An exploration of adherence and persistence in overactive bladder and other long-term conditions

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An exploration of adherence and persistence in overactive bladder and other long-term conditions

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Abstract

Background and aims

Overactive bladder is a common, bothersome, and chronic condition associated with symptoms of urinary urgency, incontinence, increased daytime micturition frequency and nocturia. Despite exerting a significant burden on quality of life, adherence, and persistence behaviours with OAB are particularly poor in comparison with other long-term conditions. The aims of the present work were to explore themes relating to medicine-taking behaviours in OAB and other long-term conditions and to suggest ways to improve them.

Methods

A systematic literature review was undertaken to understand the current landscape of qualitative work exploring adherence and persistence with OAB patients. A qualitative study involving 1:1 semi-structured interviews was conducted with OAB patients to explore the context and drivers for adherence and persistence behaviours using thematic analysis. A comparative analysis was then undertaken with qualitative papers exploring medicine-taking behaviours in a chronic bowel condition, type II diabetes, and multimorbidity to explore the themes identified in the OAB study for convergence and divergence in other conditions and to contextualise the learnings from the former study.

Results

The systematic literature review revealed a gap in the literature of qualitative exploration of adherence and persistence behaviours in OAB patients. The OAB study found a range of drivers for non-adherent behaviours including a perceived lack of treatment efficacy, side effects, unclear instructions, and drug and condition hierarchies, as well as the rich context within which these themes sit. The comparative analysis study supported the findings of the OAB study demonstrating evidence of key themes transcending across conditions, including a perceived lack of treatment efficacy and side effects, as well as nuances associated with the OAB experience.

Conclusions

The present work has identified key drivers for non-adherent behaviours in OAB patients and sets out a number of recommendations categorised within the World Health Organisation’s 5 dimensions of adherence. These include addressing the poor understanding and illness perception of OAB by patients and others, by improving the provision and availability of information, as well as the work of patient support groups; scrutiny on the support within primary care to OAB patients before and after diagnosis; and the encouragement of realistic expectations of the condition and treatment with mindful use of prescriber’s language at the point of prescribing. The present work has further highlighted the utility of conceptual models of adherence such as COM-B and the NCF in understanding medicine-taking behaviours in the context of OAB.

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List of abbreviations

Abbreviation	Definition
AE	Adverse event
APEL	Astellas Pharmaceuticals Europe Ltd
BAME	Black, Asian and minority ethnic
BBC	British Broadcasting Corporation
BJU	British Journal of Urology
BMC	BioMed Central
BMJ	British medical journal
BMQ	Beliefs about Medicines Questionnaire
BNF	British National Formulary
BPO	Benign prostatic obstruction
BPS	British Psychology Society
BT	Bladder training
BTX	Botox
CBT	Cognitive behaviour therapy
CF	Cystic Fibrosis
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CIMO	Context, intervention, mechanism, outcome
CLIP	Client group, location, improvement/ information/ innovation, professionals
CMT	Core Medical Team
COPD	Chronic obstructive pulmonary disease
COM-B	Capability, opportunity, motivation behaviour system
COVID	Coronavirus disease
CPRD	Clinical Practice Research Datalink
CRN	Clinical research network
CSM	Common-sense model
DTCA	Direct-to-consumer advertising
DTCI	Direct-to-consumer information
EAU	European association of urology
EBM	Evidence Based Medicine
ECG	electrocardiogram
ECLIPSE	Expectation, client group, location, impact, professionals, service
EMR	Electronic Medical Records
ESRC	Economic and Social Research Council
FDA	Food and Drug Administration
GMC	General Medical Council
GP	General Practitioner
HCP	Healthcare professional
HDI	Human development index
HEOR	Health Economics and Outcomes Research

HIV	Human immunodeficiency virus
HRA	Health Research Authority
HTA	Health Technology Appraisal
IBD	Inflammatory Bowel Disease
IBS	Irritable Bowel Syndrome
ICS	International Continence Society
IMS	Information motivation strategy model
IRAS	Integrated Research Application System
KSS	Kent, Surrey, and Sussex
KTP	Knowledge Transfer Partnership
LCA	Latent Class Analysis
LTC	Long-term Condition
LUTS	Lower Urinary Tract Symptoms
MHRA	Medicines and Healthcare products Regulatory Agency
MIP	Methodology, issues, participants
MMU	Manchester Metropolitan University
MPR	Medicine Possession Ratio (MPR)
MS	Multiple Sclerosis
MUR	Medicines Use Review
NCF	Necessity-Concerns Framework
NHS	National Health Service
NHSBSA	NHS Business Services Authority
NHSE	NHS England
NICE	National Institute for Health and Care Excellence
NMS	New Medicine Service
NSAID	Non-steroidal anti-inflammatory drug
OAB	Overactive Bladder
ONS	Office of National Statistics
PCO	Primary Care Organisation
PDC	Proportion of Days Covered
PFMT	Pelvic floor muscle training
PICO	Population/problem, intervention, comparison, outcome
PICOS	Population/problem, intervention, comparison, outcome, study design
PICOT	Population/problem, intervention, comparison, outcome, timeframe
PICOTT	Population/problem, intervention, comparison, outcome, type of question, best type of study design to answer this question
PMCPA	Prescription Medicines Code of Practice Authority
PPC	Pre-payment certificate
PRC	Protocol Review Committee
PRISMA	Preferred Reporting Items for Systematic Reviews
PRO	Patient Reported Outcome
PSNC	Pharmaceutical Services Negotiating Committee

PV	Pharmacovigilance
QALY	Quality Adjusted Life Year
QDA	Qualitative Data Analysis
QOF	Quality and Outcome Framework
QUOROM	Quality Of Reporting of Meta-analyses
RA	Rheumatoid Arthritis
RADAR	Royal Association for Disability and Rehabilitation
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RISP	Research Information Sheet for Practices
RPS	Royal Pharmaceutical Society
RWD	Real World Data
RWE	Real World Evidence
SABA	Short-acting beta agonists
SLR	Systematic literature review
SMR	Structured medication review
SPICE	Setting, perspective, intervention, comparison, evaluation
SPIDER	Sample, Phenomenon of Interest, Design, Evaluation, Research-type
SPSS	Statistical Package for the Social Sciences
T2DM	Type II Diabetes Mellitus
TTD	Time to Discontinuation
UI	Urinary Incontinence
UK	United Kingdom
USA	United States of America
UTI	Urinary Tract Infection
WHO	World Health Organisation

Introduction and thesis overview

This thesis will be centred on the qualitative exploration of drivers and concerns towards treatment adherence and persistence behaviours, primarily in overactive bladder (OAB). The purpose of the present section is to provide the reader with an overview of the structure and content of the work herein.

Chapter 1 forms the introductory chapter and will present the reader with the key concepts within this thesis. It provides definitions of important terms within the sphere of medicine-taking behaviours and describes the distinction and strengths of both quantitative and qualitative exploration of such behaviours and patient experiences, highlighting several areas where such an approach has been used to uncover and address non-adherence in long-term conditions. Chapter 1 also provides an overview on OAB, its burden, and treatments before describing the current literature on medicine-taking behaviours within this condition. It further describes the importance of understanding adherence, as well as several relevant conceptual frameworks used to do this, including the WHO's five dimensions of adherence, as well as the NICE guidance on this topic.

Chapter 2 describes a systematic literature review (SLR) conducted to understand the current landscape of qualitative work undertaken around adherence and persistence with treatments for OAB. Undertaken using PRISMA guidelines, the SLR encompassed studies involving adult participants (aged 18 and over) where participants were allowed to freely express themselves relating to medicine-taking behaviours. The findings of the SLR demonstrated a lack of qualitative work exploring patient medicine-taking behaviours in OAB, thus paving the way for such work to be conducted within the present thesis.

Chapter 3 describes the methodologies employed within the thesis, encompassing the organisational and philosophical backdrop of this work. Within it, I describe my ontological and epistemological perspectives, and provide a reflexive analysis exploring the relationship between my background and this work. Also discussed within this chapter are the ethics and governance processes undertaken to conduct the work within this thesis, as well as specifics on data collection and analysis processes for the central qualitative study, as well as the comparative analysis described in Chapter 5.

Following on from the identification of a gap in the literature and the problems posed by non-adherence in OAB, Chapter 4 describes the execution of such work in the form of a qualitative study involving 1:1 semi-structured interviews to explore the drivers of adherence and persistence behaviours in OAB patients. Interview recordings were transcribed and analysed through inductive thematic analysis with a specific focus on adherence to identify a set of key themes relating to these behaviours.

A subsequent exploratory study was undertaken and is described in Chapter 5, to understand how the above findings related to adherence and persistence behaviours in other long-term conditions (LTCs). Taking the learnings from the OAB study, Chapter 5 describes a comparative analysis comparing the findings from the OAB study to qualitative studies undertaken in a bowel condition, diabetes, and multimorbidity in the elderly.

The final discussions and conclusions chapter brings together the learnings and consequent recommendations of this work, as well as commentary on the strengths, limitations, and possible future works.

Chapter 1 - Introduction to central concepts

Introduction to key concepts in the thesis

In fulfilling the aim of giving the reader a background to the key subjects covered in this thesis, an overview of overactive bladder (OAB) will first be provided as it forms the central clinical area of interest within the present work. An outline of the condition itself, its prevalence, burden, and treatment options will be given, before introducing medicine-taking behaviours, key terms and their definitions, as well as the importance of studying such behaviours, and their relevance in OAB.

LUTS

Lower Urinary Tract Symptoms (LUTS) is an overarching term used to describe urinary symptoms in men and women. LUTS can be categorized into three groups: storage-symptoms (including OAB: urinary frequency, nocturia, urinary urgency and incontinence), voiding-symptoms (slow/weak splitting/spraying stream, hesitancy, terminal dribble), and post-micturition symptoms (incomplete emptying and post-micturition dribble) (Coyne et al., 2009b).

Overactive Bladder (OAB)

Within the umbrella of LUTs, OAB was a term first popularised by Drs. Abrams and Wein in 1997, and later formalised by the International Continence Society (ICS) to describe a syndrome characterised by symptoms of urinary urgency with or without urinary incontinence, usually with increased daytime frequency and nocturia, without any other causative pathology such as infection (Cardona-Grau and Spettel, 2014). Prior to this, terms to describe symptoms relating to urge and urge incontinence were based on results of urodynamic tests. In the words of the one of the proponents of the term ‘overactive bladder’, the adoption of a term based on symptoms was one that would be “useful for primary-care practitioners and specialists, that could imply initial, non-invasive therapy without the need for complicated, expensive, or invasive studies." (Wein, 2011b pg.135). Recognised as a common, bothersome and chronic condition characterised by a constellation of variable LUTS, OAB can be further categorised into OAB_{wet} or OAB_{dry} depending on the presence of incontinence (ICS, 2015). The ICS further described OAB symptoms as being suggestive of detrusor overactivity, while acknowledging other plausible causes. This description has been linked to the increased awareness within the medical community of LUTS, and has gone on to stimulate further research in this area (Peyronnet et al., 2019).

Condition burden

Prevalence

The fact that OAB symptoms are often considered by patients to be an inevitable part of ageing, combined with an embarrassment to discuss symptoms and seek diagnosis, make it difficult to accurately ascertain the true prevalence figures for this condition (Tyagi, 2006). Depending on the definition used, as well as the specific symptoms encompassed by the definition, OAB prevalence rates have been estimated to be between 3% and 43% of the population (Milsom, 2000).

The 'EPIC' study, one of the largest general population-based surveys exploring OAB in 5 countries, used the ICS definitions of LUTS and OAB to estimate the general population prevalence of OAB to be 10.8% in males and 12.8% in females. With participants aged 40-59, this rose to 51% and 56% respectively, giving support to observations made by the European Association of Urology (EAU), that there is a clear trend of increasing prevalence of OAB with advancing age (EAU, 2017b, Eapen and Radomski, 2016a, Irwin et al., 2006a). Globally, 10.7% of the worldwide population experienced OAB in 2008, with an estimated rise to 10.9% of the world population (546 million people) by 2018 (Irwin et al., 2011).

Another finding of the EPIC study was to confirm that most OAB patients experienced a combination of LUTS symptoms. It relayed that approximately half of patients had a combination of two symptoms, and about a third of patients experienced a combination of three symptoms (Irwin et al., 2006b). This finding was confirmed by the Epidemiology of LUTS (EPiLUTS) study spanning the US, UK, and Sweden, which found that it was rare for patients to experience isolated symptoms with OAB, and in agreement with EPIC, stated that the likelihood of patient bother increased with the number of LUTS experienced (Irwin et al., 2006b).

Although the prevalence of OAB is similar between male and female patients, there are differences in the incidence of gender-specific and age-related symptoms that can have consequently different impacts on HRQoL between patients. The National Overactive Bladder Evaluation (NOBLE) study in the USA found that OAB symptoms were more common in females than in men, but over the age of 60 years, symptoms were predominant in males. NOBLE showed that there was an age-related increase in the prevalence of OAB without urinary incontinence, and that this effect was more marked in the male population where it occurred more commonly than in the female population across all age groups. Urge incontinence too was shown to increase with age in both sexes, but conversely, the effect was much more marked with females than it was with males (Stewart et al., 2003, Eapen and Radomski, 2016a).

Today, OAB is increasingly recognised as a common, distressing, and chronic condition. The European Association of Urology estimates the prevalence of OAB as varying from 10% to

26% in men, and from 8% to 42% in women, with a clear trend of increasing prevalence with advancing age (Thüroff, 2011).

Economic impact of OAB

A 2009 cost of illness model based on calculating direct healthcare costs according to OAB prevalence in six countries found an estimated annual total direct-cost burden ranging from €333 million in Sweden to €1.2 billion in Germany (Irwin et al., 2009). The same study estimated the UK excess annual costs for OAB to be €1.07 billion, concluding that this was likely an underestimation of the true economic burden as nursing home costs and impact on productivity had not been factored in (Irwin et al., 2009). The impact of OAB on work productivity has been noted to be significant, and comparable to other serious LTCs including rheumatoid arthritis (RA) and asthma (Coyne et al., 2012).

Being the most recent such study undertaken in the UK, and while it may be considered dated, nevertheless, €1.07 billion in the above economic analysis equates to over £1 billion per year when adjusted for inflation to the present day (all other things kept equal), indicating a considerable financial burden in the UK (Bank of England, 2021). Such a burden is also likely to have grown in line with changes in the population and demographics over this period with the UK population having grown an estimated 8% between 2009-2021, and with the elderly population (over 65's) growing faster than other age groups (ONS, 2021). Indeed, the Office of National Statistics (ONS) projections estimate that one in four people in the UK will be over the age of 65 by the year 2050, meaning the burden of conditions such as OAB is only likely to grow (ONS, 2021). More recent annual estimates as high as £1.8 billion have been made of the cost of urinary incontinence to the NHS, with anecdotal evidence of the extreme financial pressures exerted on patients self-funding incontinence pads, on which an estimated £750 million is spent privately every year (TheUrologyFoundation, 2021).

Patient Health Related Quality of Life

Health-related quality of life (HRQoL) may be defined as *“the extent to which one's usual or expected physical, social, or emotional well-being (quality of life) is affected by a medical condition and/or its treatment”* (Finkelstein et al., 2009 pg.946), and includes physical, social, psychological and treatment-related factors as summarised by Figure 1.1 below:

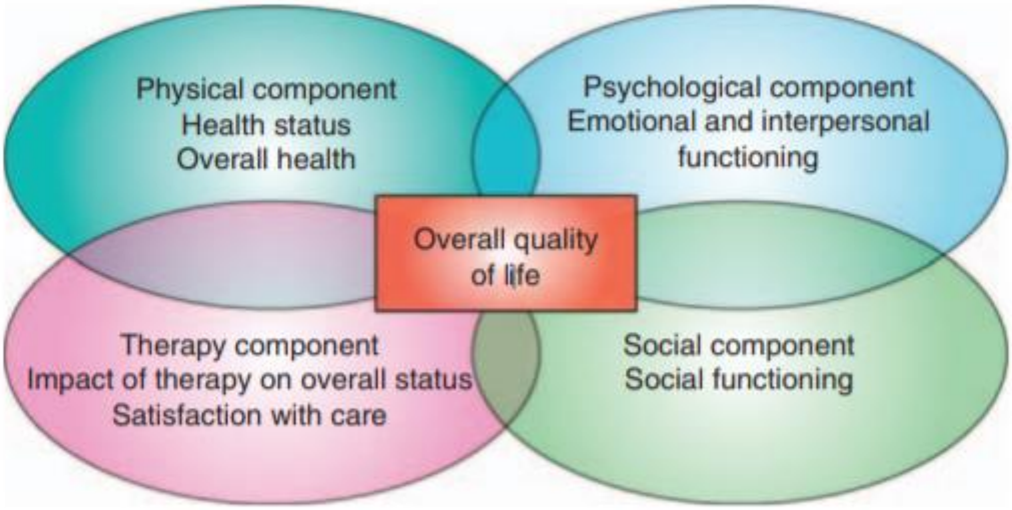

Figure 1.1: HRQoL domains (reproduced from (Finkelstein et al., 2009 pg.947)

HRQoL in OAB

Within the context of OAB, in addition to the societal burden borne from its prevalence and economic impacts, OAB can place multiple and extensive psycho-social burdens on the individual patient. OAB_{wet} in particular, is widely recognised to have a significant impact on physical, psychological, and social aspects of HRQoL (Banakhar et al., 2012, NICE, 2015, Rigby, 2003). Patients with OAB tend to restrict their participation in social activities and are more likely to isolate themselves, predisposing themselves to depression. Sexual dysfunction is frequently experienced in individuals with OAB, with OAB_{wet} patients particularly affected (Heidler et al., 2010). Frequent nocturia disrupts sleep and can lead to sleep deprivation, thereby directly affecting HRQoL for patients as well as partners

(Ouslander 2004). In a systematic literature review exploring the psychological impact of OAB, Kinsey et al. too highlighted higher levels of anxiety and depression amongst OAB patients than those without OAB, also noting the association of sudden urinary urge with significantly higher levels of depression. The authors went on to summarise similar findings for embarrassment and shame, noting OAB_{wet} was associated with significantly higher levels of shame than OAB_{dry} (Kinsey et al., 2016a). Indeed, levels of shame and embarrassment in people experiencing urinary incontinence were found to be higher than those living with depression or cancer in one European study (Elenskaia et al., 2011), with a recent systematic literature review distinguishing between the resultant social rejection (perceived discrimination in society), social isolation (the withdrawal from social activities to hide symptoms) and internalised shame (self-stigma) caused by urinary incontinence (Yan et al., 2022). The authors went on to describe the link between individuals experiencing such feelings of shame and the desire to avoid discussing symptoms, thereby missing opportunities for timely medical interventions where appropriate, resulting in poorer physical wellbeing, psychological distress, social isolation, and lower quality of life (Yan et al., 2022). OAB is also associated with other comorbidities such as fractures related to falls, urinary tract infections and skin infections (Wagg et al., 2012).

Effects on Family

Furthermore, OAB can significantly affect family members, even those who do not live with the patient (Sacco et al., 2010). As explored in a study involving focus groups to identify issues faced by OAB family members, urinary frequency in particular was the most bothersome symptom for family members as it significantly limited daily activities such as travel and social interactions due to the recurrent and urgent need to find a toilet. The study went on to confirm that nocturia resulted in sleep disturbance and fatigue for both patient and their partners, and OAB placed limitations on sexual interactions and intimacy. Family members also experienced significant emotional encumbrance, reporting feelings of embarrassment, anxiety, anger, worry, frustration and sympathy (Coyne et al., 2009a). Another study exploring the perspective of family caregivers found that "experiences of care-giving to family members with OAB were consistently difficult..." (Siu, 2017 pg.86), and that "a sense of powerlessness, helplessness, confusion and guilt, as well as grievances and social withdrawal, was prevalent … after the onset of OAB symptoms in family members." (Siu, 2017 pg.86). The study concluded that due to the chronic nature of OAB, such experiences and emotions increased over time (Siu, 2017).

OAB Treatment

Conservative Management

As there is no cure for OAB presently, treatment is concentrated on symptom management. This often begins with conservative measures such as lifestyle interventions, containment measures and physical therapies. Lifestyle interventions include weight loss and modifying fluid and caffeine intake. Containment measures such as the use of absorbent pads, urinary catheters, and external collection devices can be useful when active treatment does not adequately control symptoms, or when patients cannot take or prefer not to use active treatments. Physical therapies such as bladder training (BT), pelvic floor muscle training (PFMT) and cognitive therapy are further options that can be used as part of package of care (Robinson et al., 2017, EAU, 2017a).

Pharmacological Management

While differing in their pharmacodynamic and pharmacokinetic properties, antimuscarinics form the bedrock of pharmacological management of OAB. There is limited evidence of superiority of one antimuscarinic agent over another, however the widespread distribution of muscarinic receptors across human organ systems can lead to all antimuscarinics being associated with common, bothersome side effects including dry mouth, constipation, blurred vision, and cognitive impairment. These can be particularly troublesome for elderly patients and those taking a multitude of medications, as drugs frequently prescribed to treat common conditions such as allergies, asthma, COPD, and depression can also cause similar effects, potentially heightening the adverse event burden when used concomitantly with antimuscarinics (Nitti et al., 2014, Sexton et al., 2011b).

Mirabegron, a first-in-class selective β3-adrenoceptor agonist, offers an alternative to antimuscarinics for the treatment of OAB symptoms. While the overall efficacies and rates of treatment-emergent adverse events are broadly similar between it and antimuscarinics, mirabegron offers a differential side effects profile and is not associated with dry mouth to the same degree as antimuscarinics (Drake, 2017). Its adverse effects do however include; raised blood pressure, tachycardia, headache and dizziness (Warren et al., 2016). A second β3-adrenoceptor agonist (Vibegron) has recently been developed and approved for use in Japan in September 2018 (Keam, 2018), and has received approval from the Food and Drugs Administration (FDA) for use in the US in 2020 (de la Torre and Albericio, 2021). It is not currently available in the UK (SPS, 2021).

Invasive Management

For patients refractory or unsuccessfully treated with conservative or pharmacological treatment, more invasive options may include neuromodulation (percutaneous tibial nerve stimulation [PTNS] and sacral nerve stimulation [SNS]), intravesical injection of botulinum toxin A (BTX-A), or augmentation cystoplasty (AC) (Osman and Chapple, 2016, Willis-Gray et al., 2016, Warren et al., 2016).

Medicine-taking behaviours

Definition of terms

In addition to the appropriate prescribing of treatments, as well as their specific pharmacokinetic and pharmacodynamic properties, the effectiveness of treatments invariably hinges on the degree to which they are adopted by patients in terms of timing, dose, frequency, and duration (Martin et al., 2005, Cramer et al., 2008). Various terms have been used to describe this behaviour; a systematic literature review by Vrijens et al chronicling the development of the taxonomy on medicine-taking behaviours identified over ten different terms used in the literature, of which terms such as compliance, adherence, concordance and persistence were often used interchangeably or without clear definition (Vrijens et al., 2012). However, as these terms refer to distinct concepts, it is useful to distinguish between them here.

Compliance

The term ‘compliance’ is defined as the extent to which a patient’s behaviour matches the prescriber’s recommendations, and thus, implies that the patient is merely a recipient of healthcare, expected to comply unquestioningly with recommendations made by the prescriber (WHO, 2003, Chakrabarti, 2014, McGovern et al., 2016). With its linguistic roots in the Latin word ‘complire’, meaning to fulfil a promise, the term ‘compliance’ conveys an outdated, paternalistic attitude towards the patient from healthcare professionals (HCPs), disregarding patient autonomy and contribution to the overall process of treatment, while attributing blame to the patient for non-compliance (Aronson, 2007, Chakrabarti, 2014, Mukhtar et al., 2014).

Adherence

To account for the disparity between the implications of the term ‘compliance’ and clinical reality where the patient wields considerable autonomy and is under no compulsion to accept a particular treatment, the term ‘adherence’ has been defined by the World Health Organization (WHO) as the extent to which a person’s healthcare-related behaviours align with the agreed recommendations from a HCP (WHO, 2003). Widely gaining favour over the older term ‘compliance’, the concept of adherence offers the additional dimension of considering the patient’s agreement to recommendations made by the prescriber, thereby positioning the patient as an active partner in their own healthcare (Chakrabarti, 2014).

A further distinction between these two terms has been described in the context of the agenda’s driving their use, namely:

- the scientific/clinical agenda to describe and categorise patient behaviour in terms of how it relates to advice from the HCP,
- and the normative agenda to describe what constitutes ‘good’ and ‘correct’ medicine-taking behaviour (Horne et al., 2005).

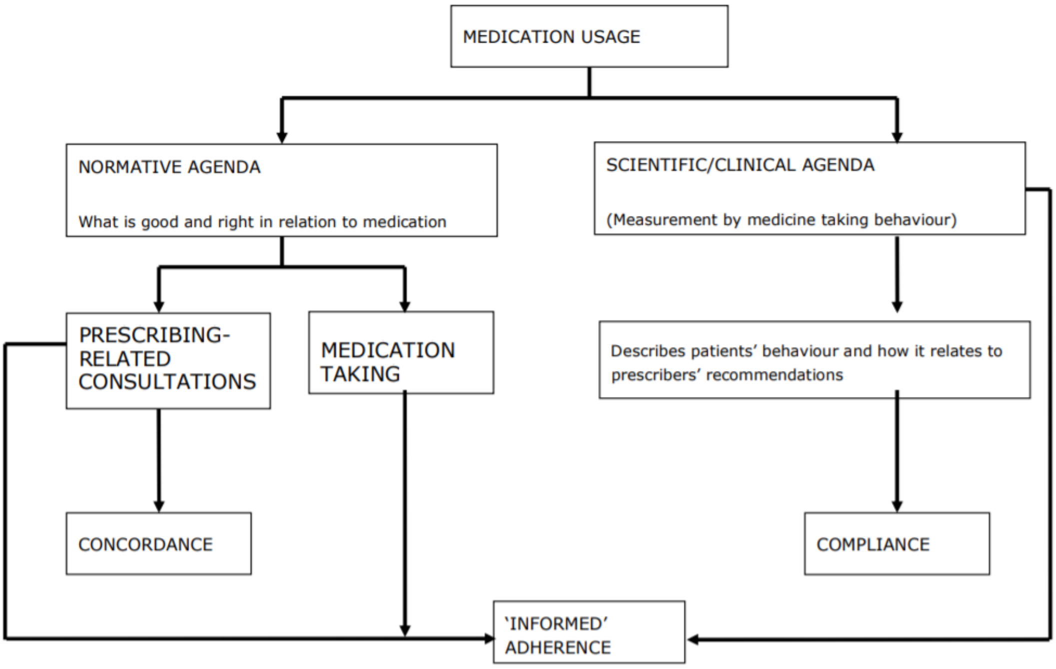

Figure 1.2: Terminology for medicine-taking behaviour (taken from figure 3 (Horne et al., 2005))

This distinction enables the further recognition that while the term ‘compliance’ works well with the scientific agenda in categorising patient behaviours, it does not address the normative agenda of whether medicine taking ‘should’ happen, and thus implies that all compliance is ‘good’ whereas all non-compliance is ‘bad’ and by extension, harmful to the patient (Horne et al., 2005).

Such a consideration of medicine-taking behaviour has been shown to be insufficient as patient decision-making around medicine-taking is influenced not only by the clinical outcomes at hand, but tempered by physical, economic, psychological and social factors also (Morris and Schulz, 1993). Furthermore, as the appropriateness of medicine taking is inexorably linked to the appropriateness of prescribing in the first instance, the decision to not follow advice to take treatment may not always be ‘bad’ for the patient as it may save them from unnecessary side effects and intolerability, as well as costs associated with inappropriately prescribed treatment (Chakrabarti, 2014).

Although more representative of medicine-taking behaviour, having recognised the interplay between patient and prescriber, the term adherence does not address the ‘normative agenda’, instead avoiding the limitation associated with ‘compliance’ by explicitly recognising the patient’s freedom to choose to adopt the advice proffered as well as emphasising the need for agreement between patient and prescriber (Horne et al., 2005). Despite this, Steiner and Earnest posited that adherence and compliance both overemphasise the physicians’ control over the medication process (Lam and Fresco, 2015a, Steiner and Earnest, 2000). The subsequent emphasis on agreement between patient and prescriber has led to the development of the term “informed adherence” in recognising both the patient’s freedom to choose their actions, as well as the responsibility of the HCP to support this choice to be an informed one (Sieber and Kaplan, 2000, Horne et al., 2005). Indeed, the aims of achieving partnership with patients to enable them, their carers, and families to make informed decisions about their care has been emphasised by the National Institute for Health and Care Excellence (NICE) in their clinical guidelines (discussed below) (NICE CG76, 2009, NICE, 2007). More recently, NICE has outlined its ‘Shared Decision-Making Collaborative’ (SDMC); a group of over 40 organisations working together to entrench shared decision-making into routine practice. Within this initiative, the definition of shared decision making has been given as “a process in which clinicians and patients work together to select tests, treatments, management or support packages, based on clinical evidence and the patient’s informed preferences”, clearly echoing many of the considerations discussed above (NICE, 2021 pg.1).

The concept of adherent medicine-taking behaviours has further been distinguished into ‘intentional non-adherence’, defined as an active decision by patients to not take prescribed therapy, and ‘unintentional non-adherence’, defined as a passive process leading to patients failing to take treatment (through forgetfulness, carelessness or circumstances outside of their control) (Wroe, 2002). While acknowledging that patients exhibit both types of non-adherent behaviours, previous work in this area have indicated that approximately half of all non-adherent behaviours over the age of 65 are as a result of intentional non-adherence (Mukhtar et al., 2014). A third type of non-adherence has been defined as 'non-conforming non-adherence', describing situations where medications are not taken in the way prescribed, with patients either skipping doses, taking medications at unadvised times or doses (Jimmy and Jose, 2011) .

Notwithstanding the above limitations of capturing the normative agenda, adherence is recognised as the most widely accepted term to describe medicine-taking behaviour, and has been explicitly designated as the preferred term for describing such behaviours by the European Patients Forum (EPF), a pan-European umbrella organisation for patient organisations and advocacy groups, as well as NICE (NICE, 2007, Vrijens et al., 2012, EPF, 2015). For these reasons, within the present body of work, adherence is the preferred term to describe medicine-taking behaviour at a given point in time (as opposed to the term persistence, describing medicine taking behaviours over time- see below).

Concordance

Recognising that consultations between patient and HCP often involve the collision of contrasting health beliefs, the term 'concordance' was posited to address the normative agenda by highlighting "good" prescribing as that entailing a negotiation between patient and HCP, taking into account the patient's beliefs and expectations, treating them as equal partners in the formation of a therapeutic alliance (Horne et al., 2005, Dickinson et al., 1999, Atal et al., 2019). Not in itself referring to the patient's medicine-taking behaviour, the term concordance describes the interaction between patient and HCP in terms of a negotiation between equals, respecting the patient’s right to decide not to take treatment (Bell et al., 2007).

A limitation of concordance is that while it explicitly addresses the normative agenda, it does not do so for the scientific/clinical agenda, and as such it too does not offer a useable term across both domains. Furthermore, while highlighting a therapeutic alliance, concordance does not address the potential tension implied between these two domains, namely: when evidence-based medical recommendations run counter to patient-choice. Finally, while better concordance may imply better adherence, this in itself is an assumption requiring further testing (Horne et al., 2005). This point was further recognised by the NICE medicines concordance final scope document, whose authors stated: “concordance reflects social values but does not address medicine-taking and may not lead to improved adherence” (NICE, 2007 pg.2).

Persistence

Treatment persistence refers to the act of following a recommendation of continuing treatment for the prescribed length of time, and may be defined as the duration of time from initiation to discontinuation of a therapy (Cramer et al., 2008). Persistence is often measured by the availability of treatment, expressed either as the proportion of patients still filling prescriptions at a set interval (such as 12 months), or as the duration of time from initiation to discontinuation of treatment, often referred to as time to discontinuation (TTD) (Guerci et al., 2019).

Importance of Adherence

Following the appropriate prescribing of a therapy, non-adherence poses a lost opportunity to maintain or improve the patient’s condition and HRQoL: the costs of which may be considered in terms of potential benefits forgone, as well as the consequent economic burden on both the individual, system and society as a whole (Elliott, 2013). Concurring with the personal and wider consequences of non-adherence, NICE has estimated between a third to a half of all medicines for long-term conditions are not taken as recommended (NICE CG76, 2009). This was also echoed in the 2003 World Health Organisation's (WHO) report on medication adherence which indicated that only around half of prescribed medication was taken as prescribed across the developed world, linking this to treatment wastage, suboptimal clinical benefit and raised avoidable mortality (WHO, 2003).

With suboptimal adherence reported in a wide range of chronic clinical areas including chronic obstructive pulmonary disease (COPD), asthma, schizophrenia and depression, the relationship between non-adherence and increased risks of poorer outcomes as well as hospitalisation and premature mortality has been widely recognised (Elliott et al., 2016, Mongkhon et al., 2018, Fitzgerald et al., 2011, Walsh et al., 2019).

Estimates of approximately 125,000 excess deaths per year in the United States are widely cited in the literature, alongside $100-300 billion each year in direct and indirect costs (Bosworth et al., 2011, Kleinsinger, 2018). Regarding the annual economic cost of non-adherence to NHS England, an estimated £930 million was associated with health gains forgone as a result of non-adherence in only five long-term conditions alone (type II diabetes, asthma, coronary heart disease, hypertension, and schizophrenia)(Elliott et al., 2016). The authors estimated that improvements in adherence across these conditions could save the NHS £500million annually (Elliott et al., 2016).

Indeed, NHS England introduced the New Medicines Service (NMS) in 2011 to support patient adherence in four strategically selected clinical areas (asthma/COPD, hypertension, type II diabetes, anticoagulation/antiplatelet treatment). The service was designed to be delivered by community pharmacists and involved face-to-face or telephone consultations with patients starting a newly prescribed medications for relevant conditions, with a view to resolve barriers to adherence. The proponents of NMS undertook several economic analyses which, although caveated with uncertainties, indicated that such an approach could deliver better patient outcomes (Quality Adjusted Life Years (QALYs)), than usual practice, with reduced costs to the NHS over a long term. Since its introduction, over 90% of community pharmacist in England have provided the service to their patients, with the service expanded in September 2021 to include additional eligible conditions (Elliott et al., 2020, PSNC, 2021c). Indeed, an analysis of the impact of the NMS has indicated that around a third of non-adherent patients became more adherent to their medicines after the NMS intervention with a HCP, indicating the wider potential of such interventions (PSNC, 2021a).

Conceptual models relating to adherence

Kardas et al (2013) carried out a systematic review of reviews in the literature to identify individual determinants of non-adherence to short and long-term therapies (Kardas et al., 2013). In assessing the 51 reviews covering an array of 19 disease areas, the authors followed the proposed adherence-related taxonomy by Vrijens et al. to distinguish these determinants in terms of treatment initiation, implementation, and persistence/discontinuation phases of adherence (also termed ‘the ABC Taxonomy’ (Maffoni et al., 2020)). As defined by Vrijens et al. (2012), treatment initiation refers to the moment the patient takes the first dose of a prescribed treatment; implementation in turn refers to the extent to which the patients actual dosing concurs with the prescribed dosing regimen from the point of initiation, with the discontinuation phase classified as the cessation of therapy (Vrijens et al., 2012). Kardas et al. found 771 individual determinants of non-adherence in the literature, and noted that although the large majority of reported factors related to treatment implementation, many reviews lacked a clear definition of adherence, causing inconsistencies in the interpretation of their findings (Kardas et al., 2013).

Numerous theoretical models have been proposed to encompass such identified factors in understanding and explaining medicine-taking behaviours, including the health-belief model, social-cognitive theory, theory of planned behaviour, and the protection-motivation theory (Chakrabarti, 2014). In fact, a recent literature review identified over 100 unique conceptual models for factors affecting medication adherence (Peh et al., 2021). According to Chakrabarti et al. although these models represent a variety of theoretical perspectives (e.g., biomedical, behavioural and cognitive perspectives), they all include elements of the patient-prescriber relationship (including the quality of communication in the therapeutic relationship), psychosocial factors concerning the patient themselves (such as personally held beliefs and attitudes), as well as immediate and distal environments (including socio-economic status, familiar support, and the wider healthcare policy and system) (Chakrabarti, 2014).

Such an approach to aggregate the plethora of constructs from various theoretical models was also undertaken by Reid et al. who selected from five well-known health behaviour models (health belief model, theory of reasoned action, theory of planned behaviour, information-motivation-behavioural skills model, and social cognitive theory) to combine selected constructs into a single integrated model (Reid and Aiken, 2011). In doing so, and building on earlier work by Noar and Zimmerman (2005), the authors classified constructs from across the 5 models into categories based on shared characteristics they described:

- Beliefs of the risks, positive, and negative aspects of the behaviour and its outcomes,
- knowledge and information,

- belief in one's own ability to undertake the behaviour (self-efficacy), and intention / plan to do so,
- belief regarding how others want the behaviour to be undertaken and the motivation to comply, and
- socio-structural factors such as health, economic or environmental systems (Noar and Zimmerman, 2005, Reid and Aiken, 2011)

The WHO's model describing the various multifactorial dimensions of adherence has been recognised as a significant contribution to understanding patient medicine-taking behaviours, and therefore offers a useable lens to frame the drivers of such behaviours within the present work (Alvi et al., 2019). Additional theoretical models of note within this space include the necessity-concerns framework (NCF), the COM-B model of adherence, and the common-sense model (CSM), which are also described herein. As a useful model in exploring the variance in patient adherence, as well as delineating variables when intervening on adherence behaviours, the three-factor model (also known as the Information-Motivation-Strategy [IMS] model) will also be presented below (Maffoni et al., 2020). Furthermore, as an key health-related organisation within the UK with significant impact on clinical practice, a summary of the NICE guidance on treatment adherence will also be provided herein (Chidgey et al., 2007). NICE's pivotal role in the availability, reimbursement, and use of treatments within the NHS, as well as in assessing their health economic impact (costs and QALYs) are further reasons for the relevance of their guidance on the present work centred on treatment adherence.

The WHO's five dimensions of adherence

In its report entitled "adherence to long term therapies", the WHO has recognised the misconception that treatment adherence is solely the responsibility of the patient, further characterising such statements as indicative of misunderstanding how patient behaviours and capacity to adhere to treatment can be affected by other factors. In describing such factors, the WHO recognises what they termed as "the five dimensions of adherence", shown in

Figure 1.3 which will be summarised herein (WHO, 2003).

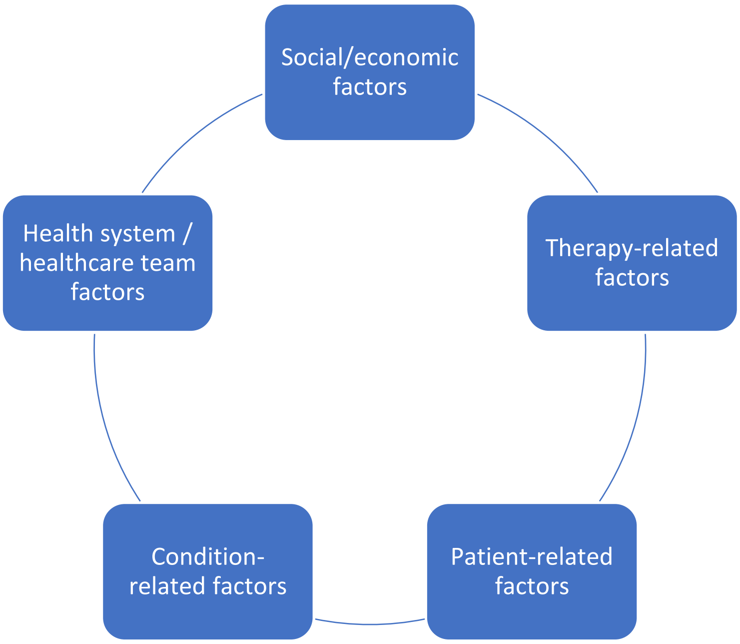

Figure 1.3: WHO five dimensions of adherence (WHO, 2003)

Social/economic factors

While distinguishing between developing and developed countries on the relative effect of socioeconomic status on treatment adherence, the WHO report went on to highlight several related factors reported to exert a significant effect on patient adherence behaviours including poverty, illiteracy, unemployment, and cultural beliefs around illness and its treatment. With UK unemployment rates of around 4% affecting an estimated 2.6million adults, the effects of this factor may be widespread with further scope to grow as the wider effects of COVID-19 unfold (Bell and Blanchflower, 2020, Francis-Devine, 2021b). Although those claiming Income Support, income-based Jobseeker's Allowance, income-related Employment and Support Allowance, or Universal Credit may be entitled to free NHS prescriptions in England (NHS.UK, 2020b), with prescription charges rising almost 30% over the last decade from £7.20 per item in April 2011 (Gov.UK, 2011), to the current level of £9.35 (NHSBSA, 2021), the financial burden of treatment has grown on those in employment also.

Linked to cultural beliefs around illness and treatments, patient race has been cited as a predictor of adherence, irrespective of native or immigrant status. Indeed, the interplay between unemployment and race itself has been characterised in a recent study investigating the ethnic dynamics of unemployment and earnings in the UK. The findings suggested that members of ethnic minorities, including those of black African, black Caribbean, Pakistani and Bangladeshi origin encounter much higher risks of unemployment and much lower earnings than their white British counterparts over the course of a lifetime (Li and Heath, 2020). Certainly, the link between race and unemployment is one seemingly exacerbated by the COVID-19 outbreak with a more marked increase in unemployment in people from a minority ethnic background (from 5.8% to 9.5%) in the same period White ethnic background unemployment rose by a smaller margin (3.1% to 4.5%) in October-December 2020 compared to the same period in the previous year (Francis-Devine, 2021a). The connection between ethnic background and treatment adherence has also been explored in the literature (McQuaid and Landier, 2018, Alhomoud et al., 2013). Amongst these, the Aston medication adherence study employed prescription data to explore non-adherence to treatment within an inner-city population, and brought together findings covering ethnic, socioeconomic, religious and age factors in relating these to adherence.

Covering a range of clinical areas including dyslipidaemia, type II diabetes and hypothyroidism, data collection spanned 76 General Practitioner (GP) surgeries over a ten-year period. The study showed that self-reported adherence levels were statistically lower for patients younger than 60 years of age, of Asian, Caribbean or African ethnicity, or whose postcode indicated they lived in the most socioeconomically deprived areas (Langley and Bush, 2014).

Relatedly, the WHO report highlighted age as an important factor in treatment adherence, albeit recognising the inconsistency in its apparent effect, recommending instead to consider age separately for each condition and the characteristics of the patient. It did however, go on to recognise the increased prevalence of cognitive and functional impairments in the elderly may contribute to a higher risk of non-adherence, as suggested elsewhere in the literature also (WHO, 2003, Dolansky Mary et al., 2016, Chudiak et al., 2018).

Also considered within the social dimension of adherence, health literacy has been defined as “the ability of an individual to obtain and translate knowledge and information in order to maintain and improve health in a way that is appropriate to the individual and system contexts” (Liu et al., 2020 pg.6). Individuals with poor health literacy are more likely to delay seeking care (Levy and Janke, 2016), and to experience difficulties in understanding health information, exhibit poorer medication adherence, and achieve worse health outcomes at a higher healthcare cost than those with adequate health literacy (Liu et al., 2020). Indeed, a Public Health England report exploring the link between health literacy and health inequalities reported approximately 42% of English adults between the ages of 16-65 years were unable to comprehend everyday health information, rising to 61% when this involved interpreting numerical information (Roberts, 2015). It stated that as the most disadvantaged and vulnerable people in society were at the highest risk of poor health literacy, improvements in health literacy had the potential to reduce health inequalities, and that health literacy was in part determined by the provision of clear and accessible information (Roberts, 2015).

Health system/healthcare team factors

While recognising that a good patient-provider relationship may help improve adherence, the WHO report went on to detail related factors that may work against this. These include health system factors such as co-payment, inadequate capacity to educate patients and provide follow-ups, poor medication distribution channels, and inefficiencies from a lack of incentives and performance feedback. Healthcare team factors such as overworked, or undertrained HCPs with inadequate knowledge on adherence and ways of improving it were also recognised as key factors.

In a two-year study examining the correlation between adherence to follow-up appointments and to medicine in patients with schizophrenia, it was found that non-attendance of appointments was related to low levels of education, worse medication adherence and poorer clinical outcomes than in those who consistently engaged with their HCPs in follow-up consultations (Balikci et al., 2013). Another study investigating health system factors affecting adherence in patients newly on antihypertensives found that medication co-payment, type of medication class initiated, and enrolment in mail order pharmacy were associated with non-adherence. The authors went on to conclude that such health system factors act as both mediators and modifiers of racial and ethnic difference in medicine-taking behaviours, noting that medicine choice, co-payment, and access were relatively modifiable factors with system-level interventions unlike socioeconomic and psychosocial factors (Adams et al., 2013).

Condition-related factors

Condition-related factors comprise any additional demands placed on the patient from the condition itself and include the rate of disease progression, symptom severity and the resultant level of physical, psychological, social, or vocational disability, as well as the availability of effective treatments. The relative impact of these factors has been recognised as being dependent on how they influence the patient's perception of risk and the importance given to treatment adherence to begin with.

Highlighting some of these factors, as well as the interplay between multiple conditions, a systematic literature review was undertaken to identify factors influencing adherence in hepatitis-C infected patients. It found evidence that having depression or psychiatric disorders in general was associated with a negative impact on adherence, while having HIV co-infection was suggested to influence adherence positively. The authors stated their findings on the effects of depression on adherence as in accordance with a meta-analysis that indicated a statistically significant negative effect of depression on adherence in chronic conditions, and went on to postulate this as being attributable to reduced motivation is such individuals. They went on to suggest the positive effect on adherence from HIV co-infection may be due to the experience of such patients in handling complex treatment regimens (Mathes et al., 2014). A metanalysis summarising the relationship between patient's beliefs around their disease severity and adherence behaviours found a strongly positive and significant relationship between these, with a greater perception of disease threat being associated with better adherence (DiMatteo et al., 2007).

Therapy-related factors

While the unique characteristics of the condition nor therapy were judged to outweigh more common factors influencing adherence, they were described as modifiers of how impactful common factors were on patient behaviours. Therapy-related factors influencing adherence include those relating to the complexity of treatment, previous treatment failures, the overall duration of treatment, as well as how frequently it is changed. Further factors include the immediacy of perceived benefits, side effects, as well as the availability of HCP support to resolve them.

Pantuzza et al. carried out a systematic review on the association between treatment complexity and patient adherence over a range of clinical areas including diabetes, epilepsy, and hypertension. They found that more complex treatment regimens were associated with lower adherence, especially in the elderly, and with those experiencing chronic, non-communicable diseases (Pantuzza et al., 2017).

Side effects too have been found to be associated with non-adherence, with one study investigating the magnitude of this association in hypertensive patients finding excessive urination and decrease in sexual drive significantly predicted lower adherence (Tedla and Bautista, 2016). In evaluating topical treatments for acne vulgaris, another study found around 46% of patients recently prescribed topical therapy had stopped treatment. Of these, 62% had discontinued due to a lack of response and 38% due to side effects. The authors also highlighted the role of condition-related factors too, noting that discontinuation due to unresponsiveness was higher in those with severe acne, whereas side effects were higher in those with comedonal-type acne (Sevimli Dikicier, 2019).

Patient-related factors

Described as not yet being fully understood, patient-related factors represent the resources, knowledge, attitudes, perceptions and expectations of the patient, as well as the complex interplay between these (WHO, 2003). Specifically, patient forgetfulness, stress, anxiety about side effects or complexity of treatment, low motivation or treatment expectations, inadequate knowledge and skill in managing symptoms, lack of a perceived need for a treatment or a negative perception of efficacy, not believing the diagnosis, not understanding treatment instructions, hopelessness or negative feelings, fear of dependency, feelings of frustration with healthcare providers or feeling stigmatized by a condition have all been reported to affect adherence (WHO, 2003).

The WHO report went on to document that a patient's adherence is influenced by the balance between the value placed on using treatment (termed the cost-benefit ratio), and their level of confidence in being able do so. It went on to recommend that alongside supporting the patient with therapy-related factors, strengthening the patient's intrinsic motivation by establishing a perceived importance of adherence, while concurrently improving their confidence in being able adhere by building self-management skills, were key levers in improving adherence (WHO, 2003).

In a cross-sectional study involving face-to-face interviews with almost 300 adult patients, multivariable logistic regression equations were used to assess the impact of the WHO's five dimensions of adherence. Patient knowledge about their treatment regimen was found to be the strongest predictor of medicine adherence, with the authors emphasising the need to meet patient informational needs and reinforcing education on their conditions and treatments (Fernandez-Lazaro et al., 2019).

An online survey was performed to assess the association between patient knowledge and initial expectations of treatment outcomes with adherence and persistence behaviours in individuals prescribed their first antidepressant. The authors found that higher persistence behaviours were associated with those who reported significantly greater mean initial expectation scores (as measured by a modified version of the credibility and expectations questionnaire), as well as significantly better mean knowledge scores (as measured by a psychometrically tested multiple choice knowledge test of depression and its treatments) (Woodward et al., 2016). Considering the suboptimal provision, accessibility, and readability of key sources of information on OAB (Koo et al., 2017) (discussed further in Chapter 6), the association of patient knowledge and expectations on persistence may be particularly important within OAB.

Necessity-Concerns Framework

Based on the findings of a study exploring beliefs about medications in 1200 participants experiencing a range of LTCs, the core tenets of the NCF state that individuals decision-making on medicine-taking behaviours are influenced by held beliefs on both the necessity of the prescribed medication, as well as concerns against taking them (Horne and Weinman, 1999). Described as undertaking a “cost-benefit assessment”, patients implicitly weigh up the perceived necessity of treatment for the maintenance of present or future health against the perceived concerns of potential adverse effects or the development of dependency, and are more likely to use treatment if their belief in its necessity outweighs their concerns about taking it (Horne and Weinman, 1999 pg.557).

The relative weights given to these beliefs can be quantified using the Beliefs about Medicines Questionnaire (BMQ), of which, the BMQ-Specific is used to assess beliefs about medicines used for a particular condition (as opposed to the BMQ-General, which is used to explore beliefs about medicines in general) (Wei et al., 2017). The BMQ-Specific is an 11-item form encompassing two subscales (for necessity and concerns respectively), with each item measured on a 5-point Likert scale resulting in a numerical total for each of the two subscales (Clatworthy et al., 2009). The scores can be combined to calculate the necessity-concerns differential, which numerically indicates the difference between the sub-scores, predicting adherent behaviours where the differential is positive (the perceived necessity outweighs perceived concerns) and the converse where the differential is negative (the perceived concerns outweigh the perceived necessity) (Horne and Weinman, 1999).

A meta-analysis was conducted to assess the utility of the NCF in explaining non-adherence to prescribed medications in a wide range of LTCs in over 90 individual studies, including patients with asthma, renal disease, cardiovascular disorders, and cancer. It found there to be a significant relationship between both necessity and concerns domains with adherence behaviours, concluding that the NCF offered a potentially useful framework for understanding such behaviours (Horne et al., 2013b). Other works assessing the NCF have also found correlations between the BMQ and adherence measures across disease areas and have further described the variable nature of this correlation. Reported in another meta-analysis by Foot et al., some studies reported positive correlations of only the necessity sub-scores to adherence behaviours, while others found only a negative correlation with the concerns sub-score. Other still found that the necessity-concerns differential itself showed a stronger correlation to adherence behaviours than necessity or concerns beliefs alone (Foot et al., 2016). The authors concluded that beliefs about medicines, while important, are one of the many factors affecting medicine-taking behaviours, linking this to the observation of relatively small effect sizes in the meta-analysis (Foot et al., 2016).

In a critique of evaluating the NCF by collapsing the necessity and concerns domains into a unidimensional measure (the NCF differential), Philips et al. (2014) suggested a polynomial regression approach, highlighting the theoretical separation between these domains, their measurement on separate subscales, as well their potential independence in predicting adherence behaviours as discussed above (Phillips et al., 2014). Going on to describe the bivariate evaluation plane theory, Philips et al. described the relationship between perceived necessity and concerns domains to be either reciprocal (one is high, the other is necessarily low), non-reciprocal (both can be high, leading to ambivalence, or both may be low, leading to indifference), or uncoupled (Phillips et al., 2014). The authors recommended that clinicians should not only discuss the relative differences between patients' beliefs on necessity and concerns (whether concerns outweigh necessity), but also the absolute levels of each domain (whether both are relatively high or low) to understand the interplay between them and potential effect on medicine-taking behaviours (Phillips et al., 2014). Within the context of OAB, where previous research has shown efficacy and side effects to be key factor in determining whether individuals initiated (Jundt et al., 2011), or discontinued pharmacological therapy (Tijnagel et al., 2017, Lee et al., 2014c), the NCF may offer a particularly useful framework for exploring adherence behaviours.

COM-B model of adherence

Michie et al. (2011) stated that many healthcare interventions were designed with inadequate attention given to the nature of the target behaviour, or a theoretically predicted mechanism of having the intended outcome. Furthermore, even where theories or models were employed, these often did not encompass the full range of factors influencing the behaviour, potentially excluding important factors. Examples given to illustrate these observations included the commonly used Theory of Planned Behaviour and Health Belief Model not addressing the roles of habits, learning, and emotional processing (Michie et al., 2011).

Recognising the importance of behaviour change interventions to the effective practice of healthcare, Michie et el. sought to design a rational system for the selection of appropriate interventions by:

- characterising intervention types,
- matching these to facets of the targeted behaviours, the target population, and the context in which the intervention would operate,
- and underpinning this with a model of behaviour and the factors influencing it (Michie et al., 2011)

This led to the creation of the capability, opportunity, and motivation behaviour (COM-B) system, summarised in Figure 1.4 below:

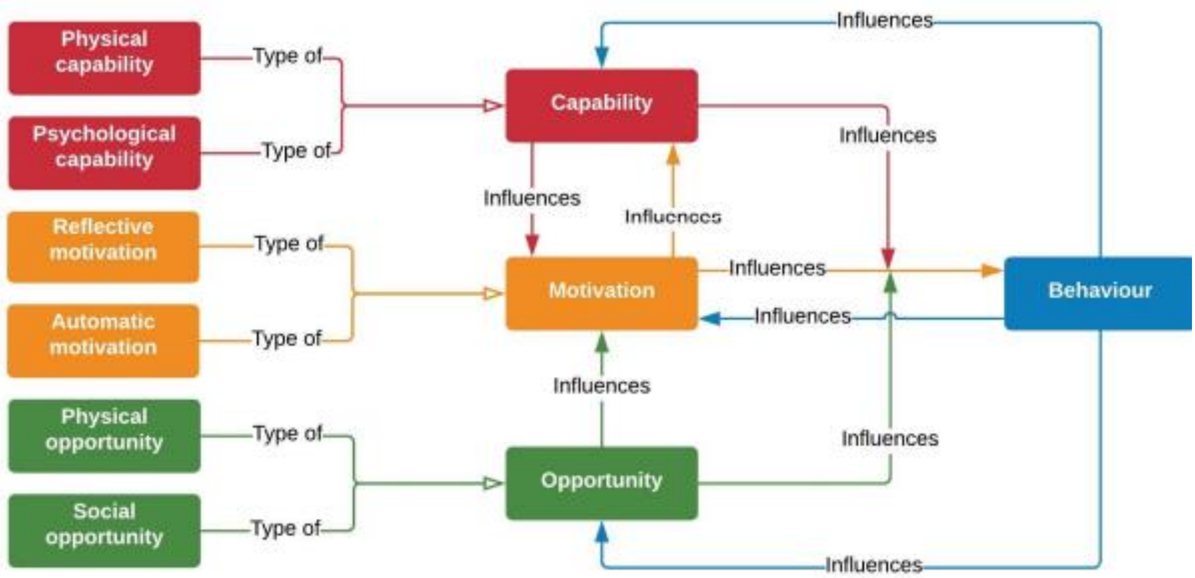

Figure 1.4 The COM-B model of behaviour (reproduced from figure 1 (West and Michie, 2020 pg.2)

At the core, the COM-B model suggests that capability, motivation and opportunity can directly influence behaviour (Jackson et al., 2014), and that a particular behaviour will only take place if the individual has the capability, opportunity and motivation to enact that behaviour above others (West and Michie, 2020). Capability and opportunity influence the relationship between motivation and the behaviour as opposed to influencing the behaviour itself, acting as “logic gates” in that both capability and opportunity “gates” need to be open for motivation to bring about the behaviour (West and Michie, 2020 pg.2). Being capable and having ample opportunity to enact a behaviour positively influences the motivation to do so, while the converse is also true. Finally, the behaviour itself can influence each of the three domains creating positive and negative feedback loops. For example, practicing a skill-requiring behaviour may improve the individual’s capability and therefore positively influence their motivation to continue to engage in the behaviour. Conversely, engaging in behaviour associated with biologically homeostatic processes such as eating, or where there are negative consequences experienced, may negatively feedback on the motivation to continue to engage in the behaviour (West and Michie, 2020).

Within this model, each domain is further distinguished as follows:

Table 1.1: COM-B component definitions

Capabilities	**Opportunity**	**Motivation**
Physical	Physical	Reflective
Relating to musculoskeletal strength, skills, and stamina for the necessary physical processes [1] e.g., ability to swallow a tablet or capsule	Opportunity provided by the environment in the form of time, resources, and location [1] e.g., treatment costs, complexity, availability, packaging, and physical characteristics of treatment [2]	Motivation influenced by evaluative and reflective practices, culminating in intentions and beliefs about what is good and bad [1] e.g., perception of condition and its cause, beliefs about treatment (necessity, efficacy, concerns about adverse events), outcomes expected, self-efficacy [2]
Psychological	Social	Automatic
Relating to knowledge, psychological or cognitive strength, skills, and stamina to engage with the necessary thought processes [1] e.g., understanding of condition and treatment, memory and capacity for judgement, capacity to plan [2]	Opportunity in terms of interpersonal influences, social and cultural norms that influence how individuals think about things [1] e.g., words and concepts making up language [3]	Instinctive processes involving emotional reactions, impulses, and reflex responses [1] e.g., habits and routines [2]
[1] (Heneghan et al., 2020) [2] (Jackson et al., 2014) [3] (Michie et al., 2011)		

In a paper to evaluate the application of COM-B to medication adherence, Jackson et al. used the findings from three extensive qualitative and quantitative literature reviews to identify a comprehensive list of over 450 factors associated with non-adherence (Jackson et al., 2014). They then mapped each of these according to the domains and sub-domains of the COM-B model, finding that the vast majority of the identified factors could readily be organised in this way. Only four identified factors could not be mapped directly into a single sub-domain of COM-B, (namely: depression, substance abuse, marital status, and forgetting) with the authors further concluding that the effects of these factors on adherence could be explained by a combination of components as opposed to a single one. Jackson et al. concluded that compared to other available models, COM-B provided the most comprehensive explanation of adherence, drawing particular emphasis on the merits of including habitual processes and system-level factors. Finally, the authors highlighted that the specificity of the COM-B domains as well as the hypothesised relationships between them, allowed for a precise determination of the relationship between individual factors of adherence, and thereby enabled the selection of a more cause-targeting intervention (Jackson et al., 2014).

Common-sense model of illness (CSM)

Illness perception has been defined as “a patient’s cognitive appraisal and personal understanding of a medical condition and its potential consequences” (Sawyer et al., 2019 pg.1). It has been shown to significantly impact health-seeking behaviours as well as adherence to treatment and self-management in the context of LTCs (Shakya et al., 2020). Individuals generally construct a pattern of beliefs relating to their condition at the point of diagnosis, which can determine their emotional response to illness, as well as the behaviour required to manage it (Petrie and Weinman, 2006). A recent review reported that positive illness perception is associated with better health outcomes than unfavourable illness perceptions, and went on to link such perceptions to the ability of an individual to cope with and manage their condition (Sawyer et al., 2019).

Such an association between illness perception and coping strategies has been characterised by the Common-Sense Model (CSM) of illness, which broadly states that it is not the disease activity itself, but the individual’s response via the selection of coping mechanisms that determines the ultimate outcomes in LTCs (Knowles et al., 2016). The CSM was originally founded from the observation that the choice and persistence with such coping behaviours was borne from a combination of a health threat representation and an action plan, and further conceptualised the patient as a highly individual problem-solver dealing with both the perceived reality of the health condition, as well as the emotional response to it (Diefenbach and Leventhal, 1996).

A schematic of the model is provided in Figure 1.5 below:

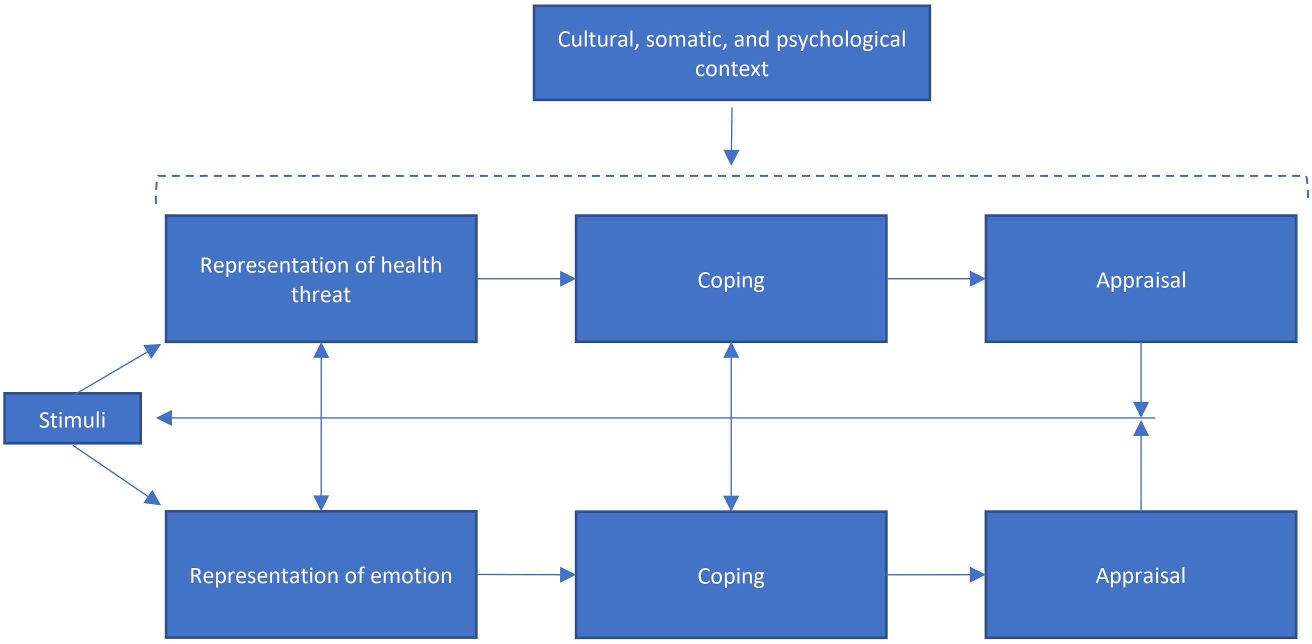

Figure 1.5: CSM of illness representation (reproduced and adapted from figure 1 in (Diefenbach and Leventhal, 1996 pg.21))

According to the CSM, internal stimuli such as symptoms, as well as external stimuli such as illness in friends and family evoke illness representations according to previous health experiences and expectations on both emotional and cognitive planes, occurring within an individualistic context characterised by history, personality, and cultural experience. The categorisation of stimuli shapes the selection and implementation of coping mechanisms, which are in turn evaluated and compared to expected outcomes (Diefenbach and Leventhal, 1996).

In terms of representations of the health threat, the CSM describes five cognitive domains: identity, timeline, consequences, cause, and perceived controllability/curability, summarised below:

Table 1.2: Summary of cognitive domains in CSM (Diefenbach and Leventhal, 1996)

Cognitive domain	Description
Identity	Labelling of a disease, as well as a representation of how the location, feel and extent of symptoms
Timeline	Expected timeframe of the stimulus, categorizing the stimulus into acute, chronic, or cyclic
Consequences	Anticipated outcomes of the illness, including personal, economic, and emotional repercussions
Cause	Perceived origin of the stimulus, determined by context within which it occurs, and shaping the labelling of the experience
Perceived controllability/curability	Responsiveness of the stimulus to self or professional intervention

The coping actions undertaken are mediated and appraised in line with the emotional representation with the CSM postulating simultaneous emotional and cognitive processing, and the consequent joint influence of these on healthcare behaviours (Huston and Houk, 2011). Illness representations as suggested by the CSM have been shown to be related to an array of health outcomes including treatment adherence, physical, and emotional well-being (Breland et al., 2020). As a well-established model, the CSM has been used to model outcomes in many LTCs including diabetes, HIV, rheumatoid arthritis and Crohn’s disease (Knowles et al., 2016).

Three-factor model of adherence (IMS)

With the initial elements presented by DiMatteo and colleagues in the 1980’s, the information-motivation-strategy (IMS) model built on the literature surrounding other prominent health behaviour models such as the Health Belief Model and Theory of Planned behaviour, to include all elements of the patient-provider interaction as well as their goals and actions (DiMatteo et al., 2012). The IMS delineates three broad categories used to tailor goals and actions for the individual patient in order to support adherent behaviours:

Information	Patient knowledge, achieved through effective patient-provider communication
Motivation	Patient belief in treatment plan and commitment to it, achieved by a strong therapeutic relationship, shared decision-making, and informed choice
Strategy	Capacity and ability of patients to overcome barriers in order to maintain treatment adherence

Figure 1.6: The IMS model (DiMatteo, 2012)

The information component of the IMS model emphasises that patients will only be able to do what they understand, highlighting that much unintentional non-adherence stems from failures in this domain. DiMatteo et al. (2012) went on to state that the healthcare team must not only ensure thorough and effective communication with their patients but should also check the patients understanding of both their condition and treatment. Such understanding is essential in the ability for patients to engage the decision-making process, and thus encourages the physician to provide information in a clear and effective manner appropriate to the patient’s level of understanding and capacity.

Relatedly, the motivation domain is characterised by the observations that patients are much more likely to adhere to treatments that they believe in, and that the belief in treatments is aided largely by their involvement in the decision-making process itself (patients are more likely to adhere to a treatment plan they have had a part in choosing). Also within this domain is the expected efficacy of treatment, and the believed consequences of non-adherence. Such areas further depend on cognitive, social, and contextual factors, and offer some overlap with other theories of adherence including the NCF described above.

The final domain of strategy encompasses the individual's capacity and ability to adhere to treatment and may be influenced by both intrinsic and extrinsic factors. The IMS emphasises the importance of HCPs to work with patients in identifying and overcoming obstacles to adherent behaviours. Such obstacles may include diminished self-regulation abilities at the time of day when treatment is due, the cost of medication, embarrassment, or the inconvenience of implementing treatment within the individual's lifestyle. Strategies to overcome some of these barriers may include leveraging available social support around the patient, the identification of other aid systems (such as workplace and community-based resources) and addressing mental health issues such as anxiety and depression which can negatively impact adherence. Further activities may include addressing treatment complexity as well as preparing the patient for likely side effects and their management.

The IMS model of adherence offers a simple and flexible heuristic framework to address the complex causes of non-adherence, helping clinicians and patients focus on the critical domains needed to improve adherence (DiMatteo et al., 2012).

NICE

Established in 1999, NICE was tasked by the UK government to advise the NHS on its implementation of new and existing health technologies in order to avoid local variations in practice (Velasco Garrido et al., 2008). While the efficacy, safety, and value of medical innovations undergo formal assessment by regulatory and payer bodies in many countries worldwide, over the last two decades NICE has developed an increasingly rigorous and formalised process of health technology assessment (HTA), and has emerged as an international gold-standard in this field (Charlton, 2020, Farrar et al., 2020, Akehurst et al., 2017). As a gatekeeper to medicines being reimbursed and therefore prescribed on NHS prescriptions within England and Wales, and with a remit to consider both the clinical and cost-effectiveness of health interventions before recommending their use within the NHS, as of 2005, health technologies are mandated to be made available by the NHS in England and Wales within 3 months from the date of a positive NICE guidance (Drummond and Sorenson, 2009).

Clinical and health economic evidence submitted to NICE is often from randomised controlled trials (RCTs), which are considered the 'gold-standard' for assessing the safety and efficacy of new interventions (Tashkin et al., 2020). However, as RCTs are subject to strict trial protocols intended to minimise bias and ensure the trial is designed to explore the study aims adequately, resulting evidence is not always representative or generalisable to the real-world setting in which the intervention will ultimately be used in (Monti et al., 2018). Adherence is a key area that may differ significantly between clinical trial and real-world settings on account of such protocols and regular contact with research personnel in RCTs, and the absence of this in the real-world (Blonde et al., 2018). Indeed adherence has been identified as a significant explanatory factor for the difference in clinical efficacy between in-trial and real-world clinical practice (Carls et al., 2017), and may thus be a fundamental driver of any differences in cost-effectiveness between in-trial and actual clinical practice also, affecting patients, the healthcare system as well as the wider economy.

In addition to the health technology appraisal programme, NICE also produces clinical guidelines (Drummond and Sorenson, 2009). Amongst these, the 2009 CG76 guidance remains the latest offering from NICE explicitly on the subject of treatment adherence, with brief references also offered within condition-specific guidelines. This guidance was reviewed in 2019 with no new evidence found to affect the recommendations it contained (Read et al., 2020, NICE, 2019), and in light of the above, is relevant for inclusion within the present work.

Guidance on Adherence

The NICE clinical guidance (CG76) covers recommendations for encouraging medicines adherence in adults aged 18 and over, with a view of supporting and involving patients in making informed decisions on medication use. Aimed primarily at clinicians, patients, and their families, the guidance highlights the need for HCPs to individualise the implementation of the guidance to the needs, preferences, and values of the patient. While its recommendations are framed through the binary distinction of intentional and non-intentional adherence, critics have highlighted the limitation of this approach due to the theoretical overlap between such a distinction, giving the example of forgetfulness arising from memory lapse (unintentional), versus forgetfulness arising from a conscious de-prioritisation of treatment (intentional), and the resultant limitation of being able to identify interventions to address these issues (Read et al., 2020). Nevertheless, the report delivers its guidance in four sections covering patient involvement, supporting adherence, reviewing medicines and the broader communication between HCPs, which are summarised below (NICE CG76, 2009).

Patient involvement in decisions about medicines

This section of the NICE guidance contains subsections covering communication, increasing patient involvement, understanding the patient's perspective, and providing information. The importance of good communication between HCP and patient is highlighted early, noting interpatient differences in how easy this might for some over others. HCPs are advised to adapt their consultation style to the needs of the individual, considering any physical or learning disabilities, as well as difficulties with written or spoken English in establishing the most effective way of communication, while encouraging patients to ask about their condition or treatment.

HCPs are encouraged to acknowledge patients' views on their condition or treatment, and to recognise the partnership with patients in making treatment decisions, while tailoring the extent to which the patient would to be involved in this process. Furthermore, HCPs are guided to clearly explain the condition and the expected benefits and risks from the intended treatment, aligning this with what the patient hopes to achieve from the same.

In acknowledging the patient's right to refuse treatment, CG76 advises HCPs to record any patient concerns in case they are helpful in future consultations. An awareness of patient concerns and beliefs surrounding treatments has been emphasised repeatedly throughout the guidance, especially at key points in the treatment journey such as medication reviews and before prescribing new treatment. HCPs are also reminded that patients may hold a goal to minimise how much treatment they take, and to address this alongside other concerns to enable informed decision-making. Relatedly, relevant, timely (pre-prescribing), and jargon-free information on the treatment should be discussed (as opposed to delivered) with the patient, checking their understanding and encouraging further requests for clarification as needed.

Supporting adherence

Acknowledging that patients do not always take their medications as prescribed, and that HCPs are often unaware of when this occurs, the purpose of assessing adherence is expressed as uncovering patient needs for further information and support, as opposed to monitoring patient behaviours, or blaming them. Indeed, in assessing non-adherence by asking if patients have missed any doses of treatment recently, the need to be non-judgemental, avoid blame-laden language and encouraging patients to share instances of non-adherence were emphasised in this section of the report.

In presenting interventions to increase adherence in non-adherent patients, the NICE guidance first advises an exploration of whether the adherence in intentional or non-intentional, as well the underlying concerns and beliefs that may be driving this behaviour. While recognising that the evidence supporting interventions to increase adherence is inconclusive, as well as the individual nature of the specific intervention to recommend, the guidance suggests the following possible interventions:

- patients record their medicine-taking
- patients monitor their condition
- simplifying the dosing regimen
- using alternative packaging for the treatment
- using a multi-compartment medicines system

The CG76 guidance also explicitly recognised the importance of side effects and their impact on adherence. In managing them, the report suggested contextualising the side effects with the expected long-term benefits and other effects of the treatment with the patient, exploration of regimental strategies such as adjustment of dosage or timing, or changing the medicine entirely, albeit with ongoing engagement with the patient to understand their preferred method of proceeding.

Reviewing medicines

The guidance recommends regular engagement with the patient in order to gauge their experience of using long-term medication in particular, as well as their evolving need for adherence support. Medication reviews are also recommended to review the patient's knowledge, understanding and concerns about the treatment, as well as any changes in their interpretation of how they should be using treatment. The latter point was in response to the observation that patients sometimes apply their own criteria to evaluate prescribed mediation and may stop, start, or alter the dosing to gauge the effects of this on their symptoms. HCPs are advised to enquire about this in order to better support adherence in patients.

Communication between healthcare professionals

In order to prevent fragmentation of care for patients who may be under the direction of multiple HCPs from various disciplines, as well as transferred between HCPs, good communication between the healthcare team is recognised as an important tenet of supporting patient adherence. The report goes on to highlight the importance of communicating the findings of reviews carried out by other HCPs to the prescriber, especially when these have identified any difficulties with adherence, or where further support may be required.

Quantitative and qualitative approaches to medicine-taking behaviours

As can be seen from the overview of approaches and understandings of adherence, above, medication-taking behaviour is extremely complex and individualistic, involving patient, physician, and process components (Brown and Bussell, 2011). Quantitative research, based on deductive interrogation of aggregated data to identify trends and frequencies, offers useful understanding of prescription-filling behaviour, which can help form insights into patient adherence and persistence behaviours, as well as their preferences. Indeed, aetiological and health service research more broadly, has historically been dominated by quantitative methodology, where it is sought to investigate and numerically express the effects of specific circumstances upon an outcome of interest. In controlling for any confounding factors, such approaches aim to establish causal inferences (often through statistical means), while maintaining high reproducibility and predictability of similar outcomes to the same set of circumstances (Lakshman et al., 2000).

Common quantitative approaches towards understanding patient medicine-taking behaviour include the use of Medicine Possession Ratio (MPR) and Proportion of Days Covered (PDC) to estimate the proportion of days during a specified observational period, in which the patient refilled their prescription and has medication available to take, as well as Time-To-Discontinuation (TTD) which estimates the time between initial and final prescription (Lam and Fresco, 2015c).

The MPR is calculated as a ratio between the days of supply for a medication (all issued prescriptions) over a specified time interval, and may yield values between zero (indicating no adherence) to one (indicating perfect adherence) (Sperber et al., 2017):

$$MPR = \frac{Days\ supply\ prescribed}{Days\ within\ interval\ period}$$

Furthermore, while values under one indicate underdosing and values above one indicate overdosing (Sperber et al., 2017), MPR is often used as a dichotomous metric, with patients exhibiting MPRs above 0.8 conventionally considered adherent (Tang et al., 2017).

Variations of the MPR calculation result from the choice of denominator, and include either fixed time intervals e.g. 1 year (termed interval based MPR, or MPRi), or variable time intervals e.g. total time between first and last prescription (termed prescription-based MPR, or MPRp) (Tang et al., 2017). Because the MPR does not account for the date of prescription, rather the number of days supplied over a number of days within a timeframe, prescription overlaps due to early requests can lead to an overestimation of adherence (MPR exceeding 1) (Canfield et al., 2019). Furthermore, as such results are often truncated at a value of 1, there may be inconsistencies between reported MPRs in the literature, further complicated in the case of measuring adherence across multiple treatments where an average MPR can conceal outliers (Meige, 2021).

PDC is a newer measure of adherence and caps its output at 100%, thereby avoiding the issue of producing estimates above this level (Canfield et al., 2019), and is typically calculated by:

$$PDC = \frac{Days\ covered\ within\ interval\ period}{Days\ within\ interval\ period}$$

The subtle distinction between days supplied as in the MPR calculation and days covered within the PDC ensures that overlapping supplies of medication are considered sequentially, enabling a truer understanding of the days a patient has medication available to take (Gallagher, 2015). Furthermore, PDC is a more suitable measure in patients on multiple medications as instead of averaging between multiple medications as is usually the case with MPR, the PDC calculation would only consider a day as “covered” with all medications were available to take (Gallagher, 2015).

TTD offers an estimation of persistence by measuring the time between initial and final prescription as defined by a maximum allowed gap between prescriptions. Upon the exceeding of this gap, the patient is assumed to no longer be persisting with treatment (Lam and Fresco, 2015b, Kim and Lee, 2016).

Useful though such measures are in addressing the scientific/clinical agenda (as described by (Horne et al., 2005)), as well as in gauging population-level behaviour, (where such metrics are commonly employed), there is an assumption that prescription-refilling behaviour corresponds to medicine-taking behaviour. Furthermore, as described by the authors of numerous quantitative papers above, MPR, PDC and TTD alone cannot describe nor explain the full picture of patient medicine-taking behaviour, as purely quantitative metrics fail to provide insight into patients' individual or personal experiences, and the meaning ascribed to such concepts as adherence and persistence by the patients being studied (Yilmaz, 2013). Taken alone, such measures also fail to provide clarity as to why observed behaviours occur as they are more suited to hypotheses-testing, than explaining complex social or cultural phenomena (Tariq and Woodman, 2013). This may, therefore, limit their usefulness in understanding and uncovering ways of improving medicine-taking behaviours (Lam and Fresco, 2015c, Peterson et al., 2007).

Qualitative methods however, are concerned with understanding context and meaning through inductive reasoning, emphasising the interpretation people make of their experiences (Yilmaz, 2013). In contrast to quantitative research, where sample size and representativeness is controlled to heighten external validity, such generalizability is not typically expected of qualitative research. Here, contextual, rather than statistical similarities determine the applicability of findings from one group of people, onto another (Sullivan and Sargeant, 2011, Tariq and Woodman, 2013, Leung, 2015, Trochim, 2015, Horsburgh, 2003).

Indeed, the value of qualitative approaches in providing powerful insights to the drivers and barriers of treatment adherence, including cultural influences, beliefs and values underlying them have been recognised in a diverse array of clinical areas including antiretroviral treatment, hypertension and breast cancer, paving the way for the present body of work centred on OAB (Sankar et al., 2006, Najimi et al., 2018, Verbrugghe et al., 2015). An exploration of such qualitative works in the context of OAB is provided in Chapter 2.

Impact of the study type on exploring medicine-taking behaviours

Alongside considering the general approach to exploring medicine-taking behaviours as outlined above, it is noteworthy to consider the impact of the chosen study design and assessment tools on the outcomes of studies exploring adherence.

Direct and indirect measures of adherence

Osterberg et al. (2005) distinguished the measurement of medicine-taking behaviours between direct and indirect methods. Direct methods include observing the ingestion of treatment or measuring the concentration of a drug, its metabolite or a biomarker in blood or urine, thereby objectively proving the uptake of treatment. Indirect measures include patient questionnaires and self-reports, pill counts and prescription refill data, and questioning care-givers (Osterberg and Blaschke, 2005). While direct methods may be useful for specific, narrow therapeutic index treatments such as sodium valproate, lithium and methotrexate, such methods are expensive, burdensome and time-consuming to undertake, and are inapplicable for treatments with long half-lives (Osterberg and Blaschke, 2005). Furthermore, direct methods are not devoid of bias as seemingly adequate serum concentrations on the day of the test can mask historic non-adherence, and underdosed prescribing and patient-specific pharmacokinetic and pharmacodynamic factors can influence serum concentrations too (Anghel et al., 2019).

Self-reported adherence, and caregiver reported adherence, while relatively easier and more economical to collect, can be subject to recall or reporting biases, and may overestimate adherence (Anghel et al., 2019), (a description of recall bias, interviewer effect, and demand characteristics can be found in Chapter 4: “strengths and limitations”). Despite offering the most useful tool in clinical practice, reporting from patients or their carers are susceptible to error, particularly with increasing intervals between visits, and are easily distorted by the patient (Osterberg and Blaschke, 2005). On the other hand, pill counts, and rates of prescription refills offer relatively objective, and quantifiable methods of characterising medicine-taking behaviours and are often favoured in population-level analyses (see below). However, the provision or possession of treatment is not a guarantee of actual ingestion, and such measures too can misclassify true behaviours (Osterberg and Blaschke, 2005) (see discussion of MPR and PDC above).

RCT’s and Real-world data

Clinical trials are time consuming and can be extremely costly to conduct (Fogel, 2018), and a high degree of treatment non-adherence within a trial can result in a failure to detect a true difference between trial interventions on account of a loss of statistical power (Murali et al., 2017). RCT’s are typically conducted on a strictly selective sample of individuals and managed under highly protocolised settings, under the overarching tenet that the outcomes from the sample are representative of the entire population (Kim et al., 2018). While the latter point may be a subject of contention given the comparative controlled homogeneity of trial participants against patient and circumstantial heterogeneity in real clinical practice, as well as differences in the characteristics, motivations, and behaviours of trial participants vs. general population, treatment adherence within a trial is inextricably linked to the clinical outcome of interest (Susukida et al., 2017). In general, observed treatment adherence rates of individuals in RCT's (typically using indirect methods) is considerably higher than that observed in clinical practice (Matsui, 2009, van Onzenoort et al., 2011). This may be contributed to in part by RCT's measuring adherence over a relatively short duration of time, RCT participants receiving more clinic time and accompanying monitoring, support, and advice than their non-participating patient counterparts, as well the provision free treatment in some RCT's (Sexton et al., 2011b, Persaud et al., 2020). Furthermore, the exclusion of individuals more likely to be non-adherent, as well as the potential motivating effect of being enrolled in a trial itself are additional reasons why individuals may adhere more closely to their treatment in an RCT (Murali et al., 2017).

Compensating some of the limitations of clinical trial data, the analysis of Real World Data (RWD) to generate Real World Evidence (RWE) leverages raw information from non-interventional and observational studies such as Electronic Medical Record (EMR) data and prescription claims records to generate insights into actual clinical practice, without the strict controls of the RCT setting (Chodankar, 2021). While RWE too is associated with some limitations (selection bias, data may be inconsistently collected or archived, there may be missing variables in the databases used), compared to RCT's, RWE is often more economical to generate, can include data from far more individuals, and typically covers longer follow up times (Nazha et al., 2021).

Within the context of OAB, differences in the characterisation of medicine-taking behaviours using RCTs and RWE has been noted in the literature. Sexton et al., in their review paper summarising persistence and adherence to antimuscarinic treatments found RCTs to understate the extent of treatment discontinuation compared to RWE such as medical claims data from clinical settings, noting a trend of substantially higher treatment discontinuation rates in studies with longer follow-ups (Sexton et al., 2011b).

Adherence and persistence to OAB oral pharmacotherapy

Being a chronic condition, control of OAB symptoms often requires long-term treatment, the bulk of which is accounted for by oral pharmacotherapy (Goldman et al., 2016, Margulis et al., 2018b, Abrams et al., 2000b). Achieving prolonged adherence with OAB medication has been shown to be associated with better symptom improvement and enhanced patient quality of life in an observational study involving 952 patients (Kim et al., 2016). These findings were mirrored by a prospective study that determined an association between self-reported adherence to fesoterodine and improved quality of life and symptom control in women with OAB (Andy et al., 2016).

Furthermore, discontinuing OAB medication was related to a relapse of OAB symptoms as evidenced by a study investigating the effects of discontinuing propiverine after a 3-month successful treatment (Choo et al., 2005). Similar findings with respect to the discontinuation of tolterodine were reported by Lee et al.,2011 who reported high symptom relapse rates (62%), regardless of treatment duration preceding the discontinuation (Lee et al., 2011). Offering evidence across more than one OAB treatment, Kim et al.2017 described their findings of a high rate of OAB symptom recurrence, particularly at one-month post discontinuation (25.6%), with patients on a variety of antimuscarinic agents (Kim et al., 2017).

It has long been understood that patient adherence and persistence in the context of treatments for OAB are generally low (Chapple, 2017b). In fact, in one study, such medicine-taking behaviour was found to be lowest with OAB treatment when compared to medication classes to treat five other chronic conditions (diabetes, glaucoma, hyperlipidaemia, osteoporosis and hypertension) (Yeaw et al., 2009). Like many quantitative estimations of medicine-taking behaviours, this study involved retrospective analysis of pharmacy claims data. Records for almost 168,000 patients from 100 health plans in the USA were analysed to compare across the six disease areas. Adherence was defined as a continuous measure of the PDC during 12-months of follow up, whereas non-persistence was defined as discontinuation of the medication following an allowable gap between refills (30, 60, and 90-day gaps were used). The study reported variable but uniformly suboptimal medication use across the six disease areas and found the mean 12-month adherence rates (PDC ≥80%) ranged from 72% with oral diabetic drugs, to 35% for OAB medications. Similarly, in comparing the 6-month persistence rates, patients taking OAB medications were found to persist the least with only 28% meeting this endpoint. According to the authors themselves, the PDC calculations used to estimate adherence in this study may in fact have overestimated adherence, as they assumed that patients took all the medications for which they had prescriptions filled. Furthermore, as the objective of this study was to identify variations in adherence and persistence in a heterogenous population of patients, it was not within-scope to explore the drivers for such behaviours. As such, taken alone, the reduction of such complex human behaviours to their resultant measurement on a unidimensional scale offers little by way of understanding the contributors to such behaviours. The authors acknowledged that improving the management of chronic conditions required better understanding of the underlying phenomena of adherence and persistence to prescribed therapy, and that that further work was needed to understand and address the underlying reasons for such behaviour (Yeaw et al., 2009).

Another study using prescriptions claims data considered persistence with OAB medication in the Medicaid population. Looking specifically at tolterodine (extended-release), oxybutynin (immediate-release and extended-release), this study employed TTD to gauge persistence, and the MPR method as a proxy for adherence and reported 12-month persistence rates of 5-9% in patients prescribed antimuscarinics for OAB. The authors reiterated the weakness in extrapolating medicine-taking behaviour from medicine-claims data as seen with the previous study. They also went on to conclude that further work was needed to understand the reasons for low persistence, in order to develop interventions to improve persistence and adherence, giving particular emphasis to the need for further clinical studies and surveys towards achieving this (Shaya et al., 2005).

These findings were supported by a systematic literature review considering reports of adherence and/or persistence with OAB therapy from a multitude of sources including randomised controlled trials, observational studies, medical claims database studies and economic analyses (Sexton et al., 2011b). Of the total 149 sources, 129 were related to RCTs and open label studies, 14 were retrospective medical claims studies, three were patient-reported observational studies and three were economic modelling studies (using existing trial data).

The results from randomized controlled trials indicated high rates of medicine discontinuation (4-31%), with significantly higher rates reported for studies with longer follow-up periods (Sexton et al., 2011b). The authors illustrated several characteristics of clinical trials that made them poorly suited to assess long-term medicine-taking behaviours, including their relatively short duration, selection bias, and use of patient incentives. They went on to describe the added bias of patients being provided free medication while on a trial, and the ongoing monitoring and reinforcement of lifestyle changes being unmirrored in real practice, thereby producing an inflated picture of adherence and persistence behaviours. This was further made clear upon considering medical claims studies, where rates of discontinuation were significantly higher than those predicted in RCTs, ranging from 43-83% of patients discontinuing their OAB medications within the first 30-days (Sexton et al., 2011b). Rates of discontinuation were seen to rise over time also, with 59-68% discontinuing by 6-months to 75-90% at 12-months (Sexton et al., 2011b).

Of the three patient-reported observational studies, the first study (Benner et al., 2010) employed population-based postal surveys to 260,000 households and collected data on demographics, clinical characteristics and beliefs and expectations of OAB and its treatments. As it displayed some qualitative features in allowing respondents to express their own reasons for OAB medication discontinuation, this study is discussed in more detail as part of the systematic literature review in this chapter. The second reference was a poster detailing a retrospective analysis of 22 patients seen in a single urogynaecology clinic over a period of 18-months. It found the compliance rates with oxybutynin fell from 91% at 3-months, to 55% at 6-months, 32% at 9-months and 18% at 12-months. It also found that side effects were the most common complaint and reason for discontinuation but did not go into detail as to how this conclusion was reached (Echols et al., 2000).

The third patient-reported study concentrated on health-related quality of life with OAB and treatment satisfaction, and employed an online survey to gather data (Newman, 2007). Having categorized respondents into those without OAB symptoms (control group), and those with symptoms (further subdivided into current users of OAB medication, lapsed users, and those never treated), this study also identified reasons for OAB medicine discontinuation (amongst lapsed users). Medicines not working (35%), side effects (31%), and unwillingness to take another pill (18%), were described as the most common reasons for discontinuing therapy, although it was not made clear whether respondents chose from pre-coded reasons or were free to supply their own (Newman, 2007, Sexton et al., 2011b).

The trends seen in this systematic review were broadly mirrored in a more recent narrative review aiming to summarise what is known about persistence and compliance with OAB medication (Kim and Lee, 2016). In this study, the key factors likely to affect adherence and persistence were identified as including adverse effects, treatment expectations, and the recognition by patients of the chronic nature of their symptoms, as well as the need for long-term treatment (Wagg et al., 2015). The study from which these findings were summarised was a retrospective claims database analysis of a Canadian private drug plan and was centred on a comparison between antimuscarinics and mirabegron in terms of adherence and persistence over 12-months. Using MPR and TTD to gauge adherence and persistence respectively, it found that patients that received mirabegron remained longer on treatment than those on antimuscarinics and had higher 12-month persistence and adherence rates. The identification of factors likely to affect adherence and persistence appeared to be speculative, and not grounded on the data generated within the study, which did not include any patient-reported outcomes, or single patient-level data.

Also included in the above narrative review was a descriptive study investigating persistence with various antimuscarinic medication for OAB. It reported that the proportion of UK patients still on their antimuscarinic treatment 12-months after having started ranged from only 14%-35%. The authors suggested that these observations could have been affected by patients taking “drug holidays” whereby they voluntarily discontinued and recommenced their OAB medications intermittently, or in response to the re-emergence of symptoms. However, in the absence of direct patient responses, and the without recorded reasons for discontinuation, this level of explanatory granularity was not possible (Wagg et al., 2012, Kim and Lee, 2016).

A UK retrospective database study used prescription data from the clinical practice research datalink (CPRD) to compare persistence and adherence between antimuscarinics and mirabegron (Chapple, 2017a). It found that discontinuation of antimuscarinics in OAB patients generally occurred within 1-3 months, compared with a median of 5.6 months with mirabegron. Furthermore, the study suggested that the rate of patients discontinuing later than 3 months was similar with all OAB drugs, and therefore the reasons for discontinuation at this stage may also be similar. As the CPRD does not contain data on reasons for medicine discontinuation or non-adherence, these could not be examined as part of this study. In considering possible drivers of such behaviours, the authors reiterated findings from Benner et al, 2010 (discussed below), as well as possibly inadequate patient counselling resulting in unrealistic patient expectations, and proactive treatment holidays as described above. The study concluded that further efforts were needed to better understand the reasons for discontinuation of OAB medications and how to support patients so that they achieved long-term adherence, further reiterating the importance of qualitative works in this area.

Chapter Summary

The present chapter has introduced the reader to the thesis and its overall aims. It has provided an overview of OAB, its burden and available treatments, and went on to describe patient medicine-taking behaviours and the importance of exploring this topic. The relevance of these behaviours to OAB were then presented with a brief overview of the literature on this area. Following this, the reader was provided with an overview of the strengths and limitation of quantitative and qualitative exploration of such behaviours, giving the rationale to collate qualitative works relating to medicine-taking behaviours in OAB as described in the next chapter.

The next chapter will describe a systematic literature review undertaken to collate qualitative research exploring medicine-taking behaviours in OAB.

Chapter 2 – Systematic literature review

What is the current landscape of qualitative research into factors affecting patient adherence and persistence with OAB medication? A systematic literature review

Summary

This chapter describes a systematic literature review of qualitative work exploring factors affecting patient adherence and persistence behaviour relating to overactive bladder (OAB) treatment. The reader is directed to the chapter entitled “Introduction to central concepts” for an overview of OAB itself, the burden of this condition as well as its treatments. Further exploration of adherence and persistence, including their context within OAB is also provided in the aforementioned chapter. In the current chapter, the value of qualitative research in healthcare and the assessment of its quality will be explored alongside search tools to help guide the literature review process. Finally, this chapter will describe the work undertaken to review relevant literature in this space, and the learnings from this exercise.

Introduction

> *“Behind every quantity there must lie a quality” (Gertrude Jaeger Selznick)*

In the words of Shoshanna Sofaer, “If we focus research only on what we already know how to quantify, indeed only on that which can ultimately be reliably quantified, we risk ignoring factors that are more significant in explaining important realities and relationships. Qualitative methods help provide rich descriptions of phenomena. They enhance understanding of the context of events as well as the events themselves” (Sofaer, 1999 pg.1102).

Qualitative research is an umbrella term used to cover a multitude of techniques seeking to discover, interpret and reveal the process, context, interpretation and meaning of observed phenomena, rather than measuring the frequency of its occurrence (Al-Busaidi, 2008, Yilmaz, 2013). Often involving inductive reasoning, the emphasis is typically placed on the contextual influences of people’s actions and interactions, and the meanings that they ascribe to their experiences (Yilmaz, 2013).

Qualitative Research in Healthcare

Within the healthcare context, qualitatively generated evidence has become increasingly used in a multitude of settings to answer questions unsuited to quantitative research, as well as to add new dimensions of understanding to existing research (Hammarberg et al., 2016, Pope et al., 2002). Furthermore, such research is increasingly used to inform the acceptability of interventions in order to gauge factors that may influence their implementation (Lewin et al., 2015), as well as to inform decision-making and the development of guidelines in the face of increasingly complex interventions (Noyes et al., 2019).

Demonstratively, qualitative data collection methods have been employed as part of the NHS Insight programme by NHS providers and commissioners to understand local healthcare experiences and needs, and to further explore the findings from quantitative surveys and other tools. Furthermore, qualitative methods have been used to provide insight on patients’ views on their care, and consequent outcomes, as well as to inform quality improvements, design and delivery of services (NHS England, 2019).

While there exists a range of measures that could be employed to aid medication adherence in OAB patients and beyond (Dhaliwal and Wagg, 2016), the choice and prioritisation of the most appropriate ones to implement at a system level, as well as on an individual basis may be better informed by a qualitative exploration of the patient experience and context than a unilaterally quantitative approach. Such an observation was made in the context of infection prevention (Forman et al., 2008). With an abundance of existing epidemiological evidence, qualitative research methods were used to help explain why certain factors influenced the use of infection control practices by staff across hospitals and to uncover the mechanisms through which these influences occurred. In this study, the authors highlighted the advantages of using a qualitative approach in generating insights of how physicians and nurses could work together to promote early urinary catheter removal (to reduce hospital-acquired infections). The authors went on to describe additional insights from taking a qualitative approach in that its findings challenged their initially held assumptions around the merits of using numerous evidence-based infection prevention practices. Before the qualitative phase of the study, it was assumed that the more infection prevention practices a hospital adopted, the more effective their overall infection control programme would be. However, the qualitative data suggested that this was not necessarily the case, finding appropriate adoption of key measures was more effective than the adoption of many approaches (Forman et al., 2008).

From a wider perspective, the World Health Organization (WHO) highlighted the value of qualitative research in supporting relevant and context-sensitive decision making as governments worldwide moved towards sustainable development of universal health coverage schemes. In a recently published bulletin, the WHO recognised the crucial contribution of qualitative research in the development of recommendations on antenatal care, as well as gauging the acceptability of these recommendations and their implementation (Langlois et al., 2018). Within the context of adherence in OAB and other conditions, understanding the level of acceptability to recommendations, as well as the underlying context behind this may offer key insights into medicine-taking behaviours and the most appropriate ways to support patients.

Further examples of the versatility of qualitative research in healthcare range widely and include the exploration of health professionals holding stigmatised views towards those they treat (Waugh et al., 2017), HCP's and patients' experiences of the conduction of NHS health checks (Riley et al., 2016), and voicing the experiences of underrepresented elderly patients (Birgit, 2019). While reflecting the diversity of areas within healthcare (mental health, cardiovascular medicine, and oncology respectively), these examples also reflect the breadth and mixtures of viewpoints able to be distilled through qualitative research, involving HCPs, patients, and practitioners collectively, and patients alone, respectively. Qualitative methods have also been used to explore the views held by important wider stakeholders in healthcare. Wye and colleagues sought to learn how academic research influenced commissioning outcomes, with a particular emphasis on exploring commissioners' information-seeking behaviour and the role of research in their decision-making. The study involved conducting 52 interviews with clinical and managerial commissioners, witnessing multiple commissioning meetings, and analysing minutes and reports from further meetings. From these, Wye et al. revealed key insights into how information pertaining to commissioning decision making was exchanged through conversations and stories and how pragmatism was adopted by healthcare commissioners in making rapid decisions (Wye et al., 2015). In the absence of universal healthcare coverage in the USA, patients pay for healthcare through a combination of employee or government paid insurances, private insurance and out of pocket payments. To improve efficiency (described as better outcomes for less cost) in such a system which employs a fee-for-services model, Williams et al. described the tension between healthcare delivery organisations having to bear the costs of investing in more efficient care, while the benefits accrued from the resulting reduced resource utilization chiefly profited insurance companies. Williams et al. employed qualitative methodology to compare the views of primary care providers and administrators with private insurance representatives (payers), revealing a high consensus across stakeholders on key areas including a call for payment reform to support a value-based system, and countered assumptions that insurance representatives would favour reduced service utilization (in a bid to minimise costs) above other outcomes (Williams et al., 2019).

Qualitative Research in Medication Adherence

In the context of non-adherence specifically, a systematic review of qualitative research has been used to understand key factors contributing to a large proportion of patients not adhering to tuberculosis (TB) medication, from the perspectives of patients, caregivers and clinicians (Munro et al., 2007). This meta-ethnography of 44 key studies, noted the importance of understanding barriers and facilitators to adherence, as well as the suitability of qualitative research in reaching this understanding and contextualising findings from quantitative approaches. In reporting the interaction of four major factors affecting adherence to TB treatment (structural, social, health service, and personal factors), this study highlighted that many of these factors affecting adherence were out of the control of affected patients, however more work was needed to address significant contributors such as poverty and gender discrimination. The authors went on to advise that future interventions should involve patients more in the decisions made about their treatments (Munro et al., 2007).

Taking a different approach to the use of qualitative methods to address the issue of poor adherence, another study employed focus groups with General Practitioners (GPs) to gather insights from prescribers into finding ways of overcoming non-adherence in chronic conditions. The study identified three main areas affecting adherence: patient-specific factors, the role of the doctor, and the health system, and suggested better interprofessional cooperation with nurses and pharmacists, improved communication with patients, and better information management to address the issues identified (Kvarnström et al., 2018).

To explore the barriers to medication adherence in patients with hypertension, Najimi et al. conducted a qualitative study involving 18 semi-structured interviews. The resulting transcriptions underwent content analysis to produce four key concepts related to non-adherence: lifestyle challenges, patient incompatibility, forgetting medication, and non-expert advice. The study went on to expand on each of these concepts to produce a comprehensive picture of the key reasons for non-adherence with hypertensive patients, to inform decision makers and future policy decisions (Najimi et al., 2018).

A similar approach has been taken with breast cancer patients in a bid to understand the complex patterns of adherence and persistence with antihormonal therapy (AHT), using semi-structured interviews. The study determined that patient experiences leading up to AHT, their expectations and perceptions of the treatment, and the impact AHT had on daily living were key factors related to patient medicine-taking behaviour. In addition to this, social support from family and friends, as well as recognition from HCPs had a direct impact on the disease burden on patients (Verbrugghe et al., 2017).

Analogous examples of using qualitative research to uncover a deeper context of matters pertaining to adherence or persistence can be found in an array of areas including diabetes (Jaam et al., 2018), hypertension (Holt et al., 2014), secondary stroke prevention (Jamison et al., 2016b, Bauler et al., 2014) and schizophrenia (Dobber et al., 2018) among others.

Importance of this Review

In recognising the burden that OAB has on patients, as well as the detrimental health effects of not persisting with its treatment (discussed elsewhere), it becomes essential to understand the drivers of such behaviour in order to identify potential strategies to improve patient outcomes in this disease area.

While notable examples exist in the literature of quantitative investigations into measuring adherence and persistence in these patients, qualitative approaches may be more suited to enable a deeper understand of the drivers for such behaviour, especially in a disease where personal, clinical and environmental factors have been noted to largely influence patients and their medication-taking behaviour (Cleland, 2017, Kim and Lee, 2016).

Conducting a literature review collating evidence from multiple sources may provide more complete knowledge than individual studies alone while helping the interpretation of the findings from single studies. Furthermore, such an approach may aid the exploration of variation or conflicting findings, as well as identifying any gaps in existing research (Munro et al., 2007).

Objective

The aim of this review was to examine the current landscape and quality of qualitative work exploring factors affecting patient adherence and persistence with oral OAB medications.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines

In recognition of the inadequate reporting quality of RCT meta-analyses in the literature, an international group produced the Quality Of Reporting Of Meta-analyses (QUOROM) guidelines in 1996 in order to standardise and improve this (Moher et al., 2009). The subsequent Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were developed as a revision and update of QUOROM guidelines to incorporate meta-analyses and systematic reviews on account of their increasing use and importance of in healthcare research (Moher et al., 2009).

First published in 2009, the PRISMA statement consisted of a 27 item checklist and a four phase flow diagram to enable authors to improve the reporting of systematic reviews and meta-analyses, and to improve the transparency of why such work had been undertaken, the methods employed, and what was found (Moher et al., 2009).

The PRISMA statement was updated in 2020 to reflect changes to technology, terminology, and methods since the publication of the original statement in 2009 (Page et al., 2021). The present systematic review of the literature was originally undertaken using the 2009 PRISMA statement and updated using the 2020 update.

The protocol for the review was registered with the International Prospective Register of Systematic Reviews (PROSPERO ID: CRD42018085333).

Eligibility Criteria

Studies meeting the following criteria were eligible for consideration within the present study:

- Involving adult participants (aged 18 or over) who were on or had previously been prescribed oral medication for the treatment of OAB,
- Involving primary qualitative data collection where participants were allowed to freely express themselves relating to factors affecting adherence or persistence to oral OAB medication. As the manner of data elicitation was the focus of the current review, studies were not restricted to having to report results in a “qualitative” way.

Inclusion and Exclusion Criteria for studies in this review

The full applied inclusion and exclusion criteria for the present study were as below:

Table 2.1: Inclusion and exclusion criteria

Inclusion	**Exclusion**
Peer reviewed	wholly quantitative work with no scope for participants to freely express themselves,
Published in English,	in vitro, paediatric, or animal studies,
Involving human subjects over the age of 18 years	not fully completed,
Involved primary qualitative data collection allowing participant to freely express themselves,	literature reviews, editorials, letters, commentaries, legal cases, newspaper articles, thesis
Investigated or explored factors affecting adherence or persistence to oral OAB medication	

Search Strategy

Search Tools

An integral part of conducting a systematic literature review is the use of a standardised search tool as an organising framework to list terms in accordance with the main concepts in the search question, thereby paving the way for a systematic search strategy. A number of such tools have been developed, each to help formulate the search strategy to answer different types of research questions, from various viewpoints (Methley et al., 2014). Population/problem, intervention, comparison, outcome (PICO) was first introduced in 1995, as a way to break down clinical questions into key searchable terms (Davies, 2011). As a widely used tool, PICO is recognised by the Cochrane Collaboration, and is most useful to identify components of clinical evidence for systematic reviews in Evidence Based Medicine (EBM). Some of its parameters (such as 'comparison' and 'intervention') however, do not lend themselves to qualitative research which does not traditionally employ interventions or control groups (Higgins, 2011, Davies, 2011).

In recognition of the differences between medical terminology, and language used in health policy/management, the client group, location, improvement/ information/ innovation, professionals (CLIP) tool was developed to be used for health and social care management or policy-related questions, which often use softer, and more variable language than that in EBM research. CLIP was further developed into ECLIPSE, in which the 'I' was changed to 'Impact' and which featured the additional parameters of 'Expectation' and 'Service' to further help shape the research question. (Wildridge and Bell, 2002)

Similarly, other tools have been developed to serve differing needs, such as CIMO (context, intervention, mechanism, outcome) for realist synthesis questions, MIP (methodology, issues, participants) for medical ethics questions, and SPICE (setting, perspective, intervention, comparison, evaluation) for evidence-based librarianship (Wong et al., 2013, Strech et al., 2008, Andrew, 2006).

In the context of research questions centred around qualitative studies, and the recognised shortcomings of the PICO model in fully accommodating such research, PICOS was a suggested as a modification to PICO whereby the 'S' referred to 'study design', to help limit the number of non-qualitative results when searching (Tacconelli, 2009). Other adaptations such as PICOT (where the 'T' reflects timeframe), PICOC (where the 'C' represents context), and PICOTT (where the T's represent 'type of question' and 'best type of study design to answer this question') have been suggested as alternative frameworks (Davies, 2011, Riva et al., 2012).

In the search for a PICO-like instrument, designed specifically for qualitative and mixed-methods approaches, the SPIDER tool (Sample, Phenomenon of Interest, Design, Evaluation, Research-type) was developed, adapting and adding to the constituents of PICO in an attempt to make them more suitable for qualitative research (Alison et al., 2012):

- The ‘P’ (population/problem) in PICO was likened to ‘Sample’, as qualitative research tends to involve smaller groups of participants, generating detailed data.
- The ‘I’ (intervention) was changed to ‘Phenomenon of Interest’ to better reflect the aims of qualitative research to explore and deepen understanding of behaviours and experiences rather than to test a specific intervention as such.
- Because of the exploratory nature of qualitative research, and the absence of control groups, the ‘C’ (comparison) in PICO was changed to ‘Design’, as the study design (including any supportive theoretical framework) influences the robustness of the study and subsequent analysis. The inclusion of ‘design’ would also serve to improve the detection of qualitative studies while conducting searches.
- The ‘O’ (outcomes) in PICO was equated to ‘Evaluation’ because outcomes in qualitative research may be seen as subjective concepts, and ‘evaluation’ was considered more appropriate for qualitative work.
- Finally, the creators of SPIDER included the additional parameter of ‘R’ (Research type), in a bid to make the tool more useful for mixed-methods and quantitative searches (Alison et al., 2012).

In the words of the proponents of SPIDER, “more development and testing of the SPIDER tool with a wide range of qualitative research topics are needed before it can be considered a viable alternative to PICO for retrieving qualitative research” (Alison et al., 2012 pg. 1441). A study was conducted to compare the specificity and sensitivity of using PICO, PICOS and SPIDER across three major databases (MEDLINE, EMBASE and CINAHL) in investigating the health care experiences of people with Multiple Sclerosis (Methley et al., 2014). It found that the SPIDER tool exhibited the greatest specificity, generating fewer hits for the team to sift through than PICOS, and substantially fewer than the PICO method. This did however, come at a price of missing five papers identified through using PICO. Although the PICOS tool was more specific than PICO, it did not identify any additional relevant hits in comparison to SPIDER (suggesting similar sensitivities). The study concluded that the SPIDER tool may offer a useful option for study teams with limited resources and time. Furthermore, it could be of benefit to projects not seeking to perform completely comprehensive searches. Studies involving qualitative synthesis may be a good example of this, where the aim of the project is to reach theoretical saturation rather than to compile an absolute collection of all research on a subject area (Booth, 2001). Methley et al. concluded that in relation to SPIDER, with the exception of the above examples, until such a time when the indexing of qualitative studies improves, PICO offers the most comprehensive search tool over a variety of databases (Methley et al., 2014).

With this in mind, this literature review employed PICO as its primary search tool and used SPIDER secondarily to generate a more comprehensive list of search terms.

Table 2.2: Using PICO and SPIDER to identify search terms

PICO Parameters	**Relevant Areas Identified**	**SPIDER Parameters**	**Relevant Areas Identified**
P (population)	Adult (≥18) (OAB) patients	S (sample)	Any sample size composed of adult (≥18) OAB patients
I (intervention)	No specific intervention. Any oral OAB medication.	P I (phenomena of interest)	Factors affecting adherence and persistence to oral OAB medication
C (comparison)	No specific comparison. No specific control	D (design)	Any study design using qualitative data collection to allow patients to self-express factors affecting their adherence and persistence to oral OAB medication

O (outcome)	Factors affecting patient adherence and persistence to OAB medication	E (evaluation)	Factors affecting patient adherence and persistence to OAB medication
		R (research type)	Any research method allowing participants to freely express themselves. Either quantitative research with qualitative elements to data collection or wholly qualitative research.

Search Terms

Using PICO and SPIDER, the following free terms were searched for in combination with database-specific indexed terms:

- "overactive bladder", "overactive detrusor", "overactive detrusor function", "overactive urinary bladder", OAB, “lower urinary tract symptom*", LUTS, "urin* storage symptom*", “urin* incontin*”
- medic*, drug*, prescri*, treat*, antimuscarin*, anticholinerg*, mirabegron, Betmiga, darifenacin, flavoxate, fesoterodine, oxybutynin, propiverine, solifenacin, tolterodine, trospium
- complian*, adher*, persist*, concord*, discont*
- qualitative, "qualitative research", interview*, "group interview*", "oral history", “focus group*”, “case note*”, "telephone interview*, questionnaire*, survey*, telephone, thematic, theme

Search Dates

The literature search was conducted on 19th January 2018 on a total of five databases (MEDLINE, Embase, Web of Science, PsycInfo and the Cumulative Index to Nursing and

Allied Health Literature [CINAHL]). MEDLINE and Embase were accessed through the ProQuest Dialogue platform, with the remaining databases accessed through EBSCOHost. Database results were limited to studies published between January 1st 1987 and January 1st 2018; this period was selected as an appropriate period based on previous work in this area exploring historic prescribing patterns for OAB in UK primary care (Odeyemi et al., 2006), as well as the fact that only oxybutynin was licenced for use in the UK in 1987 (Margulis et al., 2018a).

Manual searches for work by key researchers (as recognised by the presence of their work in the literature search) were undertaken on Research Gate as well as their institutional databases, to capture any relevant grey literature. The full search strategies can be found in Appendix A1. SLR Search Strategy.

Databases

MEDLINE is the primary bibliographic database of the National Library of Medicine (NLM), the worlds' largest biomedical library, based in Maryland USA. Spanning a timeframe from 1966 to present, MEDLINE contains over 27 million references primarily to articles in scholarly journals, indexed with NLM Medical Subject Headings (MeSH). MEDLINE has a subject scope of biomedicine and health sciences, of particular relevant to health professionals and others engaged in research, clinical care, public health, health policy development and related educational activities (NLM, 2021).

Embase is an alternative biomedical database provided by Elsevier. Covering international biomedical literature from 1947 to present, Embase contains over 32 million records (including MEDLINE titles), sourced from over 8,500 journals from over 95 countries. Containing over 2,900 journals unique to it, the Embase database employs the Emtree thesaurus containing over 75,000 preferred terms and subheadings to index its content (Elsevier, 2021).

The Web of Science Core Collection database is an expertly curated collection of over 21,000 scholarly journals, spanning over 250 sciences, social sciences, arts, and humanities subject areas. Provided by Clarivate, the database contains over 74.8 million total records with references dating back to 1900, uniquely offering cover-to-cover indexing (Clarivate, 2021).

The American Psychological Association’s (APA) PsycInfo is a leading resource for interdisciplinary citations of behavioural psychology and social science research, spanning citations from 1597 to present, and covering almost 2,500 journals from more than 50 countries. PsycInfo employs over 8,400 controlled terms and cross-references, using the Thesaurus of Psychological Index Terms for indexing its content (APA, 2021).

Provided by EBSCO, the Cumulative Index to Nursing and Allied Health Literature (CINAHL) database has indexed 5,500 journals and contains over 7.4 million records pertaining to nursing and allied health literature, including biomedicine and health sciences. The indexing of articles using subject headings following a similar structure to the MeSH headings in MEDLINE (EBSCO, 2021).

The choice of databases was informed by both guidance from the literature, as well as confirmation with academic experts with experience of conducting similar reviews in other areas. Booth et al. (2016) performed a structured methodological review of the systematic identification of qualitative evidence for qualitative evidence syntheses and cautioned against the use of a singular database. They furthermore reported MEDLINE and CINAHL as consistently being the most used sources of qualitative research, noting CINAHL’s relatively strong coverage of qualitative research (Booth, 2016). Although EMBASE contains all the records within MEDLINE, both databases were included within the present study to take advantage of their distinct methods of indexing, and to maximise the effectiveness of the search strategy (Clarivate, 2017).

The choice of databases was also partly supported by the findings of Bramer et al. who explored the optimal combination of databases to provide efficient search results for SLRs in order to minimise the burden on research teams without compromising the validity of the research by missing applicable papers. Their findings supported the use of multiple databases in conducting systematic reviews, finding that EMBASE, MEDLINE, Web of Science and Google Scholar offered the best combination of databases to aid a high recall (not missing relevant papers). The authors went on to suggest that specialised databases such as CINAHL and PsycInfo could be useful in retrieving unique references related to the focus of the database (Bramer et al., 2017).

Data management

Search results were exported into Endnote reference management software (versions X8 and X9, Clarivate). Widely supported across a multitude of literature databases and online resources, Endnote offered an intuitive and easy to use platform on which to export, organise and analyse search results.

Paper Screening

The Endnote feature of identifying duplicates was used to highlight, manually review, and remove duplicate papers from the screening process. Following this, titles, abstracts (and where required, full texts) were screened against the review inclusion and exclusion criteria by two researchers (MA & SG). Where there was any disagreement in study selection, a third independent researcher was placed to act in mediation and as final decision-maker

(FF). Full papers were reviewed by both researchers before being included within the present review.

Studies were screened for meeting the inclusion criteria in a stepwise manner to aid a thorough consideration of all potential papers for the current review. Sequential screening steps prioritised the retention of all papers related first to the relevant clinical area (OAB), followed by the treatment type (oral medication), followed by relevance to the exploration of adherence or persistence, and finally, the use of qualitative methods in data collection and/or analysis.

Quality Assessment

Quality assessment of qualitative research

Given the increasing interest in qualitative research over recent years, qualitative studies have increasingly been published in medical, nursing and related journals, as well as generating renewed interest in the field of health economics (Mays, 2000, Obermann et al., 2013, Coast, 2004, Coast, 2018, DeJean et al., 2016). Likewise, evermore decision-makers have been using qualitative evidence to strengthen their assessment of the needs, values, perceptions and experiences of stakeholders, as well as their understanding of relevant socioeconomic settings, health systems and communities, to aid complex health decision-making (Lewin and Glenton, 2018, Langlois, 2018). With the growing volume and increasing exposure of qualitative research to a wider audience, there has been rising interest to better understand the methods used, as well as to scrutinise their findings, bringing with it, the matter of assessing the 'quality' of such research (Mays, 2000, Coast, 2004, Leung, 2015). Historically, the subject of assessing the quality of qualitative research has been a contentious one, dividing qualitative researchers into three broad groups of opinion: those that believe qualitative research ought to be judged according to the same quality criteria as quantitative research; those who believe that a separate set of criteria should be defined for all qualitative research; and those who question how appropriate it is to use any predetermined criteria for judging qualitative research at all (Rolfe, 2006). A central theme of this debate has been the philosophical and epistemological range encompassed within qualitative research, which some believe precludes such work from being appraised in a manner reflecting that employed in the appraisal of quantitative research (Carroll and Booth, 2014). A contrasting view is the acknowledgment that in order for the findings of qualitative research to inform policy and practice, decision-makers need to know whether the primary research is appropriate to shape such decisions (Toye et al., 2013a). The findings of a review in 2012 which considered 82 qualitative evidence syntheses between 2005 and 2008, found that the overriding majority of research teams opted to perform critical appraisal of included studies, with only 5 out of the 82 syntheses expressly not doing so (Hannes 2012). This is indicative of the shifting of the debate from whether or not to perform quality appraisals, to what criteria to use when conducting them (Carroll and Booth, 2014).

It is important to note that while the most common application of a quality assessment has been to exclude papers deemed to be of inadequate quality from an evidence review or synthesis exercise, doing so raises two key questions: what threshold should be used to indicate “adequate quality”, and whether the exclusion of such studies actually strengthens the overall analysis performed (Carroll and Booth, 2014). In light of these, for the purpose of the present review, where the goal was to explore and summarise the available evidence sourced by qualitative means, the quality appraisal of papers has been used as a confirmatory step to illustrate the relative strengths and weaknesses of selected papers, rather than as an additional exclusion criterion for their consideration. Nevertheless, as noted by Carroll et al., and recognised in the Cochrane handbook, the use of a critical quality appraisal forms a crucial part of systematic reviews, even when not used to exclude studies on the basis of quality (Noyes J, 2021, Carroll et al., 2013).

Quality assessment tools

A study by Munthe-Kaas et.al to identify tools explicitly intended for critically appraising the methodological quality of qualitative research found 102 distinct critical appraisal tools mentioned in the literature. Almost half of these were published in the past 9 years, with little description of either the necessity of a new tool or how the proposed tools were developed (Munthe-Kaas et al., 2019). A similar observation of the multitude of tools was made by Carroll et.al who also noted work by Dixon-Woods et al. and Toye et al. in highlighting inconsistencies in quality assessment both within and across different tools (Carroll and Booth, 2015, Dixon-Woods et al., 2007, Toye et al., 2013b).

Garside et al. noted the difficulty of using a single, simple checklist to appraise qualitative research, given the range of approaches to data collection and analyses, comparing this to the relative straightforwardness of designing quality appraisal tools for RCTs. Garside et al. went on to highlight the danger of using such quality appraisal tools too prescriptively and warned that doing so could result in the judgement of the quality of reporting as opposed to the quality of the actual studies conducted. In recognising the practicalities of assessing research with the information available to the researcher, however, Garside et al. concluded that it was incumbent upon the researcher conducting the research to document the conduct of their study in sufficient detail to allow critical appraisal, and without such information, it was impossible to appraise the quality of research irrespective of what framework or tool was deemed appropriate (Garside, 2014).

Quality Assessment within this review

The Cochrane Qualitative and Implementation Methods Group (QIMG) suggest to select a tool that focusses on the assessment of methodological strengths and limitations of qualitative studies, and put forward example domains suggested for consideration in choosing an appropriate tool (Noyes J, 2021). These domains are listed as they appear in the Cochrane handbook in Figure 2.1 below:

- Clear aims and research question
- Congruence between the research aims/question and research design/method(s)
- Rigour of case and or participant identification, sampling, and data collection to address the question
- Appropriate application of the method
- Richness/conceptual depth of findings
- Exploration of deviant cases and alternative explanations
- Reflexivity of the researchers

Figure 2.1: Key quality assessment tool domains

In a paper extensively referenced in the Cochrane handbook and beyond, Garside et al. built on published works by Dixon-Woods et al. and Sparkes et al. (who outlined the schools of thought around assessing reliability and validity of qualitative research) (Sparkes, 2001, Dixon-Woods et al., 2004), in proposing a quality assessment criteria aligned with the key considerations outlined above (Garside, 2014).

The proposed quality assessment checklist tool was used for appraising the methodological quality of papers identified in the current review on the basis of its alignment with recommendations from Cochrane, the simplicity of its approach, and its applicability to works identified within this review.

Table 2.3: Paper quality assessment criteria (Garside, 2014)

Question		Yes / Partially / No
Is the research question(s) clear?		
Is the research question(s) suited to qualitative enquiry?		
Are the following clearly described?	Context	
	Sampling	
	Data collection	
	Analysis	
Trustworthiness	Are the design and execution appropriate to the research question?	
	What evidence of reflexivity is there?	
	Do the voices of the participants come through?	
	Are alternative interpretations, theories, etc. explored?	
	How well supported by the data are any conclusions?	
	Are ethical considerations given appropriate thought?	
Theoretical considerations	Does the report connect to a wider body of knowledge or existing theoretical framework? If so, is this appropriate (e.g., not uncritical verification)?	
	Does the paper develop explanatory concepts for the findings?	
Practical considerations	Does this study usefully contribute to the policy question?	
	Does this study provide evidence relevant to the policy setting?	
	Does this study usefully contribute to the review?	
(Garside, 2014)		

In line with recommendations from the Cochrane handbook to avoid the application of domain scores or an overall calculation of total quality score, each paper was coded with a ‘yes’, ‘partial’, or ‘no’ response to each of the 17 criteria questions under the four areas of clarity, trustworthiness, theoretical considerations and practical considerations (see Table 2.3) (Noyes J, 2021, Garside, 2014).

Two reviewers (MA and SG) independently coded each paper to the Garside criteria with an additional reviewer (JH) supporting the updated searches in 2021. Assignment of the ‘yes’, ‘no’ or ‘partial’ descriptions was based on reaching consensus between reviewers with full concordance reached through discussion where there was initial difference in opinion. The coding of included papers is provided in Table 2.5 below.

Results

A total of 1,315 records were found in the databases searched. After removing duplicates, screened 971 titles were screened, from which 112 abstracts were selected for retrieval and screening. Of these, a further 78 papers were excluded, leaving 34 full papers to be reviewed, ultimately resulting in 12 papers to include within the present review. No further relevant articles were found when searching Research Gate and institutional websites of authors in selected papers.

Study identification

The PRISMA flow diagram is presented in Figure 2.2 below.

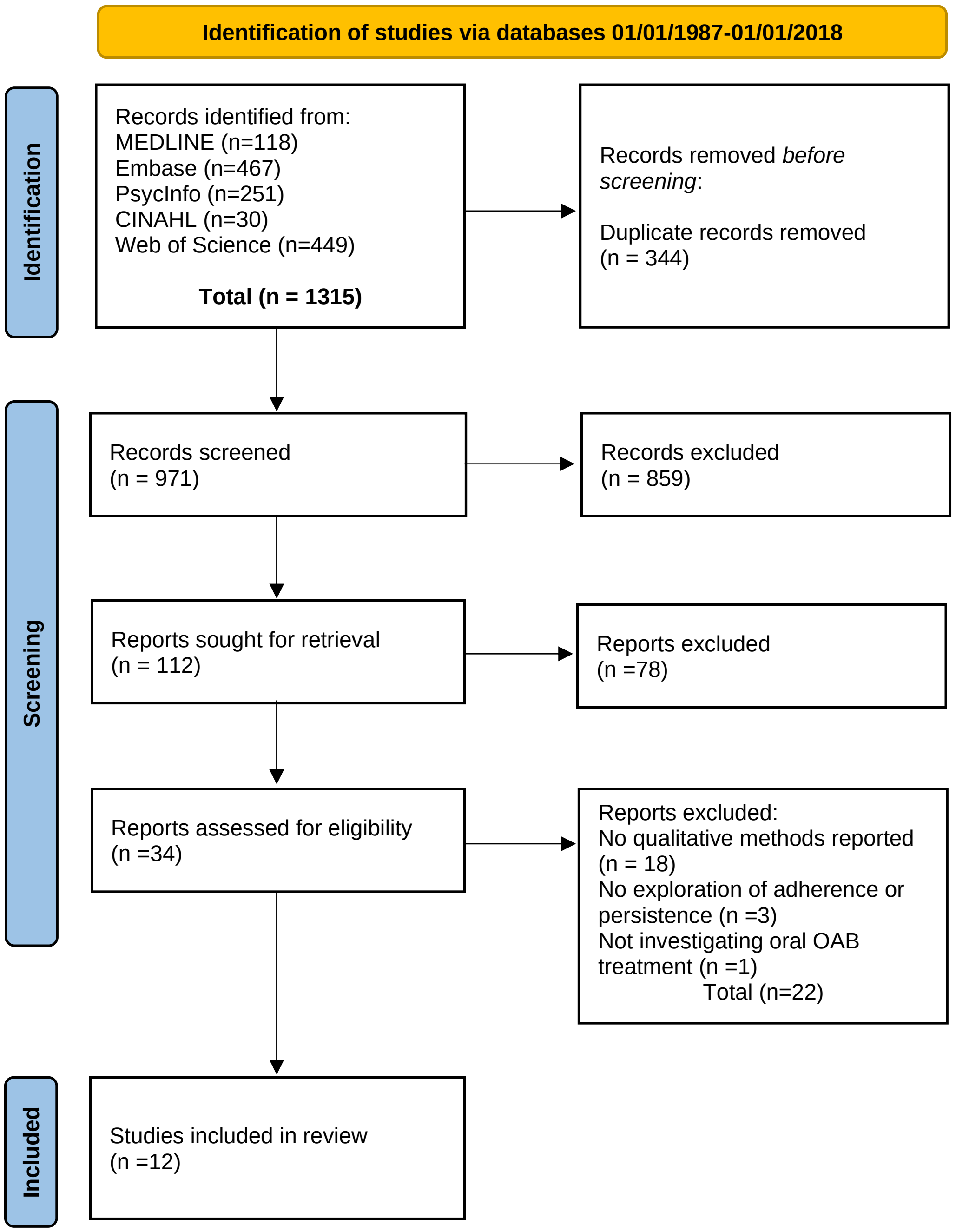

Figure 2.2: PRISMA flow diagram 1987-2018

Selected studies:

Table 2.4: Selected studies overview

#	Study Design, Participants and Objectives	Methods of Data Collection	Methods of data analysis /Presentation of results	Main Findings
1.	**Benner et al. (2009):** Patient-reported reasons for discontinuing overactive bladder medication			
	Prospective cohort symptom prevalence study. Phase 1: screening survey sent to 260,000 households in USA to identify patients using antimuscarinics for OAB. (Sample was balanced to reflect the USA population in terms of age, sex, geographical region, urban vs rural, household income, household size). Phase 2: follow-up survey with 5392 respondents (78% of participants were female, 14% were under 44, 59% were 45-75, and 27% over 85 years of age) **Objectives**: To evaluate patient-reported reasons for discontinuing antimuscarinic prescription medications for overactive bladder (OAB).	Phase 2 survey included OAB-V8 questionnaire as well as questions on: current and past use of OAB medications including self-reported start and end dates, persistence rates, and reasons for discontinuation for three or fewer OAB treatment regimens. Respondents could write their own reason for discontinuation or select among 14 pre-coded reasons: Advice of family/friend, Another condition/medication, Bladder symptoms stopped/cured, Change of insurance status, Cost/amount of co-pay, Didn't work as expected, Doctor didn't make right treatment decision, Don't like taking ANY medications, Don't like taking medications for too long, Had side-effects, Learned to get by without medication, Switched to new medication, Switched to previous medication, Told to stop by clinician/pharmacist Respondents were also questioned about demographics, comorbid conditions, beliefs about OAB, treatment expectations, healthcare-consulting behaviours, and level of satisfaction with their healthcare providers.	Latent Class Analysis (LCA) statistical method was used to identify natural groupings of respondents based on combinations of their reported reasons for discontinuation. The measurement model was developed using the Lo-Mendell-Rubin likelihood ratio test to determine the number of latent classes. The conditional probability of each reason for discontinuing OAB medication was estimated for each class. Multivariable logistic regression was used to assess the influence of age, sex, race, income, and recent history of incontinence on the most likely class assignment. Results expressed as descriptive statistics.	In all, 1322 phase 2 respondents (24.5%) reported discontinuing one or more antimuscarinic drugs during the 12 months before phase 2. LCA identified two classes based on reasons for discontinuation. Most respondents (89%) reported discontinuing OAB medication primarily due to unmet treatment expectations and/or tolerability; many respondents in this class switched to a new antimuscarinic agent. A smaller group (11%) indicated a general aversion to taking medication. Age, sex, race, income, and history of incontinence were not predictive of class assignment.
2.	**Campbell et al. (2008):** Survey assessment of continuation of and satisfaction with pharmacological treatment for urinary incontinence			
	Online survey of 1,447 adults in a US National Family Opinion World Group database. (87% of participants were female, 30% were 18-49, 54% were 50-69,	Online database of 100,000 adults screened for those having previously reported receiving medication for incontinence. A total of 33 questions on the survey relating to demographics, nature and impact of	Descriptive analyses performed, calculating means and frequency distributions of the survey variables. Logistic regression	81% of participants experienced wetting accidents while laughing, sneezing, coughing, or exercising (indicating stress incontinence). 25% reported being somewhat dissatisfied or very dissatisfied with incontinence treatment.

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	and 16% were over 70 years of age) **Objectives**: to investigate the types of treatments (pharmaceutical or surgical) used by patients with urinary incontinence, their satisfaction with treatment, and the rate of	incontinence symptoms experienced, treatments used within the last 4 weeks, treatment satisfaction, efficacy, and discontinuation. Impact of incontinence on lifestyle was answered "no/mild/moderate/severe effect", treatment satisfaction was indicated using a 5-point Likert scale from "very satisfied" to "very dissatisfied".	was used to estimate unadjusted and adjusted odds ratios (ORs) for each outcome of interest (e.g., frequency of urination and wetting accidents). Statistical significance and 95% confidence intervals were calculated to describe	651 (45%) of participants reported a reason for discontinuing drug treatment: lack of treatment efficacy (41%), side effects (22%), treatment costs (19%), lack of insurance coverage (12%), other reasons unspecified (28%). Exploring predictors of treatment discontinuation, compared to participants ≥70 years, 18–39 and 40–49 were significantly more likely to discontinue treatment (crude OR = 1.76; 95% CI 1.15–2.68 and crude OR = 2.12, 95% CI 1.49–3.01, respectively). Duration of symptoms was weakly associated with treatment discontinuation. Compared to

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	and reasons for discontinuation of pharmacological treatment.		the precision of effect estimates from the regression models.	those with symptoms for less than 3 years, OR was significant in those with duration of symptoms 6 or more years (OR of 1.45 and 1.53; 95% CI did not include 1.0)
3.	**Filipetto et al. (2014):** The patient perspective on overactive bladder: a mixed-methods needs assessment			
	A mixed-methods study involving telephone interviews with 40 participants (31 females and 9 males) and a	40 qualitative interviews were conducted with patients who were pre-screened for a history of OAB and/or urinary incontinence. Interviews lasted between 30mins to an hour.	Data analysis conducted using SPSS, descriptive statistics such as means and frequencies provided.	OAB was reported as troublesome and had a significant effect on daily life. On average, there was a 3.5-year gap between symptom onset and treatment initiation. 62% participants had been

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	quantitative survey to 194 respondents (49% female, 33% between 41-60 and 67% over 61 years of age) **Objectives:** to identify patients' knowledge, experiences and attitudes, barriers to treatment adherence, and desires and	Participants were questioned on the type of treatment and adherence in an open-ended format. A quantitative survey and assessment tool based on insights in qualitative phase was developed and emailed to those self-identified as experiencing OAB/urinary incontinence. Survey took less than 15minutes to complete.	Differences in scores determined using analysis of covariance (ANCOVA), mean scores from Likert scale compared using independent sample t test. Responses from interviews discussed in general sense	prescribed OAB medications. Only 29% and 31% had been provided bladder training and pelvic floor exercises. Non-adherence was mostly due to side effects including dry mouth, constipation, and blurred vision. Treatment cost and low effect were other key reasons. Treatment adherence was reported as initially starting high but falling over time. Adherence decreased as patients perceived medication becoming less effective. More frequent HCP communications were associated

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	tendencies regarding patient/clinician communications		alongside quantified survey results.	with higher adherence than less frequent communications (p=0.018)
4.	**Jundt et al. (2011):** Anticholinergic therapy: do the patients take the pills prescribed?			
	132 patients interviewed on average 22months post visit to outpatient's clinic. (100% women with median age of 62 years and range of 24-86 years)	Telephone interview between 2006 and 2007. Patients recruited from uro-gynaecology outpatients' department from University hospital Munich. Patients asked if they were still taking medication originally prescribed, whether the symptoms were better with	Statistical description of: drug most often prescribed, percentage of patients still taking their medication after at least 12 months, reported symptom improvement	38% of patients still took their medication after at least 12 months. 62% did not take the original medication anymore. 10% had never started with the medication. The main reason for not even trying was ''fear of side effects'' and ''not wanting to take pills''. 42% took the medication for 3 months and 8% for 4–12 months. 25% had changed to another anticholinergic

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	Objectives: To evaluate how many patients with overactive bladder still took their prescribed medication at least 12 months later and to find out the reasons for discontinuation of the therapy.	medication, and if discontinued- the reasons for stopping	percentage of patients taking originally prescribed treatment reasons for not starting treatment reasons for discontinuing therapy within the first three months	drug. The reason for discontinuation of the therapy in the first 3 months were: improvement even without medication (27%), fear of side effects (10%), no further prescription by the family practitioner or gynaecologist (9%), no improvement (20%), side effects (20%).
	Lai et al. (2011): Solifenacin use in older Australians – the challenge of non-government subsidised prescription for overactive bladder			

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5.	16 patients attending two geriatric continence clinics in Perth in 2008. Non-interventional prospective study. (94% women, mean age of 81 ± 10 years) **Objectives**: using an audit tool, this study looked to identify the barriers to the use of solifenacin	Patients prescribed solifenacin completed a three-day bladder diary at baseline and at eight weeks. They received telephone interview after one year.	Pre- and post-solifenacin bladder diary outcomes were compared by paired t-test. Parameters were compared between solifenacin users and non-users to identify prescription pattern using unpaired t-test or Pearson's c2 test where appropriate. A qualitative approach was	At four weeks, solifenacin reduced frequency by 3.2 episodes per 24 hours, urgency by 2.6 episodes per 24 hours, incontinence by 2.3 episodes per 24 hours and continence product usage by seven pads per week. These effects were sustained at eight weeks. Two geriatricians reported that many patients refused to commence solifenacin because it was expensive. Among the eight non-responders to oxybutynin or amitriptyline, half reported dry mouth or constipation from solifenacin and two discontinued by eight weeks.

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	for the management of OAB symptoms.		also used in examining prescription pattern and compliance to allow unanticipated issues arise.	Excluding two patients who deceased, compliance for solifenacin at one year was poor (28.6%). Among four patients who remained on solifenacin, one achieved continence and two reported tolerable dry mouth or slowness in thought. Three discontinuations were due to cost and three due to intolerance. Two patients did not remember that solifenacin was prescribed. Two provided no reason.
	Lee et al. (2014): Persistence with solifenacin add-on therapy in men with benign prostate obstruction and residual symptoms of overactive bladder after tamsulosin monotherapy			

6.	Prospective, multicentre, open-label, single-arm study conducted at 16 university hospitals over 52-weeks. Eligible patients prescribed Tamsulosin. After 4 weeks, men with persistent OAB symptoms were prescribed Solifenacin in addition to Tamsulosin. Total 176 patients prescribed solifenacin. (100% men, median age 63.5 years) **Objectives**: This study aimed to evaluate persistence and the reasons for the discontinuation of solifenacin add-on therapy in men with residual symptoms of OAB after tamsulosin monotherapy for benign prostatic obstruction (BPO) in a real clinical environment.	At 4, 12, 24 and 52 weeks after adding solifenacin, patients were assessed on their medication status, willingness to continue the medication or reason for discontinuation. After 30 days, patients were contacted via telephone to evaluate single most important reason for discontinuation. Individual reasons were divided into appropriate categories; adverse events, lack of efficacy, symptom improvement, withdraw consent, other diseases, protocol violation and others.	Because patient's willingness to continue/discontinue the treatment and the reasons for discontinuation were up to patient's subjective perception and decision, investigators did not define the reasons objectively. Descriptive statistics reported for persistence, reason for discontinuation, and adverse events. Statistical analysis using: univariate and multivariate regression analyses, paired T-tests, and Wilcoxon's signed rank tests.	After 52 weeks, 44 (25%) remained on solifenacin therapy. Of the 132 who discontinued solifenacin, 85 were evaluated on the reason for discontinuation. The three most common reasons for discontinuation were adverse events (AEs) (35%), lack of efficacy (33%), and improvement in symptoms (16%). The aggravation of voiding symptoms was the most common AE leading to discontinuation. Retention was observed in 11 men. None of the demographical or clinical characteristics were significantly related to persistence
7.	**Maguire et al. (2016):** Patients' experience and expectations of conservative management strategies, anti-muscarinics and treatment with intravesical onabotulinum toxin for overactive bladder - a qualitative interview study			
	Follow on "qualitative interview assessment" of 15 consenting female patients from the RELAX randomised controlled study investigating intravesical onabotulinumtoxinA (onaBoNTA) vs placebo for the treatment of idiopathic detrusor overactivity (DO). (100% female, mean age 63 years) **Objectives**: to explore patients' experience and expectations after onaBoNTA treatment for DO; to compare the experiences/ expectations between women randomised to receive active drug	Up to an hour-long, semi-structured interviews conducted with consenting participants. Discussion guide was developed by study team in combination with literature and trial experience from RELAX. There was an emphasis of allowing participants to discuss their experiences and views freely. Interviews were audio recorded.	Audio recordings were transcribed and anonymised ready for "qualitative analysis". Analysis described as breaking the transcripts down into "meaning units", condensed and analysed thematically based on a constant comparative method (from the grounded theory approach). Two reviewers were involved in data analysis, with data read and re-read at intervals of 5 completed interviews until data saturation (which occurred at interview 13).	Quality of life: impact of OAB illustrated by participants discussing feelings of anxiety, embarrassment, and restrictive effect on lifestyle. Conservative management: pelvic floor exercises were recommended to all participants, with varying degrees of support in how to do them. Most did not adhere to these and viewed them as a short-term exercise plan. All participants had experience of anti-muscarinic medication, and all had discontinued due to lack of effectiveness and/or side effects. Commonly reported side effects included headache, dry eyes/mouth, irritability, restless legs syndrome and nausea.

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	or placebo, and to explore patients' experience and understanding of taking part in an RCT		Results presented under headings of themes relating to quality of life, conservative management, and the intervention in the RCT, with quotes from participants illustrating observations made.	
	Pindoria et al. (2017): Persistence with Mirabegron Therapy for Overactive Bladder: A Real-Life Experience			

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8.	Retrospective analysis of hospital case-notes and subsequent telephone interviews. 197 patients from Department of Urology, Guy's Hospital, London, United Kingdom (63% female participants, mean age 57 years)	Retrospective analysis of case-notes to identify patients commencing mirabegron treatment between 2013-2014. Data collated from notes: previous treatments trialed for OAB, reasons for discontinuation of previous therapy, incidence of mirabegron used concomitantly with antimuscarinic therapy. Patient then contacted for telephone interview and asked to complete two	Primary endpoint measured in this study was the percentage of patients on mirabegron therapy at 6months. In those that had discontinued therapy early, reasons for discontinuation were identified and explored.	Persistence rates with mirabegron at 3 months were 69% which reduced to 48% by 6 months. Very similar persistence rates between males and females at both 3 and 6 months. Persistence rates in patients aged over 60 years of age was 64% and 43% at 3 and 6 months, respectively. Mirabegron persistence rates were similar between those patients who had stopped antimuscarinics due to side effects compared with those who had stopped due to lack of efficacy, with 6-month persistent rates of 39% and 34%, respectively. Of the subset of participants initially commenced on antimuscarinic

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	Objectives: To evaluate persistence rates of patients receiving mirabegron therapy for overactive bladder (OAB) over a 6-month period, identify determinants of early discontinuation of therapy, and assess overall patient satisfaction with treatment.	questionnaires: [1] Overall treatment satisfaction [OAB-SAT-Q] from which data from 2 questions was included (overall satisfaction and preference to Mirabegron over previous treatments [2] a new questionnaire to evaluate persistence rates and reasons for discontinuation. Average length of follow-up was 10months.	Persistence and satisfaction rates calculated from the OAB-SAT-q (telephone interview). represented with descriptive statistics. Reasons for discontinuing therapy expressed with percentage of respondents citing them.	agents, 68% discontinued therapy due to a lack of symptomatic improvement and 24% due to development of adverse effects. Reasons for discontinuation for the remainder were unknown

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9.	**Sung et al. (2015):** Interventions do not enhance medication persistence and compliance in patients with overactive bladder: a 24-weeks, randomised, open-label, multi-centre trial			
	Prospective cohort study 2012 - 2014, involving 682 OAB patients randomly assigned to health education intervention (HEI) plus fesoterodine group or fesoterodine alone group (control). (Multicentre) (100% female, mean age 56 years)	Post randomisation into groups, patients had follow-up visits in weeks 4, 8, 16 and 24 where the discontinuation of medication was evaluated. Telephone surveys were performed for those participants who failed to follow-up within a month. Pre-coded and free-format reasons for discontinuation:	Primary endpoint: percentage difference in maintaining a persistence rate of fesoterodine at 24 weeks post-randomisation. Secondary endpoints: percentage difference in persistence rate at 4, 8 and	Persistence of the HEI group at 6 months was not statistically higher than that of the control group. Compliance at 6 months was also similar between the two groups. Using OAB symptom score questionnaire, the efficacy of the two groups was not different at each follow-up. The global response was similar between the two groups. However, the HEI group was more satisfied with treatment than the control group (p = 0.034). The most common reason for discontinuation was satisfaction

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	Objectives: The aim of this study was to determine whether a health education intervention (HEI) could improve drug persistence with anticholinergics in OAB patients.	satisfaction/dissatisfaction with treatment, insufficient efficacy, adverse events, death, violation of protocol, and pregnancy. Other reasons were reported in an open-ended format	16 weeks and the percentage difference in compliance rate at 24 weeks. Statistical analysis using two-sample t-test, Chi-Squared test, and Fisher's exact test performed.	with the treatment so that they did not need to follow-up, followed by inadequate efficacy in both groups. Adverse events were reported in 12.3% of patients.
	Tijnael et al. (2017): Real life persistence rate with antimuscarinic treatment in patients with idiopathic or neurogenic overactive bladder: a prospective cohort study with solifenacin			

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10.	Prospective study following 123 patients from Urology Dept. of Erasmus University Medical Centre, Rotterdam for duration of one year. (43% female participants, mean age 62 years) **Objectives**: To investigate the persistence rate in real life among	Telephone interviews / surveys taken at 1, 3, 6 and 12 months after starting solifenacin. Patients asked whether they were continuing the medication (Solifenacin), possible side effects, and reasons for stopping if discontinued.	Statistical analysis performed using SPSS. Chi-square test was used to evaluate the differences between groups	After one year 40% of patients were still using solifenacin, 50% discontinued. 1-year persistence in neurogenic group was 58% versus 32% in the idiopathic group. The main reasons to stop taking solifenacin were lack of efficacy (39%), side effects (30%) and a combination of both (13%).

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	Welch et al. (2012): A Qualitative Inquiry of Patient-Reported Outcomes: The Case of Lower Urinary Tract Symptoms			

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11.	Qualitative interview study with 90 respondents (46% female participants, mean age of 59 years) **Objectives:** to explore the value of qualitative methods for understanding and developing patient-reported outcomes in	Respondents were a stratified random sub-sample of an epidemiological survey (Boston Area Community Health [BACH] survey), conducted in the USA. 151 1:1 Semi-structured interviews conducted to explore experiences with urinary symptoms, related beliefs and attitudes, management strategies, and histories of care-seeking in 6 subgroups of Black, Hispanic, or White men and women. Interview guide developed from literature	Interviews were digitally recorded and transcribed verbatim by an external company. Analyses were conducted in ATLAS qualitative analysis software. Inductive "initial coding" undertaken by three analysts to develop a codebook which was revised by consensus	90 participants had spoken to an HCP about their urinary symptoms, of which, compared to Black and Hispanic respondents, White respondents more often saw a urologist, gynaecologist, or other specialist about LUTS. Of those seeking treatment, complete symptom relief was achieved by 14%, partial relief by 39%, and no relief by 47%. The most common reason for no relief of symptoms was not receiving treatment, followed by non-adherence, or non-effective treatment. Non-receipt of treatment was seen as a message that symptoms were not serious or were a normal part of ageing. 4/5 participants reported

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	lower urinary tract symptoms (LUTS)	review and 8 90-minute focus groups composed of 58 participants. Adherence was elicited with: "Did you follow any of the recommendations offered by the doctor for your urinary or pelvic problems?"	between analysts. Focused coding and application of subcodes were undertaken by a single analyst, following which content and thematic analyses was performed.	they fully adhered to recommendations. Of those not adhering to prescribed treatment, reasons included a preference to avoid medications, side effects, and lack of significant symptom improvement. Respondents in this group typically weighed perceived harms and benefits of medicine in relation to their overall health, values, or alternative treatment options.
	Wyman et al. (2010): Contributors to Satisfaction With Combined Drug and Behavioral Therapy for Overactive Bladder in Subjects Dissatisfied With Prior Drug Treatment			

#	Study Design, Participants and Objectives	Methods of Data Collection	Methods of data analysis /Presentation of results	Main Findings
1.	**Benner et al. (2009):** Patient-reported reasons for discontinuing overactive bladder medication			
	Prospective cohort symptom prevalence study. Phase 1: screening survey sent to 260,000 households in USA to identify patients using antimuscarinics for OAB. (Sample was balanced to reflect the USA population in terms of age, sex, geographical region, urban vs rural, household income, household size). Phase 2: follow-up survey with 5392 respondents (78% of participants were female, 14% were under 44, 59% were 45-75, and 27% over 85 years of age) **Objectives**: To evaluate patient-reported reasons for discontinuing antimuscarinic prescription medications for overactive bladder (OAB).	Phase 2 survey included OAB-V8 questionnaire as well as questions on: current and past use of OAB medications including self-reported start and end dates, persistence rates, and reasons for discontinuation for three or fewer OAB treatment regimens. Respondents could write their own reason for discontinuation or select among 14 pre-coded reasons: Advice of family/friend, Another condition/medication, Bladder symptoms stopped/cured, Change of insurance status, Cost/amount of co-pay, Didn't work as expected, Doctor didn't make right treatment decision, Don't like taking ANY medications, Don't like taking medications for too long, Had side-effects, Learned to get by without medication, Switched to new medication, Switched to previous medication, Told to stop by clinician/pharmacist Respondents were also questioned about demographics, comorbid conditions, beliefs about OAB, treatment expectations, healthcare-consulting behaviours, and level of satisfaction with their healthcare providers.	Latent Class Analysis (LCA) statistical method was used to identify natural groupings of respondents based on combinations of their reported reasons for discontinuation. The measurement model was developed using the Lo-Mendell-Rubin likelihood ratio test to determine the number of latent classes. The conditional probability of each reason for discontinuing OAB medication was estimated for each class. Multivariable logistic regression was used to assess the influence of age, sex, race, income, and recent history of incontinence on the most likely class assignment. Results expressed as descriptive statistics.	In all, 1322 phase 2 respondents (24.5%) reported discontinuing one or more antimuscarinic drugs during the 12 months before phase 2. LCA identified two classes based on reasons for discontinuation. Most respondents (89%) reported discontinuing OAB medication primarily due to unmet treatment expectations and/or tolerability; many respondents in this class switched to a new antimuscarinic agent. A smaller group (11%) indicated a general aversion to taking medication. Age, sex, race, income, and history of incontinence were not predictive of class assignment.
12.	Qualitative study seeking to clarify reasons for treatment satisfaction in participants 7-10 months after completing a previous open-label study. Convenience sample of 15 subjects from 5 clinical centres. (87% female, median age of 57 years, range of 23-85 years)	Individual cognitive debriefing interviews using a semi-structured discussion guide.	Content analysis conducted by two independent reviewers to identify and summarise themes, issues, and concerns expressed. Descriptive statistics used to summarise and describe data.	12 out of 15 participants attributed dissatisfaction with prior antimuscarinics to lack of efficacy. Only 7 participants had positive expectations of tolterodine ER treatment, 5 did not expect it to work, and 3 did not know what to expect. Reasons given for satisfaction with combined treatment were improved OAB symptoms, attention of clinic staff, review of educational materials on OAB symptoms and treatment, and keeping a bladder diary. One-third of participants continued to take tolterodine ER for 7 to 10 months after completing the open-

#	Study Design, Participants and Objectives	Methods of Data Collection	Methods of data analysis /Presentation of results	Main Findings
1.	**Benner et al. (2009):** Patient-reported reasons for discontinuing overactive bladder medication			
	Prospective cohort symptom prevalence study. Phase 1: screening survey sent to 260,000 households in USA to identify patients using antimuscarinics for OAB. (Sample was balanced to reflect the USA population in terms of age, sex, geographical region, urban vs rural, household income, household size). Phase 2: follow-up survey with 5392 respondents (78% of participants were female, 14% were under 44, 59% were 45-75, and 27% over 85 years of age) **Objectives**: To evaluate patient-reported reasons for discontinuing antimuscarinic prescription medications for overactive bladder (OAB).	Phase 2 survey included OAB-V8 questionnaire as well as questions on: current and past use of OAB medications including self-reported start and end dates, persistence rates, and reasons for discontinuation for three or fewer OAB treatment regimens. Respondents could write their own reason for discontinuation or select among 14 pre-coded reasons: Advice of family/friend, Another condition/medication, Bladder symptoms stopped/cured, Change of insurance status, Cost/amount of co-pay, Didn't work as expected, Doctor didn't make right treatment decision, Don't like taking ANY medications, Don't like taking medications for too long, Had side-effects, Learned to get by without medication, Switched to new medication, Switched to previous medication, Told to stop by clinician/pharmacist Respondents were also questioned about demographics, comorbid conditions, beliefs about OAB, treatment expectations, healthcare-consulting behaviours, and level of satisfaction with their healthcare providers.	Latent Class Analysis (LCA) statistical method was used to identify natural groupings of respondents based on combinations of their reported reasons for discontinuation. The measurement model was developed using the Lo-Mendell-Rubin likelihood ratio test to determine the number of latent classes. The conditional probability of each reason for discontinuing OAB medication was estimated for each class. Multivariable logistic regression was used to assess the influence of age, sex, race, income, and recent history of incontinence on the most likely class assignment. Results expressed as descriptive statistics.	In all, 1322 phase 2 respondents (24.5%) reported discontinuing one or more antimuscarinic drugs during the 12 months before phase 2. LCA identified two classes based on reasons for discontinuation. Most respondents (89%) reported discontinuing OAB medication primarily due to unmet treatment expectations and/or tolerability; many respondents in this class switched to a new antimuscarinic agent. A smaller group (11%) indicated a general aversion to taking medication. Age, sex, race, income, and history of incontinence were not predictive of class assignment.
	Objectives: To assess contributors to treatment satisfaction subjects from an open-label study who had previously reported dissatisfaction with antimuscarinic treatment for OAB			label study. Among the 15 participants, 5 were still taking tolterodine ER at the time of the cognitive debriefing interviews, which occurred 7 to 10 months after completion of the open-label trial. Four were no longer taking medication, stating that it did not work; 2 had switched to a different medication; 1 had discontinued medication because of dry mouth; and 1 had discontinued because the participant was no longer being reimbursed for expenses.

Table 2.5 summarises the agreed quality assessment designations of yes, partial, or no between reviewers for the various domains in the Garside criteria described above.

Methodological quality of the selected studies

Table 2.5: Quality assessment of included papers (Garside, 2014)

		Clarity		Are the following clearly described?				Trustworthiness					Theoretical considerations			Practical considerations		
	Papers	Is the research question (s) clear?	Is the research question(s) suited to qualitative enquiry?	Context.	Sampling	Data collection	Analysis	Are the design and execution appropriate to the research question?	What evidence of reflexivity is there?	Do the voices of the participants come through?	Are alternative interpretations, theories, etc. explored?	How well supported by the data are any conclusions?	Are ethical considerations given appropriate thought?	Does the report connect to a wider body of knowledge or existing theoretical framework? If so, is this appropriate (e.g., not uncritical	Does the paper develop explanatory concepts for the findings?	Does this study usefully contribute to the policy question?	Does this study provide evidence relevant to the policy setting?	Does this study usefully contribute to the review?
1	Tijnagel et al.	Y	P	P	Y	P	P	P	N	N	P	P	Y	Y	N	P	N	P
2	Jundt et al.	Y	P	Y	Y	P	N	Y	N	N	Y	P	P	Y	Y	P	N	Y
3	Pindoria et al.	P	P	Y	Y	P	N	P	N	N	P	P	N	Y	Y	Y	Y	P
4	Sung et al.	Y	N	Y	P	N	Y	P	N	N	Y	P	Y	Y	Y	N	N	P
5	Lee et al.	Y	P	P	P	P	Y	Y	N	P	Y	Y	Y	Y	P	P	N	Y
6	Maguire et al.	P	Y	P	Y	Y	Y	Y	N	Y	N	P	Y	Y	P	P	P	Y
7	Benner et al.	Y	Y	Y	Y	Y	Y	P	N	P	N	Y	N	Y	N	Y	Y	P
8	Wyman et al.	P	Y	P	Y	Y	Y	Y	N	Y	N	P	P	Y	Y	P	P	P
9	Mei Yee Lai et al.	P	Y	P	N	N	P	N	N	N	N	N	N	N	N	N	N	P
10	Campbell et al.	Y	Y	Y	P	P	P	N	N	N	Y	P	P	Y	Y	P	P	P
11	Filipetto et al.	P	Y	P	P	P	P	Y	N	P	N	P	Y	P	P	Y	P	P
12	Welch et al.	Y	Y	Y	P	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y

Y, yes; P, partially; N, no/none.

Findings and discussion

Extent of qualitative research found

While having applied a quality assessment to the selected papers, a natural next step may have been to delve deeper into the findings and implications of those assessed as having highest quality before considering the overall body of evidence put forth by the collection of papers in this review. However, it is important to note that while the focus of this review was to identify qualitative research into factors affecting patient adherence and persistence behaviours in OAB, there was a shortage of papers exploring this area employing both qualitative data collection and analysis methods.

While the three papers describing themselves as qualitative did employ both qualitative data collection and data analysis methods (Maguire et al., 2016, Welch et al., 2011, Wyman et al., 2010), the majority of identified papers resonated more closely with the quantitative research paradigm whilst hosting "add-on" qualitative features. Principally, these entailed the use of qualitative data collection methods such as interviews or focus groups (Filipetto et al., 2014, Jundt et al., 2011, Mei Yee Lai et al., 2011, Pindoria et al., 2017b, Tijnagel et al., 2017, Wyman et al., 2010), and surveys (Benner et al., 2010, Campbell et al., 2008, Filipetto et al., 2014, Sung et al., 2015a). Such an approach was further evidenced by the language used in describing the objectives of each study, as well as in how the findings were expressed across the sample. In most cases, the stated objectives frequently included words such as 'rates', 'how many', and 'assess', signifying the intention to present results in a numerical fashion, with authors opting to present findings with descriptive statistics such as frequencies, means, Chi-squared tests, t-tests, and Wilcoxon's signed ranked tests (Filipetto et al., 2014, Lee et al., 2014b, Mei Yee Lai et al., 2011, Sung et al., 2015a, Tijnagel et al., 2017), with some featuring more complex statistical analyses such as multivariate regression analyses and latent class analysis (Benner et al., 2010, Campbell et al., 2008, Lee et al., 2014b).

The language used in the three recognisably qualitative papers departed from the above observations, with an emphasis on combination of words such as ‘explore’ (Maguire et al., 2016, Welch et al., 2011) and ‘patient’ or ‘participant experience’ (Wyman et al., 2010, Maguire et al., 2016). Methods employed also followed a similar vein, with the use of semi-structured interviews for data collection and qualitative analysis including grounded theory, content and thematic analysis, and content analysis respectively (Maguire et al., 2016, Welch et al., 2011, Wyman et al., 2010).

When closely examining the Garside criteria used in this review, we can consider that it is comprised of two kinds of elements. Those that assess areas common to quantitative and qualitative research, and those that may be used to distinguish between the two. The earlier elements (where the bulk of papers were more often assessed as yes or partially meeting the quality assessment criteria), relate to how clearly the paper describes the research questions, context, sampling, and data management. These areas offer little distinction between assessing the quality of quantitative and qualitative research, resulting in little differentiation in terms of quality assessment. Conversely, the latter elements assessing the presence of reflexivity, the voice of the participant, and contribution to policy considerations were more suited to allow distinction between papers, which were apparent in Table 2.5. These elements of assessment therefore offered more granularity in terms of the strength of evidence contributed by each paper towards assessing the qualitative research into adherence and persistence behaviour in OAB sufferers.

Notably, while not usually a feature of quantitative work, not even the fully qualitative papers showed evidence of reflexivity. Combined with what may be perceived as an established norm in the social sciences to write in the third person and avoid autobiographic accounts, another possible reason for this may be a reluctance from authors to write themselves into research, borne from the potential for embarrassment and the revelation of their flaws in the public sphere (Smith, 2006). This, combined with the observation that even when authors do place value on providing a reflexive account, word limits set by academic journals can stand in the way of them doing so in any meaningful way (Finlay, 2002).

The degree to which the voice of the participant came through in the papers also differed widely, with the papers by Maguire et al., Wyman et al., and Welch et al. all performing strongly here on account of their unfiltered transmission of the participants voice through the use of direct quotes (Maguire et al., 2016, Welch et al., 2011, Wyman et al., 2010). This had the added benefit of allowing the reader to make their own interpretations from the quotes disclosed. Papers assessed as partially meeting this criterion included Benner et al., who, while stating that participants were free to provide their own reasons for treatment discontinuation, did not clearly distinguish between these and pre-coded reasons, meaning the degree to which the manuscript offered an unaltered voice of the participant was unclear (Benner et al., 2010). While qualitative research is not independent of the researcher (O'Sullivan, 2015), the lack of reflexive analysis compounded this ambiguity meaning the extent to which the paper met the requirement to allow the participant voice to be expressed, was undisclosed.

Although Lee et al. did not use direct quotes from participants, the authors did explicitly recognise the subjectivity of patient experience and made an effort to freely capture reasons for treatment discontinuation without pre-definition or filtration from the authors (Lee et al., 2014b). The Filipetto et al. paper was also assessed as partially allowing the

participant voice through on account of focussing more on reporting the quantitative analysis, and relaying responses from the group as a whole rather than individuals, resulting in the delivery of a participant voice pre synthesised and interpreted by the authors (Filipetto et al., 2014). The remaining papers were all assessed as not allowing the participant voice to come through based on no use of quotes and a reduction of participant responses to numerical and categorical statistics (Campbell et al., 2008, Jundt et al., 2011, Mei Yee Lai et al., 2011, Pindoria et al., 2017b, Sung et al., 2015a, Tijnagel et al., 2017).
The selected papers also varied in how prominently the exploration of adherence and persistence behaviours featured in both the aims and findings sections. There were those where this was stated as part of the central objectives (Benner et al., 2010, Campbell et al., 2008, Filipetto et al., 2014, Jundt et al., 2011, Lee et al., 2014b, Mei Yee Lai et al., 2011, Pindoria et al., 2017b, Sung et al., 2015a, Tijnagel et al., 2017), and others where adherence and persistence were explored in the periphery (Maguire et al., 2016, Welch et al., 2011, Wyman et al., 2010). It is of interest to note that the papers exploring patient medicine-taking behaviours in OAB as a central phenomenon of interest exclusively employed quantitative methods to analyse or describe their findings. This mirrors the observed divergence in focus between clinicians and patients, in that while clinicians have tended to focus on the quantifiable functional impact of OAB symptoms, patients have shown more of a concern with the subjective experiences of OAB such as the ability to cope with and manage the condition (DuBeau et al., 1998). Within the context of OAB where patient adherence and persistence with oral pharmacotherapy has been shown to be poor (Dhaliwal and Wagg, 2016, Yeowell et al., 2018b, Yeaw et al., 2009), a qualitative approach to understand the drivers of medicine-taking behaviours and an exploration of these subjective experiences would therefore be valuable. Taking such an approach may allow the

expansion from quantifying patterns of behaviour to producing a more in-depth exploration of the human experiencing driving non-adherent behaviours such as those falling within the domains of key conceptual models of adherence, including COM-B and the NCF (as discussed in Chapter 1). Such an exploration may therefore pave the way to overcoming identified barriers to adherence through behaviour change theory in future works.

Within this review, however, all three papers describing qualitative approaches to both data collection and analysis, were examples of where patient medicine-taking behaviours were explored peripherally. In the Maguire paper adherence and persistence were captured as an aside from the main objectives of the study which were broad, and aimed to capture the experiences and expectations of patients after treatment with onabotulinum toxin A (Maguire et al., 2016). A similar observation was made with the Wyman paper, where, although reasons for patient non-adherence to OAB medication were discussed, the focus of the study was on overall treatment experience, rather than linking this to medication-taking behaviours (Wyman et al., 2010). The Welch paper aimed principally to explore the value of qualitative methods in developing patient reported outcome (PRO) tools. As such, while adherence behaviours were elicited from participants, this was not a prime focus of the study.

Consequently, while all the selected papers satisfied the inclusion requirements of the current review, their contributions to summarising qualitatively derived findings of adherence and persistence in OAB patients taking oral medication were limited due to their tangential exploration of these topics. This review did however highlight the lack of qualitative work centred on exploring the drivers of patient adherence and persistence behaviours in OAB patients taking oral medication, and as such, paved the way for such a study to be performed.

Reasons for non-adherence or persistence

The Jundt paper was the only one to explore pre-treatment reasons why patients did not even start their OAB medication, and found that the main reason for not trying was a fear of side effects and patients not wanting to take tablets (Jundt et al., 2011). Indeed, the patient's attitude to long-term medication and an aversion to tablet taking was identified as a contributing reason in other papers in this sample (Benner et al., 2010, Maguire et al., 2016, Pindoria et al., 2017b, Welch et al., 2011).

All 12 papers in this review identified the presence of treatment-emergent side effects as a leading reason for patients to discontinue their OAB medications. The papers by Tijnagel and Lee respectively specified patient-reported side effects included dry mouth, constipation, blurred vision, dry eyes, and abdominal pain (Lee et al., 2014b, Tijnagel et al., 2017). This list was expanded upon by Pindoria et al. (whose paper included antimuscarinics as well as mirabegron) with the addition of neurological effects including drowsiness, headache, trigeminal neuralgia, as well as vomiting and palpitations (Pindoria et al., 2017b). A participant in the Maguire paper was quoted as saying she "just couldn't use" the treatment "at all" having experienced "no saliva", a resultant inability to eat, and problems in wearing contact lenses on account of dry eyes (Maguire et al., 2016 pg. 71). Other participants added side effects including getting "very depressed", a "dry, crusty nose", an "asthma type dry cough", heartburn, diarrhoea, and voice changes, going on to describe feeling "unwell and emotionally unwell. That was the oxybutynin", and the observation that "the side effects put me off" (Maguire et al., 2016 pg. 71). These observations are in congruence with published literature on the central and peripheral effects of antimuscarinics commonly used to treat OAB, as driven by their affinity for various types of muscarinic receptors in the brain and body, as well as their and ability to cross the blood-brain barrier (Chancellor et al., 2012). Furthermore, the direct attribution of adverse effects to the treatment, as well as weighing up the negative effects of continuing, offered some support for the NCF, while the acknowledgment of the impact of adverse effects on the individual's motivation to continue treatment highlighted the reflective motivation as described by the COM-B model outlined above.

Many of the papers linked patient discontinuation to a lack of treatment effectiveness (Campbell et al., 2008, Filipetto et al., 2014, Lee et al., 2014b, Maguire et al., 2016, Pindoria et al., 2017b, Sung et al., 2015a, Tijnagel et al., 2017, Welch et al., 2011, Wyman et al., 2010), and unmet treatment expectations (Benner et al., 2010, Pindoria et al., 2017b). In recognising the role that treatment expectations play in gauging their perceived effectiveness, several papers pointed out the role of prescribers and HCPs in potentially improving medicine-taking behaviour by having frank discussions with patients regarding treatment efficacy, and fostering realistic treatment expectations (Benner et al., 2010, Pindoria et al., 2017b).

Indeed, the relationship between treatment expectations and adherence is a complex one, with some evidence suggesting expectations may be predictive of adherence where patients may continue to adhere *because* they have strong expectations from treatment (high expectations promote high adherence). Conversely, adherence has been described as being predictive of expectations, where the act of adhering in itself may produce stronger expectations from it (i.e. high adherence promoting high expectations) (Stetler, 2014). Within this review, however, while some papers did describe patients' medicine-taking behaviours in the context of their treatment expectations, this relationship was inversed, in that when expectations were not met, patients discontinued their medication (as opposed to high expectations driving adherence). Such findings also echo the reflective motivation domain of the COM-B model, as well as the NCF in that treatment expectations would invariably inform the perceived necessity of taking treatment, as it follows reason that a treatment perceived to be ineffective would not likely be perceived as highly necessary. This may also heighten the relative impact of potential concerns such as adverse events on medicine-taking behaviour.

While reflecting on this difference, it may be important to consider several linked issues:

- the context of symptoms and other subjective factors influencing and changing treatment expectations,
- over what timeframe these expectations are forged and held (and measured),
- at what point unmet expectations lead to behaviour change, and
- temporally, how this relates to the pharmacology of the treatment in question.

Indeed, related to the latter point, Pindoria et al. found that almost a fifth of patients discontinued their therapy within a month of having started, due to a perceived lack of efficacy. However, the authors went on to state that the optimal time to therapeutic efficacy of the treatment being used was 28 days, meaning that some patients were prematurely terminating treatment not only due to incongruence between expected and true level of efficacy, but also in the expected time taken to reach such efficacy. Despite briefly touching upon reasons for discontinuing medication, the Pindoria et al. paper focussed more on providing an evaluation of persistence rates and to identify rather than explore determinants of treatment discontinuation, thus meaning that these important questions remained unexplored in the context of OAB (Pindoria et al., 2017b).

Perhaps surprisingly in light of the observations made above, several papers found that a significant number of patients stopped taking their OAB medication because of symptoms resolving (Jundt et al., 2011, Sung et al., 2015a, Benner et al., 2010, Lee et al., 2014b). The Jundt paper, (which reported symptom resolution as a reason for treatment discontinuation in 27% of patients) did go on to postulate other reasons for this observation. The authors suggested that perhaps the OAB-like symptoms in these patients were due to time-limited causes such as urinary tract infections of vaginal dryness which were self-limiting, or that the improvements were induced by behavioural changes (Jundt et al., 2011). In another study with similar findings, 35.9% of participants cited the resolution of symptoms as a reason for discontinuing OAB treatment. Being composed of largely treatment naïve patients with relatively mild OAB symptoms, the authors highlighted the composition of the sample as a possible reason for this observation, while reiterating the progressive, chronic nature of OAB was naturally interspersed with periods of remission (Krhut et al., 2014a). Other identified factors affecting adherence and persistence within this review included contraindications to treatment and other health conditions (Benner et al., 2010, Lee et al., 2014b, Pindoria et al., 2017b), prohibitive costs (Benner et al., 2010, Pindoria et al., 2017b, Tijnagel et al., 2017) (including to patients as well as to the system), and recommendations from HCPs as well as family and friends to discontinue (Benner et al., 2010).

Limitations

There were several limitations of performing a systematic literature review purely in the search for qualitative literature, as have been mentioned elsewhere in the literature (Booth, 2016). Of these, the most notable challenges within this body of work lay in the limited degree of indexing of qualitative research in databases compared to quantitative research. This was possibly borne from the variety of methodologies encompassed within qualitative research, as well as the interplay between qualitative and quantitative approaches in mixed-methods research (as many of the papers in the current review were). Furthermore, there was little granularity and nuance found in the data collection and analysis methods used in many of the studies, and exactly how the qualitative methods employed were used in the ultimate findings. This was especially true of abstracts, requiring the exploration of full paper in order to best understand if the inclusion/exclusion criteria had been met. Furthermore, limiting the searches to those in the English language albeit as a consequence of resource constraints, was another limitation of the present work.

Conclusion

Several important observations emerged from this review. Of these, the frequently mentioned areas of treatment-related side-effects and lack of treatment effectiveness, in relation to treatment expectations may offer useful foci for prescribers and HCPs in the provision of their services. Such individuals are ideally placed to inform and help manage the expectations patients have of both the positive and negative effects of their treatments, as well as to advise on the best ways of overcoming medication-related barriers to adherence and persistence.

This review was comprehensive, originally expected to yield much more published work in this area, to be collated and to reveal possible areas to expand upon with future work. A major limitation of work in this area was undoubtedly the scarcity of qualitative evidence to review in order to enable a thorough and deep exploration of adherence and persistence behaviours with OAB medication. Overall, this review revealed a dearth of qualitatively generated evidence exploring factors affecting adherence and persistence behaviours with OAB medication, and a complete absence of studies prioritising the focussed exploration of this area using purely qualitative methods.

In uncovering such a gap in the research and in highlighting the evidence that does exist in this sphere, this review provides a depiction of the current landscape of knowledge in this area whilst offering a clear path forward to expand upon it by the conduction of a purely qualitative study to explore the drivers of adherence and persistence behaviours in the OAB population.

Update to SLR

In light of the original SLR having been done at the beginning of the research journey, and with a view of providing the reader with as full a picture of the current landscape of qualitative research in OAB medicine-taking behaviours as possible, the original searches were re-run in May 2021, the results, and implications for which are detailed below.

Methods

The search strategies were re-run on the same five databases as described above on 19th May 2021. The new searches were limited to papers published between January 1st, 2018 and May 19th, 2021 to bring the literature review up to date. All other methods followed were aligned to those described above.

Results

A total of 379 records were found in the databases searched. Screening was performed by two researchers (MA and JH) independently with full agreement reached on papers to retain at abstract and full-text screening stages. After removing duplicates, 277 titles were screened from which 29 abstracts were selected for retrieval and screening. Of these, a further 22 papers were excluded, leaving 7 full papers to be reviewed, ultimately resulting in only 1 paper to include within the present review. No further relevant articles were found when searching Research Gate and institutional websites of authors in selected papers.

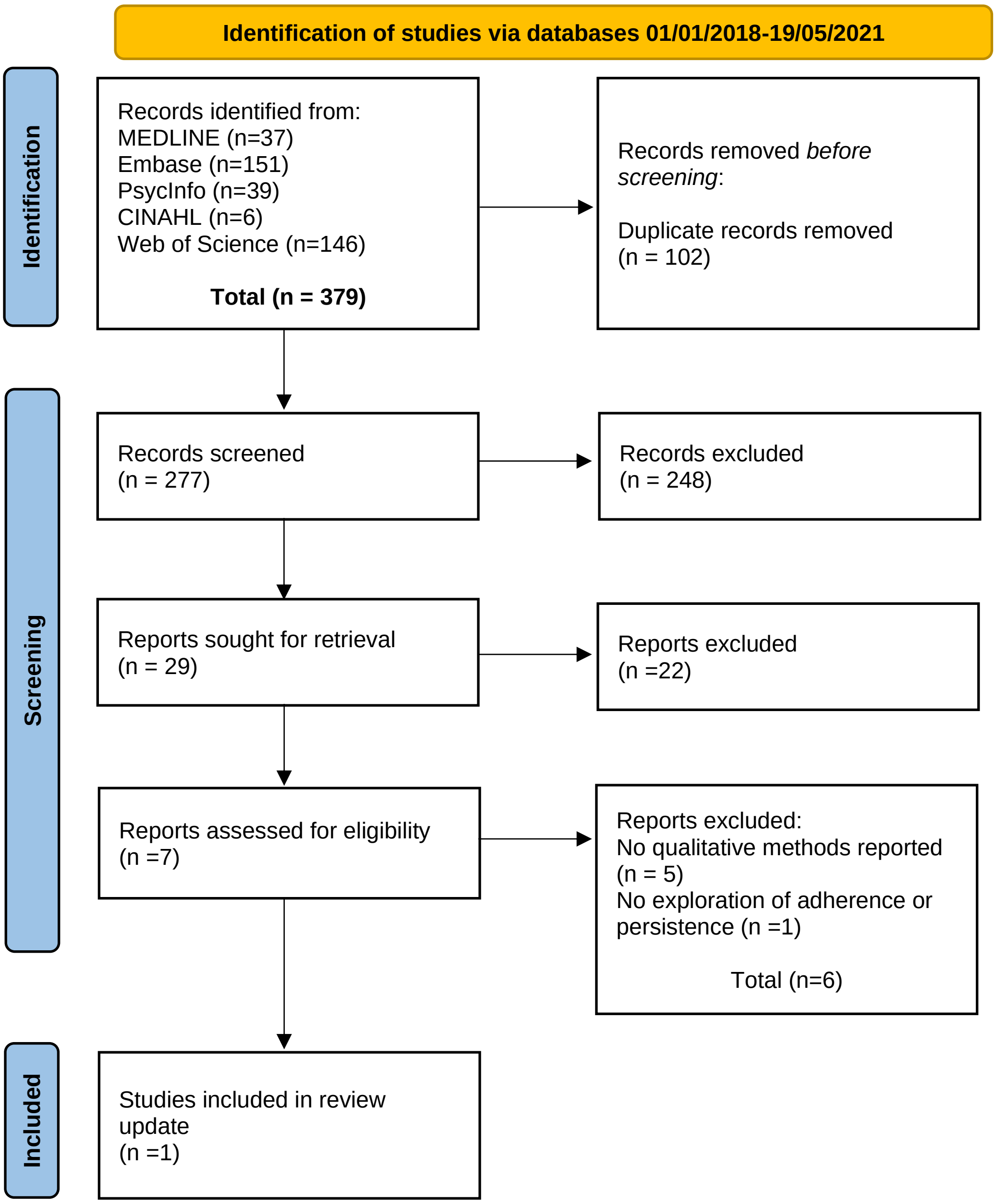


Figure 2.3: PRISMA flow diagram 2018-2021

The one paper selected for inclusion within this review between 2018 and present, was the paper entitled “Qualitative Analysis of Factors Influencing Patient Persistence and Adherence to Prescribed Overactive Bladder Medication in UK Primary Care”. This paper resulted from the original work discussed elsewhere within this thesis, and as such will not be subject to further comment here. A copy of the published manuscript can be found in Appendix B5: OAB study published manuscript.

Chapter Summary

The present chapter has described a systematic literature review undertaken to identify qualitative works exploring adherence and persistence behaviours in OAB. Searches in five databases were ran from 1987, resulting in a total of 1,315 papers identified. Of these, and after having removed duplicates, 971 papers were screened resulting in the review of 34 full papers, ultimately resulting in 12 papers included within the current review. Of these, while 9 of the 12 papers described some form of qualitative data collection, results were reduced to quantitative analysis and description. Only 3 papers employed both qualitative data collection and data analysis methods, however, medicine-taking behaviours were only tangentially explored therein. As such, the present chapter demonstrated a gap in the literature for a wholly qualitative study exploring adherence and persistence in OAB patients.

The next chapter will provide the reader with a description of the methodology used in this thesis.

Chapter 3 - Methodology

Introduction

The purpose of the current chapter is to provide the reader with a thorough grounding in the organisational, philosophical, and methodological backdrop to this thesis. As this chapter encompasses procedural as well as biographical milestones in the development of the present body of work, two ‘voices’ will be employed. The first, already familiar to the reader is a detached, scientifically ‘objective’ voice expressed in third person to relate to methodological and factual subjects contained herein. The second voice will be a first-person one where I discuss my own experiences leading and shaping this research. The two voices will at times be used in tandem to grapple with the philosophical background of this research underpinned by my personal views.

Furthermore, throughout the thesis, a distinction is made between the terms “patient”, “participant” and “people”, and it is useful here to distinguish between these, and which descriptor is given primacy when referring to both within and between individuals. The term “participant” is used to refer to individuals who took part in the OAB interview study within this thesis, namely individuals who engaged in any step of the research as those with whom the subject of interest was explored directly. In contrast, the term “patient” has been used to describe individuals within their role as those under the medical care of a HCP or the National Health Service (NHS). In the OAB study where individuals were identified and recruited through the NHS, they have been described within this thesis as patients to reflect this role during the recruitment process. Upon agreeing to take part in the study, these individuals were referred to as participants in keeping with the definition outlined above.

Finally, the term “people” was used to refer to individuals in a general sense, specifically not fitting into the definitions of patients or participants described above.

The present chapter will commence by outlining the philosophical stance underpinning the work within this thesis, exploring ontological, epistemological, and reflexive matters before providing the reader with an overview of the methods employed. Within this description, the reader will be provided with the organisational context for a part of the work within this thesis, before the ethical and governance processes followed are outlined. Finally, there will be an overview of the data collection and analysis methods used within this thesis.

Epistemological and ontological perspective / philosophical basis

While quantitative researchers rarely reveal the theoretical underpinnings of their approach, such delineation is important in qualitative research where the distance between researcher and researched is bridged, subjectivity is seen as inevitable, and the researcher is recognised as an integral instrument in the intersubjective production of knowledge and understanding (Morrow and Smith, 2000). Furthermore, as the influence of history and context are interwoven into qualitative research and because the belief systems of the researcher (assumptions and world views, also referred to as ‘paradigms’) can influence data collection, analysis, and appraisal of qualitative work, explicitly addressing such underpinnings are an indispensable part of qualitative research (Morrow and Smith, 2000, Davidsen, 2013).

Ontological perspectives

Ontology is the study of the nature of reality or existence, and what there is to know about it. Under the overarching positions of **realism** and **relativism**, central ontological questions include whether reality exists independently of human conception and interpretation, and if there exists a shared social reality, or multiple realities specific to unique contexts (Ormston et al., 2014). Realists view the world as being organised in pre-existing categories, driven by absolute natural laws and mechanisms, with reality existing independently of human interpretation of it. Research is considered to be able to uncover this apprehendable objective reality (Guba and Lincoln, 1994). In contrast, idealists posit that reality is only able to be known through the human mind and socially constructed meanings and that without these, there is no existence of reality (Neuman, 2007, Ormston et al., 2014).

Between these divergent perspectives lie a range of nuanced views including:

- subtle realism (where an external reality is acknowledged while only being known through the human mind and social construction),
- depth realism (where reality is believed to consist of various levels, distinguished between those experienced by humans, those that exist regardless of human observation, and underlying processes)
- subtle idealism (where the social world is considered to be constructed by individuals sharing their representations under particular circumstances), and
- relativism (where there exists only a collection of individual constructions of reality and no shared social reality) (Ormston et al., 2014).

Critical realist ontology suggests that reality exists independently and irrespective of its comprehensibility to the human mind. In contrast to realism, critical realists believe that reality cannot in its entirety be comprehended, with only glimpses or partial fragments of its totality accessible to the human mind. Taking a critical stance towards causation, critical realists combine explanation with interpretation to identify and describe whole phenomena from the available glimpses of such fragments. Furthermore, critical realism postulates only the results of causal forces are observable (as opposed to the causal forces of phenomena themselves), meaning truth cannot be reached purely by observation and must be achieved with reasoning (Levers, 2013, Archer, 2016).

Epistemological perspectives

Epistemology has been defined as "*a way of understanding and explaining how we know what we know*" (Crotty, 1998 pg.3), and is distinguished from theoretical perspectives, methodologies and methods, which together form the four elements of a research process (Figure 3.1). Epistemology aims to answer questions concerning what knowledge is and how it is acquired (Killam, 2013, Brown and Dueñas, 2020).

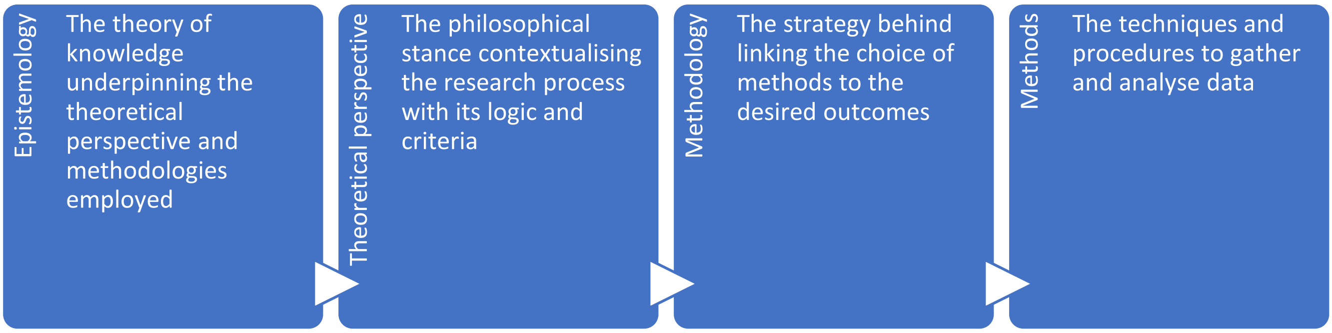


Figure 3.1: the four elements of research (adapted from (Crotty, 1998 figure 1 pg.4))

There are four main epistemological paradigms: **positivism, post-positivism, constructivism and critical theory**, supplemented by various combinations (Kovács et al., 2019). Positivist epistemology posits a direct relationship between external events and objects and human perception and knowledge of them. It suggests the existence of a single objective reality and uses mainly quantitative methods to produce impartial and unbiased knowledge, devoid of any personal influence from the researcher, and thus is considered a cornerstone of the quantitative research paradigm. A positivist approach to research emphasises how knowledge is attained, stipulating it to be objective, empirical, and scientific. The extent to which our understanding of the world can be considered an objective knowledge or truth is reflected under various other approaches ranging from naïve realism (which although rare, reflects the description of positivism above), to extreme relativism, where notions of knowledge or truth are rejected altogether, to critical realism and social constructionism in between these extremes (Willig, 2013, Kovács et al., 2019, Ryan, 2006).

Post-positivism posits the existence of a single, albeit imperfectly understood reality, while offering a more interpretative approach to research than the positivist stance, emphasising the seeking of meaning beyond the aggregation of data. Post-positivism suggests that human intellect is unable to fully capture reality, and that the role of the researcher of one who learns through conducting research among other people as opposed to one who tests by conducting research on people (as in positivism). There is an emphasis on theory falsification rather than theory verification. Both positivism and post-positivism share the central goal of explaining phenomena to predict and control, emphasising the establishment of cause-and-effect relationships through research where the researcher is detached from the phenomena under investigation (Ryan, 2006, Kovács et al., 2019, Ponterotto, 2005).

The constructionist or interpretivist view suggests that reality is individually constructed, leading to multiple apprehendable and equally valid realities, diminishing the conventional distinction between ontology and epistemology. A central tenet of this view is that objective reality cannot be separated from the subjective experience, social context, processing and labelling of that reality by the subject, leading meaning to be considered hidden and must therefore be discovered through deep reflection, an action facilitated by the interaction between researcher and participant. Indeed, under this perspective, the relationship between researcher and the participant is central. Constructivists argue that the interaction between them co-creates knowledge (Ponterotto, 2005, Guba and Lincoln, 1994).

There is no single form of critical theory, with the original proponents themselves having not developed a single, unified theory. However, a central tenet of critical theory is the influence of social and historical contexts and "*power relations*" upon the construction of thoughts and lived experiences (Ponterotto, 2005 pg 130). Furthermore, a critical theorist is one whose work takes a critical view of culture or society, aiming to use dialectic interactions between researcher and participant to empower participants to stimulate social change and the liberation of oppressed groups within society. Like the constructionist stance, critical theory puts the researcher-participant relationship at the centre of scientific enquiry. They argue that findings are therefore laden with the values of both the researcher and participant. This perspective similarly blurs the line between ontology and epistemology as it states that the nature of what can be known is intertwined with the specific researcher interacting with a specific participant(s) (Ponterotto, 2005, Guba and Lincoln, 1994).

My philosophical and theoretical perspective

In arriving at a description of my own ontological and epistemological perspective, I was compelled to reflect both upon my views, as well as my personal journey in forming them. The notion of reality existing independently and irrespective of it being comprehended by the human mind resonates with my experiences as a student of physical sciences and as a registered pharmacist, as well as with my personal theological beliefs about the nature of the universe. I believe that there is a 'real' reality out there for us to attempt to observe, comprehend and explain, but that ultimately, there are facets of this reality that are out of the scope of our conscious understanding. Our ever-evolving understanding of the reality around us is built by the continual connection of the smallest fragments of knowledge collected over time, of which I consider the present work to be very much a particle of. It is therefore in the critical realist perspective that I find a description of my reflections on the nature of reality.

I believe we all view, learn, and understand the world through our own prisms, shaped in part by extrinsic factors such as social norms and culture, but also by the choices we make and our experiences, as well as our genetic and familial predispositions. It is the interplay between all these factors (and possibly others beyond our current understanding) that shape the way we construct individual representations of reality in our minds, to grasp the world around us and conceptualise what we see. The nature of these prisms seems fluid to me as people can, and do change their approach to understanding and explaining the "reality" around them. For this reason, I do not believe an epistemological perspective is something entirely fixed, but something that may adapt and flex over time and in response to new stimuli and circumstances (albeit to varying degrees both within, and between individuals over time).

To my mind, as the "*understanding and explaining how we know what we know*" (Crotty, 1998 pg.3) is governed by such a complex web of influences, there is a degree of subjectivity in even the most objective observations, thus echoing the words of Frazer and Lacey who stated *"our knowledge of the real world is inevitably interpretive and provisional rather than straightforwardly representational"* (Frazer and Lacey, 1993 pg.182, Maxwell, 2012).

Reflexive Analysis

Reflexivity has been defined as *"the process of a continual internal dialogue and critical self-evaluation of researcher's positionality as well as active acknowledgement and explicit recognition that this position may affect the research process and outcome"* (Berger, 2015 pg.220). Put shortly, it is the self-appraisal process in research (Berger, 2015), and has been recognised as a central, or even defining part of qualitative research, aiming to explicitly lay out the role of the researcher in the co-creation of knowledge (Finlay, 2002). While the practice of reflexivity has been widely accepted by qualitative researchers, the question of how to perform such an analysis has been the subject of debate between researchers across the theoretical spectrum (Finlay and Gough, 2008). While reflexivity may be conceptualised as existing on a continuum (Lazard and McAvoy, 2020), several typologies have been suggested in the literature including that by Wilkinson et al. (1998), who distinguished between subjective, functional and disciplinary reflexivity, Lynch et al. (2000) who offered six subsets of reflexivity, and Willig et al. (2001) who delineated epistemological and personal reflexivity (Gubrium et al., 2012). Considered to be a definitive work in this field (Lear et al., 2018), the five variants of reflexivity presented by Finlay et al. have been explored in their book entitled ‘A practical guide for researchers in health and social sciences’, and have been summarised below (Finlay and Gough, 2008).

Finlay’s five variants of reflexivity

Introspective reflexivity

Stemming from an appreciation of self-dialogue and discovery, researchers undertaking introspective reflexivity use their own experiences as a primary basis for forging a psychological understanding of their subject of choice. Examples given by Finlay and Gough, (2008) included that of Moustakas (1990) whose phenomenological work on loneliness was shaped by his personal experiences of isolation when faced with a critical and urgent decision regarding the health of his daughter. One of the challenges with introspective reflexivity, however, is striking the right balance between reflections on the personal experiences of the researcher and those being shared by the participant, ensuring that personal revelation is not itself made the aim of reflexivity, *“but as a springboard for interpretations and more general insight”* (Finlay, 2002 pg.215).

Intersubjective reflection

The intersubjective approach to reflexivity explores the mutual meanings that emerge from the research relationship, concentrating on the nature of the research encounter, predicated on the structure of the researcher-participant relationship itself (Finlay and Gough, 2008). Under the present approach, the conscious reflection of the self in relation to others is both the aim and object of focus (Finlay, 2002). Examples shared by Finlay and Gough included one where the researcher explored the origins of rapport and kinship experienced with a particular participant, finding that shared familial experiences, social class and educational similarities enabled the researcher to be a "better, more informed listener", describing the interaction as enjoyable, and liking the participant because they had things in common (Hollway, 2012 pg.61). The researcher went on to describe the possible implications of such a personal resonance may also have led him to project his own past experiences and emotions on the account given by the participant (Hollway, 2012). Other examples highlighting the intersubjective approach to reflexivity characterise the strong sense of identification between the researcher and participant, and the influence of this on the data collection, analysis and reporting processes, noting the effect on the questions asked, answers heard, and materials observed (Finlay and Gough, 2008).

Mutual collaboration

Used in a wide array of research methodologies linked by their aim to recruit participants as co-researchers and vice versa, reflexivity as a mutual collaboration is predicated on the principle that research participants also hold the capacity to be reflexive, and such reflexive dialogue can be captured as part of the research process. Co-operative research, however, takes this a step further with researchers engaging within their research as participants, undergoing cycles of mutual reflection and experience. Such approaches enable the researcher to take multiple reflections into consideration, allowing the various voices in a research area as well as their agendas to be heard and considered within the context of the research activity itself as well as its outcomes. Critics however, maintain that while such an approach posits removing imbalances in the expression of conflicting voices within qualitative research, it instead merely masks existing imbalances (Finlay and Gough, 2008). Furthermore, such approaches may not be appropriate for all research contexts and individuals may not be comfortable being co-researchers in environments such as focus groups (Takhar-Lail, 2014).

Social critique

Building on the balance between the researcher and participant voices in the research process, reflexivity as social critique is concerned with the power imbalance between the participant and the researcher, borne from perceived differences in class, gender, race, and social position (Finlay, 2002). Reflexivity allows the deconstruction of the authority and distance between researcher and participant, and thereby counters the objectification of those who are being studied (Finlay and Gough, 2008, Wasserfall, 1997).

Within the social critique approach, experiences within research are used to explore the social construction of power, allowing the characterisation of multiple power balances between the researcher and various participants. However, similarly to criticisms faced by the mutual collaboration approach masking persisting imbalances, a high prioritisation of equalising the power between participant and researcher may detract from more vital issues highlighted by participants and may, contrarily strengthen the power imbalance (Finlay, 2002).

Ironic deconstruction

With some parallels with the preceding two approaches to reflexivity, the ironic deconstruction approach considers there to be a multitude of voices in the world with none more or less important than another. Within this approach, the role of the researcher is to challenge and dispel any notion of comparative importance, thereby allowing all voices to be heard. A special emphasis is placed upon the ambiguity of language and its role in how individuals present themselves (both within the researcher-participant dynamic as well as to the wider community; Finlay and Gough, 2008). Instead of conceptualising language as representing reality, researchers adopting this approach to reflexivity view language as conveying social and historical constructs, each with their own set of values and beliefs, and counter this by challenging the representativeness of language to reality, and championing its more careful use (Bager-Charleson, 2014).

My reflexive analysis

Following Willig's (2013) taxonomy of reflexivity (described above), an account of my epistemological reflexivity has been given earlier in this chapter (see "my philosophical and theoretical perspective"). In recognising the importance of performing a reflexive appraisal to strengthen the quality, credibility, and interpretation of the present work, and in line with the introspective approach to reflexivity outlined above, within the present section, I will endeavour to outline my personal reflexivity. This will entail an exploration of my own background in the context of the present research and acknowledgment of preconceptions that may have influenced it here, with further reflexive analyses provided in the relevant chapters below.

Before embarking on this research journey, I practised as a community pharmacist for over five years in various settings, encountering a range of patients, conditions, and treatments. I regularly performed medication reviews, advised patients and clinicians on treatments, their interactions and adverse effects, and counselled patients and carers on the correct use of medicines and devices in my practice. Given my background, I approached the present body of work with some prior knowledge and experience of long-term conditions, their treatments, and the patient experiences of both, as well as the relationships and interplay between these factors, patients, and various HCPs.

Being closely involved in the ordering, dispensing, and supply of medication for my patients, I had grown to be cognisant of their adherence behaviours, and more specifically how to identify non-adherence. This was of particular importance to me, given the early establishment of a strong link between adherence and outcomes during my undergraduate studies, which included a heavy emphasis on pharmacological mechanisms of action and therapeutic dosing. Such identification of non-adherence manifested itself in various ways in my day-to-day practice, from noticing a change in the frequency of medication being ordered, to logging uncollected prescriptions or returned expired medications, to more interventional discussions with patients during informal interactions or formal medication reviews.

While I have always been conscious of the individuality of people, and mindful of the personalised nature of peoples’ experiences and therefore how any intervention should be considered and communicated from a clinical sense, after having made contact with thousands of patients over the years, I do recognise the formation and evolution of mental models of perceived ‘correctness’ in the way I feel patients, prescribers and other organisations and representatives should behave in the acts of seeking, prescribing and dispensing advice, medication, and counselling. While my work as a pharmacist called on individualising my responses to the patient and making an effort to understand the drivers of their behaviours and health outcomes, it is important to note the role these preconceptions undoubtedly held, either as an unconscious starting point from which to adapt my perceptions and responses to the patient facing me, or an implicitly perceived desired output for the work I was doing. I also recognise that this has extended to an internalised model of how patients ‘should’ take their medications, both from the perspective of a HCP holding knowledge on how medications work ‘best’, as well as an internalised judgement on how patients ‘ought’ to take ownership in behaving in a manner in consonance with their own health-interests.

However, while such mental models invariably played a part in my professional practice as a HCP where I identified myself as having a direct responsibility to uphold and support adherence behaviours for the benefit of my patients, my present role as a researcher obligated no such responsibilities. As such, I took a consciously distinct approach to my research activities, where given the focus on exploring individually reported influences on adherence and persistence, I gave primacy to exploring and understanding the context within which such behaviours occurred as opposed to the behaviours themselves and their health implications (as was the demand in my previous role). Indeed, such a distinction was also an extension of my primary duty as a HCP to first understand the individuals under my care and the context of their healthcare decisions *before* taking on an advisory role in supporting any appropriate ‘corrections’ in line with my normative position on medicine-taking. Such an approach allowed me to explore the experience of individuals in the OAB study (Chapter 4), without my views of the ‘correctness’ of their behaviour consciously colouring my analysis of the drivers and barriers to their medicine-taking. However, my knowledge and experience of external factors such as the prescribing, dispensing, and review processes, the healthcare system itself, and the wider social context are likely to have influenced my interpretation of these components within this thesis. I have endeavoured to make such influences clear in my reflexive analysis here and throughout this thesis where appropriate.

In addition, while I believe that I entered the research process with a consciously open mind, some of the drivers of non-adherence such as adverse events and forgetfulness were ones I had experienced in my practice and were therefore an expected output of this work for me. Furthermore, while OAB itself was not a long-term condition I had particularly in-depth experience of in practice, other long-term conditions and comorbidities within this thesis such as asthma, eczema, and diabetes (see Chapter 5) were ones I have seen in daily practice and were therefore much more familiar to me, possibly bringing more of my presumptions to the fore. The role of an independent research assistant conducting the interviews in the OAB study did offer some mitigation against the effects of these potential biases on data collection and analysis, strengthened by the inclusion of her reflexive account (see Appendix B4: Interviewer reflexive exercise, and Chapter 4: Interviewer reflections).

Methodology

While the methodology of the systematic literature review has been described within Chapter 2, within the present section of the chapter, I will outline the background and rationale for the specific methods employed for the main study within this thesis involving 1:1 interviews with individuals with OAB, as well as describe the approach taken for the comparative analysis described in Chapter 5.

Methods for OAB study (Chapter 4)

Ethical considerations and governance

The OAB study was designed following the principles outlined in the British Psychology Society (BPS) Code of Human Research Ethics (Oates et al., 2021). As described within these guidelines, participants were treated with respect at all times; informed consent was achieved through the provision of information at various stages of their involvement, and the voluntary nature of their participation and withdrawal were reiterated to them. Participants were offered information on the nature and aims of the research before their engagement, at the pre-interviews as well as the interviews themselves, and were debriefed at the end of each interview and signposted to further support and information.

Before study commencement, ethical approval was granted by Manchester Metropolitan University (MMU). In addition to this, given its use of NHS infrastructure in identifying patients, the OAB study entailed seeking external approval from the Health Research Authority (HRA) through the integrated research application system (IRAS) and Research Ethics Committee (REC) review.

Furthermore, as the OAB study was conducted under a specific organisational backdrop, there were additional governance steps en-route to the approval and execution of the study. It is appropriate, therefore, to briefly outline the context of this backdrop here before giving an overview of the additional governance steps and their significance in the present body of work.

Organisational background: Knowledge Transfer Partnership

Knowledge Transfer Partnership (KTP) is a UK-wide, partially government-funded program that has been running for over 45 years, helping businesses improve competitiveness and productivity through improved use of knowledge and technology from the UK Knowledge

Base. Each KTP is a three-way partnership between industry and academia, linked together by an associate. The associate is most usually a post-graduate in a relevant field and works to enable the industry partner to bring in the latest skills and academic thinking to deliver a strategic and innovative project within the company (Gov.UK, 2017, Innovate, 2017, KTP-UK.org, 2021).

During the inception, design, and execution of the OAB study, I was employed as a KTP associate between MMU and Astellas Pharmaceuticals Europe Ltd (APEL), based at APEL's European headquarters in Chertsey. Launched in 2005, through the merging of Japan's third and fifth largest pharmaceutical companies, Astellas Pharmaceuticals has rapidly grown to become a global pharmaceutical organisation with regional hubs in Japan, Asia and Oceania, the Americas, and Europe, operating in more than 50 countries worldwide (Astellas, 2017).

As part of delivering on a broader strategic project within APEL, I led the design, management, execution, and reporting of a qualitative study in OAB and a quantitative study in Lower Urinary Tract Symptoms.

Context within Astellas

I began my tenure as a KTP associate at a time when Astellas was experiencing a large degree of organisational flux, with internal processes constantly being developed to cope with more diverse activities across growing jurisdictions. The pharmaceutical industry regulating bodies were also becoming more active, and there were growing examples of reputational issues in particular having severe impacts on revenue, loss of brand value and regulatory investigations across the pharmaceutical industry (Potluri, 2016).

Astellas itself had recently experienced a period of significant challenges relating to research and patient engagement practices, leading to multiple audits from the Prescription Medicines Code of Practice Authority (PMCPA) and an extended suspension from membership of the Association of the British Pharmaceutical Industry (ABPI), leading to a marked shift in culture within the organisation, with extremely high sensitivity around any patient engagement activity (ABPI, 2018).

As part of a broad goal of introducing qualitative research to Astellas, and equipping the organisation with the tools to design, orchestrate and assess such studies, the OAB study was met with exceptional levels of attention, caution, and hesitation from all levels of the organisation. It also faced extra inspection and extended delays whilst being taken through eight distinct levels of Astellas governance process (outlined below), before being allowed to go through to MMU ethics, and external approval.

Internal and External Governance Processes for OAB study

Within Astellas, these levels of governance included the steering group, the Protocol Review Committee (PRC), the Core Medical Team (CMT), the Medical Affairs Committee (MA-C), and the Medical Affairs Protocol-Approval Committee (MA-PAC) as presented in Figure 3.2 below. These bodies represented a range of cross-functional and cross-organisational individuals from various disciplines including academia, medical, health economics and outcomes research, pharmacovigilance, and compliance, and ensured scientific integrity and rigour through robust scrutiny of study synopsis and protocol.

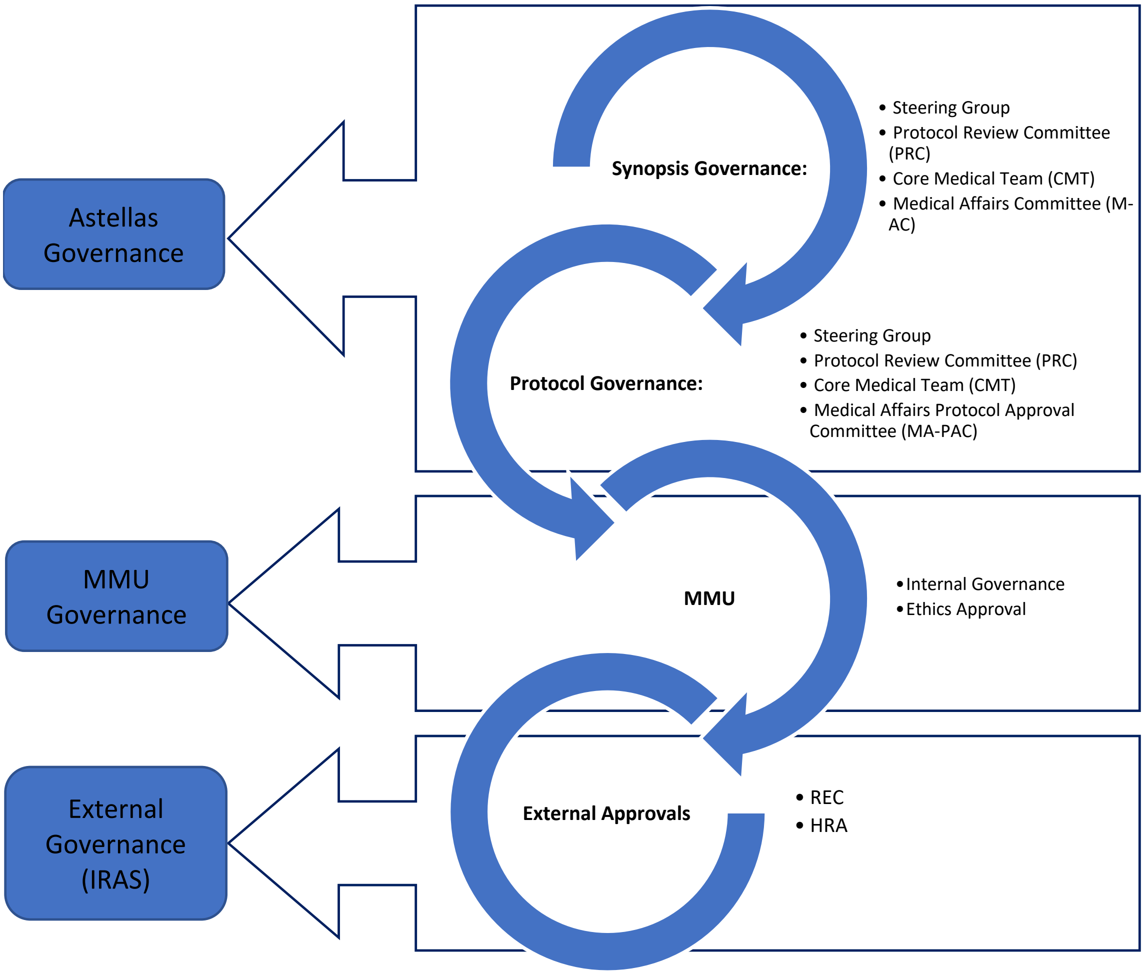


Figure 3.2: Internal and external governance and ethical approval processes

Conducting interviews

For the OAB study, after having guided the study through synopsis governance, the PRC imposed a decision to prevent the interviews to be conducted by me. This was in contravention to the preceding five review stages, including the PRC itself at the synopsis stage. In light of the regulatory climate both within Astellas and the industry, the PRC felt that although I was not an Astellas employee, I was sufficiently embedded within the organisation for it to be conceivably perceived by the industry and regulators in particular, that Astellas was directly conducting face-to-face engagement with patients. Arguably, because Astellas held a significant commercial interest in the urology space as the manufacturer of three treatments (solifenacin, tamsulosin, and mirabegron), this could have been misconstrued as the promotion of prescription-only drugs to the public (which the regulators expressly do not permit). Reflecting on this, the PRC felt it was no longer appropriate to proceed as previously planned, and so alternative means of conducting the interviews had to be sought. With support from the supervisory team, a research associate at MMU with no affiliation to Astellas was enlisted to conduct the actual interviews, with all other stages of study management agreed to continue as originally planned.

Adverse event reporting

Part of industry standards is for pharmaceutical companies to have a robust process of collecting and reporting adverse events (AE) data for treatments they hold the marketing authorisation for (MHRA, 2021). As such, a further impact of the Astellas governance process was the stipulation of having to detect and report any such AEs to Astellas products as identified through participants volunteering relevant information during their interviews with the research associate.

In usual practice, the responsibility of reporting AEs within 24 hours would have fallen to me as the first recipient of such information in my capacity as the interviewer. However, in light of the change of interviewer, this responsibility migrated to the research associate. However, upon exploring this with the research associate, a difference between industry and academic definitions of AE's was uncovered, which, alongside changes in governance for MMU employees meant that the research associate was unable to report AE's using the Astellas process, and an alternative solution had to be found.

Ultimately, in negotiation with the PRC and the pharmacovigilance department specifically, it was agreed that as part of the interview transcription and analysis process, I would identify information constituting an AE or special situation (e.g., overdose, misuse, lack of effect, or off-label use) and report it through the centralised PV process accordingly. It was agreed, that in line with participants' consent, this information would be collected and reported with anonymity and in absolute confidence with no sharing of participant data, and no possibility for further engagement from Astellas. Four such reports were submitted, for reasons described below:

Table 3.1: PV reports submitted

Report	Adverse event(s) or special situation reported
1	swollen feet, dry eyes, and dry mouth with a named Astellas product
2	dry mouth, dry throat with a named Astellas product
3	lack of effect with a named Astellas product
4	dry mouth with a named Astellas product

Data collection

To develop detailed insights from participants, qualitative research requires the collection of rich, nuanced, and holistic data (Barrett and Twycross, 2018). Data collection methods include observations, textual or visual analysis, and interviews of individuals or groups, with interviews and focus groups being the most commonly used methods in the context of healthcare research, (Gill et al., 2008). Within the current thesis, the OAB study employed semi-structured interviews to interact with participants and explore their experiences.

Interviews

Although no qualitative interview is completely devoid of structure, most interviews exist on a continuum between unstructured to highly structured processes (DiCicco-Bloom and Crabtree, 2006).

Unstructured vs structured interviews

Unstructured interviews are typically used in long-term fieldwork, often in conjunction with observational data, and allow participants to express themselves in their own way and rate, more resembling a 'controlled conversation'. Unstructured interviews range from 'non-directive' to 'informal' and 'focussed' depending on the degree to which such control is wielded by the interviewer, and can often be extremely time-consuming and difficult to navigate (Jamshed, 2014). Such interviews are therefore usually reserved for research where very little is known about the subject of interest and significant depth of enquiry is needed, or where stories of participants' lives are being explored (Gill et al., 2008, Barrett and Twycross, 2018). In the context of the present body of work, where some work has been undertaken on the subject of adherence and persistence in OAB and other conditions (which this thesis supplements and adds to), the use of unstructured interviews was not deemed necessary nor appropriate.

Fully structured, standardised interviews or surveys are where each participant responds to the same set of questions in a protocolised process with no flexibility in the questions asked, often yielding quantitative data (DiCicco-Bloom and Crabtree, 2006). While relatively easier to conduct and analyse such an interview, structured approaches do not allow participants to fully express themselves and thus limit the depth of understanding reachable via this method (Barrett and Twycross, 2018). For the current thesis, this approach too was judged to be inappropriate, given the aims of reaching a deeper understanding not only of the behaviour investigated, but its drivers and barriers in the words of the participants themselves, thus necessitating some freedom for expressing this.

Semi-structured interviews

Semi-structured interviews have been defined as an exploratory form of data collection generally following a pre-devised interview guide or protocol, thus providing some structure to the conversation albeit also allowing flexibility and the option of exploring topical trajectories (Magaldi and Berler, 2018). As such, they have been used in exploring barriers and facilitators to adherence in a range of clinical areas. Jamison et al conducted a qualitative study in GP surgeries in the east of England where they undertook semi-structured interviews with patients, caregivers, and GPs to explore perceived barriers to treatment adherence in survivors of strokes, identifying both patient-level and medication-level barriers. Semi-structured interviews were cited as particularly useful for conducting detailed investigation of people's personal perspectives (Jamison et al., 2016a). Elsewhere, a similar approach was used with adults prescribed prophylactic treatment for bipolar disease to explore their perceptions of their condition and treatment. With an emphasis on exploring the depths of beliefs, semi-structured interviews were used to uncover participants reporting non-adherence, with both the fear and actual experience of adverse effects, as well as a low perceived need for treatment being key drivers of behaviour (Clatworthy et al., 2007). More recently, semi-structured interviews have been used to understand the barriers to adhering to COVID-19 mitigation measures in Black, Asian and minority ethnic (BAME) communities in the UK. The authors interviewed participants from BAME and low-income White backgrounds to conduct a detailed exploration of adherence to social-distancing and self-isolation behaviours, and the reasons underpinning them (Denford et al., 2021).

Semi-structured interviews offer a means for conducting highly meaningful research with as few as 8 participants and are chiefly suited for where the researcher wants to deeply explore participants' thoughts, feelings, and beliefs on a topic. In the present body of work aiming to qualitatively explore medicine-taking behaviours, semi-structured interviews offered a versatile and flexible data collection method allowing participants to explain their experiences and perceptions in their own words, while retaining a framework to aid a conversational, albeit thorough exploration of key concepts with study participants (DeJonckheere and Vaughn, 2019).

Interview guide development

The interview guide for the OAB study was developed in close consultation with a cross-functional and cross-organisational study committee, and in line with the broad objectives of the Knowledge Transfer Project (KTP) outlined earlier. This thereby helped to limit potential unilateral biases from my own prior experiences and preconceptions in the development of the discussion guide. Commencing with a short briefing to remind the participant of the aims of the study, how their data were to be used, and to answer any questions before the participant gave signed informed consent, interviews were designed to last approximately an hour, and to be as conversational as possible to enhance disclosure, and to allow participants to express themselves in their own words.

In line with guidance from the literature, the interview guide was designed to include a list of guiding questions as well as follow-up/probing questions to prompt fuller exploration of responses where needed (DeJonckheere and Vaughn, 2019) (see Appendix B3: Interview Proforma). Questions commenced with an open question inviting participants to introduce themselves and to ease them into the interview. Following this, and linking to the briefing provided at the beginning of the interview, the participants were invited to give an overarching narrative of their experience with their condition, covering subsets of questions on symptoms, quality of life, interactions with HCPs, and treatment expectations and experiences, as well as experiences around adherence. The discussion guide was designed to allow the participant to relay their experiences in chronological order from early symptoms through to present reality, to both aid recall for participants, and to allow me to reach an easier understanding of the entirety of their experiences. This chronological recounting reflects the tendency of people to memory search in a temporally ordered way (Brunec et al., 2015). Participants were also given an opportunity at the end of the interview to add anything else they considered to be important to the discussion, before being debriefed and signposted in case of further questions or comments.

Data analysis

As the qualitative data generated from semi-structured interviews yields mainly unstructured, text-based data, analysing such data is not a purely technical exercise of using mathematical or statistical techniques as with quantitative research. Instead, data analysis in qualitative research is a *"dynamic, intuitive and creative process of inductive reasoning, thinking and theorising"* to explore the *"values, meanings, beliefs, thoughts, experiences, and feelings …"* of participants (Wong, 2008 pg.14).

Described as the most complex stage of qualitative research, data analysis is also the stage given the least detailed descriptions in the literature. Clear communication of the approach undertaken is pivotal in allowing others to assess and appraise both the validity and rigour of the methods used, as well as the resultant findings of the research (Nowell et al., 2017, de Casterlé et al., 2012).

Given this, a summary of the approaches to analysis and methods used within the OAB study is given below.

Inductive or deductive approach

Analysing qualitative data typically involves either inductive or deductive approaches, otherwise described as 'bottom up', or 'top down' methods respectively (Soiferman, 2010). An inductive analysis involves analysing data with little or no predetermined theory, using the actual data itself to derive the structure of the analysis. As a detailed, comprehensive, and often time-consuming process, inductive analysis is suited for when little is known about a subject, or the research has a descriptive or exploratory orientation. Deductive analysis on the other hand entails the use of a predetermined framework or structure to analyse data and is more useful when the researcher has an idea of probable responses (from previous work or insight), offering a relatively quick method of data analysis, albeit a less expansive one (Gill et al., 2008, Thomas, 2006).

In the context of the present body of work where, as explored in Chapter 2, there is a dearth of qualitative exploration of the experience of patients on OAB treatment about their medicine-taking behaviours, an inductive approach to data analysis (with an emphasis on adherence) was justifiably adopted to address this gap. On the other hand, as Chapter 5 aimed to explore the extent to which the themes identified in the OAB study were present and relevant to other conditions, a deductive approach was undertaken to compare the findings of the OAB study to those in the literature about other LTCs.

Thematic analysis

Thematic analysis aims to identify patterns (themes) in the data that are of importance or interest to the research question or surrounding issues. Distinct from other forms of analytical methods for identifying and describing patterns within qualitative data, thematic analysis is not bound to a particular philosophical framework and may be used from a realist or constructionist standpoint (Braun and Clarke, 2006). As in the present case, thematic analysis is also appropriate to be used from a contextualist or critical realist perspective, and thus offered a comprehensive and readily accessible method for this thesis. Furthermore, considering my background and as suggested by its proponents, thematic analysis houses many of the core skills useful in conducting other kinds of qualitative analyses and is therefore recommended to serve as a primary method employed by those relatively early in their qualitative research journey (Braun and Clarke, 2006, Maguire and Delahunt, 2017).

While there are many different approaches to thematic analysis, and although it is a widely used method, Braun and Clarke argued that historically, thematic analysis was poorly described and differentiated within the literature and sought to address this with an impactful paper to define its theory, application and evaluation, outlining a 6-phase process in conducting thematic analysis (Braun and Clarke, 2006). Defined by Braun and Clarke as a method for *"identifying, analysing, and reporting patterns (themes) within data*" (Braun and Clarke, 2006 pg.6), their seminal paper in 2006 has been recognised as the most influential approach to thematic analysis, offering a clear and useable framework to guide the analysis within the current thesis (Maguire and Delahunt, 2017, Braun and Clarke, 2014).

Defining a theme as capturing something of importance within the data, Braun and Clarke differentiated the identification of themes on two distinct levels. Semantic-level themes are those where the theme is identified only at the surface-level, and the researcher looks no further than what the participant stated. Latent level thematic analysis however goes beyond the explicitly stated content of the data, attempting to identify, describe, and weave together the underlying conceptualisations and beliefs driving what has been uttered by participants concerning the research question. In line with a latent level of data analysis, the current thesis aimed not only to provide an organised description of the data gathered but to produce an interpretive output (Braun and Clarke, 2006).

Analysis process

While described as an iterative and reflective process, the six phases of conducting thematic analysis are outlined in Figure 3.3 below.

Phase
1. Familiarisation with the data and transcription
2. Generating initial codes
3. Searching for themes
4. Reviewing themes
5. Defining and naming themes
6. Reporting findings

Figure 3.3: Phases of thematic analysis (Braun and Clarke, 2006)

Phase 1: Familiarisation and transcription

In the case of the OAB study, the first phase of familiarising myself with the incoming data began with the pre-interview discussions where I was able to get an overarching understanding of each participant's history and experiences, alongside some early indications on the topics to be discussed later. This was built upon by listening to the completed interview recordings in their entirety and making initial notes of interesting observations before commencing the process of transcribing.

In line with suggestions in the literature, each anonymised interview recording was transcribed verbatim and in full with an effort to represent phonetic features such as pauses, laughter, tone and emphasis (Bailey, 2008). I created a transcription form within Excel to aid this process by allowing me to touch-type who was speaking, the contents of what they said, and capture phonetic features using my own convention as described in Figure 3.4 below. Using my convention, I also included a column to timestamp various points within the interview (usually in line with each transcribing block where I would aim to complete 5 minutes of transcription in between short breaks) to allow me to quickly revisit specific points of each interview when needed.

Time/min	Speaker	Speech	Notes
Logged at the end of each transcribing block or at the point something of particular interest was mentioned.	'Participant X' or 'Interviewer'	All speech was captured verbatim, including colloquialisms, slang, dysfluencies, and fillers (e.g., *cos, erm*) reflecting differences between these where detected (e.g., *ermmm* denoting a longer filler than *erm* used within the same speech in the example below). Natural pauses between clauses of the same sentence were denoted with commas whereas cessation of a thought was denoted with a full stop. Pauses between sentences or within a sentence were distinguished using ellipses, where a longer ellipsis denoted a proportionally longer pause. Underscoring particular words or sections of a sentence signified where additional emphasis had been placed by the person speaking. Other phonetic features such as laughter were captured using parentheses (e.g. [laughs]), and double speech marks were used to capture where a participant was quoting themselves or another person within their speech (e.g., *on one of the tests they say, "oh can you just walk from A to B for me?"*). Question marks and exclamation marks were used to capture the tone of language used and dashes were used to denote where a word or sentence was changed or cut mid-way to re-emphasise or change the expression of it (e.g., *it wa-I think when it- a symptom lasts I think between a week and two weeks that it's classed as a relapse*)	The notes column served to capture any thoughts or observations I made while I transcribed, including any changes in tone or demeanour, or to link with previous observations or excerpts.
Examples			
Time/min	Speaker	Speech	Notes
	Participant 10	*ermmm, not that, much really. erm Cos I don't think I would have had a massive accident; it would have just been a little, leak probably. So I could cope with it, but I just didn't like it really.*	
4m32sec	Participant 10	*I just got, fed up with it I suppose. And also, in the night, I didn't like having to get up several times in the night, it was affecting my headaches. And also, occasionally, I would have an accident in bed? And before I'd realised? And that was the main trigger I think.mm!*	voice tone- questioning -almost as if to get validation responses from interviewer.

Figure 3.4: Transcription form

A sample of completed transcripts was then crosschecked by a member of the study team (SG) to ensure accuracy and completeness. Transcripts were then loaded into NVivo (version 11) to undergo the next stages of analysis. NVivo is a computer-assisted qualitative data analysis software package produced by QSR International. It offers a digital platform to allow the efficient organization, categorization and analysis of rich text data for qualitative analysis (Wong, 2008).

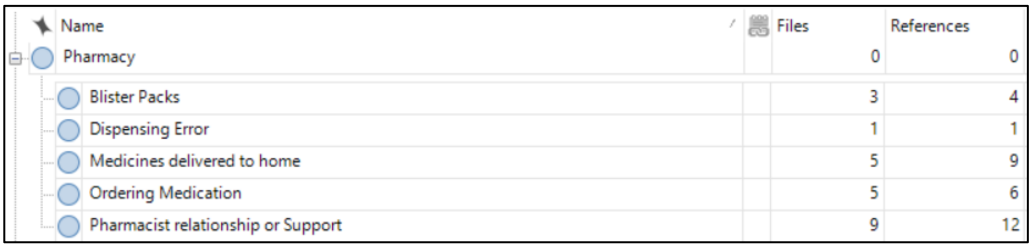
Phase 2: Generating initial codes

As codes *"identify a feature of the data (semantic content or latent) that appears interesting to the analyst"* with regards to the phenomena under assessment (Braun and Clarke, 2006 pg.18), the next phase of analysis was to generate a list of codes from the interview transcripts. In the case of the OAB study, this was a predominantly data-driven, inductive process where although there were specific questions relating to non-adherence, I wanted to address going into the analysis process, there was an early recognition of the importance to code as widely as possible to identify as full a range of codes and themes relating to treatment adherence as possible. Examples of this included coding for concepts such as alcohol consumption and mention of mobility issues. Coding was performed on NVIVO, with each transcript loaded as an individual file and each code saved as a "node" within the program. Using NVIVO made the inclusion of surrounding data and preservation of context within each code easily achievable. Furthermore, NVIVO enabled coding individual extracts of data in multiple ways, allowing for easier collation of codes and themes later.

Phase 3: Searching for themes

Having generated a list of codes within NVIVO from across individual participant files, the present phase aimed to refocus the analysis from coding to the broader level of themes. This involved analysing individual codes and identifying how they combined to illustrate an overarching theme or subthemes. Here again, the use of qualitative data analysis software enabled me to manipulate and visualise the inclusion of multiple smaller nodes (codes) under an encompassing larger one.

An example of this is given in Figure 3.5 below where various explicit mentions of the role of the pharmacy or pharmacist, as well as implicitly linked codes relating to medicine ordering and delivery were grouped under the theme of "pharmacy".



Name	Files	References
Pharmacy	0	0
Blister Packs	3	4
Dispensing Error	1	1
Medicines delivered to home	5	9
Ordering Medication	5	6
Pharmacist relationship or Support	9	12

Figure 3.5: Codes and theme

The numbers in the "files" and "references" columns also gave a readily accessible summary of the number of participants who had mentioned a particular code and with what frequency, partly informing the next phase of reviewing themes.

Phase 4: Reviewing themes and Phase 5: Defining and naming themes

The present phase involved reviewing and refining the list of themes and subthemes on two distinct levels. The first entailed reviewing the coded data extracts for each theme, ensuring they were coded correctly and fitted the theme under which they were organised, and revisiting each "node" and the coded extracts within NVIVO to do this. The second stage entailed reviewing the coding over the entire dataset to ensure the identified themes accurately reflected the entirety of the data corpus. This involved re-reading the interview transcripts in their entirety and reviewing the list of themes and subthemes to ensure congruence and representation of the participants in the OAB study.

While Braun and Clarke listed phase 4 and phase 5 as distinct steps, the defining and naming of themes was an important part of the review and refining step in phase 4. Themes were named in a self-descriptive way to capture the essence of the part of the story they told, with subthemes identified as smaller parts of themes distinctly contributing to their formation of them.

In the “pharmacy” example given in Figure 3.5 above, this theme was revised in the present phase of analysis whereby codes such as ‘ordering medication’ and ‘pharmacist relationship or support’ were retained as important components of the “support” theme. Similarly, observations for ‘blister packs’ were placed under “strategies for adherence” within the theme of “patient attitudes, experiences and responses to OAB” (see Chapter 4: “Themes”).

Phase 6: Reporting

Braun and Clarke concluded their 6-step guide to thematic analysis with the final step of producing the written report, characterising this as a means of telling the *“complicated story of your data in a way which convinces the reader of the merit and validity of your analysis”* (Braun and Clarke, 2006 pg.23). As the importance of producing a concise and coherent account of the data both within and across themes were highlighted by Braun and Clarke (as well as others), I have attempted to illustrate the results of my analyses with examples of excerpts throughout this body of work, embedding the findings within a narrative that goes beyond simply describing the data, but provides the reader with an interpretation of it also.

Further clarifications of thematic analysis

Discussing the history of thematic analysis in the book entitled the “Handbook of Research Methods in Health and Social Sciences” (Liamputtong, 2019), Braun and Clarke outlined the historical range of contexts within which the term ‘thematic analysis’ had been used. This includes, for example, the use by musicologists to describe the analysis of musical scores, and sociologists to describe a method of analysing mass propaganda. They went on to state that thematic analysis had often been used interchangeably with ‘content analysis’, noting the additional use of the hybrid term ‘thematic content analysis’ (Braun et al., 2019). Braun and Clarke went on to describe and contextualise the six-stage process detailed earlier within this chapter in their inaugural paper on the subject of thematic analysis in psychology, as an attempt to outline the theory, application and evaluation of thematic analysis (Braun and Clarke, 2006). Credited with achieving such clarification of thematic analysis, as well as the resultant increase in its interest, Braun and Clarke have since published extensively to refine and further delineate their approach to related methods (Forbes, 2022). It is useful therefore to summarise these refinements and to consider the work done within this thesis in relation to them.

In their 2019 paper entitled “Reflecting on Reflexive Thematic Analysis”, Braun and Clarke described their development of a tripartite typology of thematic analysis, namely ‘coding reliability’, ‘codebook thematic analysis’ and refinement of their own approach as ‘reflexive thematic analysis’ (Braun and Clarke, 2019b). In coding reliability approaches, thematic analysis begins with theme development with the conceptualisation of themes often driven by the questions asked to participants. This approach further emphasises consistency in analysis between multiple analysts, aiming for the ‘reliable’ or ‘accurate’ coding characteristic of a positivist approach, often measured by statistical indices such as Cohen’s Kappa (Braun and Clarke, 2019a).

Reflexive thematic analysis entails an open, exploratory, and iterative process characterised by the researcher’s transparency on their philosophical position and how it informs the analysis process and the co-creation of knowledge. In contrast to the other variants of thematic analysis, themes are considered analytic outputs of the creative process of coding and are actively constructed at the intersection of data, its analysis, and the subjectivity of the researcher (Braun and Clarke, 2019b). The underlying goal of reflexive thematic analysis is not to ‘accurately’ reflect the data nor to eradicate subjectivity, rather the aim is to provide a coherent interpretation of the data, positioning the researcher as a storyteller cognizant of their own social, cultural and theoretical underpinnings, while remaining grounded in the data (Liamputtong, 2019). The approaches taken within this thesis have adhered to a reflexive thematic analysis by taking an iterative approach to data analysis and by embedding the analytical narrative with my interpretation of not only the words being used but my perception of the drivers behind them, throughout the analysis.

Finally, codebook thematic analysis offers an in-between approach to coding reliability and reflexive thematic analysis and encompasses approaches that, while not including the term ‘thematic analysis’ in their description, nevertheless, fall into the space of employing structured coding while embedding a qualitative philosophical approach (Braun and Clarke, 2019b). Such approaches include framework analysis, template analysis, and matrix analysis where themes, conceptualised as domain summaries similarly to coding reliability approaches, are typically determined ahead of full data analysis without the need to quantify reliability and accuracy (Liamputtong, 2019). Given the approach to code as widely as possible in conducting the first fully qualitative study exploring self-described reasons for non-adherence to oral medication for OAB, such an approach was not appropriate, and instead, a reflexive approach was adopted.

Methods for comparative analysis (Chapter 5)

Chapter 5 describes a comparative analysis taking the themes identified within the OAB study described in Chapter 4, and exploring the convergence and divergence to those reported in similarly published works in inflammatory bowel disease, type II diabetes, and multimorbidity. For a detailed discussion on the rationale for the study and selection of papers, the reader is directed to Chapter 5: “LTCs explored”. Within the present section of the thesis, the methods undertaken for the comparison of outputs between the OAB study and the identified papers, as well as their presentation and subsequent analysis will be described.

Comparing thematic data

In their book entitled "Applied Thematic analysis", Guest et al. (2014) described two approaches to conducting qualitative thematic comparisons of concepts between two or more data sets. The first, offering a comprehensive approach to comparative analysis, entails the extraction of individual text excerpts associated with each code of interest, and performing an in-depth comparison of these between data sets. This method requires access to the primary data itself, from which a data matrix may be constructed (usually within a data analysis software), thereby allowing for patterns to be identified across data sets (Guest et al., 2014).

The second approach entails exploring the differential expression of thematic areas between data set, noting the similarities and differences between concepts and themes. Such an approach is driven by the overarching questions of whether the themes from one data source are expressed in the other, and how the expression of such themes may converge and diverge, discussing these observations in an analytical narrative (Guest et al., 2014).

Analysis method

The variability and extent to which direct quotes and text surrounding particular codes are available in published qualitative works have been highlighted in the literature (Eldh et al., 2020, Thorne, 2020). Given this, as well as the exploratory nature of the analysis, the latter approach focussed on the presence and differential expression of themes in published works in other long-term conditions was deemed the most suitable approach to adopt in

Chapter 5. Each theme from the papers of interest, as well as the excerpts used to support it (where available) was compared to similar concepts expressed within the OAB study to produce a narrative of where the concepts and their expression by participants converged and diverged, as well as possible reasons for this using relevant theoretical models introduced in Chapter 1.

Structure and presentation method

Chapter 5 has been subdivided into a general introduction highlighting the intent and objectives of the work, a section for each of the three comparative analyses undertaken, and a concluding section to summarise and discuss the learnings from this work. Within each comparative analysis section, the reader is provided with a background on the clinical area of interest and its treatments before being introduced to the paper under comparison. An overview of the objectives, methods, and participants is provided for each paper, followed by the content of its findings, and a narrative comparing and contrasting this to findings from the OAB study in Chapter 4.

To aid a clear comparison between the OAB study and the three studies exploring other chronic conditions, each comparative analysis was presented in both narrative and diagrammatic form. This took a phased approach in first producing a visual representation of all the themes from the papers being compared, as demonstrated in the example below:

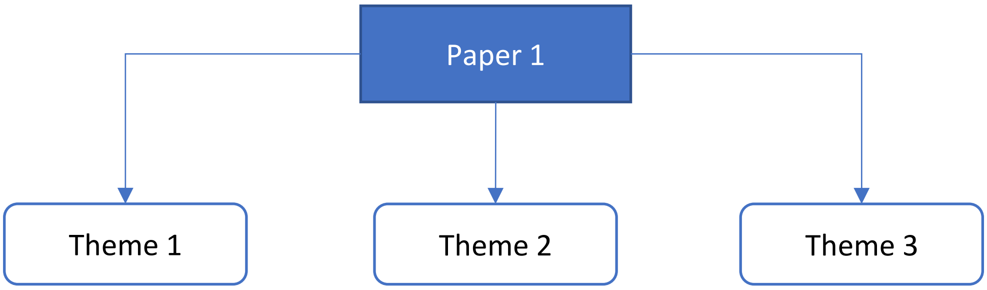


Figure 3.6: Example figure to diagrammatically represent themes in external papers of interest

After ensuring a thorough understanding of the themes described in the comparison papers, the relevant themes from the OAB study were mapped onto the diagram to visually represent their connections. The connection of each theme from the OAB study being mapped to specific themes from the paper of interest was colour coded to aid interpretation as can be seen below:

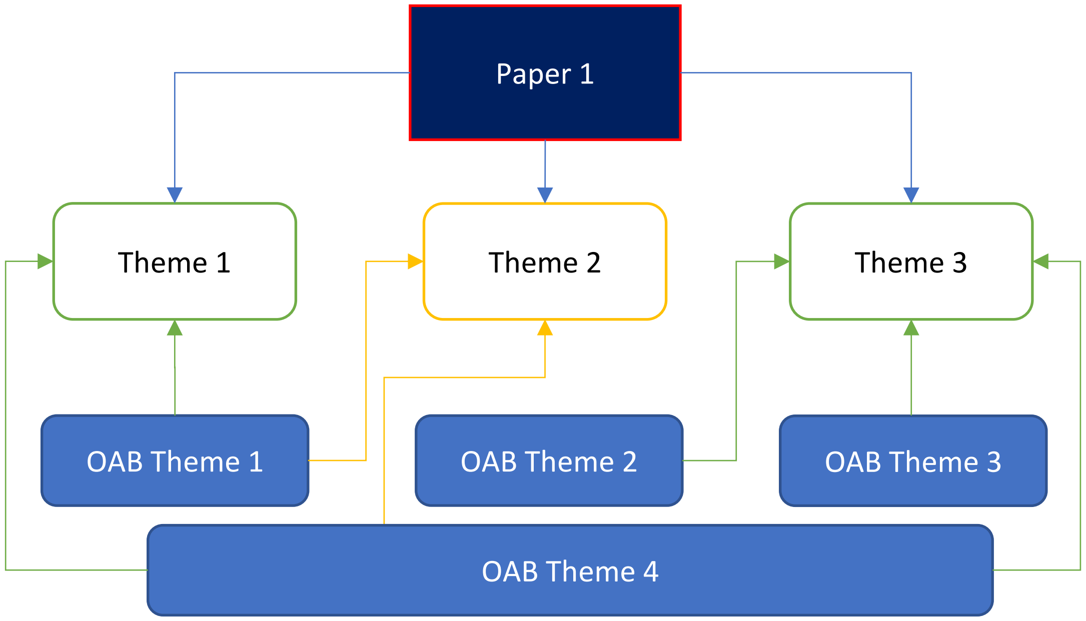


Figure 3.7: Example figure to diagrammatically represent mapping of themes between OAB paper and papers of interest

The process of producing the above diagrams and accompanying analytic narrative was itself an iterative process between early mapping based on the initial descriptions of themes given in each paper of interest, and the evolution of my understanding and the connections between concepts through writing the analytic narrative. In this way, the process undertaken was akin to the reflexive thematic analysis itself in that the comparative analysis involved iterative steps including immersion in the works being compared to, reflecting, writing, and revisiting initial impressions to develop a coherent and detailed analysis (Braun and Clarke, 2019b).

Chapter Summary

The present chapter has presented the reader with my epistemological and ontological perspectives, as well as a reflexive analysis. It has gone on to outline the methodology employed in the interactive study outlined in Chapter 4, including ethics and governance, data collection and analysis, as well as the methods used in the comparative analysis presented in Chapter 5.

The next chapter will describe a study undertaken to fill the gap identified in the literature review described in Chapter 2, in the form of a qualitative study exploring adherence behaviours in OAB.

Chapter 4 – OAB Qualitative study

A qualitative analysis of factors influencing patient persistence and adherence to prescribed overactive bladder medication in UK Primary Care

Summary

The present chapter describes a qualitative study involving 1:1 semi-structured interviews with participants experiencing overactive bladder, identified though cooperation with NHS Research and Development sites in two parts of England, UK. The study aimed to explore the OAB patient journey and identify the reasons and contexts behind non-adherent medicine-taking behaviours to oral treatment, and in so doing, filled a gap in the literature as identified by Chapter 2.

Background and Introduction

Overactive bladder (OAB) is a common, distressing, chronic condition characterized by urinary urgency with or without urinary incontinence, usually with increased daytime frequency and nocturia. The prevalence of OAB ranges from 11% to 27% in men, and from 13% to 43% in women, with a clear trend of increasing prevalence with advancing age, and highest rates reported in people aged 65-80 years (Eapen and Radomski, 2016a). An estimated 546 million people worldwide were predicted to be suffering from OAB by 2018 (Irwin et al., 2011), though this number is likely to be larger in reality due to underreporting associated with this condition (Ahmad et al., 2015). After behavioural therapy and education, pharmacological management includes the use of antimuscarinics or the beta-3 adrenergic receptor agonist, mirabegron (Yeowell et al., 2018b). The effectiveness of treatment is not solely a function of the drugs in use as non-adherence to pharmacological treatment has a major negative impact on ultimate health outcomes and quality of life (WHO, 2003).

Persistence rates with pharmacotherapy in the context of OAB are generally low with over 70% of patients discontinuing treatment within 12 months (Wagg et al., 2012). This is supported by Shaya et al. who reported 12-month persistence rates of 5-9% in Medicaid patients prescribed antimuscarinics for overactive bladder (Shaya et al., 2005). These findings were also supported by studies in the UK, US and Canada which found that around two thirds of patients discontinued their antimuscarinic medication within the first 30 days (Sexton et al., 2011b).

Adherence and persistence to OAB medications was lowest when compared with five other chronic medication classes for the treatment of diabetes, glaucoma, hyperlipidaemia, osteoporosis and hypertension (Yeaw et al., 2009). Since the introduction of the newest drug in the OAB armament (mirabegron), a recent review paper summarised evidence of the real-world adherence and persistence to OAB treatment. It found that overall, 1-year persistence ranged from 12-25% for antimuscarinics, with patients on mirabegron faring slightly better at 32-38%. The median time to discontinuation was found to be less than 5 months for antimuscarinics, and up to 7.4 months for mirabegron for the treatment of OAB (Yeowell et al., 2018a).

Similar observations were made in a 2017 UK retrospective Clinical Research Practice Datalink (CPRD) study which found that discontinuation of antimuscarinics in OAB patients generally occurred within 1-3 months, compared with a median of 5.6 months with mirabegron. Furthermore, the study suggested that the rate of patients discontinuing later than 3 months was similar with all OAB drugs, and therefore the reasons for discontinuation at this stage may also be similar. It concluded that further efforts were needed to better understand the reasons for discontinuation of OAB medications and how to support patients so that they achieve long-term adherence (Chapple, 2017b).

As part of reaching that understanding, the present study was designed to explore factors influencing participant adherence and persistence to oral medications for the treatment of OAB. The advantages offered by using qualitative methodology for this purpose have been described in earlier chapters. Given the exploratory nature to better understand the drivers of participant behaviours, no prior hypothesis was tested.

Research Question and objectives

To conduct the first fully qualitative study exploring self-reported reasons for participant non-adherence to oral medications for the treatment of OAB; to explore the context around these reasons, and the participant journey from their own perspective.

Research Methods

Study design

This was a qualitative study, conducted as part of the Knowledge Transfer Partnership (KTP) between Astellas Pharma Europe Ltd (APEL), Manchester Metropolitan University (MMU) and Innovate UK (see Chapter 3 for further details). The study was designed under the guidance of a cross-functional, and cross-organisational steering committee involving representatives from Health Economics and Outcomes Research (HEOR), Medical Affairs, Pharmacovigilance, and Academia.

Patients vs participants

It is considered that the terms ‘patient’ and ‘participant’ are both appropriate in describing the people involved in the present study. To this end, as National Health Service (NHS) infrastructure was used in the identification of people to be invited to this study, the term ‘patient’ has been used to describe the recruitment process up to the point of their consenting to take part in the study. Thereafter, people involved within the study are referred to as ‘participants’ to recognise their voluntary and active engagement in forming the research outcomes. Where the discussion and conclusion sections of this chapter relate the findings from the participants of this study to the wider context involving patients once more, both terms are employed again (Glantz, 2014).

Participants

Inclusion Criteria

Individuals were invited to participate if they meet the following inclusion criteria:

- Male or female aged 40-80 years of age,
- Fluent in English,
- Diagnosed with OAB (coded and confirmed by HCP),
- Taking, or have taken, either antimuscarinic(s) or beta-3 adrenergic receptor medications for OAB within the last 12 months,

Exclusion Criteria

Individuals were excluded if they had:

- memory impairment, cognitive decline, or dementia (as documented within medical records)

Discontinuation Criteria

The following discontinuation criteria were communicated to participants upon introduction into this study:

- Participation must be voluntary,
- Each participant was free to withdraw for any reason, at any time, without explanation nor consequences,
- If the right to withdraw was exercised, data would only be included in the study with explicit consent from the participant allowing so.
    - All such instances were to be recorded and stated in final reports

Recruitment

A description of the recruited participants is provided here. Please see "procedure" section below for a detailed description of the recruitment process. A total of 199 individual invitation packs were sent out in accordance with the reported numbers of patients meeting the inclusion criteria from each of the 16 Primary Care Organisations (PCOs). Of these, a total of 27 responses were received by the study team (13.6% response rate), and following the exclusion of 7 participants, a total of 20 interviews were performed (Table 1).

From the 20 participant interviews, two were excluded on account of poor-quality recordings not allowing accurate transcription and analysis.

Table 4.1: Summary of patient recruitment responses

		Invitation packs		Patients		
Area	**PCO**	**Sent**	**Replies**	**Excluded**	**Included**	**Reason for exclusion**
Greater Manchester	1	0	0	0	0	
	2	13	2	0	2	
	3	7	4	1	3	Inclusion criteria not met
	4	30	1	0	1	
	5	34	2	0	2	
	6	0	0	0	0	
	7	61	6	1	5	Withdrawal of consent
	8	0	0	0	0	
	Total	**145**	**15**	**2**	**13**	
Kent, Surrey, and Sussex	1	11	1	1	0	Withdrawal of consent
	2	11	6	2	4	Exclusion criteria met; no consent given
	3	0	1	1	0	No consent given
	4	12	1	0	1	
	5	4	2	1	1	Unavailable for interview, consent withdrawn
	6	9	1	0	1	
	7	5	0	0	0	
	8	2	0	0	0	
	Total	**54**	**12**	**5**	**7**	

Table 4.2: Summary of invitations and interviews

	Invitation packs sent	Patient responses received, n (%)	Patients excluded	Interviews removed	Interviews included in analysis
Totals	199	27 (13.6)	7	2	18

Participant descriptive data

Table 4.3: Participant demographic and clinical background information

Area	Participant number	Sex	Age	Occupation/background	Main OAB symptoms
Greater Manchester	1	M	64	Research/statistics (managerial) (retired)	Urgency, incontinence
	2	F	66	Retired (previous profession unknown)	Urgency, incontinence, nocturia
	3	F	58	IT programmer, currently a medical coder at a GP surgery	Frequency, urgency, incontinence
	4	F	69	Teacher (retired)	Urgency, incontinence
	5	F	71	Air stewardess (retired)	Frequency, urgency
	6	F	57	Healthcare assistant (currently on sick leave from work due to mobility issues with arthritic knees)	Frequency, nocturia, incontinence
	7	F	70	Carer in social services (retired)	Frequency, urgency, high volume
	8	F	77	Social worker (retired)	Frequency
	9	F	80	Buyer for national pharmacy chain (retired)	Incontinence, urgency
	10	F	58	Teacher (long-term migraines stopped patient from continuing teaching) “at home now”	Urgency, nocturia, incontinence
	11	F	78	Office manager (retired)	Incontinence, urgency, nocturia
	12	F	61	Accident and emergency nurse (retired)	Frequency, incontinence, high volume at night
	13	M	65	Self-employed electrician and builder	Urgency, frequency
Kent, Surrey, and Sussex	14	M	78	Planner for school projects (retired)	Nocturia, urgency
	15	F	80	Worked in plastics manufacturing (retired)	Incontinence, nocturia, urgency
	16	M	71	Chartered surveyor (retired)	Urgency, incontinence, nocturia
	17	F	67	Nurse (retired)	Frequency, nocturia
	18	M	70	Engineer (retired)	Nocturia
	19	F	76	Audio equipment failure. Participants discounted from analysis	
	20	M	75		
OAB = overactive bladder					

As shown in Table 4.3, of the 18 interviews, 5 participants were male and 13 were female. The mean age was 70 years, with a range of 58-80 in females and 64-78 in males. 13 of the interviews were conducted face-to-face with participants recruited via the Greater Manchester NHS R&D site, with the remaining 7 conducted over the telephone with participants recruited via the Kent, Surrey, and Sussex NHS R&D site. The equipment failure on 2 interviews was discovered after the team had agreed saturation point had been reached following the analysis of 18 interviews. These two interviews were not included in the analysis.

Procedure

In addition to rigorous internal governance at both Astellas and MMU, this study was subject to a thorough external governance process and ethical review (see Chapter 3 for details). The Integrated Research Application System (IRAS) is a single system for applying for the relevant permissions and approvals for health and social care research in the UK, to meet regulatory and governance requirements. As part of this process (IRAS project ID:198502), this study received approvals from the Health Research Authority (HRA) and Liverpool East Research Ethics Committee (REC) (REC ref: 16/NW/0724).

Two NHS R&D sites in Kent Surrey and Sussex (KSS) and Greater Manchester used the Clinical Research Network (CRN) and FARSITE databases respectively, to identify PCOs with eligible patients for the present study. The NHS R&D sites then sent practice engagement packs to eligible PCOs to invite them to participate in this study. These packs included the study protocol, patient information sheet, study poster to display in the practice, and a Research Information Sheet for Practices (RISP) to help PCOs gauge their level of interest and ability to allocate the necessary resources to participate in this study (see Appendix B1: Practice Engagement Packs).

Participating PCOs compiled lists of registered OAB coded patients within their practices and applied the study inclusion and exclusion criteria. A HCP from each PCO then reviewed the list of potential participants to confirm that those who progressed to be invited to participate in the study were appropriate to do so (i.e., had correctly coded OAB, had not suffered from recent bereavement or diagnosis of terminal illness, etc.). Upon sharing the final number of eligible patients with the study team, each PCO was sent the corresponding number of patient invitation packs to send out to their shortlisted patients.

Each patient invitation pack included a patient information sheet containing a summary of the study as well as contact details for further information, a consent-to-be-contacted form for patients to share their contact details with the study team, and a prepaid envelope with which to do so (see Appendix B2: Patient Pack). Interested patients returned signed consent forms to the study team confirming their wish to be engaged and discuss further involvement in the study.

Considering this was the first known qualitative study investigating this area within OAB (see Chapter 2), after consultation with academic experts in qualitative research, as well as published guidance (Dworkin, 2012, Baker SE, 2012, Gill et al., 2008), this study initially aimed to include up to 25 semi-structured 1:1 interviews (face to face or by telephone), split between the two regions. Also considering the constraints of stringent and lengthy internal governance processes (see 0), it was understood that this number represented the upper limit of interviews needed for the present study and would be subject to a data saturation point, which if reached, would make it unethical to continue further interviews (O'Reilly and Parker, 2012).

Upon receiving consent-to-be-contacted, pre-interview telephone discussions were arranged with MA (the researcher) to confirm participant suitability to the study and to answer any initial questions regarding the research. Upon mutual agreement to taking part in the research, interviews themselves were carried out by a female research associate (LS, referred to herein as the interviewer, and for reasons highlighted in 0), with prior experience in qualitative research and in conducting healthcare related semi-structured interviews. The interviews were carried out face to face (in Manchester) and over the telephone (in Kent, Surrey, and Sussex [KSS]) for logistic ease. Each interview commenced with a briefing to remind the participant on the nature of the study and how their data were to be used, and to answer any questions before the participant gave signed informed consent. Participants were also made aware that the interviewer was not qualified to give advice on healthcare, and to direct any such questions to their HCP. Participants being interviewed remotely gave verbal consent in the interviews and posted their signed consent forms via pre-paid envelopes to the researcher.

Interviews were designed to take approximately an hour each, with a view to conduct all interviews over a period of around 8 weeks (subject to arrangement with participants). The interviews were designed to be conversational to enhance disclosure and allowed participants to explain in their own words the range of reasons they might not take their medications, and their perceptions of factors that may enhance the likelihood of adherence for them and others taking similar drugs for OAB.

A discussion guide was produced with input from internal subject matter experts and experienced academic researchers to frame the interviews and to ensure full responses (Appendix B3: Interview Proforma). The discussion guide was designed to take participants through a chronological order of events in order to aid recall (Arthur et al., 2003). Subject matter experts within Astellas included HEOR leads in Urology, and Specialist Medicines, a consultant urologist with over a decade of medical experience within urology, and the

Medical Director for Urology. From MMU, qualitative academic researchers included an experienced registered nurse and Principal Lecturer in Public Health with a particular expertise in qualitative methods and interview techniques, and a Professor of Public Health with expertise in both quantitative and qualitative research methods and behavioural change, supported by a Professor of HEOR.

Each interview was concluded by a short de-brief to sign-post participants to the Chief Investigator or researcher in case of any concerns or queries related to the study, and to answer any further questions.

Study size

Although the study was designed to include up to 25 participant interviews, ultimately 20 interviews were conducted in total. Upon transcribing and analyzing the data from 18 interviews, the study team recognized that saturation point had been reached, and that it would be unethical to continue with further interviews.

The final two interview recordings were of poor audio quality and could not accurately be transcribed or analyzed, meaning that the analysis that follows is based on the data from the 18 fully transcribed interviews that led to the recognition of saturation point.

Data transcription and analysis

Following anonymization, transcription of the recordings was undertaken by the researcher and the recordings and transcripts were stored on a password-protected University computer. The transcribed data were analyzed by the researcher using thematic analysis to identify themes within and across individual interviews. Thematic analysis is defined as a method for identifying, analysing and reporting patterns within data and involves steps of data familiarization, coding, identifying, reviewing, defining themes, and bringing them together with analytic narrative to produce an accurate and coherent account of the data reviewed (Braun and Clarke, 2006). Narrative fragments from participants were also used to illustrate themes and points (Braun and Clarke, 2006, Riessman, 2008)

Each interview recording was heard in its entirety before being transcribed verbatim and in full. The transcriptions were then loaded into NVivo Pro 11 to undergo thematic analysis. NVivo is a Qualitative Data Analysis (QDA) software package produced by QSR International. It offers a digital platform to allow efficient organization, categorization and analysis of rich text data for qualitative analysis and was used to organize and expedite the process of familiarization, coding, searching for and reviewing themes (Burnard et al., 2008).

Using interviews as a means to gather data for this study allowed the generation of a rich data set to enable analysis in these ways. Furthermore, the language used by participants was used to gain a deeper insight into their perceptions and values (Ritchie et al., 2013, Newton, 2010).

Quality control

The interviewer followed the conclusion of each interview with a set of notes, to capture her own interpretations and any notable observations. These notes served as a means of cross-checking any discrepancies in the transcription stage later in the study.

A sample of transcripts (15%) in conjunction with the corresponding recordings was reviewed by the Chief Investigator (MH) to ensure completeness and accuracy of the transcripts. Any unclear or ambiguous passages were cross-checked with the interviewer to ensure that the transcripts were an accurate reflection of the recordings.

SG, an academic psychologist with extensive experience in health related and qualitative research, performed an additional cross-check validation of data coding and theme identification in 20% of interviews.

Development of themes

While the overall data analysis methods have been discussed elsewhere (within the present chapter as well as in Chapter 3: “Methods for OAB study”), it is useful to illustrate here the approach taken to coding, and the progression from this to developing a set of themes relating to adherence and persistence behaviours within OAB. Excerpts have been included below to illustrate the progression from coding to subthemes and themes, using the theme of ‘symptom perception and other people’ as an example (see section below entitled “Themes” for an overall thematic map and how this theme fits the overall findings of the present study).

Following pre-interview discussions and listening to each interview recording in its entirety (as described in Chapter 3: “Phase 1: familiarisation and transcription”), my initial notetaking during the data familiarisation and transcription was a key part of the theme development process. Illustrating this, Figure 4.1 below shows my initial thoughts noted while transcribing the interview with Participant 3, capturing my interpretation of her words in relation to other people, and the context of their expression. Such notes then became a starting point for the coding process.

Participant	Speech	Notes during data familiarisation
3	*It’s not! And one of my friend’s mums, she's stopped going to places. And I don’t actually know the outcome of what happened with her- because she was saying "oh I'm aways running to the- oh I'm not going there, I can't be bothered-oh I'll be-no I'm not-" and y'know, I might have got to the point where I'm saying well I’m not walking around the water park if there isn’t a toilet around there.*	fears of future linked to other people and their experiences. Fear of symptoms escalation- echoes previous experience. Reiteration of previous fear of becoming an old lady who keeps wetting herself. Perceived stereotype reinforced by experience of others- fuelling the personal worry of the stereotype and associated stigma?

Figure 4.1: Example of annotation during data familiarisation

Noting the commonality of this reference to other people across participants, and its proximity to the experience of OAB itself, I began to code the various forms of how people around the participant were being framed and referred to during the interview. This included instances of the participant comparing or mapping the experience of other people onto their experience of OAB (as in the example with Participant 3 above), others commenting on or passing judgement on the participant, and the effects of OAB symptoms on family and friends. Coding took both latent and semantic forms, without prioritising one over the other.

Participant	Speech
18	I-I really don't notice how often I go! [laughs] probably more than most people.

Figure 4.2: Example of semantic coding where participant expressly compared to others

Figure 4.2 above shows an instance of semantic coding whereby the participant expressly compared their own experience with that of others (highlighted text). This was of note to me as it indicated the mechanism behind how symptoms were perceived and benchmarked, which in turn would potentially impact how the health threat was represented and coped-with in line with the CSM (discussed in Chapter 1: 'Common Sense Model of illness'). Conversely, in the excerpt in Figure 4.3 below, the comparison to other people was more subtle, representing an example of latent coding.

Participant	Speech
6	[sighs] I don't know. Some people just don't seem to get [pause] I mean I'm lucky, I'm still alive, I've got use of limbs and, I can do stuff. But sometimes, I'm just a recluse. because I cannot go out, because I don't trust myself, or, it's like I can't go around town with friends cos I can't walk very far

Figure 4.3: Example of latent coding for participant comparison to others

Here, Participant 6 stopped short of direct comparison by mentioning other people before pausing and directing her comments to her own experiences. I interpreted her redirection as an interruption in making an explicit comparison, with her subsequent description of not being able to trust herself thinly veiling an implied ability of others to do so, thereby continuing the comparison in an implicit rather than explicit manner. The mentioning of friends within this excerpt also highlighted a contrast in physical abilities, reiterating a sense of comparison and its implications, with OAB symptoms at the heart of why the participant did not consider being able to go out. Finally, the self-description of “recluse” further implied the involvement of other people in the conceptualisation of her coping mechanism, reemphasising the importance of others in her perceived experience of OAB.

The codes for instances where the participant mentioned other people comparatively were refined and grouped together under the heading “comparing to others”. Similarly, where other people were mentioned in terms of them commenting on the participant’s OAB symptoms, these were coded under the heading of “others noticing/remarking/judging”. Where individuals spoke about their symptoms having an effects on others (family and friends), these were grouped together under the heading of “affecting others”.

As shown in Figure 4.4, these codes and observations came together to be considered under the initial theme of “other people” within this stage of analysis.

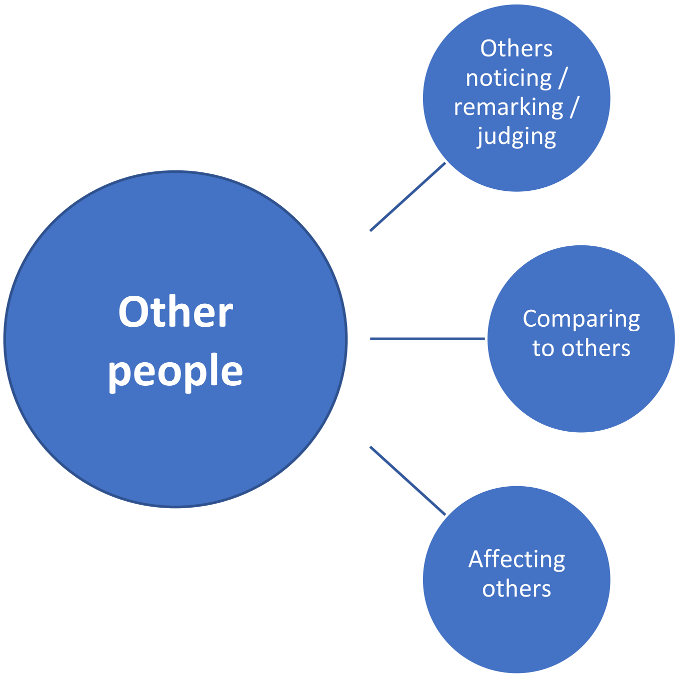


Figure 4.4: Conceptualisation of "other people" as a thematic area in OAB study

In the reviewing, defining, and naming themes stages of analysis, the theme of “other people” illustrated above was considered in relation to other themes with shared elements. This was guided by the consideration of the “central organising concept” of individual themes (Braun and Clarke, 2019a pg.2), as well as the context of the totality of thematic areas uncovered during data analysis. Such bidimensional review has been described as level one (reviewing the relationships among data items and codes informing themes and subthemes) and level two (reviewing candidate themes in relation to the entire data set) in the literature (Byrne, 2022).

The importance of social and psychological contexts in medicine-taking behaviours has been highlighted in the literature (see Chapter 1: “Conceptual models relating to adherence”) and was noted as especially important in the present study in relation to OAB (see “Themes” and “Drug/condition hierarchy” sections below). In particular, in conducting level one and level two reviews of the preceding stages of analysis, I considered the interrelationship between patient’s experiences (both of their OAB and the social context within which they experienced it), and their subsequent attitudes and approaches in managing OAB to be an important facet of interpreting the dataset.

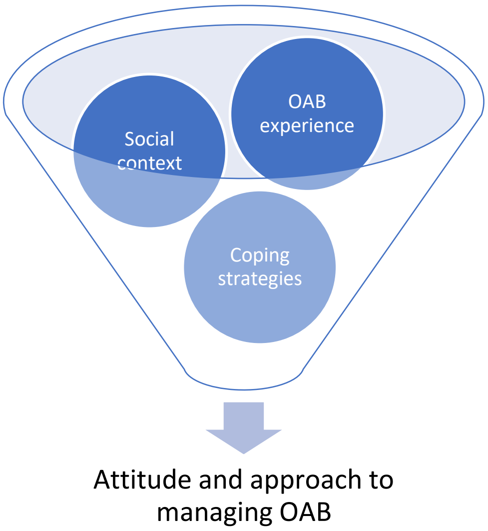


Figure 4.5: Organising concept behind "Patient attitudes, experiences, and response to OAB" theme

The attitudes individuals brought to managing their OAB, as well as the drivers behind this, therefore became the central organising concept for this theme, supported by both observations within this study, as well as conceptual models espousing the importance of attitudes and beliefs. The result of this recursive review was a reconsideration of the standalone theme of "other people" in Figure 4.4 above, and reclassifying it as a sub-theme to the overarching theme of "Patient attitudes, experiences, and response to OAB" as can be seen in Figure 4.6 below.

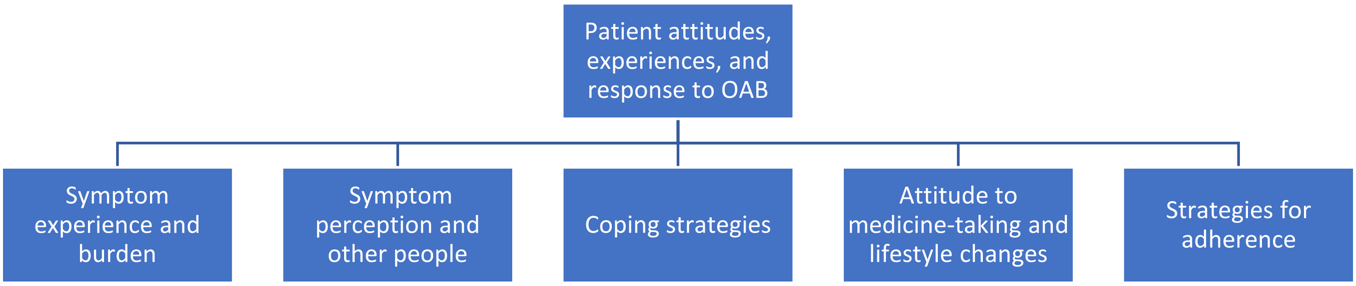


Figure 4.6: Theme of "patient attitudes, experiences, and response to OAB" and sub-themes

Results

In keeping the tone of the interviews conversational, but with sight on extracting the participants' views on a wide range of their experiences, the interview discussion guide was designed to take the conversation between participant and interviewer through a chronological experience of OAB, from initial symptoms to current situation. The discussion guide can be found in Appendix B3: Interview Proforma.

Themes

The themes identified within the present study were broadly categorized into four areas relating to medicine-taking behaviours as summarised below:

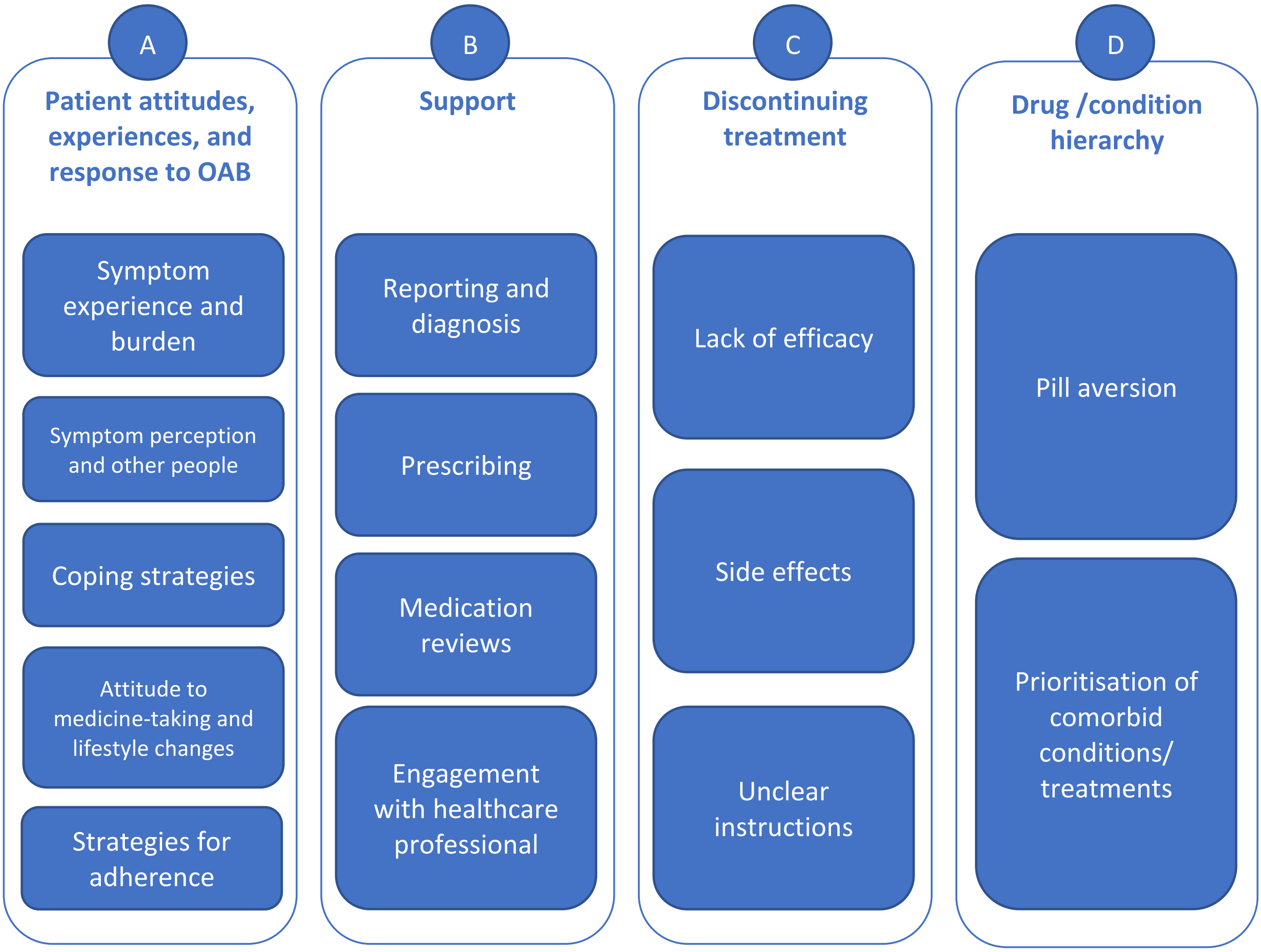


Figure 4.7: Themes relating to adherence and persistence to OAB medication

A: Attitudes, experiences, and response to OAB

The first of these four areas provides an important exploration of the context within which medicine-taking behaviours were enacted by participants. Within this overarching theme, the participant experience of symptoms, how these occurred within a social context and the effects of this, as well as their approach to medicine-taking and adopting lifestyle changes will be provided. Furthermore, how participants implemented coping strategies for symptoms, as well as strategies employed to adhere to treatment will also be outlined.

A.i) Symptom experience and burden

Consistency and severity

Participants experienced an array of symptoms, which differed considerably in their severity across the cohort. In terms of the general day-to-day OAB experience, only participants 12 and 10 described symptom uniformity, stating they did not have any days *“worse than others”*, and that the symptoms were *“quite consistent”* respectively.

The majority of participants however, reported cyclical symptoms that appeared to wax and wane over time, with descriptions such as the one provided by participant 17 who described her usual nocturnal symptoms as getting up *“just once”*, adding that this could vary and that the night before speaking to the researcher, she had been up *“about five times!”*. She went on to summarize with *“there's times that I can do without a problem! And sometimes I've got to go!”*. Participant 13 added to this theme by describing his symptoms of urgency as sometimes *“immediate”* and at other times not affecting him at all.

Participant 15 described her symptoms as *“coming and going in spasms”*, going on to describe a higher symptom burden on some days, requiring frequent changing of her absorbent pads to manage the incontinence, with other days not having any problems at all, describing her symptoms as *“a bit irregular, really”.*

With the exception of participant 14 who described the severity of his symptoms as having *"stayed the same"* over time, the majority of participants reported a gradual worsening of symptoms over time evidenced either by direct quotes explicitly describing the worsening of symptoms (e.g., participant 9: *"I can't really go on like this,* ***it's getting worse****. which it was"*), or by a description of management strategies being escalated in terms of the intervention employed, or the frequency of its use (e.g., participant 4: *"I <u>had</u> to wear a pad, a-started to <u>have</u> to wear a pad at night. Which I'd never had to do before"*).

Symptom expression

Urge and urge incontinence

Urgency and urge incontinence were often mentioned together, with several participants highlighting the suddenness of their need to use the toilet, and an inability to plan for it (e.g., participant 1: *"it was urgency, to relieve the bladder, and also, premature, release-small quantities, without too much warning, once the urgency arose",* and participant 6: *"I can have accidents now, anytime, anywhere"*). In fact, participant 15 was forced to cut the telephone interview short due to a sudden urge to use the toilet. The unexpected nature and magnitude of her urge was highlighted by the sudden shift in her demeanor from talking comfortably with the interviewer, to cautiously asking how long the interview would continue for, to having an audible urgency and quickening of her speech as she hastened to conclude the conversation. Such symptoms were also accompanied by a sense of resignation, and loss of control as highlighted by participant 7 who relayed a story where she experienced abrupt urinary urgency while away with her husband and had to run into an unfamiliar pub and ask to use the toilet. She added that the experience *"<u>really</u> started to worry me cos I thought 'if I <u>am</u> out and about and there's nowhere for me to go..." I'm-well, there's not a lot you can do is there?".* The resignation to not being able to control urinary urge was felt by other participants too who associated the unpredictability and lack of control with an emotional response. Participants described feelings of embarrassment, frustration, and apathy (e.g., participant 14: *"sometimes I do get, a little leakage, which again is embarrassing"*)

Frequency, nocturia and enuresis

A frequent need to use the toilet was one of most prevalent symptoms experienced by the participants in this cohort and was predominantly described as one of the first they noticed. Participant 7 stated: *"I was going to the toilet, and within 5 minutes I was <u>absolutely bursting</u> to go again"*, while participant 8 highlighted she *"couldn't got an hour without going"*. Due to the relative conspicuity of frequently going to the toilet, this awareness was often fuelled by the comparison to other people's frequency of toilet use, the effect of this symptom on others, or how others reacted or remarked about it. This will be covered in more detail below under 'Symptoms perception and other people'.

Nocturia was another commonly mentioned OAB symptom and appeared to be a key driver of symptom bother. Participant 9 described waking up to use the toilet three times the night before the interview and that she used a piece of tissue as an absorbent pad at night "*just in case"* of any leaks upon waking or on her way to the toilet. Participant 17 added: *"there isn't a night where I don't have to get up to go to the loo"*. Several participants mentioned the secondary effects of nocturia on their daily lives, and the additional burden caused by the resulting sleep disturbances. Most notable of these examples was participant 7 who was convinced she had dementia on account of her mental lapses, only to discover upon seeking help from her GP, that the repeated disturbances to her sleep were at the root of the issue. This participant went on to discuss the mental and emotional effects of having to get up repeatedly at night, despite having made some lifestyle changes. She admitted that the broken sleep pattern was leading to feeling *"frustrated"*, *"irritable"*, physically, and mentally fatigued, commenting: *"I lie there crying sometimes. I'm just so frustrated cos-I want- I mean I'll get up at three, go to the loo. It might be, near enough four before I get back to sleep!"*. The participant's emphasis on the words *"crying"* and *"tired"* left little doubt that the source of her distress was not solely on the experience of having to wake at night, but that the consequent secondary effects of insomnia and tiredness were particularly burdensome. The next-day cognitive effects of nocturia were also echoed by participant 2 and 4 who commented: *"sometimes I can't function. Y'know, I get up and I think 'oh I'm going senile' I forget what I'm doing!"* and "*of course it affects your tiredness the next day as well, then I went to the GP. y'know, because, well it's not on if you can't sleep, is it? you can't cope in life"* respectively.

With some parallels to be drawn with nocturia due to its effect on sleep patterns, three participants brought up their experiences with enuresis. They reiterated the lack of control with this symptom, echoing the themes seen with urge and urge incontinence. Participants strongly linked their experiences to feelings of powerlessness, embarrassment, and degradation. Participant 1 described his feeling of helplessness with enuresis was driven by a lack of awareness of the symptom occurring as he slept, and the resignation to it happening without him being able to do anything to limit or stop it. The descriptors *"flustered"* and *"degraded"* indicated the emotional and psychological effects of this symptom on him.

A.ii) Symptom perception and other people

Within this section, themes related to symptoms experienced within the context of other people will be presented.

Others noticing / commenting on condition

People around participants that noticed or commented on their condition fell into the categories of those they knew (family and friends), and those they did not.

Strangers

Distinguishing between known and unknown people while describing travelling to meet friends for a social occasion, participant 5 expressed concern about having to disclose her OAB symptoms to a stranger, clarifying that she would be more comfortable asking someone she knew to stop the vehicle but felt embarrassment at having to do so with a stranger, commenting: *"you don't really want to, inform him of my er, problems!"*.

Expanding on her embarrassing experience of extreme urgency forcing her to rush into an unfamiliar environment (described in 'urge and urge incontinence' above), participant 7 described having such a "desperate" urge, she made her husband drive into what she thought was an uninhabited alleyway in order to relieve herself into a polystyrene cup on account of not being able to *"hold it anymore!"*. The participant described being spotted by a stranger in a neighbouring bedroom window, with her demeanor relaying this story conveying the desperation of her urinary urgency, but also the extreme embarrassment of having been seen by the stranger. So much so, that she described having to abandon relieving herself there and had to find an alternative solution.

Such a preference to avoid embarrassment from strangers becoming aware of the participant's condition was echoed by participant 1 who described *"quickly running to the loo! hoping no-one's noticed!".*

Family and friends

Participant 1 went on to describe shielding his condition from scrutiny or discussion with even those close to him, opting to discuss it only with his *"medical advisors"* in a bid to avoid being judged as someone *“going to speak about his medical conditions again”.* For this particular participant, this theme of not wanting to be seen as obsessed repeated itself when he admitted to wanting additional support, but resisted going to a support group due to his previous experiences (for other conditions) leading him to feel that such groups were *“self-destructive”* and that those who did attend were too *“wrapped up in their condition”*

Participant 7’s story above also hinted at the effects of OAB symptoms on close family and friends, as the participant’s husband was mentioned as having to help find a solution. The participant went on to expand on how her OAB affected her husband, stating: *“me husband curses me for it I'm sure he does. Or used to - like I say I'm a lot better now, but a few years ago, when it wa really bad, he'd curse me cos, well- he kn-he knew what I was like! And I- he'd be feeling for me, because he knew I were desperate and he'd try and find somewhere for me to go”*, indicating a sense of conflict in that although the participant’s husband empathized with her, there was still a level of frustration of having to constantly contend with her OAB symptoms. A similar experience was relayed by participant 3 who stated: *“yeah it, makes a big difference to both* [participant and partner] *of our lives.”.*

Participant 6 described the embarrassment she felt when her close friends commented on her symptoms, stating that despite her friends *“know*[ing] *what I'm like”*, *“they make fun of it, but not in a horrible way”.* Echoing the experience of other people commenting on her urinary symptoms, as well as the resultant effect on her, participant 8 stated: *“everybody used to remark on it, you know? Like my sisters'd say, "you're not going again, are you?”*, adding: *“I used to fall out with her sometimes …”.* Participant 6 further added that she would censor her words and actions in a bid to avoid further unwanted attention from her close social group, thinking: *“’I hope I don’t need to go because they'll all make a remark...’"*. Participant 9 contributed to this theme by stating: *“I don’t speak about it* [OAB]*”*.

In contrast to the experiences outlined above, participant 12 offered a uniquely different perspective of the relationship between her OAB experience and other people’s reactions, describing no embarrassment or any need to shield her symptoms from view: *“Women, understand women don’t they. Like when I go for a wee behind the bushes, they're* [friends] *like "oh yeah ###'s gone for a wee", just- [laughs]”* adding *“I'm-don’t really care what people think about me. I'm not a worrier about what people think. Y'know, I am what I am, and take it or leave it”.*

Comparing to others and downplaying symptoms

Participants generally compared their symptoms to others in a bid to either gauge the abnormality or severity of their symptoms (problem recognition), or to reinforce a sense of normality (downplaying symptoms).

Problem recognition

Participant 12 discussed several moments of comparison. First was the long-standing comparison to friends *(“since my 20's I've always noticed that I went for a wee, more than other friends”*), and the second comparison was with fellow golfers, where she realized that her symptoms were restricting her in living out her preferences (*“Some ladies come out n they've got a flask of coffee, and I think 'ohh I wish I could have that'-”*). Both of these instances helped her to recognize the issue at hand. Describing similar experiences, participant 3’s relatively more frequent use of the toilet became apparent while comparing suspected symptoms of the menopause with her friends, whereas participant 9 realised the extent of her urinary symptoms by comparing against a friend who was suffering from problems with her digestive rather than urinary system, commenting: *“I thought 'well, y'know I don’t want to get like that'”*.

Downplaying symptoms

In contrast to the above examples where participants used comparisons to their friends/peers to recognise the presence or true severity of symptoms, the examples below illustrate where participants used the comparison to others to reassure themselves that their symptoms were not *that* bad or were easily assailable (downplayed).

Participant 10 mentioned discussing her symptoms with her family and was reassured to get the sense that they were experiencing *"similar problem*[s]*"*. She went on to draw a comparison with others to downplay the severity of her experiences: *"probably wasn't anywhere near as bad as some people..."*, relaying a sense of comfort in knowing that the presence of symptoms was not anomalous, and a sense of good fortune in them not being as bad as they could be. A similar sentiment was shared by participant 11 (*"I've got another friend who who's a lot worse than me"… "now I was never that bad"*). Participant 11 went on to draw further parallels with others when the interviewer questioned her on whether she (like others) managed her symptoms by knowing where the nearest toilets were, to which the participant replied *"I wasn't obsessed with it, it wasn't that bad that I was obsessed. I mean I know people who've <u>got</u> to know where the toilet is".* While it is possible that this participant's symptoms actually were a lot milder than those of the people that she compared herself to, her repetition of variants of the words *"I was never that bad"*, and her labelling those who did keep an awareness of where the nearest toilets were as *"obsessed"*, this participant distanced herself from those that had problematic OAB symptoms, thereby indicating that she was using the comparisons to reassure herself and downplay her own symptoms.

Downplaying symptoms independent of comparison

In addition to downplaying symptoms through comparing them to other people, there was a theme of making light of symptoms that may otherwise be considered to be burdensome, independent of other people's experiences.

Participant 17 toned down the present burden of having to get up to use the toilet multiple times every night by comparing to how much more severe her symptoms used to be previously. Participant 12 followed a similar thread of describing her symptoms as *"not that bad"*, highlighting what she could still do despite symptoms (*"I can go around shopping for an hour and half, probably without, going"*). Participant 18 phrased the length of his experience with OAB as *"just"* four years, adding *"it's not a big deal"* to reduce the impression of how much his symptoms affected him, despite describing having to get up three times a night. He went on to describe how he had to catch up on his sleep by getting up later in the day.

Participant 13, started by admitting that the nightly waking did affect him the next day, but was quick to qualify the effect with the words *"a little bit".* He went on to describe having to *"just get used to it"* and getting *"on with it"*, contributing to the theme of normalising his symptoms (discussed below). The likening of his nocturia at its worst to the dogs waking him up was another example of this participant reducing and normalising his experience of OAB symptoms.

Participant 10 admitted wetting herself if she did not reach the toilet in time, but immediately qualified the severity of this by distinguishing between the volumes involved with these episodes of urge incontinence. Stating: *"I don't think I would have had a <u>massive accident</u>; it would have just been a little, leak probably. So I could <u>cope</u> with it",* the emphasis on "massive accident" and "cope" indicated that she was distancing herself from more severe forms of this symptom, while the description of merely coping with the symptom divulged the true extent of its effects.

Normalising symptoms

Related to downplaying symptoms, was the theme of OAB symptoms being normalised. This took the form of likening OAB symptoms or the effects of symptoms to normal everyday behaviours, or the participant getting so used to the symptoms as to establish a new norm for them. Oftentimes, OAB symptoms were considered to be part of normal natural processes such as ageing or menopause.

Getting used to symptoms / new norms

Participant 12 described herself as *“so used to”* OAB symptoms that they no longer stop her from doing anything, attributing this more to an acceptance of her symptoms, rather than coping well with them (*“if I wanted to abseil down a mountain- which I wouldn’t do anyway- I'd probably leak”*). She went on to describe that even her management strategy of using pads was something she did *“naturally, now”*, further reiterating that the symptoms and their management were part of a new norm for her. Participant 7 explicitly described getting up multiple times a night as a *“norm”* and went on to say that despite having to get up five times recently, the symptom was *“manageable”*. Participant 8 gave several examples of learning to recalibrate to her symptoms (*“got used to it, yes”* and *“y'you just learn to manage things”*). The view of *“living with it”* was also shared by participant 5 who described having to make regular stops in journeys, adding: *“other than that, no I live with it”*. Participant 5 linked the sense of resignation to live with her symptoms with her self-image as someone who *“don’t go out very much”*, adding that if this was not the case, she would *“have to rethink the whole situation”.* This self-image led resignation to symptoms was also echoed by participant 2 (*"It <u>does</u> bother me sometimes, but I-I-I'm just a putter-upper. Y'know, I just put up with things"*) and participant 7 (*"that's just the way I am"*).

Considering symptoms as part of normal ageing process

Another key theme contributing to participants seeing their symptoms as something "normal" was the belief that the symptoms they were experiencing were a part of the normal ageing process.

Participant 9 provided evidence of this by describing her symptoms with: *"I thought 'oh this is old age' [laughs] quite frankly. I thought y'know, this is <u>normal</u> fo-for older people"*. This was echoed by participant 11 who described deciding her symptoms were due to old age. Participant 2 also linked her symptoms to old age and reinforced this belief with the observation that these symptoms were shared by others above a certain age, thereby producing a sense of normality both by belief, and by comparison to others (*"I put it down to old age, but I don't know! [laughs] there's that many people that are older that say 'ohh'- y'know you've mentioned anything, to them y'kno- and 'oh I'm the same' you know"*).

Participant 10 however, summed up the experience of most participants in our study, by describing a general sense of resistance to recognizing OAB symptoms (either by way or downplaying, normalising or attributing to age as seen previously), followed by a tipping point where help was sought (*"You don't want to kind of admit that you've got a problem when you're- your just think 'oh I'm getting old and it's probably <u>that'</u> but I think, when it reaches a certain level, and you-you're not prepared to put up with it anymore"*).

Summing up the theme of symptom normalization, and offering a powerful illustration of symptom normalisation, and its effect on participants' lives participant 13 stated: *"if you're not <u>careful,</u> whether it was taking medication or anything else, or making lifestyle changes, it- what's not right suddenly becomes <u>normal.</u> And you can sink into that very very quickly.*

And think "oh this is normal" and it's not. so you gotta do something about it early on I think".

A.iii) Coping strategies for symptoms

In contesting the unpredictability of OAB symptoms, and the fear of recurrence, participants often took it upon themselves to adopt precautionary measures, which was a key thread throughout the discussion of symptoms. These included the use of absorbent pads, planning ahead, sleeping tablets and other measures.

Absorbent pads

Participant 2 stated: *"if I go shopping, I always put a Tena pad on. Just in case"* describing it as a *"precaution"*. Participant 12 described adopting pads when she played golf, stating it was psychologically precautionary and for confidence, adding *"I wouldn't like to go out without my pad on"*. Participant 5 added that she would never leave the house unless she was *"padded up",* repeating the phrase *"well-padded up"* several times.

Pads were almost exclusively discussed by female participants, with a high level of acceptance of their use, even as a precautionary measure. In contrast, of the six male participants interviewed, none of them discussed using pads as a means of managing active symptoms, much less as a precaution. In the one male participant with which the interviewer brought up the subject of pads, there seemed to be much less acceptance of the use of such paraphernalia than with female participants with participant 1 stating it was not something he had considered: *"I haven't considered, but I haven't actually gone down that road".* The rejection of using pads to manage his symptoms was even more surprising given the fact that this participant had just finished describing the embarrassment of his urge incontinence. His phrasing seemed to indicate that he considered pads as somewhat of an extreme, or a distinct path from the norm, but was almost at the point of considering their use, given the nature of his symptoms. This begrudging acceptance was in contrast to what we saw with female participants and may to a large part be due to the fact that many of the pads used by the women in our study to help manage urinary incontinence were marketed as menstrual supplies, and so were both highly available and acceptable from an individual and social perspective for use by women. In contrast, as such pads for males would be exclusively for urinary incontinence, this may have contributed to them being seen as a less preferred option, meaning there was a higher barrier for their adoption for men as seen in the above example.

Forward planning

Continuing with the theme of a sense of safety achieved through adaptive behaviours, several participants described the sense of safety and confidence they fostered in their day to day lives by planning ahead and modifying their daily behaviors. The most commonly employed strategies included participants:

- keeping an acute awareness of the locations of nearest toilets,
- using the toilet pre-emptively, and
- gravitating to “safe” locations such as familiar places, and the participant’s own home

Awareness of toilets

The importance of knowing where the nearest toilets were located was summed up with several participants describing their experiences with variants of *“planning your day around being near a toilet”* (participant 13) and *“life around toilets”* (participant 7). Having a knowledge of where the toilets were was a key driver to the pursuit of a feeling of safety as illustrated by participant 5 who stated: *“Sainsburys have got loo’s, so, you think ‘if I need a* *loo, I'm alright'"*. This was echoed by participant 7 who admitted that she actively planned social interactions in places where she knew there were public toilets she could use if needed, participant 3 who stated: *"I started, planning I'd know where every toilet in series is"*, and participant 12 who summarized her experiences on holiday with *"I'm always thinking 'where's the toilet' and even I don't want to go, I need to know where they are"*.

Pre-emptive use of toilet

Many of the participants mentioned using the toilet before going out as a matter of routine, regardless of the immediate need to void their bladders. Participants 8 and 10 captured this with: *"I go because whether I wanted to or not because I need it, just to be safe"* and *"even if I-if I maybe didn't need to go, I still, went!"* respectively. Pre-emptive voiding was generally employed as a safety measure, and a way to exert some control on OAB symptoms by at least delaying the need to use the toilet while going about their day, as illustrated by participant 12 who mentioned *"I always have a wee before I go out"*, linking this to her ability to complete her shopping with relative ease. Participant 5 added: *"always make sure the last thing I do before I leave the house is- go to the loo"*, further describing pre-emptively using the toilet while at the hospital for appointments to ensure she felt safe in continuing her day without incident.

Safe spaces

Participants also mentioned places associated with feelings of being safe from the effects of OAB symptoms. These were most commonly places of high familiarity, where others would not witness or be affected by the participants' symptoms. Examples included participant 6 describing retreating to her bed upon being upset by her symptoms to *"shut off"*. She went on to discuss the perceived safety borne not only from the geographical familiarity of a friend's apartment, but by the social surroundings also (*"in- a friend's apartment, I'm safe.*

and I know like, they know that I can't control"). Participant 5 described her house as he *"safety net"* and *"safety zone",* with participant 1 discussed the relative safety of having an episode of enuresis in his own bed vs having one while staying away, citing embarrassment as the chief component of this distinction.

Other measures

Other measures employed by participants included:

- sleeping tablets,
- fluid restriction,
- avoiding triggers such as caffeine and alcohol

Sleeping tablets

A surprising strategy was the use or the attempted use of sleeping tablets to escape the sleep disturbances of nocturia specifically. In the case of participant 14, the participant recalled that the GP had prescribed him sleeping tablets specifically to give him reprieve from the regular sleep disturbances and to *"have a good night's sleep"*. The notion of entering a deep sleep to avoid nocturia was also echoed by participant 7, whose own request to the GP to prescribe sleeping tablets for this reason was denied, stating: *"but they don't-they won't prescribe sleeping tablets! They don't let you have them!"*. In contrast however, participant 6 found the effect of such tablets to be problematic as they caused her to experience enuresis due to sleeping too heavily *("because it made me sleepy, and I would go deep- I wouldn't know I'd weed"*).

Fluid restriction

The most common strategy under the theme of fluid restriction was for participants to curtail fluid intake beyond a certain time in the evening to avoid symptoms leading up to and during their sleep. This strategy was used by participants either on their own volition, or under HCP guidance. Participant 2 described experimenting with both the volume of fluid she drank as well as the timings to avoid symptoms at night, with little success. This experience was echoed by participant 10 who stated: *"I did try to not drink so late at night. I thought oh maybe it's because I'm having a drink y'know too soon before I go to bed. But even that didn't really seem to stop it"*. Participant 6 first shared her experience of restricting fluids during the day to avoid symptoms, going on to offer an example of extremely restricting her intake of both food and drink to control her symptoms. In recognizing the extremity of her restriction, the participant did go on to express concern at the risk of it becoming a regularly adopted measure to control her symptoms. Participant 15 highlighted a further motivator of fluid restriction during the day, on account of her comorbidities limiting her choice of toilet facilities to public disabled toilets, and the additional issues with doing so: *"of course being that I'm also disabled, that makes it even more difficult. Because I can't use the ordinary toilet".*

Recognizing and avoiding triggers

Caffeine and alcohol were the most commonly recognized symptom triggers that participants were aware of. Participant 17 noted: *"I know if you have alcohol, I go to the loo more frequently"*, echoed by participant 16 who stated that alcohol *"does tend to make it worse, particularly the getting up during the night"* , further adding that he restricted himself to one caffeinated drink per day.

Across the interviews, caffeine intake was described as a very habitual practice. Participant 4 summed up the contrast in alcohol consumption and caffeine intake by outlining her practice of consuming *"weak"* tea and coffee regularly but restricting alcohol to big celebrations only.

While some participants described highly ingrained habits of drinking caffeinated drinks as a matter of routine (participants 2, 11, 12, and 17), not all participants found it difficult to break the habit of tea or coffee drinking. Participant 13 recognized the diuretic effect of tea and cut down his caffeine intake, replacing his morning tea with another warm beverage, with notable effects on his OAB symptoms. Similarly, participant 6 chose to give up on caffeinated drinks after repeatedly being asked about them by her HCP: *"if I give it up, then maybe it'll make a difference, cos I keep being asked am I drinking tea and coffee- I don't drink tea and coffee anymore now"*.

A.iv) Attitude to medicine-taking and adopting lifestyle advice

Participant 8 gave an example of her perception of the necessity of taking treatment when describing her experiences with side effects to medications in general, confirming that she weighed up her perceived need to take medication against the possible side effects, describing those she adhered to as *"worth it".* This was echoed by participant 16 who described her thinking on deciding to take a medication if it was deemed *"necessary" "as long as there are no side effects that are noticeable"*.

Participant 17 added to this when discussing her thoughts on being offered a new medication for OAB (having discontinued her previous treatment). She stated her preference for not taking medication, going on to say that she would consider taking it if she knew that there would be tangible benefits: *"well if I can go without, taking the medication- fair enough but if there is any proof that it will improve the symptoms, by all means I would have a go at it".* She later put this in context with the treatment she already took for her other conditions and reemphasized her position on taking more tablets, reiterating that she would take them only if they were proven necessary, stating: *"to be taking more tablets I* *think it's the thought of taking all the extra tablets? if they're necessary y'know, by all means I-I'll take it!".*

A further example was given by participant 13, who held strong beliefs against taking long-term medication, stating he didn't *"believe it, at all".* He described himself as being careful with what he ate, linking this to his belief of it being *"madness"* to risk taking a *"concoction of chemicals".* Participant 13 reinforced this attitude later in the interview, linking it with his decision to take his OAB medication only on an as-needed basis rather than regularly, stating: *"I didn't stay on them"* despite being convinced that regular usage would mean to not *"ever have any sort of immediacy to wee. urges again".*

Participant 10 expressed a similar line of thought against increasing the dose of her OAB medication, despite knowing that it could help her symptoms, based on her judgement of the necessity of doing so. When asked how she had reached this decision despite acknowledging the potential benefits to her, she stated: *"I take quite a lot of medication anyway, for other, conditions. And I just don't want to take more than is necessary"*.

Building on this, participant 7 expressed a strong opinion relating to the risk and benefits to medicine-taking. Framing the question of necessity as *"well I think if it's a matter of life and death, or if it's definitely going to help, then ok"*, this participant admitted that she would advise others against starting OAB medication, despite having had some relief from taking some herself. The words *"sometimes the side effects are worse than what you were taking that medication for"*, reflected her own experience with what she described as waking up with a *"really thumping bad head"* which was the main driver for her having stopped adhering to her own OAB medication. She went on to reiterate her general attitude to medicine-taking with the statement: *"If it works, and I'm better with it, I'll carry on taking* *it"*, summarizing the effects of efficacy, side effects (quality of life) and impact on adherence*.*

Participant 5 gave her general attitude to medicine-taking by describing the importance of exercising her own choices, stating: *"I'm choosing to, do it my way aren't I?".* She went on to describe that despite the drawbacks of not taking medication, at least this way she was not exposing herself to more danger of suffering adverse reactions and complications. She referred to a previous episode where she had been left hospitalized upon being given the wrong blood pressure tablet, an experience that had left her with a wariness towards taking medication since. She reiterated this experience, and her resultant perception of the risks and benefits of treatment as being a key factor in shaping her attitude to medication taking. As evidenced above, in general, participant judgement of what constituted 'necessary' in terms of taking medication was largely based on their beliefs of the balance between the risks and benefits of doing so rather than acute changes in lifestyle or circumstance.

Participant 12 however, provided a contrasting view, presenting a contextual appraisal of how necessary it was to take her medication. The participant described initially deciding not to adhere to her OAB medication on the grounds of not being *"convinced they were working",* as well as doubting her OAB diagnosis, stating: "*I wasn't convinced that it was just an overactive bladder I had. It was more of a weak bladder".* She later restarted her medication when the need to control her symptoms long enough to enjoy a new hobby changed her perception of what was necessary, commenting: *"but then when I started picking up golf, it's more important to me, so I went back on 'em".*

Attitudes to lifestyle advice

On the other hand, this type of context-based adherence was more common in the adoption of lifestyle advice where participants were more likely to adhere to it if they felt it was compatible within the context of their lifestyles.

Participant 17 acknowledged that her current behavior of having a hot drink late in the evenings *“might be too late actually-for the bladder”.* She showed some reluctance in adopting a behavioral change to restrict her fluid intake in the evenings on account of the required change in a long-ingrained lifestyle routine of *“always* have[ing] *a hot drink before I go to my bed”.*

Participant 5 added to this thread by describing similar lifestyle advice she received on fluid management, recalling smiling to herself in disbelief, knowing that she would not be able to uphold the advice in relation to her lifestyle, stating: *“I came away smiling, cos I thought "this rate I’m gonna have to have an alarm clock round m'neck!”* (referring to the strict protocol of *“you should have approximately 200mls, say 8 o'clock, and then another 200mls about 11 o'clock, and keep this going”* and *“when it gets to half past eight, if you're going to bed at half past ten, don’t drink anymore!").*

In another example, while allowing for the possibility that the pelvic floor muscle exercise could have helped her symptoms had she *“done it properly”*, participant 12 admitted that it was not so much accepting their merits, as it was actually incorporating them into her lifestyle that she found difficult, and ultimately impracticable, commenting: *“pelvic floor? Hmm, well I'm not against doing them. It’s just, doing them!”.*

Participant 7 spoke about not quite managing to adhere to the lifestyle advice of avoiding caffeine, due to her preference for having coffee in the morning and throughout the day. The sense of reluctance to disrupt a routine part of life was reiterated with this participant commenting: *“I have two, caffeinated coffees in the morning, so I know if I go out before lunch, there's gonna be- maybe a problem. While I'm out”*, highlighting a preference to account for the consequences of not following this piece of advice, rather than to adhere to it. Participant 7 went on to add that she tried to follow other lifestyle modification advice for OAB but stated: *“but after a couple of weeks you forget don't you and just revert back! [laughs]”*.

Forgetting medication / ease of adherence

Generally, participants reported few problems with medicine adherence borne from forgetting to take tablets, or unintentional non-adherence.

Participant 2 described being *“ok at remembering”* to take her medications in general, drawing a distinction between the OAB medication she chose not to take, and all her other medications which she remembered to take on a daily basis, stating: *“I'm ok at remembering, I take-like I say I remember all me other tablets I take every day”*.

Similarly, participant 17 described having *“no challenges at all”* in taking her medication, with participant 8 echoing these sentiments by describing taking her medication as *“automatic”* and giving her *“no challenges at all”*.

Other participants described the process of taking their medication with descriptors such as *“simple”* as with participant 11, who went on to say she did not forget to take her medication, and *“no problem”* by participant 4.

A.v) Strategies for medication adherence

Participants described several strategies they used to try and remain adherent with their medications. Of these, the most commonly employed were incorporating medicine-taking into a daily routine, either as a matter of habit or by binding it to a daily occurrence, and keeping medication in a visible place, to remind themselves to take it.

Establishing a routine

Participant 10 described having *"a set time"* she took her daily medication, confirming it was part of a conscious routine to support her adherence. This was echoed by participant 17 who described taking her medicines *"as a routine"* and described taking treatments for multiple conditions at the same time to avoid forgetting any one of them. This was aided by the fact that her other medication (statins for cholesterol and amitriptyline for diabetic neuropathy) were already indicated to be taken in the evening. She went on to describe *"never having problems"* with her medication using this routine.

Participant 12 described taking her OAB treatment *"just before I go to bed"*, adding that on the occasions where she had failed to use her inhaler during the day as instructed, tying its use to her bedtime routine and OAB tablet-taking routine enabled her to incorporate some use of her inhaler into her day.

Participant 11 contributed to the current theme by giving primacy to her medicine taking upon waking by stating: *"I get up in the morning, I- before anything else, I take my, blood pressure tablet, and my, oxybutynin".* She went on to expand on the sense of routine by tying her evening medication-taking routine not only to her own medications but also to her husband's nightly medication-taking routine to ensure that she did not miss taking them. She commented: *"the last thing we do before going to bed is- my husband, that's all he takes, is a statin, and I take me statin and me oxybutynin!"*

Other participants established a routine by attaching their medicine-taking behaviors to daily occurrences such as mealtimes or sleep times. Participant 6 gave a good example of this type of routine by associating her evening meal as the time to take the bulk of her medication, commenting: *"soon as I sit down to eat me tea, which is normally about 8pm, I take my tablets".* She went onto link taking the remainder of her medications to her sleep and waking times. This was also emphasized by participant 9 with the words *"when I have my breakfast, I take my tablets".*

Participant 16 reiterated that with his routine of having his medication *"out, onto the table, ready for me to take as soon as I finish my breakfast"*, remembering to take his tablets was *"not a problem"*. He illustrated the point using his blood pressure treatment rather than his OAB medication to further demonstrate that non-adherence to his OAB medication was a choice, rather than an unintentional omission.

Keeping medication in a conspicuous place

Often used in combination with the above theme of establishing routines, another strategy employed by participants to help adherence was to keep their medications in conspicuous places, or within eyesight.

Participant 3 described keeping her medication in prominent places such as *"on top of the bread bin"* and in her *"eyeline"* around the house in locations linked to her morning routine (e.g., *"by the kettle"*) in a bid to further remind herself to take her medication. This was mirrored by participant 10 who kept her medication *"next to the bed yes. On my drawers, sort of, all together"* to remind herself to take them before going to bed.

Participant 12 spoke about her difficulties in remembering to use her inhaler, and as highlighted in the previous theme, attached its use to the ingrained habit of taking her tablets before going to bed. She went on to discuss leaving both her inhaler and OAB tablets in conspicuous places such as *"bathroom sink"* in order to *"see them, all the time"* to help this further, though admitting: *"I do take me inhaler, but nowhere near as rigi-everyday like I should"*, and concluding: *"So, the only strategy I've got is having it in sight".*

Other strategies

Other strategies mentioned by participants included the use of pre-packed dosette boxes, (prepared by the pharmacy to house a week's worth of medication arranged into pre-defined intervals), and one participant mentioning writing on his boxes of medicine to remind himself of what time to take them.

Participant 1 described trying to take his tablets upon waking but admitted that that *"doesn't always happen... for many reasons"* stating, *"I can be forgetful"*. He went on to describe now having his medications delivered to him in dosette boxes so as to aid his adherence. He stated that this approach was helpful as *"when you're on so many tablets, and they're all in different bottles and jars"*, remembering if he had taken a particular tablet had become more difficult. Participant 8 and participant 12 used an alternative descriptor of dosset boxes, calling them *"blister packs"* to describe a similar approach.

Participant 15 described a similar, albeit self-derived strategy to support adherence to his medications by writing on the box *"whether I take it at morning or whether I take it at lunchtime, or whether it's in the evening"*, to make it easier to stick to the correct ones at the correct times. He cited his poor eyesight as the reason why clearer demarcation was required than the label the boxes came with.

Problems faced with strategies

Strategies described in the previous section were not without issues, and further context where provided, is given here.

Although participant 12 mentioned that she kept medication in her line of sight to help her adhere, she went on to say that while this strategy did help her with her oral OAB medication, it did not quite work for her inhaled medication. Similarly, participant 9, who described her daily routine of taking medication in the mornings around breakfast time, admitted that if a new medication required dosing outside of her set routine, taking it *"probably wouldn't happen- cos I take them all together".*

Participant 10 added that despite the array of potential strategies, adhering to treatment is *"down to you isn't it really to remember to take it!".* She added that she found it easy to adhere as she didn't *"have a terribly busy life"* and was *"usually at home"* at the time she had to take her treatment, noting that she found more difficult *"if I'm out somewhere"*. These comments thus linked the fragility of a routine established by temporal or visual cues as being dependent on the extent to which a person was *"busy"* or found themselves within the same environment in which the routine was established.

Related to participant 10's comment on remembering to take treatment, participant 3 who's primary adherence strategy was keeping medication in sight, expressed concern about how effective this might remain if her memory started to lapse, commenting: *"I don't know if it'll be like that when I'm getting older and haven't got such a good memory!"*. She concluded that like her mother, she would start using alarms to remind her to take her medication.

Dosette boxes may be considered to offer a simple and regimented way for participants to get into a medicine-taking routine by encapsulating all the participant's medications into a single weekly pack. Described by participant 1 as being *"fairly straight forward"*, he went on to describe that their use was not without hazard. He stated: *"the worse one is, having a box upside down, and suddenly realize that you've taken your evening tablets first thing in the morning"*, with the realization stemming from suddenly feeling drowsy (from having taken his evening sleeping tablets in the morning).

B: Support

Participants described a consistent disconnect from their primary care provider with respect to their OAB support. This was expressed throughout the symptom reporting process, through to diagnosis, prescription of treatment, and GP medication reviews.

B.i) Reporting and diagnosis process

Reporting

There were several subthemes under this stage of the participant journey. The first, related to the previous theme of normalising symptoms, was the topic of incidental reporting where participants did not go to their HCP's specifically for their urinary symptoms but mentioned it while there for something else. Participant 8 described having bothersome overactive bladder symptoms for over 45 years and not seeking medical support, only mentioning her urinary symptoms in passing when visiting her Practice Nurse for a medication review. The nurse consequently referred the participant to a GP for diagnosis and treatment. Participant 11 recounted a similar experience, stating: *"so I went to the doctors, and I said, 'oh while I'm here, I think I've got a problem with my bladder!'"***.**

Related to this behavior was the length of time participants tolerated symptoms before actually seeking help, which was itself often related to a threshold that had to be reached before participants felt compelled to seek help. Participant 12 commented that she had *"put up with it for a while"* before seeking help. Participant 13 admitted that he *"just didn't bother"* seeking help, stating that he thought his symptoms were borne from a self-limiting infection. Other reasons given for delayed help-seeking behaviours included a perceived slow onset and progression of symptoms (participant 18), being unaware of the availability of medication (participants 3 and 10), and erroneously fearing that surgery might be needed (participant 16).

The process of reaching a personal threshold before seeking medical help was encapsulated by participant 10 with the words: *"You don't want to kind of admit that you've got a problem when you're- your just think 'oh I'm getting old and it's probably* *<u>that.'</u>* *but I think, when it reaches a certain level, and you-you're not prepared to put up with it any more"*, thus highlighting normalising symptoms by their denial, as well as a point at which the symptom bother became too great to continue this. Participant 6 described the realization of an upcoming trip abroad to see family as the prompt for her to finally seek help.

Diagnosis

The participants' experiences of the diagnosis process itself offered a mixture of views ranging from descriptions of *"easy"*, and *"simple"* (participant 10), to experiences of drawn-out testing and specialist referrals, with ultimately unconvincing diagnoses.

Positive diagnosis experiences were reported by those who described: good relationships with HCPs (participant 11: *"a GP that I could talk quite easily to"*), the perception that their GP was knowledgeable about their symptoms (participant 3: *"because she immediately said 'it could be an overactive bladder'"*), and a swift or immediate solution (participant 9: *"when she had examined me, she said 'right, I'll get you in straight away'"*).

Conversely, other participants did not have quite the immediacy between describing symptoms and receiving a diagnosis. Participant 14 described a lengthy process between going to the GP, being trialed on an antibiotic under the assumption of having a bladder infection, only to be referred to a specialist upon this not resolving his symptoms, and eventually being prescribed a drug for his symptoms. Participant 7 described a similar process of lengthy referrals and being thoroughly tested, to find *"there's nothing wrong, its fine"*, receiving an OAB diagnosis by default as *"that's all they could say cos they couldn't find* *<u>anything</u>* *wrong"*. Variants of the words "nothing wrong with me" was used by participants 13, 6 and 5, laying the ground for doubts about the diagnosis they had received when the objective tests had found no anomalies.

Unconvinced of diagnosis

With the above theme in mind, perhaps unsurprisingly, some participants were left in doubt about their condition, and the conclusiveness of their diagnosis. Participant 2 described her GP originally diagnosing and treating for a UTI before shifting to supplying OAB treatment, with the inaccuracy of the first diagnosis causing uncertainty with the subsequent one of OAB. Similar doubts with the diagnosis were expressed by participant 17 (*"one minute they'll say that "you've got <u>something</u> in the urine" and another time there is <u>nothing</u>"*), participant 7 (*"I've got an overactive bladder, but I don't know if it's an <u>irritable</u> bladder- I don't know!"),* and participant 11 who stated: *"I've <u>never</u> had anything diagnosed about it"*, indicating her perceived disconnect between the actions of her GP (diagnosing and prescribing), and her knowledge of why she had been given treatment.

The latter point was built on by participant 17 who complained of little information being given to her during the diagnosis, and the lack of a detailed investigation *("<u>All</u> I was told, "oh you've got overactive bladder" and nothing else"*). What permeated through the discussion with this participant ultimately, was less the need for diagnostic evidence, but more the absence of a good, communicative relationship with her HCP where she felt supported. This was evidenced by her asking the interviewer basic questions regarding her care, indicating that she had either not had such conversations with her HCP, or was left unconvinced by them: (*"well would it be only medication that could help the symptoms?"). H*er poor relationship with her HCP was also evidenced by her description of them being uninterested, using the descriptor *"fob you off"* to describe their behaviours toward her.

B.ii) Prescribing

Tentative language

Participants reported the common experience of having the prescribing of OAB medications framed by language that made taking such medication seem experimentative or like a trial for the participant.

Participant 3 recalled the GP using the phrase *“we’ll try these tablets”* to introduce the treatment to her, thereby hinting towards the notion that the prescriber too was experimenting by selecting this particular drug first. This was followed with the statement *"there are different ones we can try"*, thereby reinforcing the perception of trial and error. Similar experiences were relayed by participant 7 about her HCP (“*’oh well try these ones!’*”), participant 9 (*“"try the tablets, see how you get on"”),* and participant 17 *(“’I'll give you these, see how you go’”).* Participant 12, more explicitly spoke about doubting whether the GP himself was sure the tablets worked or not, and linked this to the notion of a lack of available evidence to support their efficacy, further supporting the theme of OAB medications being prescribed on a trial basis. Participant 6 recalled a similar experience with her hospital-based specialist who reinforced the idea of an experiment by using the words *“’try this one, it might be a lot better’”*.

The effect of this kind of language was seen with participant 16, who although primarily stopped his medication due to poor efficacy, used the perceived trial and error basis of prescribing as a secondary reason to do so, stating: *“it didn’t do a lot of good, no. It was a trial and I think, probably better without it to be honest”*.

Bringing together the themes of an unconvincing diagnosis and the language used by his HCP, participant 13 stated: *“I think he just wanted to get rid of me. He sent me for all the* *tests, and he couldn't find anything, so I think he just said, 'try these'"*, linking a perceived flippancy of experimental prescribing with apparent inconclusiveness of diagnosis.

B.iii) Medication Reviews / HCP engagement

Participants described a varied experience with medication reviews and support from their HCPs. Linked to the observations around the relative importance of different conditions (condition hierarchy- see below), participants broadly reported an imbalance between reviews for the OAB medication against other conditions

Participant 11 described the absence of any formal reviews for her OAB medication, drawing a stark comparison between them and the regularity of her kidney checks, which had *"nothing to do with the* [OAB] *tablets"*.

This relative difference in HCP focus between conditions was also mentioned by participant 8 who described being *"on a lot of medication"* necessitating 6-monthly medication reviews at the surgery, during which her OAB medication was *"never mentioned"*. She went on to recall the Practice Nurse broadly asking *"if I've got any problems with anything but… I just said no. and … that was it"*. While also mentioning that the reviews themselves were *"about 8 minutes"* long, participant 8 indicated that with the time constraints, only those medicines that were causing specific problems to her were given prominence during the review process, which was focused on problem solving, rather than optimizing her care.

The notion of time constraints with the review process was echoed by participant 12, who stated an absence of reviews regarding her OAB, and added that he regarded GP's as *"too busy"* to conduct monitoring reviews, suggesting *"There's plenty of continence nurses, or physios that could offer, that service".* Also stating an absence of reviews covering his OAB medication, participant 13 acknowledged that it would be *"helpful"* to have such discussions, highlighting an unmet need with the current situation.

Participant 10, offered further evidence on the perceived difference between HCP focus on treatments for OAB and other conditions, responding with *"not about that tablet, no"* when asked about reviews of her OAB medication. She echoed other participants' experiences of OAB not being featured in routine reviews with the words *"but I think, if I wanted to talk about it, I would just go and make an appointment"*, indicating the separation of her OAB medication from her usual medication reviews.

Participant 5 described the disparity between the written instructions on her OAB repeat prescription detailing the need for a review before further repeats could be issued, and the real-life practice of the repeats being issued despite no reviews occurring, stating*: "I don't think I'd ever actually be phoned up and said, 'you must come in for your review'"*. She went on to compare her experiences to those of her son, who because of his learning difficulties, was automatically offered annual reviews, thereby reiterating the sense of comparative importance of conditions in the review process. Similar experiences of repeat prescriptions being issued without the requisite reviews were also relayed by participant 13 and 7, with participant 7 adding that although one was due several weeks prior to the interview, no one had chased this with her, leaving her to conclude *"nobody's said anything, so they're not bothered!"*, contributing to the theme of clinicians not caring about OAB.

This behavior of wanting the review process to be initiated or at least prioritised by the surgery was seen with participant 17 too, who described not having any reviews, but if she was offered one, would *"happy"* to attend.

Participant 2 took this further by describing being instructed by her GP to make an appointment for a medication review, but not following up with this, admitting: *"it's my fault, my fault. Yeah"*. She went on to repeat that she would have liked for the surgery to have proactively followed up and chased her to arrange a review, again admitting her own shortcomings in arranging one, describing herself as *"lazy"*, despite acknowledging the usefulness of having reviews. She reiterated participant 7's perceived indifference from the surgery by describing their failure to notice her non-adherence: *"y'know its 18 months, you'd think th-they'd notice I'm not having it! Y'know it's, but-no".*

Participant 9 described being prescribed her OAB tablets without being given a lot of additional information: *"they didn't really go-they-this- they just said "these will help*". On the subject of medication reviews, the participant outlined those undertaken by her local pharmacy. Her account fitted the description of a pharmacy Medicines Use Review (MUR), an Advanced Service within the NHS Community Pharmacy Contractual Framework designed for pharmacists to conduct medication reviews to help participants manage their medicines more effectively (Latif, 2018). Interestingly, as a key NHS service for which pharmacies receive a fee for provision, this type of review is likely to have been initiated and pursued by the participant's regular pharmacy. Despite this, and the fact that MURs are designed to occur annually, participant 9 only reported having one every other year, describing the review as going "to a little room" to "ask about my tablets". The participant stated: *"what the outcome of it is, I don't know"*, thereby indicating a lack of explicit connection of these reviews with decisions related to her healthcare.

Participant 1 found it difficult to discuss his health concerns with his family and friends, upon fear of being seen as someone who always talked about his ailments. Similarly, he described support groups as *"self-destructive"* with attendees as *"wrapped up in their conditions"*, highlighting a potential perceived downside of being too vociferous in such matters. On the subject of reviewing his OAB medication, the participant admitted to having to take a lead with his OAB medication, something he was reluctant to do, opting to discuss his most recent OAB medication issues when he next went into the surgery for another matter. The participant went on to describe his wish for a "*regular review*" to ensure that his medication was having the desired effect, offering *"every couple of months"* as a suggested ideal frequency, to allow him to make alternative arrangements if this was not the case. He described that this review did not necessarily have to be with the GP, or even face-to-face, suggesting the practice nurse or pharmacist as well as telephone consultations as alternative routes to achieving better care for himself and others.

Not all experiences of medication reviews were negative; some participants described more supportive arrangements. Of these, participant 16 was very complimentary of his GP surgery describing them as *"readily"* receptive to feedback and willing to investigate any issues. He described his medication review process as having been lacking only due to his reluctance to go and see his GP, stating *"it's probably, my-my fault for not going back, but when you're not really that ill, you don't like to bother them"*, offering evidence of downplaying his own problems against the needs of those *"who really are ill"*.

Participant 3 also held very positive views of her surgery, describing her GP as *"really good"*, in the context of offering the participant an open invitation to return for a review or to work through any further issues the participant may have had, expressly mentioning *"she said to give her a ring if I had any problems with it-if it* [the medication] *wasn't working, if I wanted to review sooner, to go back in"*. Highlighted above, a similar instruction to participant 17 was insufficient to achieve a comparable outcome, thus demonstrating the importance of the broader context on influencing engagement behaviours.

Finally, despite being given similarly brief information at the point of prescribing as others have outlined, participant 4 described feeling *"very confident"* with her consultant. This stemmed from having had her husband under the same clinician's care previously. She described the consultant as a *"very experienced chap"* and went on to describe her overall experiences with her HCPs and their support as *“very satisfactory”*, placing extra emphasis on the word “very”. This positive experience was reinforced with her experience of the treatment he prescribed, and the impact on her lifestyle with the participant commenting: *“he'd made the right decision for me. And as I was taking it, the med-the detrusitol, th-the problems, were erased. I didn’t need a pad”,* connecting the perceived efficacy of the treatment with the clinician’s demeanor and expertise.

C: Discontinuing treatment

In the current section, core findings will be presented on the explicit reasons given by participants for not adhering to OAB medication. As this section forms the crux of this report, bringing together elements from other sections, the reasons for OAB medicine discontinuation will be presented in two ways for clarity and depth. A summary is provided in the form of Table 4.4, of the broad or overarching reason(s) given for OAB medicine discontinuation, as well as a more detailed breakdown of the participant perspective and context from those that shared this level of detail during the interview process. Often, more than a single reason was given as contributory to discontinuing treatment. In these cases, the secondary reasons will be described alongside the primary in the text below.

Table 4.4: Reasons for discontinuing OAB medication

Participant Number	Age	Sex	Primary reasons for discontinuation	Other reasons
1	64	M	Lack of efficacy	Tablet being “nothing special”
2	66	F	Side effects	
3	58	F	Did not discontinue	
4	69	F	Lack of efficacy and requirement for ECGs	Fear of unknown effects
5	71	F	Side effects	Taking too many tablets
6	57	F	Waning efficacy, side effects	Botox
7	70	F	Side effects	Taking too many tablets
8	77	F	Lack of efficacy	Suspected side effect

9	80	F	Side effects	Fear of unknown effects
10	58	F	Side effects	Aversion to dose escalation, wanting to switch medication
11	78	F	Did not discontinue	
12	61	F	Lack of efficacy, side effects	Unconvinced of OAB diagnosis (more a "weak bladder")
13	65	M	Fear of side effects	Unclear instructions
14	78	M	Lack of efficacy	Side effects
15	80	F	Lack of efficacy, side effects	Surgery stopped the medication because of potential cognitive effects
16	71	M	Lack of efficacy, side effects	Trial and error
17	67	F	Unclear instructions	Pill aversion
18	70	M	Lack of efficacy	
19*	76	F	Data not available	
20*	75	M	Data not available	

ECG = electrocardiogram, OAB = overactive bladder *discounted from analysis due to missing data

Not all of those who discontinued an OAB medication stayed off OAB treatment completely, as some continued on an alternative treatment. This information is provided it in the descriptions below where the participant described still being on OAB treatment at the time of the interview. Furthermore, while participants 3 and 11 met the inclusion criteria of having been prescribed an OAB medication in the last 12months, both were currently persisting with treatment. Their experiences were used to add weight to the experiential outcomes of interest.

Within the overarching theme of reasons for not adhering or persisting with OAB medication, the following subthemes will be explored below:

- Lack of efficacy,
- Side effects,
- Unclear instructions or engagement from the HCP,

The related drug/condition hierarchy will be explored within its own section further below.

C.i) Lack of efficacy

Participant 14 was a 78-year-old male retiree. He described his initial symptom of nocturia as *"having to get out of bed four or five times in the night"*, often with an accompanying sense of urgency, and occasional urge incontinence during the day. The participant was working offshore at the time of OAB onset and because his GP was in mainland UK, he did not seek medical assistance for two years from the initial symptoms, after which he started *"attacking the problem, seriously"*, giving an initial impression that such passage of time enabled him to recognize both the depth of the problem and the need for a proactive, combative approach to its resolution. His GP sent him off for a range of tests, to investigate his recurrent urine infections and other symptoms. After being referred to a consultant, who performed more tests including cystoscopy, the participant briefly mentioned that they had found an *"abnormality"* which he had removed from his kidney tube (without going into further detail). He went on to say that this treatment had ultimately not done anything for his initial urinary symptoms, which still woke him several times a night.

He was eventually prescribed *"a low dose antibiotic and mirabegron"*, the latter of which he described as an *"alleged"* muscle relaxant, indicating his dubiety of its effects. Upon questioning on his choice of words, he emphasized that this treatment had *"hardly any effect"*. He then went on to describe that both his consultant and he were "*hacked off that we're not making any progress!".* The participant used the phrase "hacked off" four times throughout the interview to convey his frustrations, summarizing with the phrase: *"what hacks me off is that I have not been able to get some medication that gives me a good night's sleep without taking sleeping pills. End of story*". The latter phrase indicated both an expectation of what his treatment should be able to restore to normality (having a good night’s sleep), as well as his expectations of the mechanism by which that restoration should occur. This was expressed as a continued unmet need with his urinary treatment, and dissatisfaction with sleeping tablets despite them delivering the desired outcome. At the time of the interview, the participant was due to see his consultant to review and change his medication to a more effective one for him.

Participant 14 went on to describe taking a sleeping pill three times a month to help him tackle the secondary effects of next-day fatigue from nocturia, as prescribed by his GP. He described polypharmacy consisting of eight different tablets for various ailments, expressing the possibility that some of his OAB symptoms could also be caused by other conditions (e.g., prediabetes) or the treatments he took for them, revealing elements of a doubted diagnosis of OAB. Alongside his chief concerns of the mirabegron lacking efficacy, the participant attributed a *“certain numbness in the legs, below the knees”* to taking the drug. He then went on to say that that effect in particular could also be linked with the arthritis he had in both ankles, reiterating his previous assertion as well as his earlier doubts of the link between his treatment and its effects (both positive and negative).

Overall, the primary reason driving this participant to discontinue his mirabegron was a perceived lack of efficacy. His linking of the drug to adverse events although reported, seemed tenuous even in the eyes of the participant who quickly supplied an alternative reason for them. His frustrations were added to by the secondary effects of nocturia as recognized with other participants, as well as a lack of a conclusive answer to his OAB symptoms. The fact that taking sleeping tablets did help his nocturia, but his urinary treatment (which he held higher expectations and preferences to) failed to do so was also interpreted as an additional layer of his frustrations.

Participant 12 was a 61-year-old retired nurse, whose career in healthcare had lent her a considered and pragmatic approach towards her own health as evidenced by her reasoned decisions to stop and restart her OAB medication based on her observations and judgments. Paradoxical to both her professional background and attitude to her health, she admitted that in general she *“didn’t remember to take”* medication, resulting in her having to *“come off”* treatments in the past, giving examples with the contraceptive pill, as well as her ongoing struggles with her inhaled medication for respiratory issues.

Throughout the interview, themes of a general aversion to tablets and visiting the surgery were apparent, illustrated by her self-description: *“mm! I mean I'm pretty, a big believer in the body does sort itself out”* (without treatment), which seemed at odds to her professional experience of recommending and implementing treatments in her own patients where their ailments did not “sort” themselves out. However, this belief too was marked with some realism the participant with the recognition that *"this* [bladder] *problem won’t sort itself out"*, and the acknowledgement that she would need help.

Having noticed initial symptoms in her twenties, (increased micturition frequency), participant 12 did not seek medical advice until her early fifties, indicating a perceived low importance and appetite for intervention spanning decades and the probable use of adaptive behaviours to cope with symptoms during this time. Upon being referred to a physiotherapist and having failed to incorporate the recommended pelvic floor exercises into her daily routine, she was eventually denied further visits with the physiotherapist on account of having missed two appointments which she described as *“unfair”*. The fact that the participant delayed seeking help for so long, only to be denied further appointments so abruptly may possibly have further contributed to her low sense of importance and priority to OAB. The participant was eventually prescribed OAB treatment but described it as *"on and off"* for the last decade.

The key drivers for this participant's non-adherence to OAB medication centered on her perception of its pharmacological action. This manifested in two ways; firstly, as clear doubts on the efficacy of her tablets (mentioned throughout her interview), and secondly, with the suspicion that they were causing her eyesight to worsen. She commented on the former with: *"well I went off it cos I - like I say, I wasn't convinced they were working. Didn't seem a lot better".*

The participant's perceived lack of efficacy was further reinforced by her assessment of the GP's demeanor while initially prescribing the drug as being *"unsure whether these tablets worked or not"*, signifying both the patient's perception and importance of the HCP's demeanor when prescribing. The participant linked this to an assertion that *"there's probably not loads of scientific evidence to say they definitely suit or whether or not they do work"* thus reinforcing her opinion on her treatment's lack of effectiveness.

The second reason participant 12 gave for discontinuing her OAB medication was the perceived adverse effect on her eyesight: *"ooh it might be affecting me eyesight, and that's more important than anything so, I stopped them"* giving a clear order of priority whereby urinary symptoms could be tolerated in order to protect from possible effects on her eyesight. The participant later reevaluated this perceived effect on her eyesight and attributed it to her advancing age rather than the tablets she was taking, resulting in her re-initiating treatment of her own volition. The main driver for this change of stance and re-initiating the same OAB treatment previously thought to be ineffective was the participant's adoption of a new hobby that required her to be on a golf course for several hours at a time, and the motivation to control her bladder symptoms while doing so. The increasing seriousness with which the participant took her hobby was reflected by her new approach to adhering to her OAB medication which she described now as taking *"every night"*, commenting about her inhaled medication: *"I don't even take that as much as I take these tablets!".* This highlighted the malleability of the participant's previous order of priority to changing circumstances, attitudes, and motivation.

The participant still maintained doubts on the effectiveness of her OAB medication but given their newfound importance in possibly enabling her to control her symptoms while playing golf, she had settled in continuing to take them. In effect, the priority given to the possibility of an adverse effect (and the resultant drive to stop taking treatment) had been supplanted by the possibility of a positive effect on bladder control, (and the result drive to maintain strict adherence), though both possibilities were equally tentative. This illustrated that the temporal and situational perception of the balance between risks and benefits exerted a distinct effect on medicine-taking behaviours from the actual management of such risks.

Participant 18 provided another example of a lack of efficacy being a key driver in OAB medicine non-adherence. A 70-year-old male retiree, this participant's initial symptoms were *"having to go to the loo, three or four times a night"*, which he described as having come on gradually. Having gone to the GP, who sent him for an ultrasound, he was initially trialed on tamsulosin (an alpha-adrenoceptor blocker), on account of an enlarged prostate. Having tried this for 3-months with nothing but a *"minor improvement"*, the GP then prescribed oxybutynin for OAB and advised for the participant to take the two together. The participant described the resulting changes to his symptoms as *"moderate, but I couldn't really tell it was providing any great improvement"*. He went on to describe that in addition to the lack of efficacy, the oxybutynin gave him a dry mouth, which further prompted him to stop taking it, indicating the multiplicative effect of both a lack of efficacy and the presence of adverse effects on adherence. Having told the GP of his decision to stop taking the oxybutynin, she advised him to stop the tamsulosin too. The participant was still symptomatic at the time of interview, waking *"probably three times a night"*, and managing his symptoms by waking later in the day to make up for lost sleep.

Participant 1 was a 63-year-old male retiree. He described symptoms of extreme and sudden urinary urgency leading to urge incontinence, as well as nocturia and enuresis. His GP started him on *"some medication, which, didn't work"* before referring him to a urologist who confirmed the OAB diagnosis. The participant could not recall the name of this first medication but described it as "i*t was probably the [pause] it wasn't anything special I thin- it was one of the most common they...prescribe",* indicating his low expectations for it. Such an expectation seemed to stem not only from the perceived ubiquity of what he had received, but a perception of his condition being distinct from that common to others, and therefore warranting something "special". His subsequent experience of having to go to a urologist for a more definitive diagnosis may also have affected this expectation of the treatment initiated before this stage, feeding into observations elsewhere in this work of tentative language, and trial and error in prescribing, and the impact on treatment expectations.

Having suffered from a range of medical issues, and undergone several surgeries on his bowels and liver, surprisingly, this participant's comorbidities were a driver for his adherence to his OAB medication, rather than a hinderance. Having had a fatty liver which then turned into cirrhosis, eventually requiring a transplant, meant that the participant took his OAB medication diligently to avoid any further urinary problems, despite the fact that he felt the medication did not work very well for him. This indicated that his fear of additional problems exerted a stronger effect on his medicine-taking behaviours than the actual efficacy (or lack thereof) he experienced.

After persisting with the first medication for 2-years, it was stopped by the GP following the participant’s liver surgery whereupon many of his medications were reviewed and changed. The participant described a brief period of relief from his OAB symptoms before they returned *“probably a little worse”* than before.

Having returned to the GP for another OAB medication, which he described as *“didn’t do anything at all. Still having the same problems”*, he persisted for another two months before going back and being put on solifenacin. Upon questioning on whether this third medication was having an effect, the participant reported that after two months of use, although he was experiencing no side effects, there was again no noticeable benefit from it. The participant went on to say that he would soon be making an appointment to discontinue the solifenacin and request for a fourth OAB medication. His words *“I will have to go back and see… what’s next”* indicated his understanding of the sequential nature of taking OAB treatment until he found one that did offer him the relief he sought. This also indicated his setting and resetting expectations of new medications with a set interval of time he would allow for each to show an effect before requesting a change.

Participant 16 provided another clear example of where a lack of efficacy led to discontinuation of OAB medication. A 71-year-old male, the participant described his initial symptoms as urgency and urge incontinence. He admitted to trying to cope with the symptoms for several months before deciding that he needed to *“have some investigation done”*, indicating a turning point in the previously assumed mechanism behind his symptoms and the need to determine this definitively. The participant described going to see his GP who referred him to a urologist with whom the participant underwent *“a number* *of detailed investigations"*, before being prescribed Mariosea XL (slow release tolterodine) at first, followed by mirabegron more recently. The participant reported feeling drowsy with this first tablet and decided to *"pack it up. Period"* within a few days of starting it because of this side effect. Giving conflicting accounts of his experience with mirabegron, the participant first said it *"really wasn't worth taking to be honest. Didn't seem to improve it at all",* commenting he still had to get up "*once or twice a night*". He later went on to say: *"Betmiga* [mirabegron] *calmed it down a bit",* indicating that although it may have had some effect, the mirabegron did not live up to the expected efficacy. He went on to summarise his reason for discontinuing the mirabegron with: *"I probably took a few doses of that and found it really didn't help so, I couldn't see much point in just taking drugs for, the-the benefit of just taking them, so, I thought 'well it isn't doing much good so, I, I'll leave it off'".*

C.ii) Bothersome side effects

Participant 15 was an 80-year-old female retiree. Her initial OAB symptoms were of incontinence, nocturia, and urgency, which she had started managing with incontinence pads at night, and eventually during the day too. She initially downplayed her symptoms to put off going to see her GP but eventually succumbed to seeking advice upon their worsening (higher incontinence volume and frequency). Her GP referred her to hospital specialist whereupon she was prescribed twice-a-day tolterodine.

The participant reported that the tolterodine did not improve her symptoms and left her with a dull ache in her stomach, which she put up with for four weeks before going back to her prescriber, who reduced the dose to once daily. She further added that although the ache got *"worse and worse and worse"* (a phrase she repeated throughout the interview), she persisted until the surgery called and instructed her to *"stop it immediately"* because of potential effects of the tolterodine on her memory and cognition. Although the participant seemed relieved to stop the tolterodine (commenting *“oh, thank you for that- so I came off of it”*) she had not chosen to do so on her own volition. This decision was linked to a preceding instance when the participant had tried to get the medication changed due to her OAB worsening, only to be informed by her GP: *“well, yes it* [the OAB] *does. It’s because you’re getting older and you’ve had children”*, contributing to the normalising belief that OAB is a normal part of ageing (see ‘symptom perception and other people’ above).

Following the GP practice stopping her OAB medication, the participant had been offered no alternative, and was left with the irregularity of wax and wane symptoms. The extent of her urgency was evidenced by the change in her demeanor towards the end of the interview, which had to be cut short to allow her to use the toilet. The way in which OAB treatment had been truncated without the provision of an alternative may also be a factor in the formation and reinforcement of a condition hierarchy (discussed further below).

Participant 5 was a 71-year-old female who described her bladder issues as having started in her 50’s with recurrent *“UTI’s”* (self-diagnosed). Her OAB symptoms included urinary urgency and frequency, which upon investigation by two consultants resulted in a diagnosis of OAB. The participant went on to describe her GP prescribing an (unknown) OAB drug suggested by the second consultant, which made her feel *“sick”*, which she described as *“just awful”.* Having discontinued this drug after a week and feeling the side effect dissipate, the participant was offered a change of OAB medication by her GP but opted to *“live with it* [OAB] *because I feel as though I take so much medication”*, citing this as another reason to not take her OAB medication. Considering that participant 5 had agreed to take the OAB medication to begin with, her change in stance was perhaps more attributed to her poor experience of the treatment than the feeling of being on too much medication, with the latter factor strengthened by the side effects she had experienced.

Participant 7, a 70-year-old retired carer described her initial OAB symptoms as a mixture of urge and frequency: *“I was going to the toilet, and within 5 minutes I was absolutely bursting to go again!”*. After seeing her GP who sent her for scans and tests, none of which showed abnormality, her doctor eventually gave her a diagnosis of OAB. Following this, the participant was prescribed one set of OAB medication which she described taking only for a couple of days because of intolerable side effects, commenting: *” I felt li' I was chokin'. me throat were that dry and me skin was sticking together, and o-it was really horrible. not just the mouth- all me throat”.* Upon going back to her GP and describing her experiences, participant 7 was prescribed another set of tablets which she described as having a similar effect, consequently resulting in the same decision to discontinue.

As a result of being invited to take part in the present study however, participant 7 uniquely took it upon herself to re-initiate her discontinued OAB medication a week before the interview to remind herself of her experiences and to offer a richer account to inform this study. She went on to describe a mixed experience with side effects, stating that the solifenacin did indeed still give her a dry mouth, but on a more positive note, she was not getting up so much at night and had actually slept better while on the medication. Throughout the interview, she went on to develop a postulation that the solifenacin tablets contained a sedative ingredient to aid sleep. This notion was supported by her husband’s research about the interplay between the brain and the bladder during sleep: *“there’s something int'brain, that tells your bladder, not to <u>feel</u> full, when you're asleep!".*

The experience of reinitiating the tablets led to the participant identifying another key driver of her original discontinuation. She described *“really thumping bad head[aches]”* upon waking and went on to say, *"and then I remembered, that was the main reason I stopped taking them"*. The participant concluded that she would continue to the end of her current pack but would most likely discontinue taking her OAB medication once more on account of the number of other tablets she took. She did however, state that she would reinitiate therapy if her symptoms returned upon discontinuation.

Continuing the thread of headaches curbing adherence, participant 6 repeatedly described her experiences with this side effect as something she *"couldn't get past"*. A 57-year-old female currently off work due to ongoing health problems with her bladder and knees, participant 6 presented with symptoms of increased urinary frequency and nocturia, accompanied by incontinence. Upon seeking help and being referred to an incontinence clinic, she tried and failed to gain benefit from pelvic floor muscle exercises. Meanwhile, with her symptoms worsening, and a long-haul family trip planned, the participant visited her GP again and received Regurin (trospium) which the participant described as *"wonderful! but it* [effect] *only lasted three months"*.

Upon the participant's request, the prescriber at the hospital stopped the Regurin and prescribed a second (unknown) OAB medication, which the participant took for ten days before the *"headaches, and the feeling sick was too much"* for her. The participant then called the hospital to request yet another alternative and the prescriber obliged, offering another (unknown) medication. The participant described trying four different OAB medications in this manner, all of which caused the same side effects and resulted in her unable to continue with them.

Eventually, the participant was offered Botox by her consultant, and described her experience following the first treatment as *"for 6 months, I just-it was fantastic, the Botox was unbelievable"*. However, due to a miscommunication between the hospital team and the participant, the participant failed to self-catheterize, leading to urinary retention and a series of *“really really bad”* urinary infections. After being informed by the consultant that some participants continue with their OAB medication alongside the Botox, the participant has currently settled into a routine to take her Regurin on an as-needed basis to manage symptoms between Botox treatments.

Participant 4, a 69-year-old female retiree stated her suspected connection of her urge incontinence to her hysterectomy with the comment: *“my bladder was perfect until I had a hysterectomy”.* Upon being advised by her GP and gynecologist the two were unrelated, the participant went on to pursue a resolution to her symptoms with her GP, who referred her to a *“very experienced urologist”.* The participant underwent a series of tests before being prescribed detrusitol, which she took for over 18-years, before its effects started to wane. This diminished efficacy coincided with a worsening of symptoms and the development of nocturia, which although not explicitly recognized by the participant, could have indicated a combination of waning treatment effect, and worsening of her condition.

Upon being referred to physiotherapist, and then a consultant at a local hospital, participant 4 was given mirabegron, and advised to stop taking her detrusitol for a week before initiating the new medicine. The participant went on to describe that the week without any medicine at all left her *“in a right mess”*, describing the week as a *“nightmare”* which she only managed with “*lots and lots of* [incontinence] *pads”.*

The participant described her experience with mirabegron in a cautious manner, stating it *“worked- well it-it slowed- it slowed the output down, let’s put it that way”*, followed by *“but what I didn’t like about the mirabegron, I had to have an ECG with it”*. It was this requirement of additional monitoring on mirabegron that prompted the participant to discontinue it after a few months. The participant did make a distinction between the fear of future side effects with mirabegron driving her decision to discontinue more than her direct experience of any, commenting: *“just because I didn’t in the few months- doesn’t mean that I wouldn’t have in the longer term, I thought 'no I don’t want that”***.**

After taking her off the mirabegron, the GP prescribed solifenacin, which the participant has been on for about six months. The GP also informed participant 4 that she may wish to consider Botox for the future, while warning her of the possible need to self-catheterize in case of incomplete bladder emptying after Botox treatment. The participant expressed dissatisfaction at the idea of having to self-catheterize, saying that she would rather take medication than to risk the complications of Botox: *“I'd rather just have, I-I-just I can cope with the pads, and the medication”.*

Participant 4 also mentioned experiencing side effects from the solifenacin, though none that were concerning enough to warrant discontinuing. Despite following her GP’s advice to take her tablet at night not curbing her getting a dry mouth, the participant overcame this side effect by habitually keeping a bottle of water nearby. She also commented on the drowsiness the tablet caused her, but like other participants, saw this as something advantageous in aiding sleep. The participant went on to admit that the drowsiness could spill over into the next day but felt able to manage this by changing the pace of her day on account of being retired. This difference in response highlighted the larger degree to which participant 4 was accommodating of the actual side effects of solifenacin, despite them impacting her throughout her day, over the feared effects of mirabegron, despite them being regularly monitored for with her HCP.

Participant 9, an 80-year-old retiree, had only been diagnosed with OAB several months ago. Her initial symptoms were incontinence and urgency which, upon worsening, prompted her to see her GP. The participant was referred to a consultant and sent for ultrasound which found *“three little nodules on my kidney”*, which she quickly stressed had been *“nothing to worry about”.*

While awaiting an appointment with her consultant, the GP prescribed tolterodine, which the participant had been taking for several weeks ahead of interviewing for the present study, but had already taken steps to discontinue it, citing extreme dryness especially in her nose and mouth as the primary reason for this, stating: *“I'm parched. Absolutely parched”*. Echoing participant 4 above, the actual experience of side effects was accompanied by a powerful fear of additional, unknown effects, which added another driver towards the participant’s wish to stop taking the medication: *“I’m, worried, about what else its drying up y'know?”.* This indicated that the experience of one side effect triggered the fear of other effects, the unseen nature of which, was a distinct factor in her adherence behaviours.

Participant 8 was a 77-year-old female who stated that she had *“always had an overactive bladder”*, since giving birth to her son, 45-years ago (normalising her symptoms as a result of childbirth- see ‘symptom perception and other people’ above). Having mainly experienced the symptom of urinary frequency, this participant repeatedly described her OAB as *“a bloody nuisance”*, being particularly mindful of other people noticing and commenting on the frequency with which she used the toilet.

Having gone to her practice nurse for something unrelated, the participant mentioned her urinary symptoms in passing and was seen by the GP, who prescribed her (unknown) tablets which the participant described as *“not much good”*, stating poor efficacy. The participant then went to see the GP again *“after ages”* and was informed of the availability of *“better ones”* and was subsequently prescribed solifenacin, which she described as *“brilliant”.*

Overall, the participant described herself as being adherent to her OAB medication, even when she felt as though the first medication was not working for her. She did however relay an episode where she decided to stop taking solifenacin due to a fear that they were causing her ankles to swell. When it became apparent that the medication was not the cause of this, and upon prompting by the practice nurse, the participant restarted her treatment.

Participant 2 was a 66-year-old female retiree. Like several others, she had a range of comorbidities affecting her mobility, blood pressure and digestive system. Most strikingly, was the psychological trauma she had suffered upon losing her family eight years ago, and the nervous breakdown she had experienced more recently, for which she took ongoing antidepressant treatment.

The participant's initial urinary symptom was incontinence which she described as having *"no control whatsoever!"*. Having gone to her GP, who *"said it was probably"* a urinary tract infection, she was given some antibiotics, and the symptom passed. The participant then went on to describe gaining weight after giving up smoking, leading to the return of her urinary symptom, and further noticing the development of urge incontinence and nocturia. Having tried to manage using pads, the participant went to her GP again and got prescribed (unknown) tablets. Participant 2 went on to describe that although the tablets stopped the urgency, it also stopped her from voiding her bladder at all, stating: *"it just stopped me weeing! And I don't think that's natural cos I drink a lot!"*, drawing a direct comparison to what 'normal' would be.

She went on to describe the uncomfortable feeling of knowing she had a full bladder, but not feeling able to, or having the urge to void it. She described this as a "*heavy feeling*", leading her to feel *"sluggish".* After persisting for 4-5-months in the hope of *"getting used to the medication",* she concluded that she just did not like the way the tablets made her feel and elected to stop them because of this. Plainly put, the participant described preferring to tolerate intermittent symptoms that although bothersome, were acute in their onset and resolution, than the constant discomfort of the side effect, summarizing with: *"I'd rather put up with, getting up every couple of hours in the night, than feel like I do all the time".* The participant described herself as a *"putter-upper"* and *"not pushy enough"* to go back and request for an alternative medication but would be willing to try if one was offered to her. This indicated a differential impact of the relative importance given to the condition by the participant herself and the prescriber. The participant concluded that she would pursue further treatment if her symptoms worsened, but for now was content to *"manage it"* without OAB medication.

Participant 10 was a 58-year-old retired teacher with a history of chronic migraines, which she described as the reason for a short-lived career, as well as the *"massive gap"* between having her children and summarized: *"yeah. It ruins peoples' lives, migraine"*. Her initial OAB symptoms included urgency and nocturia, for which she described not seeing her GP for a year after her symptoms started because she was unaware of there being anything they could do to help her. Worsening symptoms and the onset of occasional *"accident*[s] *in bed"* led to the participant being *"fed up with it"* and seeking advice.

The GP prescribed solifenacin, which the participant has been taking ever since, describing the diagnosis process as "simple", and her impression of the tablet as *"I thought it helped".* She went on to mention that she was presently still getting nocturia and was tempted to increase the dose to help manage her symptoms more effectively, commenting: "*I don't really want to increase the dose unless it's absolutely necessary".* She went on to develop the theme of 'necessity' with the words *"I take quite a lot of medication anyway, for other, conditions. And I just don't want to take more than is necessary".*

Having been prompted by the invitation to take part in this study, the participant has identified several side effects which could be attributed to her OAB medication, including blurred vision and gastroesophageal disturbances. Being unsure of which of her medications may be causing these, the participant mentioned planning to discontinue her OAB medication to gauge how much of an effect it may be having on these effects.

Also contributing to her decision to stop this treatment was the new knowledge that there were other OAB treatments available, something she was previously unaware of: *"I think from reading that form* [study participant information sheet]*, there appears to be quite a lot of different drugs for, the same problem. And my GP didn't offer me a choice or anything",* going on to say: "*I wasn't aware that there were alternatives really, which is probably part of the reason that I haven't gone back".*

C.iii) Unclear instructions / engagement from HCP

Participant 17 was a 66-year-old female retiree who noticed having to go to the toilet more frequently. Having gone to her GP complaining of this and the accompanying tenderness, the participant was prescribed nitrofurantoin (an antibiotic). Following the resolution of this episode, urinary frequency and nocturia symptoms had developed, which the participant showed clear signs of normalising and downplaying ('symptom perception and other people' above). Upon another GP consultation, the participant was prescribed an initial one month's supply of solifenacin 5mg tablets with the instruction from her GP: *"if it works, and you wanna come back, we can start you on it* [regularly]*"*

The participant went on to describe that the reasons she went on to discontinue her solifenacin were two-fold; firstly, because her symptoms had *"cleared up"* (something which she later contradicted by describing still getting up three times a night, offering further evidence of symptom normalisation and downplaying), and the fact that the GP did not again ask her to come back for further medication. This too was contradicted later in the interview with the comment: *“-to be honest she did say "when you come to the- when you finish, if you want to recon-continue, we can give you some more".* The participant summarized both perceived reasons for discontinuation with the statement: *“She just gave me this month’s supply and she said let’s see how you go on that, and because it had cleared up, I just didn’t go back cos she didn’t say "come back", she said "I'll give you these, see how you go" and that was it.”*

Also clear from the interview was the participant’s aversion to taking medication, her doubts on the OAB diagnosis, and the lack of a communicative relationship with her GP. The participant had compensated for these by downplaying the symptoms she was still getting, and normalising the effects of them on her lifestyle, leaving her content to continue without medication for the foreseeable future.

Participant 13 was a self-employed 65-year-old male. He described his initial symptom as *“an absolute immediacy to want to wee”*, that came and went. He described the episode that led him to seek help was actually a difficulty in voiding his bladder one morning, which led to his GP sending him for tests, not finding *“anything wrong”,* and eventually prescribing tolterodine XL tablets.

The participant went on to describe that following his observation of non-constant symptoms, he decided to adopt lifestyle changes by proactively reducing his caffeine intake and resorted to only sporadic use of his OAB tablets, taking them only when he judged he needed to. This judgement was based on the frequency of his toilet use, with the participant describing taking his tablets for a day at a time and gauging whether he needed it the following day based on his symptoms: *“I would probably take one. And then see what it was like tomorrow”.* The decision to take his medication in this manner was aided by his experience with the prescriber, who the participant described as *“off-hand”, “hostile”* and who did not stress taking the tablets daily, while framing the prescribing of them with the word “try” (see Appendix B.i) Reporting and diagnosis process

Reporting

There were several subthemes under this stage of the participant journey. The first, related to the previous theme of normalising symptoms, was the topic of incidental reporting where participants did not go to their HCP's specifically for their urinary symptoms but mentioned it while there for something else. Participant 8 described having bothersome overactive bladder symptoms for over 45 years and not seeking medical support, only mentioning her urinary symptoms in passing when visiting her Practice Nurse for a medication review. The nurse consequently referred the participant to a GP for diagnosis and treatment. Participant 11 recounted a similar experience, stating: *"so I went to the doctors, and I said, 'oh while I'm here, I think I've got a problem with my bladder!'"***.**

Related to this behavior was the length of time participants tolerated symptoms before actually seeking help, which was itself often related to a threshold that had to be reached before participants felt compelled to seek help. Participant 12 commented that she had *"put up with it for a while"* before seeking help. Participant 13 admitted that he *"just didn't bother"* seeking help, stating that he thought his symptoms were borne from a self-limiting infection. Other reasons given for delayed help-seeking behaviours included a perceived slow onset and progression of symptoms (participant 18), being unaware of the availability of medication (participants 3 and 10), and erroneously fearing that surgery might be needed (participant 16).

The process of reaching a personal threshold before seeking medical help was encapsulated by participant 10 with the words: *"You don't want to kind of admit that you've got a problem when you're- your just think 'oh I'm getting old and it's probably that.' but I think, when it reaches a certain level, and you-you're not prepared to put up with it any more"*, thus highlighting normalising symptoms by their denial, as well as a point at which the symptom bother became too great to continue this. Participant 6 described the realization of an upcoming trip abroad to see family as the prompt for her to finally seek help.

Diagnosis

The participants' experiences of the diagnosis process itself offered a mixture of views ranging from descriptions of *"easy"*, and *"simple"* (participant 10), to experiences of drawn-out testing and specialist referrals, with ultimately unconvincing diagnoses.

Positive diagnosis experiences were reported by those who described: good relationships with HCPs (participant 11: *"a GP that I could talk quite easily to"*), the perception that their GP was knowledgeable about their symptoms (participant 3: *"because she immediately said 'it could be an overactive bladder'"*), and a swift or immediate solution (participant 9: *"when she had examined me, she said 'right, I'll get you in straight away'"*).

Conversely, other participants did not have quite the immediacy between describing symptoms and receiving a diagnosis. Participant 14 described a lengthy process between going to the GP, being trialed on an antibiotic under the assumption of having a bladder infection, only to be referred to a specialist upon this not resolving his symptoms, and eventually being prescribed a drug for his symptoms. Participant 7 described a similar process of lengthy referrals and being thoroughly tested, to find *"there's nothing wrong, its fine"*, receiving an OAB diagnosis by default as *"that's all they could say cos they couldn't find anything wrong"*. Variants of the words "nothing wrong with me" was used by participants 13, 6 and 5, laying the ground for doubts about the diagnosis they had received when the objective tests had found no anomalies.

Unconvinced of diagnosis

With the above theme in mind, perhaps unsurprisingly, some participants were left in doubt about their condition, and the conclusiveness of their diagnosis. Participant 2 described her

GP originally diagnosing and treating for a UTI before shifting to supplying OAB treatment, with the inaccuracy of the first diagnosis causing uncertainty with the subsequent one of OAB. Similar doubts with the diagnosis were expressed by participant 17 (*"one minute they'll say that "you've got something in the urine" and another time there is nothing"*), participant 7 (*"I've got an overactive bladder, but I don't know if it's an irritable bladder- I don't know!"),* and participant 11 who stated: *"I've never had anything diagnosed about it"*, indicating her perceived disconnect between the actions of her GP (diagnosing and prescribing), and her knowledge of why she had been given treatment.

The latter point was built on by participant 17 who complained of little information being given to her during the diagnosis, and the lack of a detailed investigation *("All I was told, "oh you've got overactive bladder" and nothing else"*). What permeated through the discussion with this participant ultimately, was less the need for diagnostic evidence, but more the absence of a good, communicative relationship with her HCP where she felt supported. This was evidenced by her asking the interviewer basic questions regarding her care, indicating that she had either not had such conversations with her HCP, or was left unconvinced by them: (*"well would it be only medication that could help the symptoms?"). Her* poor relationship with her HCP was also evidenced by her description of them being uninterested, using the descriptor *"fob you off"* to describe their behaviours toward her.

B.ii) Prescribing). The participant emphasized his understanding from the prescriber that the treatment was *“not a course of tablets as such”*, going on to add: *“I don't-I don't think it is anyway. They just give you a prescription so, it doesn’t say 'take them to the end', or I don’t think it does anyway, so I just take them* [sporadically]”. Upon being asked about the guidance his doctor had provided him about his OAB treatment, the participant replied: *“I think he just said "try these"…if-if he said that many words- I’m not sure! He just wrote the prescription”*, reemphasising the lack of clear instructions from the prescriber, as well as the strong impression of them not caring or being invested in the improvement of his OAB. Regarding the efficacy of this treatment, participant 13 described immediate relief, stating: *“It’s unbelievable. It’s like a, well it’s like a magic bullet”.* He went on to describe his assuredness that taking the medication daily would offer him complete relief but balanced this with the fear of long-term effects: *“if I took one every day, then I don’t think I'd ever have any sort of immediacy to wee. urges again. I think that that could, I really do. but long-term effects I don’t-it might have other effects on me body”.* The description of this fear was further developed with the participant drawing a stark comparison between describing himself as *“careful”* with his diet, against ingesting a *“concoction of chemicals*”, repeating the fear of unknown effects as a driver for his adherence behaviors. The degree to which he knew he could rely on the efficacy of his treatment may also have been a key contributor to his adopted level of adherence, as the known timing and nature of treatment effect was used to determine when he felt the need to take it, in the absence of clear direction from his HCP.

D: Drug / Condition hierarchy

This theme captured instances where the participant compared or described a ranking of either conditions (theirs own or others) or their treatments in a way indicate differential importance, impact, or consideration given. Participant 13 highlighted an example of his prescriber setting a tone of low importance for OAB and its treatment, by giving the participant an impression of resorting to a diagnosis and treatment of OAB to *"get rid"* of him when *"all sorts of tests"* revealed no other diagnosis. The participant went on to mention that this disinterest continued beyond the initial consultation, with the GP not reviewing his OAB medication or sporadic adherence, despite having a face-to-face opportunity to do so, electing instead to simply supply the prescription (reinforcing the flippancy and desire to *"get rid"* of the participant, as well as the low interest previously highlighted)).

In echoing the first example (though without the perceived disinterest), participant 1 described his urologist *"didn't want to see"* him again on account of his condition not being serious enough to be outside the management of his GP, despite his worsening symptoms. The participant went on to discuss his other treatments, stating: *"immune suppressant tablets- for the transplant, uhm you've gotta take <u>them</u>-not supposed to miss a day"* placing extra emphasis on the word "them" to signify their importance. This order of relative importance was also made apparent by the participant's reluctance to go and see the GP specifically about his OAB issues, despite worsening symptoms, electing instead to wait until he had to visit for something else, to seek assistance. The participant also added: *"when I see a specialist sort of doctor, and they say "you've got xyz disease" and I've not heard of it, then yes I'll go and- 'right, what is this, and-' but erm I haven't for the bladder no"*, signifying yet another difference in approach between his OAB and other conditions.

Participant 3, who herself had experience of working in a GP surgery, drew a comparison between the relative prominence given to conditions such as asthma and prostate cancer against the dearth of such information being publicly available for *"day-to-day"* conditions such as OAB, which she asserted *"really does interfere with your lifestyle".* She highlighted that every surgery had their own website where such information could be prominently displayed to convince people that they didn't *"just have to put up with it"*.

Participant 2 contributed to the present theme by illustrating contrasting examples of stopping a medication on her own volition; having stopped her antidepressants, the participant specifically informed her GP and went on to proactively reengage with her prescriber to restart treatment once she realized that had stopped prematurely. In contrast, upon stopping her OAB medication, the participant did not inform her GP, and went on to describe avoiding a review and an opportunity to readdress the issue.

Linked to this, participant 10 described tolerating her OAB symptoms and putting off going to the GP because she did not realise anything *"could be done about it really".* This changed when worsening symptoms and *"having to get up several times in the night"* started impacting on her chronic migraines, at which point she was more open to pursue a treatment. This participant-side hierarchy of conditions was echoed in her description of the surgery never reviewing her OAB or treatments, hinting that her other medication did get reviewed in this manner, this reinforcing the lower priority given to OAB.

Participant 6 directly compared her OAB symptoms to her experience with epilepsy to emphasise the degree to which the urinary symptoms affected her lifestyle, drawing particular attention to the lack of warning and control with her OAB (as compared to her epilepsy symptoms which gave her a *"warning"*). She went on to draw another comparison between her work in healthcare, helping *"mental participants"*, and her experiences with OAB by describing parallels between the lack of control mental health participants faced, with her own inability to control urinary symptoms: "*Some of them can't help that, I can't help this"*. She also recognized the difference between being able to offer some direction or structure to a mental health participant versus not being able to do so for her bladder issues, reiterating her frustrations with the latter.

Participant 16 contributed to this theme by describing himself as *"not <u>really</u> that ill"* minimizing his needs when compared to other participants requiring the GP's time *"who really <u>are</u> ill!"*, hinting also at themes of normalisation and downplaying ('symptom perception and other people' above). Furthermore, after stating that he was *"not by nature a great drug taker"* while describing possible future OAB treatments, he went on to produce another contrasting comparison to downplay his OAB by emphasizing the word *"those"* when describing his adherence with his blood pressure tablets: *"oh I take <u>those</u> without fail, because my blood pressure <u>was</u> quite high".*

Partly echoing the attitude shared by participant 16, the subtheme of *"consequences"* related closely with the levels of importance ascribed to different conditions and treatments. Participant 7 illustrated this with her description of discontinuing several OAB medications due to side effects and a wish to avoid tablets where possible, indicating the relative strengths of these drivers where OAB was concerned. While the same driver of wishing to avoid taking too many tablets led to her trying to discontinue her omeprazole for reflux (against her GP's advice), the participant described being able to go for only a few days before being *"in agony with heartburn"*, prompting her to restart them. Similarly, she maintained the practice of adhering to her blood pressure and letrozole tablets in light of the potentially serious consequences of not doing so: *"I take a blood pressure tablet. Because I don't want to have a stoke cos-me blood pressure high, which I know is dangerous. So, I take that regularly every single night".* The divergent consequences of non-adherence between these three conditions appeared to be a central pillar in the participant's decision to discontinue her OAB treatment whilst adhering to her other treatments despite her aversion of tablets and fear of side effects.

Participant 12’s act of elevating the importance she ascribed to her OAB medication was aligned to her uptake of a new golfing hobby has already been highlighted. She went on to further contribute to the theme of relative importance of conditions in a broader sense, by describing a lack of awareness of bladder problems, linking this to a lack of research interest: *“nobody's really that interested I don’t think, in weak bladders”,* thus reiterating the perceived low importance given to OAB. She put this in the context of there not being a lot to offer to OAB participants as *“they”* (HCP’s/researchers) were too busy focusing on the *“big things”*. This echoed the earlier words of participant 16 who avoided going to the surgery as they were too busy with those *“who really are ill”*, and contributed to the link between the perception participants held of the relative importance given to OAB and their motivations and ability to seek and receive help appropriately.

Discussion

The multitude of drivers of adherence and non-adherence behaviours in OAB specifically have been recognized in previous works in this area which principally identified patients having unmet treatment expectations, issues with tolerability, and not wanting to be on treatment (Dhaliwal and Wagg, 2016, Tijnagel et al., 2017). As demonstrated in the systematic literature review presented in Chapter 2, this was the first study taking a qualitative approach to explore the drivers, reasons, and context behind observed adherence and persistence behaviours in OAB patients, and thus filled a gap in the literature. The study aimed to develop a deeper understanding of the complex and multifactorial drivers of such behaviors and emphasize a closer examination of the wider context as well as the meanings that participants ascribed to their experiences (Yilmaz, 2013).

The participants' lived experiences, attitudes and response towards their symptoms were central themes to the interviews, and a launch pad into related matters such as their attitudes to medicine-taking and their reasons for discontinuing OAB medication. The majority of participants had a cyclical experience of OAB, with periods of symptomatic activity and remission (see 'symptom experience and burden' above). Similarly, there was a collective trend of worsening symptoms over time, the degree of which varied between participants. In reflecting the findings of a study exploring unintentional non-adherence to chronic medications, participants in the present study described few problems with forgetfulness or carelessness and described several strategies they used to remain adherent with their oral medications (Gadkari and McHorney, 2012). Of these, the most commonly employed were incorporating medicine-taking into a daily routine, either as a matter of habit or by binding it to a daily occurrence and keeping medication in a visible place to remind themselves to take it. The importance of such measures has been emphasized in the COM-B model of adherence with the recognition that habits and routines are an important factor of adherence behaviours, forming part of the automatic motivation domain (Michie et al., 2011).

Within the present study, the perception of OAB itself ranged from being a natural part of ageing (e.g., participant 10: *"oh I'm getting old and it's probably that")*, its diagnosis being doubted (e.g., participant 7: *"but I don't know if it's an irritable bladder- I don't know!")*, being considered a temporary set of symptoms requiring short-term management (see participant 17: in section C.iii above), to its being accepted as a chronic condition by some participants. Participant perception of the severity and burden of their symptoms was often framed by the theme of *"other people"*, emphasizing the role of social context in illness perception in OAB (see "CSM model of illness" in Chapter 1). Participants contextualized their symptoms in terms of how other people reacted to them, how symptoms affected those close to them, and how they compared to others around them (e.g., participant 7: *"me husband curses me for it I'm sure he does",* participant 12: *"I've always noticed that I went for a wee, more than other friends".* This was particularly the case with the symptoms of urinary frequency and urgency which were relatively noticeable to friends, family, and strangers alike. A common experience was the self-consciousness about others noticing or commenting on symptoms, with several participants sharing stories of embarrassment to illustrate this. The psychological impact and embarrassment with OAB symptoms are widely documented (Stewart, 2009, Filipetto et al., 2014, Toye and Barker, 2020, Kinsey et al., 2016a), and are discussed in a wider context in relation to stigma in Chapter 6 (see "Social/economic factors").

Participants also compared their experiences with others in a bid to gauge the abnormality/severity of their symptoms (in order to identify a threshold for seeking treatment), or to reinforce a sense of normality to downplay symptoms. Examples included participant 10 stating that her experience *"probably wasn't anywhere near as bad as some people",* going on to say: "*I think, when it reaches a certain level, and you-you're not prepared to put up with it anymore".* Related to this was the theme of OAB symptoms being normalised in the form of participants likening symptoms or their effects to everyday behavior, or the participant getting so used to the symptoms as to establish a new norm for them. Often, as seen with previous works in this area, it was accepted that OAB symptoms were part of natural processes such as ageing, childbirth, or the menopause, further contributing to their sense of normality, and a sense of having to *"get on with it"* (participant 13) (Diokno et al., 2006). Indeed, self-directed stereotypes and the endorsement of ill-health as an inevitable consequence of getting older has been associated to negative health outcomes for older adults with chronic conditions (Stewart et al., 2012), and were linked to a delay in seeking help in the present work, as well as how highly OAB treatment was prioritised. Within this study, the diffuse nature of the social impact on both the conceptualization of symptoms and their treatments across participants from a range of backgrounds offered evidence of the social opportunity component of the COM-B model of adherence, as well as its importance within OAB. This was evidenced explicitly by the effect of “other people” as described above, as well as related themes of downplaying and normalizing, as well as the effect of language used in the prescribing process (see “tentative language” section above).

There were several themes related to symptom reporting and diagnosis stages of the participant journey. The first, and in some ways related to the previous theme of normalising symptoms, was the topic of incidental reporting where participants often did not go to their HCPs specifically for their urinary symptoms but mentioned them while there for something else (e.g., Participant 11: *“so I went to the doctors and I said, 'oh while I'm here, I think I've got a problem with my bladder!’”*). This was linked to the relative importance participants attached to OAB against other conditions (explored below). Related to this behavior was the length of time participants tolerated symptoms before actually seeking help, using variants of the words *“cope”* (participant 4) or *“putting up with”* symptoms (participant 10) before reaching a personal threshold or trigger to seek help. The association between participants normalising symptoms and delayed help-seeking has been noted in other chronic disease areas such as rheumatoid arthritis and cancer (Stack et al., 2012, Whitaker et al., 2014).

The participants' experiences of the diagnosis process itself offered a mixture of views ranging from descriptions of *"easy",* and *"simple",* to experiences of drawn-out testing and specialist referrals, with ultimately unconvincing diagnoses (e.g., participant 7: "*they couldn't find anything wrong")* Positive diagnostic experiences were aligned with the participant feeling assured by an immediate diagnosis from their HCP, as well as additional information such as the availability of other treatments and what side effects to be aware of. Doubts about the diagnosis often stemmed from the participant undergoing a range of tests to ultimately find *"nothing wrong"* with them (as described by participants 5, 6 and 13), before receiving a diagnosis of OAB.

One of the central themes in the consideration participants gave to adhering to medication was their perceived necessity of taking specific tablets. This involved individual participants balancing perceived risks (known and unknown long-term effects of medication), and perceived benefits (symptom control and effects on quality of life) in starting or continuing to take medication. This weighing of costs and benefits therefore offered support for the NCF described by Horne et al. (see Chapter 1: "Necessity-concerns framework") (Horne et al., 2013a, Phillips et al., 2014). The perceived benefits of taking OAB medications were often of limited value to those participants who downplayed or normalised their symptoms, where variants of the words *"learned to live with it"* were often employed (e.g., participant 8: "*y'you just learn to manage things")*. This was further contextualized by their perceived effectiveness of treatment and what other medications the participant was taking.

Underlying the explicit reasons given for medicine discontinuation were participants' general beliefs and attitudes around tablet taking. A prevalent theme in this category was one of wanting to avoid tablets/additional tablets where possible. With the use of terms such as *"I don't like being on […] lifelong medication"* (participant 12), participants expressed their general aversion to taking tablets, closely linking this to the theme of necessity described above.

Mentioned in one form or another by over half of the participants in this study, lack of efficacy was a recurring theme of conversation within the present study. Such responses ranged from a relative lack of efficacy, where more effect was sought (e.g., participant 14 stating his treatment had *"hardly any effect")*, to the medicine offering no relief of OAB symptoms at all (participant 1: "*medication, which, didn't work"*). The emphasis and consequences of this perceived lack of efficacy also varied from some participants mentioning it only as a contributory factor while others linking it more directly as a causative factor to their level of medicine adherence. Also described in the literature as a 'lack of treatment effectiveness' and 'unmet treatment expectations', this reason for non-adherence to OAB medication is well-documented in quantitative and mixed-methods explorations (Krhut et al., 2014b, Lee et al., 2014b, Sung et al., 2015b, Wyman et al., 2010). Related to this, the authors of a large-scale, two-part survey study in the USA highlighted the integral role prescribers can play in managing realistic treatment expectations in the context of OAB, and the importance of trust in the prescriber-patient relationship in helping to enable this (Benner et al., 2010). This was also echoed by others, including the authors of a UK retrospective chart review study (Pindoria et al., 2015), and featured throughout the present work. Such observations offer support to the IMS model of adherence whereby information and motivation domains are linked by an effective therapeutic relationship, supporting adherence behaviours through more effective patient understanding and capacity (see Chapter 1: "three-factor model of adherence").

The findings of the present study further highlight the potential effects of prescribers' behaviours and language at the point of prescribing OAB treatment, upon patients' attitudes and expectations. Participants commonly recalled prescribers using variants of the word *"try"* in relation to OAB medication, leaving some participants with clear misgivings on the merits of the drugs supplied and what they could expect from them (as highlighted in 'reporting and diagnosis' above). This theme was further developed in the present study by some participants describing the prescribing of OAB medication as *"trial and error"*, thereby emphasizing an expected failure of treatment. In contrast to the notion of non-adherence being driven by participants holding unrealistically high treatment expectations, the present finding offers a different perspective, that low treatment expectations, driven by interactions with prescribers also contributed to the perception of a lack of treatment effectiveness. Furthermore, the historical downplaying and normalizing of OAB symptoms may have resulted in a diminished representation of the health threat (see Chapter 1: "Common-Sense Model"). This may have led some participants to underestimate the true positive effect of their OAB medication, when comparing historical symptoms to their current ones. This was given some credence with participant 7 deciding to restart her medication for this study after a period of not taking it, and noting a reduction in her nocturia, as well as identifying headaches as a key forgotten driver for her having discontinued originally.

Non-adherence in OAB being driven by side effects has similarly been documented by previous studies (Kim and Lee, 2016, Basra et al., 2008). In the present study, although not all participants reported suffering from them, side effects ranged from gastrointestinal discomfort, sickness, and sedation (the latter of which was broadly welcomed by participants on account of positive effects on nocturia and quality of sleep). It is worth further highlighting that while sedation was broadly welcomed in the present work, such a perception is unlikely to be universally shared by those of a younger demographic who may not be able to accommodate this side effect as well as older, part/retired individuals as was the case within the present study. Consistent with the profile of OAB treatments, dry mouth and/or dry nose were the most widely mentioned side effects overall, followed by headaches and nausea.

Developing on the theme of side effects affecting adherence, the present study uncovered not only the impact of side effects actually experienced, but the fear of future or unknown effects influencing adherence behaviours also. Of these, mirabegron was strongly linked to a fear of future side effects by one participant on account of the additional blood pressure and ECG monitoring required while on treatment. Furthermore, the fear of (unknown) side effects with other OAB treatments centered on anti-muscarinic side effects of the OAB tablets and the fear as what else they could be affecting. This gave some evidence for both the experience and fear of side effects acting as stimuli in shaping the representation of the health threat as described in the CSM model of illness perceptions (see CSM section in Chapter 1). This, therefore, adds further reason for prescribers to frame both initial and subsequent consultations to provide patients with reassurance and realistic expectations of not only treatment effectiveness, but possible transient and longer lasting side effects, as well as their management.

The present study also uncovered non-adherent behaviours being driven by an inadequate understanding of either OAB itself or its treatments, often driven by unclear instructions or engagement from the HCP, leaving participants room to make their own interpretations of the advice given, or enact pre-existing judgements. Although not one of the most widely cited reasons for discontinuation in the present study, this theme highlighted participants departing from the tenet that OAB requires long-term treatment to achieve consistent symptomatic control (Abrams et al., 2000a), and thus offers further areas where a combination of disease education, public information and shared decision making with HCPs may help correct this, and improve medicine-taking behaviours as well as outcomes with OAB. The mechanism through which such interventions may support medicine-taking behaviours have been described in the IMS model where patient's knowledge is critical for their engagement in the healthcare process, motivation to adhere to treatments, and the strategies they employ to do so (DiMatteo et al., 2012) (see CSM in Chapter 1).

Participants ascribing different levels of importance between their various drugs and conditions was another key theme identified (see "drug/ condition hierarchy" above for examples). Shaped largely by the difference in consequences of not adhering to one medication versus another, this hierarchy was further contributed to by the attitude of the prescriber, the perceived necessity of taking a drug, and the marginal risk or benefit from taking a new drug in relation to the pool of comorbidities already being treated. Such behaviour has previously been described in a mixed methods study which found elderly patients held quantifiably different perceptions of the relative importance of their prescribed medications. Although the study was US-based and primarily aimed to explore cost-related medication non-adherence, the authors concluded that the relative importance of treatments was informed by a complex and interrelated set of factors they classified into drug-related, patient-related, and external factors (Lau et al., 2008). These findings were broadly mirrored within the present study, where the comparatively lower importance given to OAB by participants manifested into behaviours in the form of incidental reporting of initial urinary symptoms, the delay in seeking further support until seeing the HCP for something unrelated, or choosing instead to *"cope"* with symptoms rather than seek an immediate resolution, thereby reinforcing OAB symptom normalisation and downplaying (described in 'symptom perception and other people' above).

This comparatively low importance given to OAB was mirrored by the participants' perceptions of prescribers' attitudes towards the condition, with a collective experience of rushed or overlooked OAB medication reviews, and an issuance of repeat OAB medication without the prerequisite regular review appointment (e.g., participant 5: *"I don't think I'd ever actually be phoned up and said, 'you must come in for your review'")*. Highlighting the formation of a suboptimal representation of the health threat (in accordance with the CSM model of illness representation- see Chapter 1), this reiterated a sense of OAB being regarded with low significance in the eyes of the prescriber, and in turn, the participant. This theme was further developed by broader comments on the comparative lack of information for OAB versus other chronic conditions such as asthma and was taken further with the suggestion that there was a lack of research interest in OAB.

Reflexive accounts

The interviewer (LS) has provided her own reflections for each interview, which have been anonymized and included in full within the present chapter in Appendix Set B Appendix B4: Interviewer reflexive exercise. As a general reflexive analysis outlining my background and approach to this research has been provided in the 0, within the present section, I will give a personal account of my reflections during the data transcription and analysis process of this study, and any preconceptions that may have influenced these steps. I will then briefly summarise the interviewer's self-reflections on the process of conducting the interviews and her stated thoughts and preconceptions. It is worth noting that LS's reflexive accounts have been included within this work for information and transparency, but were conducted in complete isolation to the analysis I undertook, as well as from my own reflections.

Personal reflections

Having led the study design in all stages even up to the screening telephone discussions with participants and arranging the actual interviews, it was strange to relinquish the act of actual interviewing to another person (for reasons discussed in 0). Stanger still, was to reassume stewardship of the study in the data transcription and analysis stage, and hear the interviews that had taken place with an odd mixture of both detachment and ownership of the process and discussions, having engaged closely with both the interviewer and interviewees up to this point, as well as having shaped the materials directing the interviews.

While having listened to each interview recording with some knowledge from my own pre-interview discussion with each participant, days and sometimes weeks had elapsed between my initial discussion with a participant, their eventual interview, and subsequent sharing of the recording with me. Furthermore, I opted only to revisit my notes from the pre-interviews after coding the interview transcript for each participant in order to make sure nothing of importance had been missed post-coding. This helped to limit the effect of any preconceptions from a relatively short telephone conversation in performing a thorough inductive thematic analysis centering on medicine-taking behaviours. Furthermore, this helped the process of transcribing become the chiefly effective way for me to get close to the data quickly and to familiarize myself with the participants responses in a comprehensive manner.

Combined with my professional history as a pharmacist, my role in developing the discussion guide and my ideas for what the study would deliver in terms of the breadth and depth of subjects covered, the process of listening to the interview recordings left me conflicted. While appreciating that interview styles are inherently personal, listening to the interactions between participants and the interviewer (who in contrast did not have a background in healthcare provision, or any prior knowledge of OAB), at times made me feel as though I would have taken a slightly different approach or worded a follow up question differently. However, more often than not, the interviewer either circled back, or the participant offered further information in the course of the interview anyway. I felt that the in-depth briefing of the interviewer and ongoing liaison between us helped ensure the content of the interviews was overall well aligned to my own approach. While I was conscious of the interviewer performing her own account of the interviews and her observations, I was careful not to use these during data analysis, opting instead to do an independent analysis, corroborating my coding with others on the team, as well as the final output of the study with the interviewer to ensure congruence.

Acknowledging the importance of context on individual behaviours, I entered the process of executing the present study with a consciously open mind to the many contributing factors influencing medicine taking behaviours. This frame of mind was aided by finding myself in a totally new work setting, being exposed to not only a novel way of working personally (away from the dispensary and patients), but for both the organisations I worked for, thus requiring me to have an open and adaptable approach to both the inputs and outputs of my work. However, given my prior experience and knowledge of some of the literature in OAB before commencing this work, I was aware of and thus had expectations to find some common reasons for non-adherence such as side effects, lack of efficacy and forgetfulness which traverse across therapy areas. Whilst these preconceptions could have been the basis of a potential bias in the present study, the use of an independent interviewer with no prior experience or vested interests in the outputs of the study, as well as the judicious use of quotes to support my interpretations helped to mitigate this. It is likely however, the interviewer's perspectives and preconceptions could also be seen to be the basis of a similar bias, and this will be explored further below.

Not having often conducted hour-long interviews with patients centering on a specific condition, some of the findings were surprising to me. These included both the extreme breadth of how OAB impacts lives, as well as the depth of impact felt and described by participants, particularly in terms of the mental and social strain imposed by the condition and the sense of helplessness to its effects (predominantly where the treatment was not having the desired outcome on symptoms). On careful reflection, the source of this may have been my inceptive perception of some symptoms of OAB (e.g., increased micturition frequency, urinary urgency, nocturia) as something of an extension (mostly in terms of increased frequency) of otherwise 'normal' experiences such as occasionally experiencing urinary urgency (e.g., following a large drink) or needing to use the bathroom in the middle of the night. Holding a perception of myself and others having experienced a 'version' of some OAB symptoms in isolation led me to hold a premature view characterized by the thought: *"how bad could the experience of OAB be?"*.

Having immersed myself in the experiences shared by the participants, as well as in my role in understanding and interpreting their voices has made me much more empathetic to the extremity of symptoms experienced, as well as the otherwise largely hidden psychological and social effects of OAB. Furthermore, this study has reiterated to me the non-linearity between the frequency of symptoms and consequent impact on quality of life. In observing the experience of others at a distance, it is easy to assume that the seemingly minimal marginal impact of one more symptom event is the same at the lower end of the scale (e.g., needing to use the toilet one more time daily than 'normal') than it is at the higher end (e.g., needing to use the toilet one more time having been twice in the last hour), and that burden is simply a function of frequency. Having had a window into otherwise hidden experiences of OAB patients, and in closely engaging with the stories of the participants in this study has clearly demonstrated to me that the experiential burden associated with the same apparent 'increment' is not the same within individuals, nor across them.

This study has also made me reflect that my attempts at 'making sense' of someone else's symptoms by relating them to my own experiences left me susceptible to normalise and downplay their symptoms, especially in relation to symptoms where I could rationalize having experienced some 'version' of those exhibited. Although such a preconception would presumably be less likely to surface with more non-descript LTCs or where the symptom expression is further detached from 'everyday' experiences (e.g., joint stiffness in rheumatoid arthritis), this observation does leave me with the lasting thought of to what extent we as a society are driven to behave in this way, and the impact this might have on those experiencing such chronic conditions.

Interviewer reflections

In-between her reflections on individual interviews and the stories contained within them, the interviewer's overall reflections mirrored my own in terms of noting the impact of OAB on everyday life, as well as the seeming acceptance of its symptoms indicated by multiple participants. She permeated her description of the overall experience of each participant, with additional context where relevant, such as the body language presented by participant 1, describing this as *"more closed and hesitant and it was not a comfortable thing for him to talk and open up about."* Several themes and subthemes of this chapter were in congruence with such observations, including 'normalising symptoms', delayed 'reporting', 'condition hierarchy' and 'other people'.

On her own involvement, the interviewer noted having little prior knowledge of the context and therefore having *"minimal expectations"* at the first interview, enabling her to *"be non-judgmental"* in her questioning. She went on to acknowledge that her growing exposure to participants throughout this study informed and influenced her expectations giving her *"an inclination of what the next participant might say"* and made it easier to probe further *"due to having a prior knowledge and familiarity with the interview schedule and research topic plus common responses"*. Nevertheless, while recognizing the importance of sticking to the discussion guide, the interviewer highlighted her goal of: *"allowing the research participant to feel like they can communicate their personal experiences fully of having an OAB, their experiences of medication(s) from seeking advice to referral, to being prescribed, to reviewing their medication and adherence to this and the perceived success of it and whether they had to try alternative methods".*

Strengths and limitations

The present study was designed to encourage participants to describe their experiences in their own words, with additional questions from the interviewer if necessary, to elicit as full an exploration of the key thematic areas as possible. There were, however, several potential biases and limitations which are listed below, alongside steps taken to mitigate their effects:

- Recall bias: Given the exploration of past experiences, participants may have not remembered such events accurately, or may have omitted important details. Furthermore, the accuracy of such experiences may have been influenced by subsequent events and experiences.
    - Patients with recorded memory or cognition problems were excluded for this reason.

  - The interviews were designed to go through a chronological order of events to aid accurate recall.
  - The use of a discussion guide, as well as the same interviewer to conduct all the interviews offered some standardization of the questions asked and their formulation to limit any effects this may have had on the individual participant's ability to recall.
- Selection bias: as recruitment relied on patients firstly being shortlisted by their HCPs, and secondly coming forward to take part in the study, recruited participants may have differed from the general OAB population to which the learnings of this study will be extrapolated to. Excluding those non-fluent in English may have further contributed to this bias.
- Interviewer effect: Participants may have responded differently depending on their perception of the interviewer. This may have been particularly impactful with differences between face-to-face and telephone interviews with there being less of a chance to form impressions based on physical characteristics in a telephone interview
  - All participants were contacted by the interviewer prior to the interview as a means of introduction and to discuss the study
  - The interviewer had undergone training on interview techniques to help mitigate the effects of this potential bias
- Demand Characteristics: Participants may have formed their own interpretation of the study's purpose and changed their responses to fit that interpretation
  - The interviewer described the nature and rationale of the study to the participants at first contact. There was then a briefing before the commencement of the interview to reiterate the purpose of the study. This

  - was standardized across all participants to mitigate any differences to responses due to this potential influence (Newton, 2010).

- The interviewer's own background and experience may have introduced bias to the direction and scope of the conversations with participants
  - The use of a discussion guide to direct the conversations helped to minimize this
  - Furthermore, the interviewer performed a reflexive exercise, documenting a firsthand account of the interviewer-interviewee interaction (see Appendix Set B Appendix B4: Interviewer reflexive exercise) (Willig, 2001).
  - In addition to this, the data transcription and analysis were undertaken by the researcher with the input of academic expertise from MMU to limit the introduction of any unilateral bias
  - An Academic Health Psychologist with extensive experience in qualitative research performed a validation cross-check of 20% of the interview transcripts and analyses to confirm the completeness and appropriateness of the coding and analyses
  - Lastly, to complete the series of cross-checks, the final list of identified themes was cross-checked with the interviewer to confirm its accurate representation of the interviews held
- Using just one qualitative method of data collection, where two or more (e.g., focus groups, questionnaires, and surveys) may have provided a fuller picture.
  - However, additional data collection methods, though enriching, would have added further time and cost implications, and were excluded for this reason.

These could form the basis of future work to expand upon the findings of the current study.

The present study involved 18 individuals, of which only 5 males were able to be included. This may limit the degree to which the views and experiences of males with OAB were reflected within the data, and is reflective of findings elsewhere in the literature of the underrepresentation of males in health behaviour research (Ryan et al., 2019). Beyond this, the mean age within this study was 70 years, resulting in 14 of the 18 participants to be retired, with a further two on long-term sick leave, and only 2 participants in active work at the time of interview. While the age of participants does reflect the clinical reality of the majority of OAB patients being over 65 (Wagg et al., 2020), the degree to which the experiences of participants within the present study were representative of the entire OAB population may be limited. This may particularly be the case given an estimated 38-48% of those aged <39, and 51-56% of those aged 40-59 years experiencing OAB symptoms (Eapen and Radomski, 2016a). However, this may be a limited weakness of the present work given the focus on exploring factors affecting adherence behaviours, many of which are likely to transcend age brackets, and the exploratory nature of the present study (being the first qualitative work to explore this area). Furthermore, as the present study took a chronological approach to exploring experiences with OAB from the time of the initial symptoms, much of the participants' experiences before retirement were captured.

Conclusions

The drivers of OAB drug non-adherence identified in this study were wide-ranging and multi-layered, involving patient, prescriber, and drug-specific dynamics, as well as their interplay. Explicitly stated reasons for OAB medicine discontinuation in this study broadly mirrored those found in the quantitative literature as being principally related to a lack of efficacy, and treatment emergent side effects (Lee et al., 2014a, Pindoria et al., 2017a, Tijnagel et al., 2017). Other stated reasons included a generalized drug aversion, the patient perception of being on “too many tablets”, fear of unknown effects and unclear instructions from the prescriber or a doubted diagnosis. Furthermore, through the exploration of patient experiences and attitudes towards their symptoms, as well as the proffered treatments, this study uncovered the rich context within which these factors sit, and the relationships between them. Its findings will help in identifying future areas of research while allowing us to consider potential points of improvement in current practices.

The barriers to participants seeking initial help included a perceived dearth of publicly displayed information on OAB, as well as general unawareness of the availability of treatments for it. This presents an opportunity for public awareness campaigns to ameliorate public knowledge of OAB and encourage help-seeking behavior. From the identification of the role that “other people” and their perceptions play in the likelihood for OAB patients to seek help, more information may help patients and peers recognize how widespread such symptoms are, leading to less embarrassment in discussing and treating them, shifting the sense of normalising the symptoms, to normalising help-seeking behavior, with better outcomes for OAB patients.

Another key potential area of improvement was the reported lack of medication reviews, and in particular, those that centered on OAB. As noted, the perceived disinterest from HCPs to review OAB, alongside patients being less willing to chase such reviews may have caused a gap in patient care, with a resultant effect on adherence, healthcare resource use health outcomes, as well as wider implications on patients and their families. As medication reviews have been shown to most effective in resolving treatment-related issues (Huiskes et al., 2017), they may be of particular importance in OAB where issues with medication were a leading cause of non-adherence in the present work as well as the wider literature. Relatedly, poor adherence and persistence with OAB treatment may result in higher risks of morbidity and increased healthcare resource use compared to those with good adherence and persistence (Kim and Lee, 2016). Clearly, regularly scheduled reviews arranged by the GP practice would allow patients to raise their concerns and help optimize their care, rather than resorting to “coping” with OAB as was the case with many of the participants in this study. Indeed, a NICE guideline development group summarized that although there was mixed evidence in the literature, four randomized controlled studies in the UK had demonstrated medicine reviews increased adherence to prescribed medication (NICE CG76, 2009). As previously noted, such reviews could be conducted by nurses or pharmacists, taking advantage of existing review mechanisms such as community pharmacy services, thereby relieving pressure on GP practices. Additional publicly available information concerning OAB may also help patients to decide to directly pursue better care for their OAB, rather than incidentally reporting issues while at the GP practice for other matters. This study also highlighted the potential impact that patient-prescriber relationships and interactions had on the perception of both symptoms and treatments, and ultimately, on adherence. The key themes of prescribers offering participants assurance via confident diagnoses, warnings of common side effects, and the availability of other treatments were identified in this study as good preparators for more adherent behaviors. Conversely, the reported use of ambiguous language during the consultation led to participants harboring doubts of both the diagnosis and the treatments offered. Further work is needed on investigating how the experience of diagnosis and support shapes attitudes to adherence. Furthermore, the theme of a condition hierarchy whereby participants in particular rank their conditions in order of relative importance needs further investigation to understand its significance and how it may be used to improve patient outcomes in OAB and other conditions.

Chapter Summary

Taking the findings from a systematic literature review (discussed in Chapter 2) , describing a lack of qualitative research into medicine-taking behaviours in OAB, the present chapter has outlined the context, design and execution of a de novo piece of research to address this gap in the literature. The study described herein was a wholly qualitative exploration of the drivers of adherence and persistence behaviours in OAB patients in the UK. It employed 1:1 semi-structured interviews with patients identified through NHS R&D sites, and used inductive thematic analysis to explore their experiences relating to adherence behaviours. The resultant peer-reviewed, published manuscript is provided in Appendix B5. This chapter described a range of themes identified, including explicitly stated reasons for non-adherence, as well as those providing a rich context to medicine-taking decision-making. Chief amongst the central themes of reasons for not adhering or persisting to OAB medications were a perceived lack of efficacy, side effects, unclear instructions, and drug and condition hierarchies were explored in depth. Supplementing these, were thematic areas such as the participants attitudes towards medicine-taking, strategies employed to support adherence, and importance of medication reviews.

The next chapter will describe the conduction of a comparative review study in other chronic conditions, in order to explore the relevance of themes identified in the present chapter to the experiences of those with inflammatory bowel disease, type II diabetes and multimorbidity.

Chapter 5 – LTC Comparative analysis

A comparative analysis to compare and contrast themes relating to barriers and facilitators to adherence in OAB with those identified in the literature for other long-term conditions

Summary

This chapter describes a comparative analysis to take the learnings related to treatment adherence from the earlier OAB study (Chapter 4 (Ali et al., 2019)) and explore the extent to which the themes observed in OAB were relevant and observed in other long-term conditions. These included inflammatory bowel disease, type II diabetes, and multimorbidity in the elderly. Findings of factors affecting adherence and persistence in the context of OAB as described in Chapter 4 were compared to a qualitative study in IBD and two reviews in type II diabetes and multimorbidity, noting similarities and differences in findings. As well as exploring the relevance of findings from the OAB study in a wider clinical area, this chapter served as a means of triangulation and strengthening of the OAB study itself, and a means of widening the scope of the present thesis.

Introduction

Long-term conditions

A long-term condition (LTC) (such as OAB) is defined as one that cannot at present be cured but is managed by medication and other treatments (Roddis et al., 2016). Worldwide, it is estimated nearly 50% of all adults and approximately 8% of children have some form of a chronic condition, and this is expected to rise in line with an ageing global population (Cutler et al., 2018). According to NHS England, there are over 26 million people in the UK living with at least one LTC, with about 10 million with two or more (NHS England, 2018). People with LTCs account for around half of all GP appointments and 70% of hospital beds in the UK, accounting for about 70% of the health and social care budget in the UK (NHS England, 2018), which currently sits at £159 billion for 2021/22 (not counting the additional £22.4 billion COVID-19 specific funding) (The King's Fund, 2019). It is unsurprising, therefore, that the 2014 NHS five-year forward view highlighted LTCs as a key focus of the NHS, emphasising the need for long-term partnerships with patients, and continuity of high-quality care (NHS England, 2014). The 2019 NHS Long-Term Plan further outlined a particular focus on those LTCs causing the most morbidity and mortality, and went on to note the national importance of multimorbidity (NHS, 2019). It further outlined that a quarter of adults in the UK were living with two or more LTCs, there was a need for the training and education of HCPs to drive and accelerate the shift from a historical emphasis on highly specialised roles, to a better balance with more generalists. This, it noted, would help HCPs better manage patients with multi-morbidities alongside those with single-conditions (Alderwick and Dixon, 2019).

The management of health outcomes for LTCs is not solely reliant on treatments themselves, as non-adherence can play a large part in influencing health outcomes and quality of life. It is estimated that between 33%-50% of all medicines prescribed for chronic conditions are not taken as recommended, representing a forfeiture to the individuals affected, the NHS and society as a whole (NICE, 2009). Indeed, an estimated £500million per annum could be saved by the NHS if adherence was markedly improved in five key disease areas (asthma, type II diabetes, coronary heart disease, hypertension and schizophrenia) (Elliott et al., 2017). Furthermore, a systematic literature review considering the economic impact of medication non-adherence across multiple disease groups found that lower levels of adherence (as measured using MPR or PDC- see Chapter 1) were generally associated with higher total patient costs, concluding with the observation that *"economic, clinical and humanistic consequences of medication non-adherence will continue to grow as the burden of chronic diseases grows worldwide"* (Cutler et al., 2018 pg.9).

Comparative analysis

The use of comparative analysis within research is considered to be a cornerstone of scientific inquiry, and of immense value within the social sciences, enabling the identification of variation and consistency in patterns of behaviour (Corbin and Strauss, 2015). Indeed, within qualitative research, contrasting one set of data with another has been described as "the heart of analysis" (Krueger, 1998 pg.17). Distinguished from merely juxtaposing descriptions of individual cases, a comparative analysis aims to build upon the observation of similarities and differences between cases to develop a better understanding of the contributory processes involved in the production of an event or behaviour being studied (Pickvance, 2005).

Quantitative methods have been used to undertake comparative analyses of medicine-taking behaviours across LTCs. Such works encompass a variety of approaches including survey designs e.g., (Unni and Goren, 2018), network meta-analyses e.g., (Walsh et al., 2019), and retrospective database analyses e.g., (Quisel et al., 2019), comparing within and across conditions. A common criticism of such approaches is that identities, experiences, perceptions and beliefs influencing human behaviour cannot meaningfully be reduced to numbers, and comparative analyses taking quantitative approaches often do so devoid of the social contexts within which such behaviours occur (Choy, 2014).

A systematic review summarising evidence from 55 studies found that experiences faced by people with LTCs were associated with safety and clinical effectiveness parameters in healthcare, including treatment adherence, health-promoting behaviour, and healthcare resource use. The authors further found that this held true across a range of disease areas, study designs, settings, and population groups (Doyle et al., 2013). Peoples' experience of their care, as well as their observation of the care of others, can offer valuable insights into the everyday provision of healthcare for those with chronic conditions. As qualitative methods give voice to the contexts that influence the actions individuals take, as well as the meanings they associate with these (Yilmaz, 2013), such methods present an effective vehicle to explore these experiences within the context of medicine-taking behaviours and are therefore a central feature of this thesis.

Within the context of this thesis, while the ineffectiveness of individuals to consistently take long-term medication has been noted across the clinical spectrum (Brown et al., 2016), previous research has indicated this to be particularly pronounced amongst individuals with OAB. Indeed, when compared to treatments for five other long-term conditions, (including hypertension and diabetes), individuals taking OAB treatment were associated with the lowest 1-year treatment adherence and persistence rates (Yeaw et al., 2009). Building on such comparisons within a quantitative paradigm and armed with the first fully qualitative exploration of factors influencing medicine-taking behaviours within OAB (see Chapter 4), the present chapter will describe a comparative analysis of themes relating to barriers and facilitators to adherence in OAB (as described in Chapter 4) against those identified in the literature for other LTCs.

Objective and rationale

The OAB study (described in Chapter 4) presented several key thematic areas related to adherence and persistence behaviours in OAB. The current exploratory comparative analysis aimed to compare the themes identified within the context of OAB with published reviews of barriers and facilitators of adherence in other LTCs.

Conducting such an analysis allows the observations from one LTC (OAB) to be explored within the context of a wider clinical landscape. Considered the gold standard for quality and rigour in qualitative research (Key, 2017), of the four criteria of trustworthiness: ‘credibility’, ‘transferability’, ‘dependability’ and ‘confirmability’ (Lincoln and Guba, 1985), the constructs of ‘credibility’ and ‘transferability’ may be particularly useful to consider in the context of the present study concerning the wider content of this thesis.

The construct of ‘transferability’ has been defined as the extent to which findings from one study can be transferred to other contexts or settings (Forero et al., 2018). A key contribution of the present comparative analysis is to enable areas of convergence and divergence in medicine-taking behaviours across clinical areas to be examined. This will widen the scope of the current works as well as its applicability to a wider group of stakeholders including individuals with interests in OAB, the other LTCs considered, or the common drivers and barriers to medicine-taking behaviours more generally. Relatedly, ‘credibility’ had been defined as the ability of the readers of a study to be able to recognise the experience being represented and relayed by the researcher (Nowell et al., 2017). Supporting this construct, alongside the adoption of well-established approaches to methodology and sampling, the use of multiple methods of data collection and multiple groups of participants (termed triangulation), has been suggested as a powerful form of corroboration (Shenton, 2004). Conducting a comparative analysis between the findings of the OAB study and individuals in a comparable position experiencing other LTCs may thus serve as a means of triangulation via data sources, thereby enhancing the credibility of the findings and recommendations within this thesis (Shenton, 2004).

Finally, noting areas of convergence and divergence to other LTCs may help distinguish particularities in the experience of OAB and other LTCs, as well as drivers of adherence behaviours, thus offering actionable insights for clinicians and policy makers into the differential management and support needs for individuals across conditions.

Comparative LTCs explored

As the comparative analysis described in this chapter was exploratory in aiming to note the convergence and divergence in factors influencing medicine-taking behaviours across LTCs, key choices such as how many LTCs and which ones to compare to were subjective and the result of a deliberative process influenced by my professional and academic experiences. This followed the principles of purposeful sampling, a widely used sampling technique in qualitative research, characterised by the selection of *"information-rich cases"* (Palinkas et al., 2015 pg.534). Taking such a deliberative approach to sampling, which would be characterised as a source of bias (and therefore a weakness) in quantitative approaches, becomes an intended focus under this approach, and is therefore considered a strength (Patton, 2002).

In considering the scope of the current analysis, comparing to a single LTC felt restrictive in that while I could have considered several publications within the same clinical area to compare to, and as a result, possibly produced a deeper comparison, such an analysis would still only consider the findings of the OAB study within the context of a single LTC. This then would not achieve the aim of exploring the transferability of the findings to a multitude of LTCs. Similarly, considering a large range of LTCs to include, whilst of academic interest to me and possibly to the readership of this thesis, was not feasible given the logistical limitations of time and costs. I therefore settled on including three LTCs to compare the findings of the OAB study.

In deliberating on which LTCs to include within the comparison, I reflected upon my experiences both as an HCP and a researcher, as well as what I considered to be the most informative comparisons to make for the potential readership of this thesis. Such a judgement was informed by three key considerations: the centrality of the OAB experience, its importance to the current healthcare agenda, and its relevance to the future needs of the healthcare system.

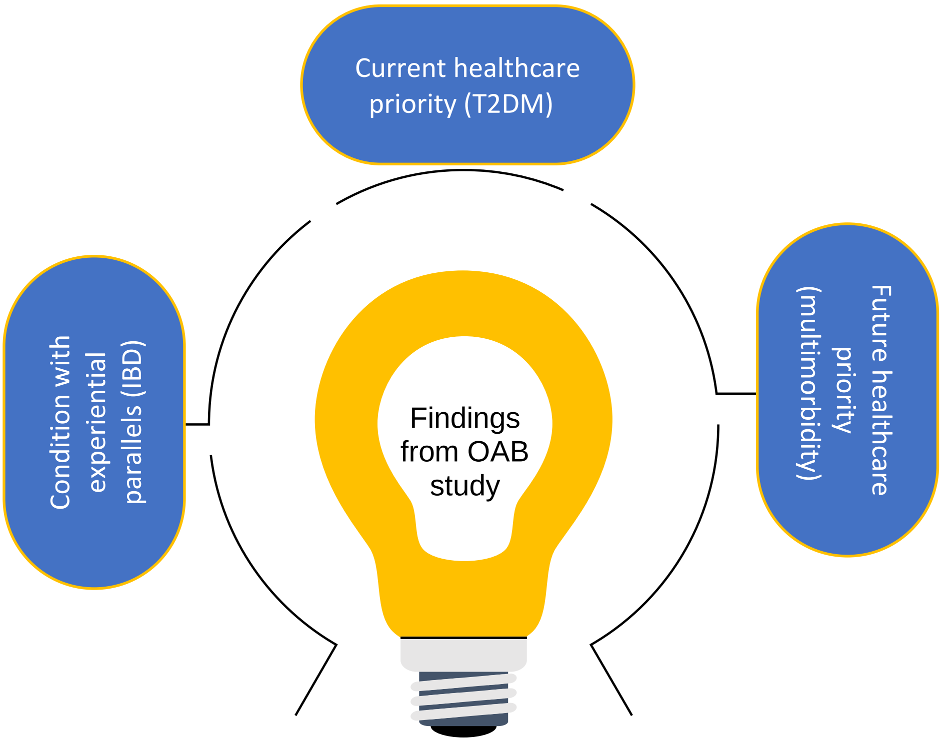


Figure 5.1: Approach taken to the comparative analyses undertaken

OAB-parallel condition

Given the findings of the OAB study where the experience of OAB symptoms themselves was central to the importance individuals attached to their condition, as well as its management, the choice of the first comparison paper centred on a bowel condition where strong parallels could be drawn to OAB both in terms of symptom expression and impact of social judgement. In addition to their proximity and common innervation from spinal afferent pathways, the bowels and bladder share primary roles within the body of collecting, storing, and expelling waste (Grundy and Brierley, 2018). There are therefore clear parallels between similar losses of control and undesirable juxtaposition of private behaviours in public between the two conditions (Robertson et al., 2022). The close relationship between bladder and bowel conditions has been noted in the literature with a higher prevalence of urinary symptoms observed in those experiencing bowel conditions than those not (Klingele et al., 2010), as well as an association between faecal incontinence and LUTS such as urinary urgency, frequency, and urge incontinence (Malykhina et al., 2012). Within the sphere of bowel-related conditions, inflammatory bowel disease (IBD) is among the most prevalent (Greenwood-Van Meerveld et al., 2017), affecting over 620,000 people in the UK, with a rising incidence (Ghosh and Premchand, 2015), and so was an appropriate choice for the present analysis.

Current healthcare priority

In exploring the findings of the present work on OAB within a broader context, it was useful to consider an LTC of high importance on the current healthcare agenda, to ensure the learnings of this thesis applied to the current healthcare priorities. While there is a wide range of prevalent chronic conditions that may be considered burdensome to the individual as well as society as a whole, one of the most challenging LTCs currently facing the NHS is type 2 diabetes mellitus (T2DM), in part due to its growing incidence, as well as due to its diffuse health effects and consequences for the individual, their family, and society as a whole (NAPP, 2019). Described as a *"health crisis"* (Rowley et al., 2017 pg.11), over 10 million people in England are at an increased risk of developing T2DM, with at least a tenth of the annual NHS budget currently being spent on the condition (UK, 2020). Type II diabetes, therefore, represents a significant current priority for the NHS (Newbound, 2019), and has therefore been considered within the present thesis as the second area of comparison to the findings in the OAB study.

Future healthcare priority

Finally, defined as when an individual has two or more medical conditions simultaneously, multimorbidity is recognised as a growing public health challenge, particularly in the elderly (Johnston et al., 2019), and is an area of increasing concern for healthcare systems globally (Head et al., 2021) both presently and in the future (Pearson-Stuttard et al., 2019).

Being a highly relevant phenomenon from a wider healthcare policy and practice standpoint, according to a recent Government White Paper, *"one in three patients admitted to hospital as an emergency has five or more health conditions, up from one in ten a decade ago"* (Health and Care, 2021 pg.5). The authors further highlighted that the proportion of people over 65 years of age with four or more conditions is expected to almost double by 2035, driven in part by demographic changes, stating that while the general population is expected to grow around 10% over the next two decades, the number of people aged over 75 years is expected to grow by almost 60% (Health and Care, 2021). Patients with LTCs, and particularly those with multiple comorbidities have been noted to engage in increased use of unscheduled care including emergency department, out-of-hours, and walk-in clinic attendances, than those without LTCS, in turn representing a large share of total healthcare costs within the UK (Langer et al., 2013). Furthermore, multimorbidity is associated with decreased HRQoL, mobility and functional ability, as well as higher mortality (Masnoon et al., 2017).

Closely related to multimorbidity, polypharmacy is generally defined as taking five or more prescription medications and may be further delineated into 'necessary polypharmacy' and 'unnecessary polypharmacy' to acknowledge the difference between the appropriate use of multiple medications to avoid morbidity and the inappropriate use of excessive medication (Lee et al., 2020). Polypharmacy may also be associated with an increased risk of non-adherence, which, while poorly understood within the context of multimorbidity, can deepen the burden of multiple health conditions in terms of both morbidity and mortality (Foley et al., 2021). It is therefore highly relevant and appropriate to explore the alignment of findings on the drivers and barriers of medicine-taking behaviours within a single LTC in the present work, with findings of works exploring similar factors in those experiencing multiple LTCs.

Methods and structure

The reader is referred to the section entitled ‘methods for comparative analysis’ in Chapter 5 for a background on the approach taken to comparing thematic data and the choice of presentation methods used within the present chapter. The remainder of this chapter will be dedicated to presenting each of the three comparison papers in their respective sections, prefaced by a brief introduction to give the reader important context to the condition and its treatments. The findings from each comparison paper will then be compared to those from the OAB study and discussed sequentially in light of the relevant theoretical considerations. The final discussion and conclusion section will bring together the noted areas of convergence and divergence between the individual analyses and summarise the learnings within this chapter.

OAB-parallel LTC

Inflammatory Bowel Disease

Background

IBD consists of two distinct conditions: Crohn's disease, and ulcerative colitis, affecting different areas of the gastrointestinal tract with a subset of patients where it is not possible to distinguish between the two (known as IBD unclassified) (Ghosh and Premchand, 2015). Many studies do not distinguish between the two conditions in the literature, and employ samples consisting of both types of patients (Wilburn et al., 2017). As described below, there are significant parallels that may be drawn between the experiences of individuals with IBD and OAB.

Crohn's disease

Crohn's disease is described as a chronic, inflammatory condition affecting the gastrointestinal tract. It causes the formation of lesions ranging along the full extent of the alimentary canal, resulting in flare-ups of symptoms such as diarrhoea, abdominal pain, rectal bleeding, fever, weight loss and fatigue, followed by periods of remission (Veauthier and Hornecker, 2018), offering parallels to the wax and waning nature of OAB symptoms over time (Fontaine et al., 2021). The aetiology of Crohn's disease is considered to be multi-factorial with genetic factors, dietary and environmental triggers, immune dysfunction and gut microbiome thought to be involved (Sandefur et al., 2019). Crohn's can affect patients of all ages, however, symptoms usually appear between the ages of 10 and 40. It is estimated that Crohn's affects one in every 650 people in the UK, with women slightly more likely to be affected than men (Crohns and Colitis UK, 2016).

Ulcerative colitis

Ulcerative colitis is a chronic inflammatory condition of the large intestine, most commonly affecting adults aged 30-40 years of age (Ungaro et al., 2017). Causing continuous mucosal inflammation, erosion, and ulceration, it too is characterised by periods of relapse and remission, resulting in hallmark symptoms of bloody diarrhoea, faecal urgency and tenesmus (the feeling of a need to pass stools, despite bowels being empty) (Gajendran et al., 2019). Such symptoms of urgency offer further parallels to people who experience OAB and urinary urgency in particular. Other symptoms of ulcerative colitis include abdominal pain, fatigue and weight loss, with more diffuse effects presenting in a flare up including painful and swollen joints, mouth ulcers skin rashes, and irritated eyes, suggesting an autoimmune causation (NHS.UK, 2019d). Ulcerative colitis affects an estimated one in every 420 people in the UK and is more common in white Europeans and black people than those of Asian backgrounds (NHS.UK, 2019d).

Treatments

Crohn’s disease

Like OAB, in the absence of a cure for Crohn’s disease, treatment aims to induce and maintain remission, with options including trigger avoidance (smoking cessation and dietary triggers), pharmacological management, and surgical intervention (BNF, 2020). Glucocorticosteroids such as prednisolone, methylprednisolone or hydrocortisone are used to induce remission in those presenting with an exacerbation. Alternative treatments at this stage include budesonide or amino salicylate where glucocorticosteroids are contraindicated or not tolerated. Mercaptopurine, azathioprine or methotrexate may be used as add-ons to manage symptoms if required. Biologic treatment options for severe active Crohn’s includes recombinant human monoclonal antibodies infliximab and adalimumab. Maintenance pharmacological treatment (where needed) includes azathioprine, mercaptopurine or methotrexate (NICE NG129, 2019).

Ulcerative colitis

Treatment is focussed on the management of flare-ups, as well as the induction and maintenance of remission, and may include pharmacological intervention, biologics, or surgery (BNF, 2022). Pharmacological treatment of ulcerative colitis may be systemic (oral) or local (topical, suppository or enema) depending on the location and severity of the inflammation (BNF, 2022). NICE guidelines recommend the use of a topical amino salicylate for the management of inflammation of the rectum or the sigmoid colon, with the option of adding a time-limited course of topical or oral corticosteroids should this not suffice. Inducing remission in more extensive disease calls for the combination of a topical and high-dose oral amino-salicylate as the first-line treatment. If remission is not achieved within 4-weeks. The oral amino-salicylate may be replaced with a time-limited course of an oral corticosteroid. Biologics may be recommended for moderate to severe ulcerative colitis, and include infliximab, adalimumab, and golimumab. Maintenance therapy may entail the use of a topical amino salicylate alone, in combination with an oral amino salicylate, or an oral amino salicylate alone. However, oral amino salicylate treatment alone is not as effective as combined treatment (NG130, 2019).

Devlen et al. (2014)- “Barriers to mesalamine adherence in patients with inflammatory bowel disease: a qualitative analysis”

While the Devlen, et al. study was not a review paper as with the other two comparative LTCs in the present chapter, it was, however, particularly apt for comparison to themes identified in OAB. In addition to the similarities between IBD and OAB noted above, the Devlen study too served as the first qualitative work exploring barriers to treatment adherence in an otherwise quantitatively dominated space. As such, it provided situational similarities alongside subject areas and clinical ones.

Describing a study to explore the causes of non-adherence to a common oral amino salicylate (mesalamine) used for the treatment of IBD, Devlen et al. began by introducing the reader to the chronic nature of IBD and the need for long-term treatment adherence to support remission. They went on to state that such medicine-taking behaviour within the context of IBD is poor, further linking this to higher rates of relapse and HCRU. Further mirroring the present work on OAB, the authors highlighted the limitations of previously used quantitative approaches to the understanding of barriers to adherence within IBD, stating *“our understanding of adherence behaviours in patients with IBD is thus incomplete”* (Devlen et al., 2014 pg. 309).

Summary of objectives and methods

This study aimed to understand the attitudes of individuals with IBD towards adherence, to inform a conceptual model of adherence in this condition.

The authors conducted a qualitative study involving four focus groups (of 2-6 individuals) and ten 1:1 interviews, with participants recruited through a specialist tertiary clinical site, according to the following inclusion criteria:

- Patients over 18 years of age with mild/moderate ulcerative colitis or Crohn’s disease,
- in clinical remission at the time of the study, and
- prescribed only mesalamine for the maintenance therapy.

A total of 27 participants gave written informed consent and received renumeration for their time. Trained interviewers used a standardised moderator guide to conduct the interviews and focus groups and continued data collection until information saturation was reached (defined by the authors as when no new information was being identified). Transcripts were analysed by a single analyst using Grounded Theory to identify themes and relationships between them.

Results

Participants

Of the 27 participants, three reported being adherent to their treatment with the remaining 24 reporting intermittent non-adherence.

Table 5.1: Participant characteristics (modified from table 1 in (Devlen et al., 2014))

Characteristic (n=27)	
Mean age	31.5 years
Age range	20-59 years
Gender	52% (M) : 48% (F)
Mean disease duration	6.5 years
% Diagnosed with Ulcerative Colitis n (%)	21 (78)
% Diagnosed with Crohn’s Disease n (%)	6 (22)
Mesalamine schedule n (%):	
Once daily	15 (55)
Twice daily	9 (33)
Three times daily	13 (48)

Themes identified

Barriers to adherence were categorised into the following themes:

Table 5.2: Summary of themes from (Devlen et al., 2014)

Theme	Description
Competing priorities	Forgetting to take treatment due to changing circumstances
Efficacy values	Suboptimal treatment efficacy. As well as situations warranting less adherent behaviours (such as being in remission).
Side effects	Experience of adverse effects associated with treatments
Pill characteristics	Size of tablets, frequency of dosing, and not wanting to take tablets.
Social stigma	Impractical, socially awkward or embarrassing to take medication in the presence of others
Refill inconvenience	Temporary interference with adherence caused by the inconvenience of visiting a pharmacy to collect a prescription
Costs	The cost of treatment was a significant concern for 5 participants

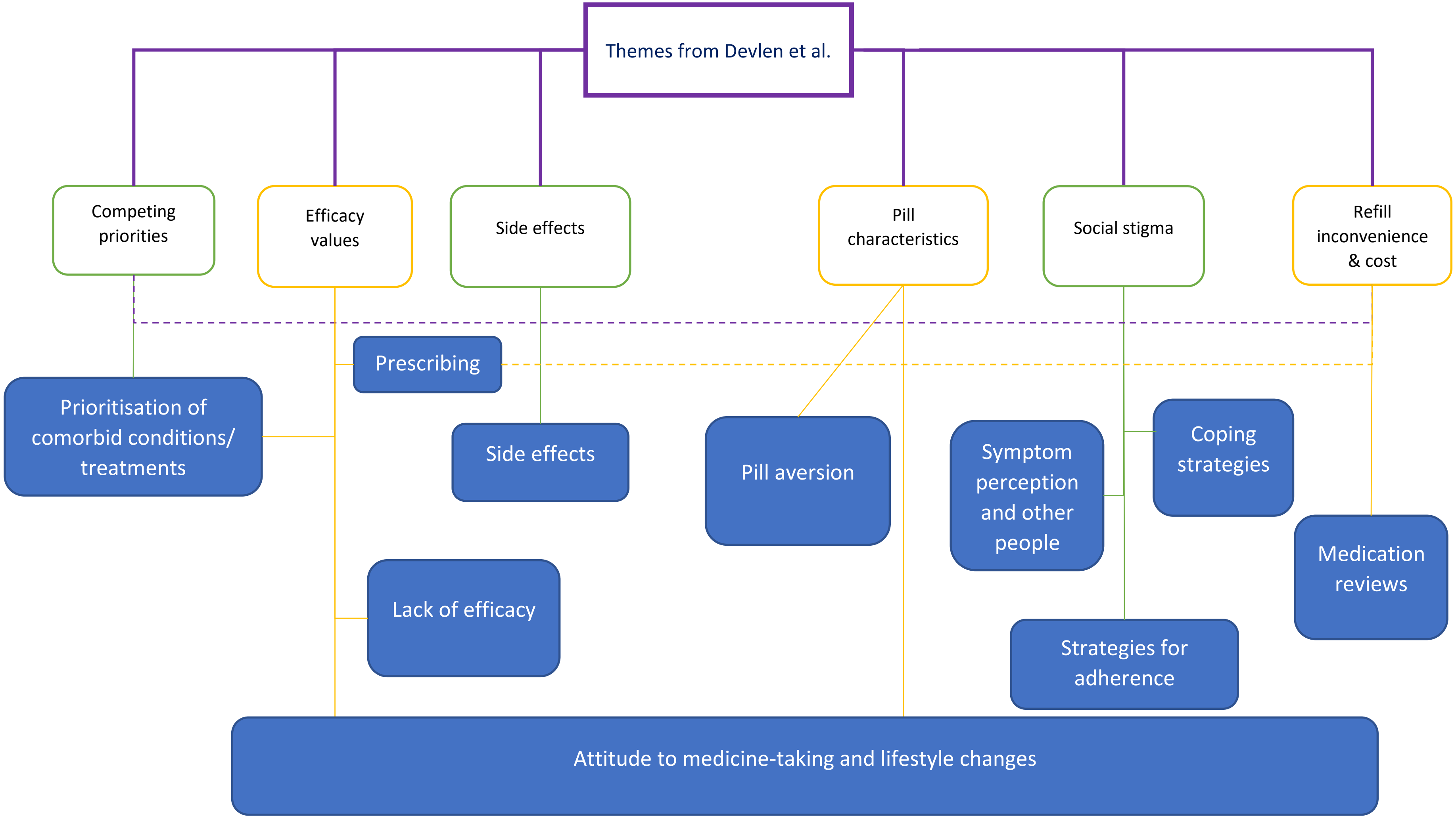


Figure 5.2: Comparison of themes from Devlen et al. and the OAB study

Discussion and comparison to the OAB study

Competing priorities

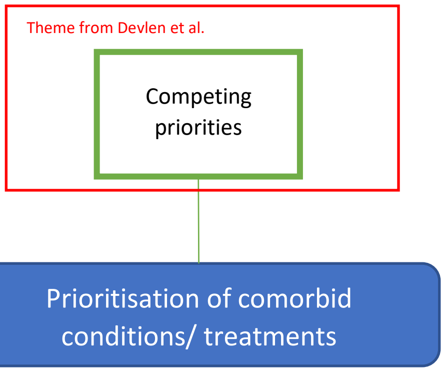


Figure 5.3: Comparing "competing priorities" theme from Devlen et al. to themes from OAB study

The theme of ‘competing priorities’ encompassed not taking IBD treatment due to forgetting, being busy or distracted, changes in routine such as weekends and holidays (where usual cues to take treatment were missed), and general disorganisation. The overall experience of the OAB cohort offered limited support for this theme as most participants reported few problems with unintentional non-adherence. However, such findings did echo the experiences of participant 10 of the OAB study who described much more difficulty with maintaining adherence *“if I’m out somewhere”*, and participant 3 who hypothesized the effects of getting older on forgetting to take her OAB treatment. While in the context of IBD, competing priorities included school and work, it is important to note that the majority of participants in the OAB study were retired, and such had much less likelihood of such competing activities exerting a similar effect on their adherence behaviours. This was also supported by the significant differences in mean age between the OAB study (70 years) and the IBD study (31 years). Offering a distinct form of competing priorities, the OAB theme of ‘prioritisation of comorbid conditions/ treatments’ gave the closest observation of where individual medicine-taking behaviours were affected by competing interests, offering considerable support for the importance of illness perceptions as delineated by the CSM. However, such observations were not described in the Devlen paper.

Efficacy values

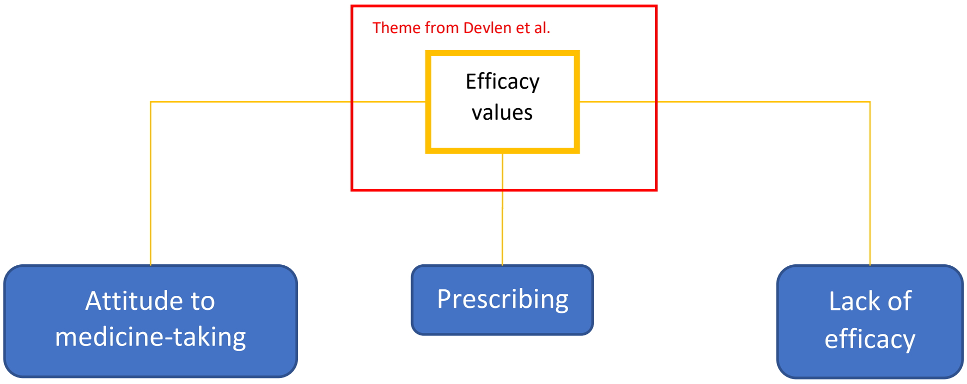


Figure 5.4: Comparing the theme of "efficacy values" from Devlen et al. to findings from OAB study

Under the theme of efficacy values, the IBD study authors noted that *"patients who claimed not to see any benefits from their medications or were not convinced of their efficacy were less likely to adhere to their medication"* (Devlen et al., 2014 pg. 312), also observing patients questioning the need to take their treatments in times of remission. This offered significant congruence to the themes around risks and necessity observed in the OAB study (described in chapter 4 under the section titled 'attitudes to medicine-taking and adopting lifestyle advice'), as well as the theme of lack of efficacy driving non-adherence. Such observations from both studies echoed the findings of the NCF whereby individuals are more likely to adhere to treatments when the results of an internally undertaken 'cost-benefit analysis' are favourable to doing so (Horne and Weinman, 1999).

The reporting of a patient commenting: *"Why should I take it if I'm not seeing any benefits?"* (Devlen et al., 2014 pg.312) echoed the requirement of proven efficacy from participant 17 in the OAB study who stated: *"well if I can go without, taking the medication- fair enough but if there is any proof that it will improve the symptoms, by all means I would have a go at it".* This also gave credence to the 'motivation' domain of the IMS model whereby the individual's belief in the treatment and their consequent commitment to it was integral to supporting adherence behaviours (DiMatteo et al., 2012).

A further common observation between the two studies included the notion of there being an acceptable time in which participants gauged the appearance of such effects, and the decision to discontinue once this had lapsed without the prerequisite treatment efficacy emerging. In the context of the IBD study, this was denoted as a subtheme called 'time to response', though was not expanded upon beyond the use of a quote from a single patient commenting: *"I was taking these pills, and I was on it for a while. I can't even tell you how long I was on it. And, I just felt I doubted that it was even doing anything for me. So I just stopped taking it."* (Devlen et al., 2014 pg.311). While the time between initiation and discontinuation was not explicitly explored in either study, similar observations were made within the OAB study where participants described 'trying' medication (a descriptor, partly fueled by HCP language while prescribing), or believing to be a recipient of a 'course' of treatment (discussed under the OAB theme of 'prescribing'), and is further bolstered by the observation that in clinical practice, the majority of OAB patients discontinue treatment within 1-3 months of commencement (Chapple, 2017a). Such an observation in both studies also highlighted the joint influence of both the 'reflective motivation', and 'psychological capabilities' domains of the COM-B model whereby individuals' knowledge and understanding of their condition and its treatments interplayed with their reasoned evaluation of these to shape instances of suboptimal adherence behaviours (Michie et al., 2011).

Also under the present theme, the authors of the IBD paper gave an example of a patient being dismissive about taking treatment for maintenance *"suggesting the medication was perceived as a less important class of drug"* (Devlen et al., 2014 pg.312). While the authors did not expand on this observation, it nevertheless offers support for the role of drug hierarchies as well as illness perceptions (from which drug hierarchies may be borne) in shaping adherence behaviours.

Side effects

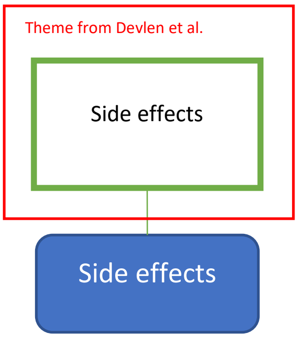


Figure 5.5: Comparing the theme of "side effects" from Devlen et al. to findings from the OAB study

While the portrayal of side effects as a barrier to treatment adherence in IBD was unsurprising given their explicit mention in several of the models described in Chapter 1, only three patients reported experiencing and attributing such effects to their IBD treatment. This was in contrast to observations in the OAB study where the majority of participants (13/18) attributed feared and actual side effects as a reason to discontinue treatment. This may be explained, in part, by the difference in participant ages between the two studies, and reinforced by the observation that the elderly are particularly predisposed to experiencing adverse effects, due to age-related changes to pharmacokinetic and pharmacodynamic processes, as well as a higher incidence of polypharmacy (Dubrall et al., 2020). Furthermore, given that over 600 medications have been identified as possessing some level of antimuscarinic effects, as well as the additive nature of such effects, the presence and impact of such treatment effects within the context of OAB are made clearer (Ghossein et al., 2020).

Pill characteristics

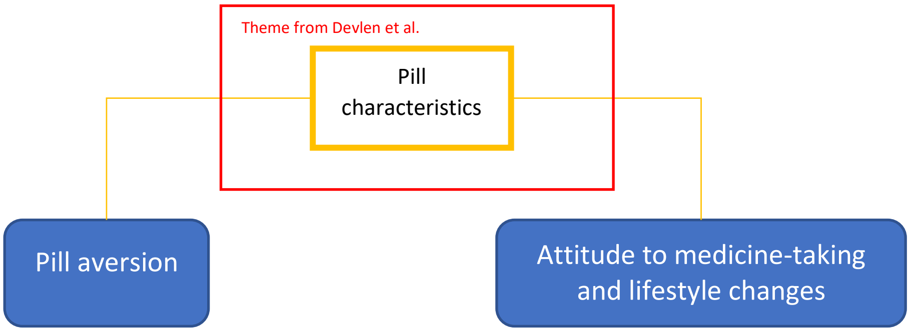


Figure 5.6: Comparing the theme "pill characteristics" from Devlen et al. to findings from the OAB study

The theme ‘pill characteristics’ within the context of IBD covered the size of the mesalamine tablets themselves, as well as the prescribed dosing frequency (with 33% of patients on a twice-daily regimen and 12% on a three-times-a-day regimen). Such observations were not made in the OAB study where most participants described once-daily treatment regimen, with some prescribed twice-a-day treatment. The physical nature of the tablets themselves was also not presented as a barrier to adherence within the OAB study, in contrast to the IBD study where the size and shape of the tablets were commented on in this context.

A final observation within this theme that did show agreement with the OAB study was of patients simply not feeling like taking their medication. Termed ‘pill fatigue’ within the IBD study, this theme fitted well with the ‘pill aversion’ theme within the OAB study which described participants exhibiting a general dislike of taking medication, preferring to stay off treatment if deemed possible and even stopping less ‘necessary’ treatments to enact this theme. Similar notions have been captured within the literature under terms such as ‘treatment burden’ or ‘medication-related burden’, describing the burden of taking treatments as distinct to that of the conditions themselves, and including facets such as the burden of adverse effects, dependence, and impact on daily living (Awad et al., 2020).

Social stigma

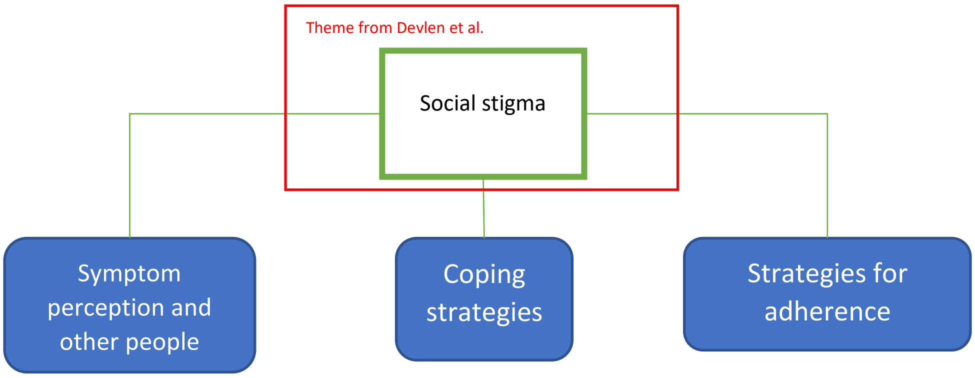


Figure 5.7: Comparing the theme of "social stigma" from Devlen et al. to findings from the OAB study

Related to the previous theme of the prescribed dosing frequency and the consequent effect of having to take treatment throughout the day, patients in the IBD study described taking treatment in the presence of others as impractical, socially awkward, and embarrassing. They further associated such observations with felt stigma, highlighting the importance of 'social/economic factors' as described by the WHO's five dimensions of adherence model, as well as the 'cultural, somatic, and psychological context' as defined by the CSM on illness perceptions (both described in Chapter 1). Examples supplied included not wanting to disturb a fellow university student with the sound of a shaking pill bottle and avoiding unwelcome medical questions whilst on a date. Such feelings manifested themselves as delaying IBD treatment or skipping doses entirely to preserve discretion. Such an observation was not made within the OAB study, partly on account of the differences in demographics and occupation. Several patients within the IBD study were reported as being at college, or beginning new relationships, whereas participants within the OAB were mostly retired, and described their medicine-taking largely within their homes. This may also have been aided by the once, or twice-daily dosing schedule in the OAB study which allowed such discrete management, as opposed to the dosing in IBD, which can be up to 3-4 times daily (BNF, 2022). Furthermore, there may have been differences in the packaging of medication between OAB and IBD, with OAB treatment typically available in standard blister packaging, as opposed to pill bottles as described in the IBD study.

The theme of 'social stigma' within the IBD study, however, resonated most strongly with the described experience of OAB symptoms themselves, as opposed to the act of taking treatment. Considering the importance of illness perceptions to adherence behaviours, it is useful to note that the distinct symptom expression and coping strategies between individuals with OAB occurred at the interface between cultural, somatic, and psychological contexts described in the CSM. Within this context, the OAB themes of 'other people', 'downplaying symptoms' and 'comparing with others' formed the bedrock of how embarrassment and social judgement were managed by participants in the OAB study (described under the overarching OAB theme of 'symptom perception and other people'). Measures employed by individuals to contain OAB symptoms were also in part, fuelled by a desire to avoid public disclosure of their symptoms, and included forward planning to know the locations of toilets, pre-emptive use of the toilet, absorbent pads, and fluid management (under the OAB theme of 'coping strategies'), as well as the strategies used to remain adherent ('strategies for adherence' theme).

Stigma has been defined as *"an attribute that makes a person different from others in a social category and…reduces the person to a tainted or discounted status"*(Goffman, 1997 pg.133). While the 'social stigma' theme reported by Devlen et al. related more towards the felt stigma of the treatment itself as opposed to IBD itself, it is likely there is a strong relationship between the two, as well as the individual's perception of IBD and that of those around them. Such relationships have been noted in the literature where medications used to treat stigmatised conditions have stigma by connection. An example is where medications needed for the treatment of mental disorders are labelled as ‘expensive’, despite their cost being much lower than the treatments used for other conditions. The authors noted that the treatments *“are not considered expensive because of their cost, but because they are meant to be used in the treatment of people who are not considered to be of much value to the society”* (Sartorius, 2007 pg.396).

The desire to avoid disclosure relating to treatment is unlikely to occur independently of a desire to avoid disclosure of IBD itself, meaning that although not explicitly mentioned by Devlen et al., the theme of ‘social stigma’ may well relate to the condition itself as well as the acts of managing it in public, thus introducing further similarities to the theme of ‘symptom perception and other people’ in the OAB study. Such a desire to avoid disclosure may stem most strongly from the ‘consequences’ cognitive domain of illness perception in the CSM model whereby an individual associates their illness with effects on their work, family, lifestyle and finances, reflecting the subjectively perceived severity of their condition (Petrie and Weinman, 2006). Such observations have been made in other studies exploring illness perception in IBD. Vegni et al. noted that IBD has a significant impact on social and personal relationships, and that poor illness perceptions in IBD (in particular relating to perceptions of consequences of IBD), were associated with significantly poorer psychological adjustment and QoL (Vegni et al., 2018).

Refill inconvenience and cost

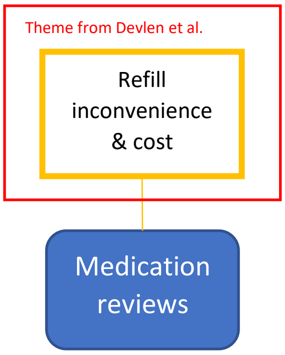


Figure 5.8: Comparing the theme of "refill inconvenience and cost" from Devlen et al. to findings from OAB study

Within the IBD study, the theme of refill inconvenience was linked to 'competing priorities' and described individuals with IBD forgetting to refill a prescription, or not being able to fit in a visit to the pharmacy, leading to not physically having the mesalamine to take. This was further complicated by having to speak to a physician to arrange the prescription to begin with, (possibly a feature of the US healthcare system where this study was conducted). This was in contrast to the experience of most participants in the OAB study who described being prescribed their treatments even in the absence of such reviews, with several participants commenting on the ease of ordering repeat prescriptions, either automatically done by the pharmacy, or via the surgery's request system (discussed under the OAB themes of 'prescribing' and 'medication reviews'). Relatedly, some OAB participants described receiving free deliveries from the pharmacy, with some getting their tablets packed into dosette boxes, further increasing the ease and convenience of taking medication.

Costs also featured as a theme within the IBD study, with 5 patients reporting it to be a significant concern, and a driver of non-adherent behaviour. This was particularly of note during times of symptom remission where the perceived need for treatment was lower, and competing priorities held more financial significance. This was not observed within the OAB study as the majority of participants were over the age of 60 and so were eligible for free prescriptions. Even in the event of being under 60 years of age, the prescription charge within England is currently £9.35 for a single item, £30.25 for a 3-month pre-payment certificate (PPC), and £108.10 for 12 months, meaning individuals can access all the prescribed treatment they need for slightly over £2/week (Gov.UK, 2022). This is in contrast to the USA-based IBD study, where the healthcare system is a complex mixture of public and private insurers, and where universal healthcare coverage has not been achieved (Shi and Singh, 2022). This is further evidenced by WHO data held by the World Bank stating that out-of-pocket expenditure per capita on health in the US was 42% higher than in the UK (World Bank, 2022).

Current healthcare priority LTC

Diabetes

Diabetes is defined as a group of metabolic diseases characterised by raised blood glucose, as a result of malfunctioning insulin secretion, the insulin itself, or both (American Diabetes Association, 2010). There are two main subtypes of the condition: type I (diabetes insipidus) and type II (diabetes mellitus) with the vast majority of adult cases (around 90%) being type 2 (NHS.UK, 2019b).

Background to type II diabetes

Accounting for between 90-95% of all diabetes cases in the UK (Xiao and O'Neill, 2017), T2DM is characterised by a reduced sensitivity and response to insulin, despite it still being produced by the body (as opposed to type I, which is characterised by insulin insufficiency). This leads to hyperglycaemia, resulting in symptoms of weight loss, polyuria and polydipsia and polyphagia (Simmons and Michels, 2015), which can produce symptoms mimicking OAB (repeated need and urgency to micturate). Left untreated, T2DM can increase the risk of cardiovascular complications like coronary heart disease and strokes (Kayyali et al., 2019). Chronic hyperglycaemia can also lead to microvascular complications including neuropathy, nephropathy and retinopathy, as well as macrovascular complications such as cardiovascular disease, stroke, and peripheral artery disease (Papatheodorou et al., 2018). Estimates from Diabetes UK suggest that 1 in 10 adults over 40 now has T2DM in the UK, with total cases of all diabetes expected to rise from 4.7 million, to 5.5 million by 2030 (Diabetes UK, 2019).

Treatments

NICE guideline NG28 highlights the need for structured education for adults newly diagnosed with T2DM and recommends annual reinforcement and review, accompanied by dietary and lifestyle modification. Pharmacological therapy is initiated with escalating doses of metformin or, if this is contraindicated or not tolerated, a sulfonylurea, pioglitazone, or a dipeptidyl peptidase-4 (DPP-4) inhibitor is given. Following the intensification of oral therapy (including dose increases, add-on therapies and combination therapies), insulin-based treatments are indicated. It is recommended that although the necessity of other oral therapies should be reviewed at the point of initiating insulin, metformin should be continued where tolerated to aid glycaemic control. Glucagon-like peptide (GLP-1) mimetics or sodium-glucose co-transporter-2 (SGLT-2) inhibitors offer additional treatment options should further intensification be required (NICE NG28, 2019).

McSharry et al. *(*2016*)*- "Perceptions and experiences of taking oral medications for the treatment of Type 2 diabetes mellitus: a systematic review and meta-synthesis of qualitative studies"

Noting the literature describing poor levels of treatment adherence in T2DM patients, McSharry et al. (2016) highlighted three areas of consequence: poor glycaemic control, increased mortality and hospitalisation rates and higher healthcare resource use. The authors went on to state the suboptimality of medication adherence in long-term conditions more broadly but emphasised the complexity of medicine-taking behaviours in T2DM, and the particularly limited success of interventions in this space. Acknowledging the strengths of individual qualitative studies in reaching a deep understanding of such complex behaviours, McSharry et al. noted the particular advantages of synthesising findings across multiple studies to generate insights beyond that of an individual study, noting that such approaches had been used in other areas such as exploring the patient understanding of diabetes itself and its management, as well as strategies to manage diabetes over time (McSharry et al., 2016).

Summary of objectives and methods

This study aimed to explore the perceptions and experiences of individuals taking oral T2DM treatment, with the authors employing a systematic literature review and a qualitative meta-synthesis to achieve this.

SLR

CINAHL, EMBASE, MEDLINE, and PsycINFO databases were searched for terms relating to T2DM, adherence, and qualitative research methods. The search was conducted in 2014 and included all available records from each database (1937, 1947, 1946, 1806 onwards, respectively).

Inclusion and exclusion criteria

Table 5.3: Inclusion and exclusion criteria for McSharry et al. (2016)

Inclusion	Exclusion
Published studies focusing on patient perceptions and experiences of taking oral medication for T2DM	Non-English articles
	Studies with a mixed sample of patients with T2DM and other conditions
Using qualitative methods of data collection and analysis	Mixed method studies where qualitative data were not reported separately
Adult patients (>18 years)	Studies focusing primarily on insulin
	Reviews or grey literature

Studies identified

A total of 1162 records were identified, from which after deduplication and title, abstract and full-text screening, 8 studies were included within the qualitative synthesis. A brief summary is provided in Table 5.4 below:

Table 5.4: Summary of selected studies for meta-ethnography reproduced and adapted from Table 1 from (McSharry et al., 2016 pg. 1334)

Study	Research question	Country and setting	Participants	Methods data collection/analysis
Lawton et al. 2005	To explore British Pakistani and British Indian patients' perceptions and experiences of taking oral hypoglycaemic agents	Scotland, Primary care and community	N = 32 (17 female) Age: 30–50 years: n = 6 51–60 years: n = 10 61–70 years: n = 13 ≥71 years: n = 3 Pakistani, n = 23 Indian, n = 9	In-depth interviews Grounded theory
Lawton et al. 2008	To examine Type 2 diabetes patients' expectations, perceptions and experiences of oral glucose-lowering agents including their reasons for taking/not taking drugs as prescribed	Scotland, Primary care and community	N = 20 (9 female) Mean age: 60.8 years 20 white	Repeat in-depth interviews Thematic analysis
Tija et al. 2008	To explore the concerns of older adults with diabetes about the complexity of their drug regimens and to determine whether they discussed medication related concerns with their physician	US, Outpatient geriatric medicine practice	N = 22 (16 female) Mean age: 75.0 years African-American, n = 16 White, n = 3 Asian/Pacific, n = 1 Islander/ Hawaiian n = 1 American Indian/ Alaskan Native, n = 1 Other n = 1	In-depth semi-structured interviews Thematic analysis
Al-Qazaz et al. 2011	To explore Type 2 diabetes patients' experience and knowledge about diabetes. To explore the experiences of diabetic patients in terms of their medication. To understand the factors contributing to medication adherence in Malaysia	Malaysia, Health clinic	N = 12 (4 female) Mean age: 54.0 8 Malay 2 Indian 2 Chinese	Semi-structured interviews Thematic content analysis
Borgsteede et al. 2011	To explore both factors related to high and lower levels of adherence that patients experienced in their medication use	Netherlands, Primary Care	N = 20 (10 female) Mean age: 70 years	In-depth semi-structured interviews Content analysis
Mygind et al. 2013	To explore patient perspectives on medicine use during Ramadan, reasons for fasting, and experiences with counselling on medicine use during Ramadan among people of Pakistani background with Type 2 diabetes and at least one other chronic condition	Denmark, Community	N = 6 (five female) Age: 42–69 years Muslims of Pakistani background, n=6	Semi–structured interviews Unclear
Stewart et al. 2013	To explore diabetes medication-taking experiences and knowledge and related cultural beliefs in American Samoan adults with diabetes and healthcare providers	American Samoa, Community health centre	N = 39 (22 F) Age: 30–39 years: n = 3 40–49 years: n = 3 50–59 years: n = 12 60–69 years: n = 12 70–79 years: n = 8 80–89 years: n = 1	Focus groups Unclear
Peeters et al. 2014	To explore perspectives of Turkish migrants with Type 2 diabetes on adherence to oral hypoglycaemic agents	Belgium, Primary Care and community	N = 21 (12 female) Age: 30–39 years: n = 2 40–49 years: n = 7 50–59 years: n = 6 60–69 years: n = 6 Muslim, n = 21	In-depth interviews Grounded theory

Meta-ethnography

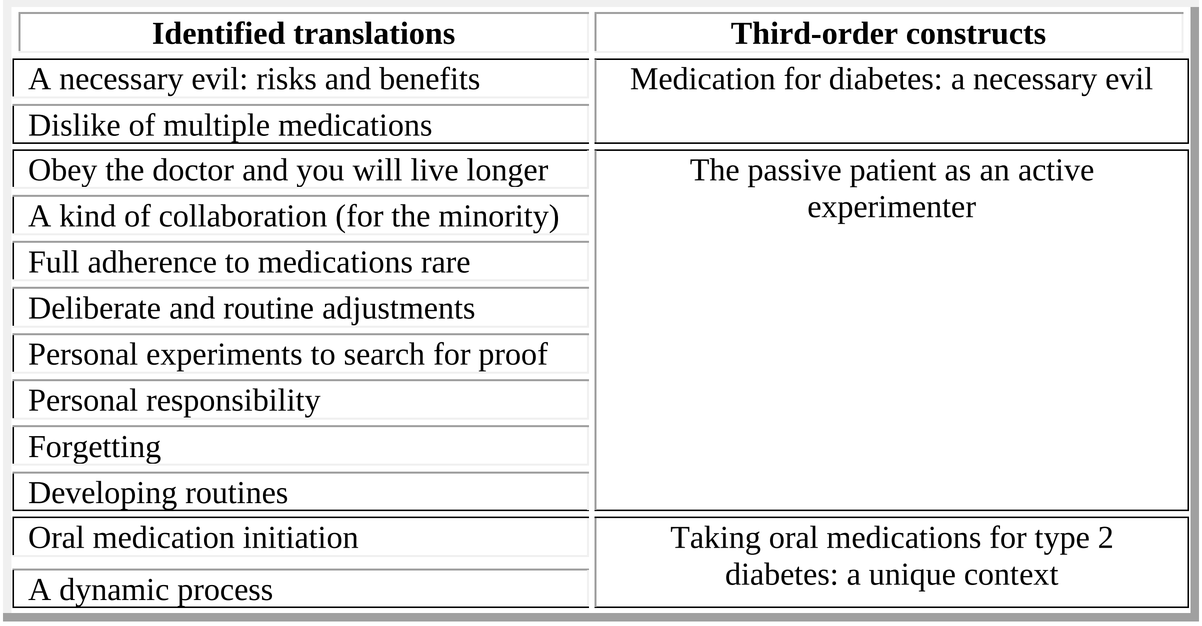
Having performed the literature searches and screened the results, the authors familiarised themselves with the selected studies before undertaking a meta-ethnography, following the methodology described by Noblit and Hare (Noblit et al., 1988). Within this methodology, the relationship between studies was determined by mapping key findings (termed 'metaphors') across studies. Extracted quotes from participants (denoted 'first-order constructs') and interpretations from study authors (denoted 'second-order constructs') were identified from each selected study, from which key concepts (termed 'translations') were developed. Such concepts were then used to develop overall models and interpretations (termed 'third-order constructs') to synthesis findings across multiple studies.

Findings and themes identified

Identified metaphors:

- Knowledge/information about diabetes and medications
- Negative perceptions and experiences of medications
- Positive perceptions and experiences of
- Medications
- Adherence-related factors
- Patient–physician relationship
- Social/cultural/religious factors
- Self-monitoring/self-regulation

Table 5.5: Identified translations and third-order constructs (reproduced and adapted from Table 2 (McSharry et al., 2016 pg.1335)



Identified translations	Third-order constructs
A necessary evil: risks and benefits	Medication for diabetes: a necessary evil
Dislike of multiple medications	
Obey the doctor and you will live longer	The passive patient as an active experimenter
A kind of collaboration (for the minority)	
Full adherence to medications rare	
Deliberate and routine adjustments	
Personal experiments to search for proof	
Personal responsibility	
Forgetting	
Developing routines	
Oral medication initiation	Taking oral medications for type 2 diabetes: a unique context
A dynamic process	

Discussion and comparison to the OAB study

As the focus and a particular strength of this study were the syntheses of findings across multiple works, it is the output of this synthesis (the third-order constructs) that shall be used as a basis of the below comparison to themes identified within the OAB study. The identified translations from the various studies will also be used to provide additional context and comparison to similarities and differences to the findings in Chapter 4.

For clarity and visual representation of the discussion further below, a diagram shall precede the discussion on all three third-order constructs below. The reader is directed to Chapter 3 ('structure and presentation method') for a background on the diagrammatic representations used in the current chapter.

Medication for diabetes: a necessary evil

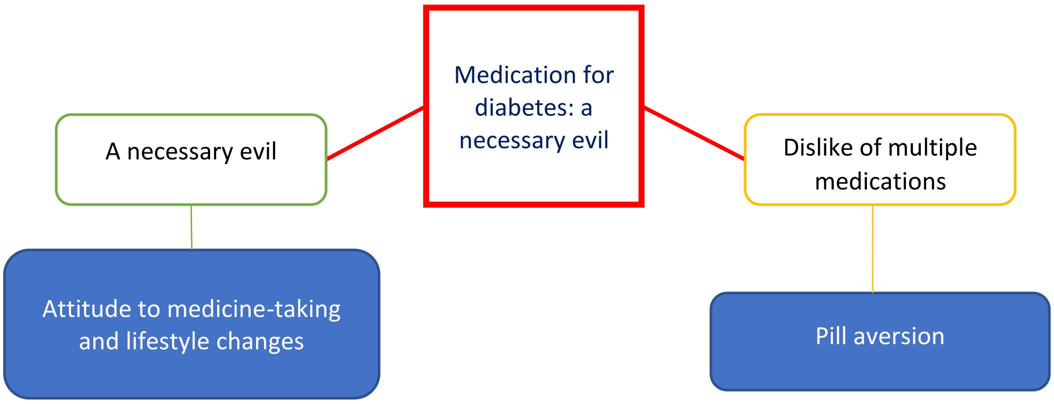


Figure 5.9: Comparing the first third-order construct from McSharry et al. to findings from the OAB study

McSharry et al. (2016) framed this construct as being descriptive of the complex nature of the way patients perceived taking T2DM treatment. Namely, within this construct, patients acknowledged the positive attributes of taking treatment but tempered this against concerns about the risks of doing so, including side effects, as well as disliking taking medication in general. This was particularly of note in those taking a multitude of treatments and was characterised by the observation that individuals were *"more likely to take medications if perceived advantages outweighed disadvantages"* (McSharry et al., 2016 pg.1333). Much of these findings closely mirrored those in the OAB study and offered a further agreement to the NCF as described elsewhere in this thesis. Particular parallels may be drawn to the theme of 'attitude to medicine-taking and lifestyle changes' in the OAB study where individuals highlighted a consideration of the benefits of taking treatment against the perceived risks of doing so in shaping their adherence behaviours. McSharry et al. reported relatively broad perceived benefits of taking oral diabetes treatment including *"controlling blood glucose, preventing complications … staying healthy and increasing physical well-being"* (McSharry et al., 2016 pg.1333). These were in contrast to the findings of the OAB study where treatment benefits were more specifically focussed on symptom control and the resultant effect on the immediate quality of life as opposed to long-term health consequences. Such a difference may be due in part to the pathophysiology of the conditions themselves, the wax and wane symptoms of OAB, and the high awareness of the long-term (and often life-changing) complications of T2DM (Taylor et al., 2021) compared to OAB. McSharry et al. noted that T2DM patients understood the need for treatment and considered themselves fortuitous in receiving it. This was largely not the case within the OAB study as the theme of 'unconvinced of diagnosis' highlighted an unacceptance of the diagnosis underpinning the benefits of treatment. The theme of 'tentative language' during the prescribing process in the OAB study also gave rise to a more doubtful reception to treatment, which at times was seen as given *"to get rid"* of the recipient.

The risks highlighted by McSharry et al. broadly mirrored those found in the OAB study including a dislike of taking drugs and their long-term effects, perceived inefficacy of long-term treatment, as well as side effects. A further area of agreement included individuals wanting to avoid taking too much medication (relating to the 'pill aversion' OAB theme), however, McSharry et al. also noted further barriers stemming from cultural beliefs with the observation that some individuals held a general dislike of Western medicine. The latter point is related to the 'social/economic factors' domain in the WHO's model of adherence, as well as the 'social opportunity' domain as highlighted by the COMB-B model.

The passive patient as active experimenter

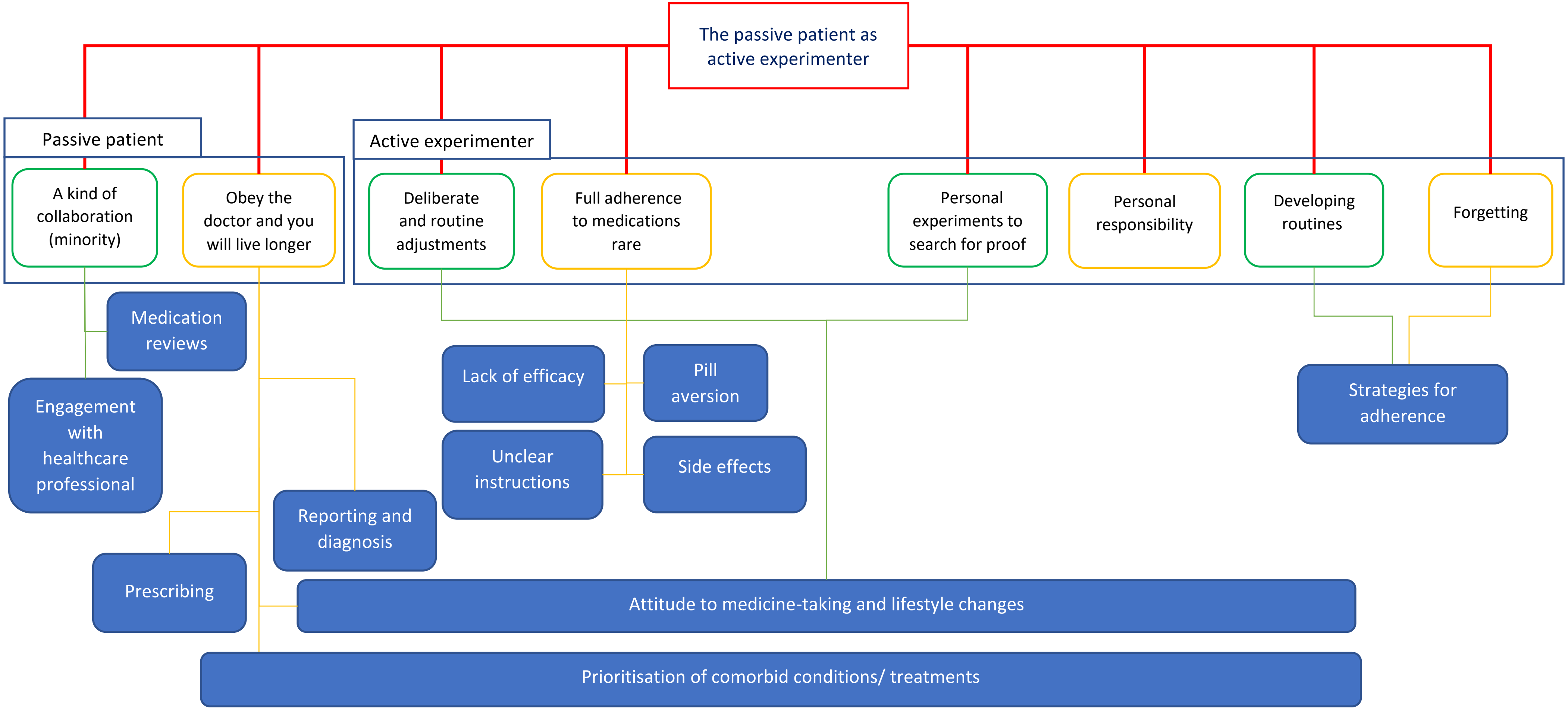


Figure 5.10: Comparing the second third-order construct from McSharry et al. to findings from the OAB study

The present construct described the within-patient contrast of individuals adopting both a passive role in accepting prescribed medication, as well as their more active decision-making and approach to taking treatment for T2DM within their day-to-day lives.

The passive patient

Outlining the passive element, McSharry et al. noted that while there was a minority of younger, educated patients who engaged in ‘a kind of collaboration’ with their HCP, treatment decisions were described as being made without negotiation, with a limited provision of information, and were accepted by patients without question. This was partly in contrast to experiences in the OAB study where, while treatment decisions were often described in a similarly directive manner and without much information shared, such recommendations were seldom accepted by the patient in any sustained way. This was evidenced by both the 1:1 discussions in the OAB study, as well as retrospective database analyses demonstrating the median time to discontinue OAB treatment was less than two-months (Chapple, 2017a). Mirroring the findings by McSharry et al. a small subset of individuals with OAB commented on having a collaborative relationship with their HCP with comments describing how receptive they were to feedback (captured in the OAB theme of ‘engagement with HCP’). The description of suboptimal information delivery at the point of diagnosis or prescribing within both studies was in strong contrast to the prominence given to effective patient knowledge, and the role of the HCP in ensuring this in the various models of adherence described in Chapter 1. Reasons for this may include the lingering effect of a paternalistic approach to healthcare within the NHS (Grünloh et al., 2018), as well as the rising workload on NHS practitioners given both the historical expansion of demands and restrictions in funding (BMA, 2018).

McSharry et al. also highlighted a hierarchical relationship between the HCP and patient, with the power principally resting with the HCP, and patients seldom questioning the authority of the prescribing physician. In contrast, participants in the OAB study largely described lengthy diagnoses, underpinned by uncertain language while prescribing, leading to doubt on both the knowledge and accuracy of their HCP's conclusions and decisions ('reporting and diagnosis' and 'prescribing' themes). While this may have been driven by the perceived disinterest in OAB by the HCP and more widely by society ('condition hierarchy' theme), it was also demonstrative of participants exercising some autonomy in deciding how appropriate the HCP's advice was to their experience. This was further captured in the OAB study under the theme of 'attitudes to lifestyle advice' where individuals largely only adopted lifestyle changes if they judged them to be compatible with their existing lifestyles. Where individuals with OAB described positive diagnostic experiences, this was largely predicated on participants having good prior experience with their HCPs and positive preconceptions of their knowledge and experience (OAB theme of 'medication reviews/HCP engagement').

The active experimenter

Within the description of 'active experimentation', McSharry et al. found that in practice, full adherence to T2DM treatment was rare, and individuals' behaviour was not consistent with the hierarchy between patient and practitioner (described above and characterised by the translation 'obey the doctor and you will live longer'). Individuals with T2DM tended to perform 'deliberate and routine adjustments' to their treatment, varying both the dose and timings of their treatment autonomously for a variety of reasons including managing side effects, due to a dislike of taking multiple medications, and in response to when blood glucose was perceived to be high. Further reasons included the belief that T2DM medications provided symptomatic relief and were not needed when feeling well. McSharry also noted some individuals modulated their T2DM treatment in response to a ‘personal understanding of their own body’s needs’ as well as a preference for traditional treatments. Such findings offered considerable overlap to those of the OAB study where this kind of non-conforming non-adherence behaviour was also adopted, as well as the reasons given for non-adherence. Discussed under the OAB themes of ‘attitudes to medicine-taking and adopting lifestyle advice’ and ‘drug/condition hierarchy’, OAB participants gave examples of self-imposed treatment caps (e.g., participant 10), purposefully missing doses (e.g., participant 13), or undergoing periods of treatment discontinuation and reinitiation (e.g., participant 12). Further areas of agreement included some overlap in illness perceptions as individuals in both studies expressed beliefs that consistent adherence was not necessary to manage their chronic condition, with this linked to the theme of ‘unclear instructions’ within the OAB study. This offered some support for both the ‘consequences’ and ‘controllability/curability’ domains of the CSM playing a part in adherence behaviours in both conditions.

In a further area of similarity to individuals within the OAB study discussing their estimation of the necessity of treatment, individuals with T2DM described engaging in ‘personal experiments’ to gain proof that their treatments were working, further highlighting the role of illness perceptions, and that individuals may retain scepticism of their treatment in the absence of such evidence. Patients with T2DM continued to take treatment if they experienced negative effects when medications were discontinued. This was also mirrored in the OAB study, by individuals using the re-emergence of symptoms as a signal to recommence treatment. Such reinforcement of the condition itself being the source of symptoms, and the resultant effect on adherence behaviours may also be attributed to changes in the ‘cause’ and ‘perceived controllability’ domains of the CSM. The concept of proof too was seen in the OAB study and was linked to the estimation of treatment necessity discussed under the theme of ‘attitudes to medicine-taking’. The observation of such similarities between OAB and diabetes may disguise several differences in the mechanisms underlying them. While the experiments performed by individuals with diabetes arguably have well-defined endpoints in that the desired effect (controlled blood glucose) is directly measurable via a blood glucose meter, the same cannot be said for the results of OAB treatment. Similarly, while the effectiveness of diabetes treatment can be measured at set daily intervals when blood glucose levels are expected to have risen (e.g., after meals), the unpredictability of OAB symptoms renders such regimented experimentation infeasible (Daly et al., 2021). This may then imply that the nature of the experimentation within the context of OAB may be more speculative than that within T2DM. This, combined with the fact that the majority of OAB patients discontinue treatment within the first 30 days (Sexton et al., 2011b), whereas the full response to OAB treatment can take up to several months (Hsiao et al., 2015), may indicate a differential need for patients to be better informed within the context of OAB. Achieving this may inform more accurate expectations from treatment, and thus better frame treatment experimentation and subsequent medicine-taking behaviours.

The translation of ‘personal responsibility’ in the McSharry paper described the individual’s feelings of guilt and concern about the health consequences of not being adherent to T2DM treatment. With the exception of some OAB participants acknowledging their own responsibility to pursue medication reviews and additional support when required, no such observations were made within the context of OAB. Reasons for this may include the observation of ‘downplaying and normalisation’ of OAB, and therefore its consequences, the variety of adaptive behaviours as described within the OAB theme of ‘coping strategies for symptoms’, as well as OAB having low priority in the ‘condition hierarchy’, potentially leading to it attracting less guilt from any perceived or actual undermanagement. Furthermore, in line with the NCF, as the perceived necessity of treatment was observed to be a key consideration behind treatment adherence in the OAB study, the low perceived necessity of OAB treatment may also have contributed to less negative consequences to be associated with its omission, leading to the translation of ‘personal responsibility’ being less prevalent amongst individuals in the OAB study. Within the context of the CSM, individuals with OAB exhibited a low estimation of the ‘cause’ and ‘consequences’ domains and variable attitudes to the ‘controllability/curability’ domain in that coping mechanisms were broadly associated with higher controllability of the condition than the treatment was.

The McSharry study also described the translation of ‘forgetting’ as a major cause of non-adherence, going on to describe the strategies used by T2DM patients to improve adherence, including the use of prompts and the establishment of ‘routines’. Indeed, the establishment of a medicine-taking routine has been noted to facilitate adherence, especially where forgetting is a cause for non-intentional adherence (Hogan et al., 2015). In contrast, forgetting was not a significant cause for non-adherence in the OAB study, however, similar use of strategies to support adherence was described, including the establishment of routines, using visual or temporal prompts, and adherence aids. This may be illustrative of non-adherence in OAB being largely intentional (Ali et al., 2019) (and therefore not subject to forgetfulness as a barrier) in contrast to that seen in T2DM, highlighting the need for differential management strategies to address this. As disruptions to daily routines have been associated with forgetting to take treatment (Atinga et al., 2018), age and lifestyle factors that may contribute to the likelihood of such disruptions may also be part of the differences seen between the OAB study and the McSharry study.

Taking oral medications for type 2 diabetes: a unique context

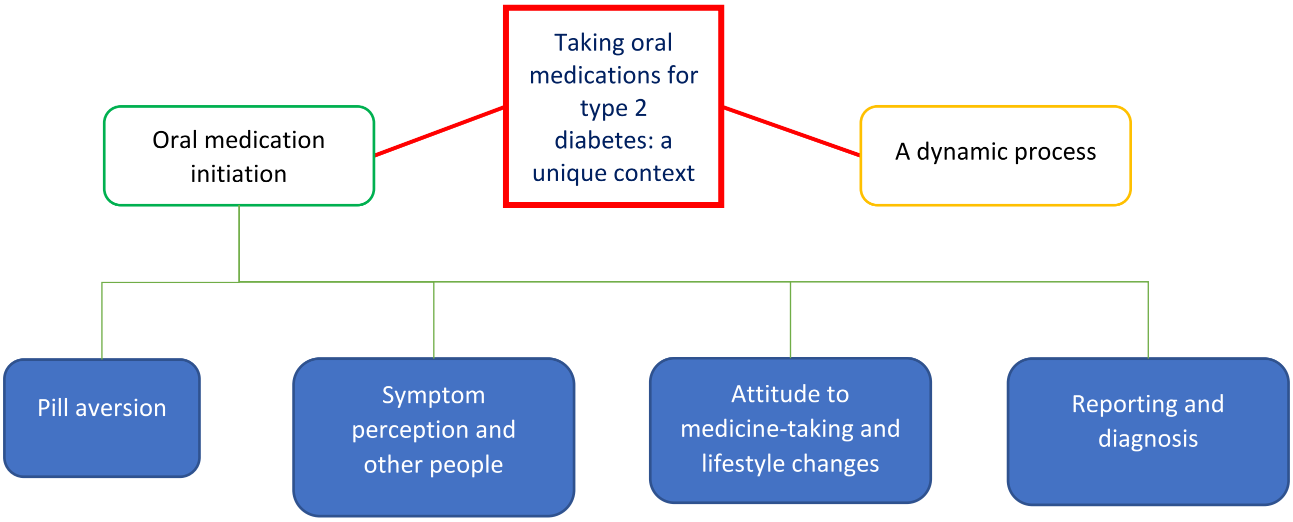


Figure 5.11: Comparing the final third-order construct from McSharry et al. to findings from the OAB study

The final third-order construct in the McSharry et al. study considered the characteristics of medicine-taking behaviours that were deemed unique to T2DM. Within this construct, the authors highlighted that a period of lifestyle modification usually precedes the initiation of oral therapy in T2DM management, stating that most individuals held negative views about transitioning from diet-controlled to pharmacologically controlled management. Reasons for this included unease about taking oral treatment, a perception of personal failure to maintain control using diet alone, and descriptions of such a move as the beginning of a "*slippery slope*" of treatment intensification, which would eventually lead to injectables such as insulin (McSharry et al., 2016 pg.1336). Such ranking of treatments was suggestive of parallels to the 'drug hierarchy' theme from the OAB study. Beliefs of personal failure to control T2DM suggest an interplay between the 'identity' and 'controllability' domain of the CSM where individuals may hold judgements over themselves (with or without labels) due to how well their actions have managed their condition.

The understanding in T2DM of treatment intensification and change over time was captured with the translation ‘dynamic process’. Despite some parallels in the initial use of lifestyle modifications in the management of OAB, as well as the unease some participants in the OAB study voiced in taking pharmacological treatment (e.g., in the ‘pill aversion’ theme), there were notable differences observed between T2DM and OAB. While the fear of treatment intensification within the context of T2DM was indicative of individuals’ understanding of the treatment pathway and the necessity of treatment escalation in response to a chronic condition (the ‘dynamic process’ translation), no such observation was made in the OAB study. Steeped in the belief that OAB symptoms were a normal part of ageing (as discussed under ‘symptom perception and other people’), and the resultant ‘downplaying’ and ‘normalising’ of symptoms, many participants in the OAB study described incidental reporting of symptoms, demonstrating (in part) an absence of the knowledge that something could have been done about them. This further extended into examples of not knowing there were alternative treatments available for OAB in the instances where the initial treatment was suboptimal, with several participants only becoming aware of this as a result of participating in the OAB study itself. Such observations again highlighted the importance of individuals having knowledge of both the condition and treatment and may also indicate misbeliefs relating to the ‘timeline’ domain of the CSM among individuals with OAB, in contrast to those with T2DM where the nature of the condition and its chronic course appeared to be better understood. However, it is important to note that neither study aimed to specifically measure knowledge of the respective LTCs, and further work may be needed to further develop this observation.

Related to the overall perception of illness within T2DM, a further finding was that the successful control of T2DM by diet alone could result in individuals questioning whether they had diabetes at all, whereas taking oral treatment was associated with a better understanding of the nature of the condition. This echoed a similar observation captured by the ‘unconvinced of diagnosis’ theme in the OAB study, with the distinction that the doubted diagnosis in the OAB study was fuelled chiefly by the unconvincing diagnosis process itself, as opposed to treatment escalation required to control the condition. The questioning of having T2DM at all could also be compared to the observations of ‘downplaying’ and ‘normalising’ OAB symptoms (described under the theme of ‘symptom perception and other people’). Here, individuals minimised the acknowledgement of troublesome symptoms (or indeed OAB itself) through comparison to peers, likening symptoms to everyday occurrences and natural processes such as ageing, as well as through successful coping mechanisms (the latter of which may be considered analogous to making lifestyle changes in T2DM).

Overall, there were several areas of congruence identified within the present comparison, giving further support for the relevance of NCF across conditions, the interplay between condition and social influences, as well as the role of the HCP in influencing medicine-taking behaviours. Areas of divergence included illness perceptions between OAB and T2DM patients, and therefore the approach to adherence (including differences in non-intentional non-adherence).

Future healthcare priority- multimorbidity

Maffoni et al. (2020)- “Medication adherence in older adults with chronic multimorbidity: a systematic review of qualitative studies on patient’s experience”

Pointing to advances in science and technology as a driving force behind the general growth and ageing of the global population over the last few decades, Maffoni et al. further delineate the disproportionate growth of the older strata of society, particularly in developing countries, hailing this as a significant challenge for healthcare systems worldwide.

The authors linked this demographic change to the growing phenomena of multimorbidity, commenting that less than 10% of older adults do not require prescribed medications, with over 50% requiring five or more, and 10% requiring 10 or more treatments. Maffoni, et al. went on to highlight that appropriate adherence was a prerequisite for the safe and effective use of treatment, and although treatment adherence among older adults varied by context and by treatment, such behaviours were often sub-optimal.

In addition to the conceptualisation of the adherence process into three phases (initiation, implementation, and discontinuation) as described in Chapter 1 of this thesis (see ‘conceptual models relating to adherence’), Maffoni et al. also briefly described the Three-Factor model (also called the Information-Motivation-Strategy [IMS] model), as theoretical frameworks to guide the present study. Chapter 1 also contains a description of the IMS model.

Summary of objectives and methods

This study aimed to identify barriers and facilitators of treatment adherence in older adults with chronic multimorbidity. The authors employed a systematic literature review of qualitative studies in Scopus and PubMed databases capturing the perspective of older patients. Clinical areas concentrated on included hypertension, heart disease, COPD, and asthma.

Inclusion and exclusion criteria

Table 5.6: Inclusion and exclusion criteria for Maffoni et al. (2020)

Inclusion	Exclusion
Peer-reviewed articles	Quantitative studies
Published between 2000 and 2017	Medication adherence on marginally reported
Qualitative studies focused on patients' perspective	HCP perspective
English language	Studies with less than 10 patients or those based only or extensively on telephone interviews
Involving patients over the age of 65 years	Patients aged <65 years or >18 years without any further details on age composition
Relating to medication adherence in chronic conditions	Reviews, book chapters, editorials, grey literature

Studies identified

1,234 papers were identified. After deduplication and title, abstract, and full-text screening, 39 research articles were considered eligible, a descriptive summary of which is provided below:

Table 5.7: Summary of studies (adapted from Table 2 Maffoni et al. 2020)

Study design	Papers n, (%)	Condition(s)	Papers n, (%)	Sample size	Papers n, (%)
Semi-structured interview	23 (58.9)	Hypertension	19 (48.7)	13–19 participants	10 (25.6)
Semi-structured interview; Focus group	6 (15.4)	Multiple chronic conditions	6 (15.4)	20–38 participants	17 (43.6)
Focus group	5 (12.8)	Cardiovascular disease	5 (12.8)	40–50 participants	8 (20.5)
Structured interview; Focus group	3 (7.7)	Diabetes mellitus	2 (5.1)	86–106 participants	4 (10.2)
Structured interview	1 (2.6)	Hypercholesterolemia	2 (5.1)		

Qualitative interview	1 (2.6)	Rheumatoid arthritis	2 (5.1)	
		Asthma	1 (2.6)	
		Chronic Kidney Disease	1 (2.6)	
		Diabetic Kidney Disease	1 (2.6)	
		Gout	1 (2.6)	
		Osteoarthritis	1 (2.6)	
		Parkinson	1 (2.6)	
		Single condition	26 (66.7)	
		Two or more conditions	13 (33.3)	

Maffoni et al. noted the significant heterogeneity in methodologies employed for data collection and analysis, drawing particular emphasis on the varied nature of reporting. Semi-structured interviews and focus groups were the most prevalently used method of data collection, and the majority of studies identified were performed in English-speaking countries.

Analysis

The presence of each model domain within the ABC Taxonomy (initiation, implementation, discontinuation), and the IMS model, was identified via content analysis (termed "*a qualitative methodology*" in the paper (Maffoni et al., 2020 pg.371)). This was analysed both in terms of the questions asked (interviewer/inquiry themes), and responses given by patients (patient/response themes). Additional themes were reviewed and agreed upon by each author.

As the purpose of the present chapter is to compare themes from a wider clinical area to those generated by individuals experiencing OAB, the emphasis of the comparison will be against those generated by the patient themselves as opposed to the interviewer/inquiry themes.

Findings and themes identified

In viewing the results of the literature review through the lens of the ABC taxonomy, Maffoni et al. found that only a few papers concentrated on the initiation phase of adherence, with the majority jointly focussing on the implementation and persistence/discontinuation phases, further interpreting this as a possible lack of interest in the precursors to adherent behaviours. Regarding the IMS model, the authors found that motivation was the most difficult domain to find evidence of in the papers reviewed, concluding that as a cognitive-emotional driver it may have been implicitly featured in the studies, warranting further work on its definition and role in medicine-taking behaviours. Regarding the patient-reported barriers to adherence in chronic multimorbidity Maffoni et al. grouped patient/response into the following themes:

Table 5.8: Summary of patient-reported themes as barriers and facilitators from Maffoni et al. 2020

Themes
Patient beliefs and concerns about treatment
Patient beliefs about polypharmacy and drug prioritization
Patient’s experience and capabilities
Prescriber-patient relationship
Health literacy
Treatment characteristics and complexity
Family and social support

Discussion and comparison to the OAB study

Maffoni, et al. did not go into detail on the definition and derivation of each of the identified barriers and facilitators to adherence, choosing instead to integrate these barriers and possible facilitators to generate a patient decisional flowchart. As the present chapter aims to compare the findings from the OAB study, each of the identified themes will be considered in turn.

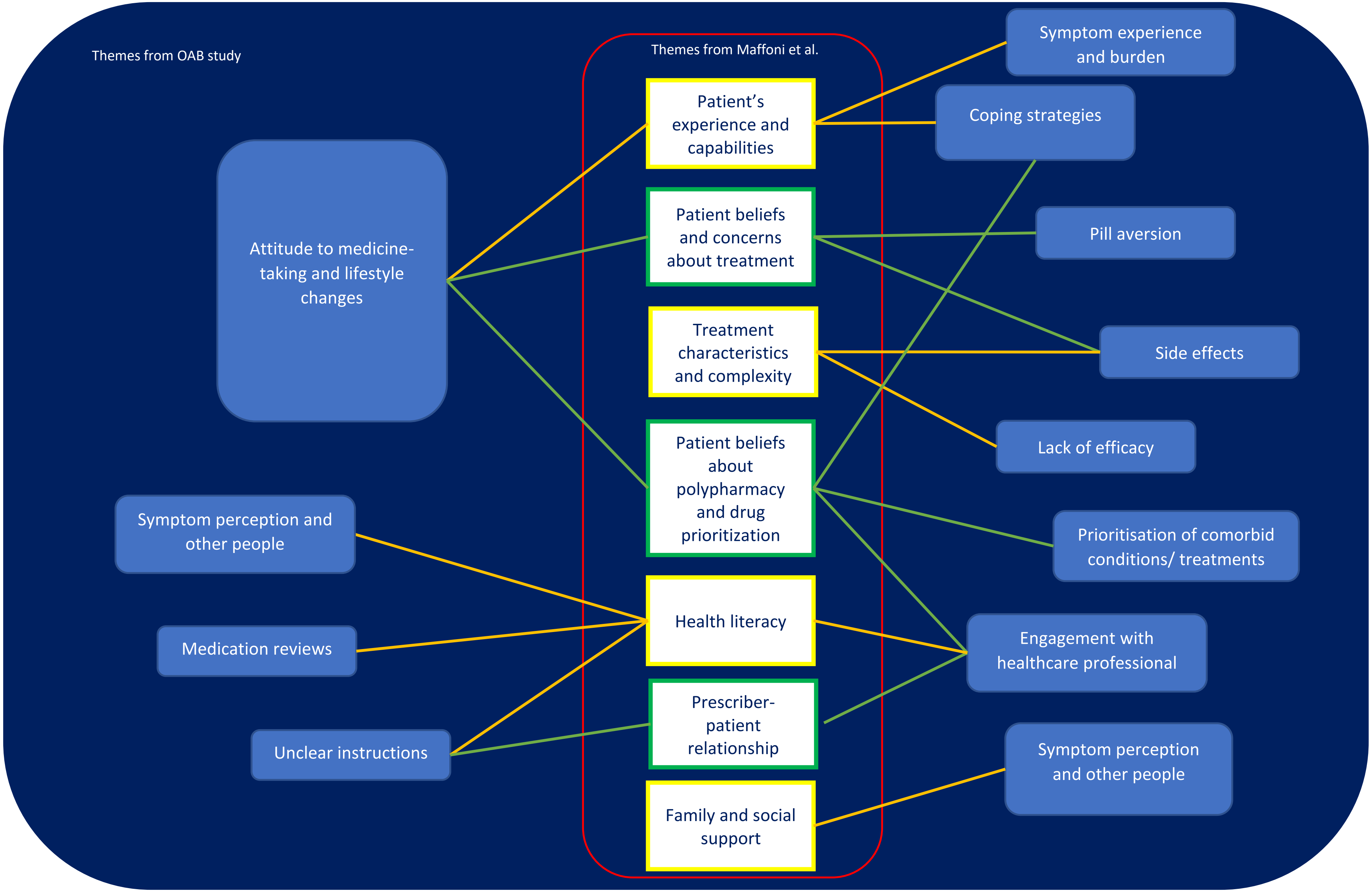


Figure 5.12: Overall comparison of themes from Maffoni et al. and the OAB study

Patient's experience and capabilities

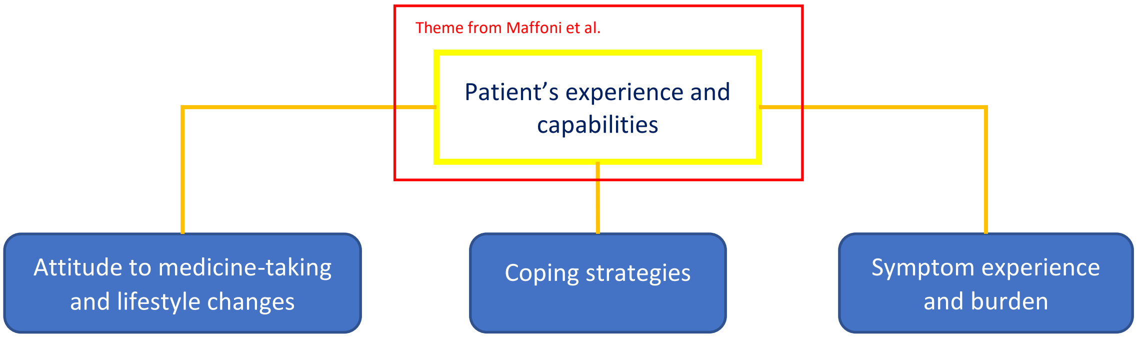


Figure 5.13: Comparing 'patient experience and capabilities' theme from Maffoni et al. to themes from the OAB study

The theme of 'patient experience and capabilities' identified as a barrier or facilitator to adherence in the Maffoni paper overlaps with several themes identified in the OAB study within this thesis. The theme of 'symptom experience and burden' in the OAB study provided the historical and present experiential context within which adherence behaviours occurred, and informed further themes such as 'symptom perception' and 'attitudes to medicine-taking behaviours and lifestyle changes'. The latter theme, as well as 'coping strategies' from the OAB study also offered areas of agreement with the Maffoni paper in describing subdomains of patient capability, as described by several conceptual models of adherence (discussed in Chapter 1). Such capability included the influence of the patient's attitude to proposed medicine-taking and lifestyle changes, as well as their knowledge and ability to engage with coping strategies for their condition. The ability to adopt adaptive behaviours and cope with symptoms, as well as the resultant effects of this on their estimation of treatment necessity were shown to be key contributors to patient medicine-taking behaviours in the OAB study. However, it is worth noting that even within the context of OAB, the capability of engaging in such adaptive behaviours differed between individuals depending on lifestyle, condition severity, and even gender. Furthermore, in instances where symptoms do not present conspicuously, acute adaptive behaviours may not be viable, nor helpful in avoiding the negative effects of some chronic conditions. Such adaptive behaviours may further be untenable in cases of chronic multimorbidity, and with the introduction of conflicting demands.

Furthermore, while the above overlaps in thematic areas offer some congruence in findings between the two studies, there were further dimensions of the present theme which did not feature within the OAB study. The Maffoni, et al. paper took learnings from studies from a diverse range of clinical, geographical, and socio-economic settings, and included studies conducted within countries with widely disparate levels of development, as measured by the Human Development Index (HDI). The HDI provides a measure of human potential and quality of life, measuring health, education, and standard of living to provide a widely cited statistic as a measure of well-being across the world (Dasic et al., 2020). The HDI rankings of countries included within the Maffoni paper ranged from 3 (Australia) to 179 (Eritrea). This compares with the UK (ranked 14 within the Maffoni paper at the time of publication). Such differences in well-being, as well as healthcare systems, support and culture may largely colour both the 'experience' and 'capability' domains of the present theme, capturing some facets of both that may not have been present in the OAB study.

Patient beliefs and concerns about treatment & treatment characteristics and complexity themes

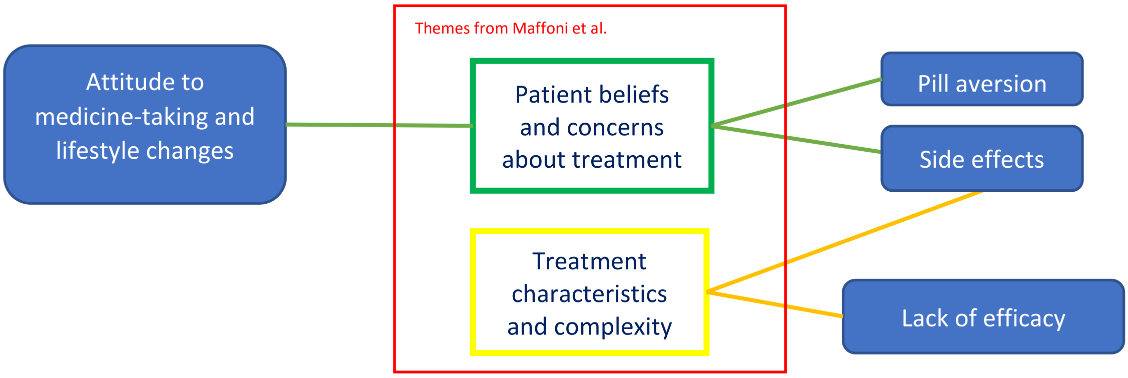


Figure 5.14: Comparing 'patient beliefs and concerns about treatment' and 'treatment characteristics and complexity' themes from Maffoni et al. to themes from the OAB study

The theme of ‘patient beliefs and concerns about treatment’ from the Maffoni paper in the context of chronic multimorbidity in the elderly too related to the OAB theme of ‘attitude to medicine-taking and lifestyle changes’, and the observation within the OAB study of patients balancing perceived risks and benefits of taking treatment. Also related to the previous theme of how patient experiences and capabilities shaped such beliefs, this congruence between the Maffoni paper and OAB study further offered support to the NCF, and its role in adherence behaviours (as discussed in Chapters 1 and 4),

The patient’s general attitude to behaviour change as well as a desire to avoid treatment where possible (‘pill aversion’ theme from the OAB study), may be likely precursors to the patient’s beliefs and concerns about treatment, as well as the evolution of this belief throughout their treatment journey, further informed by the experience of actually taking treatment (including side effects). The themes of ‘side effects’ and ‘lack of efficacy’ from the OAB study were also related to the theme of ‘treatment characteristics and complexity’ from the Maffoni paper as pertaining to the experience of taking treatment itself, and the effect this had on subsequent medicine-taking behaviours. In addition to the influence of experienced side effects, the OAB study also provided insights into the impact that preconceptions about side effects could have on adherence behaviours. However, such a distinction was not discussed in the Maffoni study.

While the OAB study captured the most important facets of treatment characteristics within the context of OAB, the broadly titled theme from the Maffoni paper likely encompass further treatment characteristics stemming from the wider range of clinical areas considered. While the description of such granularity was omitted from the Maffoni paper, examples may include the size of tablets and frequency of dosing as highlighted in the Devlen paper reviewed above, as well as treatment complexity, previous treatment failures, the overall duration of treatment, as well as frequency of treatment changes. Further areas may include the immediacy of perceived benefits or adverse events, as well as the availability of support to resolve such issues as highlighted in the therapy-related domain of the WHO’s five dimensions of adherence (described in Chapter 1).

Patient beliefs about polypharmacy and drug prioritization

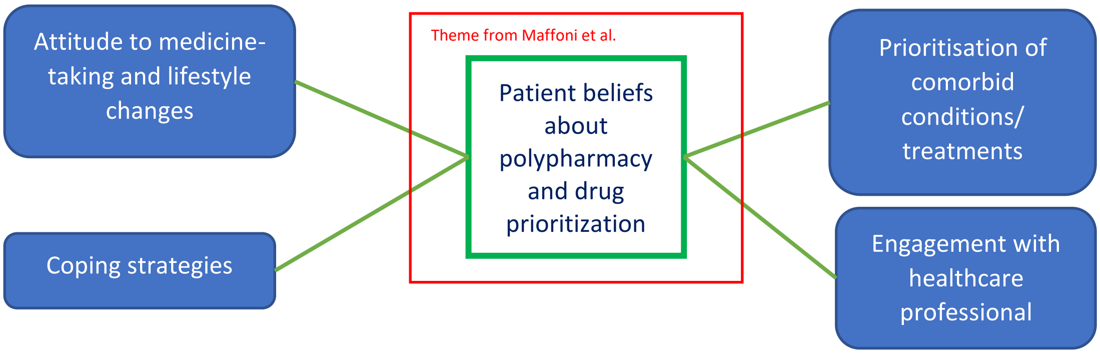


Figure 5.15: Comparing ‘patient beliefs about polypharmacy and drug prioritisation’ theme from Maffoni et al. to themes from the OAB study

With a similar precursory relationship between the theme of patient attitudes to medicine-taking in the OAB study and beliefs about polypharmacy and drug prioritization in the Maffoni paper, the present theme related most strongly to the theme of ‘prioritisation of comorbid conditions/treatments’ (also referred to as drug and condition hierarchies) in the OAB study. In contrast to the OAB study where both drug and condition prioritisation were considered from a diverse perspective, the Maffoni paper centred this theme solely on drug prioritisation from the patient perspective and did not offer comment on the role of peers and HCPs on the formation or propagation of such prioritisations. The OAB study supplied evidence of individuals with OAB applying relative importance to OAB and other comorbidities, as well as their treatments, stemming from both the ability to use adaptive behaviours to cope with symptoms of OAB, the suboptimal engagement with HCP’s (including a perceived disinterest), as well as symptom normalisation and downplaying. Given the support for the NCF seen in both studies, it is plausible that an individual with multimorbidity undertakes the cost-benefit analysis (as described Chapter 1- see 'Necessity-Concerns Framework') for each treatment and ranks the results of this comparison across their different conditions, thereby driving the act of treatment prioritisation noted in both studies. Such activity may cause treatment side effects to be considered differently across conditions. Related to this, a recent systematic literature review indicated that individuals perceiving treatment as having limited effectiveness were more likely to have increased expectations of side effects (Smith et al., 2020). Further work is required to understand if such a mechanism does indeed occur and to identify factors that may influence this decision-making.

Health literacy, prescriber-patient relationship & family and social support themes

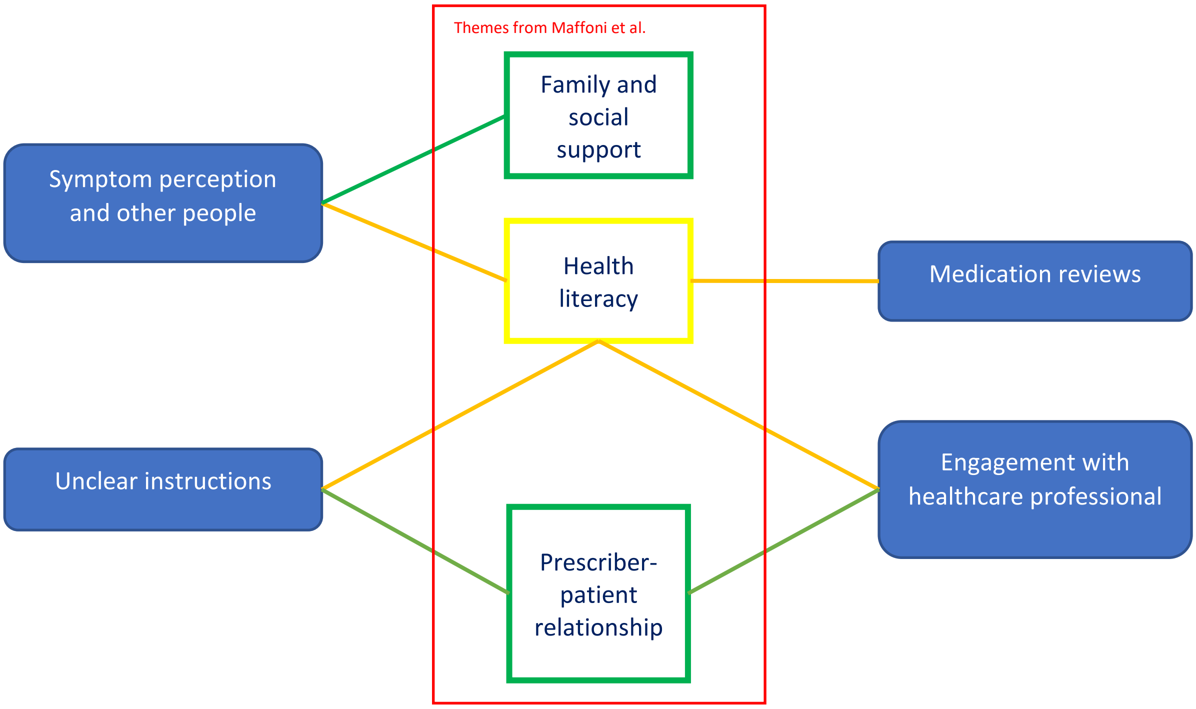


Figure 5.16: Comparing 'family and social support', 'health literacy' and 'prescriber-patient relationship' themes from Maffoni et al. to themes from the OAB study

With significant overlap in the Maffoni paper between the themes of 'health literacy', 'prescriber-patient relationship', and 'family and social support', all three will be discussed together here. As presented in Chapter 1 (see 'social/economic factors' under WHO's five dimensions of adherence), health literacy is defined as *"the ability of an individual to obtain and translate knowledge and information in order to maintain and improve health in a way that is appropriate to the individual and system contexts"* (Liu et al., 2020 pg.6). While facets of health literacy were covered by the various models of adherence discussed in Chapter 1 (e.g., 'psychological capability' in COM-B and the 'information' domain in IMS), the WHO's 5 dimensions of adherence was the only one to explicitly discuss the role of health literacy in treatment adherence within its domain of 'social/economic factors', noting a link between low health literacy and delayed help-seeking behaviours, poorer adherence behaviours, and worse health outcomes (WHO, 2003).

As one of the themes affecting medicine-taking behaviours identified by Maffoni et al., the inability of individuals to obtain and translate information through appropriate engagement with a HCP was a key related observation and area of improvement identified within the context of OAB, and further linked to the Maffoni theme of 'prescriber-patient relationship'. OAB participants reported delayed engagement with HCPs, consistently protracted and often unconvincing diagnoses, and inconsistent medication reviews, which were focussed on problem-solving as opposed to optimising care, as well as receiving unclear instructions from HCPs. Indeed, a further facet of the condition hierarchy theme within the OAB study was how little information there was in the public domain about *"day-to-day"* conditions such as OAB when compared with other chronic conditions (OAB participant 3). Such experiences may unsurprisingly lead to additional difficulties for individuals to seek, receive and process information relating to their condition and treatment. However, the availability of information as a component of health literacy was not discussed in the Maffoni, et al. paper.

Another theme from the OAB study with areas of overlap with the current themes from Maffoni et al. included that of ‘symptom perception and other people’. Within this theme, the downplaying and normalising of OAB symptoms may have limited the degree to which symptoms were seen as abnormal, thereby reducing the motivation of individuals to seek knowledge of OAB management. This is in line with the CSM of illness perception, the representation of a health threat is directly related to the selection and appraisal of the coping mechanisms employed. Evidence of suboptimal knowledge was also supplied within the OAB study with multiple participants mentioning they did not realise there was anything that could be done about their symptoms, with others only seeking treatment information from their HCP when incidentally engaging them about something else. The perceived dismissiveness of HCPs may also have contributed to patients being less likely to engage in help-seeking behaviours. Further examples included patients not engaging in medication reviews, and not taking up the opportunity to revisit their HCP for further treatment. Such perceived trivialisation by HCPs has been observed to be linked to poorer consulting behaviours in other LTCs such as acne vulgaris (Ip et al., 2021).

The theme in the Maffoni paper of ‘family and social support’ may also have covered areas not significantly evidenced within the OAB study, including more direct support from family members or the wider healthcare team. Social support, defined as the perceived and received level of support from an individual’s social network including friends and family, neighbours, colleagues, and other patients, as well as online connections, in particular, is a key mediator of adherence in conditions such as heart failure, diabetes, and HIV (Gu et al., 2017). While participants in the OAB study did mention family and friends, this was more in the context of being judged (e.g., Participant 8: *“And everybody used to remark on it, you know? Like my sisters'd say, "you're not going again, are you?”*), conscious avoidance of discussing OAB (e.g., Participant 1: *"I tend not to erm speak about my medical conditions to many people",* or concealing the need for support (e.g., Participant 6: *"'it's not something you want to do dad, you don't want to ask your dad- can I borrow some pads?'")*. Such a difference in the involvement of family and friends between OAB and other conditions may be indicative of both individual and social causes. While individuals with OAB may limit the extent to which they seek or are open to receiving support from family and friends due to embarrassment and reluctance to share, this dynamic may also be contributed to by the perceived and actual low prioritisation of OAB in wider society as mentioned by participants in the OAB study.

Finally, support from family and friends may be particularly relevant within the context of multimorbidity within elderly patients, and in managing specific chronic conditions such as rheumatoid arthritis or gout which may limit mobility, ability for self-care, and independence (Grimmer et al., 2019).

Discussion and conclusions

In congruence with findings from the OAB study, there was considerable support for the NCF across the conditions considered. This ranged from observation by McSharry et al. (2016) that individuals reported they would adhere to diabetes treatment if the advantages outweighed the disadvantages, to Maffoni et al. (2020) outlining patient beliefs and concerns about treatment were a key barrier factor to medicine-taking behaviours. Devlen, et al. (2014) described individuals questioning the need to take maintenance medication when in remission for IBD, suggesting that the perceived 'necessity' of taking such treatment diminished during these periods, increasing the likelihood of non-adherence. Such observations give clear rise to the importance of patients having an appropriate understanding of both the risks and benefits of their treatments to inform their medicine-taking behaviours. Differences were also observed between the expression of the ‘necessity’ domain in the three studies. In particular, individuals in the T2DM study characterised their treatment as a ‘necessary evil’ and considered themselves as fortuitous in having it prescribed to them. The authors further noted that patients with T2DM included long-term benefits of diabetic control as part of the reasons why treatment was considered necessary. This was in contrast to the IBD study where the necessity of maintenance treatment was questioned, and the OAB study where the benefits of treatment were only considered in the immediate sense, and the need for treatment at all was questioned due to a combination of symptom downplaying, normalisation, and doubted diagnosis. Despite this, McSharry et al. (2016) described some individuals questioning the need for diabetic medication when feeling well, indicating that while individuals generally understood T2DM and its treatment in the context of long-term health outcomes, there were some gaps in understanding the acute role of treatment. The role of the HCP in helping patients understand the need for treatment is well documented and so may be an apt area for correcting such beliefs in the context of T2DM (Voigt-Barbarowicz and Brütt, 2020). However, enduring beliefs of OAB symptoms being a natural part of ageing or menopause may indicate the role of wider society in forming and potentially dispelling such views. Correcting these beliefs through public education may be a key strategy in increasing both the awareness of OAB (identified as a need in the OAB study), as well as the correct estimation of the need for long-term treatment to manage it (Przydacz et al., 2018).

Further areas of agreement included the observation of individuals not wanting to take multiple medications, and side effects being the leading constituent of the estimation of risks. Relatedly, a lack of efficacy was a driver for non-adherence in the IBD study, offering some agreement with a similar observation in the OAB study. These findings reinforce the importance of patients being made aware of the reasons for medicines being prescribed, the management of potential side effects, and realistic expectations on the onset and extent of treatment effectiveness. Indeed, the provision of clear treatment information and informed treatment expectations have been shown to support adherent behaviours (Fernandez-Lazaro et al., 2019). Such reminders may be appropriate to share not only at the point of diagnosis but at subsequent consultations with prescribers and other HCPs to ensure their continued relevance to patient behaviours.

A further observation of note was the reporting of some form of patient experimentation in all three comparison studies. While the IBD study described this as patients waiting a finite time for the emergence of effectiveness or side effects, the T2DM study described individuals exhibiting non-conforming non-adherence in routinely adjusting their treatment dose and timings. Although there was evidence of a similar theme of experimentation with the OAB study, it is important to note differences in the causes and mechanisms of this behaviour. Within the T2DM study, individuals were described as autonomously making changes to their treatment in response to side effects, their blood sugar levels, as well as due to beliefs on the non-requirement of treatment when feeling well. Given the treatment goal of reducing blood sugar levels, such decisions may be influenced by meals and activity levels and may echo the expected dose adjustments with other treatments in diabetes such as insulin therapy (Meece, 2006). In contrast, the sense of experimentation within the OAB study stemmed from the language used at the point of prescribing and the perceived demeanour of the HCP as being unsure of the treatments being offered. This reinforces the recommendation of prescribers to be mindful of this and to offer the patient a clear and complete understanding of their treatment at the point of prescribing (GMC, 2019). Such care may be particularly important in OAB given its low social awareness and prioritisation (as noted in the OAB study).

On a similar note, while individuals doubting their diagnosis was observed in both the OAB and T2DM studies, a similar disparity in the origin of this was observed. McSharry et al. (2016) noted that individuals who managed to control their diabetes using lifestyle interventions questioned whether they had diabetes at all (i.e., doubting their diagnosis following the successful implementation of HCP advice). In contrast, the doubt in the OAB study stemmed from the long process of diagnosis itself and the perceived trial and error of prescribing, contextualised by the long-held beliefs of the normality of symptoms. This again, indicates the value of increasing public awareness of the nature and prevalence of OAB, thereby helping to shift attitudes to recognise its importance and the value of its treatment.

Relating strongly to similar observations in OAB, the theme of social stigma in the IBD study highlighted most strongly the role of wider social dynamics on the management of a LTC within the analyses conducted. While in the OAB study, the theme of 'symptom perception and other people' was characterised by individuals feeling judged based on their symptoms as opposed to their treatment, the reverse was true for the IBD study. Reasons for this may include a difference in demographics and lifestyle, as well as the possibility that stigma associated with IBD treatments is intrinsically linked to the embarrassment of shame stemming from the condition itself (see 'social stigma' above).

The present chapter aimed to compare the findings from the OAB study to studies exploring medicine-taking behaviours in other diagnosed LTCs. In doing so, the analyses uncovered areas of significant overlap, suggesting that some barriers to adherence were common across conditions, and so could benefit from a pan-condition approach. The findings also suggested some nuances in the experience of individuals with OAB, the wider context within which these occur, and the impact of these on medicine-taking behaviours.

Strengths and limitations

The present study served a key role in contextualising the findings of the OAB study within a wider clinical landscape and in triangulating the learnings from the OAB study by considering additional data sources. While only three such sources were included, these we considered sufficient given the exploratory objectives of this study, as well as pragmatic factors including the availability of time and funds. In addition, all three sources were informed by systematic literature reviews, thereby serving to widen the foundation of knowledge used for comparison.

While the choice of papers to compare to was not determined by a formally systematic methodology, the reflexive framing of such a choice placed me as the researcher in the centre of the analysis undertaken and thereby reinforced the reflexive approach taken throughout the thesis. The inclusion of the Devlen paper additionally strengthened the analysis due to the parallels it allowed to be made to the OAB study, not only in the experience of the condition itself but as the first piece of qualitative work in exploring barriers to IBD treatment adherence (mirroring a similar position for the OAB study). Considering such a disparate range of conditions to compare to was also a strength of the present work as it allowed the comparisons to be made on several planes including experiential similarities, healthcare priorities, and the evolution of these in the future. This furthermore added to the transferability and relevance of the work to a wider group of stakeholders, helping to maximise the utility of not just the present study but the corpus of work as a whole.

Chapter Summary

The present chapter has described an exploratory comparative analysis of qualitative studies in two LTCs and multimorbidity, and compared their findings to those in the OAB study described in Chapter 4. The review has described many areas of overlapping barriers and drivers for adherence and persistence behaviours across LTCs, as well as the nuances within the context of OAB.

The next chapter will present the overall discussion and conclusions from this body of work, taking the learnings from the present and previous chapters to provide the reader with a set of recommendations to support medicine-taking behaviours, and therefore outcomes, for individuals experiencing OAB.

Chapter 6 – General discussion and conclusions

Summary

The overall aim of this thesis was to explore the reasons and context for non-adherence to medications for overactive bladder, a common, bothersome, and burdensome condition, and to explore how these findings related to other LTCs. The final chapter of this thesis aims to distil and discuss the learnings from these studies into actionable next steps and policy recommendations with the ultimate aim of improving adherence and persistence behaviours, and therefore outcomes in OAB.

Findings and implications

Reasons for non-adherence

This thesis has identified several self-reported reasons for non-adherence in OAB as well as in other LTCs through the conduct of both primary and secondary research. Within the context of the WHO's model of adherence (described in Chapter 1), the individual-centric aims and methodology of the present thesis were best suited to explore the patient-related dimension to medicine-taking behaviours in OAB and other LTCs. However, while the thesis aimed to understand the *patient* perspective on medicine-taking behaviours, it is important to recognise both the centrality of the patient in each of the five domains as identified by the WHO, as well as how the experiences relayed by participants were related to themes encompassing dimensions beyond what may be considered exclusively "patient-related factors". The significance of factors pertaining to these additional dimensions is underscored by the fact that individuals in the OAB study broadly commented on these issues without prompt (signifying the relative importance to them), as well as the corroboration of these findings in other LTCs. It is therefore both useful and important to explore the findings and implications of the present thesis within the wider context of the full 5 dimensions of adherence, as seen through the eyes of the patients whose accounts have been foundational to this work.

In doing so, Figure 6.1 below depicts the patient-related dimension in the centre with key themes from the remaining four WHO dimensions as seen through the eyes of the patient. Where identified themes spanned more than one dimension, these have been listed under all those they related to. The present chapter will explore themes in each of these dimensions in turn, detailing implications and recommendations stemming from their consideration.

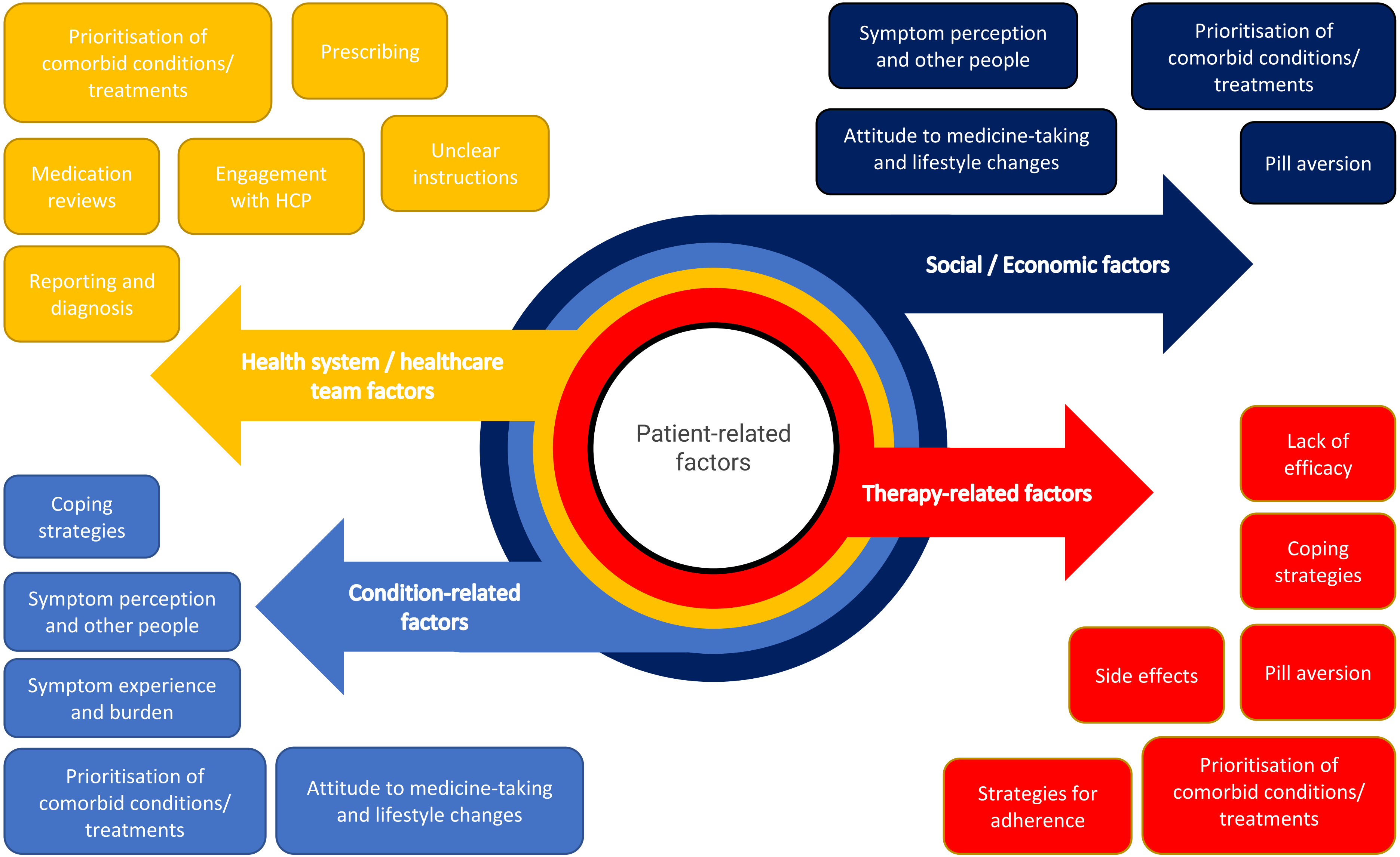


Figure 6.1: Themes within WHO five dimensions of adherence

Social/economic factors

While the WHO report outlined socioeconomic status, unemployment, illiteracy and cultural beliefs around illnesses and treatments under this dimension, several related themes were identified within the present thesis.

Key amongst the themes under social factors was the broad impact of “other people” (captured within the OAB theme: “symptom perception and other people”), both on the actions directly related to adherence, as well as on indirect themes including the formation of a condition hierarchy (and relatedly, a drug hierarchy). These themes together offered some granularity to the formation of the WHO-described cultural beliefs around conditions and their treatments, as participants within the OAB study stated that their estimation of their condition or treatment was shaped or affected by the actions and words of others. The influence of the wider social context on medicine-taking behaviours has been explicitly recognised in the COM-B and CSM models of adherence under the ‘social opportunity’ and ‘cultural context’ domains respectively (see Chapter 1: ‘Conceptual models relating to adherence’). Within the OAB study, the influence of other people took on various guises, including the views expressed by those in positions of authority (HCPs), as well as those of peers, and the perceived beliefs of wider society too.

The role of the HCP will be explored further below, however, a recent summary of systematic reviews found that social support may have a positive influence on adherence, though the evidence in the literature was inconsistent (Gast and Mathes, 2019). While arguably in a different patient demographic, research exploring the role of social support and peer groups in adolescents may be illustrative in this context. Work by Núñez-Baila and colleagues within the context of diabetic adolescents suggested the distinction of three types of peer roles: protective, indifferent, and offensive (Núñez-Baila et al., 2021). Broadly, the protective role was characterised by peer behaviours promoting patient self-management and healthy habits supportive of treatment adherence. The indifferent peer-role, was neither supportive nor hindering, granting patients social inclusion while allowing them space to wield autonomy in their health-related behaviours. The offensive role, however, was characterised by discriminatory behaviours toward the patient and their need for self-care, often manifesting in patients feeling mocked, or compared to less socially desirable people (in the case of the above study, this took the form of diabetic patients being compared to drug users on account of their having to inject insulin) (Núñez-Baila et al., 2021). While the three peer roles above could conceivably also apply to adults experiencing LTCs, it may be that in contrast to adolescents seeking social integration, adults are more likely to feel socially integrated, and thus either more immune to the effects of a specific offensive peer or more equipped to distance themselves from one. It is also possible that the role of offensive peer is one felt more generally in adulthood, and more likely to be attributed to wider society rather than specific individuals, particularly in the case of embarrassing or stigmatised conditions such as OAB, as there was evidence of within the present work.

In his seminal work on the subject, Erving Goffman described stigma as an act of reducing an individual from a whole, complete person, to a tainted, discounted one (Goffman, 1963). Goffman's work described how such reductions were based on the characterisation of social identities centred on the attributes of individuals, and that specific attributes could be considered stigmatising or not, depending on the context. In this way, stigma he argued, occurred at the intercept of attributes and stereotypes (Hector and Khey, 2022), and disqualified individuals from full social acceptance (Fitzpatrick, 2008). Stigma is distinguished into three forms: physical (relating to bodily attributes), character (blemishes inferred from mental disorder, imprisonment, addiction and unemployment), and tribal (relating to race, nationality and religion) (Goffman, 2017). Falling into the ‘physical’ form of stigma, urinary incontinence is particularly stereotyped within the context of OAB symptoms (Siu, 2016). While earlier definitions of stigma focussed within the context of visible signs of unusualness, the definition has developed to include ‘discredited stigmatised identity’ where the stigmatized individual assumes their visible differences are immediately apparent to others) and ‘discreditable or concealable stigmatised identity’, where the individual feels, their differences, while still potentially discrediting, are not immediately discernible to others (Werner et al., 2019). Further distinctions allowing the encapsulation of behaviours toward the individual, as well as their own feelings include ‘enacted stigma’ where the individual perceives an act of discrimination against them on account of their condition, and ‘felt stigma’ which refers to the individual’s own shame and embarrassment in relation to their condition (Frank et al., 2018).

Several OAB symptoms may be associated with the individual being or feeling stigmatised (spanning both discreditable and discrediting identities), including urinary urgency, incontinence, increased daytime micturition frequency and nocturia, all of which may result in shifts in behaviour or demeanour which could be discernible to others either by sight or smell. Indeed, Elstad and colleagues summarised stigma within healthcare as being associated with poorer health access and outcomes, increased stress, and reduced quality of life, going on to distinguish the stigma felt by OAB patients was not limited to incontinence, but the range of accompanying LUTS including urinary frequency and urgency (Elstad et al., 2010). Elstad and colleagues went onto note the root of such stigma in LUTS symptoms to be in social interruption, loss of socially expected control of the body, and the undesirable juxtaposition of private behaviour in public spaces, further highlighting the influence of gender and ethnic background on these (Elstad et al., 2010).

Relatedly, and overlapping with other dimensions of adherence, individuals attributed felt stigma to the poor understanding of OAB amongst “other people”. This manifested itself as embarrassment, shielding or downplaying symptoms in the presence of others, as well as patients feeling the need to compare their symptoms to those of others to justify an otherwise elusive feeling of normality and acceptance. Such observations give support to the socially exclusionary effect of stigma as highlighted by Hoffman’s work, and the human motivation for acceptance and belonging (Allen et al., 2022). Such feelings of embarrassment and social judgement were also raised by individuals with IBD in relation to their treatment in the Devlen et al. (2014) paper. Here, such experiences were associated with delayed treatment-seeking behaviours and non-adherence to avoid disclosure (see Chapter 5: “Social stigma” theme).

Related to considerations on stigma, parallels may also be drawn between OAB patients downplaying or normalising their symptoms and the disclosure behaviours of patients with other LTCs. A literature review on self-disclosure in mental health patients found that discussing their psychological LTCs was not a simple choice for individuals but involved the complex weighing up of the costs and benefits of doing so (Hyman, 2008). Benefits included the possibility of additional assistance, connecting with others having similar experiences, and being more open) whereas costs included risking social exclusion, encountering discriminatory behaviours, and having to regulate behaviours even more so in the future as a consequence (Hyman, 2008). The authors went on to distinguish between ‘selective disclosure’, where patients choose who, when, and how much of their condition to share with others and ‘indiscriminate disclosure’ where patients had undergone a change in attitude and no longer concealed their mental illness, signifying the expulsion of the hesitancy or shame in doing so (Hyman, 2008). The majority of participants within the OAB study described a degree of selective disclosure to peers and wider society, referencing social judgement and embarrassment as primary reasons for this. Only one participant gave evidence of indiscriminate disclosure with peers, but as this was not the focus of the discussion, it is unclear how far beyond peer groups such behaviour extended (see Participant 12 in "symptom perception and other people" in chapter 4).

The need for better awareness of the condition in the general public, as well as an empathetic understanding of the experience lived by patients amongst HCPs was highlighted throughout this thesis. In the case of some OAB participants, these external influences were also linked to difficulty in adopting lifestyle changes, blaming themselves for the development or persistence of symptoms and delayed seeking of help. While the adoption of lifestyle advice will be discussed in therapy-related factors below, the link between the stigma of urinary symptoms and patient self-blame has been discussed in the literature with roots attributed to individuals' perceived responsibility to maintain urinary control and a failure to fulfil a social obligation when they are unable to (Toye and Barker, 2020). Both the resultant shame and tendency to secrecy (Toye and Barker, 2020), as well as the fear of stigma, have been recognised as barriers to help-seeking behaviours in OAB patients (Elstad et al., 2010).

With a content policy outlining a commitment to the delivery of objective and trustworthy material (NHS.UK, 2021a), information relating to both conditions and medications is readily available on the NHS.UK website through its "Health A to Z" and "Medicines A to Z" web pages, as well as through the NHS mobile app (NHS.UK, 2021b, NHS.UK, 2021c). Here, individuals can find alphabetised information on a range of conditions (including an overview, symptoms, causes, treatments, and complications), as well as on specific treatments (including an overview, key facts, who the treatment is suitable for, how and when to use the treatment, side effects and management advice, special precautions, and advice on use in pregnancy or lactation, as well as common questions). Information is presented in accordance with the NHS central principles of accuracy, impartiality, accountability to its users, and serving the ‘ordinary citizen’ in order to enable them to understand and implement advice consistently. In keeping with this, the website adheres to the principles of the Information Standard, a quality standard composed of 6 principles ranging from the production of information and the sources used, to the involvement and understanding of the end user, as well as feedback and review (NHS.UK, 2019a).

Despite its prevalence and burden, OAB does not appear in the self-described ‘complete guide to conditions, symptoms, and treatments’, encompassing the A-Z list of conditions on the NHS.UK website (NHS.UK, 2021b). While ‘urinary incontinence’ appears as the record with the closest relevance, this does not address the multifactorial nature of OAB symptoms, including urinary urge, frequency and nocturia (NHS.UK, 2019c, ICS, 2015). Paradoxically, medications used to treat OAB such as tolterodine, solifenacin, oxybutynin and mirabegron are listed in the medicines A-Z list, as ‘medicines for treating symptoms of overactive bladder’ (NHS.UK, 2021c), however, as those without clinical knowledge are unlikely to know to look for specific drug names, the usefulness of having a more complete record on the medicines A-Z list, while not having a dedicated record for OAB on the conditions A-Z is questionable. As NHS.UK is described as the UK’s biggest health website with over 50 million visits every month (NHS.UK, 2019a), the lack of dedicated information to OAB on this central resource may be a contributor to patients describing a lack of understanding from peers and beyond, while also contributing to the lower importance given to OAB on the condition hierarchy, with implications on health-seeking and adherence behaviours as highlighted within this work. This was in contrast to complete records for IBD and T2DM on NHS.UK, as well as the high awareness exhibited by individuals in relation to T2DM in the McSharry (2016) paper (see Chapter 5: "Medications for diabetes: a necessary evil") (NHS.UK, 2019b, NHS.UK, 2020a).

From a wider perspective, it is unclear what proportion of the 50 million monthly site visits to NHS.UK are from patients, HCPs, or the general public. It is also noteworthy that resources such as websites, are typically reactive in nature and depend on engagement being initiated by members of the public in order to benefit from the information they contain. This may introduce a further challenge borne from the degree to which these resources are known to the public, even if they did hold adequate information on OAB. This, coupled with the issue of not listing OAB as a stand-alone condition, raises questions on the degree to which patients and non-patients may be well-informed by the most widely used platform for this purpose in England.

Other well-known sources of information include the Patient.info website, which contains thousands of leaflets and articles on conditions and treatments, written by medical authors as a resource for medical staff and patients (Patient.info, 2021). As a further provision, Patient.info (as part of EMIS Health) has developed the Patient Access mobile application, allowing patients to arrange access to GP services to make appointments, order repeat prescriptions, view their medical records, and access health information (Patient.info, 2021). While OAB does appear as a standalone article on the Patient.info website and app, it is listed under 'women's health'. The authors of the article justified this with the reasoning that OAB is more common in women than men and clarified with a statement saying that OAB can affect men also (Jarvis, 2021). However, as highlighted in Chapter 1 of this thesis, and in fact, in the reference cited in the Patient.info article itself, the prevalence of OAB is similar between males and females, and so such a justification is ill-founded (Truzzi et al., 2016). Furthermore, the term ‘women’s health’ may be perceived as issues unique to women and thus in a more general context where men are less likely than women to look for health information on the internet (Bidmon and Terlutter, 2015), such a categorisation of information relating to OAB may further hinder males in particular in accessing and benefiting from it. This resonates with the findings of a recent UK-based retrospective database analysis for which I led the design and execution and for which the manuscript is provided as Appendix C1 (referred to herein as the monotherapy and combination-use [MACU] study). The study used the CPRD to explore patterns of drug use and persistence with treatments for LUTS and OAB and found evidence to suggest that men were comparatively undertreated for OAB than its prevalence would otherwise suggest (Ali et al., 2021). This was further qualified by the observation that despite the similar prevalence of OAB in men and women (Irwin et al., 2006a), the MACU study identified over twice as many female patients based on the prescription of OAB drugs than male ones (Ali et al., 2021 (data on file)).

A further facet of sex in a social context is the historical distinction between “self-contained” men and the antithetically “leaky” nature of women and their denigration for lacking control over bodily functions (Shildrick, 1994 pg.26). Such observations may be at the heart of an expressed lack of control by multiple individuals with OAB within the present work (see Chapter 4: ‘symptom expression’). Similar findings of women with OAB expressing that they should be able to control urinary symptoms and relating an inability to do so to a form of personal psychological weakness have also been noted in the literature (Anger et al., 2011). The social situation of women has historically been defined and reinforced by their biology and the scientific model of modern medicine tends to “essentialize, naturalize, and idealize women’s bodily destiny and reduce them to motherhood” (Nisha, 2022 pg.26). More broadly, the medical profession has had a key role in the development of universal biological standards and their consideration as social norms, as well as the linkage of female normality with expected bodily dysfunction such as urinary incontinence and menopause (Peake et al., 1999). The medicalization of women’s health has been observed to occur at conceptual, institutional, and doctor-patient levels, with women’s acceptance of such negative biomedical narratives adversely affecting their attitudes and experiences of natural bodily changes such as menopause (Felice et al., 2021). Such observations offer a distinct context for the experience of OAB symptoms for women and may explain differences in how health threats are represented and subsequently coped with between men and women (according to the CSM of illness- see Chapter 1). Indeed, according to epidemiological research exploring differences in OAB between the genders, women were twice as likely to use physiotherapy and absorbent pads as coping mechanisms for their OAB symptoms than men, mirroring similar findings within the present work (Eapen and Radomski, 2016b).

More broadly, beyond the simple provision of information, the nature of its delivery is an important consideration for its ultimate resonance with individuals. A study analysing the readability of online information about overactive bladder was conducted by Koo et al. to appraise a wide range of online sources. Analysing the first 100 search results on the most widely used search engines (Google, Bing, and Yahoo!) for information on OAB, the authors appraised 296 unique websites and concluded that the vast majority of online information about OAB treatments exceeded the reading level of the average adult in the U.S. making it extremely difficult to comprehend. Furthermore, they found no websites suitable for low-literacy readers (Koo et al., 2017). Such findings were mirrored by a similar study, which concluded patients looking for information on OAB using popular search engines were likely to encounter incomplete and potentially commercially biased information, also noting that high-quality, patient-oriented materials had the potential to empower and more effectively inform patients on their LTCs, as well as improve adherence (Clancy et al., 2018).

These observations give rise to the recommendation for simple, accessible online information for OAB, and for OAB to feature as a stand-alone condition on well-used centralised online resources such as the NHS A-Z list, for patients and others to find and use with the same ease and assuredness as that held for other conditions. This, coupled with the correct categorisation of OAB as one affecting males and females may help debunk some of the beliefs held by patients and others on the prevalence, causes, and impact of the condition on patients and their families and friends. Better access to clear, understandable information may also help patients initiate conversations on their symptoms with peers, as well as HCPs, helping to counter some of the delays in seeking help as seen in the OAB study, which may in turn enable better treatment adherence, improved control of OAB symptoms and HRQoL, as well as wider effects on healthcare resource use and associated costs.

It is important to note however, that while helpful to patients, even the effective provision of information may not be enough to increase public awareness and empathy with those experiencing a LTC, especially ones marred with embarrassment and stigma. This may be because understanding and acceptance of the experiences of others is not merely a result of producing more information on a subject, especially if such information is unlikely to be accessed by those who are not experiencing the condition themselves.

On this front, proactive engagement and support from patient groups have been shown to be of benefit in both sharing and championing the voice of the patient, as well as increasing awareness amongst non-sufferers (Hu, 2017). Building on the comparative analysis with an LTC with strong experiential parallels to OAB as discussed in Chapter 5, IBD may offer a good example of this. As a leading patient organisation within this space, Crohn’s and Colitis UK has “been here for everyone affected by Crohn's and Colitis” since 1979 (Crohnsandcolitis.org.uk, 2022). Aside from the organisation’s work in promoting a better understanding of IBD and helping patients adjust to living with a LTC, their prominent offering of support materials is notable. These include a RADAR key to access disabled toilets, and a ‘Can’t wait card’ designed to be handed to members of the public when needing assistance or urgent access to a toilet (Figure 6.2).

URGENT CAN’T WAIT

PLEASE HELP – The holder of this card has Inflammatory Bowel Disease and needs to use your toilet facilities urgently.

Thank you.

CROHN’S & COLITIS UK

Registered charity numbers
1117148 (England and Wales)
SC038632 (Scotland)

Figure 6.2: Can't wait card (Crohnsandcolitis.org.uk, 2021a)

A RADAR key is a universal key designed to open compatible locks commonly installed in over 9,000 public accessible toilets, restaurants and other venues in the UK, meaning the holder does not need to wait for the toilet to be unlocked and can use it at their discretion (Crohnsandcolitis.org.uk, 2021b). Both the card and the RADAR scheme thereby give those with IBD the choice of how much they wanted to verbally disclose their experience, allowing them to maintain a comfortable level of selective disclosure more easily with strangers. Both tools furthermore allow individuals to avoid the embarrassment of having to breach their preferred disclosure level from necessity and have to verbally explain their condition or symptom being experienced, while simultaneously promoting a greater understanding of their experience amongst non-sufferers.

Interestingly, despite the obvious parallels between bowel and bladder symptoms, none of the patients within the OAB study mentioned involvement with a patient group, nor having access to similarly helpful materials such as the RADAR key to access disabled toilets, nor an information card to use in public. Describing itself as the largest bladder patient support charity in the UK, Bladder Health UK offers members a range of services to support those suffering from cystitis, OAB and continence issues. This includes articles on living with bladder illness, an advice line for sufferers, and a UK-wide network of local support groups, as well as active engagement on social media (BladderHealthUK, 2021b). However, despite appearing as the first result on an internet search for “overactive bladder support UK”, in contrast to the example of Crohn’s and Colitis UK website above (where information detailing the entitlement of members to both a RADAR key and ‘can’t wait card’ were listed very prominently under ‘member benefits’), no such information was presented for Bladder Health UK. In fact, even after searching for the term ‘RADAR key’ on the homepage, the user is directed to a page where the RADAR scheme is briefly mentioned, informing the user of the possibility of purchasing a key (separately and in addition to membership fees, and without the provision of a specific place where such a purchase of the key is possible). This is supplemented with an external link to an 8-year-old news article explaining the scheme (BladderHealthUK, 2021a, BBC.co.uk, 2013).

The Bladder and Bowel Community (B&BC) was formed in 2008 as a UK service for people with bladder and bowel control problems and states its central aim to raise awareness of bladder and bowel control problems amongst the general public and HCPs, as well as to provide information and support surrounding the conditions, treatments, and available products and services (Bladderandbowel.org, 2021b). In contrast to the more established Bladder Health UK, the B&BC website clearly promote a 'just can't wait toilet card', offering both a physical and free digital version for mobile phones, as well as a RADAR key as part of a membership of their home delivery service (Bladderandbowel.org, 2021a).

There is, therefore, a further opportunity to shape the consistent and coordinated support given to OAB patients from outside a purely medical sense, prompting a further recommendation of the present work to improve the availability and provision of aids to OAB patients, through the proactive engagement with patient groups, learning from organisation both across the urological landscape, as well as beyond this in other conditions where such measures have been welcomed by patients and the wider community (Young, 2019).

Therapy-related factors

The WHO report discussed the effects of treatment duration, complexity, and failure of previous treatment as key therapy-related factors that affect adherence. It went on to discuss frequent changes in treatment, the immediacy of beneficial effects, side effects and the availability of support to help manage them. Much of this was reflected in the themes identified within the current thesis both within the sphere of OAB and beyond.

The findings of the present work indicate that as an overarching theme; the patient's assessment of the necessity to take treatment was shaped largely by their perceived balance of the risks and benefits of doing so, with this trade-off forming a central pillar to their adherence behaviours in OAB and other LTCs. Such a trade-off, while being indicative of the evaluative process characterised by the 'reflective motivation' domain of the COM-B model of adherence, offers substantial support for the NCF. As described within the NCF, the key beliefs influencing patient evaluation of prescribed medication (and in turn influencing adherence behaviours) can be grouped into those contributing to a perceived personal need for treatment (necessity beliefs), and those contributing to concerns about potential adverse effects (concern beliefs) (Horne et al., 2013a). The NCF was based on previous works that found patient-held beliefs about medicines were stronger predictors of reported adherence than clinical and sociodemographic variables (see Chapter 1: Necessity-Concerns Framework)(Horne and Weinman, 1999).

Within the present work, the experience or fear of experiencing side effects, a general aversion to taking pills and an ability to exercise choice formed the main contributors to the assessment of risk. These were strengthened by polypharmacy where patients were on multiple medications, often for different conditions, heightening the sense of risk and aversion to taking anything 'additional', as well as the sense of choosing between medications. While polypharmacy and the perceived need for treatment have been recognised as individually affecting adherence, adherence is also affected as a result of the interaction between them (Marcum and Gellad, 2012).

The MACU study (Appendix C1) also found that compared to combination therapies for OAB comprising of multiple antimuscarinics or an antimuscarinic and mirabegron, treatment persistence was greater with monotherapy, noting persistence was greatest with mirabegron monotherapy, and particularly worse with combinations of two antimuscarinics in both men and women (Ali et al., 2021). Such an observation may not be surprising given the cumulative effects of multiple antimuscarinic medications as well as the prominence of adverse events in the stated reasons for discontinuing OAB treatment both in the literature as well as in the present work (Jaggi et al., 2021).

In this thesis, participants largely described measuring benefits in terms of treatment effectiveness at controlling symptoms, which in turn was linked with condition-related factors where the severity of the symptoms provided the context in which the above assessment was carried out. Perceived benefits of taking medication for OAB were also reinforced by the explicit and implicitly perceived input from HCPs as well as ‘other people’ as described under other dimensions of adherence. The relative balance of risks and benefits was described qualitatively by patients within the present work and mirrored the dynamics in the NCF of the necessity-concerns differential, a quantitative expression of the difference between the perceived necessity driving adherence, against the perceived concerns weighing against this (Horne and Weinman, 1999). Similarly, as voiced in both OAB and the comparative study with other LTCs, patients adhered to (and indeed in some instances reinitiated) treatment when the perceived benefits outweighed the perceived risks of doing so.

At the heart of the themes identified under this dimension of adherence, it is of value to examine the factors contributing to the formation of patient expectations of both risks and benefits. While the importance of the availability of objective, trustworthy information for OAB has been discussed above, the initial formation of OAB treatment expectations stemmed from the diagnosis and prescribing processes patients experienced with HCPs. While these experiences differed across patients, it is important to note the interplay of condition-related, health-system, and therapy-related factors, as the diagnosis process, while primarily centred on the condition, impacted the formation of expectations around the treatment also. Principally, the immediacy of the diagnosis and the assuredness of the HCP in diagnosing and prescribing were seen to have an effect on the patient acceptance and expectations of the diagnosis and treatments respectively. In the case of OAB, the similarity of symptoms to those seen with other conditions including urinary tract infections, benign prostatic enlargement, and bladder cancer (Wein, 2011a), and the fact that diagnosis of OAB is made upon the exclusion of these (Cardona-Grau and Spettel, 2014), may hinder the provision of a prompt diagnosis or treatment as suggested by the General Medical Council’s (GMC) guidance for good medical practice (GMC, 2019). Nevertheless, while some patients did report positive diagnosis processes (in terms of speed or ease), a protracted diagnosis process was a common theme amongst other OAB patients and was seen to be linked to patients harbouring doubts about its accuracy, thereby impacting the perceived balance of risk and benefits in taking treatment for it. Further work is therefore needed to understand the experience of diagnosing OAB, and whether a more thorough explanation to those coming in with non-descript urological symptoms, or better exchanges throughout the process of secondary care referrals may aid patient engagement and acceptance of an eventual diagnosis of OAB.

Following diagnosis, the experience of patients being prescribed treatment for OAB was also seen to negatively shape their expectations due to patients recalling the language used by the prescriber as being tentative, and one of experimentation, rather than conveying assured confidence in the treatment being prescribed. As antimuscarinics are the first-line pharmacological treatment for OAB, such language may be well grounded in knowledge of their shared mechanism of action, resulting in comparable efficacy and impact on HRQoL (Marcelissen et al., 2019), as well as the observation that not all patients respond to the first antimuscarinic received (Kuo, 2018). However, while it is important for patients to be aware of other agents in the event that the first one does not work, introducing this concept through what is perceived as experimentative language at the point of diagnosis and initial prescription may not be the most appropriate time or manner in which to do so, and may influence the formation of poor expectations. This is especially noteworthy given the suggestion in NICE guidelines to offer a face-to-face or telephone review 4 weeks after starting a new medication for OAB, and ongoing annual or biannual reviews for those on long-term treatment, giving subsequent opportunities to hold such discussions (NG123, 2019).

The observation that patients and prescribers bring pre-existing beliefs about conditions and treatments that can influence adherence behaviours has been made elsewhere in the literature (Horne et al., 2013a, Shahin et al., 2019). Furthermore, the characteristics of the patient-prescriber relationship, the prescribers' explanation, and their confidence in the therapy being prescribed have been noted to contribute to patient treatment expectations (Rief, 2016), which in turn have been linked to treatment adherence and persistence behaviours in several places in the literature (Woodward et al., 2016, WHO, 2003, Jimmy and Jose, 2011). Indeed, patient expectations about their treatments and the effects of these have been studied within the context of the placebo effect. While often referred to as an inert substance commonly used in double-blind RCTs, the term placebo encompasses the administration of this inert substance within a sensory and social context that indicates to the patient that a beneficial treatment is being given, and includes the use of words, rituals, symbols and meanings that help shape this (Benedetti et al., 2011). A useful distinction is between the inert nature of the physical entity being administered (which has no physiological effect of its own), and the meanings individuals ascribe to the experience of taking such a substance (which enable the 'placebo effect' often observed). Patients may perceive placebos as 'metonymic simulacra' (artificial objects embodying parts of an experience [e.g., taking a pill], which in turn represent the entirety of the medical experience) thus acting as repeated reminders of the medical interaction as a whole (Moerman, 2013). Within this interaction, the role of the physician and the transmission of their own beliefs about treatment (and by extension, about the condition) can enhance or detract from the meaning the patient ascribes to treatment, ultimately shaping its effectiveness. For this reason, Moerman emphasised the role of meanings and called for the term ‘placebo effect’ to instead be thought of as a “meaning response”, stating that the former focussed on the inert and avoided the meaningful (Moerman, 2013 pg.1). Relatedly, the formation of positive expectations has been established as a key process in the placebo effect, alongside the recommendation that promoting positive treatment expectations may enhance the benefit of all treatments (Brown, 2015). While optimistic treatment expectations have been noted to amplify the positive effects of treatment as described above (placebo effect), negative treatment expectations can have the opposite effect and potentiate adverse effects, or nullify treatment-typical improvements (nocebo effect) (Rief, 2016). Within the context of OAB, as side effects and lack of treatment effect have been reported as leading reasons for treatment discontinuation as noted in the present work as well as others in the literature (Ali et al., 2019, Yeowell et al., 2018b), the formation of positive treatment expectations and avoidance of negative expectations may address these reasons for non-adherence. The clinician’s role in the formation of such expectations, is rightly governed by strict ethical standards that form the foundation upon which holistic patient-centred care is built (GMC, 2019). The GMC’s “Good practice in prescribing and managing medicines and devices” guidance instructs doctors to prescribe the treatment only if they are satisfied that it will serve the patient’s needs. Furthermore, prescribers are expected to explain the likely risks and benefits of treatment, as well as how to resolve common side effects. It goes on to highlight the value of reassurance and the provision of additional information where individuals do not adhere to treatment in the first instance (GMC, 2021). Because of this and the findings of the present work, OAB patients would benefit from the provision of balanced information and assurance in line with the clinician's belief that the treatment will be of benefit to them.

A recommendation from the present work would therefore be for prescribers to aid the formation of positive expectations and avoid the formation of unduly negative treatment expectations by assuring the patient of the choice of treatment at the point of prescribing and reserving conversations regarding the next possible agent for reviews designed to periodically assess the performance of prescribed OAB treatment. Such practice would also be consistent with the GMC prescribing guidance which advises against "*overloading or confusing patients with excessive or inconsistent information*" (GMC, 2021 pg.7). Having the prescriber's demeanour and language reflect their prerequisite positive expectations from the treatment being prescribed may increase patient assuredness. This in turn may limit the potency of words and actions of others in having a detrimental effect on medicine-taking behaviours in individuals with OAB, as well as the associated poorer health outcomes and healthcare resource costs to the healthcare system (Yeowell et al., 2018b).

Related to treatment expectations, research has indicated the median duration to determine responsiveness with antimuscarinics in OAB is 3-months, indicating that antimuscarinic therapy should therefore be continued even when there is a poor response within the first few months (Hsiao et al., 2015). However, as noted by a retrospective real-world study of clinical practice in the UK, discontinuation of antimuscarinics in OAB patients generally occurred within 1-3 months of commencement (Chapple, 2017b), indicating that more realistic expectations may also contribute to addressing the perceived lack of efficacy being a chief reason for discontinuation as seen in many patients within the current work and beyond. Reflecting the GMC prescribing guidance, the duration of treatment should therefore be a key point of discussion during diagnosis and prescription processes, as well as subsequent reviews, to ensure medications have enough time to be adequately assessed for effectiveness (GMC, 2021).

Antimuscarinics are commonly the first treatment to be prescribed for OAB, with estimates from the MACU study (Appendix C1) suggesting 92-94% of patients undergoing monotherapy treatment for OAB received antimuscarinics (Ali et al., 2021). The exercise of trying different antimuscarinics sequentially for the treatment of OAB has been termed 'antimuscarinic cycling' and is common in clinical practice (Yeowell et al., 2018b). However, evidence from a clinical retrospective database analysis found that OAB symptom burden did not change as patients cycled through multiple antimuscarinics, suggesting that the practice of cycling may not provide any additional clinical benefit, and may actually result in sub-optimal care for OAB patients (Chancellor et al., 2016). Indeed, despite the availability of mirabegron, which differs in mechanism of action to antimuscarinics, and thus may provide a viable alternative in those unresponsive to antimuscarinics, antimuscarinic cycling is implicitly encouraged within the NICE guidelines, with clinicians prompted to offer an alternative of "low acquisition cost" from a list of antimuscarinics in the case the first is ineffective or not tolerated (NG123, 2019 pg.19). For guidance on how to prescribe mirabegron, NICE guidelines refer to its technology appraisal (TA290), which suggests for mirabegron to be used as an option only for those in whom antimuscarinics are contraindicated, are ineffective, or produce intolerable side effects (TA290, 2013). In light of the clinical case against antimuscarinic cycling, I am a part of an effort to investigate the health economic effects of this practice in UK clinical practice, through a retrospective database analysis study being designed presently to address this gap in the literature. This work may provide further evidence for the recommendation to limit the number of antimuscarinic agents that patients cycle through before being treated with an alternative type of treatment such as mirabegron, with implications on the patient experience, clinical outcomes, as well as health care resource use within the healthcare system.

Finally, the theme of ‘routine’ or habits around treatments was found in both the OAB study as well as other LTCs compared in Chapter 5 (IBD and T2DM) as a key factor in whether patients maintained adherence to treatments and lifestyle advice. The term ‘habit’ has been defined as a “non-conscious process by which a situational cue…automatically generates an impulse toward enacting a behaviour…based on learned associations between the cue and the behaviour” (Hoo et al., 2019b pg.284). Patients within this work employed a range of habitual techniques to aid adherence including taking all medications together, taking them at set times (aided by reminders), tying medicine-taking to daily events such as waking schedules or mealtimes, and employing visual cues to remind themselves to do so. Conversely, patients discussed the difficulty in establishing treatment and other lifestyle routines for OAB such as pelvic floor muscle training exercises as well as in relinquishing routines which were detrimental to their condition including excessive or mistimed consumption of caffeine. Indeed, while the association between strong habits and high adherence has been established across a range of conditions including asthma, type II diabetes, hypertension, and Cystic Fibrosis (CF) (Badawy et al., 2020, Hoo et al., 2019a), the adoption of lifestyle changes and adhering to training techniques for the management of OAB has been acknowledged to require significant behavioural changes to patients’ daily activities and habits (Wyman et al., 2009).

While the NICE guidance on adherence mentions the establishment of a medicine-taking routine, it only does so in the context of highlighting that patients may wish to discuss with a HCP how to fit taking medications into their daily routine, as opposed to leveraging habits to achieve and maintain adherent behaviours (CG76, 2009). Medicine-taking behaviours have been shown to be susceptible to disruption by breaks in everyday routine such as the arrival of the weekend (Boucquemont et al., 2020) or going away as has been seen in the present work. The establishment of habitual, ‘automatic’ medicine-taking has however been noted to aid adherence even in such circumstances which might otherwise make it challenging to maintain adherence (Arden et al., 2019).

In light of the observations within this work, a further recommendation is for clinicians to actively establish a tailored medicine-taking routine as a shared goal with the patient, having addressed any reasons for intentional non-adherence. To maintain its relevance in changing life circumstances, this should be revisited at discussions with the prescriber as well as other HCPs such as pharmacists at regular reviews as part of the ongoing assessment and support of adherence. Such a recommendation may be applicable to other LTCs as evidenced by the importance of routines in IBD, and T2DM (discussed in Chapter 5), and particularly in the case of supporting individuals with multimorbidity, which can amplify the burden of maintaining treatment adherence (Foley et al., 2022). Enabling and encouraging the safe and effective use of medications has been supported in the Royal Pharmaceutical Society (RPS) competency framework for all prescribers, and the RPS adherence guides for pharmacists, respectively, highlighting the potential role of the wider multidisciplinary health team in this activity (RPS, 2016, RPS, 2021).

Observations by Eze-Nliam et al. indicated considerable variability in the degree of agreement between medical records and reports from patients on important aspects of medical history such as demographics and conditions experienced (Eze-Nliam et al., 2012). The possibility of similar discrepancies regarding the accurate understanding of patient adherence to treatment, as well as the effects this might have on subsequent clinical decisions such as dose escalations, treatment changes, and more invasive procedures, may be avoided by assessing and addressing medicine-taking in the context of patient-specific routines and habits at regular reviews with the prescriber and other HCPs.

Condition-related factors

Patients described OAB as burdensome whilst outlining a range of symptoms including urge, urge incontinence, frequent need for micturition, nocturia and enuresis. Despite this, patients typically considered OAB as a low priority for pharmaceutical intervention as noted in Chapter 4, reflecting low reflective motivation as captured by the COM-B model of adherence. Chapter 4 also noted the range of adaptation measures patients used instead to manage and cope with these symptoms, including fluid restriction, the use of urinary pads, planning trips and journeys around the availability of restrooms, pre-emptive bladder emptying, and reliance on safe spaces (see 'coping strategies for symptoms' in Chapter 4). The experience of OAB was often framed in terms of other people noticing or commenting on symptoms or their solutions, with patients emphasising a sense of embarrassment, self-consciousness, and a feeling of abnormality, especially when comparing to others in their peer groups. This was countered by measures to normalise and downplay symptoms, as well as safe spaces where patients felt shielded from such scrutiny and emotions. Given the observations that cultural metaphors about illness play a significant part in defining identities of 'self' and 'others' (Siu, 2016), and that stigma "*is fundamentally a threat to one's self-identity*" (Southall et al., 2017 pg.2), such behaviours to downplay, and particularly normalise OAB symptoms may be mechanisms to avert identifying the self with urinary problems. Indeed, the negative effect of urinary incontinence on self-esteem, stress, and depression has been widely noted in the literature (Lee et al., 2021, Kinsey et al., 2016b, Gumussoy et al., 2019)

While the previous section of this chapter has touched upon some patients harbouring doubts towards the diagnosis of OAB, this was accentuated by the belief by some that OAB symptoms were a natural part of the ageing process, with others linking them to the menopause, or childbearing, further distancing the patient from a definitive and accepted diagnosis. On one occasion, this link was actively reinforced by a patient's recollection of a comment from their HCP regarding her OAB symptoms (see Chapter 4: bothersome side effects). While the pathophysiology of OAB may differ from patient to patient, OAB is often labelled 'idiopathic' due to the difficulty in identifying the underlying cause. Nevertheless, OAB should be regarded as complex and multifactorial, resulting from multiple possible physiological pathways (Peyronnet et al., 2019), and thus the uninvestigated attribution of symptoms to a single life event or even to ageing may be unhelpful and indeed contribute to the low prioritisation given to OAB. Such suboptimal and potentially erroneous perceptions of OAB and its causes, as well as the resultant context for OAB treatments, may cause the observed deprioritising of OAB through the mechanisms described in the COM-B under the reflective motivation domain. This in turn may adversely influence the psychological capability of individuals to manage their OAB via all available tools, as opposed to the coping mechanisms discussed in Chapter 4 (see 'coping strategies for symptoms'). Relatedly, the way older adults view the ageing process has been noted not only to affect their health status but also their help-seeking behaviours, with those with more negative self-views of ageing being less likely to seek preventative health services and more likely to require hospitalisations (Sun and Smith, 2017). In the context of OAB, despite the considerable burden on their HRQoL, rates of treatment-seeking behaviours in older patients are low with some evidence that individuals show reluctance in discussing symptoms with a HCP, partly because they believe them to be a normal part of ageing (Sexton et al., 2011a). The provision of robust, up-to-date information and accessible information on the pathophysiology of OAB may enable a more accurate view of OAB and its possible causes among patients as well as HCPs.

The normalising of symptoms as ‘natural’ was one of the ways that the importance of OAB was understated by many patients, with others reinforcing this by noting a perceived systemic disinterest in OAB. This ranged from that of individual HCPs, to the lack of information reported for OAB in the public domain, supporting earlier observations and recommendations to remedy this. Indeed, building upon the availability and quality of information for patients and those around them to access, direct-to-consumer advertising campaigns (DTCA) have been shown to increase the uptake of pharmaceuticals in the US and New Zealand, where such industry-funded campaigns directly naming treatment brand names are permitted (Zaitsu et al., 2018). In the case of the UK, where according to the Association of British Pharmaceutical Industry (ABPI) code of practice, the pharmaceutical industry, while not permitted to advertise prescription-only medication (POM) to the public, are able to encourage members of the public to seek treatment, direct-to-consumer information (DTCI) campaigns (also known as disease awareness programmes) are permitted (ABPI, 2021). A recent study found that following a 5-week DTCI campaign for OAB using television, internet, and print advertising in Japan (where there are similar regulations to the UK regarding POM promotion), patients were more likely to receive OAB treatment for 15 weeks with a 15-week delay (Zaitsu et al., 2018). This suggests that improved awareness of OAB and its symptoms may encourage those experiencing symptoms to seek help, either through the provision of correct information, or the dispelling of misinformation and incorrectly held views. Indeed, the reluctance of OAB patients to seek help has been noted both within the current thesis and elsewhere in the literature also (Norton, 2003).

The hierarchisation of conditions (and by extension, their treatments) by patients was made all the more prominent when compared against the management of other comorbidities, where OAB was seen as comparatively less important, driven primarily by the differences in consequences of not adhering to its treatment versus that for another LTC. This further highlighted the importance of the ‘concerns’ domain of the NCF and its potential role in the ranking of conditions given their long-term complications. Further evidence of this was seen in the comparative analysis in Chapter 5 where patients’ view of T2DM and their perceptions of its treatment were heavily influenced by the long-term consequences of the condition (see Chapter 5: ‘medications for diabetes: a necessary evil’).

Continuing within the NCF, the perceived necessity of OAB treatment may also have been diminished by the wide adoption of coping mechanisms and adaptive behaviours, which in turn may have shaped the perceived marginal risk or benefit from taking a new drug for OAB in the context of a pool of treatments already taken for other LTCs. A similar theme of ‘beliefs about polypharmacy and drug prioritization’ was noted in the Maffoni (2020) study exploring multimorbidity discussed in Chapter 5. Linked to observations in ‘Therapy-related factors’ above, the immediacy of treatment effectiveness was described as a key factor in this prioritization, thus reiterating the need for patients to hold clear expectations and understanding of both their conditions and treatments.

Health system/healthcare team related factors

Many of the topics relating to this dimension of adherence, such as the level of information on OAB in the public domain have been touched on in other sections, however, there are several observations from the present work highlighting useful recommendations to be made in the context of the healthcare system and OAB.

While the role and influence of people around the patient have been discussed in relation to OAB as well as other LTCs throughout this work, it is useful to recognise the pivotal role held by HCPs, and especially prescribers within this, to considerably affect patient medicine-taking behaviours. Indeed, the interpersonal dynamics of the patient-prescriber relationship have been noted to influence the degree to which the patient trusts their prescriber. This in turn can affect the level of emotional disclosure and communication between patient and prescriber, the patient's motivation to adhere, as well as the degree and effectiveness of shared decision-making (Martin et al., 2005). Actively involving patients in decision-making about their treatments has been highlighted by NICE in their guidance on adherence (see Chapter 1). Elsewhere, while not explored directly within the present body of work, the role of non-prescribing HCPs such as pharmacists has been recognised as important in improving medication adherence and health outcomes in a range of conditions including hypertension, hyperlipidaemia, COPD and asthma (Milosavljevic et al., 2018).

The existence and issues associated with historic paternalism in the NHS have been recognised for several decades (Coulter, 1999), and although patient participation and partnership are increasingly being encouraged, there is evidence of paternalistic practices still remaining due to a variety of factors including a desire to maintain control, a lack of time, and personal beliefs of the HCP, which can lead to mistrust between patients and prescriber (Grünloh et al., 2018). Even in the absence of this, the physician's advocative position in the relationship with the patient as well as an imbalance of knowledge may assign to them a level of power and influence, which they should remain respectful and mindful of in their clinical practice (Nimmon and Stenfors-Hayes, 2016). In the case of OAB, in combination with the eliminatory process of diagnosis, patients commented on the words and demeanour of the prescriber contributing to a sense of OAB holding low priority and having low confidence in the treatments prescribed. This was in contrast to the experience of individuals with T2DM in the McSharry (2016) study where patients were well convinced of the rationale for using the treatment and considered themselves fortunate in having access to it (see Chapter 5: ‘medications for diabetes: a necessary evil’). This then gives rise to the recommendation for further work in understanding the diagnosis and prescribing process experienced by OAB patients. Although such work may help determine specific recommendations on this topic, it is clear from the current work that these factors are contributory to the wider context behind the medicine-taking behaviours in OAB, and physicians should exercise care in the language used to enable patients to maintain confidence in both diagnosis and treatment. The importance of skilful communication by physicians (captured most explicitly by the ‘social opportunity’ domain in COM-B, and the ‘information’ domain of the IMS models) has been noted in the literature as a “central factor in achieving patient adherence”, through several potential mechanisms including the provision of support and encouragement (Zolnierek and Dimatteo, 2009 pg.6).

Given that OAB is primarily managed in primary care (Itam and Singh, 2017), linked to the above, was the varied experience of HCP medication reviews with OAB, with patients broadly reporting an imbalance (both in frequency as well as time spent) between those for OAB and those for other conditions, again contributing to the sense of differential importance between conditions, and low importance of OAB. HCP time constraints and the presence of more prioritised conditions were reported by patients as underpinning this, while the preference of some patients to only discuss OAB symptoms and treatments when seeing the HCP for other matters and not proactively, exacerbated the lack of focus on OAB.

On the subject of HCP time constraints, the reality of increasingly heavier and complex workloads in general practice has been recognized by a retrospective database analysis of GP and nurse consultations in almost 400 English practices between 2007 and 2014 (Hobbs et al., 2016). This study found a sizeable increase in consultation rates, average consultation duration, and total patient-facing clinical workload over this time, not including non-clinical and professional duties, which the authors expected to have also increased (Hobbs et al., 2016). Work by the King's Fund on the pressures in general practice confirmed these findings while noting that the trending growth in workload had not been matched by a growth in funding or workforce (Baird et al., 2016). Further compounding this workload is the increasing prevalence of multimorbidity with higher rates associated with increased age or socioeconomic deprivation (Cassell et al., 2018) (see Chapter 5: "Future healthcare priority" for further discussion on multimorbidity). Such pressures have been shown to result in prescribers perceiving a trade-off between conducting thorough reviews involving the patient, and the time taken to do so, opting instead to conduct the majority of medication reviews remotely (Duncan et al., 2019).

An additional factor in shaping the emphasis given to the review and support of different conditions in UK Primary Care is the funding arrangements behind the provision of such care. The Quality and Outcome Framework (QOF) is an annual NHS reward and incentive program for GP practices in England, Wales, and Northern Ireland, designed to reward GP practices for the quality of care they deliver to their patients. 'Indicators' based on the proportion of patients with defined LTCs receiving defined interventions dictate the number of QOF points a GP practice receives, which in turn affects the level of payments given (NHSDigital, 2022). The selection and employment of these indicators have been recognized to affect the prioritization of primary care with a longitudinal analysis revealing that although the implementation of the QOF incentives improved quality indicators from 2001 to 2007, this was at the expense of non-incentivised aspects of care (Doran et al., 2011). Presently incentivised conditions include coronary heart disease, hypertension, T2DM, asthma, COPD, mental health conditions and cancer (NHSEngland, 2021). A more recent systematic review found no evidence of the QOF improving care for people with LTCs, drawing comments that given the historic underfunding of primary care relative to demand, the QOF had, in essence, become a part of the core funding, without which many primary care practices would collapse (Limb, 2017). The dominance of QOF points in directing HCP-patient interactions has been highlighted by a qualitative study involving audio-recorded primary care consultations and a series of interviews with both patients and practitioners (Chew-Graham et al., 2013). It found that consultations were predominantly conducted by a checklist approach driven by the biomedical agenda set by the QOF indicators, which reinforced a paternalistic relationship with HCPs, whose desire to earn QOF points overrode the ethos of patient-centered care (Chew-Graham et al., 2013).

In the context of findings from the present work showing some OAB patients delaying symptom reporting and being reluctant to discuss their urinary symptoms in the absence of other reasons for engaging HCPs, such practices may further limit opportunities to raise, review, and refine the management of their OAB, raising the possibility of inequality in healthcare. Indeed, a key component of the present work has been the differential experience of individuals in relation to OAB versus that of other LTCs, including a difference in the provision and access to healthcare as highlighted throughout this thesis (see: ‘social/economic factors’ above and Chapter 4: ‘drug/condition hierarchy’). Despite the emphasis in the NHS Long-Term Plan on reducing inequalities and providing individuals with the personalised care they need (NHS, 2019), such differences may instead be indicative of disparities in the provision and access of healthcare for those experiencing OAB. This may be further exacerbated by the stigmatizing nature of OAB itself, as, in addition to being a global barrier to health seeking behaviours, stigma has been recognized to fuel social inequalities and ultimately exacerbate poor health (Stangl et al., 2019).

A further area identified in the present work under the healthcare system/team dimension of adherence included the procedural actions of the surgery itself (systems and support staff). The latter especially manifested itself as patients describing the surgery not pursuing them to come in for OAB reviews where these had not occurred, nor enforcing written rules around patients having to ensure they had arranged reviews before further repeat prescriptions could be authorized. This reemphasized the perception of OAB and its treatment as not being important and therefore forms the basis of recommending that systems encouraging and requiring reviews should be adhered to, in order to offer patients more timely reviews and opportunities of support, as well as to readdress the perceived condition hierarchy.

In recognition of the increasing pressures within primary care, NHS England commissioned a study to quantify the demand on GP time, and possible areas to release pressure upon them. One of the findings was that 16% of primary care appointments at GP surgeries were appropriate for diversion to other allied HCPs, including community pharmacists, and could be improved by more active signposting and information (Freeing, 2015). Within community pharmacy, one of the mechanisms this may previously have been done through was Medicines Use Reviews (MURs), which were available in England since 2005 as an Advanced Service within the NHS Community Pharmacy Contractual Framework, and were designed to allow pharmacists to conduct a one-to-one consultation with patients in order to help them manage their medicines more effectively (Latif, 2018). MURs were a free service to the patient and could be raised either at the pharmacy itself or through GP referral. Before being decommissioned recently, MURs offered the opportunity to use the combination of the community pharmacist's clinical knowledge as well as records of prescription medications dispensed at the pharmacy, to hold a private and personalised discussion of a patient's medication, adherence, and general lifestyle advice.

A qualitative study found that patients generally viewed MURs positively, valuing the pharmacist's time, reassurance and confidence felt having engaged in one. The same study however, raised concerns about the failure of the MUR service to result in inter-professional collaboration between GPs and community pharmacists and in optimizing the delivery and outcomes of MURs in those most likely to benefit from them (Latif et al., 2013). The lack of clarity in the link between an MUR and the outcomes in GP-managed care was also raised by patients in the present work where MURs were mentioned. Latif et al. concluded by emphasizing the potential of the MUR service in supporting patients in obtaining greater benefits from their treatments and reducing the occurrence of medicine-related problems being presented to GPs (Latif et al., 2013).

Supporting their historic widespread use in community pharmacy, figures from the Pharmaceutical Services Negotiating Committee (PSNC) suggest over 3.4million MUR consultations took place in the year 2018/19 from over 10,000 pharmacies in England (PSNC, 2021b). However, the MUR service was decommissioned in March 2021 for not offering good value for money, putting a stop to such reviews being carried out in the community pharmacy setting (Cox, 2019). This policy decision, however, was part of the 5-year pharmacy funding plan, which unveiled further steps such as the replacement of MURs with "structured medication reviews" (SMRs) to be conducted by clinical pharmacists working in GP practices instead of community pharmacists (practice-based pharmacists)

(Cox, 2019). The development of this new role for pharmacists within GP practice aims to not only address over-medication, and support the government's antimicrobial resistance strategy, but to use the SMRs to allow patients to get the most from their medication, while aiming to reduce waste and promote self-care. A further remit of the role will be to integrate GP services with other healthcare teams in the area including community and hospital pharmacy, thus helping to address some of the limitations of the previous system discussed above (Finch, 2019). With over 1,000 clinical pharmacists currently working in general practice (NHSEngland, no date), and with this number expected to grow up to 7,500 by 2023/24, such changes to the healthcare system may place strain on the pharmacy profession to meet the needs in pharmacy settings across the system (Andalo, 2019). Furthermore, while MURs were accessible through over 10,000 community pharmacies without an appointment, and at any time during the pharmacy's opening hours (typically longer than a doctor's surgery), it is unclear what difference the provision of SMRs through 6,822 GP surgeries in England (Bostock, 2021) may make to patient uptake of reviews in OAB and other conditions, and whether this will be outweighed by the more targeted and coordinated nature of SMRs. Based on the stated preference of some OAB patients to hold incidental discussions with HCPs regarding their urinary symptoms, as well as the perceived low importance given to OAB vs other LTCs, the change in accessibility from the community pharmacy-based MUR service with an appointment-based one within GP surgeries may make it even less likely for such reviews to be taken up by patients. This may be particularly true considering the diverse role of the pharmacists conducting such reviews within GP practices including medicines reconciliation following hospital discharge and reviewing prescription requests, making the conduction of medicines reviews only a portion of what they are employed to do (Duncan et al., 2019).

Conclusions

Summary of recommendations

- Addressing poor understanding of OAB and the support available:
    - Ensure there is a standalone page on online resources such as the NHS.UK and patient.info websites with the correct categorisation of OAB for patients, prescribers, and the general public to reach accurate and reliable information in an accessible way.
    - Encourage more proactive provision of information to patients and the general population through the work of patient groups.
    - Make better use of existing supportive mechanisms such as the RADAR scheme and other resources to make available consistently.
    - The execution of disease awareness programs for OAB in general media to increase awareness of the condition and possible treatment.
    - Such resources may also help stem the belief of OAB being a natural part of the ageing or menopause processes.
- Addressing patient expectations of risks and benefits
    - Further work is needed to understand the experience of OAB diagnosis, with emphasis on the immediacy and assuredness of diagnosis, referral, and patient acceptance of the diagnosis.
    - Cross-examining this with work on the experience of the prescriber may also help identify further areas of improvement
    - Ensure HCPs employ care with the language used at the point of prescribing, avoiding phrases that give an impression of experimentation (e.g., the word “try”). While expressing to patients that there is a range of treatments

available is likely to be an attempt to reassure the patient at the point of diagnosis and prescribing, it is important for prescribers to emphasize their confidence in the treatment being prescribed, while reviewing the need for subsequent options as part of the ongoing reviews as recommended by NICE.
    - The prescribing process should emphasize the median length of time taken for the onset of response to OAB treatment being around 3-months, thereby encouraging patients to persist with treatment before deeming it ineffective.
    - Linked to this, prescribers should be mindful of the act of antimuscarinic cycling and the limitations associated with this practice, especially with the availability of treatment with a differing mechanism of action.
- Supporting adherence
    - The establishment of a medicine-taking routine should be a shared goal between the patient and their HCPs, revisited at routine reviews with the prescriber as well as other HCPs such as pharmacists and nurses.
    - Medication reviews for OAB: further exploration is needed to investigate if reviews with prescribers are happening as irregularly as indicated by the present work, and the reasons behind this.
    - The use of alternative mechanisms of providing easily accessible support via pharmacists or nurses akin to the recently decommissioned MUR service may be needed to be explored to ensure patients can access regular 1:1 support.

Strengths, limitations, and future work

This thesis encompassed the first fully qualitative exploration of reasons for non-adherence to OAB treatment, and as such gave OAB patients a voice hereunto unheard in the literature. While among the central aims of the thesis was to uncover the self-reported reasons for non-adherence (with a focus on OAB), the present work has further explored the rich context behind these reasons in both OAB and other LTCs, giving several actionable next steps to support patients and their medicine-taking behaviours.

The multiorganizational governance processes followed for this work certainly helped to reinforce the rigour of study design and execution, giving it the benefit of input from experienced industry and academic professionals. Furthermore, the use of an independent interviewer for the OAB study, and the performance of independent reflexive analyses by both interviewer and analyst were key strengths of the present work, giving the reader transparent insights into the background and approaches taken to the present research. Undertaking thematic analysis in the step-by-step process outlined by Braun and Clarke, 2006 ensured the themes generated were well-established both from data within each data item, as well as across the entire dataset. Furthermore, the inclusion of brief quotes to highlight observations and interpretations throughout the thesis has offered the reader continuous context and justification of the interpretations made, as well as the opportunity to make their own interpretations. In addition to illustrating the journey from data to insight, the use of quotes has been used to evoke a more immersive experience for the reader, bringing to life the direct experience of each participant, and presenting it to the reader to process and make meaning of in their own unique way as discussed under the philosophical basis for this thesis (Chapter 3).

The present work, however, could have been further strengthened in several ways, some of which may form the basis of future work in this area. The sampling methods employed, though pragmatic, did result in a relative imbalance in the recruitment of men (30% of the sample), as well as a concentration of participants over 65 in the OAB study (75% of the sample). Both of these factors may be due to suboptimal reporting and diagnosis processes for OAB, the relative undertreatment and reluctance of men to be involved in similar research to this, as well as the increased prevalence of OAB symptoms with advancing age (Eapen and Radomski, 2016a). While such imbalances may limit the degree to which the learnings can be applied to individuals not represented within this work, it is important to recognise the potential effects of these parameters on adherence as noted in the literature. A systematic literature review of observational studies exploring real-world adherence and persistence to OAB treatment found that rates of medicine-taking were higher in females and older patients than their counterparts (male and younger patients, respectively) (Yeowell et al., 2018b). This may indicate that the present work understates the extent and potency of identified drivers of behaviour (while retaining the possibility that some drivers may have remained uncovered due to choices in sampling). A similar consideration may be given to the effects of geographic representation and ethnicity in the present work. Although ethnicity was not explicitly captured within the OAB study and recruitment was spread over two geographical regions of England, it is unlikely that the sample included a range of ethnicities thoroughly representative of the UK populace. This may be particularly important given the influence of social context and norms on OAB management as discussed throughout this work. The importance of geography and ethnicity has also been considered within the same literature review above. It found that there were no notable trends between the data on medicine-taking behaviours across geographic locations (including the UK, Germany, Norway, Spain, USA and Canada), however, White individuals were more likely to adhere to OAB treatment than those of Black, Hispanic and Asian ethnicities (Yeowell et al., 2018b).

A useful starting point for the extension of the present work may be to address such limitations by including participants from a larger age range, employing more concentrated efforts into recruiting a higher proportion of males and considering the expression and relative strengths of drivers and barriers to adherence in individuals from different cultural backgrounds. The findings in Chapter 5 of some individuals holding a dislike for Western medicine may offer valuable insight into exploring such influences (see Chapter 5: ‘Medication for diabetes: a necessary evil’). Related to the impact of age on the findings, the exploration of how factors affecting medicine-taking behaviours are influenced by working life may be another area of future work.

The use of interviews alone, while also reflective of the time and cost constraints of the thesis may have been strengthened by the use of other methods of data collection such as focus groups. Focus groups may have encouraged even more candid responses in the presence of others with shared experiences, and participants may have been able to build on each other’s responses to provide an even richer account of the collective experience of participants within this work (Leung and Savithiri, 2009). Such an approach may also have enabled the collection of wider perspectives from caregivers and HCPs.

Relatedly, using a mix of qualitative and quantitative approaches with additional data collection methods such as surveys and questionnaires may also have aided the robust comparison of experiences of patients within the sphere of OAB, as well as beyond it in other LTCs. Indeed, while the OAB study in the present work involved a single interview with each patient, future developments could identify newly diagnosed patients and conduct repeated interviews with them to reach further depth to the understanding of their experiences over time, and the implications on their medicine-taking behaviours. This may thereby help reduce the recall bias which may have affected the present work, where patients were relaying events from months, and in some cases years ago.

A further area of development includes the effect of cycling from one OAB treatment to another and exploring the effects this may exert on treatment expectations and medicine-taking behaviours, as well as health outcomes and healthcare resource use. As mentioned earlier in this chapter, I am currently involved in such an effort with findings expected to be published in a manuscript in 2023.

While the present work has identified and interpreted the rich context behind medicine-taking behaviours in OAB and other LTCs, a future development could also include the exploration of behaviour change models that would likely offer the greatest benefit to account for the factors identified, in order to improve adherence and related health outcomes in patients experiencing OAB.

Finally, while antimuscarinics form the mainstay of oral pharmacological management of OAB and were thus reflected within the experiences of the majority of OAB patients within the present work, a further area of future work may entail exploring differences in drivers and barriers of medicine-taking behaviours between those taking antimuscarinics and those on beta-3 agonists such as mirabegron. With a distinct tolerability profile to antimuscarinic agents (Huang et al., 2020), it is feasible that in a disease area where adverse events have been shown to be a key factor in medicine-taking behaviours, differences between treatments could amplify these. Some quantitative work exploring how this affects persistence has already been undertaken and included in Appendix C1. Exploring such drivers more granularly could further aid the identification of interventions to aid both adherence and persistence behaviours, as well as health outcomes in OAB patients.

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Appendices Set A:

Appendix		Title
A1		SLR search strategies
	A	MEDLINE
	B	Embase
	C	CINAHL
	D	PsycInfo
	E	Web of Science

A1. SLR Search Strategy

A: MEDLINE

Search	Terms	Results
S1	Ti,ab ("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder" or OAB or "lower urinary tract symptom*" or LUTS or "urin* storage symptom*" or “urin* incontin*”) or MESH.EXACT.EXPLODE("Urinary Bladder, Overactive")	4936
S2	(ALL) (medic* or drug* or prescri* or treat* or antimuscarin* or anticholinerg* or mirabegron or Betmiga or darifenacin or flavoxate or fesoterodine or oxybutynin or propiverine or solifenacin or tolterodine or trospium)	55016837
S3	(complian* or adher* or persist* or concord* or discont*) or MESH.EXACT.EXPLODE("Medication Adherence")	2759181
S4	(qualitative or "qualitative research" or (interview* or "group interview*" or "oral history" or “focus group*” or “case note*” or "telephone interview*") or questionnaire* or survey* or telephone or thematic or theme) or MESH.EXACT.EXPLODE("Qualitative Research")	4945174
S5	S1 AND S2	4904
S6	S5 AND S3	796
S7	S6 and S4	193
S8	Ti,ab (“paed*” OR child* OR “adolescen*” OR “pediat*” OR “pubescen*”) OR MESH.EXACT.EXPLODE("Pediatrics")	60669
S9	S7 NO S8	192
	Abstract included, humans, English, adults, dates	155

B: Embase

Search	Terms	Results
S1	ti("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder" or OAB or "lower urinary tract symptom*" or LUTS or "urin* storage symptom*" or “urin* incontin*”) OR ab("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder" or OAB or "lower urinary tract symptom*" or LUTS or "urin* storage symptom*" or “urin* incontin*”) OR (MJEMB.EXACT("overactive bladder"))	64934
S2	(((medic* or drug* or prescri* or treat* or antimuscarin* or anticholinerg* or mirabegron or Betmiga or darifenacin or flavoxate or fesoterodine or oxybutynin or propiverine or solifenacin or tolterodine or trospium)))	26801039
S3	(complian* or adher* or persist* or concord* or discont*) OR (MJEMB.EXACT("medication compliance"))	1615220
S4	(((qualitative or "qualitative research" or (interview* or "group interview*" or "oral history" or “focus group*” or “case note*” or "telephone interview*") or questionnaire* or survey* or telephone or thematic or theme))) OR (EMB.EXACT("qualitative analysis") OR EMB.EXACT("qualitative research"))	3047482
S5	S1 AND S2	57264
S6	S5 AND S3	7286
S7	S6 and S4	2027
S8	ti(“paed*” OR child* OR “adolescen*” OR “pediat*” OR “pubescen*”) OR ab(“paed*” OR child* OR “adolescen*” OR “pediat*” OR “pubescen*”) AND (EMB.EXACT.EXPLODE("pediatrics") OR EMB.EXACT("adolescent"))	1514628
S9	S7 NO S8	1959
	(S16 NOT S17), abstract included, humans, English, adults, dates	618

C: CINAHL

Search	Terms	Results
S1	Ti,ab (("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder") or OAB or "lower urinary tract symptoms" or LUTS or "storage symptom*" or urin* or incontin*) or (MM "Overactive Bladder")	1426
S2	TX (medic* or drug* or prescri* or treat* or antimuscarin* or anticholinerg* or mirabegron or Betmiga or darifenacin or flavoxate or fesoterodine or oxybutynin or propiverine or solifenacin or tolterodine or trospium)	4127906
S3	TX (complian* or adher* or persist* or concord* or discont*) or (MM "Medication Compliance")	285618
S4	(qualitative or "qualitative research" or (interview* or "group interview*" or "oral history" or “focus group*” or “case note*” or "telephone interview*") or questionnaire* or survey* or telephone or thematic or theme) or (MM "Qualitative Studies+") OR (MM "Ethnographic Research") OR (MM "Ethnological Research") OR (MM "Ethnonursing Research") OR (MM "Grounded Theory") OR (MM "Naturalistic Inquiry") OR (MM "Phenomenological Research")	1076633
S5	S1 AND S2	1245
S6	S5 AND S3	177
S7	S6 and S4	49
S8	Abstract included, humans, English, adult, dates	36

D: PSYCINFO

Search	Terms	Results
S1	TI ((("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder") or OAB or "lower urinary tract symptoms" or LUTS or "storage symptom*" or urin* or incontin*)) OR AB ((("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder") or OAB or "lower urinary tract symptoms" or LUTS or "storage symptom*" or urin* or incontin*))	17182
S2	TI ((medic* or drug* or prescri* or treat* or antimuscarin* or anticholinerg* or mirabegron or Betmiga or darifenacin or flavoxate or fesoterodine or oxybutynin or propiverine or solifenacin or tolterodine or trospium)) OR AB ((medic* or drug* or prescri* or treat* or antimuscarin* or anticholinerg* or mirabegron or Betmiga or darifenacin or flavoxate or fesoterodine or oxybutynin or propiverine or solifenacin or tolterodine or trospium))	1058806
S3	(complian* or adher* or persist* or concord* or discont*) or MM "Treatment Compliance" OR DE "Compliance" OR DE "Treatment Barriers")	205711
S4	(qualitative or "qualitative research" or (interview* or "group interview*" or "oral history" or “focus group*” or “case note*” or "telephone interview*") or questionnaire* or survey* or telephone or thematic or theme) or (DE "Qualitative Methods") AND (DE "Focus Group" OR DE "Grounded Theory" OR DE "Narrative Analysis" OR DE "Semi-Structured Interview" OR DE "Thematic Analysis" OR DE "Mixed Methods Research" OR DE "Qualitative Measures")	1209686
S5	S1 AND S2	8987
S6	S5 AND S3	1290
S7	S6 and S4	413
S8	TI ((“paed*” OR child* OR “adolescen*” OR “pediat*” OR “pubescen*” DE "Pediatrics" OR) OR AB ((“paed*” OR child* OR “adolescen*” OR “pediat*” OR “pubescen*”)	865908
S9	S7 NO S8 Abstract included, humans, English, adult, dates	290

E: Web of Science

Search	Terms	Results
S1	TI=("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder" or OAB or "lower urinary tract symptom*" or LUTS or "urin* storage symptom*" or “urin* incontin*”) OR AB=("overactive bladder" or "overactive detrusor" or "overactive detrusor function" or "overactive urinary bladder" or OAB or "lower urinary tract symptom*" or LUTS or "urin* storage symptom*" or “urin* incontin*”)	41266
S2	(medic* or drug* or prescri* or treat* or antimuscarin* or anticholinerg* or mirabegron or Betmiga or darifenacin or flavoxate or fesoterodine or oxybutynin or propiverine or solifenacin or tolterodine or trospium)	13352265
S3	(complian* or adher* or persist* or concord* or discont*)	1527966
S4	ALL=(qualitative or "qualitative research" or (interview* or "group interview*" or "oral history" or “focus group*” or “case note*” or "telephone interview*") or questionnaire* or survey* or telephone or thematic or theme)	3368413
S5	S1 AND S2	24460
S6	S5 AND S3	2713
S7	S6 and S4	709
S8	TI=(“paed*” OR child* OR “adolescen*” OR “pediat*” OR “pubescen*”) OR AB=(“paed*” OR child* OR “adolescen*” OR “pediat*” OR “pubescen*”)	1986406
S9	S7 NO S8 Abstract included, humans, English, adult, dates	595

Appendices Set B:

Appendix		Title
B1		Practice engagement packs
	A	PCO invitation letter
	B	PCO poster
	C	Study protocol
	D	RISP
B2		Patient pack
	A	Patient information sheet and consent to be contacted form
	B	Patient study consent form
B3		Interview proforma
B4		Interviewer reflexive accounts (all patients)
B5		Published manuscript

Appendix B1: Practice Engagement Packs

A: PCO invitation letter

RE: Patient name

Date of birth: DD/MM/YYYY

RE: **A Qualitative Analysis to Explore Factors Influencing Patient Adherence to Prescribed Overactive Bladder (OAB) Medication, in UK Primary Care. HRA Approval IRAS ID 198502**

Dear Dr……….

I am writing to inform you that your patient (name) has agreed to take part in the above qualitative research, which will involve a one-one interview with a researcher about their experiences of OAB and its treatment. Questions will focus on perceptions and attitudes to OAB and its treatment, as well as the range of reasons why patients may not take their medications for OAB, and likely factors that might enhance adherence for them and for others taking similar drugs.

This research is being carried out as part of The UK Knowledge Transfer Partnership (KTP) programme (Europe's leading programme for helping businesses to innovate, develop, and grow through better use of the knowledge, technology, and skills that reside within the UK knowledge base). The research partners are Manchester Metropolitan University (MMU) and Astellas Pharma Europe Limited.

This research aims to explore factors influencing patient adherence to medications for OAB. A greater understanding of these issues has the potential to drive the development of personalised value-added services, and guide new product and service development that could significantly improve health outcomes in patient groups. In addition to the development of new products, the research will also contribute to the teaching and learning of health professions, the development of healthcare policy and practice and improve access to, and quality of, healthcare by providing cost-effective treatment interventions for people with OAB.

If you would like any further information about this project, please contact me using the details below.

Yours sincerely

Dr Maxine Holt (Chief Investigator)

Principal Lecturer in Public Health
Manchester Metropolitan University
Tel 0161 247 2240
Email m.holt@mmu.ac.uk

B: PCO poster

DO YOU TAKE PRESCRIBED MEDICATION FOR AN OVER ACTIVE BLADDER?

We want to hear from you !

Your GP practice or clinic has agreed to ask its patients who have been prescribed medication for an **Over Active Bladder (OAB)**, to consider participating in our research to help:

- Understand patient's view of OAB and its treatment
- Explore what factors may influence whether you continue taking your medication or not

If you have taken any of the following medication, and are interested in participating in this research, please let your reception staff or prescriber know, and they will provide you with further information:

OAB is more common than you might think. It affects 1 in 6 adults in the UK (1)

Darifenacin (Emselex®), **Fesoterodine** (Toviaz®), **Flavoxate** (Uripass®), **Mirabegron** (Betmiga®) **Oxybutynin** (Ditropan®/Lyrinel®), **Propiverine** (Detrunorm®), **Solifenacin** (Vesicare®), **Tolterodine** (Detrusitol®), **Trospium** (Regurin®),

*Generic name (Brand names).

Either generic, brand, or both may appear on packaging and on prescriptions.

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(1) Bladder Health UK 2017 http://bladderhealthuk.org/bladder-conditions/overactive-bladder

C: Study Protocol

Study Protocol

Title: A Qualitative Analysis to Explore Factors Influencing Patient Adherence to Prescribed OAB Medication, in UK Primary Care.

Background:

This research is being carried out as part of The UK Knowledge Transfer Partnership (KTP) programme (Europe's leading programme for helping businesses to innovate, develop, and grow through better use of the knowledge, technology, and skills that reside within the UK knowledge base). The research partners are Manchester Metropolitan University (MMU) and Astellas Pharma Europe Limited.

Rationale:

Overactive bladder (OAB) is a common, distressing, chronic condition characterised by urinary urgency with or without urinary incontinence, usually with increased daytime frequency and nocturia. Non-adherence to pharmacological intervention has shown to have a negative impact on health outcomes and quality of life. Research conducted using a US based claims database showed adherence with OAB medications to be the lowest amongst six chronic conditions.

This research aims to explore factors that influence patient adherence to medications for the treatment of OAB. Findings from this research have the potential to equip healthcare professionals with a greater understanding of the drivers of patient non-adherence, and the potential to modify clinical practice and improve health outcomes.

Research Outcomes:

- This research will provide a deeper understanding of patient's attitudes to medication, the support they receive during interactions with healthcare professionals and the main reasons for non-adherence to OAB medications.
- This research will also provide Astellas a greater understanding of the patient perspective and the qualitative methods used to gain patients insights that can be embedded into the organisation to ensure that patient-centricity runs through all Astellas activities.

Methodology:

It is anticipated that approximately 25 participants will take part in semi-structured, face-to-face interviews with the researcher.

Participants will be recruited from two R & D sites (Manchester University Hospitals NHS Foundation Trust and Surrey and Sussex NHS Trusts) through GP practices and clinics.

Interviews will be designed to enhance disclosure of the full range of reasons for non-adherence, and will leave space for patients to explain in their own words their experiences with OAB, the reasons why they may not take their medications, and factors that might enhance adherence for them and for others taking similar drugs.

Inclusion Criteria:

1. Male or female aged 40-80 years old

2. Fluent in English
3. Diagnosed with OAB (coded)
4. Stopped taking or have switched from either antimuscarinic(s) or Beta-3 adrenoceptor agonist medications within the last 12 months for Overactive Bladder (OAB)

A purposive sampling method will be used to involve participants who meet the above criteria.

Exclusion Criteria:

Due to the reliance of this study on patients being able to recall and describe their experiences, we will exclude those patients with memory impairment, cognitive decline, or dementia (as recorded within their medical records).

Analysis:

This is a predominantly qualitative study. Any statistical data analysis that is used will be presented as simple descriptive statistics (e.g., number of yes/no answers).

Thematic analysis is the treatment of stories or narratives as data and using analysis to arrive at themes. Themes can illustrate both similarities and differences across data and can undergo further analysis and refinement to produce sub-themes using a form of thematic networks, or web-like illustrations. Narrative fragments from participants will be used to illustrate themes and points. (Attride-Stirling, 2001)

Consent

Patients will provide their consent to be contacted by the research team in the first instance after initial contact by the GP practice, introducing this study.

Written consent [see patient consent forms] will be obtained by the research associate at the time of the interview.

Data Management

Each participant will be assigned a unique study identifier number, which will be used for all research data and will enable log linking the data to the participant. This information will be kept separately to the research data on a University Password Protected computer and will only be accessed by the research team.

Interview audio recordings will be transferred by the researcher to secure University computers, and then moved to storage as per University Data Protection Policy. Once done, original recordings will be deleted from the audio tape recorder.

Transcription of the research data will be undertaken by an employee within the university who is specifically employed for such project work, and has undergone relevant training covering the issues of patient confidentiality. The transcription process will be undertaken within the University during working hours and transcripts will be stored on password protected university computers.

While analysing the anonymised transcripts, information regarding possible adverse events (AE) relating to medicines produced by Astellas will be passed on to the manufacturer. Information shared will relate only to the drug and the event itself; no patient-identifiable information will be passed on.

No data will leave the country. Completed consent forms will be stored in a locked cupboard in a password-protected room in the university. As the data in storage will be anonymized and there is no danger to the participants about the release of information. Files will be stored up to 5 years as they may provide useful background information for continued research. After 5 years they will be destroyed.

Ethical Approval

This research has gained ethical approval from the required NHS Research Ethics Committees. You may verify the ethical approval of this study, or raise any concerns you might have, by contacting Ethics and Research Governance Manager at ethics@mmu.ac.uk.

For any other questions about this research contact Dr Maxine Holt (Chief Investigator) on m.holt@mmu.ac.uk or telephone 0161 2472240.

Ethics number: **198502**

Dissemination of Results

It is anticipated that the results of this research will be shared with others in the following ways: directly to the participants, the research team, Astellas Pharma Ltd, healthcare professionals, exhibits and presentations, reports, thesis, and published articles.

References

Attride-Stirling J (2001) Thematic networks: an analytic tool for qualitative research. Qualitative Research, 1 pp385-405.

D: RISP

Dear Colleagues,

Your practices are currently inviting patients to participate in a qualitative study to explore Overactive Bladder (OAB) in the UK.

The Clinical Research Network would be obliged if your sites would take part in a study looking to gain a deeper understanding of patient adherence to medications for the treatment of OAB.

STUDY TITLE

A Qualitative Analysis to Explore Factors Influencing Patient Adherence to Prescribed OAB Medication, in UK Primary Care.

STUDY OVERVIEW

Background:

This research is being carried out as part of The UK Knowledge Transfer Partnership (KTP) programme. The research partners are Manchester Metropolitan University (MMU) and Astellas Pharma Europe Limited.

Rationale:

Overactive bladder (OAB) is a common, distressing, and chronic condition. Non-adherence to pharmacological intervention has shown to have a negative impact on health outcomes and quality of life. Research conducted using a US based claims database showed adherence with OAB medications to be the lowest amongst six chronic conditions. This research aims to explore factors that influence patient adherence to medications for the treatment of OAB.

Methodology:

It is anticipated that approximately 25 participants will take part in semi-structured, face-to-face interviews with the researcher. Participants will be recruited from two R&D sites (Greater Manchester and Kent, Surrey, and Sussex) through GP practices and clinics.

Inclusion Criteria:

1. Male or female aged 40-80 years old
2. Fluent in English
3. Diagnosed with OAB (coded)
4. Stopped taking or have switched from either antimuscarinic(s) or Beta-3 adrenoceptor agonist medications
   within the last 12 months for Overactive Bladder (OAB)

Exclusion Criteria:

Due to the reliance of this study on patients being able to recall and describe their experiences, we will exclude
those patients with memory impairment, cognitive decline, or dementia (as recorded within their medical
records).

EXPECTED START & CLOSURE DATE

START DATE: 1st May 2018

EXPECTED CLOSING DATE: 31st July 2018

STUDY TARGET

Practices in Greater Manchester

PRACTICE INVOLVEMENT

- Display study poster in surgery
- Search surgery database for eligible patients and send them study materials through post (patient information sheet, consent-to-be-contacted form, prepaid envelope for reply)
- Notify research associate upon receipt of reply slips from patient and store them until collection.

PRACTICE PAYMENT

GP time (60 minutes):	£80.00
Practice Nurse time (60 minutes):	£26.96
Total:	**£106.96**

FURTHER INFORMATION

Please contact:

Mrs. Emma Oughton
Assistant Research Delivery Manager
emma.oughton@nihr.ac.uk

Mr Mahmood Ali
Research Associate
M.Ali@mmu.ac.uk
Mobile: 07919302616

Dr Maxine Holt
Chief Investigator
M.Holt@mmu.ac.uk

Appendix B2: Patient Pack

A: Patient Information Sheet and consent-to-be-contacted form

Patient Information Sheet

Version 4:19/2/18

IRAS Number: 198502

A Qualitative Analysis to Explore Factors Influencing Patient Adherence to Prescribed OAB Medication, in UK Primary Care

Your GP practice or health care professional is sending this to you as you have been identified as someone who may be interested in participating in the above research. The research is part-government funded, and is being undertaken by researchers at Manchester Metropolitan University in association with Astellas Pharma Europe Ltd.

Overactive bladder is a common condition. Symptoms can include an urgent feeling to go to the toilet, going to the toilet frequently and sometimes waking to go to the toilet more than once at night, and leaking urine before you can get to the toilet (urge incontinence).

We are exploring what factors affect the adherence to medications for patients with an Overactive Bladder (OAB). We are asking people aged 40-80 years who have either stopped or changed their medication for OAB (see below for names) in the last 12 months, to participate in this research. We would like to know what your views are about OAB, as well as the medication(s) used to treat it, and what factors may influence whether you continue to take these medications or not.

Darifenacin (Emselex®), **Fesoterodine** (Toviaz®), **Flavoxate** (Uripass®), **Mirabegron** (Betmiga®), **Oxybutynin** (Ditropan®/Lyrinel®), **Propiverine** (Detrunorm®), **Solifenacin** (Vesicare®), **Tolterodine** (Detrusitol®), **Trospium** (Regurin®),

*Generic name (Brand names). Either or both names may appear on packaging or on prescriptions.

Research of this type is important as it enables a greater understanding of the issues, which affect patients' decisions to continue to take their medication. The findings from patients like yourself who contribute to the research has the potential to drive the development of personalised medicine, improve existing services and guide new products and service development that could significantly improve health outcomes in patients with Overactive Bladder. In addition to guiding the development of new products, the research will also contribute to the teaching and learning of health professionals.

What is involved?

If you agree to participate in this research, you will be invited to take part in a face-to-face interview with a researcher, to discuss your thoughts, opinions, and experiences of OAB and any of the above medications you have taken for it. The researcher will interview you in a place convenient to you (e.g., your own home or local public space). The interview will be tape-recorded and may last up to an hour (longer if you require). All recordings will be destroyed after transcription.

Voluntary Participation

Your participation in this research must be voluntary. If you do decide to participate, you may withdraw at any time without any consequences or giving any explanation. If you do withdraw from the research, your data will only be used if you give permission for its use. Your participation **does not** affect your care pathways and current care provision in any way. The researcher is not a clinician and will not be able to answer any personal clinical questions. Should you have any concerns about your Overactive Bladder and medication, it is advised that you consult your healthcare professional (e.g., GP).

In appreciation of your time, we would like to offer you a £10 Voucher for either Tesco or Amazon.

Benefits to Taking Part

There are no immediate benefits to the participant, but the results could help inform future clinical practice and care pathways for those who have an Overactive Bladder. However, achieving this goal will require up to an hour of your time to participate in the study.

Adverse Events Reporting

Patients sometimes respond in different ways to the same medicine, and some side effects may not be discovered until many people have used a medicine over a period of time. For this reason, any information around side effects mentioned during the interview may be passed onto the manufacturer to help them learn more about the safety of their medicines. This will be done in a completely anonymous way and your personal information will **not** be shared with anyone outside of the University research team.

Anonymity & Confidentiality

To protect your anonymity, no names will be used in any reports. All identifying features will be removed from transcripts before they undergo analysis so that your answers will not be identifiable. Your confidentiality and the confidentiality of the data will be protected by ensuring that all data from the interview is stored in password protected computer files.

Information that you will be required to give to the Researcher

- Some form of contact number or address
- Any medications that you take or have taken for an Overactive Bladder

Dissemination of Results

It is anticipated that the results of this research will be shared with others in the following ways: directly to the participants, the research team, and its partners in Astellas Pharma Europe Ltd, healthcare professionals, exhibits and presentations, reports, academic theses, and published articles.

Storage and Disposal of Data

Data will be stored in a locked cupboard in a password-protected office or on a password-protected computer in the university. The research team are the only people who have access to this. As the data in storage will be anonymised and there is no danger to the participants about the release of information. All of the data will be stored for a period of 5 years as they may provide useful background information for continued research. After 5 years all data will be destroyed.

What if Something Goes Wrong

No intentional questions will be asked during interview that may cause upset or embarrassment. The research associate will have undertaken interview- techniques training. It will be made clear at the onset that the research associate is not qualified to give advice on any health or clinical issue. All efforts will be made to ensure that the participants understand that they can speak to their health professional about any issue that may have upset them during the interview.

Ethical Approval
This research has gained ethical approval from the required NHS Research Ethics Committees. You may verify the ethical approval of this study, or raise any concerns you might have, by contacting Manchester Metropolitan University Ethics and Research Governance Manager at ethics@mmu.ac.uk

For any other questions about this research contact Dr Maxine Holt (Chief Investigator) on m.holt@mmu.ac.uk or telephone 0161 2472240.

The scientific quality of the study has been assessed by the following:
1. Innovate UK for the purpose of KTP funding
2. ESRC - Economic and Social Research Council UK
3. The Stratified Medications Cohort
4. The research review team

Agreement to Participate
Your signature and contact details on the next sheet indicates that you understand the above conditions of participation in this research and that you wish to be contacted by the researcher, who will answer any further questions you may have and to arrange your most preferred method of contributing to the research.

CONSENT TO BE CONTACTED FORM

Name of Researchers: Dr Maxine Holt, Mr Mahmood Ali, Mrs Leanne Staniford

Please initial each of the following if you agree to them:

1.	I confirm that I have read and understand the information sheet (already provided) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
3.	I understand that details about my medications for Overactive Bladder will be shared with the Researcher.	
4.	I agree to take part in the above study and to provide the following contact information for the researcher to contact me to arrange my preferred method of participating in the study	

Participant Full Name:		
Month and Year of Birth:		
Contact Details:		
	Home telephone:	
	Mobile:	
Signature: Date:		

B: Patient study consent form

Manchester
Metropolitan
University

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INTERVIEW CONSENT FORM Version 3…2/1/18

IRAS ID: **198502**

Centre Number:

Study Number:

Participant Identification Number for this trial:

CONSENT FORM

Title of Project: **A Qualitative Analysis to Explore Factors Influencing Patient Adherence to Prescribed OAB Medication, in UK Primary Care**
Name of Researchers: Dr Maxine Holt, Mr Mahmood Ali, Dr Leanne Staniford

Please initial box

1. I confirm that I have read the information sheet dated.................... (version............) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. (If appropriate) I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from [company name], from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. (If appropriate) I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers. ☐
5. (If appropriate) I agree to my General Practitioner being informed of my participation in the study. / I agree to my General Practitioner being involved in the study, including any necessary exchange of information about me between my GP and the research team. ☐

6. (If appropriate) I understand that the information held and maintained by the Health and Social Care Information Centre (or amend as appropriate) and other central UK NHS bodies may be used to help contact me or provide information about my health status. ☐

7. I agree to take part in the above study. ☐

______________________	______________________	______________________
Name of Participant	Date	Signature
______________________	______________________	______________________
Name of Person taking consent	Date	Signature

Appendix B3: Interview Proforma

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Interview Performa

Thank you for agreeing to take part in this interview. The interview will last about an hour.

As discussed when you first agreed to take part, this interview will be part of a study to explore Overactive Bladder and why some people take their medications as prescribed, and some do not.

Please be completely honest, as this will help us to get a clear understanding of your experience of OAB and how you feel about it and the drugs you take, including any reasons why you may or may not take them as prescribed.

As I explained previously, the interviews will be tape-recorded and we may use direct quotes from what you say to us in our reports and other publications, but your name will not be used. The anonymised recordings will be kept securely at the University for a period of 5 years. Your privacy is important to us and any information you provide will be kept anonymous.

If you feel uncomfortable at any time, we can pause or stop, and if you do not want to answer any questions that is also fine. Just let me know.
The purpose of this research is to:

- Understand attitudes towards medication adherence in OAB patients,
- Understand the patient's perspective and experience of OAB as a disease, as well as their expectations around its management.

Questions:

1. **Introduction**: [to document: age, occupation, gender]
   "So first of all, can you tell me a little about yourself?"

2. **Overarching narrative of patient journey: attitudes and expectation:**

   a. **OAB History**: [Presenting symptoms, bother, and how long before help was sought and why -get a sense of initial attitude to OAB/engagement with own health]

      "Can you tell me a bit about your experience with OAB up to now, how did it all start?" [Probe: can you tell me any more about that/ and then?]

      "What were the initial symptoms you noticed, and how much did they bother you at first?" [Probe: and then?]

"How long after noticing them did you go to see your HCP?" [If waited before seeing HCP, probe: "why did you wait xxx before seeing your HCP?"]

"How much do your symptoms affect you/ your lifestyle?" [probe: "do they change what / how you do things?" "Are some days better/worse than others? Can you tell me more about this?"]

b. **HCP interactions**: [ascertain whether diagnosis/management was led by GP or Specialist? Establish how patient felt with HCP response to OAB at diagnosis stage. Gauge patient feelings on advice/monitoring received and own engagement with healthcare.]

"How would you describe the HCPs response to your initial concerns?" [Probe: "What was said/offered?"]

"How did the GPs/Specialists advice make you feel?" [Probe: worried? Re-assured? Confident in next steps?]

"Did you find the advice they gave was enough to answer your questions, or did you do your own research too?" [Probe: "where did you look for advice?"]

"How often was your OAB monitored/followed up by your GP or Specialist?"

"Were these routine appointments or did you have to request more frequent follow ups?" [Probe: why is that?]

c. **Treatment History & Expectations:** [to explore treatment expectations, experience and engagement, Discuss HCP response when asked to change OAB med by patient. How <u>far into treatment</u> and reasons for this?]

"What sort of response (if any) did you expect from lifestyle changes?" [Probe: why is that?]

"How easy or difficult was it to follow the GP's/Specialists advice on lifestyle changes?" [Probe: why is that?]

"What (if anything) did you expect from your OAB medication?" [Probe: why is that?]

"How easy or difficult has it been to keep to your drug regime?" [Probe: why might that be?]

"Are there any particular OAB drugs that have been more difficult to take as prescribed than others?" [Probe: Why might that be? Can you tell me more about that?]

“Have you ever asked your HCP to change your OAB drug from one to another? How did that come about, and what happened?” [Probe: how soon after starting did you stop/ask to change the drug? Why?]

“Can you think of any occasions where you have missed taking your OAB medicines?” [Probe: Tell me a bit about what happened] Ascertain here whether there was a particular event linked with non-adherence with relevant probes.]

“What are the key challenges in taking your OAB medication as prescribed?” [Probe: Can you tell me more about that? What is the key challenge do you think?]

“What do you generally do if you realise that you have not taken your OAB medication on time?” [Probe: Tell me a bit more about that]

“How do you feel when you realise you have missed taking your OAB medication?” [Probe: Tell me a bit more about negative feelings. Were there any positive feelings? [Try to get information on both positive and negative aspects here]

“Do you think your expectations from your OAB treatment have changed since first being diagnosed?” [Probe: why is that? In what way?]

3. **Improving Adherence:**

“Are there any strategies that you use to ensure that you take your medicines on time?” [Probe: Can you tell me a bit more about that?]

“Is there anything that HCPs could do to make it easier for you take your medication as prescribed?” [Probe: Is there anything else?]

“Is there anything that drug manufactures could do to make it easier for you to take your medication as prescribed?” [Probe: Anything else?]

4. **General:**

“finally…is there anything else you would like to add?"

5. **Debrief:**

Thank you for taking part in our study. We really appreciate your support and your involvement.

If you have any questions about the study after you leave us, please feel free to contact:

Dr Maxine Holt on m.holt@mmu.ac.uk. Telephone 0161 247 2240.

We will be contacting all participants with a summary of results from this study and to get feedback on our analysis.

Please do not hesitate to ask us about anything at all relating to this study.

Appendix B4: Interviewer reflexive exercise

The participants in this section are presented in the order in which they were encountered by the interviewer, and in the interviewers own words verbatim.

Participant 8

As I often find in these interviews immediately when the voice recorder is switched off the participant speaks much more openly and often as in the case today makes interesting points related to her own experience. It makes me wonder for future research (just a general point related to qualitative research) on such topics would it be worth participants recording their own reflective journal after the interview for things that come to mind afterwards that might be useful to know from a research perspective and then use triangulation of interview data, the researchers reflective journal and the participants reflective journal.

She did say even though she had learnt to live with having an overactive bladder she felt this was because she had made the conscious decision of having the mindset it would not stop her living her life i.e., she would still partake in the social activities that she wanted to do with friends and family. She would just plan ahead to go to the toilet prior to going out and mapping out toilet stops so she could go when necessary and she said she would sometimes go almost 10 times in a day.

She did not let it stop her doing exercise nor did she change what she ate and drank. She felt as her overactive bladder and associated symptoms seemed a lot less severe than some of her friends she considered herself lucky. Some of her friends were incontinent and suffered a leaky bladder related to their OB she says that is probably why she did not ever seek help for this condition specifically for over 40 years.

It was eventually an issue she raised in a medication review appointment for other conditions she had with a practice nurse who she felt comfortable to talk to. The doctor prescribed the first lot of medication that she had to take twice daily but she could not recall the name of it. She did not notice any change or relief from the urgency to go to the toilet so eventually gave up taking it and did not want to try another medication. It was not until years later that she eventually decided 'why not' try another one to see if it could help with relief from her OAB symptoms she got described. She was clear this one was effective and started to work almost immediately as she recalls. She felt a huge relief that she no longer had to consider planning in toilet stops as part of days out.

The main annoyance for participant 8 was around people's comments and lack of understanding about her needing to go to the toilet frequently. She said she wished people could be more understanding and this was the one thing she kept highlighting as she reiterated several times. I feel this was her main annoyance over the symptoms she experienced from her OB. Also I think she naturally felt it would have been a lot easier finding this medication earlier rather than later. It was interesting that she raised the overactive bladder issue with her practice nurse who she has her six monthly review with over her other medications. She suggested she developed a good trust and rapport with this nurse and it seemed that this is why she felt comfortable to raise the overactive bladder issue.

One other point was participant 8's son was present during the interview. This might not have had any impact but it might have led her to be a bit less open about the overactive bladder and her experiences as she did say it was since having her son that she had the symptoms.

My thoughts following the interview was of her acceptance of the symptoms of OAB due to others in her social circle also experiencing such symptoms after having children. I was surprised at how long this acceptance went on for and then also the time lag between trying a second medication for the symptoms as the first one had not worked. It made me think that there should be a regular review/monitoring process when the original prescription has finished to check if it has worked, if any side effects had been experienced and the need to consider other medications where it has been ineffective. Even if this review could be done with the pharmacist over the phone or online just to ensure the patient is happy with the medication. It also may be important for the doctor or nurse to ask women (particularly those who have given birth) questions around bladder related symptoms. This could help identify early on whether they might be suffering OAB as it should not just be accepted. Patients might be embarrassed to open up about OAB symptoms and might have just accepted them as part of life when there could be an OAB medication which would improve their symptoms and make everyday life easier.

From a researchers perspective an interesting point to explore in the qualitative data analysis would be to look at potential similarity and differences in participants views depending on the age of the participant experiencing the OAB, severity of OAB symptoms and how much it impacts what they want to do in their daily life and how long they have experienced the symptoms?

Participant 5

From both interviews it is clear that OAB symptoms impact everyday life in that they have to plan in toilet stops, avoid visiting places that do not have easy toilet access and alter their drinking patterns to reduce the symptoms of urgency to go to the toilet. The main reason for participant 5 only trying her prescribed medicine for a very short period of time (under a week) was the side effects she experienced as it made her feel very sick. She said even if she had persisted on the medication and it started to work it was not worth it because of the negative side effects. She wanted to take control so asked the GP rather than to prescribe an alternative OAB medication she would rather manage it as she did not really want to be on another tablet.

It was interesting that both participants *(participant 8 and this one)* did not present with OAB symptoms to their doctor or any other health professional until much further down the line (40 years plus) – both had accepted it as part of life. It seemed that with both participants' they had other health conditions that were more debilitating which might explain why they had a more accepting attitude towards their OAB symptoms and reluctance to seek advice or support related to the symptoms as they did not want to be on another tablet. By managing it with lifestyle alterations both participants viewed this as better than going on another tablet as they suggest once you go on them you never come off them so ideally they did not want to start on another tablet for this alongside the other medications.

Participant 5 expressed satisfaction with her support from her GP and that her GP worked alongside her letting her make the final decision to not try any other OAB medications after the first one failing. It seemed from what participant 5 said this empowered her by letting her have the final decision on the proposed treatment for her OAB. How OAB medication interacts with other tablets that participants are taking for other conditions is one area she felt could have been more clearly explained and she would have liked more information on this. This might have reduced her apprehension and reluctance to try other OAB medications and given her the confidence to try another tablets after the initial one she prescribed. One clear point participant 5 made was that as she has a supportive network of people around her who understand her OAB condition and symptoms this helped in the process of making it a manageable condition through lifestyle adaptations.

A point related to transparency in this research process – I recognise myself as the main research instrument (i.e.the interviewer). I have little knowledge in this context so have minimal expectations when I went along to the first interview. I recognise that as I go on to conduct more and more interviews I have the views of the previous participants in my mind and can not erase these. This influences my expectations or gives me an inclination of what the next participant might say. This makes it important to stick to the areas covered in the semi structured interview guide covering the key areas of the semi structured interview schedule. I feel the benefits of this not being my research area is that I can be non-judgmental in my questioning. I have no investment to be biased in one way or another as I have no professional or personal investment. My main goal is allowing the research participant to feel like they can communicate their personal experiences fully of having an OAB, their experiences of medication(s) from seeking advice to referral, to being prescribed, to reviewing their medication and adherence to this and the perceived success of it and whether they had to try alternative methods. I think from my personal experience it was important to understand their experience of the symptoms of the OAB and whether this has impacted their lifestyle and the way they have lived their life.

Participant 7

Participant 7 was really insightful in terms of speaking about the need to trust your own judgement when it comes to taking medications. Listening to your own body and managing your medication in line with how your body feels not what is written on a guidance leaflet or doctors advice unless they have said it is a ‘life or death’ situation. She said she would immediately stop a medication if she experienced negative side effects unless it had been made clear by a health professional that she had to take it. She did not feel she had ever been given a clear diagnosis of OAB but it was explained to her as irritable bladder so she did seem a bit confused over what she had specifically but knows her symptoms are commonly associated with OAB and has noticed the change in the severity of the symptoms throughout her life.

It was clear within days of being prescribed the first medication for OB the side effects presented as dry mouth which could lead her to feeling like she was choking when waking from sleep. The headaches she was getting and the fact it was not helping her sleep which was her main symptom of concern associated with the condition (she was waking at least 5-6 times in a night) meant she give up taking the medication. She has started to give the same medication another try just to see if it could help with her waking so many times in the night to go to the toilet. She feels this time the medication may be helping as she has felt a reduction in the times she wakes up to go to the toilet in the night is 2-3 rather than 5-6. She is putting that change down to this medication but she said she is not certain it is this and this gain outweighs the side effect of getting the dry mouth this time round so is going to persist with it.

Similar to the first two interview participants there was a final trigger that encouraged her to go and ask for help and guidance from her GP which was the lack of sleep quality due to waking up to 6 times a night to go to the toilet. Similar to the other participants interviewed she had experienced the symptoms of an urgency to go and an increased frequency of going to the toilet for years before she finally sought guidance. The medication she received was not explained by her GP she was just prescribed it and told that it would help with her bladder condition. She did not feel she had much guidance on how to take the medication, the side effects to be expected and which ones are likely to be more severe or which side effects (if any) she should be more worried about and how it interacts with other medications she is on. She did feel it would have been useful for a health professional to explain the side effects and whether they would be temporary and whether they should persevere until the side effects subside or whether they are likely to be long term. This way she could have made a more informed decision over whether to stop or not and she might have persevered longer in the first try of the medication. She feels the leaflet accompanying the medication providing guidelines on the side effects, dosage etc is so long she always avoids reading it. She feels a lot of people are the same and it is more likely people would read it if it was more succinct. Also she feels it is overwhelming sometimes to see how long the side effects list is and is off putting from the start to motivate you to want to take it. Having the option to have a chat with a health professional in a less formal situation than review appointments to reassure you how to take the medication, the side effects that are more likely and less likely and the guidelines to follow if you do experience side effects would have made her feel more reassured in taking the medication. She feels other patients feel more confident and reassured taking their medications if they had them explained. Reflecting on this interview it was easier to probe issues further in this interview due to having a prior knowledge and familiarity with the interview schedule and research topic plus common responses. It seems that when participants are on other medications they choose to manage their OAB up to a point through lifestyle adaptations as they do not want to be on any more tablets and this condition is not a case of life or death. From a research perspective, it would be interesting to explore if women who are not on other medications for other health conditions are more adherent or give OAB medications a longer trial before giving up when side effects do present than those already on so many tablets?

Participant 1

Having interviewed three women previously, I was interested to see whether participant 1 as a male had experienced similar symptoms and how he had dealt with his OAB condition as well as his success with medication. participant 1’s overwhelming feeling that he conveyed towards the symptoms he experiences that are associated with an OAB was of frustration, lack of control and degrading- which was the word that stuck in my mind when he described it. His main symptoms are of a sudden urgency to go to the toilet which sometimes leads to leakage due to not being able to make it to the toilet quick enough and every few weeks he experienced incontinence in his sleep which would mean he needs to wake, shower, change clothes and the bedding and then settle back down to try and sleep again so very disruptive and frustrating for him. I felt a hesitancy from him when he was speaking about these symptoms as he suggested it can be embarrassing and he almost gets annoyed and frustrated with himself that he does not feel no control over these incidents. You could see from his body language when speaking specifically about these symptoms and incidents he was more closed and hesitant and it was not a comfortable thing for him to talk and open up about. He is now trialling a third medication type but does not feel this one is working much like the first 2 having no noticeable effect or control over his OAB symptoms. I think he is open minded to the prospect a medication may be able to help the symptoms but he did not seem that hopeful that any medication could but I think this is understandable because no medication to date has been successful at treating the symptoms.

It was interesting that similar to the other ladies his mindset is to not let the condition affect the way he lives his daily life or to stop him doing anything he wants to do. There is a general sense that he will not let this condition control the way he goes about his daily life.

The only aspect of his life he did communicate it puts him off doing is going on holiday due to the fear he may be incontinent in his sleep in the hotel bed and says he would find that highly embarrassing if staying in a hotel. I think it was clear that participant 1 remains generally positive towards this and his other health conditions. Interestingly even though there is a suggestion that it is males who tend to just put up with health conditions and have a reluctance to go to their GP with health concerns participant 1 went quite quickly to seek advice from his GP about his OAB symptoms particularly comparatively to the women interviewed thus far who went to seek help years down the line as they almost had that expectation it was just part of life.

Participant 1 suggested it would be helpful if a health professional could have a regular review/monitoring of your medications and the effectiveness of them - even if this was over the phone to avoid the wasted time that he has experienced being on them whilst them still being ineffective. He was clear that he feels everyone is different and what helps one person might not help another so regular reviews with a health professional can make sure the medications are reviewed and changed efficiently and a tailored medication/treatment plan is then provided to patients like himself who has multiple health conditions and medications to manage.

It was interesting that he prefers not to speak about his condition and he suggested this is because it can almost make you overly focus on it and that he would then be defined by it. I did have a feeling when he was hesitant to speak about the symptoms and was pausing a lot when we spoke around the symptoms that he does feel a little embarrassed which may also be a reason he chooses not to speak about it too much to any friends or family – I only make that assumption as he did use the words degrading, frustrated and annoyed and these are quite strong feelings.

From a researcher perspective I feel there was a limit to the depth I probed the issues around the experience of his symptoms just as I did not want to make him feel uncomfortable about something he did seem more hesitant to speak about. It was interesting to see similar to the women I have interviewed so far that they do not want to be defeated by their OAB so did not let it affect their day to day lives so work to manage it. He had a file which had the details of his latest medication they had given him to try but he said this was not helping so he will actively seek a review of this and would be open minded to try another alternative until he finds one that works. An observation point that I had from the four interviews so far was that each participant were on multiple medications for multiple health conditions and it was just accepted as a normality for the people I have interviewed and an expectation and acceptance that with ageing comes more health conditions and medications. Again from a research perspective it would be interesting to see if younger people diagnosed with the conditions express similar or differing views.

Participant 3

The interview went really well and it was different to the other interviews as participant 3 had such a positive experience and you could tell by the way she was communicating the information. She said her GP had been really helpful and reassuring and the medication kicked in straight away. The GP worked alongside participant 3 understanding that she ideally does not want to be on medication for life but if it kept the symptoms of the frequency and urgency to go to the toilet then she would do that under the advice of her GP. I think the only improvement would be raising awareness of the symptoms of overactive bladder in health settings so people question their symptoms and go and seek advice as many people are unaware there are medications that will get rid of those symptoms.

I felt although the interview was quick that all the relevant information was communicated as the conversation flowed and participant 3 addressed issues within a more informal conversation than needing to ask every question in a structured manner. She also said feel free to contact her if we required any further information or clarification on the information she provided. Interesting to hear that the long lists of the potential side effects meant she avoided reading the associated guidance leaflet for the medication and just followed her GPs guidance for taking the medication. The feeling was much more positive of both her GP support and medication experience but I suppose this may have been less positive if the medication had not worked yet I can not assume that. Participant 3 was taking oxybutynin hydrochloride and was very happy with her medication and experiences of support from her GP for taking this medication.

Participant 4

Participant 4 was really thorough in the description of her experience and in terms of her support for her concerns over her experiences of OAB symptoms she received specialist support from the outset from consultants qualified in urology and gynaecology. Her experience of the initial medication was that it was successful in reducing the urgency and leaking symptoms so she stayed on this medication for around 18 years. In the last period of time taking it the medication it seemed to have stopped working - the symptoms started to reoccur of the leaking bladder, urgency to go, waking throughout the night, and not even making the toilet in the night. During this period participant 4 admitted she was not quick to go to the doctors to express her concerns of the reoccurring symptoms and just managed them with buying pads in case of accidents and planning in toilet stops. It was when the lack of sleep through constantly waking to go to the toilet started to really impact her daily life that she returned to the doctor.

The doctors treatment to refer participant 4 to a specialist again was positively recognised by participant 4. An interesting point related to this was that participant 4 had a level of trust and rapport in the specialist she received support from given previous contact from supporting her husband through his treatment. As participant 4 mentioned women are quite embarrassed to speak about symptoms around OAB and maybe having the relationship already with this specialist was important to make it easier for her to raise these issues and speak openly. Having a rapport with healthcare professionals or even local community pharmacists and them being approachable and opening up conversations around symptoms related to OAB might be helpful for patients as it might open the door to seek support or help and allow patients to realise they do not just have to put up with symptoms related to OAB and there are medications that will take these symptoms away and ultimately improve their quality of life.

Awareness raising in healthcare settings is what came to mind again as there is a common theme being communicated around participants just choosing to manage OAB symptoms and an acceptance of OAB symptoms as part of life and a lack of awareness and knowledge of the availability of medication to stop the symptoms of OB. Posters and leaflets in pharmacies and GP surgeries etc to make people think about symptoms they are experiencing and that they could be related to OAB are something she feels would be useful. Also when people go to GP surgeries and pharmacists if a patient expresses concerns over symptoms that could be OAB they should be encouraged to investigate further and seek further advice and guidance to increase awareness and trigger someone seeking support/further guidance.

Just a note on the three medications she has been on (in case this has not already been confirmed or was not clear from the recording:

1)Tolterodine (Detrusitol) – on this medication for around 18 and a half years it was immediately effective with just one daily tablet but then increased this to two as the medication instructions advise to do so. It was then effective until the last period of taking it and then the specialist advised her to have a week without this before moving onto to try another medication - Mirabegron and in that week the symptoms made her feel house bound as there was just no control over the OB and she could not even make the toilet in time when she woke in the night.

2)Mirabegron (Betmiga) only took this for a month as it required you to get regular ECGs as it can affect the heart rate - she decided this medication was not for her due to her concerns over this potential side affect and need for regular ECGs

3) Solifenacin (Vesicare)- this new drug has been effective in taking the symptoms away again and as it can make you drowsy she was advised to take before bed. She said it does make her feel a little drowsy and have a dry mouth as was also pointed out to her as a potential side affect but as long as it has taken the OAB symptoms away these side affects are not a problem she just makes sure she has a glass of water by her bed to drink when she wakes with the dry mouth. She is happy with this current medication and is not interested in the option of having botox alongside it as she said she did her own research around it and she said there is no long term evidence so she is not sure what side effects it could cause in the long term and does not want to commit to botox every 6 months particularly as she will still have to stay on the medication anyway so in her eyes there is no benefit to this but will discuss this further in her review appointment in October. I have given her my email if anything else comes to mind as she said she usually remembers something after that she wants to say.

Overall she has had a positive experience of medication and specialist support for her OAB and also an understanding partner which she says helps a lot as OAB can lead to embarrassing situations. She said she would much rather stick to a tablet than resorting to botox or surgery. She has a belief that an earlier sterilisation process where she was told that the bladder and bowel attached to the uterus plus putting on weight and the hysterectomy could have all contributed in some way to disrupt the bladder but she was happy with taking the medication under specialist advice in the long term as long as it continues to be effective.

Participant 14

First telephone interview and it seemed the overwhelming feeling from participant 14 was frustration over not finding a medication that has been effective in reducing or stopping the OAB symptoms. He was satisfied with the thoroughness of investigation from the specialists yet suggested a feeling that it might be the other medications he takes that are causing the bladder related symptoms as some of the side effects for example on the pre diabetes medication leaflet suggest this increased need for the toilet might be an associated symptom. It seems participant 14was prescribed the antibiotic alongside the Mirabegron for the OAB and despite taking it for an extended period of time suggests it has not been effective but would never stop taking medication without the guidance to from the specialist or GP hence why he continues to take the medication. The main symptom that effects participant 14’s life is the loss of sleep through waking at least 3-4 times a night with the urgency to go to the toilet and urgency can be experienced in the day times which can result in leakages. Participant 14 was quite short with his answers and upon using more probing questions to ask further he did not seem to open up his responses much more. From the communication though it seems he can feel embarrassed and frustrated understandably so when he does get a leakage due to not being able to make it to the toilet on time. The other main frustration is him not being able to have a nights sleep which lead to him telling the doctor about this symptom and being prescribed sleeping tablets – he was hesitant about wanting these and avoids using them on a daily basis but just rather when he feels he is exhausted as the tablets leave him feeling sleepy and drowsy the next day.

I think from doing the seven interviews from a researcher point of view I have felt patients would like to understand more about bladder conditions, management of it it and then further guidance on how the OAB medication interacts with other medications and can certain medications make the OAB medication ineffective or result in side effects that might be related to the bladder. Participant 14 seemed frustrated that a specialist could not answer whether the bladder related symptoms could be a result of other medications he is taking for other health conditions or whether there could be an interaction effect of taking so many tablets. This is interesting as the three participants I have interviewed who did not take as large a number of other medications and just the OAB one seemed to have more success with the medication and adherence to this. I think participants' do suggest this want and need to understand their OAB medication given that some medication guidance leaflets list symptoms that are bladder related so you can understand why it would be frustrating to not get answers on this and it would just be reassuring to know from their perspective.

Participant 14 made an interesting point that no other participant made this far in the interviews. This was related to making medication more accessible/user friendly as especially when people are older they might have conditions that reduce their strength in their hands and he suggests the medication are very difficult to get out of the packaging.

Participant 15

This was a telephone interview and her line was not brilliant. I did feel because of this and with having to repeat questions it did interrupt the flow of the interview slightly yet I do feel I was able to get the information required communicated. Just to mention towards the end of the interview she sounded a little in discomfort as she needed the toilet so I did rush the final part.

I feel it has been an interesting observation of the difference in levels of support and monitoring associated with different participants medication and their follow up procedure and who specifically they seen in this period i.e. GP, pharmacist, specialist. Participant 15 received a referral to a specialist doctor upon raising her concerns over her OAB symptoms to her GP and then was prescribed a medication which she had a one month review for. Once starting the medication she raised her initial concerns over a dull ache in her stomach she was experiencing since starting to take the tablet and the doctor told her to just take one tablet a day rather than the two advised on the (morning and night) directions for use on the medication packet. Beyond this one month review she had no further review and as it was only the dull ache she recalls as a side effect which disappeared after reducing it to one tablet. She carried on taking the medication despite her feeling it had no impact on reducing any of her OAB symptoms because her attitude is to fully trust the doctor and their guidance and she was almost hopeful it might start to work and that she was at least doing something to try and address her OAB symptoms.

Like other participants, she has learnt to manage her OAB symptoms and accept them as part of life and growing old. She has her own strategy to manage the leakages and not making it to the toilet in time through using washable flannels. She did say the only time she stopped taking the OAB medication was five weeks ago when she received a phone call from her GP surgery informing her to not take the medication as it could be associated with memory loss and deterioration and be associated with dementia.

From a researcher perspective it seems a face to face review meeting may have been more appropriate than a phone call for such a serious potential side effect as those that were explained to her over the phone around memory loss and associations with dementia which could easily lead a patient into a state of panic and worry (given they thought they were doing something good trying to manage their OAB yet could have actually unintentionally been doing harm to their body). A face to face appointment would at least allow the patient the opportunity to speak about their concerns related to such serious potential harmful effects and their concerns and worries so that the doctor could put her mind at more ease and discuss steps moving forward and options for other medications.

In relation to medication monitoring and support I feel there should be a standard review and monitoring procedure in place across the healthcare system for example standard review times e.g. every 6 months, guidelines that must be covered – how this medication might interact with other medications a patient is on, side effects, when to seek further guidance, when to stop taking a medication if it is not being effective in anyway? I feel this would have put the patients minds at ease and reduce frustrations and uncertainties that were communicated in this interview and a lot of other interviews. From this particpant’s perspective if she did not have to be on long term medication she clearly would not be so at least if there was a review procedure she would feel reassured in the need for medications and could come off ones that did not have to be lifelong. I had a feeling this would reduce her negative attitude towards avoiding seeking help from her doctor unless she really has to which seems to be a lonely place.

Participant 2

Participant 2 was on a lot of other tablets so did go off track quite a few times speaking about her other medications. I did try to bring her back to focus smoothly without interrupting her so the conversation still flowed. It seemed very much that with being on so many other tablets and the uncomfortable side effects of feeling like she was heavy in the bladder region and thus making her feel sluggish had led her to make the decision to stop taking her OAB medication. It seems when participants are on a lot of medication it becomes a very personal choice/decision irrespective of the professional advice of weighing up whether the side effects they experience in relation to the medication is worth persevering with for the level of relief they experience from the OAB symptoms they experience. Also it is a more reactive decision in that if it seems to be ineffective then they will give up adhering to the medication much quicker as ultimately they do not want to be on another tablet.

I think this participant clearly did not want to be on another tablet. The side effects meant it was an easy decision to decide to stop taking it at around 5-6 months. She gave the impression that she does not like to bother going to the doctors and finds it a negative experience so leaves it until she has to go to seek support. I found it interesting that there is no monitoring or follow up when a patient just decides themselves to stop ordering the repeat prescription (which is what Participant 2 did) and even if it was a follow up with the pharmacist it might be useful to monitor/review such changes just as a support mechanism for patients and to ensure that they give medications a long enough trial.

I think one thing I noticed is that when a patient like Participant 2 who is retired and does not go out so much then they seem to accept they are able to manage the OAB symptoms of potential leakages by using pads for accidents if they do not make it to the toilet. She only goes out once a week so for her lifestyle it is manageable so it is understandable why she would not want to deal with the side effects of a medication and how it made her feel with the general heaviness and sluggishness given she can manage her symptoms in her current lifestyle situation. However she did say she remained open minded to try another medication if it allowed her to sleep without waking for the toilet and feeling the urgency to go to the toilet. In the ideal world though she would rather not on be on medication at all this was a point she made several times.

Participant 17

This was really interesting to hear participant 17's experiences. The immediate comparison in my thoughts were the comparisons between the different GPs treatment participant 17 experienced when going to see them over her bladder symptoms. The GPs she seen all had a different approach to diagnosis and treatment. participant 17's first experience with her first GPs diagnosis was that the GP seemed uninterested and it was almost just an attitude of take these pills and the discomfort and tenderness in the bladder region and the urgency to go to the toilet will go away. There was no attempt to understand her condition or reassure her which you could imagine would be disheartening if you have gained the courage and go and open up about bladder symptoms that can be an embarrassing issue to talk and open up about.

The other comparison I thought of in my head was with other participants experiences as there is no consistency - some have been referred to specialists for more thorough investigation and treatment and others just tested then given a tablet for OAB. It seems there is no consistent approach to the diagnosis and treatment of the common OAB symptoms and then the subsequent medication provided as participants' are prescribed different OAB related medications, some have been prescribed a series of antibiotics and other participants' were also told about alternative options to treatment such as botox. Participant 17 is the only participant I have spoke to who has been guided to take a medication for a trial period and that she should then stop the medication after the symptoms were reduced and she followed this guidance as the symptoms did reduce. This was interesting given that other participants I have interviewed have just been told to continue to take their medication indefinitely. Similar to other patients there was no formal review process for participant 17 medications and her OAB and she suggested some review process even if this was with her pharmacist to reassure her she is doing the right thing to not take any medication in the long term would have been useful.

It seems the pharmacist could provide an important support source for OAB patients in taking the medications, patient experiences, understanding why patients stop taking their medication (they can enquire about this when recording if a patients stops ordering a specific medication meant for repeat prescription). Also if the pharmacist has a closer relationship with the patients they are then more likely to confide and seek their guidance regarding their medication and options if they feel they are causing side effects, potential other options for oral medication for OAB. As an observational point a closer relationship between the GP-patient-pharmacist would be an ideal way to better support patients in understanding their experience of their OAB condition, attitude and experience of the medication prescribed, adherence or non-adherence to medication. Having the pharmacist more involved in this support loop would also better support GPs if they take the lead role related to the medication once diagnosis and medication has been decided upon.

Participant 17 seemed to not feel the OAB symptoms had not had much of an impact on her life which could be why she was content on the whole with the treatment and support process. The main annoyance for her in terms of symptoms was the need to wake throughout the night to go to the toilet but she felt it was manageable and her symptoms have never stopped her from doing her physical activities or taking long journeys etc so her symptoms did not seem as severe as other participants I have spoken to.

Participant 19

As a first reflection I would say that participant 19 was the most open about the emotional effect of her bladder symptoms and it was clear she felt isolated and alone in her experience of her symptoms. Clearly when she has had an accident in the past and not managed to make it to the toilet on time she describes the feelings of embarrassment, panic, out of control, and frustration. It was quite upsetting to hear how it made her feel and that she just feels it is something she needs to manage as a part of getting older. I think a key feeling conveyed from participant 19 is that had she have had someone to talk to and reassure her that this is something that many women and men experience and there are medications to support you in this that can reduce those symptoms would have been very helpful and made her less reluctant in trying medications. She also felt more information leaflets should be readily available in health settings providing tips related to OAB for example tips about how to plan for a potential accident. She suggested this would have been very helpful in terms of her feeling less embarrassed, less alone and more prepared for the symptoms.

I think participant 19 does have a negative attitude toward being on long term medication and an under riding feeling she does not want to be on any long term medication which is why she chooses to manage the symptoms while she can. Now that she is prepared for potential symptoms through knowing where toilets are whenever she is out and about and having clean clothes and cleansing wipes just in case of an accident this clearly makes her feel more relaxed. Being prepared gives her a level of control and she says she would only seek further support if the severity and likelihood of having these accidents of not making it to the toilet in time when out and about worsened.

I felt that for her more than for any other participant I have spoke to the most helpful thing would be more opportunities to talk about her bladder condition and her experiences. This again reiterates not one size fits all for planning treatment for OAB related symptoms and a tailored treatment is needed for each specific patients case of OAB that is matched to their symptoms and preference for treatment. This allows them to still feel a level of control/empowerment and autonomy in the management of their treatment plan. Online support groups or face to face support groups would be useful for someone like participant 19 as it would provide more opportunity to talk about her experience and be reassured in knowing she is not the only one that experiences such feelings related to her OAB and would make her feel better given that she perceives she is happy with how she manages her symptoms at this point in time.

Participant 11

This was a very short interview which might be explained by the fact participant 11 perceived her experience of symptoms, diagnosis, treatment plan and success as a simple process and was positive about her experience of the medication she was prescribed and its effectiveness on relieving her OAB presenting symptoms.

She had no side effects, the medication started to work within a few days. She estimates has been on the medication for four years and a period of a few days is the only time when she has not adhered to it (only because she had forgotten to phone for a repeat prescription). In this few days when she had run out and was not taking her medication the symptoms did return but as soon as she started taking it again the symptoms were reduced again. She would have been open to try another medication had this not have worked despite her only describing her symptoms as a 4/10 in severity in terms of how they impact her life. It was interesting that at 4/10 her symptoms were still enough to make her want to seek guidance and support.

There was a sense again that is consistently occurring across participants that there needs to be more information in health care settings eg pharmacies, GPs, hospital, community and alternative healthcare settings regarding bladder symptoms and availability of medications to treat them. It would be useful potentially to make personal trainers or physios working on GP referral schemes or participant rehab programmes in health care settings aware so that they can bring this up as a lot of people find it uncomfortable to exercise with bladder conditions as they quickly have a need to go to the toilet or a leakage. If PTs could refer them to their GP to try a medication that could remove these symptoms then it would be a great improvement. It is having this holistic more whole systems approach to treatment and care that might enhance their experiences it seems. One possible explanation for a lot of participants suggesting they just manage their bladder symptoms is this perception it is just a natural/normal part of ageing and there is nothing that can help with it. Participant 11 mentioned even spoke of a friend who had worse symptoms but would not go to see anyone but just manages the symptoms by taking a change of clothes and wearing pads in case of an accident. Increasing the awareness of the symptoms of OAB and oral medication that can reduce these symptoms is key as then people might feel less embarrassed to talk about it and accepting it as a part of ageing and offer more chance of finding a medication that could reduce and remove the symptoms.

Participant 20

Participant 20 was another participant who chose to manage the symptoms when they started to present around 4-5 years ago. It seems again when people have other more severe health problems that cause discomfort and pain they are always managing a level of pain so learn to live with things as on a scale of 1-10 they are less severe symptoms. The bladder symptoms were relatively minor compared to other issues that Participant 20 was dealing with. There seems to be a tipping or trigger point and with Participant 20 his tipping point was when the symptoms worsened and he felt he was going to get caught out whilst out in public, not make it in time to find a toilet and just resort to go in a bush. He felt this was the point were it was embarrassing and no longer perceived his symptoms as manageable.

It was good to hear he has a very open and honest attitude with his GP and always seeks out help from his Doctor when he feels it is necessary. He expressed he feels satisfied with the support he receives. He conveyed he sees the value in medication and that as long as it is relieving the symptoms that he is happy to continue to take it in the long term and has no issue with taking it over a long term period.

It seems he had a good review process although this was with a private doctor so might explain why other participants have not had any review or monitoring process as they have not had access to a private doctor. Also because he is on several medications for different conditions it might be more important to have a formal review once a year of his medications . For participant 20 this review process of his medications did seem like it was a reassuring process for him and allowed the opportunity to express any concerns or queries about his OAB medication. Having this review process would be helpful for patients just to reassure them they should or should not still continue their medication and make sure the medication is still not having any side affects.

I do feel from the previous interviews some form of medication review process would be valued by patients. Even if the review was with the pharmacist, it would be useful to promote and enhance medication adherence through reassuring patients they should continue to take the medication, helping them understand the medication and how it may interact with other medications particularly if they have started any new medications since their last review and also the opportunity to discuss any worries or concerns.

I feel when the participant has immediate relief from their bladder symptoms upon starting the medication (i.e. within a few days) accompanied by no side effects this seems to be associated with a positive attitude towards medication and increased likelihood of adherence as in participant 11’s case.

Whereas participants with no notable or obvious relief from symptoms when first taking a medication prescribed for OAB or experiencing negative side effects are more cautious and skeptical in their attitudes towards the potential benefits of the medication and the potential side effects and less likely to adhere to the medication.

From the different diagnosis and treatment process participants have discussed it seems there is an inconsistency in the treatment of bladder symptoms across the healthcare system. For example, some participants have been referred to a specialist to investigate symptoms further whereas other GPS have ruled out a urinary tract infection then prescribed an OAB medication for the participant to trial.

Participant 12

Participant 12 did mention before starting the interview that she her stomach was not feeling 100% and she may need to pause at some point. She still suggested she felt well enough and wanted to do the interview. I was mindful of this and did reassure her if she did feel uncomfortable at any point to let me know as we could pause or stop and rearrange. I think from this interview it was clear Participant 12 is generally quite open and honest and this is the same approach she has taken to the symptoms she has experienced related to her bladder.

She had a different initial response from her doctor than any participant I have interviewed so far as he referred her to a physiotherapist in the first instance. The physio was a positive experience for participant 12 although she said she cancelled her last appointments as she did not really feel the need to go anymore. The physio mainly focussed and encouraged her to do pelvic floor exercises regularly. Participant 12 felt she did not adhere to the physio's guidelines regarding the amount of times she should do her pelvic floor exercises the physio so thought this was why she did not get any notable relief from symptoms following these physio sessions.

Unlike some other participants I have spoken to she said as a person she does not get overly embarrassed about needing to go the toilet a lot and just makes a joke of it when she needs the toilet so much when she is out with her friends. She expressed a positive attitude towards managing her bladder symptoms and from her point of view perceives it as a weak bladder rather than overactive. She feels she has learnt to manage it as from her perspective she does not think her symptoms are that severe. Despite not perceiving her symptoms as sever it was interesting she did decided to give the medication another try even though she expressed they give her no relief from symptoms. She suggested she does not feel like there is much relief from the symptoms this second time round and is questionable whether she will continue to take them long term. The driving factor in her trying the medication again is that now she is retired and doing more golf (which means not being able to get to a toilet as quickly when out on a golf course) she wants to try and be able to do a full round of golf without the urgency to go as currently she has a toilet break half way through. She thinks it might have a placebo effect taking this medication again in the sense of if thinking I am taking a medication then it must be doing something rather than her actually feeling a noticeable physical change or any relief in symptoms when taking the medication. She does suggest she would try another medication if her GP suggested it but it was clear she would not actively seek this out unless the severity of her symptoms worsened.

Participant 12 did express an attitude that she did not want to be on lifelong medication and was honest that she was not good at adhering to medications in the long term. I think her negative attitude towards lifelong and long term medication might be a reason associated with why she does not adhere well to medication and often stops off her own accord. She did express a belief ‘ the body always has a way of sorting itself out’ and that some things you just expect as you get older again these attitudes may be underlying reasons why she does not adhere to medication.

It was good to hear that participant 12 has not let her bladder symptoms stop her from doing anything in her life but just uses precautionary tactics i.e. wearing pads in case of leakages, knowing where the nearest toilet is , drinking decaffeinated drinks, not drinking fizzy drinks, avoiding alcohol (although that is not specifically because of the bladder condition but she does note that as a specific trigger for her symptoms).

She did suggest it would be nice if it was more openly discussed and acknowledged as a condition as she feels it is less acknowledged in the healthcare world yet the symptoms can impact your daily life which can be frustrating in the long term. She also suggested she would be open to try another medication if it had the potential to remove her symptoms- this again suggests the relevance of some type of follow up/ medication review process (even if this be with the pharmacist to review the medication). One other point is when she was initially referred to the physio – the physio is another person who could speak more openly about bladder conditions and encourage patients to ask and try a medication alongside doing their pelvic floor exercises. Participant 12 did take my email in case she did have any further information she thought was relevant and came to mind.

Participant 18

I feel with this interview I established quickly Participant 18 was quite minimal on detail in his responses despite using probes and cues. I thought it was likely he would open up in any great depth which would explain why it was a short interview.

I feel there was not necessarily a need for Participant 18 to speak at length about his OAB and medication experience given that Keith's symptoms did not really impact his life in any huge way. The only symptom he reported was waking frequently in the night but he was clear this had no negative impact on his life as he was able to sleep in in the mornings.

He did not feel the medication he was prescribed had any notable impact or relief of his symptoms and given that he experienced the dry mouth as a side effect it was an easy decision for him to weigh up and decide to not take the medication any longer.

One point to make was Participant 18 also suggested he would be open to try another medication. Again this suggests the potential value of a review of medication even within that first 6-12 weeks as this could be one positive strategy to promote adherence or in cases when patients feel the medication prescribed is having no impact it would offer the opportunity to prescribe and trial another medication.

Participant 13

It was really interesting to speak to participant 13 as his experience did differ from other participants. He expressed a general attitude that he does not like to take any medication long term as he does not like the idea of what it could be doing to his body. This attitude governed why he only took the bladder medication sporadically despite him saying the medication worked immediately and having no side effects. He still keeps the medication and takes it like you would take a pain killer and his attitude was that the doctor never told him how to take it so just takes it when the symptoms flare up and then just stops when they settle again. He feels that seems to work so just makes sure he has some in case of a flare up and then takes them sporadically again. He also said he altered his lifestyle trying to drink less tea and he feels that has reduced the urgency to go. It was interesting that when he went to the doctor to get a repeat prescription the doctor did not seem to do much further investigation to see how he had been taking the medication, how his symptoms were related to his bladder now i.e. whether they were worse or there were different symptoms and his attitude was interesting that he just felt the doctor just wanted to get rid of him so was happy to just do the repeat prescription despite no review process. It was also interesting to note that when he did go to get the repeat prescription there was a different named tablet given to him yet no explanation by the GP or pharmacist of why this was and he has just assumed that this tablet will do the same as the last but he has not had to take this yet as his symptoms have not flared up again recently. It does seem that it could be quite worrying for someone if the tablet they received on repeat prescription was under a different name as without this being explained a patient is likely to be a little worried about what might be in them and might be a factor that could contribute to non adherence. Another worrying point was when participant 13 eventually did decide to go to the doctor and seek advice about the bladder symptom of this increased urgency to go which he honestly admitted he did not do until much later down the line than the symptoms first presenting and was only because they worsened and he experienced pain and spoke to a few friends who said it could be a water infection. But on this first visit to the GP it was a woman GP and he felt she was quite dismissive of his concerns over a potential water infection suggesting only women get them so he went to see a male GP then and felt more comfortable in his assessment yet still there was a feeling it was trying to get you in and out and limited information was provided re the medication. participant 13 clearly would have found it useful to have a more detailed discussion over his symptoms and had more information about the medication including a monitor or review process- this again might be a factor that could make it more likely a patient adhered to medication. However I do feel from the attitude expressed from participant 13 that he prefers prevention rather than cure so ultimately his aim is to not stay on any medication long term as he is sceptical about putting it in his body and the potential long term effects.

Participant 16

I feel from the attitudes conveyed from this participant his experience was largely positive towards the support and investigation and subsequent process of deciding what treatment course was best for him. It seems the process of investigation was very thorough and the GPs support for the participant was reassuring for them. His dissatisfaction was more about the actual medications prescribed, the associated side effects and the minimal effect that the medications had on his bladder symptoms as ultimately there was a suggestion that he feels there needs to be more research to ensure medications for this condition achieve more success with less side effects and he feels and others he has spoke to of his friends feel a general sense of dissatisfaction with the available medications for OAB. He suggested that he would be open to try other medications and seek further support if this was recommended by his GP. He seemed like he had a good relationship and trusted in the process of investigation with his GP and the treatment prescribed it was just a disappointment that neither of the medications had any impact and given the side effects of feeling drowsy and depressed from the first and no effect from the second he did seem a bit disheartened and unimpressed by the medications available.

As a general point from a researcher perspective there are common themes consistently being portrayed from participants account now. The most obvious being:

- Generalised negative attitude to long term medication unless completely necessary as a reason for poor medication adherence
- Side effects outweighing benefits as a reason for non adherence to medication
- Severity of bladder symptoms associated with participants efforts to seek medical advice and adhere to medication
- Lack of monitoring of medication success and patient adherence to their medications from health professionals
- Generalised feelings of acceptance and management of bladder symptoms as a consequence of ageing
- Planning and preparation for days out and long journeys as part of life to reduce anxieties over urgency to go and potential leakage
- Need for understanding and reassurance from GPs – include thorough investigation of bladder symptoms', explanation of medication/treatment, invitation for review of this plan and explanation around potential side affects and interactions with other medications and when it is a priority to stop taking a medication.

Participant 10

Participant 10 was clear that the medication she had been placed on had reduced the severity of her symptoms to the point it was manageable and the symptoms no longer give her cause for concern to go back to the GP to review the medication. It was interesting that since she had the phone call related to doing this interview it made her review the medication in her own mind to the point she went back and read the medication leaflet more thoroughly. She avoided doing so for the fear of paying too much notice to the long list of side effects that tend to be detailed. However having now read back she feels that there are some side effects listed related to reflux and blurred vision that she feels she has experienced and now has a little concern about the potential for these symptoms to be related to the medication. She is thinking about going to the GP to review and even has considered coming off the medication yet still has not which suggests she is not convinced and the reduction in symptoms is enough to make her want to continue with the medication. She also believes that the side effects could equally be from one of her other medications so maybe the uncertainty is enough to make her continue the medication despite some concerns.

I feel Participant 10 suggested that she would have liked a little more information about options and choice for treatment for her irritable bladder as she suggests that there was little supporting information or investigation nor was there any suggestion there was other medications for the condition which she said had she have known she would have been more likely to contact the GP and review her medication as ideally she wanted a medication to totally reduce the symptoms. I think the need for informed choice came across from Participant 10 and despite being content with the GP support and understanding of her symptoms she would have liked more information so she could have felt empowered to make an informed decision rather than ‘take these tablets these will work’.

Again there was a delay of a year before Participant 10 went to seek support for her bladder condition. She suggested she almost felt embarrassed about the symptoms and a denial the symptoms were occurring as it was almost admitting oh I am getting old as these are the type of symptoms she associates with getting old. It was when she had an accident in the night and did not make the toilet that was the tipping point to seek guidance from her GP as it is no longer manageable. The feeling of having no control and that was concerning and upsetting.

From the participants interviewed there is a level of acceptance of the bladder symptoms being associated with age and a choice made to manage the symptoms up to a point. Each person has had their own trigger or tipping point with these bladder symptoms where a symptom presents that is no longer manageable where it feels out of control so it seems seeking advice and support from the GP allows the patient to take control again. Participants choosing to take the medication again is them feeling they are taking control and feeling more empowered over the symptoms of their bladder condition.

Participant 6

I think it is important to mention that participant 6 cancelled on four occasions over the past couple of weeks. Hearing the effect of her bladder condition on how she feels and how she lives her life it became clear how badly she has been suffering with her bladder condition. On a severity scale it was at 10 on a scale of 1 to 10 given that her life has seriously been impacted by her bladder condition and to this day it is still unpredictable and not fully under control. I feel as an interviewer I do recognise it is important to remain as neutral and objective as possible. It is always more difficult to do that when a participant gets emotional over the topic they are talking about and in this circumstance I feel it is important to be sensitive and reassuring to the participant and to check they are happy to continue to talk about the topic which participant 6 reassured me she wanted to as in her head she said if she can speak about her experience and it can help even one other person that’s what she would like to do.

It was difficult seeing participant 6 get upset several times when explaining how her bladder condition makes her feel. It really brought to life how much of a negative impact a bladder condition can have on someone's life, the emotion this brings with it including the detrimental effect it can have on a persons confidence to go out in public and do every day routine tasks. participant 6 used the word 'reclusive' several times and it did feel that to avoid the potential frustration, embarrassment and panic associated with a potential accident when out and about she just avoided going out at all the effort in to go out and at her worst times just went to bed.

I did try to reassure and comfort participant 6 and as I mentioned I checked with her that she was fine to continue and she reassured me she wanted to. I think she opened up and was very honest and it was important to hear her story of how her OAB symptoms and treatment path had governed her life. The realness of her story made me realise the importance of medication for the relief of bladder symptoms and supporting people with bladder conditions. The speed of diagnosis and review of their condition is key to ensure it is brought under control and tackled to a point it is manageable so they can still live their routine life and avoid cases like participant 6's experience of her OAB.

She seemed frustrated in the time it has taken to get to the point she is at now on her second round of botox and finally finding a medication that seems to deal with the internal symptoms associated with her bladder and the botox. Having had '4 dry days' in her words she seemed in a more positive frame of mind and is hopeful that this might be a turning point and intends to continue on the route of botox and the medication she is on (not a OAB medication).

It was interesting that she said the only time she actually feels completely relaxed is when swimming and does not even have the urge to go to the toilet. I related this to a few other interview participants accounts as it seems once they are aware of the potential for an accident there is a constant panic and worry and I wonder if the anxiety this brings can sometimes heighten the likelihood of an accident? It would also make sense that in the water it is the only time she relaxes and does not feel the urge to go to the toilet as she is more relaxed and less worried about an accident so this could be why she does not have an accident in this context. The associated worry and panic can almost make it a viscious cycle increasing the likelihood of an accident. I think an important point related to this is that a patient needs to feel confident and believe in their treatment plan thus participant 6 suggest it is important to understand why they are receiving the treatment, how it works and review the treatment regularly with their specialist or GP or even the pharmacist in the case of medication reviews.

There needs to be more clear guidance whether patients should take the medication alongside the botox as participant 6 just stopped taking it although she was not told to. She assumed she should just stop medication once having had the botox but does keep it as a precautionary measure for when the botox wears off. The need for understanding and reassuring attitudes from health professionals and the persons support system was clear. Participant 6 clearly finds it useful to have the opportunity to vent so maybe a support group for bladder conditions specifically. This could be organised by sufferers themselves at clinics they attend for botox treatment. I think this could be a really useful way for OAB sufferers to sit and talk and ‘vent’ as participant 6 said- just about their experiences of the condition and medication for it and alternative treatments it seems from the participants I have spoke to this would be a useful outlet valued by OAB sufferers. I think from a general perspective there needs to be more awareness of bladder conditions so people feel less embarrassed. It would allow us as the general public to be more reassuring and understanding of people who display bladder symptoms that are likely to be related bladder conditions.

Participant 9

Just a note that at the start of the interview the gardeners were in the back so I think this may have caused a bit of interference with the sound at the first stage of the interview. Similar to other participants Participant 9 only seeked help for her bladder symptoms (which were mainly having a leak or accident which she managed through wearing pads) when she came back from a holiday that was her tipping point. She thought this can not be acceptable just because of my age which was the reason she was justifying not seeking out medical guidance.

She just assumed the bladder symptoms were a natural part of ageing but it was getting too much a few months ago and that is when she decided to go to see her GP. Her GP was reassuring and understanding and she says the tablets she is willing to take 'for now' as they do relieve her symptoms of urgency. She said they are not acceptable for the long term as she would rather have a tablet or surgery so she does not have to experience the associated side effects of dry mouth and nose and tiredness that have accompanied the relief of the bladder symptoms since taking the tablets.

It is very early stages for Participant 9 and she is going to speak to a gynaecologist next week so said she would be happy for us to contact her again if necessary to see what the outcome of that is. The only thing she said she would be against is the mesh operation as she heard a lot of negative stories about this. One thing similar to other people I have spoke to was that she does not let the bladder symptoms stop her doing anything and does not speak about the topic as she feels it is something she is just dealing with and would rather chat about other more positive topics. She has a friend who always has to go for pit stops and notes where they are when they are out and she said she does not want to be like that as you can become obsessed with it but she does not believe that is helpful. Overall it felt a lot of the themes Participant 9 was bringing up were very much in line with those discussed by previous participants it is just she is very early on in her taking of the medication so it would be interesting in six months whether she has decided to take the tablets still despite the side effects given the relief they provide from her bladder symptoms.

Appendix B5: OAB study published manuscript

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ORIGINAL RESEARCH

Qualitative Analysis of Factors Influencing Patient Persistence and Adherence to Prescribed Overactive Bladder Medication in UK Primary Care

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ABSTRACT

Introduction: Pharmacotherapy for overactive bladder (OAB) is generally associated with low rates of persistence and adherence. This study was conducted to explore the patient journey in a UK primary care setting (experiences, perceptions, attitudes, and levels of engagement and expectations) and identify self-reported reasons for patient non-adherence and/or non-persistence to medications for OAB.
Methods: This was a qualitative, non-interventional study involving one-to-one semi-structured, face-to-face or phone interviews with individuals aged 40–80 years, diagnosed with OAB, and currently taking, or having taken, either antimuscarinic or β_3-adrenoceptor agonist medications within the last 12 months. Thematic analyses of interview transcripts identified themes surrounding the participants' experiences with OAB.
Results: A total of 20 interviews were conducted (face-to-face, $n = 13$; telephone, $n = 7$). Interviews from five men and 13 women (mean age 70 years) were included in the final analysis. The most common OAB symptoms reported included urgency, frequency, incontinence and nocturia. Several key themes of factors influencing persistence and/or adherence to prescribed OAB medication were identified: patients' attitude and condition adaptation behaviour; support with treatment; unmet efficacy/tolerability expectations; drug/condition hierarchy. Non-adherence and/or non-persistence to OAB medication was largely intentional, with patients balancing side effects against perceived clinical benefits. Perceived lack of efficacy was the primary reason for discontinuing treatment. Other factors cited included side effects of medication (either experienced or a fear of future effects), a general aversion to long-term medication taking, drug/condition hierarchy relative to other comorbidities, and limited healthcare professional (HCP) support/engagement. Patients expressed condition adaptation behaviours to help self-manage their condition.
Conclusion: Persistence and adherence to OAB medication may be suboptimal. HCPs might be able to improve persistence and adherence by fostering realistic treatment expectations and

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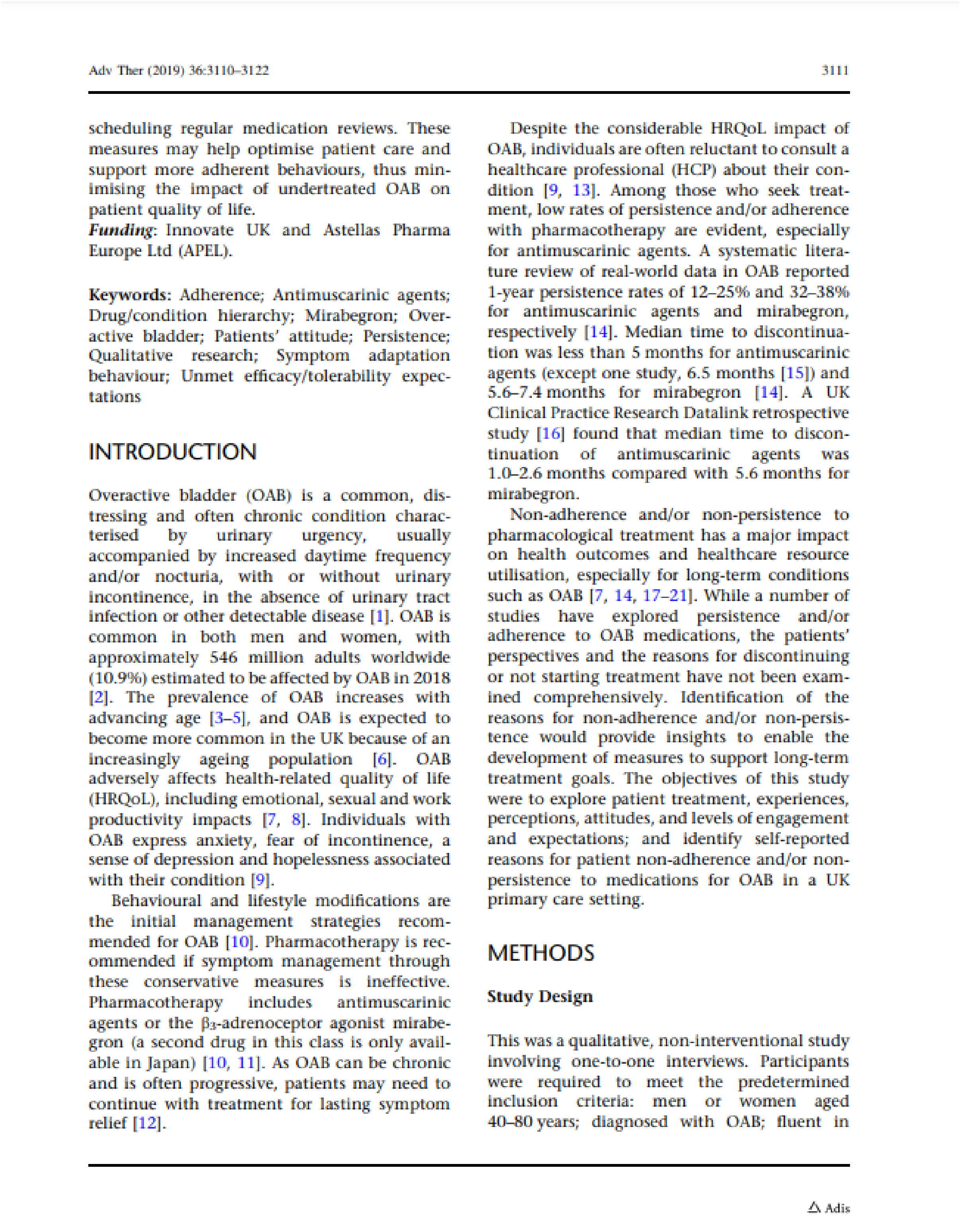

scheduling regular medication reviews. These measures may help optimise patient care and support more adherent behaviours, thus minimising the impact of undertreated OAB on patient quality of life.

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Keywords: Adherence; Antimuscarinic agents; Drug/condition hierarchy; Mirabegron; Overactive bladder; Patients' attitude; Persistence; Qualitative research; Symptom adaptation behaviour; Unmet efficacy/tolerability expectations

INTRODUCTION

Overactive bladder (OAB) is a common, distressing and often chronic condition characterised by urinary urgency, usually accompanied by increased daytime frequency and/or nocturia, with or without urinary incontinence, in the absence of urinary tract infection or other detectable disease [1]. OAB is common in both men and women, with approximately 546 million adults worldwide (10.9%) estimated to be affected by OAB in 2018 [2]. The prevalence of OAB increases with advancing age [3–5], and OAB is expected to become more common in the UK because of an increasingly ageing population [6]. OAB adversely affects health-related quality of life (HRQoL), including emotional, sexual and work productivity impacts [7, 8]. Individuals with OAB express anxiety, fear of incontinence, a sense of depression and hopelessness associated with their condition [9].

Behavioural and lifestyle modifications are the initial management strategies recommended for OAB [10]. Pharmacotherapy is recommended if symptom management through these conservative measures is ineffective. Pharmacotherapy includes antimuscarinic agents or the β_3-adrenoceptor agonist mirabegron (a second drug in this class is only available in Japan) [10, 11]. As OAB can be chronic and is often progressive, patients may need to continue with treatment for lasting symptom relief [12].

Despite the considerable HRQoL impact of OAB, individuals are often reluctant to consult a healthcare professional (HCP) about their condition [9, 13]. Among those who seek treatment, low rates of persistence and/or adherence with pharmacotherapy are evident, especially for antimuscarinic agents. A systematic literature review of real-world data in OAB reported 1-year persistence rates of 12–25% and 32–38% for antimuscarinic agents and mirabegron, respectively [14]. Median time to discontinuation was less than 5 months for antimuscarinic agents (except one study, 6.5 months [15]) and 5.6–7.4 months for mirabegron [14]. A UK Clinical Practice Research Datalink retrospective study [16] found that median time to discontinuation of antimuscarinic agents was 1.0–2.6 months compared with 5.6 months for mirabegron.

Non-adherence and/or non-persistence to pharmacological treatment has a major impact on health outcomes and healthcare resource utilisation, especially for long-term conditions such as OAB [7, 14, 17–21]. While a number of studies have explored persistence and/or adherence to OAB medications, the patients' perspectives and the reasons for discontinuing or not starting treatment have not been examined comprehensively. Identification of the reasons for non-adherence and/or non-persistence would provide insights to enable the development of measures to support long-term treatment goals. The objectives of this study were to explore patient treatment, experiences, perceptions, attitudes, and levels of engagement and expectations; and identify self-reported reasons for patient non-adherence and/or non-persistence to medications for OAB in a UK primary care setting.

METHODS

Study Design

This was a qualitative, non-interventional study involving one-to-one interviews. Participants were required to meet the predetermined inclusion criteria: men or women aged 40–80 years; diagnosed with OAB; fluent in

English; and currently taking, or having taken, either antimuscarinic agents or β_3-adrenoceptor agonists for OAB within the last 12 months. Individuals with memory impairment, cognitive decline or dementia (as documented within medical records) were not eligible for inclusion. Two UK National Health Service Research and Development sites (covering Kent, Surrey, and Sussex; and Greater Manchester) invited primary care practices (PCPs) from these regions to participate in this study. PCPs were sent the study protocol, copies of the patient information sheet, a study poster to display in the practice, and a research information sheet for practices form to help them decide whether they were able to participate in this study.

Participating PCPs compiled lists of their registered patients with OAB and applied the study inclusion and exclusion criteria. An HCP from each of the PCPs then reviewed the list of potential participants to confirm that those who progressed to be invited to participate in the study were appropriate to do so (correctly coded OAB, not suffered recent bereavement/terminally ill, etc.). Invitation packs were posted to the home address of eligible participants. This included an information sheet outlining the area of research and rationale (Supplementary Appendix A). Participants who returned consent-to-be-contacted forms were telephoned by the study team to reiterate the purpose of the research, confirm their consent to take part in this study, and to arrange interviews. This study has gone through a health research authority and ethics review with NW Liverpool East REC (Central Manchester is the lead Research & Development site). IRAS project ID 198502. All participants provided their written consent to take part in this study.

Interviews

Semi-structured interviews were conducted face-to-face or over the telephone by L.S., a research associate with more than 5 years' experience in qualitative research. A reflective journal recorded by the interviewer detailed that this was not a familiar topic of research, thus interviews were initiated with no preset assumptions or bias regarding medication persistence and/or adherence in relation to OAB. Participants were briefed on the interviewer's research experience and the purpose of the interviews prior to the interview commencing; they were also made aware that the interviewer had no commercial interests related to the study. Interviews were designed to take approximately 1 h and followed a discussion guide (see Supplementary Appendix B). They were conducted in participants' homes (Greater Manchester) and over the telephone (Kent, Surrey, and Sussex). Presence of non-participants (i.e. partners/family members) was at the discretion of the participants. Each interview was voice recorded and notes taken. Participants received a £10 store voucher upon interview completion. Participants had no further involvement following the interviews and repeat interviews were not performed.

The discussion guide was produced by academic researchers with expertise in qualitative research methods, with input from subject matter experts. Questions were framed to elicit full responses and obtain a narrative of the patient journey in their own words: starting with OAB history and coping strategies, interactions with their HCPs, treatment history, and treatment expectations; following up with a discussion of their strategies for adherence and finally the opportunity for any further comments (Supplementary Appendix B).

Analyses

Interviews were transcribed verbatim (by M.A.). A sample of transcripts (3/18 transcripts; 17%) was reviewed against corresponding recordings by the Chief Investigator (M.H.) to ensure completeness and accuracy of the transcripts. In addition, an academic Health Psychologist (S.G.), with more than 20 years' experience of conducting and publishing qualitative research, performed a validation crosscheck of the resulting themes.

Transcribed data were collectively analysed, using NVivo Pro 11 software (QSR International, Warrington, UK), to identify a set of themes on the basis of the method of thematic analysis by Braun and Clarke [22]. Data

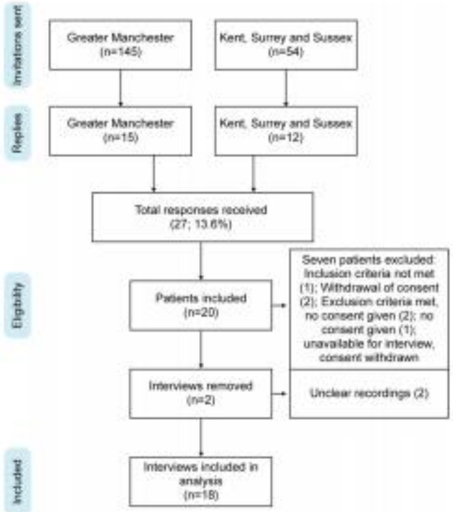

Fig. 1 Summary of patient recruitment and participation

collection and analysis were discontinued when data saturation was achieved (i.e. no new information was discovered) [23]. Identified themes were agreed by all authors.

RESULTS

Study Size

Of the 199 invitation packs sent, 27 positive responses were received and 7 respondents were excluded (Fig. 1). A total of 20 interviews were conducted (face-to-face, n =13; telephone, n =7), between June and August 2018. Subsequently, two interviews were excluded because of poor-quality recordings not allowing accurate transcription and analysis. Upon transcribing and analysing the data from the 18 interviews, the study team recognised that saturation had been reached.

Participant Demographics

Interviews from five men and 13 women, with an overall mean age of 70 years (range 57–80), were included in the final analysis (Table 1). The most common OAB symptoms reported included urgency, frequency, incontinence and nocturia.

Factors Influencing Persistence and/or Adherence to Prescribed OAB Medication

Several key themes of factors influencing persistence and/or adherence to prescribed OAB medication were identified, broadly categorised into four subgroups: patients' attitude and condition adaption behaviour; support with treatment; discontinuing treatment; drug/condition hierarchy (Fig. 2).

Patients' Attitude to Medication and Condition Adaptation Behaviour

Some participants questioned the necessity of taking medication and balanced the perceived risks (side effects) against the clinical benefits in their decisions to start or continue taking OAB medication—'If it is necessary to take the medication, then it should be taken as long as there are no noticeable side effects', (participant #16). Other participants (#7, 8 and 17) expressed that they would take medication if there were tangible benefits (improvement in OAB symptoms). However, one participant (#7) would advise others against starting OAB medication, despite experiencing some symptom relief, due to a side effect (headache) that led to their non-adherence.

Negative beliefs regarding risk of side effects were the basis of one participant's (#13) decision to only take OAB medication on an 'as-needed' basis, despite a conviction that regular usage would be beneficial, while another participant (#10) was reluctant to accept a dose increase of OAB medication, although acknowledging it might improve symptoms. One participant (#5) chose not to be exposed to any potential danger from side effects/complications, on the basis of a prior hospitalisation following an incorrect prescription for hypertension.

Non-adherence was largely intentional (e.g. participants did not forget to take their

Table 1 Study participants demographic and background information

Area	Participant number	Sex	Age (years)	Main OAB symptoms
Greater Manchester	1	M	64	Urgency, incontinence
	2	F	66	Urgency, incontinence, nocturia
	3	F	58	Frequency, urgency, incontinence
	4	F	69	Urgency, incontinence
	5	F	71	Frequency, urgency
	6	F	57	Frequency, nocturia, incontinence
	7	F	70	Frequency, urgency, high volume
	8	F	77	Frequency
	9	F	80	Incontinence, urgency
	10	F	58	Urgency, nocturia, incontinence
	11	F	78	Incontinence, urgency, nocturia
	12	F	61	Frequency, incontinence, high volume at night
	13	M	65	Urgency, frequency
Kent, Surrey, and Sussex	14	M	78	Nocturia, urgency
	15	F	80	Incontinence, nocturia, urgency
	16	M	71	Urgency, incontinence, nocturia
	17	F	67	Frequency, nocturia
	18	M	70	Nocturia

F female, *M* male, *OAB* overactive bladder

medication). One participant (#2) distinguished between their OAB medication, which they had decided not to take, and their other daily medications that they continued to take. Descriptors from participants in reference to remembering to take medication included 'no challenges at all' (participant #17) and 'automatic' (participant #8). Strategies for avoiding non-intentional adherence included incorporating medicine taking into a daily routine (e.g. taking tablets with breakfast or just before going to bed); keeping medication in conspicuous places and in the line of sight; and using dosset boxes. Although these strategies were highly effective, they were not without certain challenges e.g. if the usual schedule was disrupted by a change in location or setting. One participant (#9), who described a routine of taking medication around breakfast time, stated that adherence would be difficult if a new medication was prescribed that needed to be taken at a different time of the day.

Participants modified their daily behaviours and planned ahead in order to foster a sense of safety and confidence, including keeping an acute awareness of toilet locations, using the toilet pre-emptively, and gravitating towards familiar places, such as their own home, where others would not witness or be affected by their symptoms. Among female participants, absorbent pads were commonly used as a precautionary measure. Several participants described variants of 'planning your day around being near a toilet' and 'life around toilets'. This was a

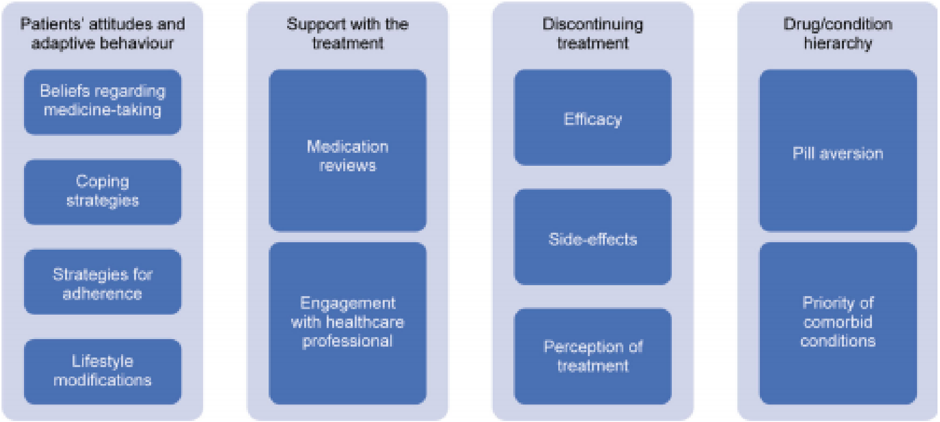

Fig. 2 Identified themes from interviews on persistence and adherence to OAB medication

key element in the pursuit of feeling secure—'Sainsbury's have got loos, so… if I need a loo, I'm alright' (participant #5). One participant (#7) mentioned planning social interactions specifically in places where they had knowledge of the availability of public toilets. One participant (#6) described a reluctance to go on holiday—'I haven't been this year, 'til I wanted to sort me bladder out', and being around people they were comfortable with—'In a friend's apartment, I'm safe… they know that I can't control'.

Some participants demonstrated a reluctance to make recommended lifestyle modifications, including two participants (#12 and 17) who perceived difficulties/impracticalities of incorporating pelvic floor exercises into their routine, and another (#7) who did not adhere to caffeine avoidance advice, as this entailed giving up a daily habit.

Support with Treatment

Several participants described a lack of formal reviews for OAB medication, in contrast to routine medication reviews conducted for their other conditions. Some participants felt their general practitioners (GPs) were 'too busy' to conduct monitoring reviews. Reviews for OAB were rushed or overlooked, and medicines that caused specific problems were given prominence during the review process, which was focused on problem-solving, rather than optimising their care. In other cases, repeat prescriptions were issued without medication reviews.

One participant (#16) mentioned that the lack of their own reviews was due to a reluctance to visit the GP, downplaying their own needs against those of others who 'really are ill'. A lack of communication with the HCP, a preference to avoid medication, and a doubted OAB diagnosis were the reasons given by another participant (#17) for not attending a repeat visit after initially being prescribed a 1-month supply of OAB medication. One participant (#13) decided to take OAB medication sporadically to manage their inconsistent symptoms, because the HCP appeared uninterested and did not stress taking the tablets daily. Although convinced that daily medication would offer complete symptom relief, this was tempered by a fear of unknown long-term effects. However, some participants described their GP as being supportive, providing invitations for reviews and imparting confidence.

Unmet Efficacy/Tolerability Expectations

Over half of participants cited lack of efficacy as a reason for non-adherence and/or non-persistence of OAB medication (Table 2). One

Table 2 Reasons for discontinuing OAB medication

Participant number	Sex	Age (years)	Primary reasons for discontinuation	Other reasons
1	M	64	Lack of efficacy	Tablet being 'nothing special'
2	F	66	Side effects	–
3	F	58	Did not discontinue	–
4	F	69	Lack of efficacy and requirement for ECGs	Fear of unknown effects
5	F	71	Side effects	Taking too many tablets
6	F	57	Waning efficacy, side effects	OnabotulinumtoxinA
7	F	70	Side effects	Taking too many tablets
8	F	77	Lack of efficacy	Suspected side effect
9	F	80	Side effects	Fear of unknown effects
10	F	58	Side effects	Aversion to dose escalation, wanting to switch medication
11	F	78	Did not discontinue	–
12	F	61	Lack of efficacy, side effects	Unconvinced of OAB diagnosis (more a 'weak bladder')
13	M	65	Fear of side effects	Unclear instructions
14	M	78	Lack of efficacy	Side effects
15	F	80	Lack of efficacy, side effects	Surgery stopped the medication because of potential cognitive effects
16	M	71	Lack of efficacy, side effects	Trial and error
17	F	67	Unclear instructions	Pill aversion
18	M	70	Lack of efficacy	–

ECG electrocardiogram, *F* female, *M* male, *OAB* overactive bladder

participant (#14) expressed frustration due to poor efficacy and the need to take sleeping pills to counteract the secondary effects of next-day fatigue from nocturia. According to many participants, side effects further prompted their decision to discontinue ineffective medication. Reported side effects affecting persistence and/or adherence included dry mouth and headaches. Drowsiness was mentioned by several participants, but mostly in a positive context as an aid to sleep (reducing the effects of nocturia). One participant (#18), who initially experienced a 'minor improvement' in urinary symptoms from α-blocker monotherapy, subsequently received an add-on antimuscarinic agent, but did not perceive any 'great improvement' from combination therapy. Together with the side effect of dry mouth, this led to complete treatment discontinuation; this participant was still symptomatic and waking several times a night. One participant (#15) experienced a dull stomach ache from a twice-daily antimuscarinic agent, which resulted in once-daily treatment and eventual discontinuation (advised by the HCP) due to potential effects on memory. Subsequently, they were not offered an alternative treatment and continued to experience the wax and wane of OAB symptoms. β_3-adrenoceptor agonists were linked to a fear of future side effects by another participant (#4) due to additional blood pressure and electrocardiogram monitoring required while on treatment.

Doubtful efficacy together with a suspicion that the treatment was causing a deterioration in eyesight led to one participant (#12) discontinuing treatment. This perceived lack of efficacy was further reinforced by an assessment of the HCP's demeanour (while initially prescribing the drug), interpreted as being 'unsure whether these tablets worked or not'. The participant subsequently re-evaluated the side effects of the medication, attributing the decline in eyesight to advancing age instead, which coincided with a renewed motivation to control symptoms after taking up golf. They remained adherent despite still doubting the effectiveness of medication. Another participant (#10) was unsure as to which of their medications were responsible for their symptoms of blurred vision and gastro-oesophageal disturbances and intended to discontinue the OAB medication to gauge how much of an effect this might have. They also cited a lack of awareness about the availability of a range of medications for OAB as one of the reasons for not returning to the GP to try a different drug—'I think from reading that form [patient information sheet], there appears to be quite a lot of different drugs for, the same problem. And my GP didn't offer me a choice or anything'.

Drug/Condition Hierarchy

Participants showed a general pill aversion, choosing to discontinue OAB medication while prioritising other conditions. For example, one participant (#7) had discontinued several OAB medications because of side effects and a wish to avoid tablets where possible, while maintaining adherence to hypertension medication and letrozole, on the basis of the potentially serious consequences of not doing so. This was echoed by participant #16 who described adherence to hypertension medication: 'Oh I take those without fail, because my blood pressure was quite high'. Some participants chose to delay OAB treatment until they could no longer endure the symptoms and associated consequences. One participant (#10) became more open to treatment following a worsening of OAB, due to the effect of their OAB symptoms on chronic migraines. Conversely, the presence of comorbidities, including liver disease culminating in a liver transplant, was a driving factor in adherence to OAB medication for one participant (#1), who persisted with treatment despite lack of efficacy; now on their third OAB medication (an antimuscarinic agent), they were planning to request a fourth. Nevertheless, they were reluctant to seek HCP advice specifically for OAB (despite worsening of symptoms) and were delaying consultation until another healthcare need arose.

When participants did consult their HCP about their OAB, they often felt that the condition was regarded with low priority by the HCP. According to one participant (#13), the HCP set the tone of low importance of OAB and its treatment by giving the impression of providing a diagnosis and treatment to 'get rid' of the patient when an ultrasound test did not reveal any particular issue. This was compounded by there being no review of OAB medication, with the HCP supplying prescriptions only. One participant (#3), who worked in a GP clinic, drew a comparison between the relative prominence given to conditions such as asthma and prostate cancer against the dearth of information publicly available for 'day-to-day' conditions, such as OAB, which 'really interfere with your lifestyle'. This was mirrored by another participant's (#12) opinion that there is a lack of effort into developing OAB medication, as researchers focused on the 'big things'.

DISCUSSION

Non-adherence and non-persistence with treatment are behaviours that feature prominently among patients with OAB [24, 25]. Through qualitative patient interviews, this study provides insights into the complex and individualistic factors driving such behaviours in patients who have undergone pharmacological treatment for OAB.

The interviews uncovered several common themes surrounding non-adherence and/or non-persistence of OAB medication. Failure to take OAB medication was largely intentional, with many participants making decisions on the basis of a perceived balance of benefits and risks and/or lifestyle choices. Unintentional non-adherence was not identified as a problem, as participants tended to alter their behaviour to facilitate medicine taking. In this study, the main reasons for treatment discontinuation, as reported by participants, were, firstly, a perceived lack of efficacy, resulting in unmet treatment expectations and, secondly, experience of side effects (or fear of potential side effects). There was also a general aversion to taking chronic medication, as well as a tendency to prioritise medications on the basis of the perceived prominence of the condition and the consequences of not taking the medication, giving rise to a drug/condition hierarchy. Lack of engagement and support from HCPs were also factors that may have contributed to poor treatment persistence for OAB.

Dry mouth was the most widely mentioned side effect leading to discontinuation of OAB medication, followed by headache and nausea—effects typically associated with antimuscarinic therapy and commonly cited as reasons for treatment discontinuation [26, 27]. Improved rates of persistence and/or adherence have been reported with the β_3-adrenoceptor agonist mirabegron compared with antimuscarinic agents [16, 28, 29], perhaps owing to lower rates of typical antimuscarinic adverse events [14]. Many participants were receiving multiple medications for comorbidities, but sometimes incorrectly attributed other undesirable effects to their OAB medication. The choice to discontinue the OAB medication over other treatments may suggest a poor perception of the benefit–risk balance of available OAB treatment options, as well as assigning a low priority to managing OAB.

The findings of the current study are aligned with the results of a survey from 5392 respondents using antimuscarinic agents for OAB in the USA [18], among whom 1322 (24.5%) reported discontinuing one or more antimuscarinic medications during the previous 12 months. The most commonly reported reasons for discontinuation were that 'it didn't work as expected' (46.2%), 'switched to a new medication' (25.1%), 'learned to get by without medication' (23.3%), and 'I had side effects' (21.1%). A proportion of participants (11%) indicated a general aversion to taking any medication. In another US survey of OAB, among the 138 women who reported that they had taken or were currently taking OAB medication, half of them had discontinued OAB medication at some point; the most common reasons were inadequate efficacy (42%) and adverse events/intolerability (30%) [30].

The issue of drug/condition hierarchy was evident in several participants who opted to discontinue OAB treatment while prioritising other conditions, such as hypertension, for which the consequences of stopping treatment would be more drastic in their opinion. This verifies the findings of other studies showing that rates of persistence and adherence appear to be particularly low for OAB medications (specifically antimuscarinic agents) compared with other chronic conditions, such as diabetes, glaucoma, hyperlipidaemia, osteoporosis and hypertension [25].

Better persistence and/or adherence to OAB medication is associated with improved urinary symptoms and HRQoL [19, 20]. OAB management primarily through coping strategies in preference to HCP consultation has been highlighted in several studies [9, 13, 31]. Similarly, in the current study, some participants downplayed or normalised their symptoms and 'learned to live with it' by employing coping strategies—these may have a negative impact on patients' HRQoL and may also hinder the realisation of potential clinical benefits from OAB treatment. This was exemplified by one participant who had resumed OAB medication in order to pursue a new hobby.

In the current study, barriers to patients seeking initial help included a perceived lack of publicly displayed information on OAB, as well as a general unawareness of the availability of treatments. More information may help patients recognise how widespread such symptoms are, leading to less embarrassment in discussing them and thereby facilitating help-seeking behaviour. This may also help patients to decide to pursue better care for their OAB, rather than incidentally reporting issues while visiting the GP for other health concerns. Raising awareness to the multiple medications available for OAB may also provide motivation to pursue alternative treatment. The progressive use of coping strategies may also prevent patients from presenting to their HCP by masking the extent of their condition until the psychological burden becomes too great or they have a significant event, such as an incontinence episode in public.

The finding that many participants discontinued treatment because of unmet efficacy/tolerability expectations suggests that HCPs might be able to encourage persistence and/or adherence by fostering realistic expectations about the onset of efficacy and the extent of benefits [18, 30]. This could include educating patients that side effects of medication may manifest before improvements in symptoms become apparent, and discussing how side effects could be managed. Furthermore, realistic treatment goals could focus on practical factors that are limiting the patient's HRQoL, such as attending more social events or travelling longer distances, rather than simply focusing on symptoms.

The demeanour of HCPs during consultations led to participants harbouring doubts of both the diagnosis and the treatments offered. The perceived disinterest of HCPs to review OAB medication, alongside participants being reluctant to chase such reviews, has left a gap in patient care, leading to poor treatment persistence. HCPs can support treatment persistence and/or adherence through: the use of patient-centred communication with more discussion of critical topics (e.g. the impact of OAB on HRQoL, and concerns about treatment) [32]; involving patients in treatment decisions; reviewing medicines; communication with other HCPs involved in the patient's care [33]. Treatment 'cycling' did not appear to be widespread in the current study (participant #1 received three OAB medications and was planning to start a fourth), but as patients may need to try different treatments to find a suitable one, regularly scheduled reviews would allow patients to provide feedback and help optimise their care. Such reviews could be conducted by nurses or pharmacists (e.g. the Medicine Use Review service), thereby relieving pressure on GPs.

There were a number of strengths associated with the current study. Interviews were open-ended and designed to encourage participants to respond fully in their own words (enabling the generation of rich information). Additionally, data were collected from participants living in two regions, in the North West and in the South of England. The study also had a number of limitations: invited individuals were preselected by HCPs, thus selecting only those who had sought healthcare for their OAB (selection bias); the study was restricted to English language speakers only; socio-economic factors were not considered; the duration of treatment for OAB medications was not captured; and the type of medication taken for other conditions was not formally collected and, therefore, anticholinergic burden may have been a factor influencing OAB medication-taking behaviour.

In addition to no improvement or deterioration of health, non-adherence and/or non-persistence may lead to higher economic costs with respect to wasted medicines and increased demands for other healthcare resources; economic considerations of poor persistence and/or adherence in OAB could be a feature of future research. Additional data collection methods (e.g. focus groups, questionnaires/surveys), which may provide a more complete picture, could be employed in future studies. Further work is needed to investigate the extent to which previously reported determinants of persistence and/or adherence, such as female (sex), older age group, use of extended-release formulations and treatment experience [14], influence OAB medication persistence and/or adherence. These could take the form of longitudinal studies following a patient's journey through medication taking to understand their decision-making processes better. Drug/condition hierarchy and its effect on disease management and outcomes is also a potential area of interest for further investigation. This is particularly relevant in OAB, where patients may have other long-term comorbidities.

CONCLUSION

In the current study, the primary reason for non-adherence and/or discontinuing OAB medication, as reported by patients, was perceived poor efficacy/unmet expectations, followed by side effects. Patients also showed an aversion to long-term medication taking and opted to discontinue OAB treatment, according low priority to OAB relative to other comorbidities. By providing confident diagnoses, managing expectations of treatment benefit, educating patients on managing side effects, and raising awareness of the availability of multiple treatments, HCPs may be able to support more adherent and persistent behaviours among patients with OAB.

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Disclosures. Margarita Landeira is a current employee of APEL. Patrick Covernton is a current employee of APEL. Jameel Nazir was an employee of APEL at the time the study was conducted and is now an employee of Sobi. Francis Fatoye was a member of the KTP team, which received research grants from APEL. Maxine Holt was a member of the KTP team, which received research grants from APEL. Sarah Grogan was a member of the KTP team, which received research grants from APEL. Sue Powell was a member of the KTP team, which received research grants from APEL. Mahmood Ali completed secondments at APEL. Ashley Jaggi completed secondments at APEL. Leanne Staniford has nothing to disclose.

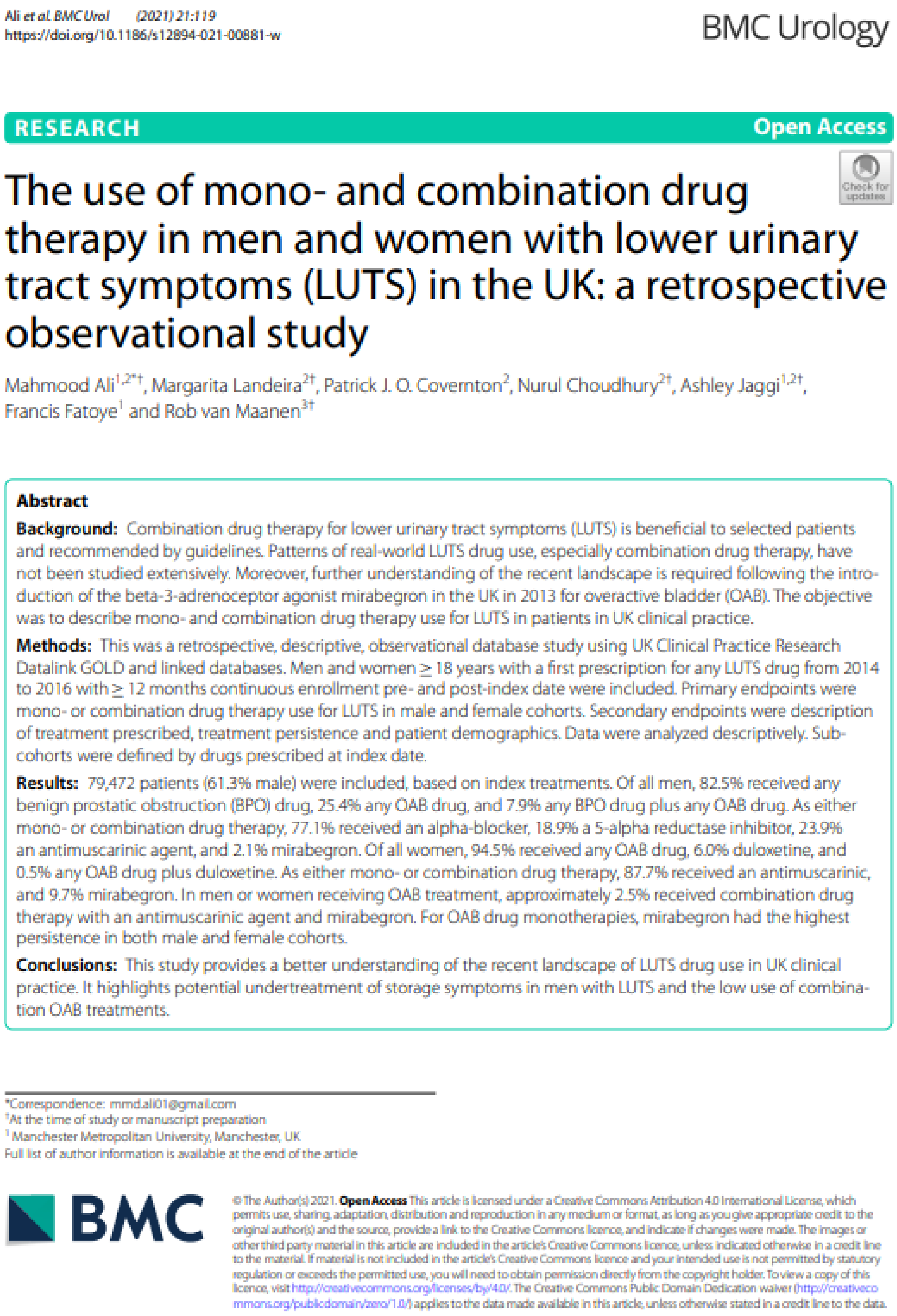
Compliance with Ethics Guidelines. This study has gone through a health research authority and ethics review with NW Liverpool East REC (Central Manchester is the lead Research & Development site). IRAS project ID 198502. All participants provided their written consent to take part in this study.

Data Availability. All data generated or analysed during this study are included in this published article or as supplementary information files. Access to anonymised individual participant level data will not be provided for this trial as it meets one or more of the exceptions described on http://www.clinicalstudydatarequest.com under 'Sponsor Specific Details for Astellas'.

Appendices Set C:

Appendix	Title
C1	MACU Study Manuscript: Monotherapy and combination use in men and women with lower urinary tract symptoms (LUTS) in the UK: a retrospective observational study

Appendix C1: MACU Study Manuscript



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BMC Urology

RESEARCH

Open Access

The use of mono- and combination drug therapy in men and women with lower urinary tract symptoms (LUTS) in the UK: a retrospective observational study

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Abstract

Background: Combination drug therapy for lower urinary tract symptoms (LUTS) is beneficial to selected patients and recommended by guidelines. Patterns of real-world LUTS drug use, especially combination drug therapy, have not been studied extensively. Moreover, further understanding of the recent landscape is required following the introduction of the beta-3-adrenoceptor agonist mirabegron in the UK in 2013 for overactive bladder (OAB). The objective was to describe mono- and combination drug therapy use for LUTS in patients in UK clinical practice.

Methods: This was a retrospective, descriptive, observational database study using UK Clinical Practice Research Datalink GOLD and linked databases. Men and women ≥ 18 years with a first prescription for any LUTS drug from 2014 to 2016 with ≥ 12 months continuous enrollment pre- and post-index date were included. Primary endpoints were mono- or combination drug therapy use for LUTS in male and female cohorts. Secondary endpoints were description of treatment prescribed, treatment persistence and patient demographics. Data were analyzed descriptively. Sub-cohorts were defined by drugs prescribed at index date.

Results: 79,472 patients (61.3% male) were included, based on index treatments. Of all men, 82.5% received any benign prostatic obstruction (BPO) drug, 25.4% any OAB drug, and 7.9% any BPO drug plus any OAB drug. As either mono- or combination drug therapy, 77.1% received an alpha-blocker, 18.9% a 5-alpha reductase inhibitor, 23.9% an antimuscarinic agent, and 2.1% mirabegron. Of all women, 94.5% received any OAB drug, 6.0% duloxetine, and 0.5% any OAB drug plus duloxetine. As either mono- or combination drug therapy, 87.7% received an antimuscarinic, and 9.7% mirabegron. In men or women receiving OAB treatment, approximately 2.5% received combination drug therapy with an antimuscarinic agent and mirabegron. For OAB drug monotherapies, mirabegron had the highest persistence in both male and female cohorts.

Conclusions: This study provides a better understanding of the recent landscape of LUTS drug use in UK clinical practice. It highlights potential undertreatment of storage symptoms in men with LUTS and the low use of combination OAB treatments.

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Keywords: Benign prostatic obstruction (BPO), Overactive bladder (OAB), Lower urinary tract symptoms (LUTS), Persistence, Stress urinary incontinence (SUI)

Background

Lower urinary tract symptoms (LUTS) is an overarching term for symptoms in men and women, comprising storage, voiding and post-voiding components [1, 2]. In both men and women, storage LUTS are commonly attributed to overactive bladder (OAB) syndrome [1–3], which is defined as urinary urgency, usually with increased daytime frequency and/or nocturia, with/without urinary incontinence, and with no urinary tract infection or other detectable disease [1, 2, 4]. Stress urinary incontinence (SUI) is another common cause of LUTS, especially in women, and involves involuntary urine leakage associated with physical activity (e.g., coughing, sneezing), often as a consequence of childbirth [1, 3, 5]. Voiding LUTS in men are commonly attributed to benign prostatic obstruction (BPO: bladder outlet obstruction [BOO] due to benign prostatic enlargement) [1, 6].

Although conservative treatment, including lifestyle intervention and behavioral therapies (such as bladder training), remains the foundation of LUTS management, several pharmacological treatments are available [6–8]. If conservative treatment fails, pharmacological therapy for OAB/urgency urinary incontinence (UUI) includes antimuscarinic agents or the beta-3 agonist, mirabegron [7]. Combination of an antimuscarinic agent plus mirabegron has also been shown to be effective [9] and is recommended as an option if patients respond inadequately to monotherapy [7, 8]. In patients with SUI where surgery is not indicated, duloxetine is the only recommended pharmacotherapy [7]; it is unknown to what extent duloxetine is used in combination with OAB drugs. Women with LUTS can experience symptoms of both OAB and SUI [10], but there are no recommendations regarding combination therapy with OAB/UUI drugs for such patients.

In men with LUTS suggestive of BPO, the main treatment options include alpha-blockers for rapid symptomatic relief [11, 12] and 5-alpha reductase inhibitors (5-ARIs) to delay progression of BPO and help manage symptoms over the long term in men at risk of disease progression [6, 12]. Alpha-blockers are usually used as first-line treatment [6], but the European Association of Urology (EAU) guidelines recommend combined alpha-blocker and 5-ARI treatment in men with moderate-to-severe LUTS and an increased risk of disease progression [6]. However, many men with LUTS (approximately 50%) experience mixed symptoms suggestive of both OAB and BPO [13]. Only one-third of these men with mixed symptoms will achieve adequate symptom control with an alpha-blocker alone, with the remainder requiring additional pharmacotherapy to manage residual storage LUTS [14]. Clinical trials in men on alpha-blocker monotherapy who still have bothersome storage LUTS have shown that adding an OAB drug can significantly reduce storage symptoms and improve quality of life [15–18]. The addition of an antimuscarinic agent or beta-3-agonist if storage symptoms are not relieved by alpha-blocker monotherapy is a recommended treatment strategy in clinical guidelines [6].

Patterns of real-world LUTS drug use, especially combination drug therapy, have not been studied extensively in the UK. Our study investigated the recent landscape of pharmacotherapy for men and women with LUTS in UK clinical practice, including the types and extent of combination therapies used, and persistence with treatment.

Methods

Study design

This was a retrospective, descriptive, observational database study of LUTS treatment in the UK primary care setting. Data were extracted from the UK Clinical Practice Research Datalink (CPRD) GOLD, a national longitudinal primary care database, which contains anonymized electronic health records of over 15.6 million patients (September 2018 version) [19]. Only de-identified data were obtained, and patients could opt out if they did not wish to have their data used for research purposes. CPRD GOLD was linked to the Hospital Episode Statistic database in England for the exploration of resource use, and the Index of Multiple Deprivation (IMD). The IMD provides an indication of patients' socio-economic status measured at the GP surgery level. All methods were carried out in accordance with relevant guidelines and regulations.

Population

The study included adults (≥ 18 years of age) identified with LUTS (evidenced by prescription of drugs used to treat LUTS) between 1 January 2014 and 31 December 2016, with ≥ 12 months continuous enrollment pre- and post-index date (index date was the date on which patients were prescribed a new index pharmacotherapy [one pharmacotherapy or combination of two or more pharmacotherapies] for the first time between 1 January 2014 and 31 December 2016). Patients prescribed the same index drug in the 12-month pre-index period were excluded. Male and female cohorts were considered separately. Sub-cohorts were defined by the drugs received at index date (Additional file 1: Table S1), and combination therapy was categorized by index drug with patients placed into one sub-cohort only. If > 1 drug was prescribed at index date and this indicated assignment to different sub-cohorts, the order of preference was as follows: LUTS (including OAB) had priority over BPO in the male cohort and LUTS (including OAB) over SUI in the female cohort. Patients were classified as being on combination therapy if the additional drug(s) was prescribed within the prescription duration of the first drug (prescription duration was calculated by total tablets prescribed divided by total daily dose) and the index date was the first prescription of the most recently prescribed drug.

The LUTS (including OAB) cohort were patients receiving an OAB drug (antimuscarinic agent and/or mirabegron), with or without a BPO drug (alpha-blocker and/or 5-ARI) in the male cohort and with or without a SUI drug (duloxetine) in the female cohort. BPO patients were those receiving an alpha-blocker and/or 5-ARI without an OAB drug. SUI patients were those receiving duloxetine without an OAB drug (Additional file 1: Table S1).

Endpoints

Primary endpoints were use of mono- or combination drug therapy for LUTS in a) male or b) female cohorts. Secondary endpoints were socio-demographic and clinical characteristics, and description of monotherapy/combination drugs. Exploratory variables included treatment persistence and presence of a LUTS diagnostic Read code in the pre-index period.

Data analyses

Socio-demographic characteristics were recorded by age, sex and IMD; clinical characteristics were recorded by comorbidity (number of chronic diseases from the Quality and Outcomes Framework [QOF]), polypharmacy (number of distinct British National Formulary headers from CPRD GOLD), and antimuscarinic treatment experience (≥ 1 antimuscarinic agent prescription, other than index treatment, in CPRD GOLD), within the 12-month pre-index period.

Statistical analyses

Data were analyzed descriptively for the overall population and by cohort and sub-cohort. Analyses were conducted using SAS Studio version 3.5.

Persistence was analyzed by median time (from index date) to first discontinuation (TTD, during the 12-month post-index period), and persistence rate at 12 months, calculated using the Kaplan–Meier method. Discontinuation was defined as exceeding the maximum allowable gap duration (MAGD) between prescriptions. For the base-case, the MAGD was defined as 1.5 times the estimated duration of the most recent prescription. Combination treatment was classed as discontinued upon discontinuation of any one of the component drugs. Data were classed as Not Observable when the number of patients still at risk was below the 20% of the initial sample threshold required to allow for persistence to be calculated or, the median was not reached.

Sensitivity analyses

Sensitivity analyses (SA1-7) varied the combination drug therapy definition, MAGD definition and presence of LUTS diagnostic code. The combination drug therapy definition was changed to: a second drug of interest is prescribed within 1.5 times the estimated prescription interval of the first drug (SA1); two drugs of interest are prescribed on the same day (SA2); both drugs continue to be prescribed for ≥ 90 days from index date (SA3). MAGD definition was changed to: equivalent to (SA4) or double (SA5) the length of most recent prescription. To be considered a patient with LUTS, patients required a LUTS diagnosis code (Additional file 1: Tables S2a–c) registered any time before the index date (SA6). In the final sensitivity analysis, patients diagnosed with hypertension were excluded (SA7).

Results

Patients

Of 223,831 patients with one or more LUTS drug prescription between 1 January 2014 and 31 December 2016, 79,472 were included in the study (61.3% [$n = 48{,}690$] in the male and 38.7% [$n = 30{,}782$] in the female cohort) (Fig. 1) (Additional file 1: Table S3a and b).

At index date, the mean age was 65.5 years. In the 12-month pre-index period, patients had a mean of 0.2 new diagnoses of QOF chronic diseases and were prescribed a mean of 9.6 drugs; 5.1% of patients had received an antimuscarinic agent (Tables 1, 2). Approximately one in five patients (16.3%) had a LUTS diagnostic code, the notable exceptions being for doxazosin and duloxetine monotherapy (3% each).

Extent of monotherapy and combination drug use

Of all men ($n = 48{,}690$), 82.5% received any BPO drug (alpha-blocker and/or 5-ARI), 74.6% received any (one or more) BPO drug without an OAB drug, 25.4% received any OAB drug (antimuscarinic agent and/or mirabegron) (17.5% received any [one or more] OAB drug without a BPO drug, and 7.9% received any BPO drug plus any OAB drug). As either mono- or combination therapy, 77.1% were receiving an alpha-blocker, 18.9% received a

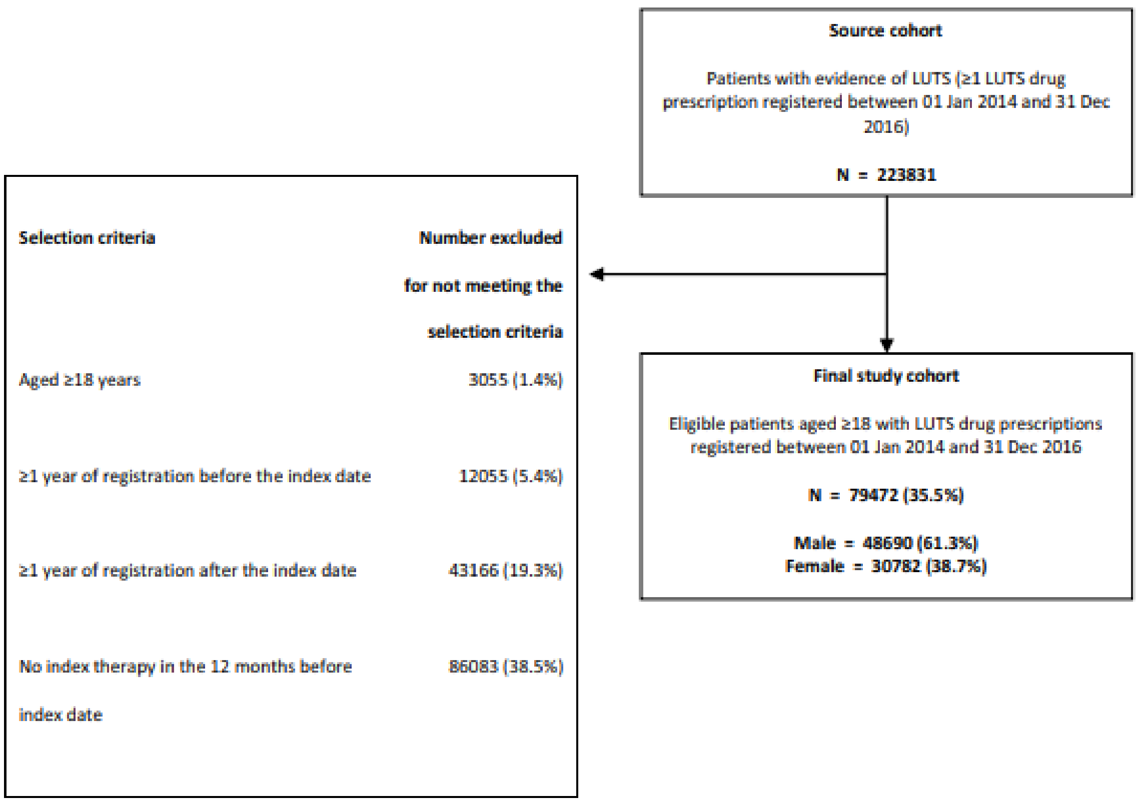


Fig. 1 Selection criteria and study cohorts

5-ARI, 23.9% an antimuscarinic agent and 2.1% mirabegron. The most common drug received either as mono- or combination therapy was tamsulosin (61.2% of all men) and the most common combination was finasteride plus tamsulosin (8.6%, with or without additional drugs). Of all women ($n = 30{,}782$), 94.5% received any OAB drug, 6.0% received a SUI drug, and 0.5% received any OAB drug plus a SUI drug (Additional file 1: Table S3b). As either mono- or combination therapy, 87.7% were receiving an antimuscarinic agent and 9.7% mirabegron. The extent of drug class use is summarized in Tables 3, 4 and 5, and in Additional file 1: Tables S3b and 4.

Male LUTS (including OAB) sub-cohort

In this sub-cohort of 12,383 men treated with any OAB drug, 64.2% received monotherapy with an OAB drug and 35.8% received combinations (31.2% with any OAB drug plus any BPO drug and 7.8% with two or more OAB drugs [3.2% with and 4.6% without a BPO drug]) (Table 3). In addition, 94.1% received any antimuscarinic agent, 8.4% received mirabegron, 2.5% received any antimuscarinic agent plus mirabegron and 5.4% received two or more antimuscarinic agents (Table 3). In this sub-cohort 26.9% of patients received combination therapy including any alpha-blocker and any antimuscarinic agent and 2.6% received any alpha-blocker plus mirabegron. Furthermore, 7.7% of this sub-cohort received triple therapy with any alpha-blocker plus any 5-ARI plus any OAB drug (Table 3).

The most frequently prescribed OAB monotherapies in this sub-cohort were solifenacin (22.3%), oxybutynin (21.1%), tolterodine (11.7%) and mirabegron (4.1%) (Table 3; Additional file 1: Table S5).

The most common OAB drug either alone or in combination was solifenacin (40.6% of the OAB sub-cohort). The most frequently prescribed combination was solifenacin plus tamsulosin (7.3% of sub-cohort for this two-drug combination alone; 11.7% when also including additional drugs), followed by oxybutynin plus tamsulosin and then tolterodine plus tamsulosin, with 2.9% and 2.0% of sub-cohort, respectively. A total of 0.8% of this sub-cohort received mirabegron plus solifenacin alone (1.4% when also including additional drugs).

Table 1 Population demographic and clinical characteristics for male sub-cohorts

		LUTS (including OAB) N = 12,383	**BPO only** N = 36,307
Age at index date	n	12,383	36,307
	Mean (SD)	65.54 (15.73)	67.98 (12.47)
	18–24	192 (1.6%)	119 (0.3%)
	25–34	434 (3.5%)	356 (1.0%)
	35–44	736 (5.9%)	997 (2.7%)
	45–54	1438 (11.6%)	3586 (9.9%)
	55–64	2188 (17.7%)	7746 (21.3%)
	65–74	3379 (27.3%)	11,905 (32.8%)
	≥ 75	4016 (32.4%)	11,598 (31.9%)
Index of multiple deprivation at index prescription (GP surgery level)	n	5112	16,534
	1 = least deprived	633 (12.4%)	2770 (16.8%)
	2	1124 (22.0%)	3654 (22.1%)
	3	968 (18.9%)	3175 (19.2%)
	4	963 (18.8%)	2926 (17.7%)
	5 = most deprived	1424 (27.9%)	4009 (24.2%)
New comorbidities	n	12,383	36,307
Count of newly diagnosed chronic diseases from the QOF within the 12-month pre-index period	Mean (SD)	0.21 (0.50)	0.22 (0.51)
	0	10,228 (82.6%)	29,480 (81.2%)
	1	1790 (14.5%)	5700 (15.7%)
	2	313 (2.5%)	978 (2.7%)
	3+	52 (0.4%)	149 (0.4%)
Polypharmacy	n	12,383	36,307
Number of distinct BNF headers within the 12-month pre-index period	Mean (SD)	9.81 (7.27)	8.52 (6.45)
	0	576 (4.7%)	1757 (4.8%)
	[1; 3]	1931 (15.6%)	6668 (18.4%)
	[4; 7]	2936 (23.7%)	10,342 (28.5%)
	[8; 19]	5707 (46.1%)	15,220 (41.9%)
	20+	1233 (10.0%)	2320 (6.4%)
Antimuscarinic treatment experience within the 12-month pre-index period	n	12,383	36,307
	Yes	908 (7.3%)	397 (1.1%)
	No	11,475 (92.7%)	35,910 (98.9%)

Male LUTS (including OAB) sub-cohort patients were those receiving an OAB drug (antimuscarinic and/or mirabegron) with or without a BPO drug (either an alpha-blocker and/or 5-ARI). Male BPO sub-cohort patients were those receiving an alpha-blocker and/or 5-ARI without an OAB drug. Percentages may not total exactly 100 due to rounding

BNF: British National Formulary; *BPO*: benign prostatic obstruction; *GP*: general practitioner; *LUTS*: lower urinary tract symptoms; *OAB*: overactive bladder; *QOF*: Quality and Outcomes Framework; *SD*: standard deviation

Male BPO sub-cohort

In this sub-cohort of 36,307 men, 81.9% received monotherapy (75.6% with any alpha-blocker; 6.3% with any 5-ARI) and 18.1% received combination therapy (15.3% with any alpha-blocker plus any 5-ARI). Tamsulosin monotherapy was the most commonly prescribed (58.3% of sub-cohort patients), followed by doxazosin (15.0%) (Table 4; Additional file 1: Table S6). For combination therapy, 49.7% of combination therapy patients were prescribed finasteride plus tamsulosin (9.0% of this sub-cohort for these two drugs alone; 10.0% when also including additional drugs), followed by dutasteride plus tamsulosin and doxazosin plus tamsulosin. In addition, 93.6% of patients in this sub-cohort overall received an alpha-blocker and 21.7% a 5-ARI.

Female LUTS (including OAB) sub-cohort

In this sub-cohort of 29,094 women, 90.5% of patients received monotherapy (83.4% any antimuscarinic, 7.1% mirabegron) and 9.5% combination therapy (9.0% with two or more OAB drugs). In addition, 0.5% of women in this sub-cohort received any OAB drug plus duloxetine

Table 2 Population demographic and clinical characteristics for female sub-cohorts

		LUTS (including OAB) N = 29,094	**SUI N = 1688**
Age at index date	n	29,094	1688
	Mean (SD)	62.92 (16.77)	54.24 (16.29)
	18–24	604 (2.1%)	32 (1.9%)
	25–34	1121 (3.9%)	159 (9.4%)
	35–44	2536 (8.7%)	315 (18.7%)
	45–54	4835 (16.6%)	399 (23.6%)
	55–64	5264 (18.1%)	315 (18.7%)
	65–74	6446 (22.2%)	248 (14.7%)
	≥ 75	8288 (28.5%)	220 (13.0%)
Index of multiple deprivation at index prescription (GP surgery level)	n	11,999	665
	1 = least deprived	1534 (12.8%)	86 (12.9%)
	2	2418 (20.2%)	148 (22.3%)
	3	2292 (19.1%)	137 (20.6%)
	4	2285 (19.0%)	105 (15.8%)
	5 = most deprived	3470 (28.9%)	189 (28.4%)
New comorbidities	n	29,094	1688
Count of newly diagnosed chronic diseases from the QOF within the 12-month pre-index period	Mean (SD)	0.20 (0.48)	0.23 (0.53)
	0	24,327 (83.6%)	1374 (81.4%)
	1	3950 (13.6%)	248 (14.7%)
	2	712 (2.4%)	56 (3.3%)
	3+	105 (0.4%)	10 (0.6%)
Polypharmacy	n	29,094	1688
Number of distinct BNF headers within the 12-month pre-index period	Mean (SD)	10.77 (7.49)	11.55 (7.42)
	0	681 (2.3%)	29 (1.7%)
	[1; 3]	3766 (12.9%)	165 (9.8%)
	[4; 7]	6944 (23.9%)	384 (22.7%)
	[8; 19]	14,178 (48.7%)	873 (51.7%)
	20+	3525 (12.1%)	237 (14.0%)
Antimuscarinic treatment experience within the 12-month pre-index period	n	29,094	1688
	Yes	2681 (9.2%)	56 (3.3%)
	No	26,413 (90.8%)	1632 (96.7%)

Female LUTS (including OAB) sub-cohort patients were those receiving an OAB drug (antimuscarinic and/or mirabegron) with or without a SUI drug (duloxetine). Female SUI sub-cohort patients were those receiving duloxetine without an OAB drug. Percentages may not total exactly 100 due to rounding

BNF: British National Formulary; *GP*: general practitioner; *LUTS*: lower urinary tract symptoms; *OAB*: overactive bladder; *QOF*: Quality and Outcomes Framework; *SD*: standard deviation; *SUI*: stress urinary incontinence

(Table 5). Mirabegron plus duloxetine was prescribed to 0.04% of patients in this sub-cohort. A combination of any two or more antimuscarinic agents (± mirabegron) was used by 6.3% of sub-cohort patients and any antimuscarinic agent plus mirabegron by 2.7%. The most common OAB drug either alone or in combination was solifenacin (41.0% of the OAB sub-cohort) and 10.2% of this sub-cohort overall received mirabegron.

Solifenacin was the most frequently prescribed monotherapy (34.7% of this sub-cohort), followed by oxybutynin and tolterodine (Table 5; Additional file 1: Table S7); 92.8% of sub-cohort patients were prescribed any antimuscarinic agent. The most frequently prescribed combinations were solifenacin plus tolterodine, oxybutynin plus solifenacin and mirabegron plus solifenacin.

Female SUI sub-cohort

Duloxetine was prescribed to all ($n = 1688$) sub-cohort patients and was the only drug used in women with SUI, as defined in the base-case.

Persistence

Kaplan Meier curves of TTD by mono- and combination drug therapy for the male BPO sub-cohort, and for

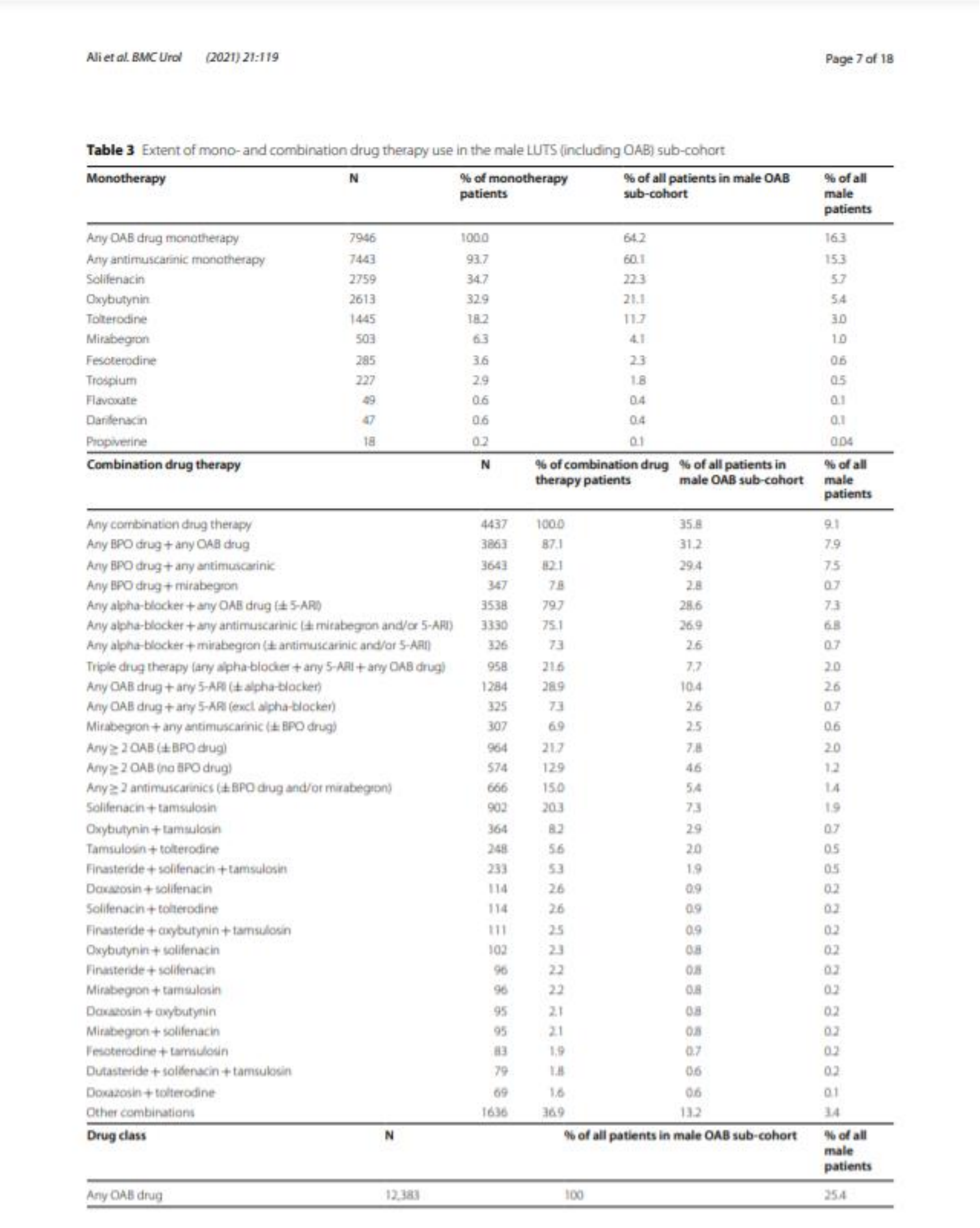


Table 3 Extent of mono- and combination drug therapy use in the male LUTS (including OAB) sub-cohort

Monotherapy	N	% of monotherapy patients	% of all patients in male OAB sub-cohort	% of all male patients
Any OAB drug monotherapy	7946	100.0	64.2	16.3
Any antimuscarinic monotherapy	7443	93.7	60.1	15.3
Solifenacin	2759	34.7	22.3	5.7
Oxybutynin	2613	32.9	21.1	5.4
Tolterodine	1445	18.2	11.7	3.0
Mirabegron	503	6.3	4.1	1.0
Fesoterodine	285	3.6	2.3	0.6
Trospium	227	2.9	1.8	0.5
Flavoxate	49	0.6	0.4	0.1
Darifenacin	47	0.6	0.4	0.1
Propiverine	18	0.2	0.1	0.04

Combination drug therapy	N	% of combination drug therapy patients	% of all patients in male OAB sub-cohort	% of all male patients
Any combination drug therapy	4437	100.0	35.8	9.1
Any BPO drug + any OAB drug	3863	87.1	31.2	7.9
Any BPO drug + any antimuscarinic	3643	82.1	29.4	7.5
Any BPO drug + mirabegron	347	7.8	2.8	0.7
Any alpha-blocker + any OAB drug (± 5-ARI)	3538	79.7	28.6	7.3
Any alpha-blocker + any antimuscarinic (± mirabegron and/or 5-ARI)	3330	75.1	26.9	6.8
Any alpha-blocker + mirabegron (± antimuscarinic and/or 5-ARI)	326	7.3	2.6	0.7
Triple drug therapy (any alpha-blocker + any 5-ARI + any OAB drug)	958	21.6	7.7	2.0
Any OAB drug + any 5-ARI (± alpha-blocker)	1284	28.9	10.4	2.6
Any OAB drug + any 5-ARI (excl. alpha-blocker)	325	7.3	2.6	0.7
Mirabegron + any antimuscarinic (± BPO drug)	307	6.9	2.5	0.6
Any ≥ 2 OAB (± BPO drug)	964	21.7	7.8	2.0
Any ≥ 2 OAB (no BPO drug)	574	12.9	4.6	1.2
Any ≥ 2 antimuscarinics (± BPO drug and/or mirabegron)	666	15.0	5.4	1.4
Solifenacin + tamsulosin	902	20.3	7.3	1.9
Oxybutynin + tamsulosin	364	8.2	2.9	0.7
Tamsulosin + tolterodine	248	5.6	2.0	0.5
Finasteride + solifenacin + tamsulosin	233	5.3	1.9	0.5
Doxazosin + solifenacin	114	2.6	0.9	0.2
Solifenacin + tolterodine	114	2.6	0.9	0.2
Finasteride + oxybutynin + tamsulosin	111	2.5	0.9	0.2
Oxybutynin + solifenacin	102	2.3	0.8	0.2
Finasteride + solifenacin	96	2.2	0.8	0.2
Mirabegron + tamsulosin	96	2.2	0.8	0.2
Doxazosin + oxybutynin	95	2.1	0.8	0.2
Mirabegron + solifenacin	95	2.1	0.8	0.2
Fesoterodine + tamsulosin	83	1.9	0.7	0.2
Dutasteride + solifenacin + tamsulosin	79	1.8	0.6	0.2
Doxazosin + tolterodine	69	1.6	0.6	0.1
Other combinations	1636	36.9	13.2	3.4

Drug class	N	% of all patients in male OAB sub-cohort	% of all male patients
Any OAB drug	12,383	100	25.4

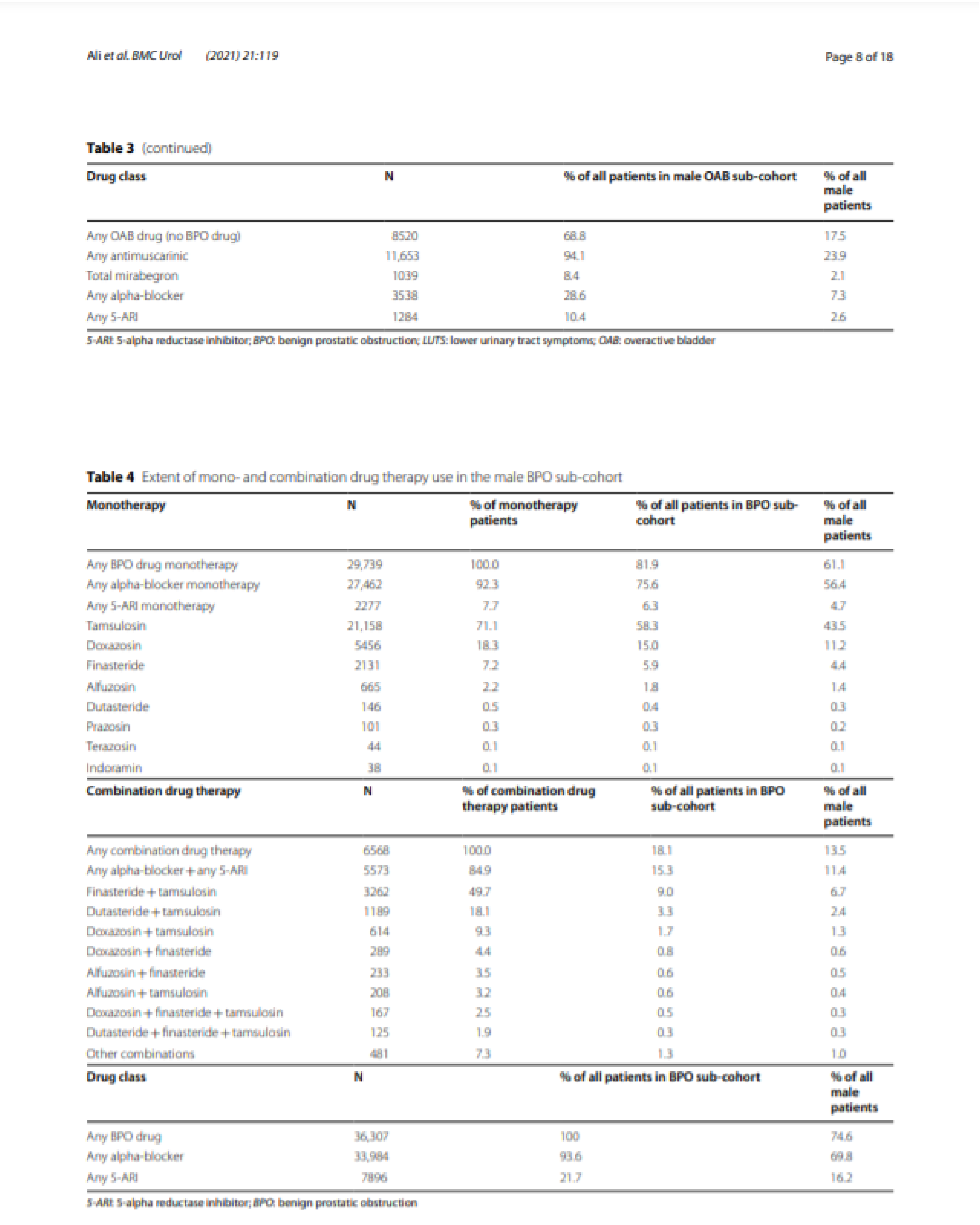


Table 3 (continued)

Drug class	N	% of all patients in male OAB sub-cohort	% of all male patients
Any OAB drug (no BPO drug)	8520	68.8	17.5
Any antimuscarinic	11,653	94.1	23.9
Total mirabegron	1039	8.4	2.1
Any alpha-blocker	3538	28.6	7.3
Any 5-ARI	1284	10.4	2.6

5-ARI: 5-alpha reductase inhibitor; *BPO*: benign prostatic obstruction; *LUTS*: lower urinary tract symptoms; *OAB*: overactive bladder

Table 4 Extent of mono- and combination drug therapy use in the male BPO sub-cohort

Monotherapy	N	% of monotherapy patients	% of all patients in BPO sub-cohort	% of all male patients
Any BPO drug monotherapy	29,739	100.0	81.9	61.1
Any alpha-blocker monotherapy	27,462	92.3	75.6	56.4
Any 5-ARI monotherapy	2277	7.7	6.3	4.7
Tamsulosin	21,158	71.1	58.3	43.5
Doxazosin	5456	18.3	15.0	11.2
Finasteride	2131	7.2	5.9	4.4
Alfuzosin	665	2.2	1.8	1.4
Dutasteride	146	0.5	0.4	0.3
Prazosin	101	0.3	0.3	0.2
Terazosin	44	0.1	0.1	0.1
Indoramin	38	0.1	0.1	0.1
Combination drug therapy	**N**	**% of combination drug therapy patients**	**% of all patients in BPO sub-cohort**	**% of all male patients**
Any combination drug therapy	6568	100.0	18.1	13.5
Any alpha-blocker + any 5-ARI	5573	84.9	15.3	11.4
Finasteride + tamsulosin	3262	49.7	9.0	6.7
Dutasteride + tamsulosin	1189	18.1	3.3	2.4
Doxazosin + tamsulosin	614	9.3	1.7	1.3
Doxazosin + finasteride	289	4.4	0.8	0.6
Alfuzosin + finasteride	233	3.5	0.6	0.5
Alfuzosin + tamsulosin	208	3.2	0.6	0.4
Doxazosin + finasteride + tamsulosin	167	2.5	0.5	0.3
Dutasteride + finasteride + tamsulosin	125	1.9	0.3	0.3
Other combinations	481	7.3	1.3	1.0
Drug class	**N**		**% of all patients in BPO sub-cohort**	**% of all male patients**
Any BPO drug	36,307		100	74.6
Any alpha-blocker	33,984		93.6	69.8
Any 5-ARI	7896		21.7	16.2

5-ARI: 5-alpha reductase inhibitor; *BPO*: benign prostatic obstruction

Table 5 Extent of mono- and combination drug therapy use in the female LUTS (including OAB) sub-cohort

Monotherapy	**N**	**% of monotherapy patients**	**% of all patients in female OAB sub-cohort**	**% of all female patients**
Any OAB drug monotherapy	26,338	100.0	90.5	85.6
Any antimuscarinic monotherapy	24,263	92.1	83.4	78.8
Solifenacin	10,083	38.3	34.7	32.8
Oxybutynin	7852	29.8	27.0	25.5
Tolterodine	4020	15.3	13.8	13.1
Mirabegron	2075	7.9	7.1	6.7
Fesoterodine	1173	4.5	4.0	3.8
Trospium	754	2.9	2.6	2.4
Darifenacin	209	0.8	0.7	0.7
Flavoxate	96	0.4	0.3	0.3
Propiverine	76	0.3	0.3	0.2
Combination drug therapy	**N**	**% of combination drug therapy patients**	**% of all patients in female OAB sub-cohort**	**% of all female patients**
All combination drug therapy	2756	100.0	9.5	9.0
Any ≥ 2 OAB drugs	2621	95.1	9.0	8.5
Mirabegron + any antimuscarinic	788	28.6	2.7	2.6
Any ≥ 2 antimuscarinics (± mirabegron)	1847	67.0	6.3	6.0
Duloxetine + any OAB drug	144	5.2	0.5	0.5
Solifenacin + tolterodine	507	18.4	1.7	1.6
Oxybutynin + solifenacin	458	16.6	1.6	1.5
Mirabegron + solifenacin	417	15.1	1.4	1.4
Fesoterodine + solifenacin	174	6.3	0.6	0.6
Oxybutynin + tolterodine	174	6.3	0.6	0.6
Other combinations	1026	37.2	3.5	3.3
Drug class	**N**		**% of all patient in OAB sub-cohort**	**% of all female patients**
Any OAB drug	29,094		100	94.5
Any antimuscarinic	27,010		92.8	87.7
Total mirabegron	2972		10.2	9.7

LUTS: lower urinary tract symptoms; *OAB*: overactive bladder

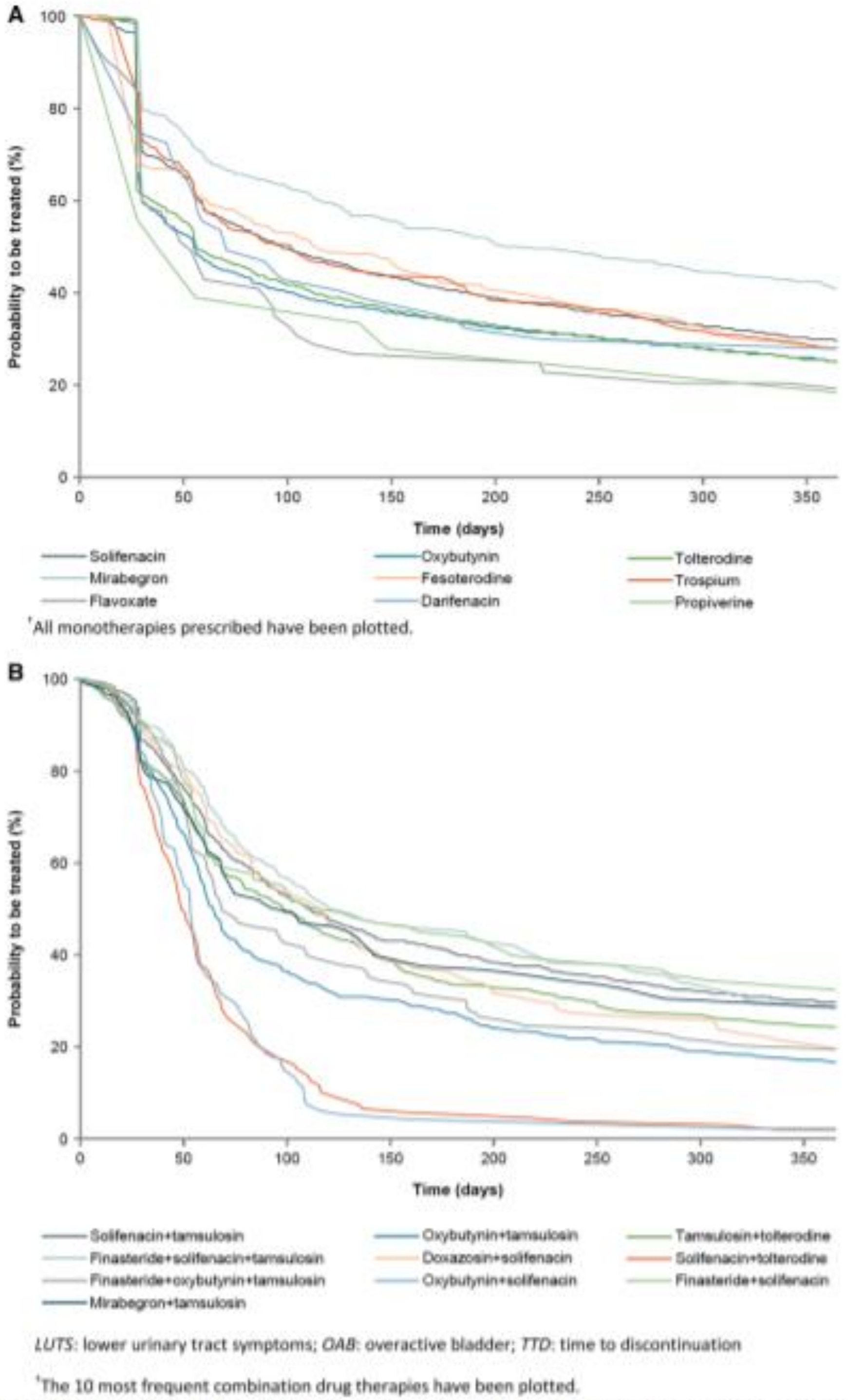
duloxetine in the female SUI sub-cohort, are included in Additional file 1: Figures S1–S3.

Male LUTS (including OAB) sub-cohort

For monotherapy, mirabegron had the longest median TTD (205 days), followed by fesoterodine (115 days), trospium (102 days) and solifenacin (97 days) (Fig. 2a; Table 6). These drugs also displayed the highest 12-month persistence rates (Table 7). For combination therapies, tamsulosin plus trospium had the longest median TTD (144 days); however, the sample size was small ($n = 65$). The longest median TTD for combination therapy with a sample size > 100 was 121 days for finasteride plus solifenacin plus tamsulosin (Fig. 2b). The highest 12-month persistence was with finasteride plus solifenacin (32.3%) (Table 7).

Male BPO sub-cohort

For monotherapy, median TTD was longest for doxazosin and finasteride (> 365 days each [median not reached]), followed by tamsulosin (329 days) and dutasteride (305 days) (however, see sensitivity analyses below). Doxazosin had the highest 12-month persistence (67.8%) followed by finasteride (53.3%) and tamsulosin (48.4%). For combination therapies, the highest 12-month persistence was for dutasteride plus tamsulosin (56.3%) followed by doxazosin plus dutasteride (55.6%) (Additional file 1: Tables S8 and S9).



†All monotherapies prescribed have been plotted.

LUTS: lower urinary tract symptoms; *OAB*: overactive bladder; *TTD*: time to discontinuation

†The 10 most frequent combination drug therapies have been plotted.

Fig. 2 TTD in male LUTS (including OAB) sub-cohort (Kaplan–Meier estimates)† for **A** monotherapies. †All monotherapies prescribed have been plotted. **B** Combination drug therapies. *LUTS*: lower urinary tract symptoms; *OAB*: overactive bladder; *TTD*: time to discontinuation. †The 10 most frequent combination drug therapies have been plotted

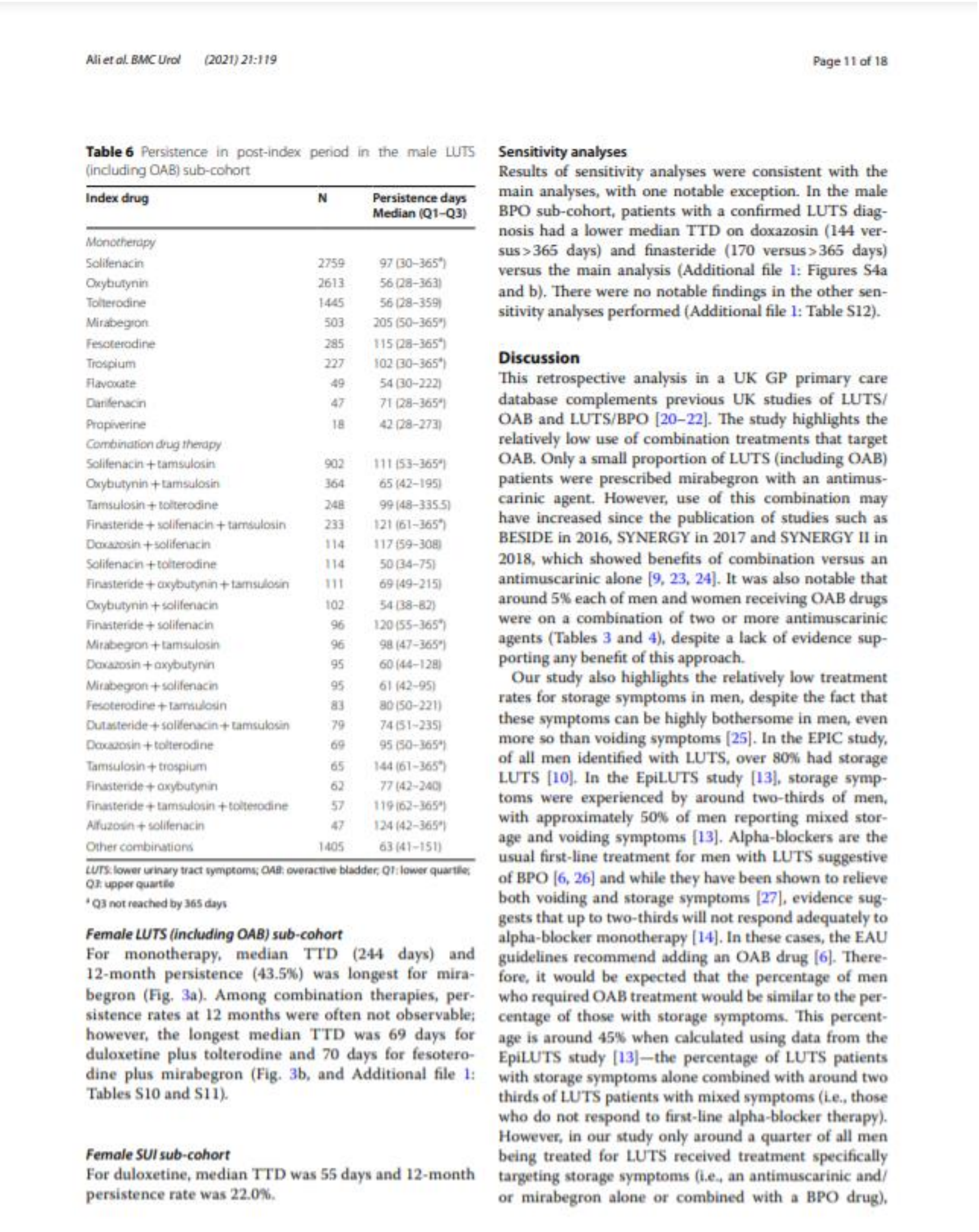


Table 6 Persistence in post-index period in the male LUTS (including OAB) sub-cohort

Index drug	N	Persistence days Median (Q1–Q3)
Monotherapy		
Solifenacin	2759	97 (30–365[a])
Oxybutynin	2613	56 (28–363)
Tolterodine	1445	56 (28–359)
Mirabegron	503	205 (50–365[a])
Fesoterodine	285	115 (28–365[a])
Trospium	227	102 (30–365[a])
Flavoxate	49	54 (30–222)
Darifenacin	47	71 (28–365[a])
Propiverine	18	42 (28–273)
Combination drug therapy		
Solifenacin + tamsulosin	902	111 (53–365[a])
Oxybutynin + tamsulosin	364	65 (42–195)
Tamsulosin + tolterodine	248	99 (48–335.5)
Finasteride + solifenacin + tamsulosin	233	121 (61–365[a])
Doxazosin + solifenacin	114	117 (59–308)
Solifenacin + tolterodine	114	50 (34–75)
Finasteride + oxybutynin + tamsulosin	111	69 (49–215)
Oxybutynin + solifenacin	102	54 (38–82)
Finasteride + solifenacin	96	120 (55–365[a])
Mirabegron + tamsulosin	96	98 (47–365[a])
Doxazosin + oxybutynin	95	60 (44–128)
Mirabegron + solifenacin	95	61 (42–95)
Fesoterodine + tamsulosin	83	80 (50–221)
Dutasteride + solifenacin + tamsulosin	79	74 (51–235)
Doxazosin + tolterodine	69	95 (50–365[a])
Tamsulosin + trospium	65	144 (61–365[a])
Finasteride + oxybutynin	62	77 (42–240)
Finasteride + tamsulosin + tolterodine	57	119 (62–365[a])
Alfuzosin + solifenacin	47	124 (42–365[a])
Other combinations	1405	63 (41–151)

LUTS: lower urinary tract symptoms; *OAB*: overactive bladder; *Q1*: lower quartile; *Q3*: upper quartile

[a] Q3 not reached by 365 days

Female LUTS (including OAB) sub-cohort

For monotherapy, median TTD (244 days) and 12-month persistence (43.5%) was longest for mirabegron (Fig. 3a). Among combination therapies, persistence rates at 12 months were often not observable; however, the longest median TTD was 69 days for duloxetine plus tolterodine and 70 days for fesoterodine plus mirabegron (Fig. 3b, and Additional file 1: Tables S10 and S11).

Female SUI sub-cohort

For duloxetine, median TTD was 55 days and 12-month persistence rate was 22.0%.

Sensitivity analyses

Results of sensitivity analyses were consistent with the main analyses, with one notable exception. In the male BPO sub-cohort, patients with a confirmed LUTS diagnosis had a lower median TTD on doxazosin (144 versus > 365 days) and finasteride (170 versus > 365 days) versus the main analysis (Additional file 1: Figures S4a and b). There were no notable findings in the other sensitivity analyses performed (Additional file 1: Table S12).

Discussion

This retrospective analysis in a UK GP primary care database complements previous UK studies of LUTS/OAB and LUTS/BPO [20–22]. The study highlights the relatively low use of combination treatments that target OAB. Only a small proportion of LUTS (including OAB) patients were prescribed mirabegron with an antimuscarinic agent. However, use of this combination may have increased since the publication of studies such as BESIDE in 2016, SYNERGY in 2017 and SYNERGY II in 2018, which showed benefits of combination versus an antimuscarinic alone [9, 23, 24]. It was also notable that around 5% each of men and women receiving OAB drugs were on a combination of two or more antimuscarinic agents (Tables 3 and 4), despite a lack of evidence supporting any benefit of this approach.

Our study also highlights the relatively low treatment rates for storage symptoms in men, despite the fact that these symptoms can be highly bothersome in men, even more so than voiding symptoms [25]. In the EPIC study, of all men identified with LUTS, over 80% had storage LUTS [10]. In the EpiLUTS study [13], storage symptoms were experienced by around two-thirds of men, with approximately 50% of men reporting mixed storage and voiding symptoms [13]. Alpha-blockers are the usual first-line treatment for men with LUTS suggestive of BPO [6, 26] and while they have been shown to relieve both voiding and storage symptoms [27], evidence suggests that up to two-thirds will not respond adequately to alpha-blocker monotherapy [14]. In these cases, the EAU guidelines recommend adding an OAB drug [6]. Therefore, it would be expected that the percentage of men who required OAB treatment would be similar to the percentage of those with storage symptoms. This percentage is around 45% when calculated using data from the EpiLUTS study [13]—the percentage of LUTS patients with storage symptoms alone combined with around two thirds of LUTS patients with mixed symptoms (i.e., those who do not respond to first-line alpha-blocker therapy). However, in our study only around a quarter of all men being treated for LUTS received treatment specifically targeting storage symptoms (i.e., an antimuscarinic and/or mirabegron alone or combined with a BPO drug),

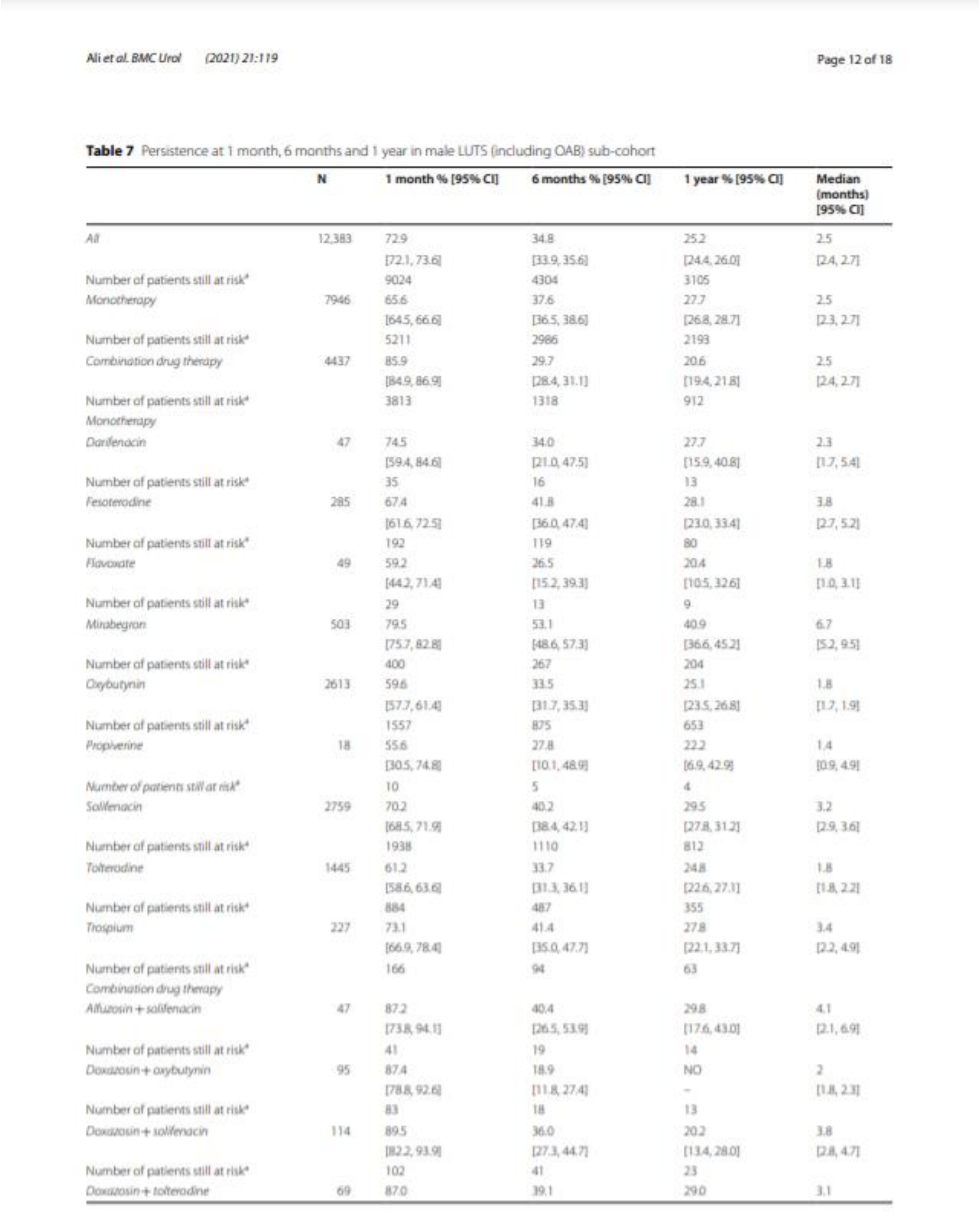


Table 7 Persistence at 1 month, 6 months and 1 year in male LUTS (including OAB) sub-cohort

	N	1 month % [95% CI]	6 months % [95% CI]	1 year % [95% CI]	Median (months) [95% CI]
All	12,383	72.9	34.8	25.2	2.5
		[72.1, 73.6]	[33.9, 35.6]	[24.4, 26.0]	[2.4, 2.7]
Number of patients still at risk[a]		9024	4304	3105	
Monotherapy	7946	65.6	37.6	27.7	2.5
		[64.5, 66.6]	[36.5, 38.6]	[26.8, 28.7]	[2.3, 2.7]
Number of patients still at risk[a]		5211	2986	2193	
Combination drug therapy	4437	85.9	29.7	20.6	2.5
		[84.9, 86.9]	[28.4, 31.1]	[19.4, 21.8]	[2.4, 2.7]
Number of patients still at risk[a]		3813	1318	912	
Monotherapy					
Darifenacin	47	74.5	34.0	27.7	2.3
		[59.4, 84.6]	[21.0, 47.5]	[15.9, 40.8]	[1.7, 5.4]
Number of patients still at risk[a]		35	16	13	
Fesoterodine	285	67.4	41.8	28.1	3.8
		[61.6, 72.5]	[36.0, 47.4]	[23.0, 33.4]	[2.7, 5.2]
Number of patients still at risk[a]		192	119	80	
Flavoxate	49	59.2	26.5	20.4	1.8
		[44.2, 71.4]	[15.2, 39.3]	[10.5, 32.6]	[1.0, 3.1]
Number of patients still at risk[a]		29	13	9	
Mirabegron	503	79.5	53.1	40.9	6.7
		[75.7, 82.8]	[48.6, 57.3]	[36.6, 45.2]	[5.2, 9.5]
Number of patients still at risk[a]		400	267	204	
Oxybutynin	2613	59.6	33.5	25.1	1.8
		[57.7, 61.4]	[31.7, 35.3]	[23.5, 26.8]	[1.7, 1.9]
Number of patients still at risk[a]		1557	875	653	
Propiverine	18	55.6	27.8	22.2	1.4
		[30.5, 74.8]	[10.1, 48.9]	[6.9, 42.9]	[0.9, 4.9]
Number of patients still at risk[a]		10	5	4	
Solifenacin	2759	70.2	40.2	29.5	3.2
		[68.5, 71.9]	[38.4, 42.1]	[27.8, 31.2]	[2.9, 3.6]
Number of patients still at risk[a]		1938	1110	812	
Tolterodine	1445	61.2	33.7	24.8	1.8
		[58.6, 63.6]	[31.3, 36.1]	[22.6, 27.1]	[1.8, 2.2]
Number of patients still at risk[a]		884	487	355	
Trospium	227	73.1	41.4	27.8	3.4
		[66.9, 78.4]	[35.0, 47.7]	[22.1, 33.7]	[2.2, 4.9]
Number of patients still at risk[a]		166	94	63	
Combination drug therapy					
Alfuzosin + solifenacin	47	87.2	40.4	29.8	4.1
		[73.8, 94.1]	[26.5, 53.9]	[17.6, 43.0]	[2.1, 6.9]
Number of patients still at risk[a]		41	19	14	
Doxazosin + oxybutynin	95	87.4	18.9	NO	2
		[78.8, 92.6]	[11.8, 27.4]	–	[1.8, 2.3]
Number of patients still at risk[a]		83	18	13	
Doxazosin + solifenacin	114	89.5	36.0	20.2	3.8
		[82.2, 93.9]	[27.3, 44.7]	[13.4, 28.0]	[2.8, 4.7]
Number of patients still at risk[a]		102	41	23	
Doxazosin + tolterodine	69	87.0	39.1	29.0	3.1

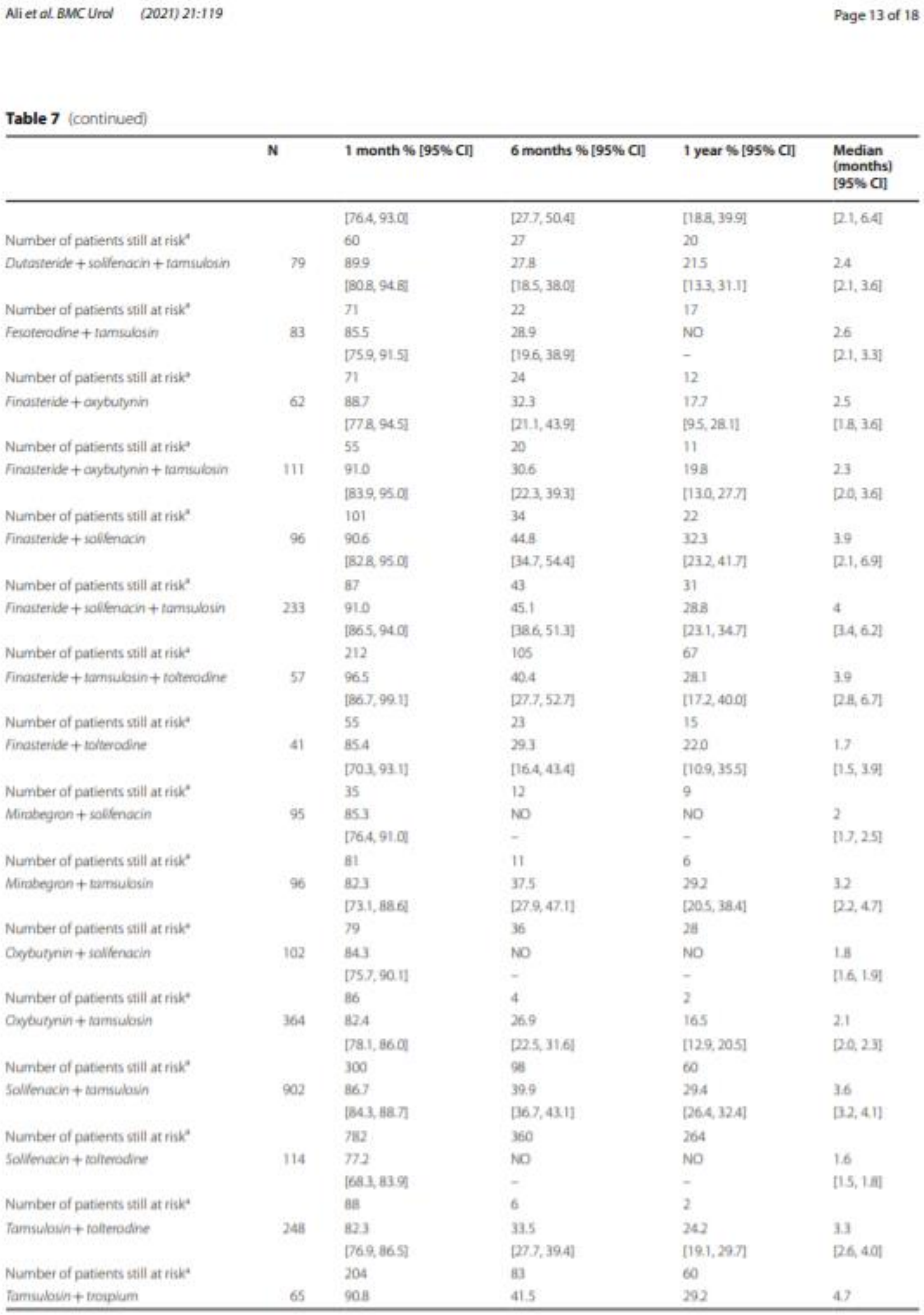


Table 7 (continued)

	N	1 month % [95% CI]	6 months % [95% CI]	1 year % [95% CI]	Median (months) [95% CI]
		[76.4, 93.0]	[27.7, 50.4]	[18.8, 39.9]	[2.1, 6.4]
Number of patients still at risk[a]		60	27	20	
Dutasteride + solifenacin + tamsulosin	79	89.9	27.8	21.5	2.4
		[80.8, 94.8]	[18.5, 38.0]	[13.3, 31.1]	[2.1, 3.6]
Number of patients still at risk[a]		71	22	17	
Fesoterodine + tamsulosin	83	85.5	28.9	NO	2.6
		[75.9, 91.5]	[19.6, 38.9]	–	[2.1, 3.3]
Number of patients still at risk[a]		71	24	12	
Finasteride + oxybutynin	62	88.7	32.3	17.7	2.5
		[77.8, 94.5]	[21.1, 43.9]	[9.5, 28.1]	[1.8, 3.6]
Number of patients still at risk[a]		55	20	11	
Finasteride + oxybutynin + tamsulosin	111	91.0	30.6	19.8	2.3
		[83.9, 95.0]	[22.3, 39.3]	[13.0, 27.7]	[2.0, 3.6]
Number of patients still at risk[a]		101	34	22	
Finasteride + solifenacin	96	90.6	44.8	32.3	3.9
		[82.8, 95.0]	[34.7, 54.4]	[23.2, 41.7]	[2.1, 6.9]
Number of patients still at risk[a]		87	43	31	
Finasteride + solifenacin + tamsulosin	233	91.0	45.1	28.8	4
		[86.5, 94.0]	[38.6, 51.3]	[23.1, 34.7]	[3.4, 6.2]
Number of patients still at risk[a]		212	105	67	
Finasteride + tamsulosin + tolterodine	57	96.5	40.4	28.1	3.9
		[86.7, 99.1]	[27.7, 52.7]	[17.2, 40.0]	[2.8, 6.7]
Number of patients still at risk[a]		55	23	15	
Finasteride + tolterodine	41	85.4	29.3	22.0	1.7
		[70.3, 93.1]	[16.4, 43.4]	[10.9, 35.5]	[1.5, 3.9]
Number of patients still at risk[a]		35	12	9	
Mirabegron + solifenacin	95	85.3	NO	NO	2
		[76.4, 91.0]	–	–	[1.7, 2.5]
Number of patients still at risk[a]		81	11	6	
Mirabegron + tamsulosin	96	82.3	37.5	29.2	3.2
		[73.1, 88.6]	[27.9, 47.1]	[20.5, 38.4]	[2.2, 4.7]
Number of patients still at risk[a]		79	36	28	
Oxybutynin + solifenacin	102	84.3	NO	NO	1.8
		[75.7, 90.1]	–	–	[1.6, 1.9]
Number of patients still at risk[a]		86	4	2	
Oxybutynin + tamsulosin	364	82.4	26.9	16.5	2.1
		[78.1, 86.0]	[22.5, 31.6]	[12.9, 20.5]	[2.0, 2.3]
Number of patients still at risk[a]		300	98	60	
Solifenacin + tamsulosin	902	86.7	39.9	29.4	3.6
		[84.3, 88.7]	[36.7, 43.1]	[26.4, 32.4]	[3.2, 4.1]
Number of patients still at risk[a]		782	360	264	
Solifenacin + tolterodine	114	77.2	NO	NO	1.6
		[68.3, 83.9]	–	–	[1.5, 1.8]
Number of patients still at risk[a]		88	6	2	
Tamsulosin + tolterodine	248	82.3	33.5	24.2	3.3
		[76.9, 86.5]	[27.7, 39.4]	[19.1, 29.7]	[2.6, 4.0]
Number of patients still at risk[a]		204	83	60	
Tamsulosin + trospium	65	90.8	41.5	29.2	4.7

Table 7 (continued)

	N	1 month % [95% CI]	6 months % [95% CI]	1 year % [95% CI]	Median (months) [95% CI]
		[80.6, 95.7]	[29.5, 53.1]	[18.8, 40.5]	[2.9, 7.1]
Number of patients still at risk[a]		59	27	19	
Other combinations	1364	85.1	22.4	15.9	2.1
		[83.1, 86.9]	[20.2, 24.6]	[14.0, 17.9]	[2.0, 2.2]
Number of patients still at risk[a]		1161	305	217	

Not Observable indicates that the number of patients still at risk was below the 20% of the initial sample threshold required to calculate persistence, or the median was not reached

CI: confidence interval; *LUTS*: lower urinary tract symptoms; *NO*: not observable; *OAB*: overactive bladder [a]Number of patients still observable at a given time and for whom no events occurred

although this figure refers only to men with treated LUTS, in contrast to the other studies which were based on the general population. Thus, some men with storage symptoms may be receiving inadequate treatment in clinical practice, despite storage symptoms often being the most bothersome component of LUTS [28].

We might also expect to see OAB/BPO drug combination therapy in up to one-third of all men being treated for LUTS (i.e., two-thirds of those with mixed symptoms) [13, 14]. However, in the current study, only 7% were receiving alpha-blocker plus antimuscarinic combination treatment therapy (and only 8% were on any OAB/BPO drug combination), which is consistent with another UK study in which 15% of men with mixed LUTS were reported to be receiving an alpha-blocker combined with an antimuscarinic agent [20].

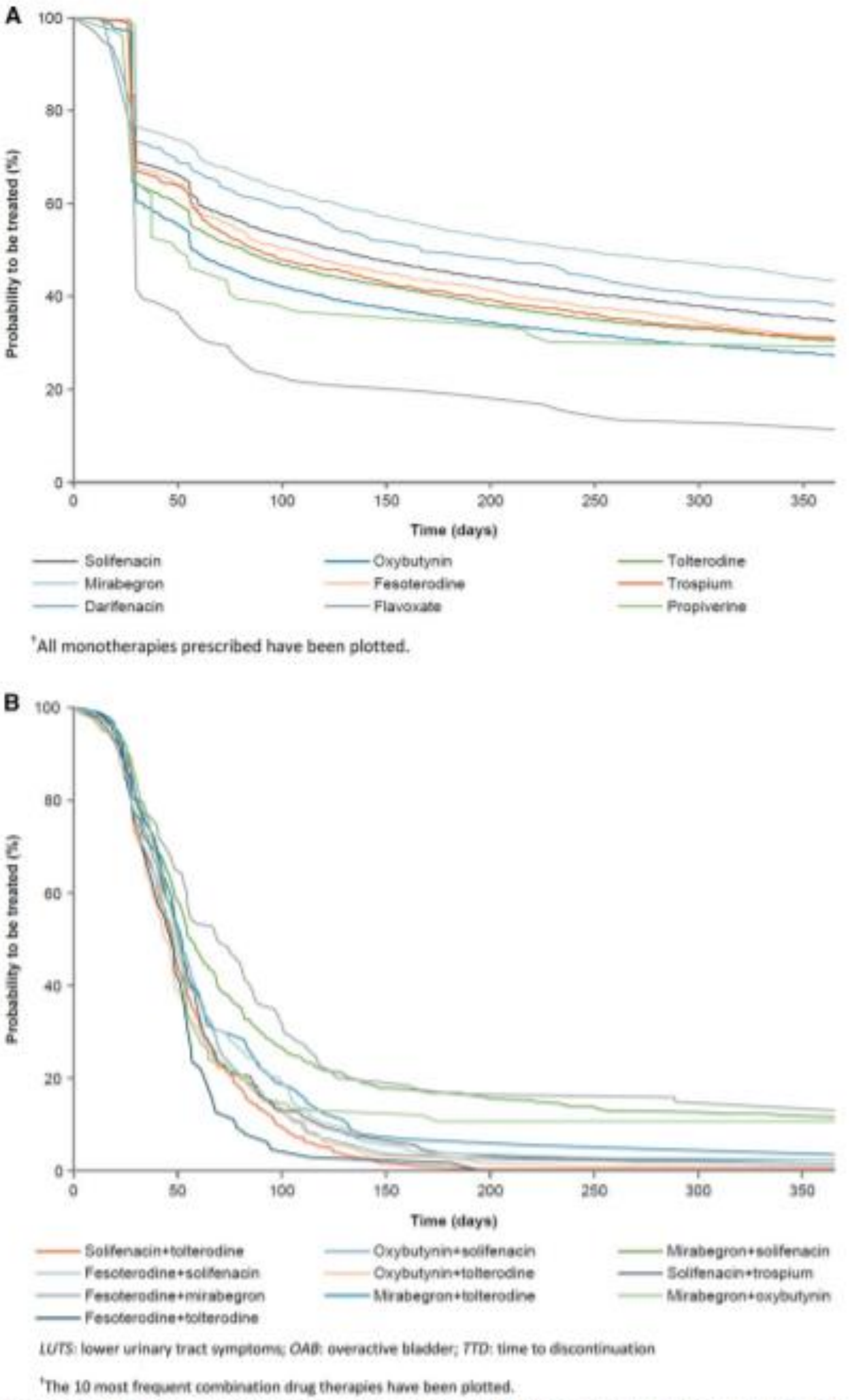
As well as alpha-blockers and 5-ARIs, the EAU guidelines recommend the use of phosphodiesterase type 5 inhibitors (PDE5Is) for the treatment of men with moderate-to-severe LUTS with or without erectile dysfunction [6]. Tadalafil, the only currently licensed PDE5I for male LUTS [6], has been shown to relieve both voiding and storage symptoms [29], although additional therapy may be required for patients with severe LUTS related to BOO [30]. However, this study did not look at tadalafil use due to potential misclassification of patients receiving the drug for erectile dysfunction.

The reasons for the low treatment of storage symptoms in men may be historical, reflecting overemphasis on the prostate-related component of LUTS rather than bladder-related issues. Furthermore, there may be a perceived risk of precipitating urinary retention when using bladder antimuscarinic agents in men with evidence of obstruction, although the available evidence suggests that this risk is low [31]. There is already good evidence supporting the use of alpha-blocker/antimuscarinic combination therapy in men with mixed symptoms [16, 17]. More recently, two randomized, placebo-controlled trials have also demonstrated that mirabegron add-on therapy in men who have residual OAB symptoms while being treated with tamsulosin for LUTS is both effective and well-tolerated [18, 32]. It is hoped that this new evidence will help to improve the overall management of men with mixed symptoms.

Antimuscarinic agents and beta-3 agonists are recommended first-line pharmacological treatments for both men and women with OAB [7, 8] and men with moderate-to-severe LUTS with predominant bladder storage symptoms [6]. However, with antimuscarinics, long-term persistence is often poor due to unmet treatment expectations or adverse events [33]. In our study, mirabegron monotherapy had the highest persistence (both in men and women). Several observational studies also reported higher persistence with mirabegron vs antimuscarinics [22, 34]. Persistence was greater with drug monotherapy than in combination drug therapy, and was particularly poor with combinations of two antimuscarinics in both men and women.

For monotherapy targeting BPO and voiding symptoms (e.g. alpha-blockers and 5-ARIs), persistence was highest for doxazosin and finasteride, but this was not evident in sensitivity analyses based on confirmed LUTS diagnosis. This suggests that the higher persistence with these agents in the main sub-cohorts may be driven by their use in other disorders (e.g., doxazosin for hypertension) and it is notable that only 3% of patients on doxazosin had a LUTS diagnostic code.

A limitation of our study is that in CPRD GOLD, GPs do not systematically report prescriptions issued in secondary care, and reasons for discontinuation were not available in CPRD, which limits interpretation of persistence results. In addition, some treatments are prescribed for conditions other than OAB, LUTS, BPO or SUI (e.g., doxazosin, finasteride and duloxetine), which may influence some of the treatment pattern and/or persistence estimates. The inclusion of fixed-dose combinations may



†All monotherapies prescribed have been plotted.

LUTS: lower urinary tract symptoms; *OAB*: overactive bladder; *TTD*: time to discontinuation

‡The 10 most frequent combination drug therapies have been plotted.

Fig. 3 TTD in female LUTS (including OAB) sub-cohort (Kaplan–Meier estimates)†for **A** monotherapies. †All monotherapies prescribed have been plotted. **B** Combination drug therapies. *LUTS*: lower urinary tract symptoms; *OAB*: overactive bladder; *TTD*: time to discontinuation. ‡The 10 most frequent combination drug therapies have been plotted increase the overall persistence with tamsulosin/solifenacin combination therapy [35]; for tamsulosin/dutasteride fixed-dose combination, the available evidence suggests it may have no impact on persistence [36]. Finally, as this study was performed using a UK general practice database, it is unclear to what extent the results would be generalizable to other healthcare systems.

Conclusions

This study provides new real-world evidence suggesting that men with LUTS may be under-treated with pharmacotherapies that specifically target storage symptoms. Only around a quarter of the men being treated for any LUTS received treatment specifically targeting storage symptoms and around 8% of men received a combination of BPO/OAB drugs for mixed symptoms. In addition, use of combination OAB treatment was low in both men and women, which may reflect the lack of evidence for this approach at the time these patients were being treated. Of all OAB medications, numerically the highest rates of monotherapy persistence were seen with mirabegron in both men and women. Persistence was worse when using combination drug therapy and particularly poor when using two antimuscarinic agents. By highlighting the possible under-treatment of men with treatments that target storage symptoms and the low use of combination OAB treatment (especially with mirabegron plus an antimuscarinic agent), this may help clinicians in the UK to re-assess their approach to pharmacotherapy for patients with bothersome LUTS.

Abbreviations

5-ARI: 5-Alpha reductase inhibitor; BNF: British National Formulary; BOO: Bladder outlet obstruction; BPO: Benign prostatic obstruction; CI: Confidence interval; CPRD: Clinical Practice Research Datalink; EAU: European Association of Urology; GP: General practitioner; IMD: Index of Multiple Deprivation; LUTS: Lower urinary tract symptoms; MAGD: Maximum allowable gap duration; NO: Not observable; NRES: National Research Ethics Service Committee; OAB: Overactive bladder; PDE5I: Phosphodiesterase type 5 inhibitor; Q1: Lower quartile; Q3: Upper quartile; QOF: Quality and Outcomes Framework; SA: Sensitivity analysis; SD: Standard deviation; SUI: Stress urinary incontinence; TTD: Time to discontinuation.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12894-021-00881-w.

Additional file 1. Supplementary Tables 1 to 12 and Supplementary Figures 1 to 4.

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Authors' contributions

Conception and design of study: MA, ML, PJOC, NC, AJ, FF and RvM. Data acquisition: MA and ML. Data analysis and interpretation: MA, ML, PJOC, NC, AJ, FF and RvM. Statistical analysis: MA and ML. Obtaining funding: MA, ML, NC, AJ and FF. Administrative, technical or material support: MA, ML, AJ and FF. Supervision: MA, ML and FF. Study report preparation, review and finalization process: MA and ML. Critical revision of the publication for intellectual content: MA, ML, PJOC, AJ, FF and RvM. All authors read and approved the final manuscript.

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Availability of data and materials

Researchers may request access to anonymized participant level data, trial level data and protocols from Astellas sponsored clinical trials at www.clinicalstudydatarequest.com. For the Astellas criteria on data sharing see: https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx.

Declarations

Ethical approval and consent to participate

The CPRD has obtained ethical approval from a National Research Ethics Service Committee (NRES), for all purely observational research using anonymized CPRD data; namely, studies which do not include patient involvement. The independent scientific advisory committee is responsible for reviewing protocols for scientific quality, but may recommend that study-specific ethical approval is sought if ethical issues arise in relation to an individual study. This study met the requirements under the CPRD obtained ethical approval from NRES. Only de-identified data were obtained, and patients could opt out if they did not wish to have their data used for research purposes.

Consent for publication

Not applicable.

Competing interests

MA, ML and PJOC are employees of Astellas Pharma Europe Ltd.; NC was an employee of Astellas Pharma Europe Ltd. when the manuscript was written; MA and AJ were working as associates as part of the Knowledge Transfer Partnership (KTP) between Astellas and Manchester Metropolitan University during the time this research was carried out; FF received grant funding from Astellas Pharma during the conduct of the study; RvM was an employee of Astellas Global Development, Leiden at the time of this work.

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