Incremental gains within an assisted conception service – utilizing evidenced based quality improvement strategies in a novel setting

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Incremental gains within an assisted conception service – utilizing evidenced based quality improvement strategies in a novel setting

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Abstract

Background Quality Improvement (QI) principles conceived from the manufacturing industry were evaluated within a fertility clinic. Model for improvement (MFI) and Lean can accelerate performance improvement within an organisation making it faster, better, and more affordable. There are examples of successful application of these approaches within healthcare (Silvester, 2015; Graban, 2016; Mazzocato et al., 2010). Little has been published regarding application of MFI or lean within assisted conception.

Aims This study aimed to assess the usefulness of these QI principles within a fertility clinic. To continuously improve through an aggregation of marginal gains in clinic performance, patient support and testing a novel self-administered psychological intervention.

Methods The MFI and lean were applied to identify areas for improvement within the clinic processes. Areas of focus included optimisation of culture conditions and exceptional patient support. Changes for improvement were explored. Application of QI principles were also used to troubleshoot a reduction in one of the clinic's key performance indicators (KPI). This quality improvement project is a time series study analysed with statistical process control methodology.

Results Staff engaged with the project which emphasised the importance of QI within the clinic. This work resulted in improvement in the workflow of the embryo culture system through refining processes without impacting on clinical results, maintaining good patients support despite the Covid-19 pandemic, and successful troubleshooting of a drop in a KPI value back to benchmark. The study demonstrated application of PDSA cycles and behaviour charts to evaluate improvement interventions, and provides a novel report of Quality of Life (QoL) assessment and use of an innovative self-administered psychological intervention during routine clinical practice.

Conclusion The exploration of QI principles is a valuable learning experience encouraging a mindset of continuous QI and accelerated performance improvement within the fertility clinic. Application of this approach to a larger clinic might bring greater rewards but further research is needed and more publications to SQUIRE standards.

Acknowledgements

This doctoral thesis completes a 12-year journey for me from starting a career as an embryologist fresh from graduation in 2010, to completion of my training and gaining HCPC registration as a clinical embryologist in 2015, and now to completion of the RCPath examinations and gaining consultant clinical scientist status with FRCPath. Many people have advised and supported me along the way, I would especially like to thank Dr Nicola Monks for the opportunity to get into the field of clinical embryology, for her continued support and pushing me to aspire to become a consultant clinical scientist and a fellow of the college. I would also like to thank Dr Aarti Umranikar who took over my Doctoral programme workplace supervision in 2019, enabling me to complete the research element doctoral thesis.

I would like to thank my academic research project supervisor Dr Michael Carroll for his advice and support during the doctoral thesis proposal, planning and writeup revisions of this thesis. Completing a doctoral thesis remotely from the academic university institution delivering the DClinSci has its challenges especially within the context of an NHS Trust fertility clinic without strong research links and facilities. Dr Carroll's guidance and advice has been invaluable in enabling me to complete my Doctoral research project and the last component of the Higher Specialist Scientific Training (HSST) Programme.

I would also like to thank Professor Jacky Boivin, Cardiff University School of Psychology, for her advice and permission to use the Positive Reappraisal coping Intervention (PRCI). All the clinic staff and the external observer, Bryan Woodward, for their involvement and contributions to this project. I must also thank the team at the Alliance Manchester Business School for inspiring me regarding the topic of my doctoral thesis. It has not been a straightforward project, but it has delivered benefit directly to patients and staff at Salisbury Fertility Centre.

Most importantly I would like to thank the staff at SFC who engaged with my project and supported me, and the patients who gave their time to provide additional feedback for continuous quality improvement. Finally, I would like to thank my partner, friends and family for their continuous support and for always asking "how's the training going?" over the past 5+ years.

Declaration

As part of the 5-year HSST some proportion of this work referred to in the thesis has been submitted in support of another qualification of this university (MMU) (C1) and Alliance Manchester Business School Manchetser University (Unit A4 PgDip programme in Leadership and Management in the Healthcare Sciences). See Appendix 8 for further information.

Outputs from work

1. Preliminary work for this study was accepted and presented as an abstract and poster at Fertility 2020. The work was well received by conference delegates and won the ARCS best post-registration poster award. This provides evidence that the proposed project is valued by professional colleagues, is relevant and has the potential to contribute new knowledge. Delegates were keen to take away handouts to present and share within their own clinical settings.

https://fertilityconference.org/wp-content/uploads/2020/03/Abstract-book.pdf

P131 Exploring the tool kit: application of Quality Improvement (QI) principles founded from manufacturing within the IVF laboratory using the Model for Improvement (MFI) and lean

2. Quality improvement report manuscript entitled "Improving ICSI success rates following root cause analysis and use of system behaviour charts: the devil is in the detail!" has been successfully submitted online and is presently being given full consideration for publication in BMJ Open Quality.

List of abbreviations

ART	Assisted Reproductive Technology
IVF	In-Vitro Fertilisation
HFEA	Human Fertilisation and Embryology Authority
NICE	National Institute for Health and Care Excellence
QI	Quality improvement
PDSA cycle	Plan-Do-Study-Act Cycle
MFI	Model for Improvement
VMMC	Virginia Mason Medical Centre
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
SQUIRE	Standards for Quality Improvement Reporting Excellence
KPI	Key Performance Indicator
SPC	Statistical Process Control
QoL	Quality of life
HADs	Hospital anxiety and depression scale
PRCI	Positive Reappraisal Coping Intervention
ICSI	Intracytoplasmic sperm injection
DSU	Day surgery unit
CPR	Clinical pregnancy rate
OHSS	Ovarian hyperstimulation syndrome
FAE	Freeze all embryos
FET	Frozen embryo transfer
HCG	Human chorionic gonadotropin
CoP	Code of Practice
2WW	Two-Week-Wait
MDT	Multidisciplinary team
SMART	Specific, Measurable, Achievable, Relevant, and Time-Bound
IAPT	Improving Access to Psychological Therapies

List of figures

List of tables

Chapter 1. Introduction

1.1 Background

Assisted Reproductive Technology (ART) is a dynamic and rapidly developing field of medicine (Paulson et al., 2018). Since the first live birth through In-Vitro Fertilisation (IVF) over 40 years ago it has been estimated that >8 million babies have been born worldwide (ESHRE, 2018). The UK has seen a continuous increase in the number of IVF cycles from 6,700 in 1991, when the Human Fertilisation and Embryology Authority (HFEA) was set up, to 69,000 in 2019 (HFEA, 2021). During this time there have been significant innovations in clinical practice (reduced multiple gestations, improved embryo culture systems, invasive and non-invasive screening technologies (Cutting et al., 2008; Harbottle et al., 2015; HFEA, 2007; Kovacs, 2014)).

The single biggest risk of fertility treatment is multiple pregnancy (HFEA, 2007). Since 1991 the national multiple birth rate dropped from 28% to 6% (HFEA, 2021) without reducing birth rates, which have improved significantly since 1991 (Figure 1). IVF treatment in the UK has become more effective and safer. An increase of >85% in live birth rates, now means 1 in 3 treatment cycles result in a birth for patients under 35 (HFEA, 2018a), and clinical improvements have led to an increased chance of a live birth for all patients under 43 (Figure 2).

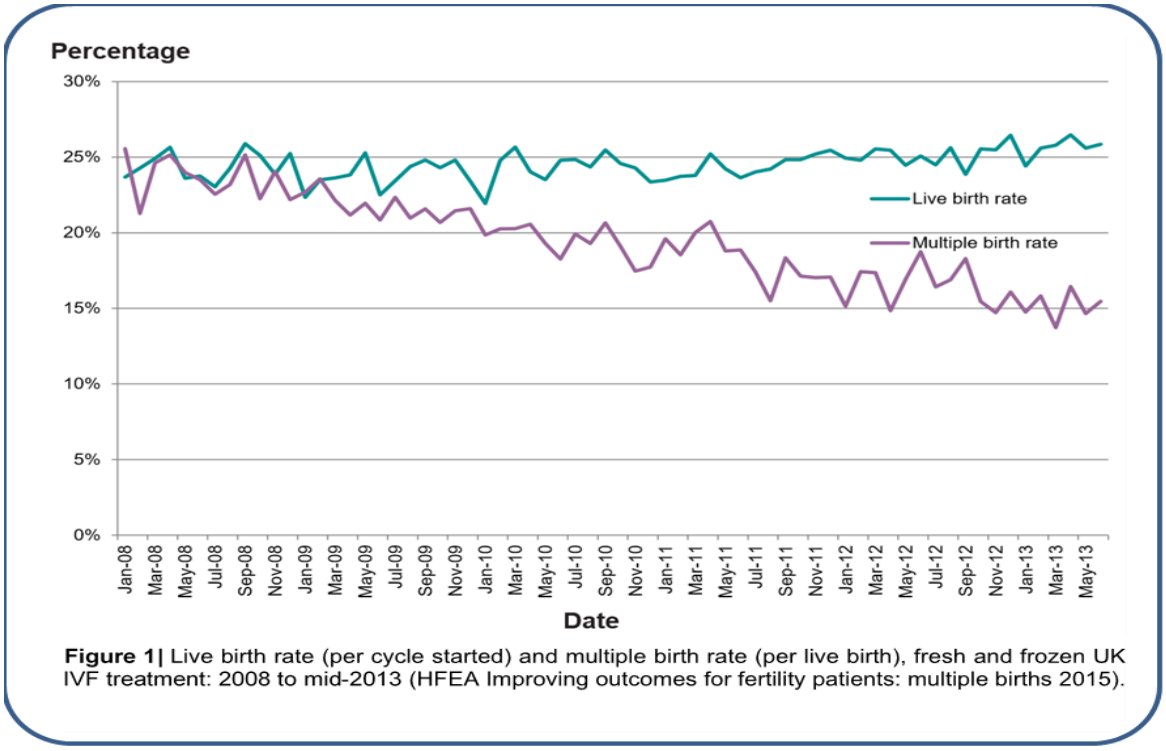


Figure 1| Live birth rate (per cycle started) and multiple birth rate (per live birth), fresh and frozen UK IVF treatment: 2008 to mid-2013 (HFEA Improving outcomes for fertility patients: multiple births 2015).

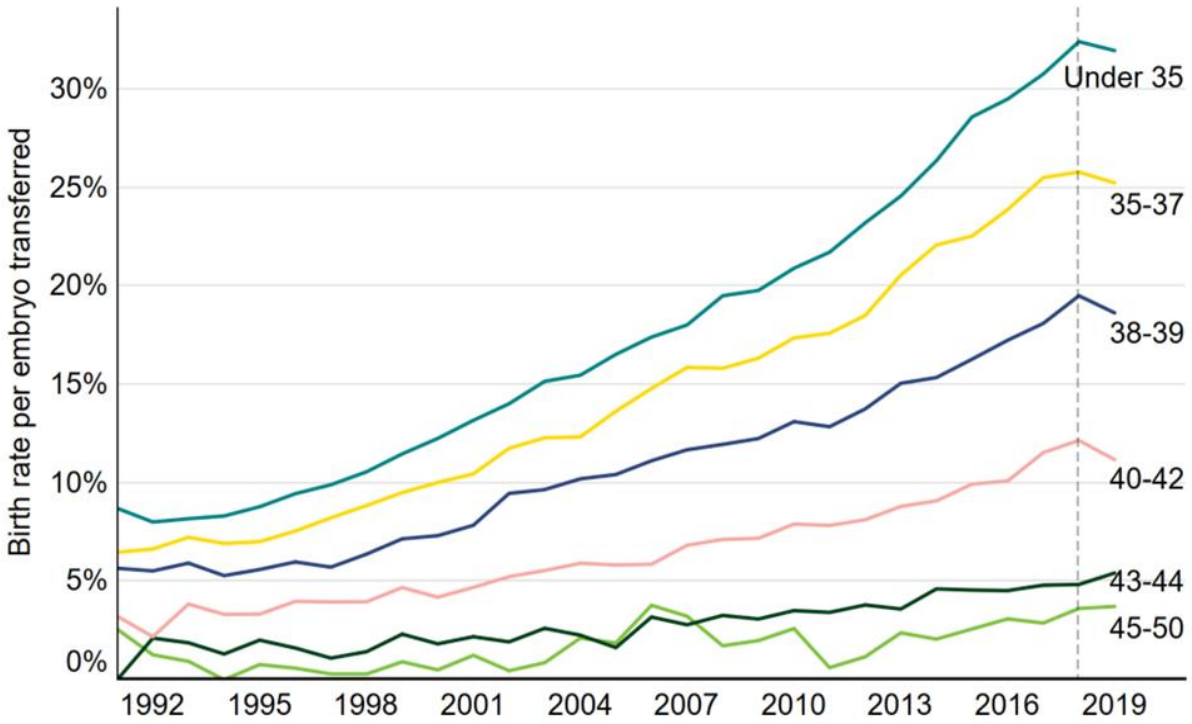


Figure 2|UK IVF birth rates per embryo transferred have increased for all patients under 43 in the last 30 years. Birth rates per embryo transferred using patient eggs by age band, 1991-2018, provisional 2019 data (yet to undergo validation), (HFEA trends and figures 2021)

However, despite advances in technology and clinical practice embryo implantation rates remain relatively low (Kovacs, 2014). As one patient explains in the HFEAs patient feedback survey "*This is the only part of my treatment I am worried about. Essentially you are gambling £6k on a 70% chance it won't work*" (HFEA, 2018c, Pilot national fertility patient survey p58). More recently the latest HFEA provisional birth rate data, published May 2021, suggest there may be a slowing in birth rates and the upward trend has plateaued, but this data needs to be confirmed.

Innovations in technology hold great promise to improve the chances of a live birth. One example is the use of time-lapse and morphokinetic algorithms to aid embryo selection, which early studies suggested could improve the relative chance of a live birth by 56% (Campbell et al., 2013). This study was well reported in the media, with headlines such as "*Most exciting breakthrough in IVF treatment in 30 years could triple number of births*" (The Independent, 2013). However, this has not been the case. A recent Cochrane review of randomized controlled trial data suggest there is insufficient evidence of differences in live birth rates between time-lapse technology (with or without embryo selection software) and conventional incubation and assessment (Armstrong et al., 2018). It

appears that this technology has not delivered on expectations (Figure 3), however its use has led to major changes in the way that embryos are observed and handled, affecting the logistics of the IVF laboratory, and its great utility meant its introduction to clinical use has not been held back (Paulson et al., 2018; Harper et al., 2017).

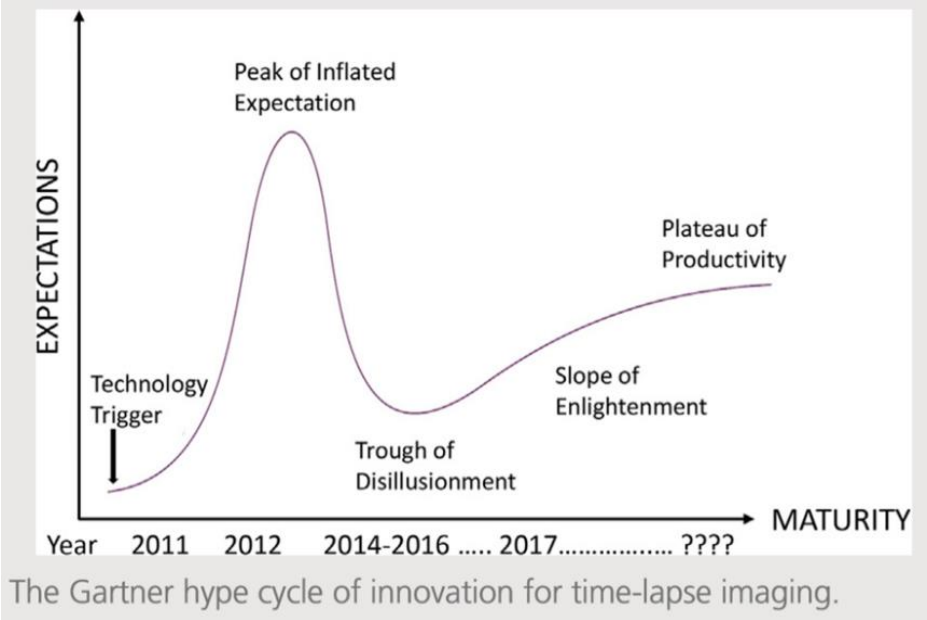


Figure 3| The Gartner hype cycle of innovation for time-lapse monitoring technology. Taken from Paulson et al., 2018. From the technology trigger in 2010 of the first live birth, the steep incline of raised expectations following further media attention and success stories to the peak in 2013 where many clinics in the UK considered investing in the technology. Publication of RCTs and a Cochrane review in 2015 concluding insufficient evidence of the benefit of TL compared to conventional incubation and selection, creating disillusionment with the technology. It has not delivered what was promised however it has served many other functions of the IVF laboratory.

The pregnancy rate per egg collection in Europe has increased to and remained stable at approximately 28% as shown in Figure 4 (Ferraretti et al., 2017). In the UK birth rates from IVF have steadily increased over time with the average birth rate per embryo transferred at 24% in 2018, compared to 7% in 1991. Now roughly one in every four embryos transferred results in a live birth (patients under 35 have the highest birth rate per embryo transferred at 32%) (Figure 2) (HFEA, 2021). Therefore, many patients will be unsuccessful at their first IVF attempt and will require more than one round of embryo transfer to achieve a live birth. The reality remains that a single cycle of IVF is more likely

to fail than to succeed and recent HFEA data, although provisional, indicates that live birth success rates could be slowing or even plateauing.

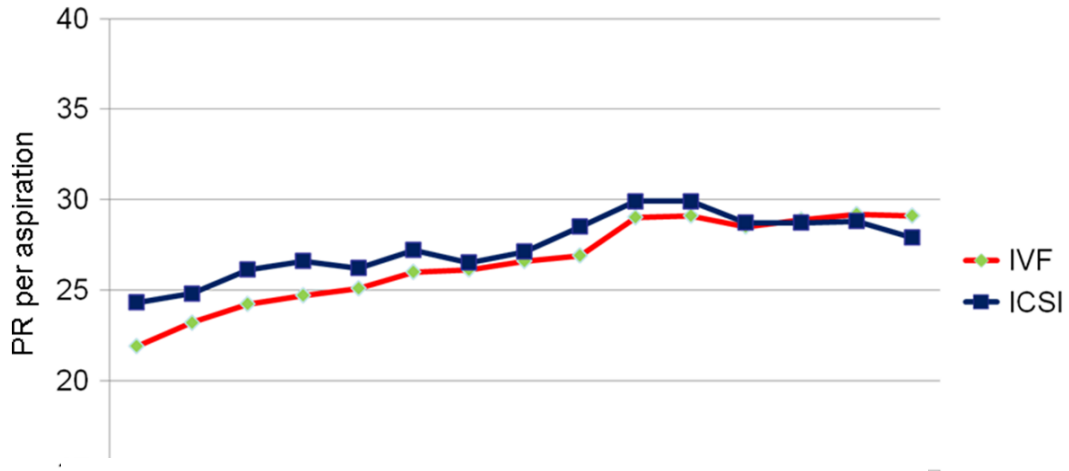


Figure 4| Effectiveness of IVF treatment in Europe over 15 years (Ferraretti et al., 2017), the overall clinical pregnancy rate per egg collection increased for both IVF and ICSI until 2007, where it remained relatively stable at 28%.

The live birth rate per patient could be 49% (Stern et al., 2010) or higher (Verhagen et al., 2008) if patients undergo the optimal number of treatment cycles. In the UK it is recommended that women under the age of 40, and who meet certain criteria, should be offered three full cycles of IVF (National Institute for Health and Care Excellence, NICE, 2013). A full cycle refers to all embryo transfers (including frozen) resulting from one episode of ovarian stimulation. NICE evidence-based guidelines for fertility treatment access criteria aim to ensure the efficacy of treatment and to optimise outcomes, providing the most cost and clinically effective use of IVF. This is because although most patients typically see success rates of 20–35% per cycle, the chance of pregnancy decreases with each successive round, while the costs increase (Harrison et al., 2021). The cumulative effect of three full cycles increases the chances of a successful pregnancy up to 45–53% for women under the age of 40 (NICE, 2013). However only 13% of Clinical Commissioning Groups follow NICE guidelines (Fertility Fairness, 2016). This leads to suboptimal outcomes and poor patient experience (NICE, 2013). Patients may be unsuccessful in their first IVF treatment cycle but then unable to return for further treatment cycles on a self-funded basis. Studies have shown that roughly 50% of patients

confronted with a failed cycle decide to continue and undergo at least three cycles of treatment, but patients have strong intentions to do as much treatment as needed to achieve pregnancy (Gameiro et al., 2013a; McLernon, 2016). Two out of ten patients discontinue treatment earlier than expected with more patients discontinuing treatment after the second (24.7%) than first failed cycle (18.2%) (Gameiro et al., 2013b). Harrison et al. (2021) suggest that IVF treatment should be planned on a multi-cycle rather than a single-cycle basis to better manage patient expectations.

Infertility can lead to stress, anxiety, depression, and the breakdown of relationships (Fertility Fairness, 2016). When treatment is provided it is emotionally and physically burdensome (Boivin & Takefman, 1995). The Covid-19 pandemic and fertility clinic closures resulting in delay of fertility treatment has compounded psychological distress for infertility patients further (Lawson et al., 2021; Boivin et al., 2020). The clinic's obligations for and the importance of offering counselling and emotional support to fertility patients has never been more crucial and has been highlighted in the recent HFEA Code of Practice (9th ed HFEA, 2019a). The Impact of Fertility Problems (2016) survey highlighted that 90% of respondents reported feeling depressed; 42% suicidal; nearly 50% reported on average feeling out of control, frustrated, and worried most of the time; with 70% reporting some detrimental effect on their relationship with their partner (Payne & van den Akker, 2016). It is unsurprising that many couples do not undergo multiple treatment cycles, even when there is a favourable prognosis and ability to cover the costs of treatment (Brandes et al., 2009). Reported discontinuation rates range from 15% (Brandes et al., 2009) to 65% (Rajkhowa et al., 2006). The most common reason given for discontinuing treatment is the psychological burden of treatment, or personal/relational problems (Gameiro et al., 2012). The experience of a failed treatment cycle can discourage patients re-engagement with treatment (Domar et al., 2018; Gameiro et al., 2012).

If patients were supported to undertake the optimal 3 full cycles, through reducing the burden of treatment, the pregnancy rate could be increased by an estimated 15% (Boivin et al., 2012; Gameiro et al., 2013b). Birth rates are important, but patients' emotional needs should not be overlooked (HFEA, 2018b). There is good evidence to show a positive association between the experience of patients and improved outcomes and patient

safety (HFEA, 2018c), therefore improving the experience of the patient should improve the chances of a successful outcome. The main drivers of patient satisfaction, according to the 2018 HFEA National Patient Survey, are the interest shown in them as a person, the quality of counselling, and the coordination and administration of treatment. Holter et al, (2017) suggest that there is a disconnect between how patients and staff perceive quality of care, with staff underestimating patient satisfaction, and Huppelschoten et al, (2013) warn that audits and feedback alone are insufficient to identify areas for improvement of patient-centeredness. Clinic staff have a huge impact on patients receiving a positive experience (HFEA, 2018c). Perhaps more could be done to enhance patient satisfaction which in turn may indirectly improve treatment outcomes.

In summary, live birth rates per treatment cycle appear to have plateaued, at best a patient's chance of success is one in four, infertility and the fertility treatment experience can be incredibly difficult, and many patients discontinue treatment because of this. However, completing the optimum number of cycle attempts would increase the patients' chance of ultimately succeeding with a live birth.

With increased operational costs and limited financial resources how can NHS fertility clinics improve the chances of a live birth per treatment cycle, help patients to stay in treatment, and lessen the psychological burden associated with infertility and fertility treatment? Even more pertinent following the Covid-19 pandemic.

It is helpful to break this large challenge into lots of smaller parts utilising the concept of incrementalism. Focusing on the fine detail (the margins) and creating rigorous small tests to determine what works and what does not, will provide a deeper understanding of each aspect of performance (Syed, 2015). Each small optimisation can aggregate to significant improvement overall. This philosophy has been successfully applied with impressive results to British cycling and Formula One (Syed, 2015). David Brailsford turned British cycling from mediocre to world dominating (Syed, 2015) winning Olympic medals, setting world records, and winning the Tour de France five times in six years (Clear, 2018). With the aim of getting from A to B as fast as possible it is easy to see the small parts, as illustrated below (Figure 5). Cycling is very different to ART and the complexities of healthcare.

Focusing on doing everything well will ultimately, directly and indirectly, result in improved financial performance, outcomes, safety, patient satisfaction and activity (Graban, 2016). Application of quality improvement (QI) strategies could be used to identify small areas for improvement within a complex assisted conception service. Quality improvement (QI) can be defined as '*systematic, data-guided activities designed to bring about immediate, positive changes in the delivery of health care*" (Baily et al. 2006, S5). The following will discuss the use of 'incrementalism' within healthcare, and the application of performance improvement QI frameworks within clinical science and specifically assisted conception.

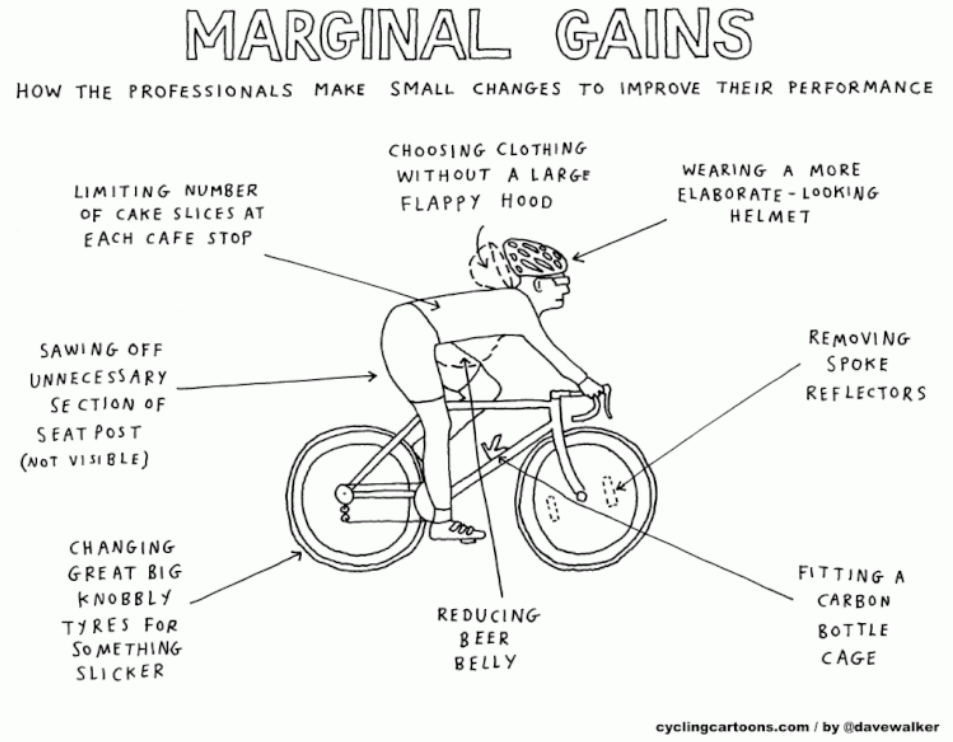


Figure 5| A light-hearted take on Marginal Gains in cycling, break everything down into component parts and improve (Cartoon by Dave Walker taken from Williamson 2018).

1.2 The relevance of marginal gains theory and quality improvement science.

1.2.1 Incrementalism (marginal gains theory)

a. Brief description of theory

Application of marginal gains requires the break down and identification of every tiny step and component of the larger process (Durrand et al., 2014). The concept is illustrated in Figure 6. Starting at point A small steps are taken in any direction, with testing after each step to ensure travel in the correct direction, repeated in this way eventually the optimum point is reached, the smaller summit, called the local maximum. Dividing a big challenge into small parts can deliver small improvements that may be negligible on their own, e.g., 1% increases, but over time these small incremental improvements can accumulate into impressive gains (Syed, 2015). The illustration also reveals the limitation of marginal gains which focuses on local optimisation, once the local maximum summit has been reached taking further steps makes no difference. At this point a focus on the bigger picture and bold leaps to new conceptional terrain is required, referred to as innovative change (Syed, 2015).

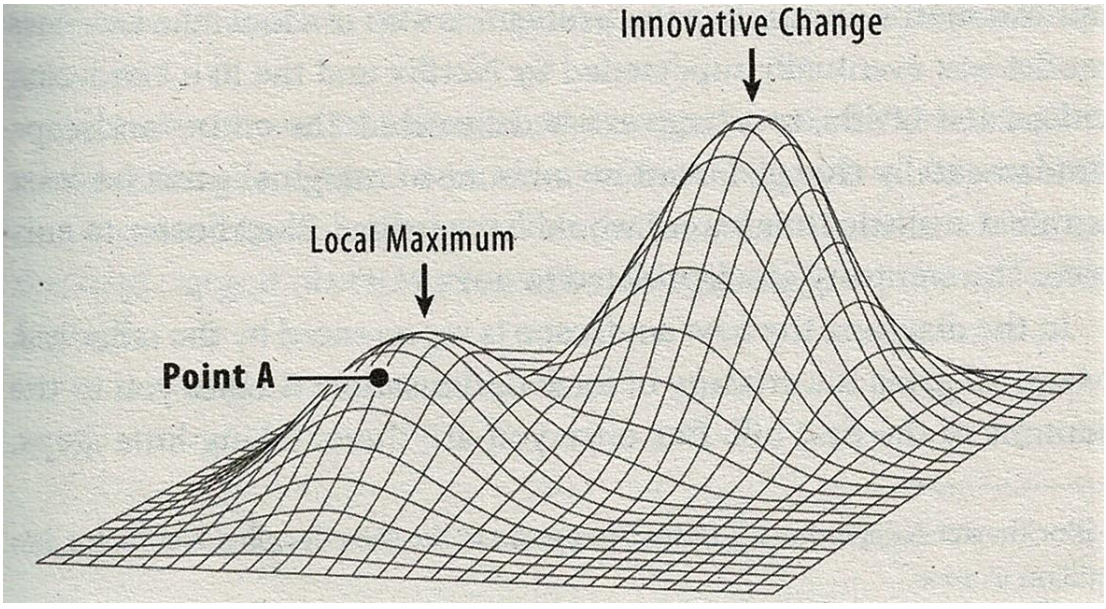


Figure 6| The concept of marginal gains in visual form in which the process of optimisation can be compared to trying to get to the top of a summit (taken from Syed, 2015).

The most astonishing application of marginal gains is found in Formula One (F1). The attention to detail is incredible, with 16,000 channels of data from every parameter on the car which enables identification and isolation of key metrics that help them improve through optimisation loops (Syed, 2015). There are thousands of components which collectively determine whether an F1 team is successful, the pit stop is one example. A group of people with clearly defined tasks and co-ordinated procedures can complete the stop in 1.95 seconds (Syed, 2015). The team will practice and use feedback on thousands of tiny failures to make performance improvements.

b. Review of the marginal gains approach within healthcare

The complex rapid tasks and roles during a pit stop are considered analogous to the group effort of medical staff to transfer patient, equipment, and information safely and quickly from operating room to the intensive care unit (ICU). Doctors at Great Ormond Street Hospital visited a F1 team to witness how a pit stop happens and asked the team to review a video of a surgery handover. They wished to improve the handover of patients from surgery to the ICU and reduce possible harm (Syed, 2015). This resulted in a new handover protocol with better choreographed groupwork and clearer roles of overall responsibility for coordinating the team and stepping back to look at the big picture. This new procedure reduced errors from 30% to 10%, improving patient safety (Sower et al., 2007).

Five medical databases were searched using the terms in Appendix 1 to create a set of results around the topic of the aggregation of marginal gains and healthcare. There are very few articles in the medical databases on this topic (n=40) and none within the field of assisted conception. Most results are within peri-operative care and cancer (Figure 7), showing that the marginal gains approach has been adopted in healthcare among various patient populations from cancer surgery, stroke recovery, prehabilitation, cardiac surgery and anaesthesia (Powell-Brett et al., 2021). Many articles within peri-operative care discuss enhanced recovery after (elective) surgery (ERAS) (Fleming et al., 2016; Chen et al., 2018; Tan et al., 2018; Smith et al., 2014). Adoption of ERAS has resulted in performance improvement though an aggregation of marginal gains parallel to GB cycling (NHS improving quality, 2013; Fleming et al., 2016).

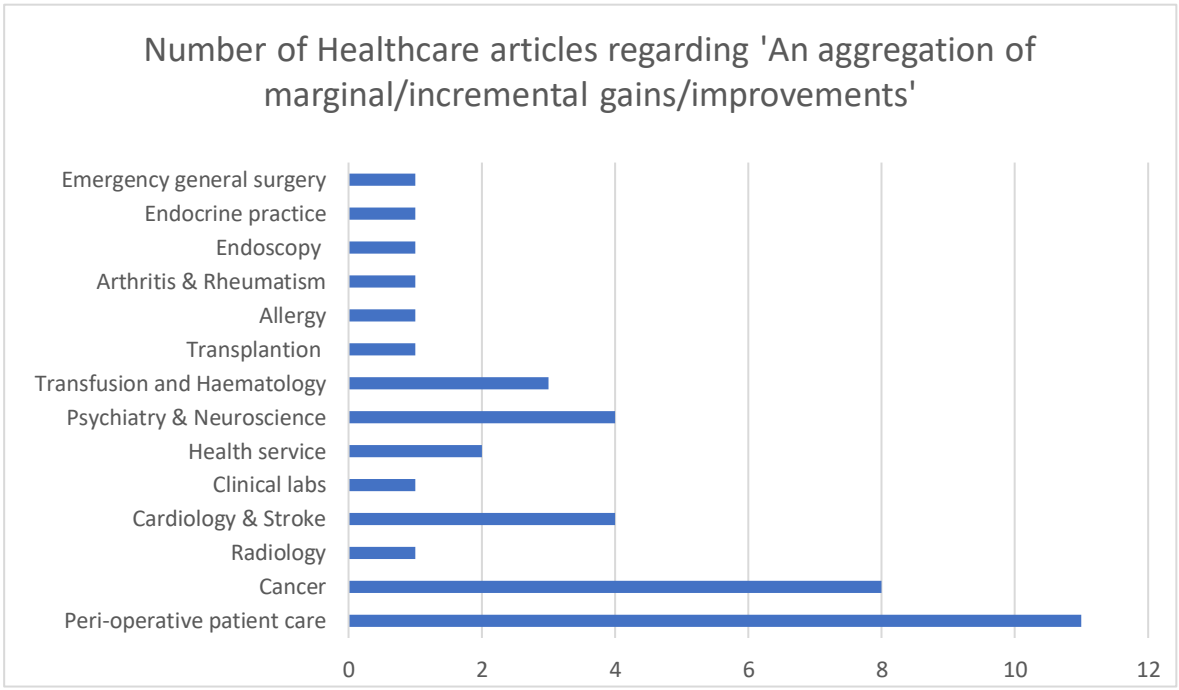


Figure 7|The number of healthcare publications regarding an 'aggregation of marginal gains'.

Elimination of small, often insignificant, imperfections in patient care provides cumulative benefits and contributes to improved overall outcomes, including patient satisfaction, cost-effectiveness, reduced morbidity and length of stay (Fleming et al., 2016). Smith et al, (2014) implemented changes to the surgical pathway (changes to the culture, patient education, intra-operative techniques, proactive de-medicalisation and post-discharge) which aggregated to create a statistically significant improvement in length of stay (50% reduction). Durrand et al, (2014) suggest there is further opportunity to implement a marginal gains approach to optimisation of patients' outcomes by action in the pre-operative phase, a concept called 'prehabilitation'. Evidenced based interventions are already used (e.g., anaemia correction, optimising underlying medical co-morbidities, and smoking cessation) but others are emerging that may further optimise the care pathway (e.g., musculoskeletal conditioning, aerobic fitness, and nutrition). There are parallels with assisted conception, e.g., smoking cessation and BMI, however this could be an area of improvement, to provide patients with the opportunity or support to optimise their physical and mental circumstances for a pregnancy to occur (Ockhuijsen et al., 2011).

Eisen et al, (2014) made efficiency and satisfaction improvements to a busy multidisciplinary paediatric allergy clinic though the use of staff engagement and improvement techniques which enabled multiple small fast-track changes to be implemented. These included an optimised clinic template, new patient history proforma, appropriate patient information, and engagement of service-users. This resulted in a 15% increase in clinic capacity (3 patients), with an average 17% reduction (20minutes) in visit duration, and improved patient experience and no additional costs.

Panagiotopoulou et al, (2019) demonstrated incremental gains to all constituents of their high-volume emergency service achieved by service reorganisation of the emergency general surgical service. The changes made reduced unnecessary inpatient stays, expedited decision making and improved financial efficiency.

To conclude, the marginal gains approach has been applied to healthcare with success, mostly within elective surgery recovery. Moreover, the application of the aggregation of marginal gains within the entire perioperative patient journey has been recognised by the National Enhanced Recovery Partnership consensus statement (NHS IQ, 2013). Identifying and improving many steps in the whole care pathway can lead to higher quality outcomes (NHS IQ, 2013). There is no current evidence of this approach being applied to assisted conception.

1.2.2 Quality improvement (QI) science

a. Summary of QI frameworks, approaches, tools and techniques

The QI movement began in industrial manufacturing and evolved through the work of several quality gurus (including Shewhart and Deming) who developed different approaches to improve organisational performance (e.g., The Toyota Production system). Some QI approaches and tools are listed in Table 1.

Table 1 QI approaches and tools (Adapted from Boaden & Furnival, 2016; Singh & Singh, 2015; NHS improvement 2017).

QI frameworks / approaches
Model for Improvement: Based on three key questions (thinking part) which are then used in conjunction with Deming's plan-do-study-act (PDSA) cycle (small scale testing or doing part).
Lean: Elimination of waste through identifying customer value and respects people and society. Originated from manufacturing the Toyota production system.
Plan-Do-Study-Act (PDCA): Or Deming/Shewhart circle (PDSA cycle), a four-step method used for the control and continuous improvement of processes and products.
Six Sigma: A process that has at least six standard deviations between the process mean and the nearest specification limit. A focus on reducing variation. Not widely applied to patient care.
Total Quality Management: Organisational approach to QI, focused on meeting customer needs, a product of the organisational processes
Theory if constraints (TOC): Each system will have a constraint that limits higher performance. Constraints are opportunities for improvement.
Clinical governance: Quality in the NHS, formal audit programmes, increased focus on clinical effectiveness and risk management. Focuses on clinical issues and culture.
Clinical guidelines/pathways: Structured multidisciplinary plans of care designed to standardise and support implementation of guidelines and protocols.
QI tools and techniques (or Quality, service improvement and redesign (QSIR) tools)
• **Checklists:** lists of key features of a process. • **Design of experiments:** techniques that identify and control parameters that have a potential impact on performance, to make a system immune to variation. • **Process mapping:** Type of flow chart to explore the chain of activities in a process i.e., patient pathway, walking the journey. Helpful for understanding the current process. Often reveal that processes are ad hoc and not designed! Reveals 'flow' improvement ideas. • **Driver diagrams:** Used to break down a goal into sub-goals, breaks a project down into activities that will act upon factors to achieve your goal called 'primary' and 'secondary' drivers. • **Statistical process control (SPC)/Run/Control charts:** Used to understand variation in a process and effects of interventions in a PDSA cycle. SPC used to identify different between 'natural variation' in processes and that which could be controlled. • **Pareto charts:** An ordered bar chart of the frequency of which causes lead to the problem. Usually, 80% of the occurrence of a problem results form 20% of the causes. Helps you target your intervention idea. • **Root cause analysis (Ishikawa/fishbone diagrams & 5 whys):** exploration of causes of a problem to find the root cause. Asking why? As many times as required until the cause is identified. • **A3 Problem solving (associated with lean):** A visual, single sheet of A3 for project management and updates. Combines the plan and tools used in one place. • **PDSA cycle:** Learning through rolling cycles of rapid, small, safe and informed trial-and-error testing. • **5S (or 6S) (lean):** An improvement technique, early step in lean, to clean standardise and maintain work space/processes etc.

QI draws on a wide variety of methodologies and tools, but they share some simple underlying principles and are based on the 'process view' of organisations (Slack et al., 2004) which focus on the 'needs of the customer' but with differing emphasis on flow, variation, and involvement of people (Boaden & Furnival, 2016). A 'process view' is a key characteristic of organisations that are successful at improvement (Plsek, 1999). The basis for this is systems thinking, the organisation must be viewed as a system and the system must be understood before questions of measuring performance can be accurately answered (Nolan, 1998; Seddon, 2008). Deming argued that performance (i.e., cost, quality, outcomes etc) is a consequence of how the work is organised to be carried out and every system therefore is perfectly designed to get the results it gets (poor outcomes are the result of a poor system). People are a part of the system and are often blamed when errors occur. However, 94% of errors are down to the system itself (Deming, 1994). Any unintended variation in a process creates inefficiencies (duplication, re-work, error etc) (NHS Wales, 2010).

Deming's system of profound knowledge provides insight into how to make changes that will result in improvements in a variety of settings (Table 2). QI approaches therefore help us look at complex systems, and organisations can harness this knowledge to drive forward improvements. Effective QI methods which support iterative development to test and evaluate interventions for improvement are essential to deliver high-quality and high-value care in a financially constrained environment (Taylor et al., 2014).

Table 2 Deming's 'system of profound knowledge' (Deming, 1986; Best & Neuhauser, 2005)

Appreciation of a system	Understanding the overall processes involving suppliers, producers, and customers (or recipients) of goods and services
Knowledge of variation	The range and causes of variation in quality, and use of statistical sampling in measurements
Theory of knowledge	Peoples' views of the world, the concepts explaining knowledge and the limits of what can be known.
Knowledge of psychology	Concepts of human nature and behaviour

Often referred to as a lens which helps you to think about the complexity of a system when looking to improve something or dealing with a complex problem. Different elements interact with each other e.g., knowledge about psychology is incomplete without knowledge about variation. This thinking prevents you from oversimplifying complexity.

There are parallels between QI approaches and marginal gains theory. David Brailsford was inspired by the Japanese practice of Kaizen, meaning 'continuous improvement' (Malik et al., 2007) ("Kai" meaning change and "Zen" meaning for the better (Newitt, 1996)). A managerial approach to achieve competitive advantage through continuous learning and small, gradual improvements in the processes of any organization (Lewis, 2000). Kaizen is a part of Lean (Singh & Singh, 2015). Although very similar, each QI approach varies according to how it prioritises its focus. Four approaches are compared in Table 3.

Table 3 Comparison of Improvement approaches (adapted from Nave, 2002; Proudlove et al., 2008; Boaden et al, 2008; and IHI.org, 2018).

Approach	Six Sigma	Lean	Theory of constraints	Model for improvement
Theory	Reduce variation	Remove waste	Manage constraints	Accelerate improvement
Application guidelines 'framework'	1. Define 2. Measure 3. Analyse 4. Improve 5. Control	1. Identify value 2. Identify value stream 3. Activities flow 4. Customers pull 5. pursue perfection	1. Identify constraint 2. Exploit constraint 3. Subordinate other processes 4. Elevate constraint 5. Repeat cycle	1. Set aims 2. Establish measures 3. Select change 4. Test change / experiment (PDSA) 5. Implement change / stop 6. Repeat / learn from honest failure
Focus	Problem focused. Good for root cause/ solution unknown problems.	Flow focused. Good for obvious flow problems.	System constraints. Good for high throughput processes.	Quick and substantial results in quality and productivity in diverse settings
Assumptions	A problem exists. Figures and numbers are valued. System output improves if variation in all processes is reduced.	Waste removal will improve performance. Many small improvements are better than systems analysis.	Emphasis on speed and volume. Uses existing systems. Process interdependence.	Multiple cycles of testing small scale change ideas can enhance learning and lead to improvement. Small teams and rapid tests. Reduced risk.
Primary effect	Uniform process output. Reduced defects and associated costs.	Reduced flow time increasing speed and capacity. Reducing cost.	Fast throughput. Increasing speed and capacity. Reducing cost.	Enhanced learning, accelerating improvement
Secondary effects	Less waste. Fast throughput. Less inventory. Fluctuation – performance measurement system. Improved quality.	Less variation. Uniform output. Less inventory. Flow – performance measurement system. Culture change. Improved quality.	Less inventory/waste Throughput cost accounting. Throughput – performance measurement system. Improved quality.	Outcome, process and balancing measurement system. Buy-in for large scale change. Reduced cost/ waste/ variation. Improved quality.
Criticisms	System interaction not considered. 'Top down' in practice. Processes improved independently. Not widely taken up in healthcare yet.	Statistical or system analysis not valued. Hard for buy-in, in practice language used can put people off.	Minimal worker input. Data analysis not valued.	Temptation to jump to large single PDSA. Testing should be very short no more than a few days. Missing out the study and act.

When secondary effects are considered in addition to the primary focus, all four approaches may achieve the same result (Nave, 2002; Proudlove et al., 2008) and there are also hybrid approaches to consider e.g., Lean-Six-Sigma. All four approaches have Shewhart's and Deming's PDSA quality cycle at their foundation and the concept of iterative tests of change (Reed & Card, 2016).

The PDSA is a four-step cyclic learning approach to adapt changes aimed at improvement within a complex system (Taylor et al., 2014; Provost & Murray, 2011; Mohammed et al., 2008). A change aimed at improvement is identified in the 'plan' stage, the 'do' stage sees this change tested, whether the change is successful or not is examined in the 'study' stage, and the 'act' stage identifies adaptations and next steps to inform a new cycle (Taylor et al., 2014). The PDSA cycle presents a pragmatic scientific method for testing changes in complex systems in comparison to more traditional healthcare research methods such as randomised controlled trials (in which the intervention is determined in advance and variation is attempted to be eliminated or controlled for) (Moen & Norman, 2006). The four steps mirror the scientific experimental method;

- Formulating a hypothesis, collecting data to test it, analysing and interpreting the results and making inferences to iterate the hypothesis (Speroff & O'Connor, 2004).
- Prediction of the outcome of a test of change and subsequent measurement over time (quantitative or qualitative) to assess the impact of an intervention on the process/outcome of interest (Taylor et al., 2014).

The PDSA cycle promotes the use of a small-scale, iterative approach to test interventions with rapid assessment and flexibility to adapt the change to ensure fit-for-purpose solutions are developed (Plsek & Wilson, 2001; Tyalor et al., 2014). Starting with small-scale tests removes barriers to action, enables learning and minimises risk to patients, the organisation and resources required. Enabling the opportunity to build evidence supporting change, increase confidence in the intervention and engage stakeholders. PDSA cycles offer a mechanism for iterative development and scientific testing of improvements within complex settings (such as healthcare) with inherent variability. Measurement of data over time helps understand natural variation in a system, increase awareness of other factors influencing processes or outcomes, and understand the impact of an intervention (Taylor et al., 2014).

The importance of PDSA cycles have been questioned with suggestion that all that is needed is to adopt proven 'best practices' recommended by other health systems and government bodies (Graban, 2016). However, transferring practices which work well elsewhere depends on context and culture, e.g., the adoption of the Hendrich II fall risk scale (considered best practice) resulted in more falls until staff were allowed to develop their own scale based on their own data and patients (Graban, 2016).

b. Review of QI literature within healthcare science

QI approaches have been successfully applied to healthcare, examples include NHS Scotland using the model for improvement to improve patient safety, and the Virginia Mason Medical Centre (VMMC) applying the Lean approach to its processes to create a 'better, faster and more affordable' healthcare system (Boaden & Furnival, 2016). QI is about getting faster, better, cheaper healthcare with zero defects (Arthur, 2016). Waste, duplication, re-work, and errors in our healthcare system are created through unintended variation in processes (NHS Wales, 2010), reducing unintended variation improves outcomes.

The VMMC created the Virginia Mason Production System® in 2002 based on the principles of the Toyota Production System to provide the perfect patient experience and it is now the safest hospital in the USA (Kenny, 2011). In 2008, due to worldwide demand from healthcare organisations to understand and apply Lean methods, VMMC founded Virginia Mason Institute (VMI), a non-profit organisation specialising in health care transformation. Five NHS trusts are working with VMI to develop a 'lean' culture of continuous improvement which puts patients first (NHS improvement, 2016). The impact of this 5-year partnership on the quality, efficiency and culture of each trust is being evaluated by a team of researchers at Warwick Business School and this research was due to be completed in 2021, but has yet to be published.

The suitability of a whole-scale adoption of 'production line' Lean within professionally dominated healthcare has been questioned, the terminology and poor application of lean has created resistance with some describing Lean as a management fad (Waring &

Bishop, 2010; McCann et al., 2015). However, there are many reports of successful improvements following application of Lean within diagnostic services (Mazzocato et al., 2010) (Figure 8). Lean and Six Sigma have been more popular in US healthcare than the UK, and mostly within diagnostic laboratories. Examples of application of QI approaches within healthcare are shown in Table 4. All demonstrate significant improvements within the area of focus, some were simple and cost-effective whereas others required additional resources and staff time.

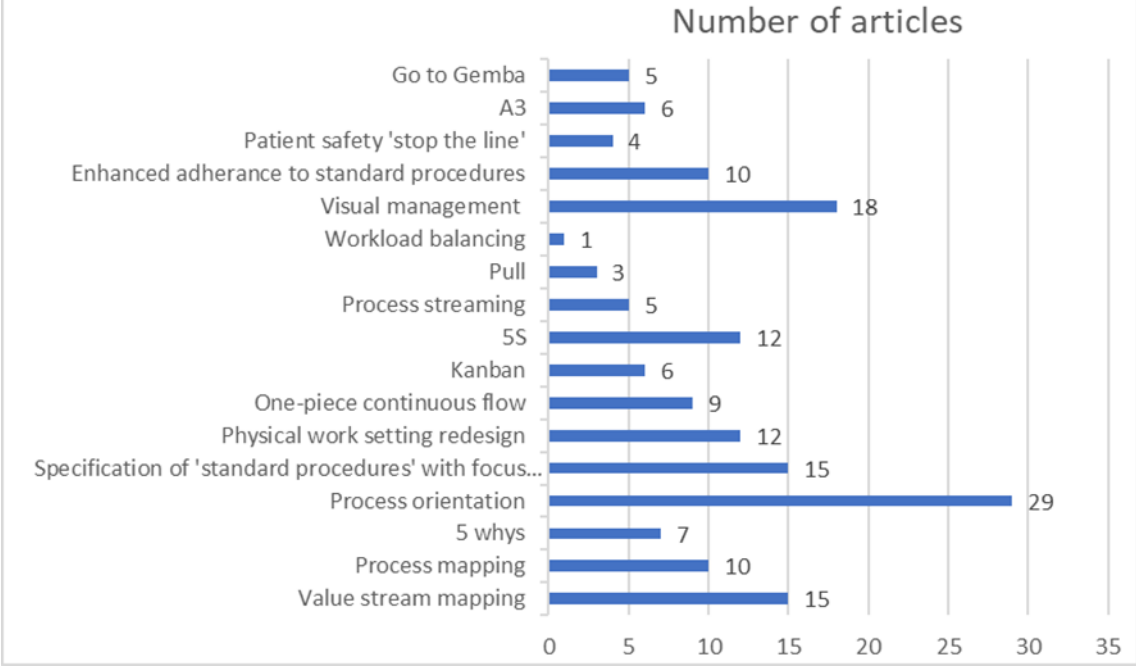


Figure 8| Articles published between 1998-2008 related to diagnostic services that have applied Lean Thinking to improvement approaches. All report successful improvements. Services included pathology, clinical chemistry, radiology and cytology. No articles within this review were related to assisted conception. (Adapted from Mazzocato et al., 2010).

Table 4| Examples of QI methodology (MFI, Lean and six sigma) being applied within healthcare. Most are within clinical laboratories but there are examples of use of PDSA within wards. Lean and MFI/PDSA are more popular in the UK and appear to require less resources to implement and sustain any improvement changes.

Reference	Application of QI method	Outcome
Denver Health laboratory (Arthur, 2016)	**Lean** approach; they used *5S* analysis (to clean 10 years of clutter), mapped the value stream and redesigned the workflow.	By rearranging workstations and equipment in the laboratory they reduced staff movement, floor space, and sample travel which resulted in a 25% reduction in test turnaround time and saved $88,000.
North Shore Long Island Jewish Health System (Arthur, 2016)	**Six Sigma** approach; to reduce laboratory errors in ordering and labelling processes. An analysis showed 5 of 100 samples were inaccurate or incomplete, of 5667 laboratory requisitions 285 errors were identified, and the most common was social security number errors from skilled nursing facilities.	A root cause analysis revealed skilled nursing facilities used addressographs instead of bar-code labels for sample identification. Changes within these facilities resulted in improvement, their defect per million opportunities fell from 7210 to 1387 and staff productivity increased from 20 to 23 requests per hour, which led to increased revenue and cost reduction of $339,000.
Riebling & Tria (2005)	**Six Sigma** approach; focused on the root cause of variance in quality and long-term maintenance of improvement (continued improvement two years later).	Defects were initially attributed to two pieces of equipment until further analysis (5 whys) revealed the cause to be operator errors due to training standards. Resulted in reduced analytical errors and improved operator competency in an automated laboratory. However, the project was guided by a Six Sigma consultant and required allocation of staff and resources to its purpose.
A clinical laboratory in Uganda (Elbireer, 2013)	**Six Sigma** approach; to help with an increased workload and manual data entry errors. Evaluating the current system and processes and identifying data-entry error root causes. The team implemented changes and control measures to address the root causes and to maintain improvements.	This resulted in a 60.5% reduction in data entry errors and an estimated cost saving of $50,115 a year from not having to identify and fix errors. However, the project required considerable dedicated resources and additional personnel time to maintain the gains.
Pathology labs at South Warwickshire (Silvester, 2015)	**Lean** A3; problem-solving process was used to support patient flow by reducing delays in blood tests (time to laboratory and lead-times through the laboratory) when it was revealed that clinical decisions were being made on out-of-date blood tests.	Reduced delays in blood tests. Key to the success of this project was laboratory staff realising that flow is a design issue and overcoming a 'blame' culture and initial scepticism/resistance of staff.
Musleh *et al.,* (2016)	**PDSA** and process mapping	Helped to significantly improve time to diagnosis for patients with congenital cataracts, leading to the development of a new care pathway.
Inpatient phlebotomy service UK NHS	**Model for improvement (PDSA)**; a lack of communication and standardised practice across wards causes delays in obtaining blood test results, impacting	Baseline data demonstrated poor handover rates of untaken bloods, ranging from 0-40%. This increased to a consistent 100% handover rate following introduction of the Phlebotomy

(Saunsbury & Howarth 2016)	detrimentally on patient safety and management. A box file system offered a set location for blood stickers to be situated within wards. The 'phlebotomy box' was implemented and optimised through PDSA cycles to improve communication between phlebotomists and doctors.	Box and ongoing staff education. The simple low-cost phlebotomy box has led to 100% of untaken bloods being effectively handed over in several different wards. Significant improvement in communication and efficiency within the phlebotomy service has tangible benefits to patient care, as minimising time lags can prevent delays in clinical decisions.
Surgical intensive care units USA (Erdek & Pronovost, 2004)	**PDSA** cycles; implementation of four consecutive interventions to improve pain assessment and treatment. Simple changes included education of staff of the importance of a standardised measure of pain, ensuring each bed had a pain score card attached, modifying the forms used during rounds to improve reporting of patients' pain scores, and making it unacceptable to have pain scores >3.	The baseline assessment of pain was 42% and treatment of pain was 59%. After 5 weeks, pain assessment improved to 71% and pain management improved to 97%. The simple low-cost interventions were associated with significant improvements in pain assessment and treatment without modification of hospital protocols and without an increase in adverse events related to pain therapy in several ICUs. However, this study was limited by a small sample size of patients (10-15 per week).

c. Literature search and review of QI work in Clinical Embryology

A review of QI work within assisted conception revealed few publications that explicitly utilise a QI framework or tools to drive improvement. Medline and EMBASE, and specific journals (BMJ Quality & Safety; Implementation science) were searched using the terms in Appendix 2 to create a set of results around the topic of assisted reproduction and QI. The search strategy followed the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) (Liberati et al., 2009) reporting guidance and is illustrated in Figure 9. From the search 32 relevant results were identified for further analysis using a realistic evaluation review design, developed by Pawson and Tilley (1997) and used by Mazzocato et al, (2010) called CIMO (an intervention (I) in a context (C) triggers a mechanism (M) which generates an outcome (O)) (Table 5). This framework assumes that social interventions are complex and dependant on context (Mazzocato et al., 2010).

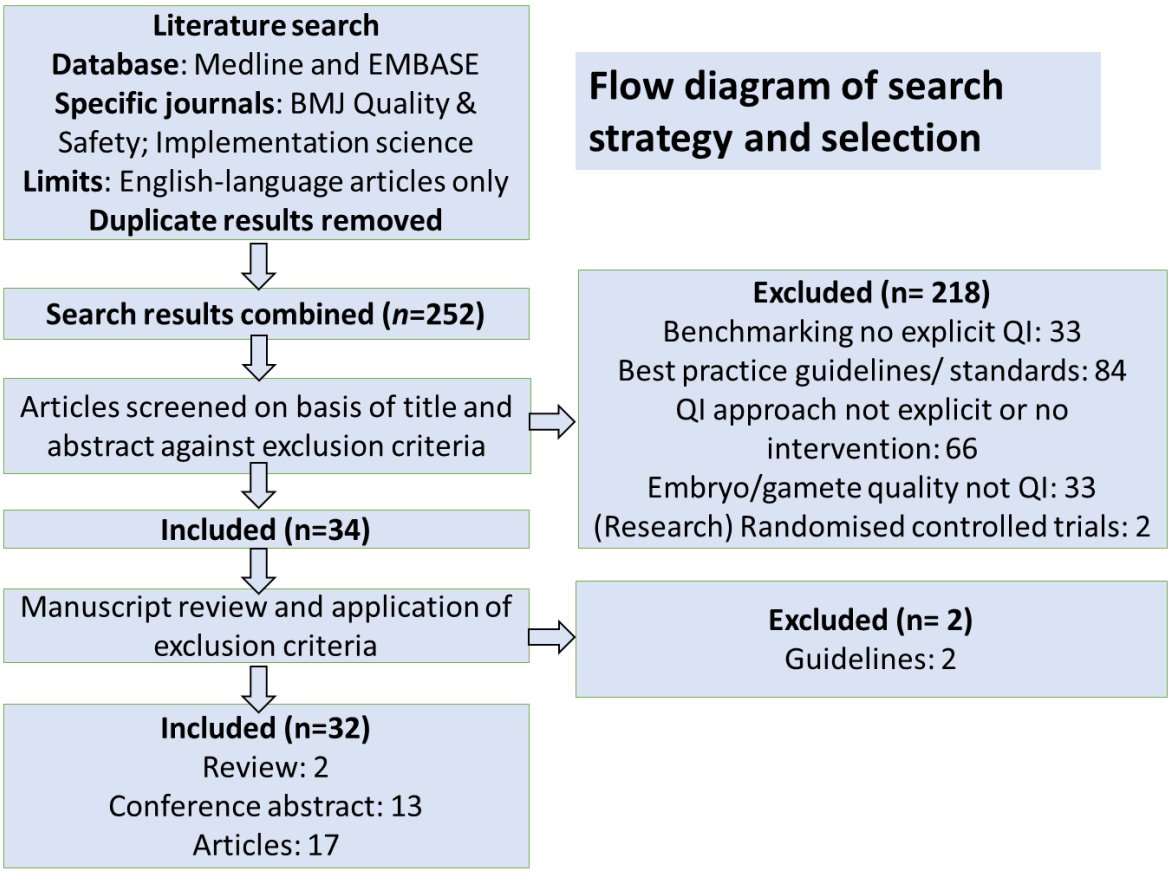


Figure 9 Flow chart illustrating search strategy and selection of literature.

Table 5 Analysis of the 32 included results using the CIMO framework.

Reference and type	Intervention	Context	Mechanism	Outcome
Romanski et al., (2021) Article	Quality management tool; implementation of an electronic whiteboard	Retrospective single centre study 2012-2018	In 2014 an electronic whiteboard was introduced into the IVF laboratory to aid staff to perform critical evaluations within standardised optimum pre-set time ranges. Metrics included time of fertilisation checks & embryo grading (Day 3 & 5), number of usable embryos, and mean evaluation time per embryologist per procedure.	Embryo grading within the optimal time frame improved but no change was observed for fertilisation checks. The mean evaluation time for the embryology team shifted closer to the midline of optimum time ranges for all evaluations except for fertilisation check. Post intervention saw an increase in the number of usable embryos per patient. The intervention helped maintain consistency in performance within the IVF laboratory.
Sharma et al., (2020) Article	PDSA to test two change ideas identified by process flow diagrams and	Single centre QI study, India	A QI project to decrease the mean waiting time from the first visit to initiation of infertility treatment by 70% within 4 weeks. Use of process flow diagrams and	After the first change idea, the average waiting period reduced to 3.25 months, a 51.8% reduction from baseline within a 2-week interval. The waiting time

	fishbone analysis		fishbone analysis identified area for change, the patient pathway for HSG caused much of the delay to start of treatment.	further reduced to 2 months after the second change idea. It was a 70% reduction from 3.25 months over 2 weeks' time. The results were sustained to the average waiting period of 2 months after the first visit for 6 months without any additional resource.
Lovesky et al., (2019) Conference abstract	PDSA, testing of two change ideas	Single centre study	A QI project to reduce HSG-related radiation exposure to patients and staff through two quality improvement interventions. Control charts were used to demonstrate improvement over time.	Fluoroscopy time, and therefore radiation exposure, was successfully reduced by approximately 75% by applying basic quality improvement methodology. This change in practice was sustained over time.
Moore & Arthur (2019) Article	Multiple site-specific change ideas were developed by front-line staff using lean methodology including standard processes & work, supportive tools, visual management, and staffing and scheduling to meet Takt time.	Using lean methodology in an ambulatory fertility setting, Canada	A QI project aiming for 85% of cycle monitoring patients to have a turnaround time (TAT) of 20 minutes or less from arrival until checkout. A time series study analysed with statistical process control methodology. Patient and staff satisfaction surveys were conducted.	Increased efficiency enabled a 17% increase in patient volumes, thereby increasing access to care. There was a decreased average patient TAT from 38.2 to 34.7 minutes, 85% of patients could complete their visit within 43 minutes rather than 52 minutes at baseline, and 35% did so within 25 minutes. The quality of care increased by providing education to every patient at every visit and waste decreased because more of the total visit time is now spent in this value-added step rather than waiting. Staff and patient feedback following the interventions was positive. The clinic was able to improve efficiency in the morning monitoring process to decrease patient TATs while accommodating increased patient volumes and improving the quality of patient care.
Mourad et al., (2019) Article	Testing of a validated questionnaire from another country	Three fertility clinics in New Zealand	Evaluation of the Patient-Centred Questionnaire-Infertility (PCQ-Infertility).	The PCQ-Infertility has been shown to be a valid quality assessment instrument to assess the patient-centredness of fertility care in New Zealand. A useful benchmarking instrument to measure performance and provide feedback for quality improvement opportunities.

Hy et al., (2019) Conference abstract	PDSA, fishbone analysis	Single centre, IVF theatre, Singapore	Use of simulation exercises with root cause analysis to evaluate the efficiency of workflow within a new environment.	Improvements were made to patient safety during recovery in the new location, by two simulation exercises.
Kirk et al., (2019) Conference abstract	PDSA	Early pregnancy assessment unit, across 4 hospitals UK	A QI project to reduce the clinical variance and improve the quality of care in an early pregnancy assessment unit. Baseline data was evaluated and patient feedback obtained.	Limited information, a clear improvement was demonstrated in outcome measures and patient satisfaction on test days compared to baseline and after introduction of the 'ideal' pathway. There was a reduction in variation.
Rienzi et al., (2017) Article	Process mapping & multicentre failure mode and effects analysis (FMEA)	IVF laboratory India Multiple IVF centres and risk analysis	Multicentre multidisciplinary process mapping to assess risk during processes. Centres can learn from each other and adopt the lower risk practices identified.	Process mapping identified areas of high risk. The results of the FMEA analyses were investigated and consistent corrective measures suggested.
Agarwal et al., (2017) Article	PDSA	IVF laboratory India, Laboratory remodelling to implement good laboratory practices	Realising that a problem exists with air quality. Implementation of best practice such as a high-efficiency particulate air CODA system, steel furniture instead of wooden, use of new disinfectants (oosafe), and restriction of personnel entry and staff avoidance of cosmetics. Baseline data (group A) (VOC meter readings throughout laboratory, embryonic development parameters) compared with current data after laboratory remodelling (group B).	Laboratory redesign, improved staff awareness. Reduction in VOC readings, enhanced air quality, improvement in blastocyst formation rate, implantation, and clinical pregnancy rate were observed in the laboratory after implementation of new facilities.
Holter et al., (2017) Article	Validated questionnaire	All 16 IVF public and private clinics in Sweden	Healthcare professionals and patients participated voluntarily through answering the same validated questionnaire "Quality from the patients' perspective of in vitro fertilization treatment" (QPP-IVF).	IVF healthcare professionals significantly underestimated the patients' satisfaction with all aspects of patient-centred quality of care. Study results increase the professionals' understanding of the patients' experiences during IVF treatment and provide additional knowledge when identifying areas to prioritize to improve quality of care.
Holter et al., (2014b) Article	Development of validated instrument for	Two centre study in Sweden	Development of a validated instrument to evaluate the patient's perspective. The questionnaire specific to	The QPP-IVF may be of use for purposes of quality improvement and national comparisons. Future studies

	measuring quality of care		IVF treatments (QPP-IVF) is based on the theoretical foundation of the validated general instrument, quality of care from patient's perspective (QPP), for both women and men.	should focus on establishing the QPP-IVF as a valuable instrument for measuring the quality of care outside Sweden.
Holter et al., (2014a) Article	Quality function deployment	Two IVF centre study, Sweden	Quality from the patient's perspective, what the couple values. Two centre study.	Men and women value aspects of care differently (results could be affected by selection bias).
Huppelschoten et al., (2013) Article	Audit	Fifteen Dutch fertility clinics	Audit of the level of patient centeredness of care, and feedback provided to clinics by a personalized paper-based feedback report.	Audits and feedback alone are not enough to improve the level of patient-centeredness in fertility care. Increasing professionals' desire to change and their ability to translate feedback about their performance into an optimal quality improvement strategy appear to be the key issues.
Tilleman et al., (2013) Conference abstract	PDSA, process mapping, LEAN Six Sigma, SIPOC (suppliers-Inputs-Process-Outputs-Customers)	IVF laboratory (no further details available)	One laboratories experience of extending to a total quality management system. Learning and shaping TQM, using different tools and approaches in a trial-and-error way.	Development of clear end-to-end process maps for key processes. Which are used to overview a treatment plan or specific laboratory process, and as a measuring and analysing tool for quality and financial management.
Shnorhavorian et al., (2012) Article	3-day rapid process improvement workshops (RPIW), involving oncology, adolescent medicine, urology, parents, patient & two sperm banks	Single hospital, USA	The use of continuous process improvement methodologies to identify barriers and create a standard process for referral for fertility preservation for young males with cancer. Rates of sperm banking before and after standardization were compared.	12 months following implementation of a standardized process, 90% of patients were offered sperm banking. There was an 8-fold increase in the proportion of AYA males' sperm banking, and a 5-fold increase in the rate of sperm banking.
Caballero et al., (2012) Conference abstract	PDSA to meet ISO 9001:2008 guidelines	IVF clinic Europe	Evaluation of metrics to improve patient satisfaction and reduce waiting times.	Ongoing (limited information available).
Nunez-Calonge et al., (2012)	PDSA	IVF laboratory Europe.	Six procedures were changed following an audit, results were compared before and after. Metrics	Clinical pregnancy rate significantly increased to 48% from 30%. Embryo

Conference abstract			included fertilisation, embryo utilisation and pregnancy rate.	utilisation rate significantly increased to 74% from 57%.
Pirkevi et al., (2012) Conference abstract	Implementing QC. Multiple PDSA cycles to meet ISO15189 standards.	IVF laboratory, Turkey. Retrospective study.	Comparing clinical and ongoing pregnancy rates over two years during implementation of QC programme. Including increased monitoring of pH, CO2, and data logger for medium transport. Decreased incubator to patient ratio by purchase of more incubators to reduce door openings. Implementing consumable tracking/testing and an internal/ external quality assurance programme for embryologists.	Increased clinical and ongoing pregnancy rates for women below 35 years old. No significant improved outcome for women 35 and over.
Huppelschoten et al., (2011) Conference abstract	1) Audit and feedback; 2) Educational outreach visits; 3) Patient-mediated interventions.	Couples (N = 1250) attending 30 Dutch clinics for a fertility treatment	A cluster-randomised trial, the effects of the three approaches were determined by a baseline and after measurement with couples. Primary outcome measures are Quality of Life (FertiQoL questionnaire), levels of anxiety and depression (SCREENIVF questionnaire) and patient centredness (PCQ-Infertility).	Suggest that by measuring patient centredness and quality of life and providing clinicians with plural feedback could improve patient centredness of fertility care which could remove some emotional burden.
Huppelschoten et al., (2011) Conference abstract	PDSA, process evaluation, audit and feedback, educational outreach visits, patient mediated interventions	30 Dutch IVF clinics	Providing clinics with a multifaceted approach for care improvement to focus on patient centredness and quality of life. Baseline metrics collected before and after the approach was used via quality of life and care experience questionnaires.	Results are benchmarked and fed back to all clinics. Each clinic feedback report is discussed and improvement goals with a clear action plan are formulated. Ongoing (limited information available).
van Empel et al., (2010) Article	Focus groups	Thirty Dutch fertility clinics	The PCQ's content, addressing 53 care aspects, was generated by seven focus groups with 54 infertile patients.	Generation of a valid, reliable and strongly discriminating instrument for measuring patient-centredness in fertility care. The PCQ-infertility can identify shortcomings and can be adopted for quality improvement.
Sun et al., (2010)	Quality improvement research? Looking at	Large IVF clinic. Limited information.	To evaluate the influence of a high hyaluronan-containing transfer medium on clinical pregnancy,	A high hyaluronan containing medium significantly increases the clinical pregnancy, implantation and

Conference abstract	retrospective data long after a change was implemented	Retrospective study.	implantation and delivery rate. Data from 2004 – 2008 and change in routine practice implemented late 2006.	delivery rates. Limited information available.
Kelly et al., (2010) Conference abstract	Six sigma to reduce variation via DMAIC	IVF clinic, limited information.	Over 8-month period. Identification and measure of the controllable variables across the entire cycle. Temperature and processing time were measured as the most significant variables during culturing. The most significant element affecting temperature variation was the multiple opening of the incubator door.	Maximum temperature variation during embryo assessment was reduced from 2.9ºC to 0.4ºC. Time eggs and embryos spent outside the optimum 37ºC culturing was reduced by 18%. Temperature regain time after the incubator door was opened was reduced by 68%. The distance eggs and embryos travelled within the laboratory was reduced by 36%.
Castilla et al., (2008) Article	Control chart	Data from the IVF/ICSI register of the Spanish Fertility Society	Comparing the quality of assisted conception programmes i.e., league tables. Using different classification methods. Selection bias within data due to poor performing clinics not choosing to submit data.	Large discrepancies arise between different methods in classifying performance as poor or optimum.
Kelly et al., (2008) Conference abstract	LEAN Six Sigma, DMAIC roadmap, fishbone diagram, process mapping, 5S, Kaizen.	Large IVF clinic, Ireland	Identify the patients' key needs and remove unnecessary waste and variation within treatment. Limited information available.	28% reduction in the time the patients spent in the clinic, 22% reduction in waiting time, 40% reduction in patient records.
Knuppel et al., (2007) Article	LEAN (not explicit but focus on removing waste in IVF), experimenting with 'niche' care management model.	Office-based telephonic nurse case management and pharmacology management practice (USA study)	Reducing cost in IVF due to overutilisation, drug wastage, and adverse outcomes such as multiple gestations (resulting in preterm births, chronic adult diseases, and lifelong neurological impairments). Cost of IVF often equals the cost of providing care to these babies (neonatal intensive care unit). Integration of IT case management to improve effectiveness and quality.	Improved transfer of real-time information to give better patient satisfaction and outcomes i.e., fewer twins. Therefore, lowering costs, safer outcomes for babies' families and society. However, no data provided.
Kennedy & Mortimer (2007) Review	Process mapping to understand risk. Root cause	Review, educational exploration of risk management	Review of tools and approaches that help to implement an effective risk management programme.	Adoption of the processes described will contribute to improved patient safety.

	analysis. Control charts.	in assisted conception.		
Mohammed & Leary (2006) Article	SPC, control charts, Shewhart's theory of variation, Pyramid Model of Investigation	Analysing the performance of IVF clinics in the United Kingdom using HFEA data.	Live births, multiple births and cancellations data from 66 licensed UK clinics between 2002/2003.	Evidence of IVF clinics exhibiting special cause variation. Help to identify areas for improvement. Control charts are a more informative representation of clinic performance compared to league tables.
Frydman et al., (2004) Article	PDSA	IVF clinic, France.	To improve QC by switching from non-stop treatment (2000-2001) to intermittent activity (2002) (treating patients in series). Therefore, the same batches of products and culture medium would be used within a series which reduces variation and make it easier to control for quality.	Significant increase in the clinical pregnancy rate per egg retrieval from 28.9% & 25.2% (2000/2001) to 41% (2002) in IVF and from 23% & 26% (2000/2001) to 38.5% (2002) in intracytoplasmic sperm injection (ICSI). A significant increase in implantation rate, from 14.8% and 13.4% to 20% in IVF and from 12.1% and 12.9% to 23.5% in ICSI. This was achieved without an increase in the multiple pregnancy rate.
Parker (2004) Review	Process mapping	Review/ educational use of process maps	N/A	Importance of process mapping to improve efficiency and effectiveness.
Mayer et al., (2003) Article	Total quality improvement	Jones Institute, USA.	Exploring metrics and quality indicators in assisted conception.	Considerations and examples of how QI initiatives may be introduced in clinics.
Hammond & Morbeck (2019) Article	Control chart/ statistical process controls (SPCs)	Retrospective, multicentre, analysis of KPIs	Embryology key performance indicators were analysed over 3 consecutive 5-month periods. During which the culture medium was changed in the middle period. Fertilisation rate, Day 5 usable blastocyst rate (D5BUR), total usable blastocyst rate (TBUR) and clinical pregnancy rate (CPR) were tracked monthly and analysed for SPC using control charts.	Day 5 usable blastocyst rate (D5BUR) decreased from 32 to 25% after the culture medium was changed. The decrease was detected within 1 week after the change. D5BUR increased after a change back to the original medium. Demonstrating that statistical KPI monitoring systems have the potential to provide systematic, early detection of adverse outcomes in ART laboratories after planned or unexpected shifts in conditions.

Specific frameworks and approaches were only discussed in a few publications, mostly Lean (n=5), Six Sigma (n=3), and Shewhart's theory of variation (SPC / control charts) (n=4). The most popular tools used were process mapping (n=5 (16%)) and PDSA (n=13 (41%)). Some of the publications that used PDSA were retrospective studies or involved data over long-time scales. Some were not strictly PDSA cycles, as no 'testing' occurred, but changes were made based on best practice guidelines and resulting effects were measured pre- and post-intervention (Agarwal et al., 2017). Of the results, 25% (n=8), regarded patient satisfaction and quality of care highlighting the importance of this area as a focus for QI and how clinics could do more to reduce the psychological burden of treatment. A novel report of embryology performance tracking across a large number of fresh treatment cycles from a multicentre clinic demonstrated KPI behaviour during a defined laboratory change (Hammond & Morbeck, 2019). Further research is encouraged to validate the effectiveness of statistical KPI monitoring within different laboratory settings and in response to alternative process changes within the laboratory.

The results show that use of QI approaches within fertility can lead to significant improvements. Frydman et al, (2004) acknowledged how hard it is to measure improvement in IVF due to so many variables which are often out of the clinic's control. There are few exemplar QI fertility publications with multiple small PDSA cycles or explicit QI approaches possibly due to the delay in outcome metrics (the best measure is a healthy child), great potential for special cause variation within IVF processes that is difficult to control for (i.e. batches of consumables/drugs, staff levels and skill-mix, equipment, patient population, case-mix, air quality, etc), and a culture of accepting new technologies without a solid evidence base (Harper et al., 2017). This is even more pertinent with the changes made to service delivery due to Covid-19 pandemic.

Much QI work goes on within this field, probably duplicated across clinics, but little is documented to the SQUIRE (Standards for Quality Improvement Reporting Excellence) guidelines (Goodman et al., 2016) or even published. There is room for improvement of routine practice within assisted conception clinics to make services 'faster, better and cheaper', to provide higher quality care and outcomes whilst utilising the same or fewer resources.

1.3 Importance of this research

The literature review revealed no publications within assisted conception that apply marginal gains theory and few that explicitly use QI frameworks and tools as a means of service improvement. QI literature indicates that these approaches and tools can be used in healthcare to accelerate performance improvement making it faster, better, and more affordable. Therefore, assisted conception services could benefit greatly from their application. Even if changes lead to marginal improvements or no improvement at all. This is because learning from the process of utilising these tools, similar to Formula 1, should result in learning from small failures which inform further future improvements, i.e., trying something sensible (derived from thinking about the system), testing it in a small, safe way, and measuring its effects for improvement, and stopping if no improvement is seen, but learning (and sharing the learning) from the experience and preparing to try something new.

However, these approaches have been available for a long time, and many attempts have been made to apply them to the complexity of healthcare organisations. It took VMMC a decade to succeed at improving quality and lowering costs (Kaplan et al., 2014). Perhaps not a short-term fix, successful application must require understanding of QI science, appreciation of context and buy-in from stakeholders. A QI approach would not work without engagement from the team using it and supportive leadership (Kaplan et al., 2014; Dodds, 2007).

Exploring these approaches and tools across a multidisciplinary team (MDT) should lead to learning and improvement of our IVF service without additional costs or staff time. Asking questions about our service should identify small, simple changes that could be tested by multiple PDSA cycles. The effects on three areas, or '3 wins' must be considered; patients (service quality), staff (workload, stress), and organisation (performance, cost, regulation) (Dodds, 2007). Continuous improvement of service performance, whether clinical outcomes or patient support, is in line with the aims and strategies of the fertility sector regulator (HFEA) and NHS Trust organisation.

1.4 Summary

The problem: Although IVF success rates have greatly improved over 40 years and treatment is now much safer (reduced multiple births) a single cycle of IVF is still more likely to fail than succeed. If multiple cycles are undertaken the chance of a success increases however emotional and financial reasons often lead to patients dropping out. Fertility treatment is emotionally burdensome, and patients can suffer from mental illness as a result. Birth rates are important, but patients' emotional needs should not be overlooked. Operational cost of IVF services has increased alongside reducing NHS funding for IVF cycles increasing pressure on NHS services to do better with less. This is a complex problem with many stakeholders. The Covid-19 pandemic has served to exacerbate these issues further with increased stress and uncertainty for patients and reduced access to fertility treatment with increased delays. Fertility centres have had to implement and adapt to many changes to service delivery required to provide safe treatment following the pandemic.

Possible solution: Perhaps a marginal/incremental gains approach, used by Formula 1 and British cycling, could lead to better outcomes within an NHS IVF service. Looking at clinic processes to test small, safe changes for improvement might result in the aggregation of a significant improvement overall to the service, without increased cost. There are no publications of this approach being applied to IVF clinics. Combined with the vast theoretical and evidenced Quality Improvement (QI) methods for enhanced performance this approach could identify areas of waste or improvement to ultimately increase the chance of live birth and patient satisfaction. The QI movement started outside healthcare and has evolved through the work of visionaries (including Shewhart and Deming) who developed different approaches to improve performance within manufacturing companies (e.g., Toyota). QI approaches (e.g., MFI and Lean) with associated QI tools can accelerate performance improvement within an organisation making it faster, better and more affordable. These approaches have been successfully applied within healthcare e.g., the Virginia Mason Medical Centre. A review of the literature revealed very few publications regarding application of these approaches and tools within fertility clinics.

Chapter 2. Aims and objectives, and overall theme of proposed research

2.1 Hypothesis based on literature reviewed

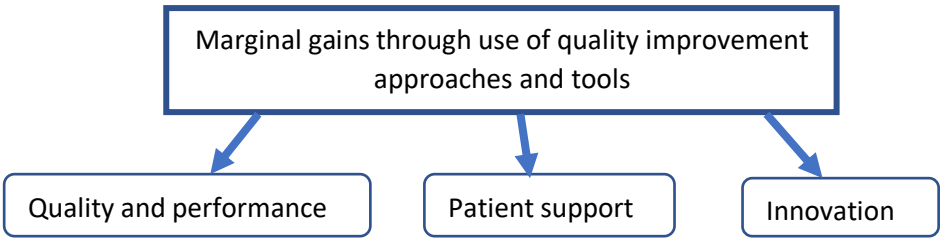
Application of QI approaches and tools can improve the performance (e.g., optimise time to live birth / success rates per cycle and patient satisfaction or quality of care) of an assisted conception clinic through an aggregation of marginal gains.

When measuring for improvement, the learning develops through the process, and as a result, the hypothesis might change throughout the project. The project aimed to determine if and how interventions through QI can be made to work within one IVF clinic and what constitutes 'success'.

2.2 Aims and objectives of the project

With increased operational costs and limited financial resources how can NHS fertility clinics improve the chances of a live birth per treatment cycle, help patients to stay in treatment, and lessen the psychological burden associated with infertility and fertility treatment? Even more pertinent following the Covid-19 pandemic.

This research project aimed to examine how standard care is delivered within an NHS IVF service with the use of novel QI tools and approaches to identify areas for marginal improvements. The main aim is to assess whether the IVF clinic could benefit from application of industrial manufacturing principles to drive continuous improvement through the aggregation of marginal gains. The research project focused on different aspects of the fertility service and included three areas:



Focusing on both performance and patient support should produce improvements in clinic success rates whilst also ensuring patients receive excellent supportive care and a good experience at our clinic. The objectives may change as QI approaches and tools are

used to look at our services systems and processes to identify areas for improvement. Preliminarily data have helped to identify the aims and objectives listed in Table 6 below. It is hoped that marginal gains from each objective may aggregate to significant improvement overall and deliver the aims of the project. The learning from this study would be shared on different platforms.

Table 6| Preliminary aims and objectives of the project.

Aims	Preliminary objectives which developed over the period of C2
Quality and performance; use QI methods to make improvements to the quality and performance of our assisted conception service i.e., efficiency and ultimately increase successful outcomes.	• Improve stability of culture conditions by 10% by July 2018 • Improve ICSI clinical pregnancy rates per embryo transferred to benchmark as soon as possible • General improvements through efficiencies and removing non-value adding 'waste' within systems such as stock control, data entry, record keeping
Patient support; use QI methods to make improvements to lessen the emotional burden of treatment.	• Offer psychological assessment training to all staff • Increase assessment of patient quality of life by 100% with the implementation of validated questionnaires • Improve patient support so that standard patient feedback reached >80% within the 'excellent' field by the end of the project • Determine clinic patient discontinuation rates and reduce by 5% compared to 2018/2019 data • Determine clinic cumulative pregnancy rates and increase by 5% compared to 2018/2019 data • No cancelled cycles due to the physiological burden of treatment
Innovation; test an innovation that could make a positive contribution to service delivery and patient experience	• Trial an innovative positive reappraisal coping intervention as part of a QI PDSA cycle related to patient support
Share the learning	• QI discussed at every team meeting, added to agenda template • Submit abstract at international conference meeting • Submit to Trust QI projects and present to Trust management (clinical management board meeting) • Submit quality improvement report article to BMJ Open Quality peer reviewed journal using SQUIRE guidelines

2.3 The relevance of the project to the research area

Team exploration of QI approaches is likely be a valuable learning experience encouraging a mindset of QI. Trialling a new approach with fresh thinking and measurable outcomes allows the safe testing of change for better systems, processes and outcomes. Preliminary work has indicated potential from the application of manufacturing principles within the IVF setting for accelerated performance improvement. This project aims to increase our understanding of how QI approaches and tools can be applied within an IVF service, identifying any barriers and enablers along the way, and whether their application can lead to incremental improvement of a clinic's performance in terms of both outcomes (success rates, financial) and quality of care. It is important to disseminate any learning from QI so that our profession can benefit from understanding how industrial manufacturing principles can be applied to fertility clinics to drive continuous quality improvements for patients (service quality), staff (workload, stress), and clinic (performance, cost, regulation). It can be challenging to write about improvement science but sharing successes, failures and developments through scholarly literature is an essential part of the complex work required in order to improve healthcare services for patients, professionals and the public (Ogrinc et al., 2016).

2.4 Stakeholder engagement

The project aligns with the requirements and strategic aims of our organisation (Trust) and regulator (HFEA). For example, use of data and feedback for continuous improvement, best outcomes and support, and responsible innovation to promote new and better ways of working and contribute to financial position of the Trust. Predicated cost savings should improve value for money for commissioners. This service evaluation project was chosen because it should directly benefit the IVF clinic and patients, and alignment with everyone's agendas should reduce barriers to the project.

2.5 Costing

Use of quality-of-life questionnaires may result in increased requirement for the counsellor, this was monitored, and patients could be signposted to other sources of support e.g., Improving Access to Psychological Therapies (IAPT) programme. MFI and

Lean should not require additional resources or cost and should lead to cost savings within the service through identification and removal of non-value adding waste. There are no consumable or equipment costs.

2.6 Innovation

Included within the improvements to patient support the project trialled an innovative tool developed to help support patients cope during medical waiting periods i.e., the wait for pregnancy outcome. The Positive Reappraisal Coping Intervention (PRCI, developed by Cardiff University) is an evidenced based, inexpensive intervention that could be delivered by medical staff. Evidence suggests PRCI can increase emotional quality of life and help patients stay in treatment. This was implemented as part of a PDSA cycle with collection of patient's quality of life data. The Author had permission from Jacky Boivin to use the PRCI within the clinic.

2.7 Ethics

This project falls into the category of service evaluation and does not require NRES approval. This was confirmed by completing the NHS Health Research Authority questionnaire, discussion with the Trust's Research and Development office, and an ethOS application with Manchester Metropolitan University (EthOS reference number 12242) (Appendix 3). Changes being tested may not lead to improvement but should not affect standard patient care as changes would be tested in a small and safe way. Any changes made for improvement involved all patients having treatment at that time, as it was the standard clinical pathway i.e., introduction of the HADS questionnaire as standard for all patients planning treatment.

2.8 Context

This service evaluation project was undertaken over ~4 years (2018-March 2022) within a small NHS fertility centre (~250 fresh cycles a year, ~150 frozen embryo transfers) offering IVF, ICSI, embryo freezing/thawing, and fertility preservation. The project was interrupted by the Covid-19 pandemic March 2020-August 2020 when all IVF clinics were closed by law to prevent the spread of the virus, from the 11th of May 2020 clinics could apply to the regulator (HFEA) to recommence treatment and this process included developing a

Covid-19 treatment commencement strategy. This strategy described the steps and measures taken to ensure treatment offered would not increase transmission of the virus (staff and patients kept safe) and that treatment could be offered safely with minimal disruption (contingency plans in case of staff shortages; sickness, isolation, redeployment) and would not put pressure on the NHS (e.g., care to not overstimulate women who might then develop OHSS and require admission to hospital). Changes implemented included social distancing measures (reduced reception seating, reduced face to face appointments, reduced footfall through the clinic, attending alone, longer allocation of time for appointments to allow for cleaning of surfaces and airing the rooms etc), mandatory PPE, and increased hand washing. The IVF clinic successfully applied to the HFEA to recommence treatment in June 2020. However, the clinic relied on the use of the Trust's Day Surgery Unit (DSU) theatre to collect eggs for fresh treatment cycles under sedation. The unprecedented times meant that the Trust was unable to provide a theatre list for fertility patients until August 2020, when one Friday morning list was acquired. Pre-pandemic the clinic had the flexibility of two theatre lists (Wednesdays and Fridays). Therefore, the pandemic presented many additional changes to the IVF clinic's processes and procedures which were not anticipated during the project planning. The single theatre list remains to April 2022 and likely beyond.

2.9 Potential risks and challenges

Risks: Changes being tested may not lead to improvement but should not affect standard patient care as changes were tested in a small and safe way. Introduction of a quality-of-life questionnaire as standard care did reveal individuals who were signposted onwards for appropriate support. This might have increased the workload of the clinic counsellor and/or required signposting or referral to additional psychological therapies (IAPT) (there were 6 available within 35 miles of the Trust). Staff needed to be supported with training; a psychological assessment skills course was available within the Trust. As this area was outside of the QI lead's expertise collaboration with the independent counsellor and the Trust's psychology department was required to safely deliver the patient support QI aspects of the project.

Challenges: This project relied on engagement with the whole team in order to work and therefore context and culture were important, and had to be considered. Significant staff

changes within the team could have presented additional challenges for engagement with the project. However, the laboratory team found the preliminary work interesting and engaging. The project proposal was presented to the team and regular updates were provided. The Covid-19 pandemic presented additional challenges due to the impact that additional unforeseen changes made to service delivery might have had on the data during quality improvement cycles and data analysis.

2.10 Expected value and impact

QI approaches with associated QI tools can accelerate improvement within an organisation making it faster, better and cheaper. An example within healthcare is the Virginia Mason Medical Centre (VMMC) applying the Lean approach to its processes to become the safest hospital in the USA. The NHS is currently in partnership with Virginia Mason Institute (VMI) to develop a 'lean' culture of continuous improvement which puts patients first. A review of the literature revealed there are few published papers within reproductive science that explicitly utilise these theories/tools. This project aimed to increase our understanding of how QI approaches and tools can be applied within an IVF service, identifying any barriers and enablers along the way, and whether their application can lead to incremental improvement of a clinic's performance in terms of both outcomes (success rates, financial) and quality of care. It is important to disseminate any learning from QI, even if changes are unsuccessful, so that our profession can benefit from understanding how industrial manufacturing principles can be applied to fertility clinics to drive continuous quality improvements for patients (service quality), staff (workload, stress), and clinic (performance, cost, regulation). Exploring these approaches and tools as a team should lead to learning and improvement of the IVF service without additional costs or resources. Continuous improvement of service performance, whether clinical outcomes or patient support, is in line with the aims and strategies of the clinic's regulator (HFEA) and NHS Trust organisation. Therefore, the clinic could benefit from employing industrial manufacturing principles to drive continuous improvement.

Chapter 3. Methodology

3.1 Experimental approaches and QI tools used

Systems thinking was used to understand the current 'system' of the IVF laboratory and clinic to identify parts that are not working well. This was not limited to a single QI approach but combined Lean and the 'MFI' because they have been more widely adopted by UK healthcare and could be better received within the clinic. The 'MFI' roadmap was used to explore metrics and root causes to identify areas for improvement by PDSA cycle. Lean thinking was explored with a focus on identifying and removing waste within the system.

There are pit falls to avoid when trying to successfully apply Lean (Blackmore & Kaplan, 2017), a focus on cost-cutting, short term gains, or not prioritising the patient first limits improvement. Although the existing research is far from complete there are many examples as proof of concept that, under many circumstances, Lean can be effective (Mazzocato et al., 2010; D'Andreamatteo et al., 2015). In the complex social systems of healthcare, the flexibility and adaptability of PDSA are important features that support the adaption of interventions to work in local settings (Reed & Card, 2016). Unlike randomised controlled trials, PDSAs allow new learning to be built in to the experimental process, if problems are identified with the original plan, the theory can be revised to build on this learning (Reed & Card, 2016). Successful application of the PDSA methodology can achieve QI goals more efficiently or reveal goals are unachievable under realistic constraints or it identifies new problems to tackle instead (Reed & Card, 2016). There is no guarantee that desired outcomes or improvement will be achieved but authentic execution of PDSA methodology guarantees learning and informed action (Reed & Card, 2016; Leis & Shojania, 2016). PDSA cycles have been used poorly in healthcare due to oversimplification of the method as it has been translated into healthcare, and a lack of rigour and tailored application of the approach (Reed & Card, 2016). Taylor et al, (2014) reported that fewer than half of published studies met the minimum characteristic of PDSA. Authentic application of PDSA methodology should require refinements to the intervention or the plan to implement it (Leis & Shojania, 2016), leading to greater benefits.

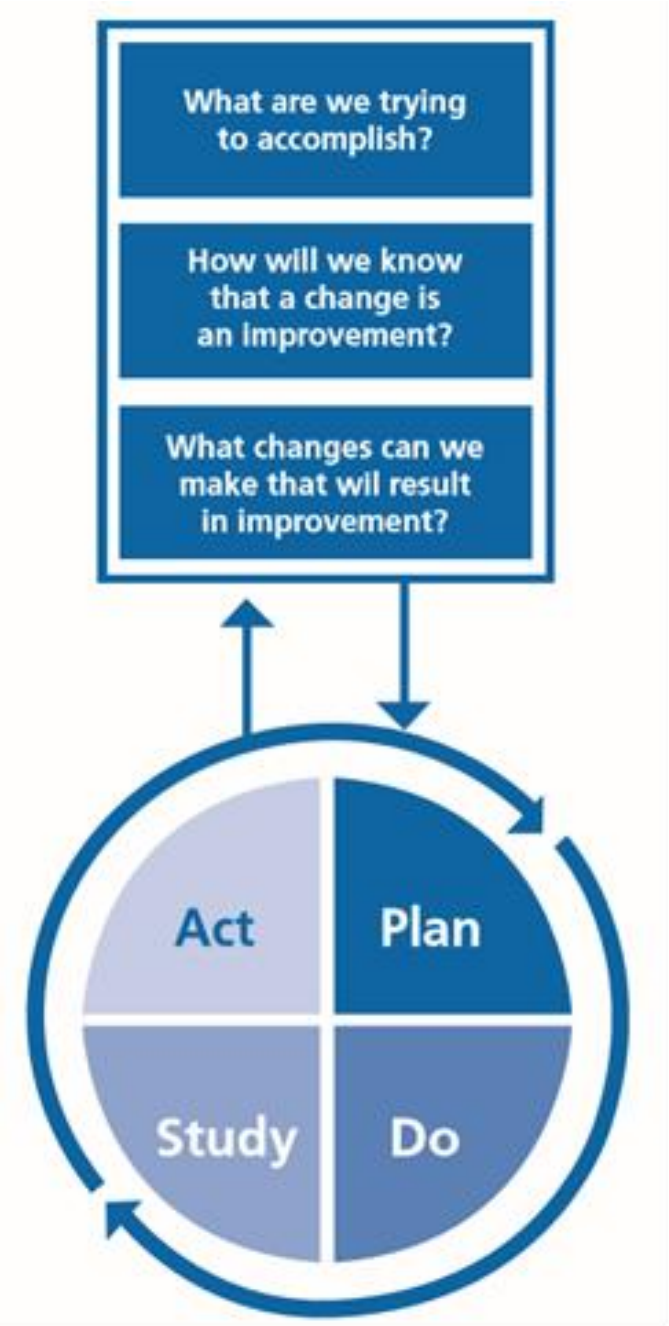


Figure 10: The Model for Improvement. Used to accelerate improvement work when used as a roadmap to help structure improvement activity to ensure the best chance of achieving set goals and wider adoption of ideas. Based on three key questions (the thinking part) which are then used in conjunction with small scale testing (the doing part) Plan-Do-Study-Act cycles (PDSA). (Langley et al., 1996; Boaden et al, 2008; Taken from ACT academy 2018)

3.1.1 The Model for improvement (MFI)

The 'MFI' was used as a roadmap to guide the quality improvement work through exploration of metrics and root causes to identify areas for improvement by PDSA cycle (Figure 10). This was combined with a Lean thinking approach to focus on identifying and

removing waste within the systems of our IVF service. The aim was to focus on value, purpose and metrics to create ideas for an intervention for improvement and produce a plan for improvement that could be tested within an appropriate time frame. The effects of the intervention could either lead to improved process or at least learning from failure. When making QI changes it is important to measure balancing, process and outcome metrics to determine if the change is an improvement.

During the duration of the 4 year project there were three areas of focus for improvement identified through staff engagement (4N chart (Dodds, 2018)), review of patient feedback, constant review of clinic key performance indicator data, equipment failure (incubators out of service), changes to way of working (move from cleavage stage embryo transfers to extended culture and blastocyst transfer, ceasing of slow freezing and implementing vitrification), adverse events (e.g. cancelled treatment cycles due to patient anxiety). These are addressed in 3 separate results chapters, listed below, the format and content of which are written with SQUIRE (Standards for Quality Improvement Reporting Excellence) guidelines. SQUIRE guidelines provide a framework for high quality reporting of new knowledge about how to improve the quality, safety, and value of healthcare (Ogrinc et al., 2016). They outline how quality improvement programmes are set up, the nature and impact of interventions intended to improve healthcare and lessons learnt.

1. **The need to improve the stability of culture systems for extended culture of embryos.**
2. **To perform a root cause analysis for a drop in fresh ICSI success rates and implement changes for improvement.**
3. **To continue to provide excellent patient support but for the clinic to do more to support patients before, during and after treatment.**

3.1.2 QI tools

The QI tools used in this project include Simon Dodds's (2007; 2018) 4N chart, process mapping (Trebble et al., 2010), cause-effect (fishbone) diagram (Best & Neuhauser, 2008), driver diagram (Bennett & Provost, 2015), 5S (Bicheno, 2005), and Statistical-Process-Control (SPC) charts (Provost & Murray, 2011; Mohammed et al., 2008) (generated using

the BaseLine© SPC software). (Further information regarding these tools can be found within the NHS Institute guide).

The implementation of Statistical process control (SPC) requires the production of control charts, of which there are different types; XmR-chart, p-chart, G-chart, and xBar-chart. The project used the robust and versatile XmR chart for simplicity and access to software (XmR is used in Baseline software (SAASoft, 2011)). Control charts include a plot of the data over time with three additional lines—the centre line (usually based on the mean, the green line drawn with BaseLine© software) and an upper and lower 'control' limit or natural process limit, typically set at ± 3 standard deviations (SDs) from the mean (the red lines drawn with BaseLine© software for the range of expected variation (± 3 sigma)) (Mohammed et al., 2008). Control limits are estimates of the limits of natural (common cause or chance) variation. A process is in statistical control (or stable) when considered to be exhibiting common cause variation; when data points appear, without any unusual patterns, within the control limits (Mohammed et al., 2008). Control charts can be used to identify special (or assignable) causes of variation. There are several guidelines that indicate when a signal of special cause variation has occurred, and this is then a trigger for investigation to learn, identify the cause and, where appropriate, action to eliminate it (Mohammed et al., 2008).

The study used the 5S tool (sorting, setting in order, systematic cleaning, standardising and sustaining) to de-cluttered and reorganise areas within the fertility centre space for a more effective working environment. Areas included the main laboratory, lab offices, and store cupboard. Refer to Appendix 17.

3.2 Chosen measures

Measurement and gathering data are vital elements of systems thinking and quality/performance improvement and are also needed to assess the impact of any interventions for change. Standard key performance indicator data and additional metrics (patient questionnaires, incubator door opening frequency), depending on the intervention, were monitored throughout the project, as listed in each result chapter.

3.3 Statistical analysis

BaseLine©, a system behaviour chart software, was used to plot the time-sequenced data. Data were evaluated by Statistical-Process-Control (SPC) charts (generated using BaseLine© SPC software (SAASoft, 2011)) (Appendix 15 for rules). IBM SPSS Statistics 27 was used to perform the statistical analysis. X^2 was used to examine the difference in treatment outcome between 2 groups (pre and post intervention) and Kaplan-Meier survival analysis was used to determine time to pregnancy.

3.4 Validated quality of life questionnaire (QoL)

As an intervention in itself and an additional data measure the fertility clinic implemented the use of a validated QoL questionnaire for its patients in October 2020. There were a number of options to choose from, such as; QPP-IVF (Holter et al., 2014b) quality of care from patient's perspective specific to IVF treatments and validated in Sweden, FertiQol (Boivin et al., 2011) internationally validated instrument to measure quality of life in individuals experiencing fertility problems, or HADS (hospital anxiety and depression score) (Zigmond & Snaith, 1983).

There is a need to measure and take into account the QoL in infertility patients (Boivin et al., 2011). Many publications demonstrate a high incidence of negative reactions to infertility and its treatment, impacting on overall life satisfaction and well-being, chance of success, and ability to continue with treatment (Boivin et al., 2011). Therefore, fertility clinics addressing patients QoL could lead to improved patient outcomes and experience.

The QoL questionnaire selected for this study was the Hospital anxiety and depression scale. Following feedback from clinic staff and counsellor it was perceived to be more acceptable to patients (less detailed questions asked compared to the other two) and the Trust was already using HADs clinically in other departments e.g., clinical psychology, maternity.

Full details of the method of construction of the HADS is presented by Zigmond & Snaith, (1983). Patients complete a questionnaire composed of statements relevant to either generalised anxiety or depression. HADs has been shown to be acceptable by patients (Snaith 2003) and only takes 2 to 5 minutes to complete. Patients complete it in order to

best indicate how they felt in the past week. The HADS consists of 14 items (7 items for each subscale) that are rated on a 4-point Likert scale, so the possible scores range from 0 to 21 for anxiety and 0 to 21 for depression. Scores on each scale can be interpreted in ranges: normal (0–7), borderline (8–10), clinical (11-21). As a self-assessment scale, it is only valid for screening purposes and definitive diagnosis must rest on the process of clinical examination.

Patients were assessed for a HAD score at initial consultation to the clinic and following all subsequent fresh or frozen embryo transfer. Patients were provided with a HADS patient information sheet with the HAD questionnaire and it was their choice to consent to and complete it. Please refer to Appendix 4 for documents created for patients and clinic regarding the offer of the HADS.

3.5 Patient involvement and additional questionnaires

The clinic's standard patient feedback questionnaire data was used as a measure for the QI work. Additional patient questionnaires were created for the QI project and used to gather data before and after implementing any changes. Refer to Appendix 5 for questionnaire used.

3.6 Innovation: The use of the Positive Reappraisal Coping Intervention (PRCI)

As part of the continuous quality improvement of clinic patient support an innovative theory-based coping psychological intervention tool was evaluated. The tool was developed to promote the use of a meaning-based coping intervention called positive reappraisal coping to help support patients cope during medical waiting periods, which are unpredictable, uncontrollable and stressful situations, when patients wait for test results that could potentially threaten their well-being. In the context of fertility waiting for the outcome of treatment following embryo transfer is one of the most stressful periods for patients, this intervention helps by encouraging women waiting for an IVF pregnancy test to redefine the waiting period more positively. The Positive Reappraisal Coping Intervention (PRCI) was developed during the PhD studies of Deborah Lancastle (Lancastle, 2006, Cardiff University) supervised by Jacky Boivin (Lancastle & Boivin, 2008). It was designed to be theoretically derived, simple enough for patients to use with no

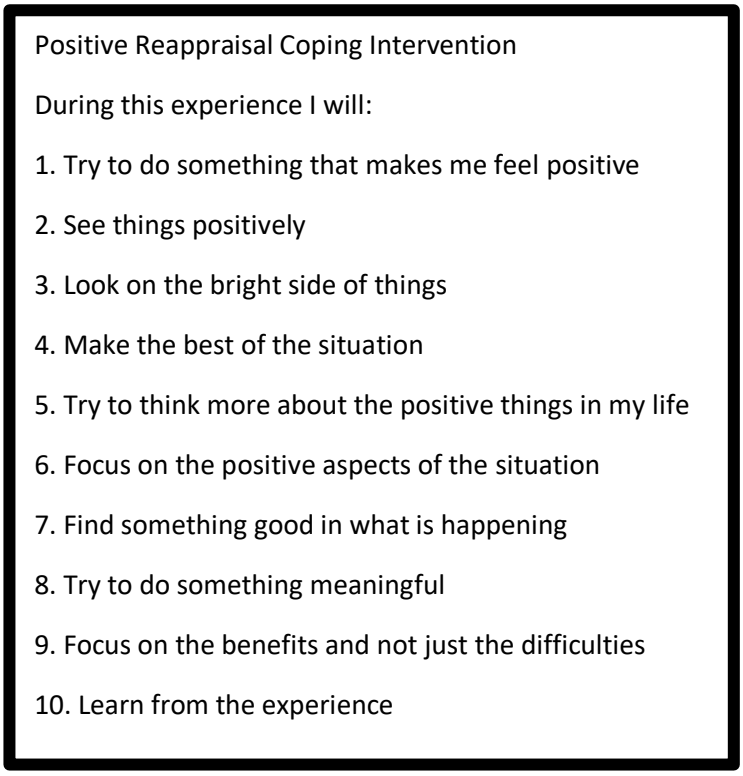


Figure 11 PRCI intervention. (Lancastle, 2006; Lancastle and Boivin, 2008)

training and to use whenever and wherever they feel the need, and cost-effective enough to be made freely available to all patients (Lancastle & Boivin, 2008). This criterion resulted in development of a simple, pocket-sized card containing 10 statements designed to prompt or promote positive reappraisal coping efforts (Figure 11). PRCI is an evidenced based, inexpensive, self-administered intervention that could easily be delivered by clinic staff and which might help patients to manage their worries during the IVF waiting period. The intervention comes with an explanatory rationale in addition to the statements (Appendix 6), patients are instructed to read the statements at least twice a day or more frequently when required (Refer to Lancastle & Boivin, 2008; Ockhuijsen et al., 2013; Ockhuijsen et al., 2014).

Evidence suggests PRCI is acceptable to patients and can increase emotional quality of life and help patients stay in treatment (Lancastle & Boivin, 2008). PRCI is widely used in the USA/Netherlands in IVF and also in recurrent miscarriage in the UK (*J Boivin 2019, pers. comm., 25th January*). Research so far suggests that use of the PRCI promotes positive reappraisal coping, positive emotions and sustains overall coping effort, it variably reduces negative emotions and seems mainly to make the stressful situation of waiting

more tolerable (Lancastle & Boivin, 2008; Ockhuijsen et al., 2013; Ockhuijsen et al., 2014a; Ockhuijsen et al., 2014b). The qualitative research indicates women adapt the PRCI, for example some have favourite statements, others statements in their phone, this shows engagement with the PRCI and learning of positive reappraisal. It may also help to build resilience for future adversity (e.g., when treatment fails) but further research is needed. Further investigation could help establish the extent to which this intervention is a beneficial addition to the routine care women receive when waiting for a pregnancy test during fertility treatment. The PRCI was implemented as part of a PDSA cycle with collection of patient quality of life data. The author gained permission from Jacky Boivin to use the PRCI within the fertility clinic.

Chapter 4.

Results chapter 1

Reducing disruption of culture conditions within an IVF laboratory using the model for improvement / lean approach

The MFI and lean were applied to identify areas for improvement within the laboratory processes. An area of focus was optimisation of culture conditions and changes for improvement were explored. Incubators were utilised differently. This was a prospective study. Many QI tools were used including Statistical-Process-Control charts (BaseLine© SAASoft), spaghetti diagrams, process mapping, and cause/effect diagram. Measurements included incubator door openings and stability, practitioner 'paces', procedure timing, and standard clinical outcome data.

Results chapter 1.1 Background

The purpose of the IVF laboratory system must be to maintain the viability of gametes and embryos during processing and manipulation, and to reduce any possible harm or risk. The key physiochemical factors that affect gametes and embryos in every IVF laboratory: temperature control, maintaining osmolarity and pH, and protection from oxidative stress and toxic substances (Mortimer et al., 2018). A good chance of successful pregnancy and healthy babies are the ultimate outcome for clinics, patients, and society. A previous improvement change to practice within the laboratory and across the sector was the use of extended culture to the blastocyst stage of development, with its associated increased chance of implantation and reduced multiple births (ASRM, 2013, Harbottle et al., 2015). However, embryos being cultured for longer periods within the laboratory could be more vulnerable to suboptimal conditions.

The lab team identified culture conditions as an area of concern through engaging with Simon Dodds's 4N chart (used to identify areas of concern and their impact, frequency and our influence over them) (Dodds, 2007; 2018). This exercise identified two areas with a high impact factor, overloading of incubators due to equipment failure and changes in caseload.

The IVF laboratory had experienced the equipment failure of two box type incubators (Incubators 1 and 2) leading to the decommissioning of one and the other to be out of

service. The situation forced unplanned changes in our processes and led to overburdening the remaining 3 incubators (3, 4 & 5). During the process of procuring, installing, and validating new bench top incubators the lab had to manage with existing equipment and reconfigure how remaining incubators were used. Incubators 3 and 5 are low oxygen, timelapse incubators used primarily for embryo culture, as undisturbed as possible. This means limiting the number of times you open the door and reducing how often you take embryos out of the incubator to observe development under a microscope. Reducing physical perturbation of the incubator environment is required for embryo viability (Consensus group, 2020). It is also important to have a 'holding' incubator dedicated to non-culture activities such as dish equilibrations, sperm preparations, etc, Incubator 4 was used to equilibrate culture dishes for the next day.

The clinic also saw a shift in its caseload. There are two days of egg collection every week, Wednesdays and Tuesdays. Historically the clinic offered cleavage stage day-2/3 embryo transfers (not blastocyst stage day-5/6). Blastocyst extended culture could only be offered to those patients planned for egg collection on a Wednesday (the clinic could not offer a day-5 transfer on a Sunday for Tuesday cases). The clinic saw an increase in demand from patients for the option of extended culture which starts on a Wednesday (day-0) and embryo transfer on Monday/Tuesday day-5/6. This led to busy clinical days on a Wednesday with frequent incubator door openings and quiet Tuesdays (day-2 transfers on Friday) (Figure 12).

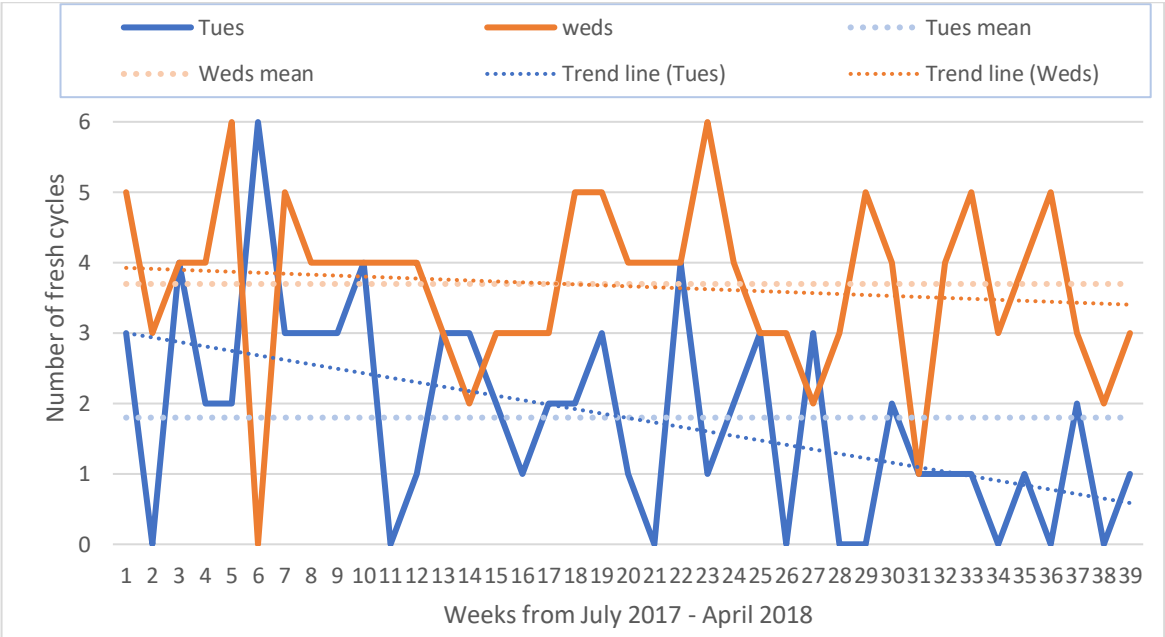


Figure 12a number of fresh cycles per day. Graph to show change in case load on a Tuesday and Wednesday over time. A drop in numbers of fresh cases on a Tuesday (Day-2 embryo transfer) compared with the more popular blastocyst treatments (Day-5/6) offered on a Wednesday. Leading to heavier workloads on Wednesdays. Over this period there was a total of 70 cases over Tuesdays and 143 over Wednesdays.

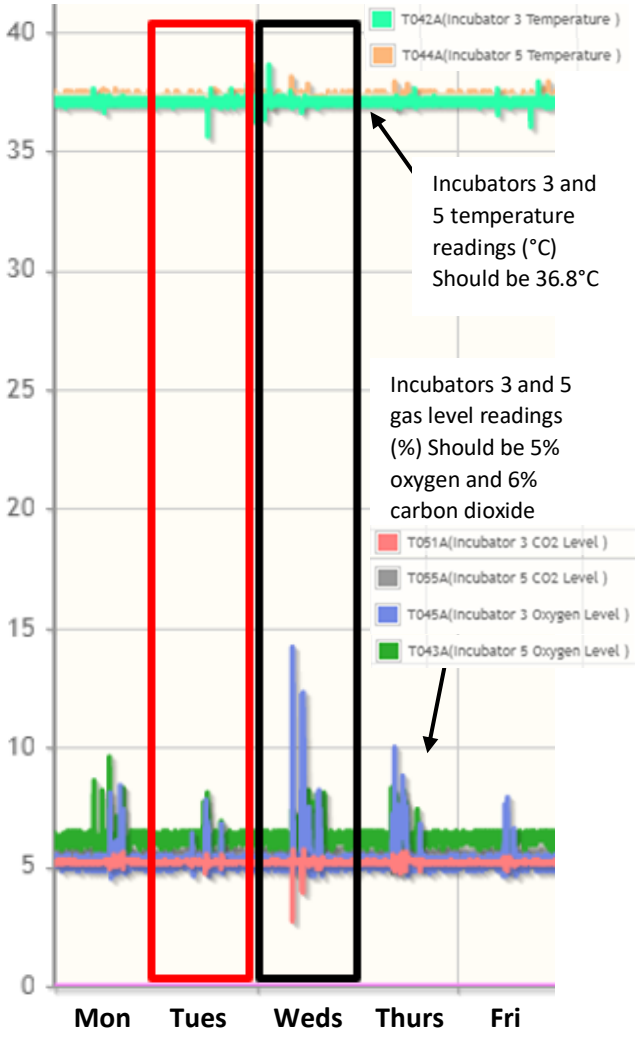


Figure 12b Daily temperature and gas fluctuation due to incubator door openings. Monitoring of box type incubators 3 & 5 (low oxygen, CO_2 buffered pH system, temperature) used for 'reduced interruption' culture. Set at 5% oxygen, 6% CO_2 and 36.8 ºC. Spikes indicate disruption to optimal culture conditions as incubator doors are opened. Busy days intuitively result in higher disruption. Monitoring of the frequency of door openings across incubators 3/5 in one week was an average of 15 openings on a Tuesday and 30 on a Wednesday. The higher and more frequent spikes are seen with incubator gas levels, especially oxygen, it appears that incubator door openings are more detrimental to optimal gas levels rather than temperature. Oxygen levels would be expected to increase (20% ambient) with repeated door openings and carbon dioxide would decrease (0.03% ambient).
Red box= Tuesday
Black box= Wednesday

Low oxygen incubators 3 and 5 are used to culture all eggs and embryos (fresh and frozen) from thaw/collection to transfer. The changes in used of incubators due to incubator failure led to overburdening these incubators, with frequent door openings disrupting gas and temperature, therefore disturbing optimal stable culture conditions. This has been exacerbated by the increase demand for extended culture to blastocysts stage which can only be offered to patients having an egg collection on Wednesdays. The clinic had future plans with the Trust Day Surgery Unit to provide this treatment to all patients with a change in egg collection theatre days from Tuesday currently to a Friday. However, in the meantime this leads to very busy egg collection days on a Wednesday. Two new bench top incubators became in service and now an opportunity existed to look at how to utilise all 5 incubators to minimise disruption to culture conditions.

The 'MFI' was used as a roadmap to guide QI work through exploration of metrics and root causes to identify an intervention for improvement. A process map of the current journey of eggs through the laboratory on day-0 identified the ICSI (Intracytoplasmic sperm injection) pathway (denudation and injection) might be more vulnerable to exposure to suboptimal conditions and would result in more interruption of culture conditions of incubators 3/5 (especially with large egg numbers) (Figure 13). The map also highlighted the overuse of incubators 3/5 and underuse of the new bench top incubators.

A closer look at the laboratory layout revealed how many practitioner 'paces' are taken during procedures (Figure 14). It highlighted motion and product transportation waste within the system, this may cause unintended harm due to an increased risk of cooling dishes, extended time taken during a procedure to retrieve a dish and increased chance of an incidence by carrying dishes through a door during procedures. This happens because of changes made following equipment failure when incubators 1/2 were lost to the service. Counting 'paces' taken revealed how far ICSI dishes are carried and therefore vulnerable to cooling and identified the paces to incubator 4 could be removed from procedures by using the new incubators. The benchtop incubators cannot hold all pre-prepared dishes like incubator 4 but they could hold dishes required for the next procedure. Process mapping of egg/embryo flow through the laboratory for ICSI vs IVF revealed that ICSI eggs/embryos are more vulnerable to fluctuation in culture conditions.

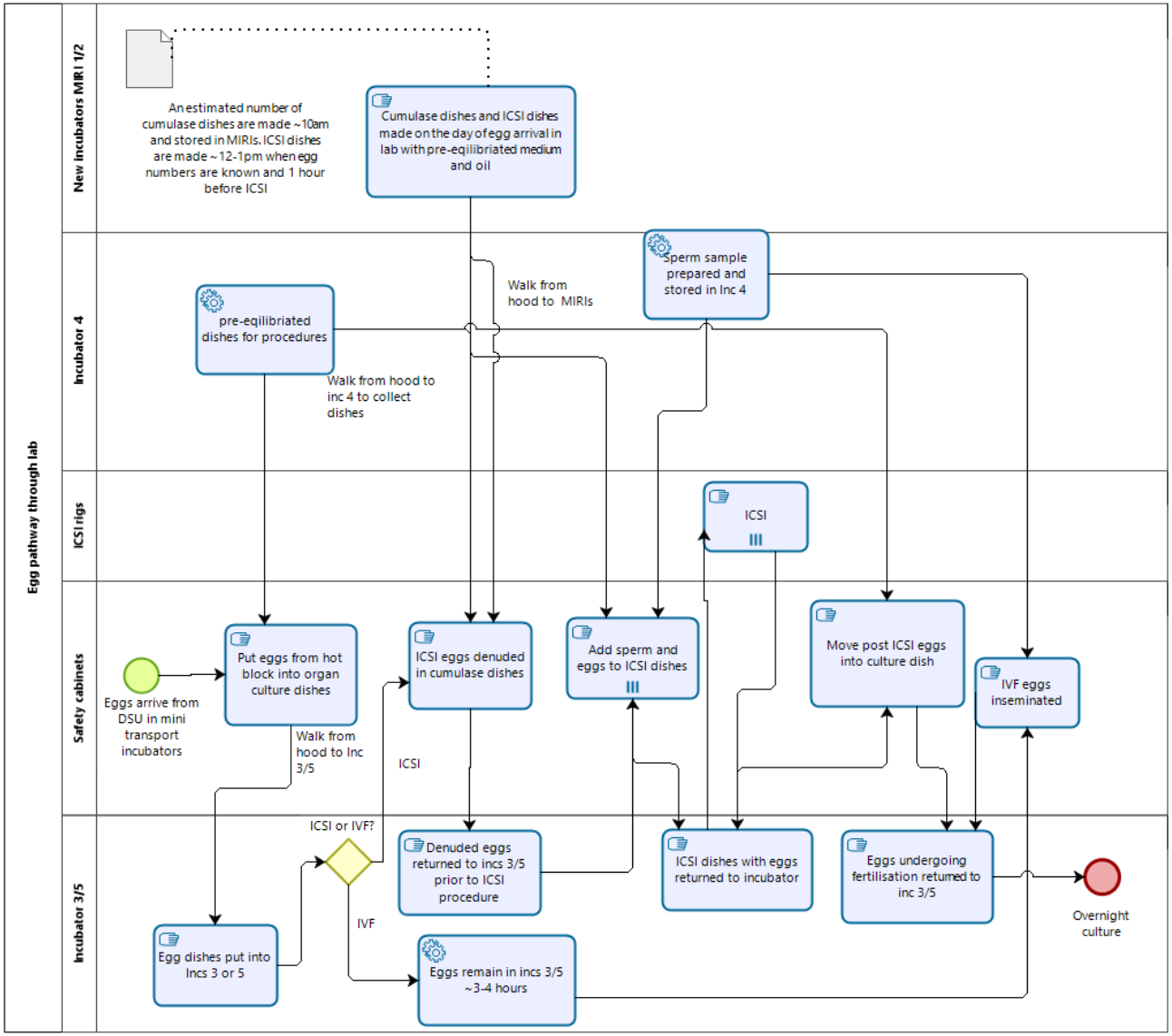


Figure 13: The current state: swim lane process map

Process map of the flow of eggs through the IVF laboratory current system. Each lane represents a piece of key equipment within the laboratory which eggs are exposed to (incubators, ICSI rigs and safety cabinets) each should be set to maintain optimal conditions for embryo culture. When eggs are outside of the incubators they are placed on heated stages and procedures must be completed quickly to reduce exposure to suboptimal conditions (e.g., cooling, overheating, change in pH).

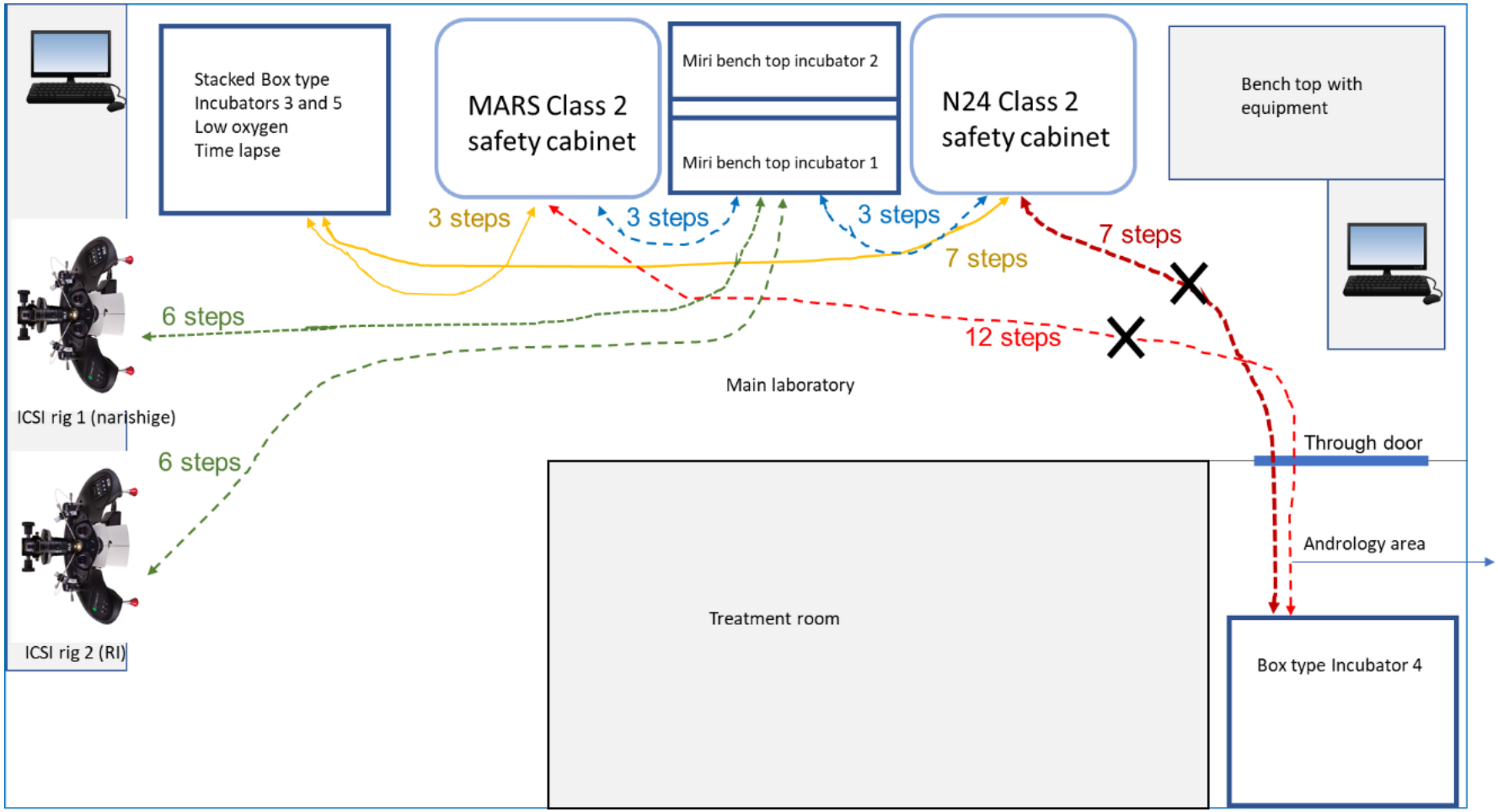


Figure 14: The current state: Distance diagram. Floor layout of IVF laboratory with 'paces' taken between equipment carrying dishes with embryos/eggs. Dishes cool while out of the incubator/heated stage. Walking to incubator 4 to retrieve fresh pre-equilibrated dishes to move embryos/eggs into during a procedure, perhaps this could be changed? Miri 1 & 2 (new incubators) are benchtop incubators with faster recover times following door openings. ICSI is performed on ICSI rigs. Safety cabinets are used for all procedures except ICSI.

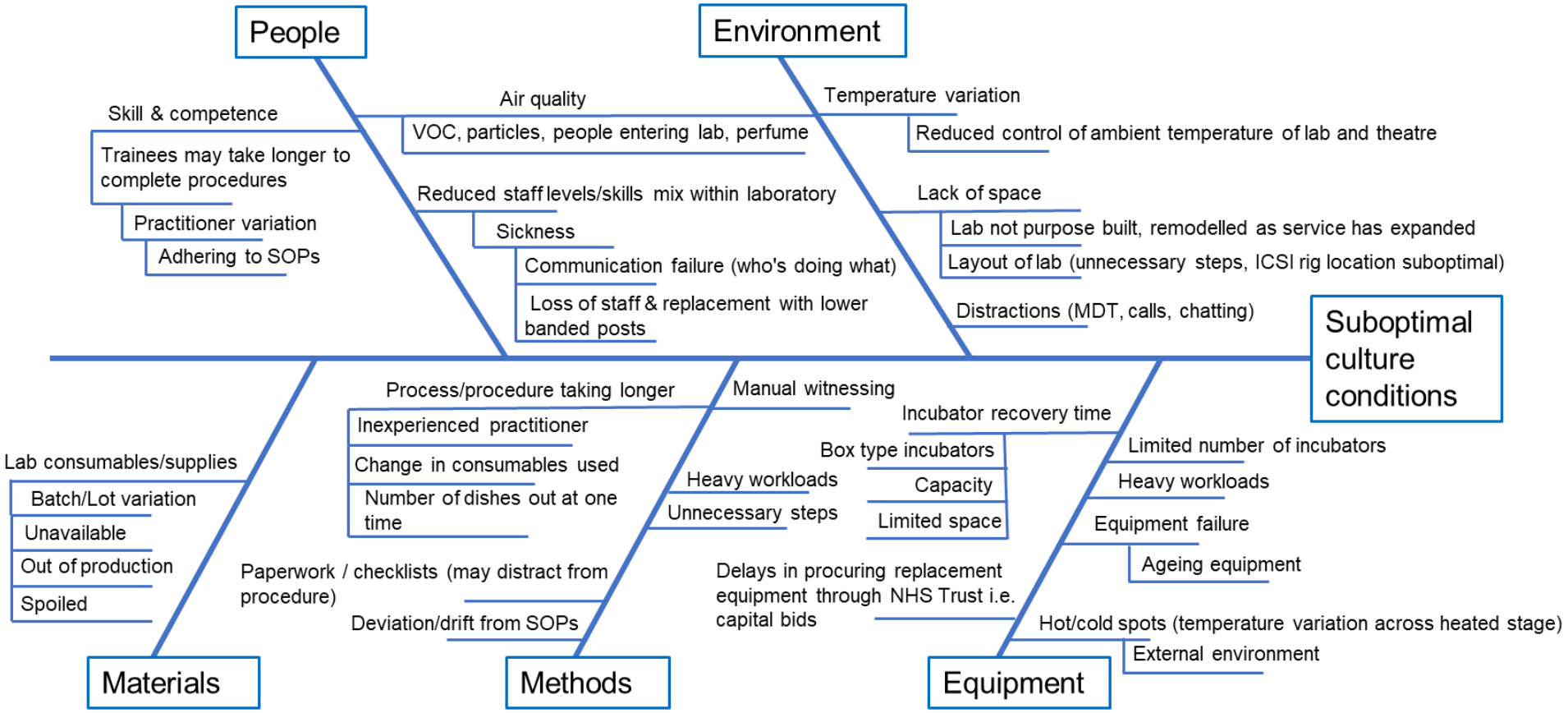


Figure 15 Cause and effect diagram. used to identify all potential causes of suboptimal culture conditions within the current system

A cause-effect diagram was used to identify all potential causes of suboptimal culture conditions within the current system (Figure 15). Limited incubators, heavy workloads and equipment failure were difficult to influence but changes in procedures could help reduce incubator culture disturbance.

Systems thinking had identified busy Wednesdays and a focus on the ICSI pathway and reducing disruption to culture conditions through better utilisation of new incubators and removing waste from processes. Therefore, the project goal was to improve the stability of culture conditions. A driver diagram helped to identify factors to influence and measures to consider (Figure 16). Interventions to achieve the primary and secondary drivers should through an aggregation of marginal gains accomplish the aim of this project; to improve by 10% stability of culture conditions by July 2018.

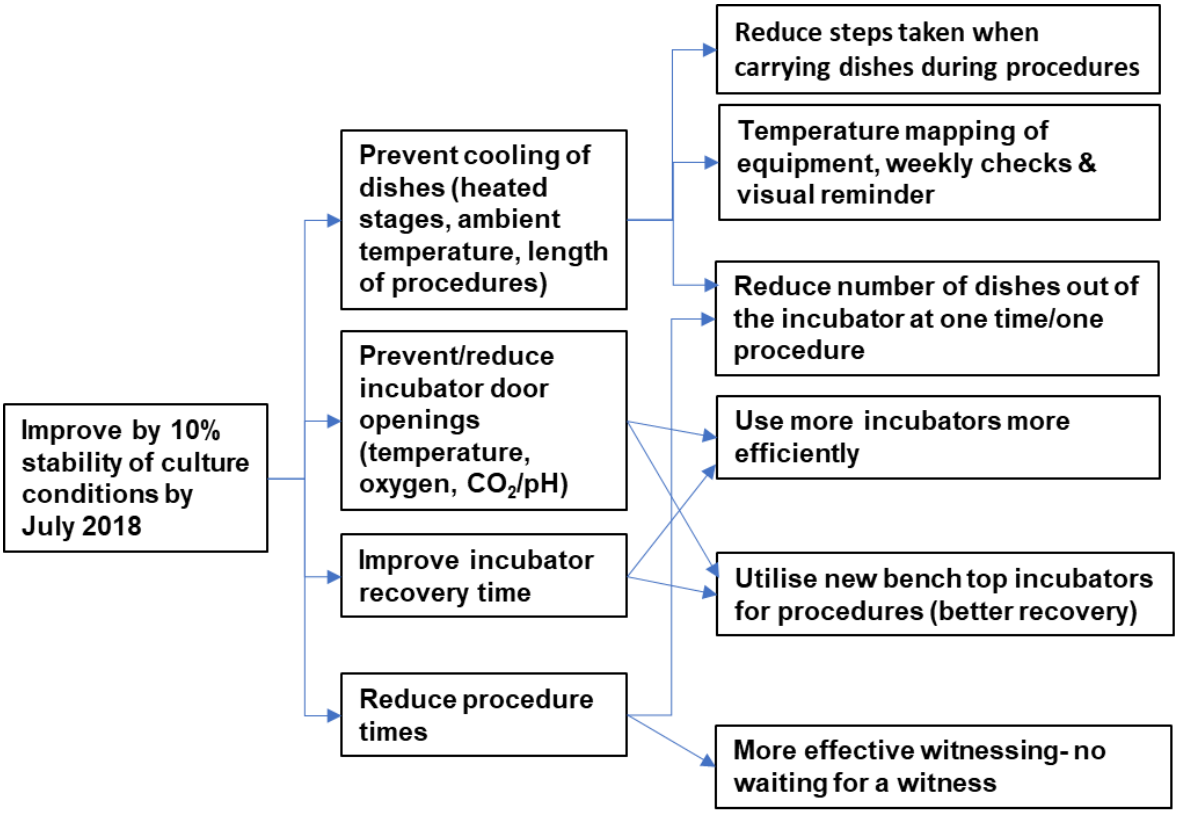


Figure 16 Driver diagram to identify primary and secondary drivers to achieve the proposed quality improvement goal

Results chapter 1.2 Methods

The QI project was implemented within a small fertility laboratory (~7 fresh IVF cycles a week) with prospective data collection from the 4th of April 2018 (metrics already

measured by the clinic were looked at retrospectively from February to April 2018 to improve baseline data prior to the PDSA cycle). The laboratory team needed to engage with the project as they were responsible for accurate data gathering and adhering to proposed processes changes. The team is small, and the project only involves laboratory staff thereby reducing complications of crossing professional silos and communication across the MDT.

To achieve the project aims an intervention 'bundle' of 4 changes was introduced in May 2018. Each of these changes should be assessed separately in multiple PDSA cycles, however due to project timescale limitations, weekly metric collection, and variation and delay in outcome metrics with IVF this is not possible. The clinic tested 4 interventions simultaneously and hoped to see a 'marginal gain' effect on culture stability through comparison of baseline data with post intervention data over SPC charts (ACT academy, 2018). However, this 'bundle' approach would complicate attribution of improvement to specific changes made.

The QI project proposed interventions were to;

1. **Standardise working, limit the number of dishes allowed out of the incubator during a procedure and a visual reminder of temperature variation across heated stages,**
2. **Reduce practitioner 'paces' taken during procedures (member of staff responsible for dish set-up to move dishes from incubator 4 to MIRI 1 or 2 prior to procedure when they are needed),**
3. **Improved utilisation of bench top incubators (MIRI 1 & 1) and box type incubators 3/5 on Wednesdays,**
4. **Keeping eggs for ICSI in benchtop incubators (MIRI 1 & 2) from denudation until after ICSI (space and case-load permitting).**

The MFI and PDSA were used to assess the impact of the intervention bundle. The best measure of optimal culture conditions are healthy babies however this is not the most appropriate measure for a short PDSA cycle. The driver diagram and cause-effect diagram were used to identify appropriate measures for the project. These measures were further defined into outcome, process and balancing measures (Table 7). When making QI

Table 7 Definition of measures

Outcome measures	Process measures	Balancing measures
• Implantation rate (%) (per embryo transferred) • Live birth rate (%) (per embryo transferred and per embryo transfer procedure) • Fertilisation rate (%) • Embryo utilisation rate (%)	• Temperature (incubators, heated stages, ambient) • CO_2/O_2 level of incubators • Frequency of incubator door opening • Time taken for procedures • Practitioner 'paces' taken during procedure	• Maternal age of patients having fresh treatment • Workload (volume); fresh and frozen cycles, egg numbers • Lab staff levels

changes it is important to measure balancing, process and outcome metrics to determine if the change is an improvement. As much baseline data as possible was collected prior to implementing the interventions to establish the natural variation within the laboratory system. Balancing measures of temperature, maternal age, workload, egg numbers, and staff levels were monitored in case poor outcomes were associated with higher workloads, equipment failure, or low staffing and not due to the changes made. Results are presented in SPC charts. Due to the delayed nature of outcomes with IVF treatment (pregnancy rate 2 weeks following treatment, fetal heart/implantation rate 7 weeks following treatment, live birth rate ~9 months following treatment), the process measures were the main focus to assess for impact of the intervention. All data measures except frequency of incubator door openings, 'paces' taken and procedure timings are standard clinic KPIs that are tracked, validated and analysed. Data collection sheets are shown in Appendix 11. Ethical approval for these changes was not required for this service evaluation and improvement project, small changes made to lab processes and tightening up of standard operating procedures could be tested in a safe way and all cases were treated with the same processes and procedures.

The proposed future journey of eggs through the IVF laboratory system is shown in Figure 17. This should result in better utilisation of all incubators, reduced door openings and disruption of low oxygen extended culture incubators 3/5, and reduced 'paces' taken by practitioners carrying dishes during procedures. Ultimately improving culture stability. The intervention bundle was implemented during week 15 of the project 13th June 2018.

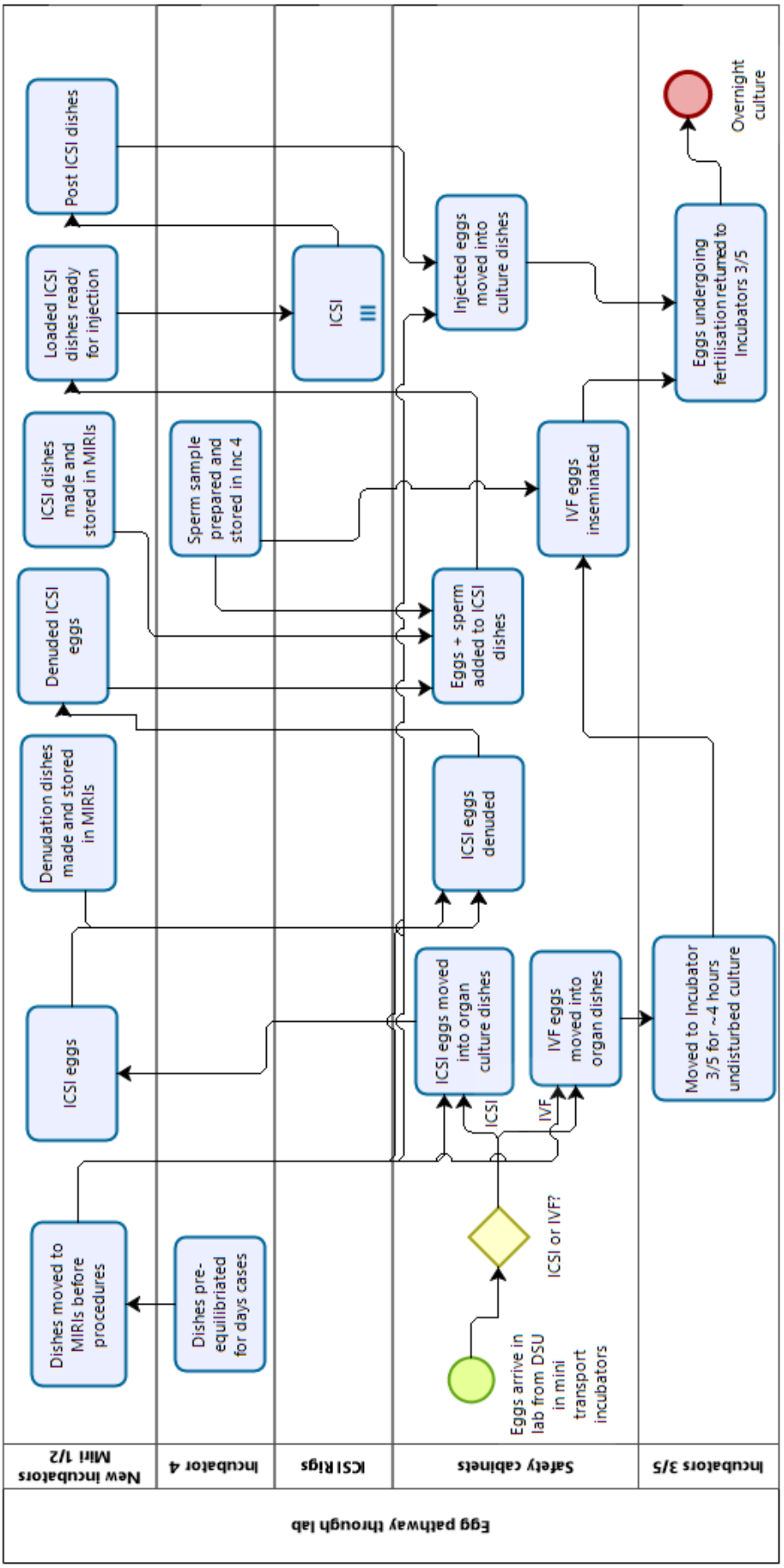


Figure 17 Process mapping the journey of eggs through the IVF laboratory. Each lane is a piece of critical equipment eggs are exposed to which must maintain the viability of eggs/embryos by maintaining optimal conditions. This pathway makes better utilisation of all incubators whilst minimising practitioner 'paces' taken during procedures and therefore time required for procedures.

Results chapter 1.3 Results

1.3.1 Visual management

A visual management approach was used to help improve the standardisation of procedures by reminding practitioners of the temperature variation present within heated stages. Heated stage temperature for workstations were remapped and the data is displayed within the cabinets (Figure 18). Practitioners were to also reduce the number of dishes out of the incubator at one time as this can vary per practitioner. Visual management is a principle of Lean management that allows problems to be visible to everyone in the work process, so that a corrective action can be taken in real time (Singh & Singh, 2015).

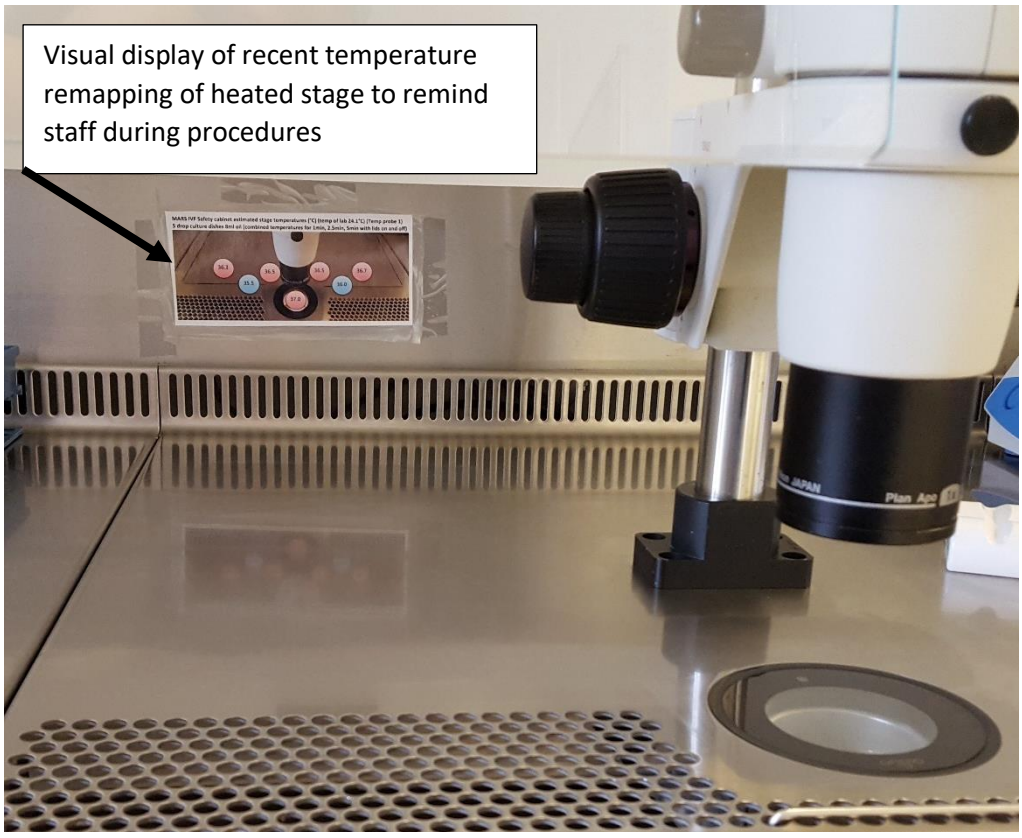


Figure 18 Visual display of temperature mapping of heated stage to remind practitioners of hot and cold spots within the work station during procedures.

1.3.2 Balancing measures

Ambient temperatures of the laboratory and day surgery unit (DSU) theatre environments and all heated stages in use were monitored on Wednesdays (Figure 19). Very little variation was observed except for the DSU ambient temperature which the IVF clinic has little control over. All readings showed no special cause variation when run on an SPC chart (data not shown).

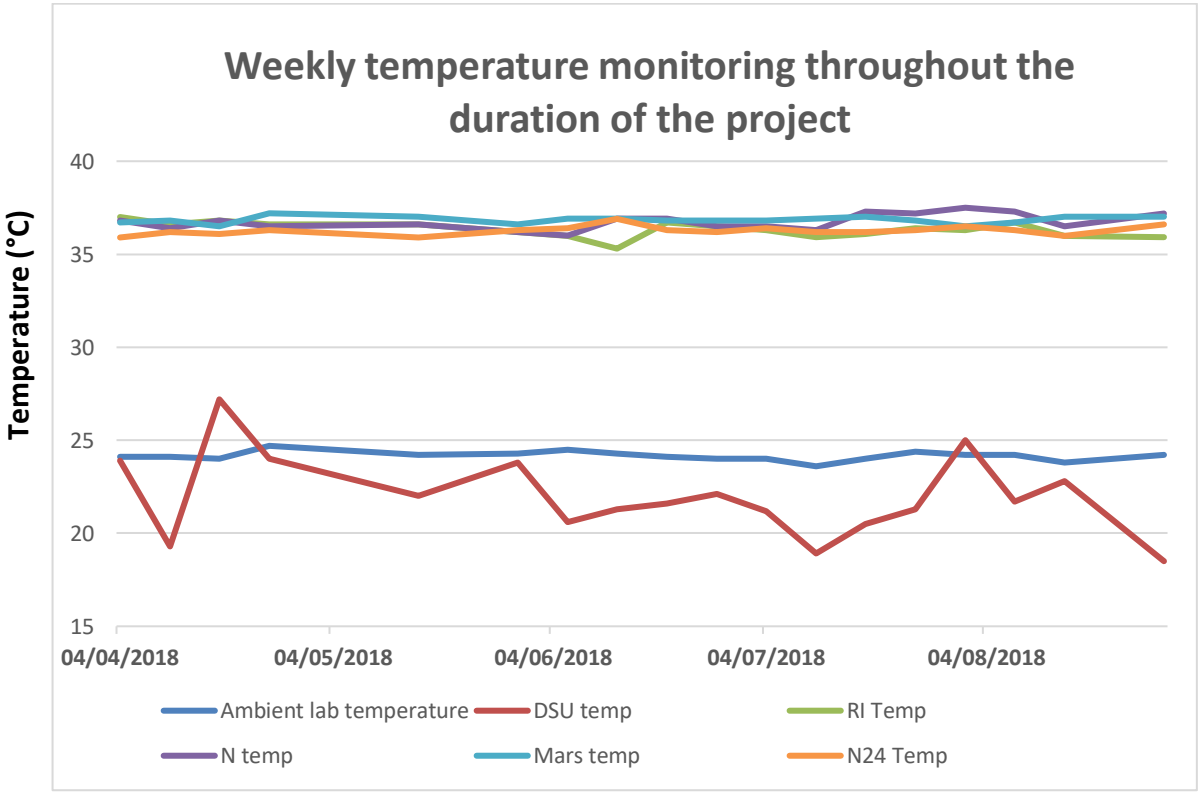


Figure 19 Balancing measures: Measurements of all heated stages and ambient temperature within the laboratory and day surgery unit (DSU). Temperatures are stable and within correct thresholds to maintain cell viability. Any changes in outcome metrics would likely not be attributed to working stage temperatures (providing practitioners avoided cool/hot spots and did not take longer than 5 minutes working on each dish outside of the incubator).

Maternal age can strongly influence chance of success during an IVF treatment cycle (Elder & Dale, 2011). The average age of women having treatment of Wednesdays was monitored on an SPC chart, age varied as to be expected but no special cause variation was observed during the duration of the project (Figure 20).

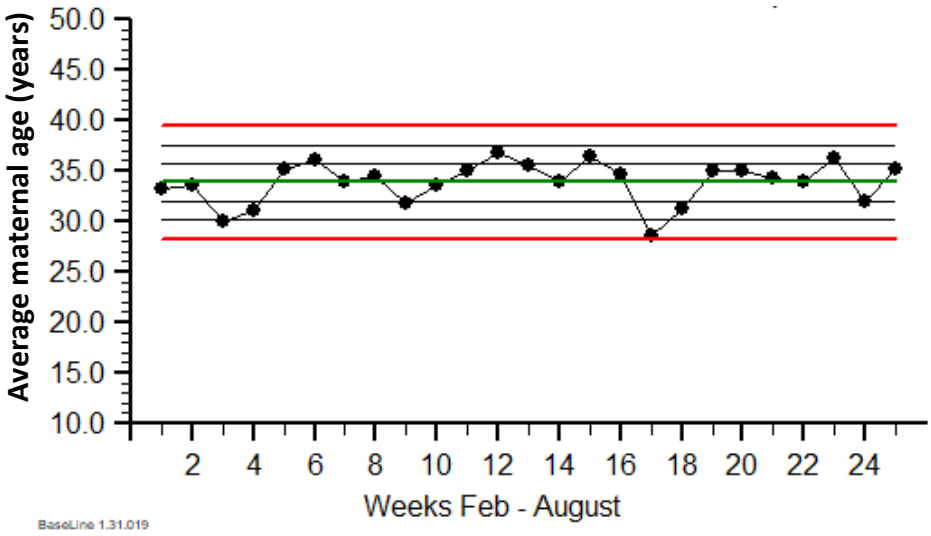


Figure 20 SPC chart of the weekly average maternal age (Y axis= maternal age) for fresh treatment cycles over time (X axis = weeks)

The workload can vary considerable over time but shows no special cause variation over the period leading up to and during the start of the intervention on week 15 (Figure 21). Workload is also affected by how many eggs are collected per patient and in total for the day, something that cannot be controlled effectively with super ovulated treatment cycles. Lots of eggs results in increased incubator door openings. No special cause variation was observed but egg numbers as expected show vast common cause variation (Figure 22).

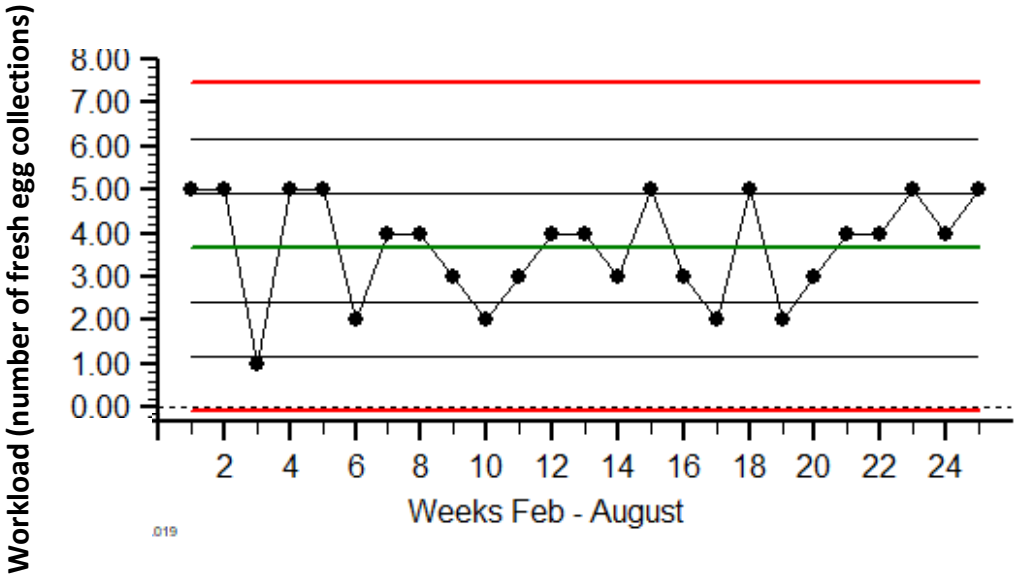


Figure 21 SPC chart of fresh cycle case numbers on a Wednesday list (Y axis = number of cases) over time during the period of the project (X axis = weeks). Treatments may be cancelled or moved dates depending on response to stimulation and therefore case load is difficult to keep consistent and naturally varies.

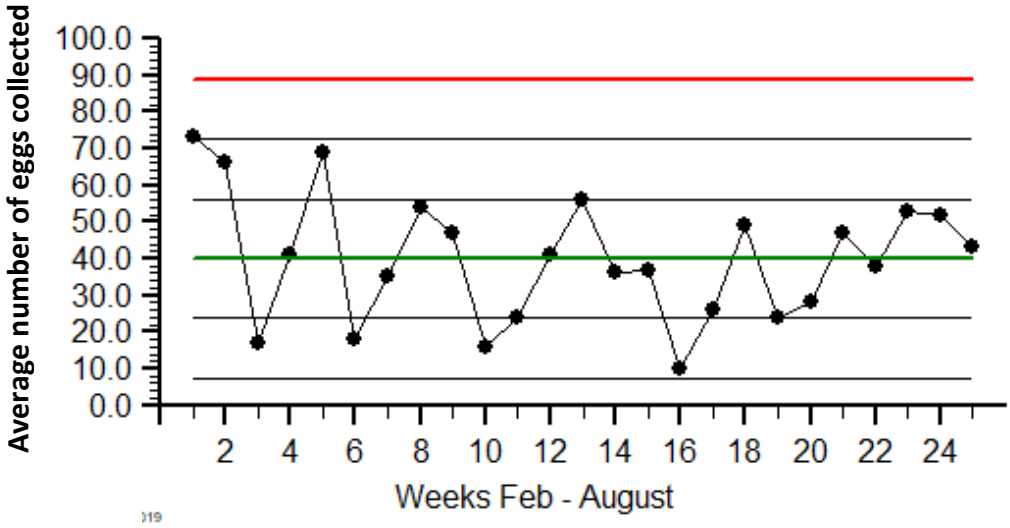


Figure 22 SPC chart of average weekly number of eggs collected (Y axis = average egg number) over time during the period of the project (X axis = weeks). Number of eggs collected varies depending on patient age and response to stimulation, therefore is difficult to keep consistent.

Staff levels within the IVF laboratory may influence process and outcome measures, low staff numbers might negatively affect outcomes. Skill mix may also have a great influence on procedure length and process measure (for example a trainee getting a single dish out of the incubator instead of two at a time resulting in more disturbance to culture conditions) however this was not monitored because it would vary depending on who performed which procedures during the day. Staff levels varied but no special cause variation was observed (Figure 23).

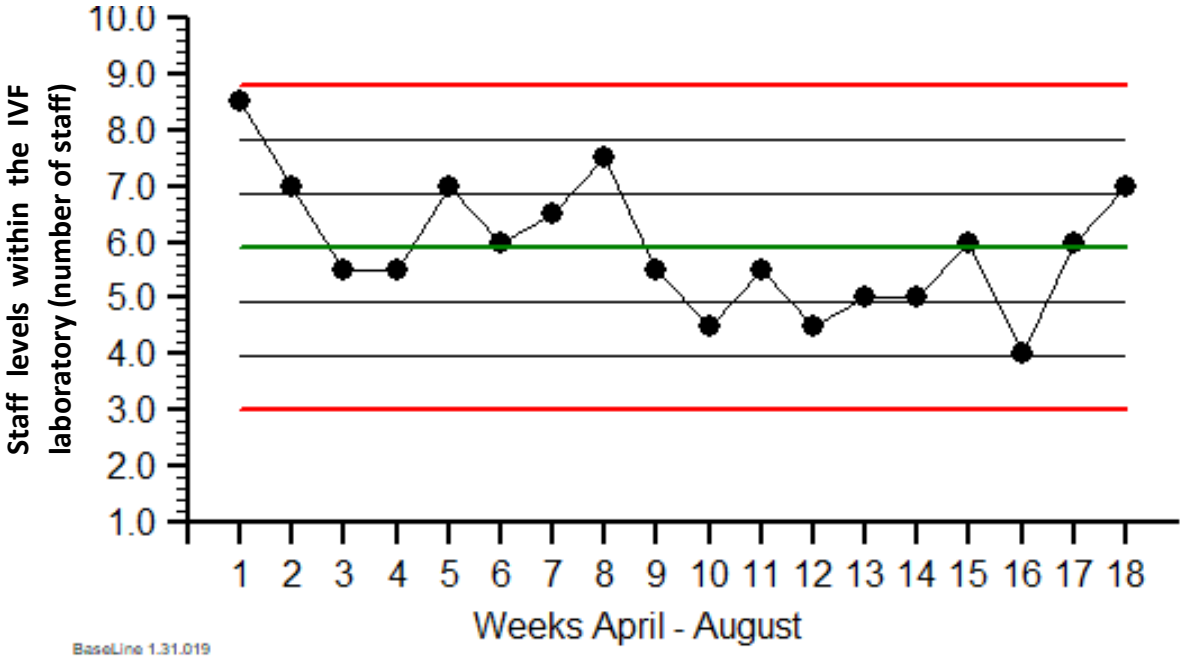


Figure 23 Staff levels within the IVF laboratory from April to July 2018. SPC chart of the number of lab staff working (Y axis = number of lab staff) over time during the period of the project (note data only recorded during the project April -August 2018, the intervention began on week 8 on this SPC).

In conclusion, balancing measures show vast common cause variation but no special cause variation or runs in the data that could be identified throughout the project timeline. Therefore, any impact observed during the PDSA can likely to be attributed to the intervention being tested.

1.3.3 Process measures

Low oxygen incubators 3 and 5 were monitored; the number of times the doors were opened during the day on a Wednesday (data for both incubators was combined due to complications of data collection in terms of treatment numbers and type located in each incubator (i.e. one may be more overloaded than the other)), and the range of variation in measurements observed each Wednesday (8am-4pm) with oxygen, carbon dioxide and temperature readings of both incubators combined. Incubator 3/5 door openings were reduced by 36% following the intervention, dropping from an average 43.00 openings to

22.55, intuitively this must result in less disruption to culture conditions within these large box type incubators which have a slow recovery time (Figure 24).

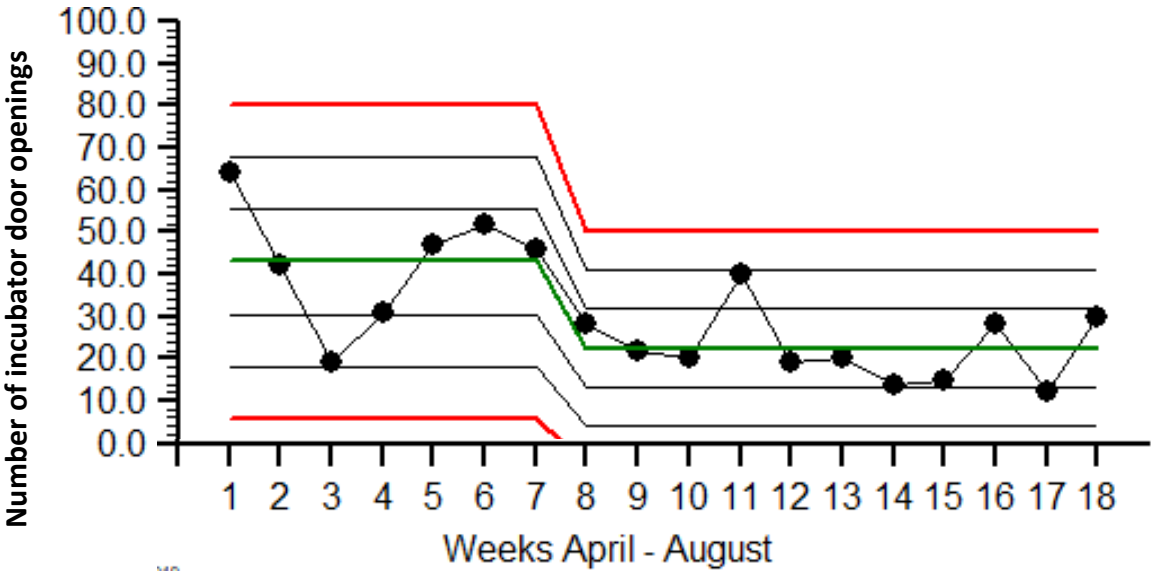


Figure 24 SPC chart of total weekly combined incubator 3 & 5 door openings for the day on a Wednesday (Y axis = total daily incubator door openings) over time during the period of the project. Note the intervention starts at week 8 (13th June 2018) on this SPC as this is not a standard clinic KPI, data collection for baseline data only began in April 2018 (no data from Feb-April 2018)

By keeping ICSI eggs within the benchtop Miri incubators throughout the day the distance ICSI eggs travelled within the laboratory was reduced by 22%. An average of 15.5 seconds was saved per culture dish used on day-0 and therefore the time eggs spent outside of the optimum 37˚C culture was reduced by 9%. On average practitioner 'paces' taken during procedures was reduced by 9.5 per fresh culture dish retrieved, which should reduce the risk of incidences while carrying dishes around a busy laboratory.

SPC charts of the average range (difference between the lowest and highest reading measured on a Wednesday between 8am and 4pm for incubators 3 and 5 combined) of measurements of oxygen, carbon dioxide and temperature levels are shown below (Figures 25, 26, 27). A large range indicates greater disturbance to the incubator and loss of optimal culture conditions. The intervention started on week 15 and appears to have reduced the mean range of $CO_2/0_2$ measurements in both incubators and the overall common cause variation. Therefore, the daily fluctuation of incubator gas levels appears to have reduced following implementation of the intervention.

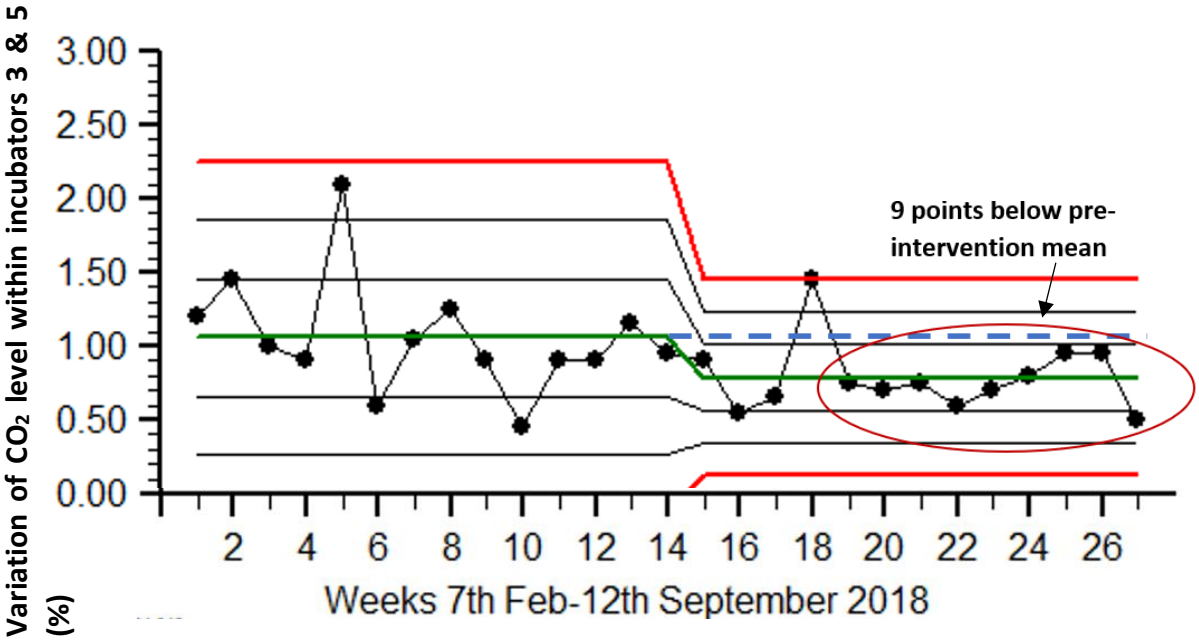


Figure 25 SPC chart of combined incubator carbon dioxide variation. The range (difference between lowest and highest reading measured) of carbon dioxide measurements on Wednesdays (between 8am and 4pm) for incubators 3 and 5 combined. A large range indicates greater disturbance to the incubator and loss of optimal culture conditions. Box type incubators have a longer recover time. The intervention started on week 15 and appears to have reduced the mean range of CO_2 measurements in both incubators, and decreased the common cause variation. The last 9 data points indicate a significant shift in the data and a new lower mean (Y axis = change is CO_2 gas level %).

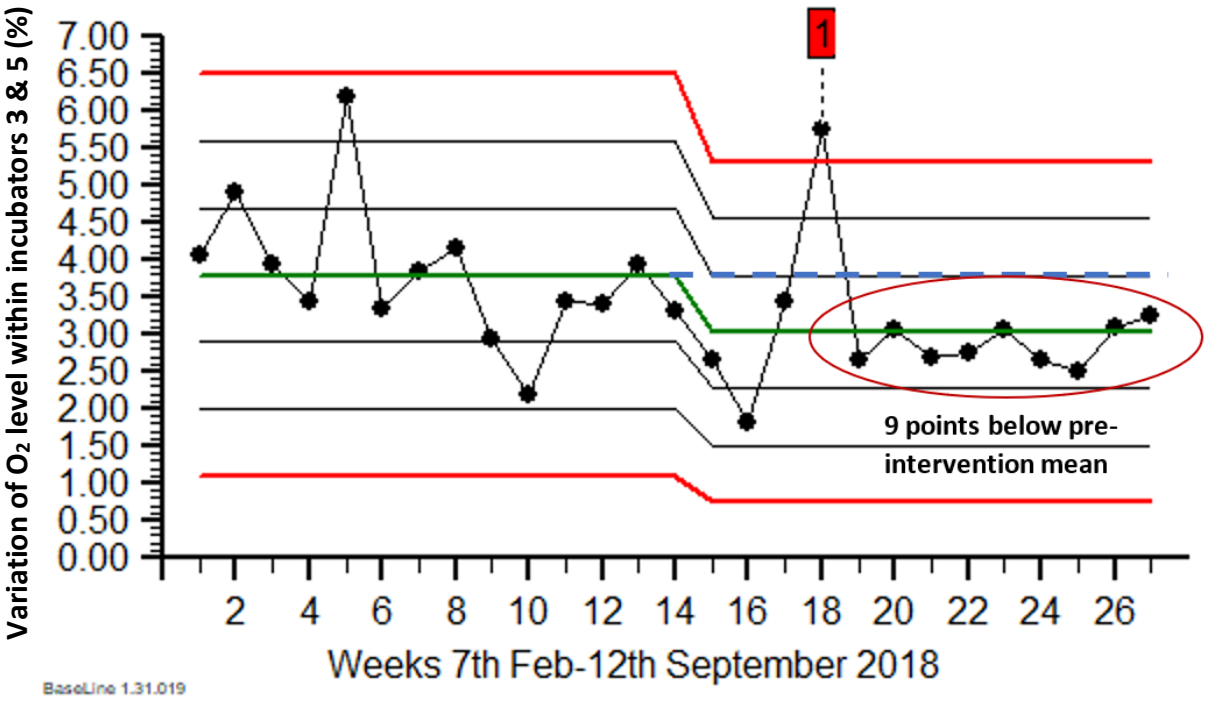


Figure 26 SPC chart of combined incubator oxygen variation. The range (difference between lowest and highest reading measured) of oxygen measurements on Wednesdays (between 8am and 4pm) for low oxygen incubators 3 and 5 combined. A large range indicates greater disturbance to the incubator and loss of optimal culture conditions. Box type incubators have a longer recover time. The intervention started on week 15 and appears to have reduced the mean range of oxygen measurements in both incubators, and decreased the common cause variation. Special cause variation was identified on week 19 with greater incubator disturbance than expected due to an increased number of door openings for incubator 3 due to an ICSI case with larger egg numbers. The last 9 data points indicate a significant shift in the data and a new lower mean (Y axis = change in 0_2 gas level %)

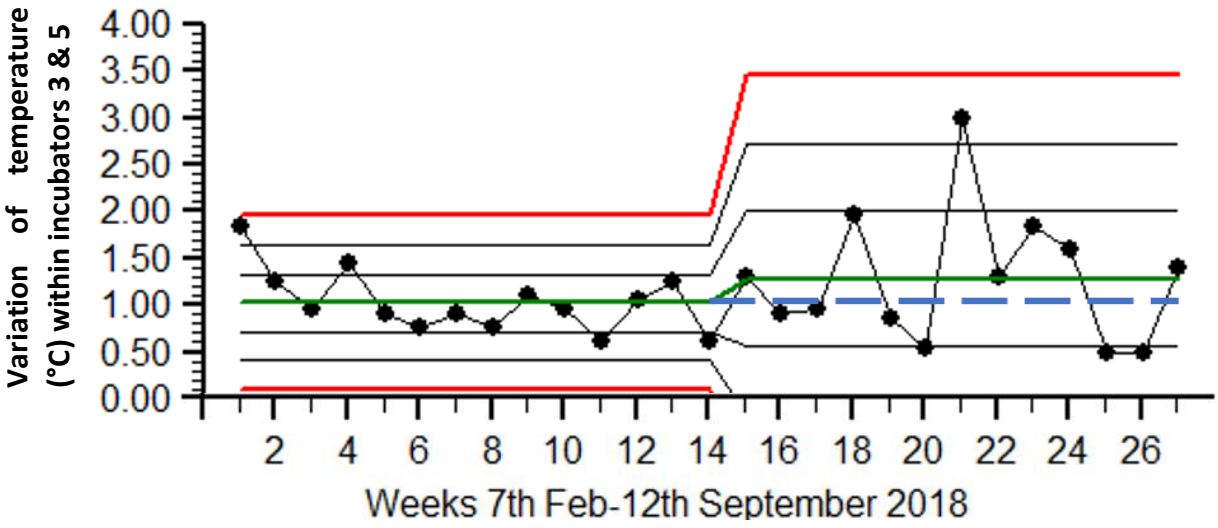


Figure 27 SPC chart of combined incubator temperature variation recorded for incubators 3 & 5. The range (difference between lowest and highest reading measured) of temperature measurements on Wednesdays (between 8am and 4pm) for incubators 3 and 5 combined. The intervention started on week 15 and appears to have no effect on the mean between 8am-4pm Wednesday plotted weekly. The mean increases slightly and the common cause variation increases. It appears that reducing the incubator door openings increases the variation seen with this measure (Y axis = temperature °C).

Special cause variation was identified on week 18 of the project for oxygen measurements only. This warranted further investigation to establish the cause of this. High gas level disturbance on this day (4th July 2018) occurred in incubator 3 only, a high number of eggs (49) were collected this day, one difficult ICSI cycle and 4 IVF cycles. Three cases were cultured in incubator 3 (including the ICSI) leading to a higher than usual number of incubator door openings (24 openings of incubator 3). Refer to Appendix 12 for further analysis of special cause variation of incubator 3.

Both CO_2 and O_2 SPC charts indicate that the process changes made to reduce the incubator disturbance was effective and a direct result of the intervention because they each have 9 data points on the same side of the mean, indicating a shift in the data towards less variation in gas levels. The reduction in the mean was materially significant (CO_2 1.057 pre change to 0.788 post intervention) (O_2 3.796 pre change to 3.027 post intervention).

The temperature SPC chart did not show any materially significant changes post intervention, the common cause variation appears to have increased since the intervention but this is not materially significant (mean temperature pre change 1.025 to 1.281 post intervention). Perhaps temperature stability of box type incubators is not as

directly influenced by door openings when compared to gasses escaping. The fluctuation spikes in figure 12b (pp59b) demonstrated less disturbance of temperature due to clinic activity and door openings when compared with gasses oxygen and carbon dioxide. Overall, the intervention has helped break the relationship between high workload and associated egg numbers with incubator door openings and therefore incubator culture condition stability (Figure 28).

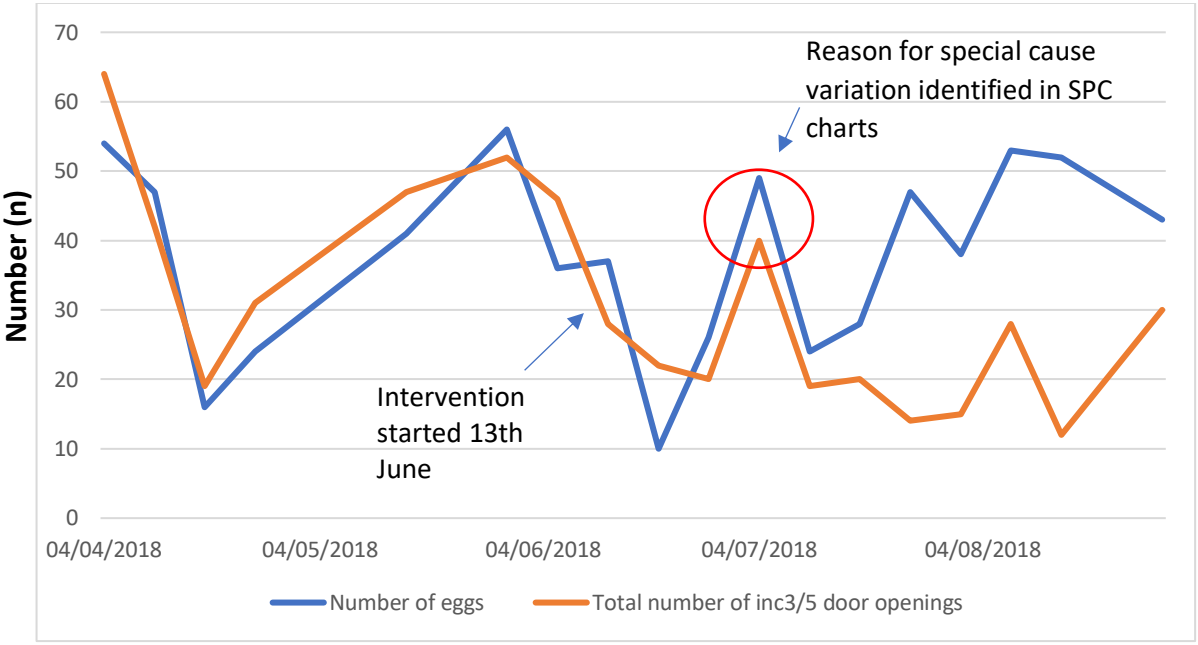


Figure 28 Relationship between egg number in laboratory and incubator door openings.

In conclusion, process measures show a reduction in practitioner 'paces' taken whilst carrying culture dishes, reduced time of culture dishes outside the incubator, reduced incubator door openings, and reduced gas level disturbance of incubators 3 and 5. Small changes to processes of the laboratory and uses of each incubator removed the link between high numbers of eggs coming into the laboratory on a busy Wednesday list with the number of door opening of the low oxygen timelapse incubators. Reducing the incubator door openings did not improve the variation or mean of temperature disturbance.

1.3.4 Outcome measures

Due to the delay with IVF outcome measures which are most critical to patients and clinics, live birth rates and implantation rates per embryo transferred, these are not great measures for QI PDSA cycles. Process measures were more vital in informing of reduced culture disruption for this project, however it is interesting to follow up the longer-term measures to establish whether the changes made to improve the stability of embryo culture in the clinic led to an increase in chance of fertilisation, good embryo development and successful pregnancy. Weekly average fertilisation rates (number of normally fertilised embryos/ number of inseminated eggs IVF/ICSI combined), embryo utilisation rates (number of usable embryos (frozen and transferred)/ number of available embryos), implantation rate (number of Fetal Heart/number of embryos transferred), and live births (per embryo transferred and per embryo transfer procedure) were plotted on SPC charts over time. The mean fertilisation rate remained the same since the intervention but common cause variation has reduced indicating better reproducibility and stability of this measure (Figure 29). Embryo utilisation rate appears to have increased slightly (mean of 45.0% increasing to 53.4% following the intervention) which would suggest a greater proportion of embryos are of good quality, however there is much greater common cause variation in the data (Figure 30).

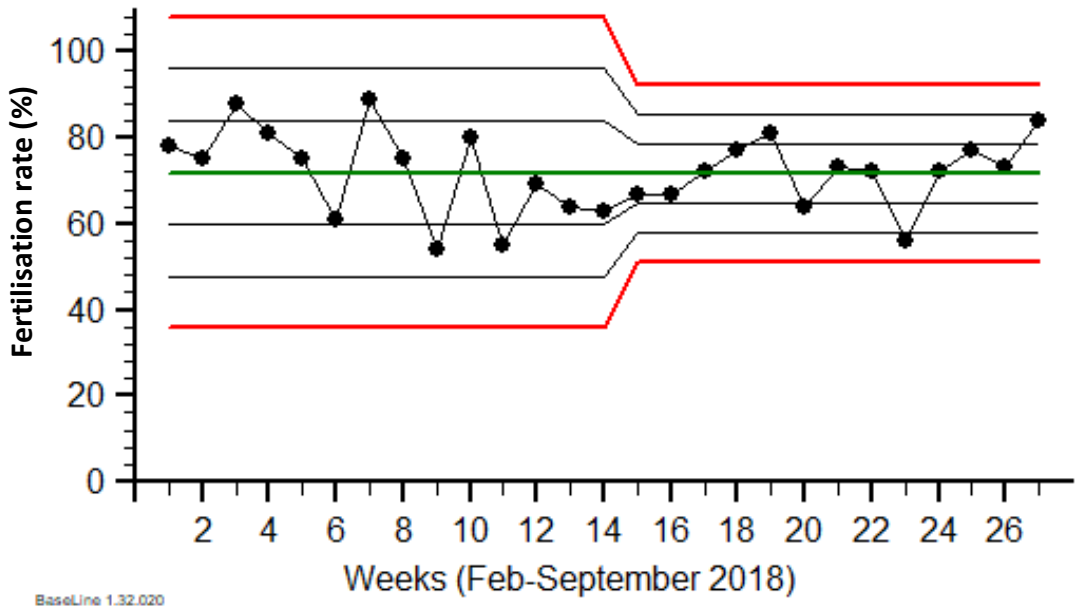


Figure 29 SPC chart of fertilisation rates over the project period. The intervention for improvement started on week 15. The mean remains unchanged at 71.9%. The common cause variation reduced following the changes.

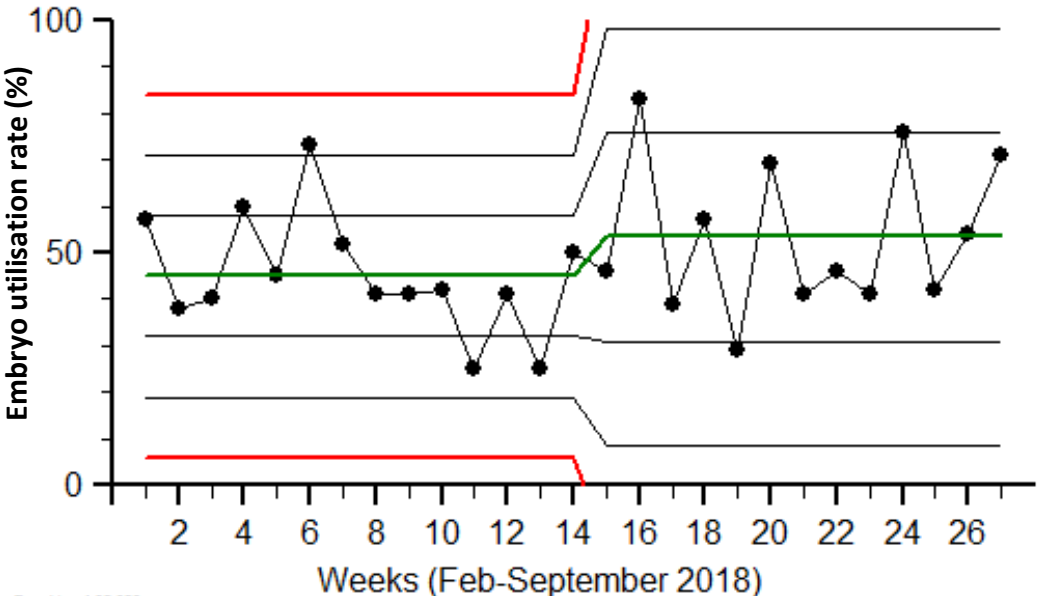


Figure 30 SPC chart of embryo utilisation rates over the project period. The intervention for improvement started on week 15. The mean increases (45.0% increasing to 53.4%) suggesting a higher number of usable embryos (better quality) are available after the intervention but this was not materially significant. The common cause variation increases following the changes.

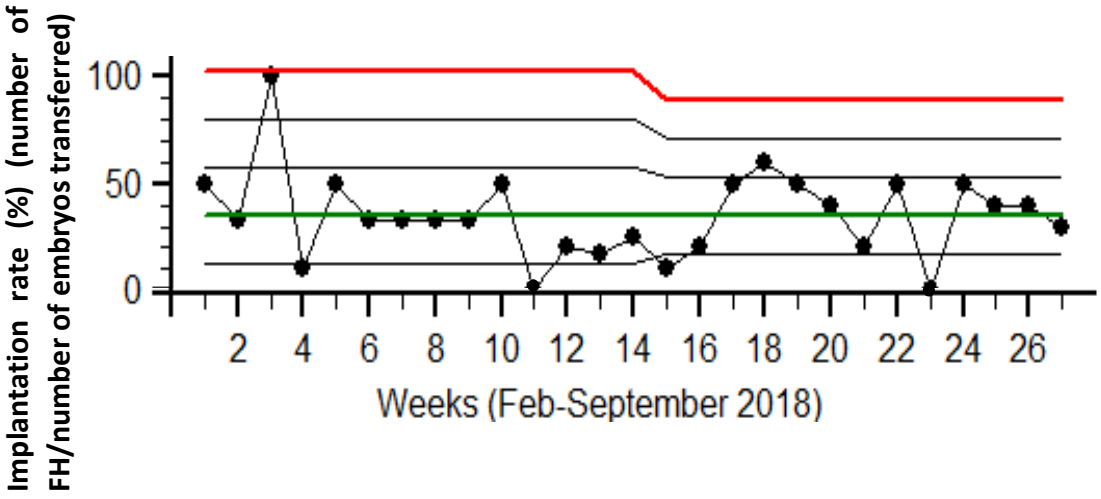


Figure 31 SPC chart of embryo implantation rates over the project period. The intervention for improvement started on week 15. The mean remains consistent across the split in the data (34.8% to 35.4%). The common cause variation decreases slightly but is vast due to the nature of weekly pregnancy averages of low case numbers in a small clinic e.g., one week 100% the next 0%. Minimum number of embryos transferred weekly = 1, maximum = 9.

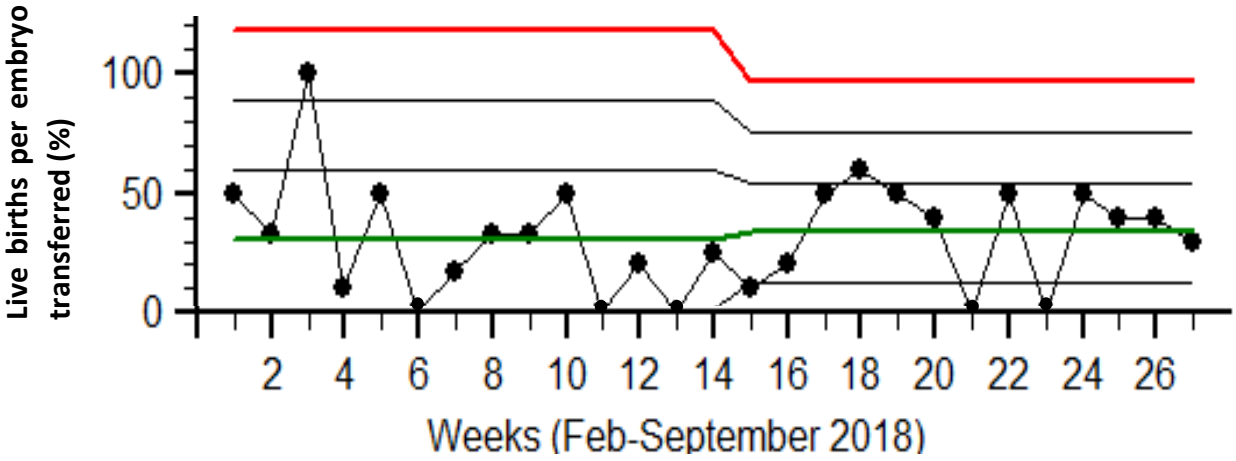


Figure 32 SPC chart of live birth rates per embryo transferred over the project period. The intervention for improvement started on week 15. The mean increases slightly after the split in the data (30.1% to 33.9%) (not materially significant). The common cause variation decreases slightly but is vast due to the nature of weekly pregnancy averages of low case numbers in a small clinic e.g., one week 100% the next 0%. Minimum number of embryos transferred weekly = 1, maximum = 9.

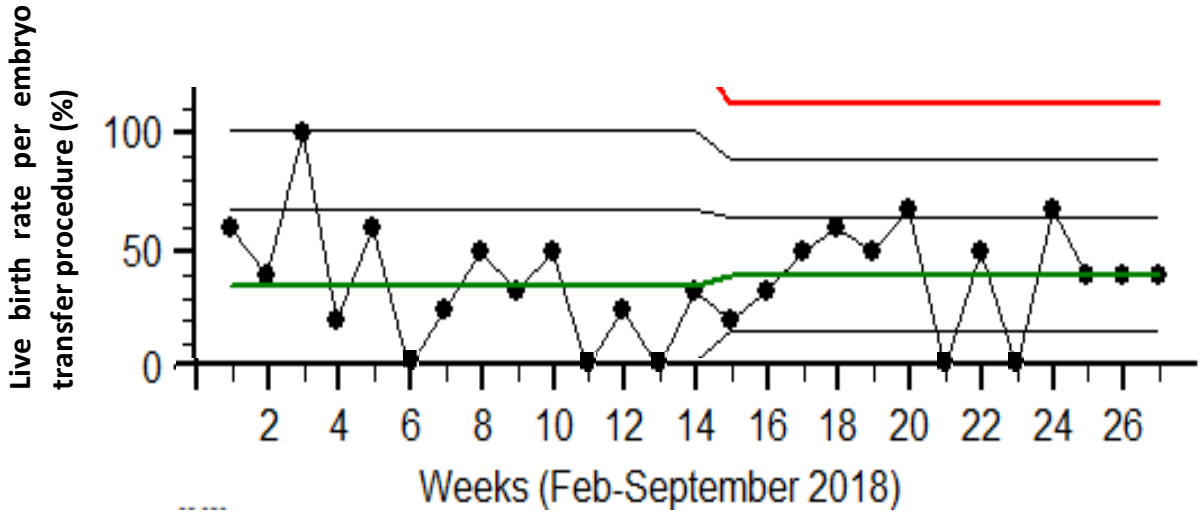


Figure 33 SPC chart of live birth rates per embryo transfer procedure over the project period. The intervention for improvement started on week 15. The mean increases slightly after the split in the data (35.4% to 39.8%) (not materially significant). The common cause variation decreases slightly but is vast due to the nature of weekly pregnancy averages of low case numbers in a small clinic e.g., one week 100% the next 0%. Minimum number of embryo transfer weekly = 1, maximum = 5.

Pregnancy outcome data in figures 31-33 demonstrate materially insignificant positive trends towards better success rates and reduced common cause variation following the changes made to improvement. However, there is still a lot of common cause variation is each chart. Weekly average outcome measures in a small clinic with low numbers of cases and embryos transferred will be expected to have increased inherent variability. This is apparent in the SPC charts. It is reassuring to determine that the change made to some laboratory processes to increase culture stability on busy days did not have a detrimental effect on the main outcomes which remain consistent with baseline data and show possible trends for improvement.

Better culture stability would ultimately result in better outcome measures if more data was available within the project time frame. This is because prolonged exposure of cultures to temperatures other than optimal 37°C, reduces the ability of fertilisation and hinders the ability of cell cleavage, implantation potential, and subsequent achievement of pregnancy (Anifandis, 2013).

To conclude, outcome measures were followed up to establish whether the changes to improve the stability of the clinic's culture system eventually led to any observable improvement in embryo number, quality and implantation rates. The rates remained consistent with baseline data but showed upward trends of improvement.

1.3.5 Summary of results

Clinic staff engaged with the project which emphasised the importance of QI within the laboratory. Certain process measures indicated an improvement. The frequency of incubator door openings was reduced by 36%. The distance oocytes travelled within the laboratory was reduced by 22% and each culture dish was out approximately 15.5 seconds less during procedures. This resulted in a 9% reduction in the time that oocytes spent outside of optimum incubator culture conditions and removed approximately 9.5 'paces' taken by practitioners during procedures. The daily fluctuation of incubator O_2/CO_2 gas levels appeared to have reduced. Other process measures showed no meaningful change (incubator temperature, fertilisation rates and embryo utilisation rates). Outcome measure of live birth rate and implantation rate remained consistent.

This work resulted in improvement in the culture system workflow by refining processes, without impacting on clinical results. Team exploration of QI principles was a valuable learning experience encouraging a mindset of continuous QI and accelerated performance improvement within the IVF laboratory.

Results Chapter 2

Improving ICSI success rates following root cause analysis and use of system behaviour charts: the devil is in the detail!

The MFI and system behaviour charts were applied to identify areas for improvement within the laboratory processes. An area of focus was troubleshooting and optimisation of Intracytoplasmic sperm injection (ICSI) success rates. Changes for improvement were explored. This was a prospective study. Many QI tools were used including Statistical-Process-Control charts (BaseLine© SAASoft), PDSA, Gemba walks and seeing with fresh eyes, cause and effect diagrams, and 5 whys/root cause analysis. A root cause analysis was conducted including the input from an external observer reviewing all systems and processes. Measurements included standard clinic KPIs. A bundle of recommended changes was implemented as part of an improvement cycle with the aim to increase fresh ICSI success rates. The data set was interrupted by the Covid-19 pandemic when the clinic was shut from March 2020 until August 2020. The success rates improved for fresh ICSI cycles.

Results chapter 2.1 Background

An established fertility clinic with over 10 years of delivering successful ICSI treatment to infertile couples observed a drop in fresh ICSI implantation rates, a KPI for success, below benchmark level. The fertility clinic at Salisbury District Hospital NHS trust is a small sized clinic performing approximately 250 fresh egg collections a year, approximately half of which are ICSI treatments. The clinic expects to achieve a benchmark of combined maternal ages (<40 years) of at least >35% clinical pregnancy per embryo transfer and >25% implantation rate for fresh ICSI cycles. During 2019 the clinic identified a dip in its fresh ICSI success rates, however the low number of cycles at this clinic and common cause variation expected with fertility treatment can lead to unstable indicators which should be investigated with caution. Results will be influenced by patient factors (e.g., maternal age, previous repeated unsuccessful attempts, significant clinical adverse factors), clinical factors (e.g., uterine receptivity) and the policies for deciding the day of embryo transfer and number of embryos to replace. Other ICSI KPI's at the clinic continued to reach benchmark levels, e.g., fertilisation rate, damage rate. There is an

inherent delay for clinical performance indicators related to pregnancy success, because of the wait for pregnancy blood result and 7-9 weeks before ultrasound data is available (Hammond & Morbeck 2019). Therefore, although implantation rate is a sensitive indicator of laboratory performance it has a limited ability to rapidly detect suboptimal laboratory performance shifts. This has more impact on smaller clinics performing fewer cycles as larger multi-centered clinics with much higher caseloads would have more stable indictors to enable identification of any issues much quicker. Once a trend had been identified the clinic further monitored the fresh ICSI implantation rate and undertook a route cause analysis of any recent changes around the affected period that could be having an impact. Implantation rate is judged an important indicator that reflects the overall performance of the laboratory and an overall low implantation rate is a serious sign of a systemic problem (ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine, 2017). The clinic continued to see this indicator not reaching expected values and a plan for improvement was made and implemented to achieve benchmark fresh ICSI implantation rates as soon as possible.

The clinic collected eggs two days a week (Tuesdays and Wednesdays) and changed its days of egg collection from Tuesday to Friday, from September 2018. This enabled all patients to be offered extended culture to the blastocyst stage. The proportion of day-2/3 transfers would reduce seeing an increase in fresh blastocyst transfers and anticipated better success rates. There can be up to 6 egg collections per Wednesday list and up to 3 per Friday list, with 30-45 minutes between cases. All patients have the same time for ovulation trigger injection, regardless of whether they are first or last on the list. This is based on the premise that 36-37 hours post-trigger is acceptable, and that eggs are collected from patients near to 40 hours post-trigger without compromising egg viability.

Egg collections take place in Trust DSU theatres rather than in the treatment room next to the embryology lab. This has historically been the situation due to lack of space in the IVF unit. Whilst egg collections could feasibly take place in the treatment rooms, there is limited space for patient recovery.

ICSI is a technique used to overcome male factor infertility and fertilisation failure (Palermo et al., 1992). A single sperm is selected, immobilsed and injected into each mature egg that has been stripped of its cumulus cells using micromanipulation tools. The

first measurable and important parameter of successful ICSI is normal fertilisation and egg degeneration rates. While success of ICSI is often measured in terms of clinical pregnancy or live birth, high rates for laboratory parameters such as fertilisation or embryo development significantly contribute to the overall efficacy of a treatment cycle. The Alpha-ESHRE consensus meeting suggested KPI's with competence and benchmark levels for different parameters, but each clinic should establish their own benchmarks based on their experience and clinical practice (ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine, 2017). Implantation rate, defined at the number of fetal hearts observed per number of embryos transferred, provides an indication of the overall performance of the laboratory. Values would be expected to be lower for cleavage stage embryo transfers (Days 2/3) than for blastocyst stage transfers (Days 5/6), and higher for women under 37 years.

ICSI is a multifaceted, highly technical, invasive procedure that involves manipulation of gametes and is time intensive for the laboratory. Success of ICSI can be influenced by many factors during several consecutive steps, when evaluating one you cannot exclude the end effect of the previous (Simopoulou et al., 2016). Patient factors, gamete quality/competence, clinical stimulation protocols, upstream and downstream procedures, timings, practitioner variation, environment, culture conditions and the ICSI technique itself are just a few examples. Published studies have led to various options for performing ICSI and despite >20 years of use there is no agreed standardized optimal protocol, resulting in many clinics around the world using slightly different approaches (Simopoulou et al., 2016).

Blastocyst embryo transfer is considered a gold standard for fertility treatment improving chances of success whilst reducing the risk of multiple births. Fresh cycle live birth rate is higher for blastocyst transfers (Glujovsky et al., 2016; Wang and Sun, 2014). The clinic changed its egg collection days to be able to offer extended culture and blastocyst transfer to all patients, with the view to continuously improve outcomes and equity of care. With the expectation that more cycles would have blastocyst embryo transfer and success rates would increase.

To ensure that a problem is correctly understood and framed prior to starting the use of PDSA an imperative part of the wider methodological approach is to conduct

investigations (Reed & Card 2016). Investigations can include process mapping, failure mode effects analysis, cause and effect analysis, data analysis and review of existing evidence. All clinic fresh and frozen treatment cycle information is collected within an electronic database and a number of standard KPI's are analysed and reported at quarterly KPI meetings. Background measures such as environmental monitoring, consumable tracking, equipment monitoring, and non-conformances/adverse outcomes are monitored and records kept. All of this information was used by the team (both clinical and laboratory) to perform a root cause analysis to identity a possible cause for the reduction in fresh ICSI pregnancy rates. A fishbone diagram was used to assess cause and effect (Figure 34).

The clinic's frozen ICSI implantation rates were above benchmark which suggested that ICSI embryo viability may not be compromised, based on the assumption that the optimal embryo is transferred in the fresh embryo transfer and suboptimal embryos are transferred in the frozen embryo transfer.

An external review was invited by the clinic and undertaken to scrutinize all procedures and processes to help identify any areas where improvements could be made. This process mirrors the Lean management philosophy of 'fresh eye approach' and 'Gemba'. Fresh eyes method is the introduction of people to an area or process in which they are not familiar. By doing this, the people are not biased toward one method or another and may quickly see some improvement opportunities that people working in the area have overlooked. The basic idea is to go to 'gemba' (the workplace) and define the current state, then a future state or 'should be' process is defined (Bicheno 2008). The gap between the two and what actions are needed to get to the future state becomes the implementation plan (Bicheno 2008). The external review, conducted by Dr Bryan Woodward, identified 43 recommendations covering clinical/laboratory policy and procedures, equipment and facilities. A plan was made to implement as many recommendations as was feasibly possible within the NHS service and the team designed a plan for improvement.

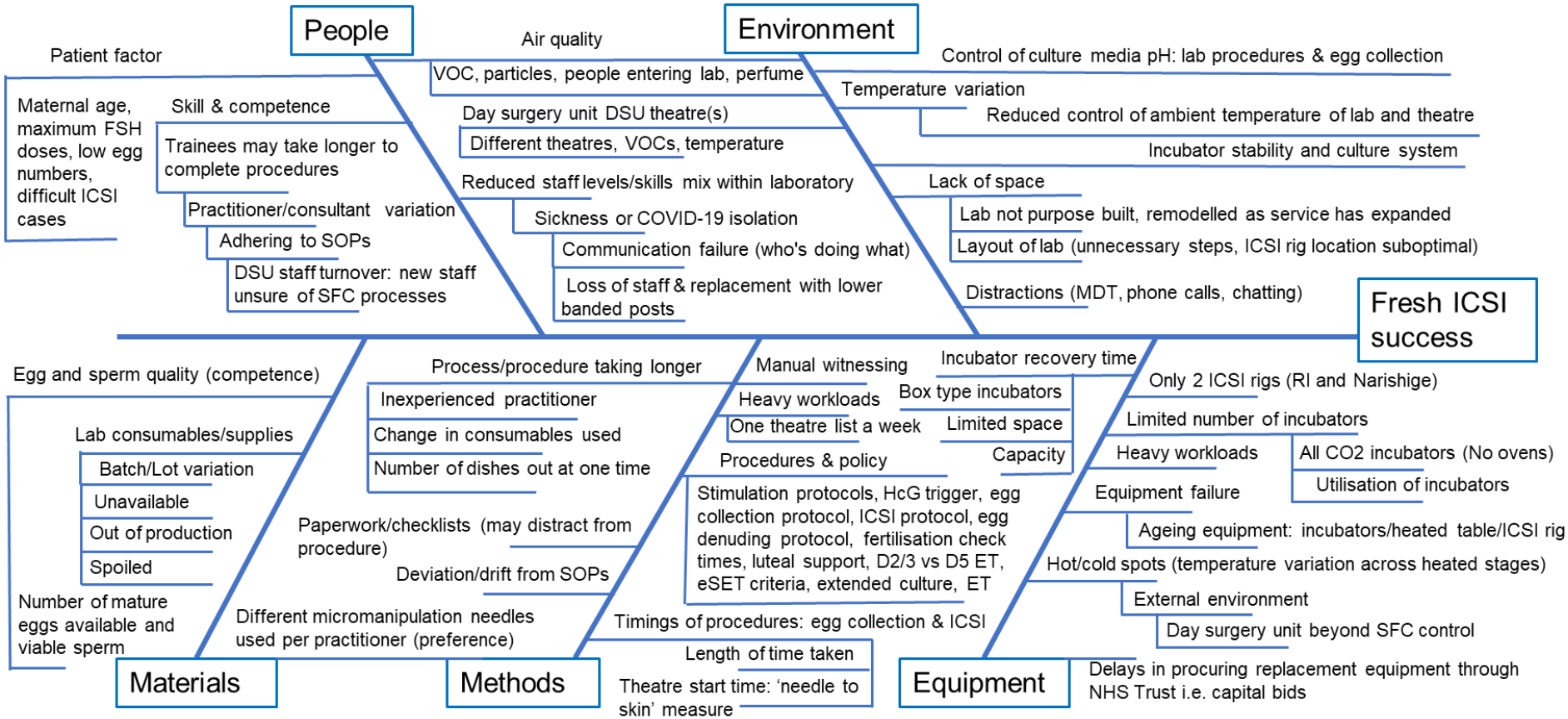


Figure 34 Fishbone diagram of factors that influence fresh ICSI success rates (cause and effect / 5 whys?).

The ICSI process prior to changes was as follows. All patients were given the same HCG trigger time and eggs were collected between 36-40 hours post HCG. ICSI patients were always first on the egg collection theatre list because of the additional downstream processing that was required for these cases. Culture dish preparation (cumulase and ICSI dishes) takes place up to 2 hours prior to use, with dishes pre-equilibrated in a CO_2 incubator. All dishes use CSCM culture medium. All eggs for ICSI were denuded between 11am-12pm maximum of 7 eggs per dish. ICSI dishes were prepared after this with culture media and PVP, stored in a CO_2 incubator. ICSI injections were started at 2pm and followed the list of egg collection 1st to last ICSI case. Eggs were then returned to culture dishes. Patients started progesterone support on the morning after egg collection and took Crinone ® vaginal gels (Merck Serono Ltd) once a day until blood test result.

The team's extensive analysis of the clinic's data and existing evidence revealed areas for process improvement. An increased frequency of egg collections being performed <36 hours post HCG trigger was noticed, being first on the list all of these cases were ICSI. These cases had a lower success rate than cases performed at 36 hours for IVF and 37 hours for ICSI. This was caused by a Trust wide theatre operational improvement initiative to reduce operating theatre running cost by optimizing start times of list (defined as first contact; needle to skin). Resulting in egg collections starting earlier in the morning than previously. The clinic would implement staggered personalised HCG trigger times for patients based on the theatre list order and type of treatment to ensure 36 hours for IVF egg collections and 37 hours for ICSI, based on clinic data. Adding more flexibility to the day of egg collection, e.g., Mon/Wed/Fri, might further optimise the time of egg collection to improve viability and could also ease the pressure on the embryology team by allowing for a more even distributed workload. However, as the clinic relies on the Trust theatres for egg collection procedures this would be controlled by hospital management.

The airflow and temperature in the DSU theatre has historically been cool and inconsistent, but temperature control is critical for maintaining egg viability (Pickering et al., 1988). The theatres are open plan with many types of operations taking place, including dentistry, so there could be volatile organic compounds in the background air that might adversely be impacting on egg quality. The team put in a capital bid to

purchase an enclosed portable biological safety cabinet (IVFTech Unica) to gain more control of the environment during egg collection procedures and replace the aged embryology equipment. Bids were also put in for electronically controlled heated stages to replace aged equipment within the IVF laboratory for more consistent temperature control.

The clinical team engaged with the improvement work and proposed the high E2 levels associated with the superovulation protocols may be causing suboptimal progesterone levels in fresh cycles. This may help explain why the clinical pregnancy rate in fresh ICSI cycles is lower than in frozen cycles. Corrective action was proposed to double the dose of progesterone (Crinone) from January 2020 for all patients having stimulated IVF/ICSI.

The clinic had always placed cumulase enzyme and PVP (buffered for ambient air) within a CO_2 incubator prior to use because the culture media also used needed to be gassed. This may alter the pH of the enzyme or PVP however the culture period is short (~2 hours) and this process had been used for >10 years with good success. With an appropriate heated workstation, the use of zwitterion-buffered media for pH maintenance during very brief visual assessments (<2 min) is not considered justified, although when denuding eggs and assessing their maturity prior to ICSI such media can be used to provide a more stable environment (Koustas and Sjoblom, 2011). The clinic would now switch culture media for an ambient air buffered handling media for the egg collections and denudation wash droplets to prevent any risk of pH change. If the denuding dishes are warmed in an ambient air incubator, this prevents any risk of gassing the cumulase. A bench top incubator would be switched to temperature only (no CO_2) for this purpose on an egg collection day. Due to historic toxicity concerns of some zwitterion buffers (Zigler et al., 1985) during ICSI injection the clinic took a cautious approach to changing to a new injection media. A process of validation began in the first quarter of 2020 of split sibling eggs between current culture media and the new handling media. This was cut short by the clinic closure in March 2020. After reviewing the data in 2021 from this small cohort of eggs and outcomes the clinic could establish that the new media was not inferior to the current culture media used (clinical pregnancy/ET; 20% (1/5) current Irvine CSCM-C media, 29% (2/7) new Irvine MHM-C media). There was an increase in the damage rate of eggs with the new medium but still within benchmark. This change was implemented for

all ICSI cases in March 2021, with monitoring of both success rates and fertilisation/damage rates.

The optimal timings for ICSI remain unclear and existing results are not fully conclusive. Most articles are concordant that a pre-incubation time before ICSI is beneficial on ICSI results, and cumulus–corona cells may have a positive effect during this pre-incubation (Rubino et al., 2016). Improvements in egg maturation, fertilisation rate and embryo quality have been reported following incubation periods of 2-4 hours between egg collection and ICSI (Rienzi et al., 1998; Ho et al., 2003; Isiklar et al., 2004). A longer culture period prior to cumulus cell removal has been associated with an increase in clinical pregnancy and live birth results (Carvalho et al., 2020), however other studies have shown there is no influence on ICSI outcome (Garor et al., 2015; Pujol et al., 2018).

The current clinic process there is usually a 3-hour delay between denuding eggs and performing ICSI, e.g., denudation takes place after 11am and ICSI begins at 2pm. This delay might adversely affect egg quality and competence as eggs may be more vulnerable to temperature and environmental changes without protective cumulus (Carvelho et al., 2020). The overall suggestion from the majority of studies is for the injection to be performed straight after the denudation procedure (Simopoulou et al., 2016). The lab team proposed to change the process to incubate eggs for ~3 hours after collection, denudation would then take place at 40 hours post HCG trigger and ICSI injection to commence straight after this. Clinic data also supported this with optimal success rates in groups that had ICSI injection at 40-41 hours post HCG trigger. ICSI and cumulase dishes would be made up in the morning at 11am. PVP would be added to the ICSI dishes 10 minutes before use.

The ICSI procedure itself was assessed during the external review, both ICSI practitioners were observed to perform mock ICSI injections and were highly skilled at this task, so it was not a cause for concern. The only suggested improvements were time saving during the procedure. Rotation of the egg on the holding pipette with the injection pipette for perfect alignment of the first polar body at 12 or 6 o'clock takes additional time. The optimal positioning of the first polar body, thought to be associated with the presumed location of the meiotic spindle, has not been determined (Simopoulou et al., 2016). Immunostaining and polscopy techniques have demonstrated that the two do not always

coincide (Wang et al., 2001) therefore the location of the polar body is only a crude measure for spindle position (Silva et al., 1999). If the 3 and 9 o'clock are avoided egg position should be quickly enforced using the holding pipette only and the ICSI swiftly performed.

One of the problems with troubleshooting at the clinic was that there are two different types of ICSI workstation: one Narashige with oil syringes and one Research Instruments (RI) with air syringes. Both ICSI practitioners also have different ways of pre-equilibrating the injection pipettes and use different micromanipulation products. For consistency and during troubleshooting and improvement work all practitioners would use the same type of syringes, tool holders, pipettes and pre-equilibration technique. This will help with competency assessments and also ensure that new staff are trained to perform ICSI in the same way.

The team also decide to tighten up on timings for fertilisation checks, with ICSI the optimal time to observe the maximum number of normally fertilised eggs is 16 hours post injection (HPI) (Nagy et al., 1998). Clinic data indicated that checks were not strictly performed at 16 hours but between 16-18. Strict fertilisation check times were to be followed going forward with ICSI cases being checked at 16 HPI and IVF within 16-18 HPI.

Another recommendation was to clear all paperwork from the laboratory (excluding patient notes) and generally declutter some areas. This tidying up process mirrors the housekeeping Lean tool know as '5S', a method for organising the work place with five steps: sorting, setting in order, systematic cleaning, standardising and sustaining (Radnor et al., 2012).

To summarise the changes determined by the team for improvement of fresh ICSI success rates following a root cause analysis, troubleshooting, data analysis and recommendations from an external review are listed in the driver diagram (Figure 35). The changes for improvement cover three areas; clinical, laboratory and equipment. The entire team showed a strong commitment to these changes which involved a great deal of process alterations, one example being the DSU theatre list order of egg collections previously completed and controlled by the lab team (as all patients were given the same HCG trigger time) was now the responsibility of the nursing team.

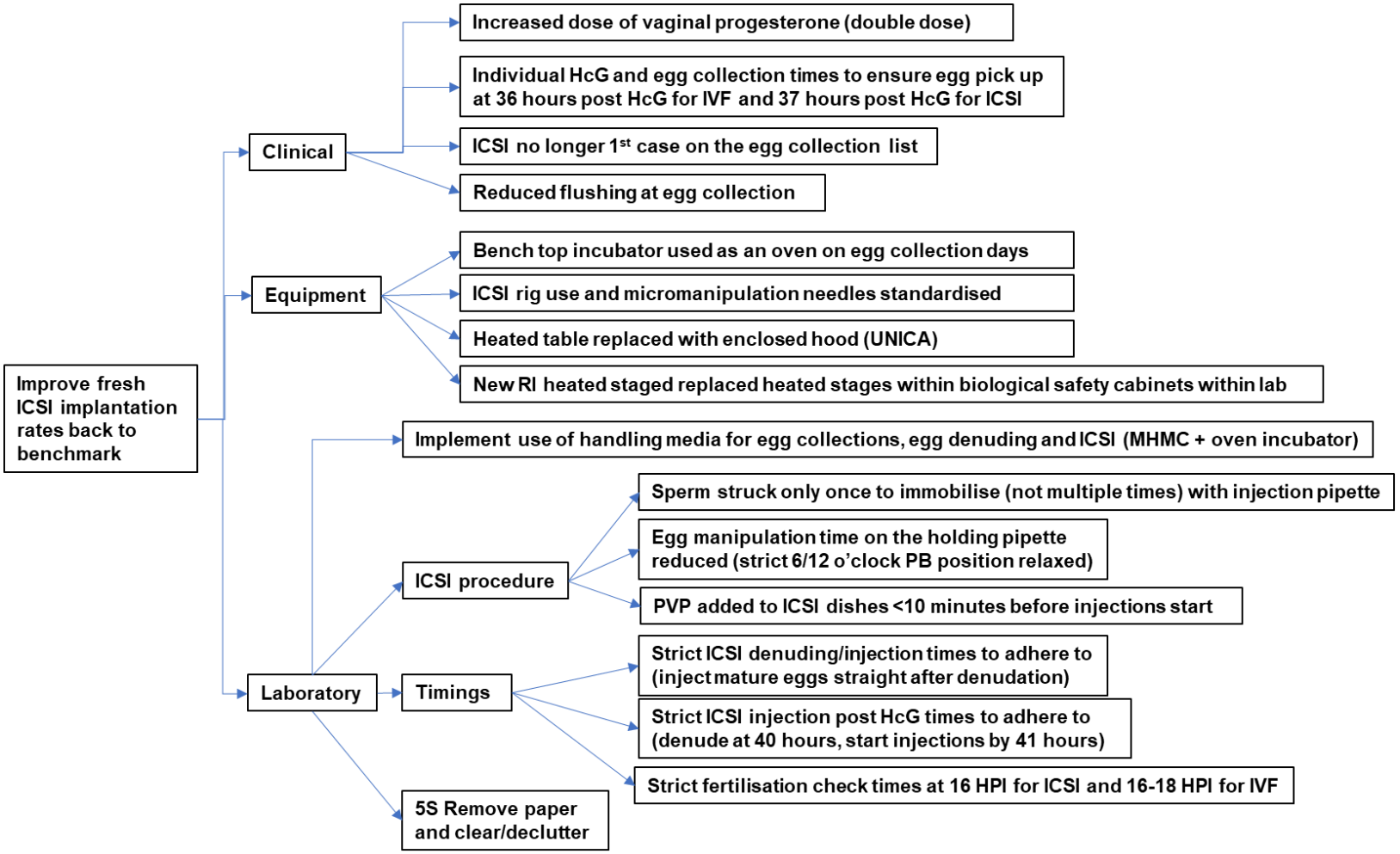


Figure 35 Driver diagram

Following final scans the lab team would review the notes and create the order, passing the notes back to the nurses to call the patients with personalised egg collection times, semen production times, and HCG trigger times. This increased the workload for the nursing team and with a notes handover also increased the risk of an error occurring. The changes would be made and sustained with close monitoring of KPIs.

Our SMART (Specific, Measurable, Achievable, Relevant, and Time-Bound) aim was to improve the fresh ICSI implantation rates to benchmark as soon as possible.

Results chapter 2.2 Methods

The strategy for implementation was based closely on the driver diagram. The main outcome measure for the improvement work was the fresh ICSI implantation rate which is defined as the number of fetal hearts divided by the total number of embryos transferred per ~25 ICSI case. Process measures included ICSI damage rates, ICSI fertilisation rates, and ICSI utilisation rate were to be collected weekly. As well as background measures including egg maturity, maternal age, and egg number (Table 8).

Table 8 List of improvement project measures, their definitions and benchmarks.

Measure	Performance indicator	Definition	Benchmark %
Outcome	**ICSI Implantation rate 25 case average (combined cleavage and blastocyst embryos) (weekly data also plotted)**	**Number of fetal hearts / Total number of embryos transferred**	**>25%**
Outcome	**ICSI clinical pregnancy rate per embryo transfer 25 case average (combined cleavage and blastocyst embryos) (weekly data also plotted)**	**Number of fetal hearts / Total number of embryo transfer procedures**	**>35%**
Process	**ICSI damage rate (weekly and 25 case average)**	**Number of degenerated eggs / Number of MII eggs injected**	**<10%**
Process	**ICSI normal fertilisation rate (weekly and 25 case average)**	**Number of eggs with 2PN & 2PB / Number of MII eggs injected**	**>65%**
Process	**ICSI embryo utilisation rate (weekly) (excludes cleavage stage transfer cycles)**	**Number of ICSI blastocysts transferred or frozen / Number of ICSI 2PN**	**>40%**
Balancing	**ICSI blastocyst cycle percentage (25 case average)**	**Number of ICSI day 5/6 transfers / Number of embryo transfers**	**n/a**
Balancing	**Proportion of MII oocytes at ICSI (25 case average)**	**Number of MII eggs at ICSI / Number of eggs collected for ICSI**	**75-90%**
Balancing	**Average number of eggs collected for ICSI cases (weekly & 25 case average)**	**Average number of eggs collected for ICSI**	**n/a**
Balancing	**Average maternal age ICSI cases (weekly and 25 case average)**	**Average maternal age of ICSI patients**	**n/a**

Running the data on SPC charts over time might reveal patterns in the data that indicate improvement due to the changes made. BaseLine©, a system behaviour chart software, was used to plot the time-sequenced data. BaseLine© graphically displays actual performance to create a platform for robust system improvement. Behaviour charts enable users to tell an informed story of how a system's performance has changed over time via the simultaneous three perspectives of the individual values, the average, and the variation, and enables continually assessment of whether systemic change is occurring. It can distinguish between what is a genuine trend or a significant event (assignable/special cause variation or signals) and what is just natural variation (common cause/chance cause variation or noise). It is easier to see and interpret patterns that would otherwise have been missed when data is converted to a picture displaying variation over time. SPC was used diagnostically to identify causes of reduced performance and prognostically to establish whether changes made to the process of ICSI led to outcome measure improvement.

Measures were plotted either as a weekly average and/or a consecutive 25 ICSI case average. Averages can hide information and patterns so plotting data weekly would reveal more information but might not be helpful for pregnancy outcome data due to vast common cause variation.

The root cause analysis and external review occurred over a series of months after the problem was identified and the bundle of improvement interventions was to be put in motion as soon as possible at the end of December 2019. Any change that could be implemented with immediate effect was e.g., double dose of progesterone, personalised HCG time. Other changes involved the purchase of new equipment or media that took time to procure and then validate safely prior to first use. This led to a three-phase approach to the intervention PDSA bundle as shown in the study flow table (Table 9), which displays the changes that occurred over time.

The improvement work was interrupted by the Covid-19 pandemic when the fertility sector was legally required to stop all treatment (except for fertility preservation for cancer patients). In the period between 1st January 2020 and the 27th March 2020 there were 29 ICSI cases, of which 21 cases went on to have a fresh embryo transfer of between 1-3 embryos. The clinical pregnancy rate per embryo transfer procedure improved to 38%

Table 9 Study flow table for planned ICSI improvements.

Summary of working group improvement efforts by phase of implementation			
	Interventions by working groups		
Phase	**Date completed**	**Laboratory team**	**Clinical team**
1	1st January 2020	ICSI procedure changes: • PVP added <10 minutes before ICSI, • sperm struck only once to immobilise, • egg manipulation on holding pipette reduced, • Eggs injected straight after denudation, • Strict ICSI HcG injection times 40-41 hours, • Handling media used for egg collections and denuding (trial use of handling media for ICSI dishes e.g. split cases), • Washing step when eggs placed within culture dishes after egg collection (wash off handling media) • Use of ovens (switch off incubator gas) • Efficiencies with old equipment (until replacement available) heated table used for egg collections in DSU • Strict fertilisation check times; 16 HPI ICSI, 16-18 HPI IVF • Max eggs per dish; 3 eggs per ICSI dish, 5 eggs per denuding dish 5S within lab: remove all paper and declutter as much as possible	• Double dose of progesterone • Strict individualised HcG trigger times for each patient to ensure egg collection times at 36 hours for IVF and 37 hours for ICSI cases • Nurses to call patients after scan to give times following review with lab team once final list and order is established • First egg collection to not start before 36 hours post HcG trigger, no longer an ICSI case due to requirement to check fertilisation at 16HPI the following day • Reduced follicular flushing at egg collection
COVID-19 pandemic – nation wide fertility sector closure, fresh cycles stopped from March 27th 2020 until 14th August 2020. **Forced change to procedures;** only one theatre list provided to fertility due to pressure on the NHS, egg collections only on Fridays going forward, IVF centres required to have a recommencement strategy in place to apply to reopen this included how patients would be prioritised once treatments restarted e.g. who was offered treatment first on the waiting list, those cancelled in March/April, advanced maternal age, funding criteria/expiration.			
2	26th Feb 2020 14th August 2020 8th October 2020	New equipment installed, validated and implemented; Unica enclosed hood for egg collections (heated table decommissioned) RI heated stages x 3	New Cook suction pump used in DSU (replaced old unserviceable equipment)
3	10th March 2021	Implement change to ICSI injections procedure: ICSI dishes made using handling media (MHM-C)	

(8/21) above the benchmark of 35% set by the clinic. The implantation rate increased to 22% (8/37). This looked like a promising improved effect from the changes made before the clinic ceased treatments, however further data would be required to confirm a sustained improvement.

During the shutdown period the clinic was required to apply for a license to recommence treatment with safeguards in place to protect staff, patients, and to not burden the NHS e.g., safe superovulation strategies reduced risk of ovarian hyperstimulation syndrome (OHSS). The clinic was required to have a strategy to prioritise patients on the waiting lists to be offered treatment in a fair manner. Those with funding requirements, advanced maternal age, or who's treatments were cancelled in March/April were given priority to start treatment when the clinic obtained one theatre list from the Trust in August 2020. Due to the pressure on the NHS services the Hospital Trust could only provide the IVF clinic with one of its egg collection lists. Therefore, the number of egg collection performed on a Friday increased from a maximum of 3 to a maximum of 7 to prevent capacity dropping by a half. The clinic had to optimise the egg collection process even further to ensure timely starts and efficient handovers. This was aided with the use of light sedation (not a general anaesthetic) as required by the Trust which did not require level 3 PPE or additional time between procedures to allow for extended ventilation.

New equipment was introduced later in 2020, an enclosed flow cabinet for egg collections and three electronic heated stages. The third quarter of 2020 after the shutdown saw reduced ICSI success rates for the first 17 ICSI cases, however this was likely due to poor prognostic patients being prioritised for treatment first, low ovarian reserve, reduced average egg numbers and increased maternal age. As identified in results below.

Critical phase 2 and 3 changes were implemented post lockdown when new equipment was available and validated. The clinic switched ICSI injection media to handling media from March 2021 onwards following satisfactory review of data from split cases performed pre lockdown.

Results chapter 2.3 Results

2.3.1 Outcome measure results

Both ICSI implantation data and clinical pregnancy rate per embryo transfer were plotted on SPC charts (BaseLine©) over time as a weekly average (to help identify more patterns in the data with more data to establish baselines) and an average of 25 consecutive ICSI cases. At least 25 cases are recommended when monitoring pregnancy KPI's to provide a more accurate picture.

Date range for consecutive 25 ICSI cycle cases is shown in the table below (Table 10) for reference to SPC charts. This data includes women <40 years old having fresh ICSI cycles, all semen types, and includes split cases where ICSI embryos were transferred in the fresh cycle.

Table 10 Date range for SPC charts displaying an average of 25 consecutive ICSI cases over 5 years

Date range for SPC chart (5 years of data 2017-2021) (# period of poor performance of ICSI implantation rates identified) (* ICSI improvement interventions begin)					
1	**Jan - March 2017**	**7**	**March - June 2018**	**13**	**Oct - Dec 2019**
2	**April - May 2017**	**8**	**July - October 2018**	**14***	**Jan - Sept 2020**
3	**June - July 2017**	**9#**	**Nov 2018 - Feb 2019**	**15**	**Sept - Dec 2020**
4	**August - Oct 2017**	**10**	**Feb - April 2019**	**16**	**Dec 2020 - May 2021**
5	**Oct - Dec 2017**	**11**	**May - July 2019**	**17**	**May - August 2021**
6	**Jan - Feb 2018**	**12**	**August - Oct 2019**	**18**	**August - Nov 2021**

2.3.2 ICSI implantation rate outcome

The SPC chart (Figure 36) shows the average ICSI implantation rate over 5 years at the clinic. The red flags are signals within the data that suggest assignable cause variation, there is a pattern caused by something other than the usual data variation you would expect. For the 6 data points (3-8), June 2017-October 2018, there is a materially significant shift towards a higher implantation rate. Possibly due to an increase in fresh blastocyst cycles and a higher proportion of patients having elective single embryo transfer. There is an opposite shift detected in the data for 6 points (9-15) from November 2018 to December 2020 of a materially significant lower implantation rate

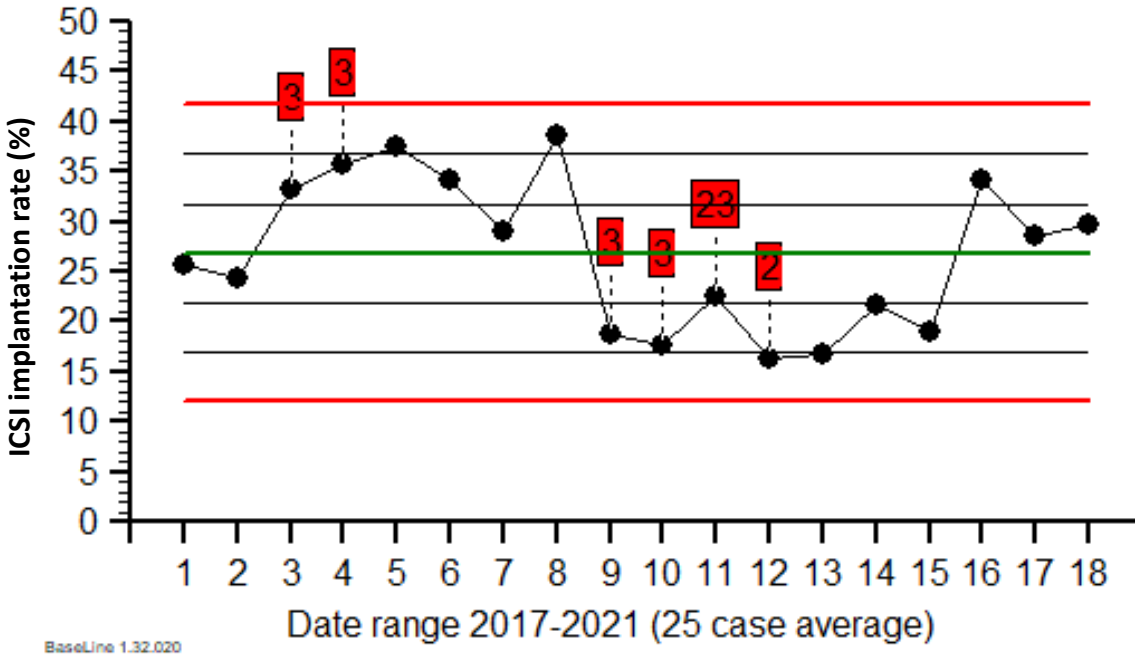


Figure 36 SPC chart of ICSI implantation rate (%) plotted over 5 years in consecutive 25 ICSI case averages. Showing signals within the data as red flags. The data is not stable. The mean implantation rate over this 5-year period 26.85% just within the clinic's benchmark of 25%.

over this period, the reason for this is unknown. The mean implantation rate for the 5 years of data was 26.85%. The data is not stable due to the signals identified. There is assignable cause variation. The data can be split into appropriate segments to remove the signals and leave segments of stable data. As shown in Figure 37 SPC chart with the data

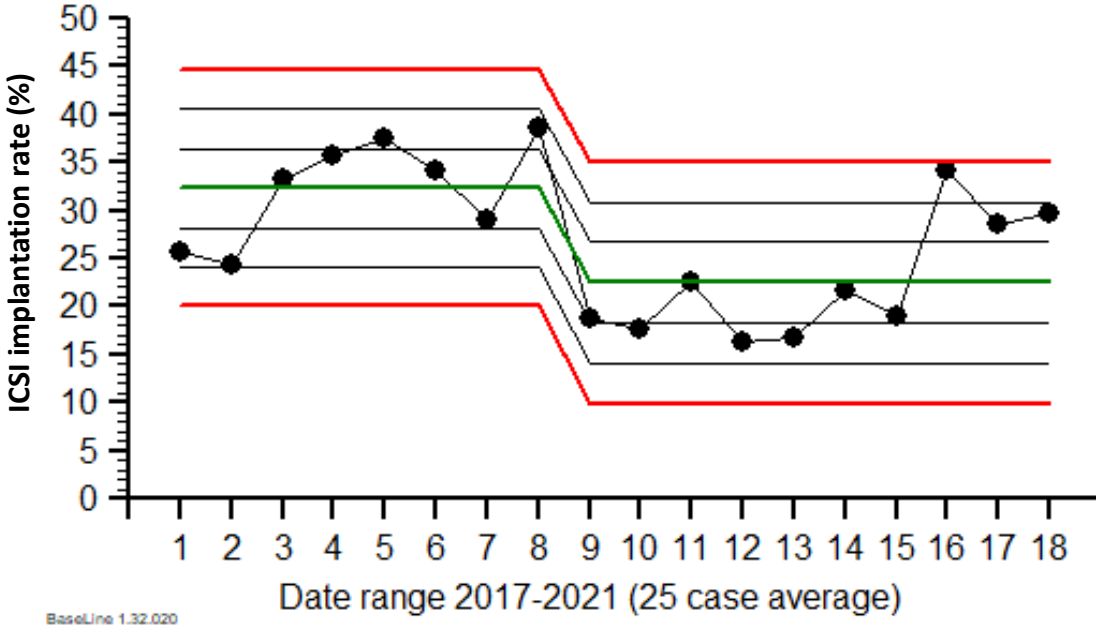


Figure 37 SPC chart of ICSI implantation rate (%) plotted over 5 years in consecutive 25 ICSI case averages. Same data but split at point 9 November 2018 as indicated by the signals. This stabilises the data into two segments of better and poorer performance. Mean implantation rate shifts from 32.31% to 22.49% below the clinic's benchmark 25% and reason for root cause analysis to identify the cause of this shift.

split at point 9. The data within both segments is now stable (no signals), the mean implantation rate baseline of the first 2017-2018 period (points 1-9) was 32.31% and the second segment (points 9-18) was much reduced at 22.49%. This is a significant reduction in the implantation rate as the clinic identified and the reason for the RCA and improvement work.

The data is then split prognostically at the point that the intervention bundle was started to monitor any improvement in the baseline mean implantation rate that could be attributed to the changes made from the improvement work. Data shown in Figure 38. The 5 data points post intervention implementation (from data point 14, January 2020) are all above the previous poor baseline mean of 22.49% implantation rate, and there are many signals present indicating a significant shift in the data. The first 2 data points post intervention are not as high as the other three. Ideally more points (at least 9) are needed to establish a new data baseline mean but showing data as the average of 25 consecutive ICSI cycles over time this is not possible within the project timeline. However there does appear to be an upward shift towards a better implantation rate attributable to the changes made from January 2020, the 5 data points giving a mean implantation rate of 26.61% reaching clinic benchmark. Refer to Figure 39 showing the same SPC chart but a

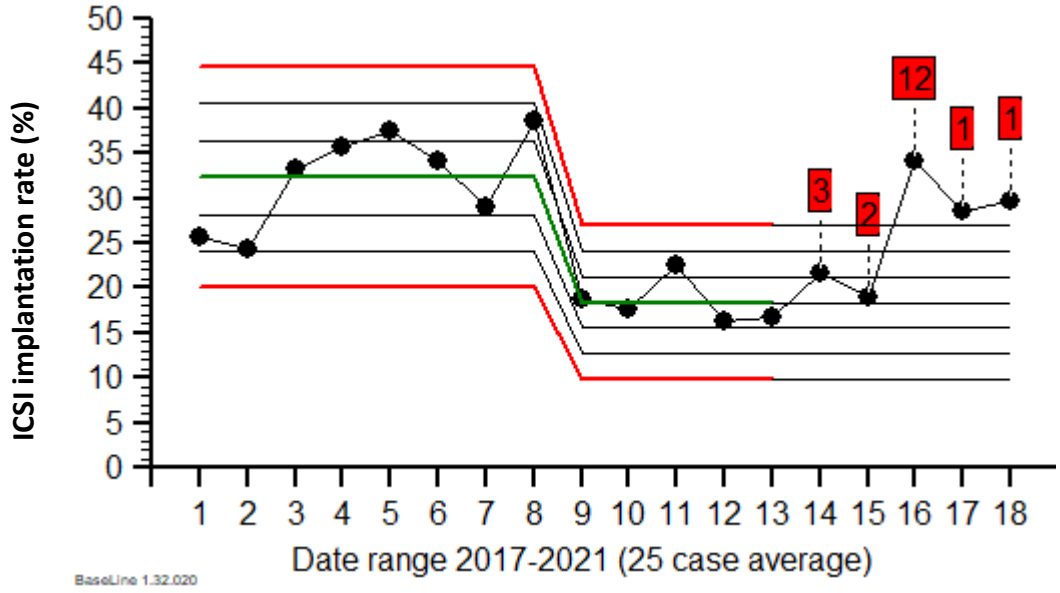


Figure 38 SPC chart of ICSI implantation rate (%) plotted over 5 years in consecutive 25 ICSI case averages. Same data but looking prognostically at the improvement intervention and its impact on the data. The data is now locked at point 14 when the intervention was started (January 2020). There are two previous implantation rate means of 32.32% (period of 1-8 January 2017-Otober 2018) and 18.37% (period of 9-13 November 2018-December 2019). The 5 post intervention data points are all above the poor performance segment mean and all have signals (red flags 3, 3, 1, 2, 1, 1) which indicate special cause variation and a significant shift in the data upwards, suggest improvement due to the changes made.

new baseline with improved mean which removes the signals, data within all segments is now stable.

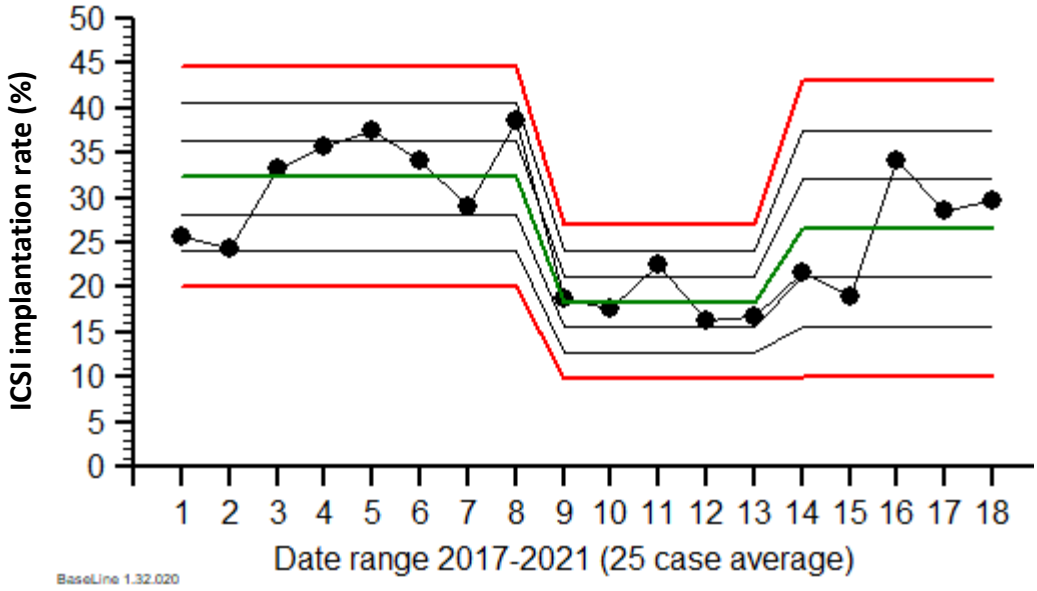


Figure 39 SPC chart of ICSI implantation rate (%) plotted over 5 years in consecutive 25 ICSI case averages. Same data but showing post intervention data as its own established baseline. Removes the previous signals and all data across all three segments is stable.

Weekly data was also monitored over a four-year period (2018-2021) and includes all ICSI cases (all maternal ages and semen types) but excludes IVF/ICSI splits. Understandably the data shows vast variation as some weeks there are no ICSI pregnancies and others a 100% implantation rate was achieved, especially if the number of weekly ICSI cases are low, or even one patient. However, looking at data in this format helps to identify patterns or shifts that would otherwise go unnoticed when looking at larger averages. The weekly implantation rate for ICSI cycles between 2018 and 2021 is shown in Figure 40. The mean implantation rate for this period was 24.19%. The period of reduced clinic performance can be seen in the weekly data between 22/10/2018 and 30/12/2019. This does not show any signals likely due to the large variation in the data set 0-100%. October/November 2019 was a particularly poor period with 9 consecutive data points below the mean showing a significant shift in the data. The intervention was implemented as indicated with the blue arrow on the chart with the first egg collection list being the 06/01/2020. This resulted in a significant shift towards a better implantation rate as indicated by the signal in the data however this was not maintained and once again the data dropped below the mean following the last list before clinic closure due to the Covid-19 pandemic and persisted during the clinic recommencement of treatment. Process and balancing measure analysis could help to explain reasons for this. The first 17

ICSI cases following clinic recommencement of fresh cycles did not achieve a pregnancy. From October 2020 the success rates improved and a regular up and down pattern of data across the mean can been seen. Few signals are present except for a period around July 2020 where there was a shift in the data towards a higher implantation rate. The data was further analysed by breaking it up into segments in Figures 41 and 42.

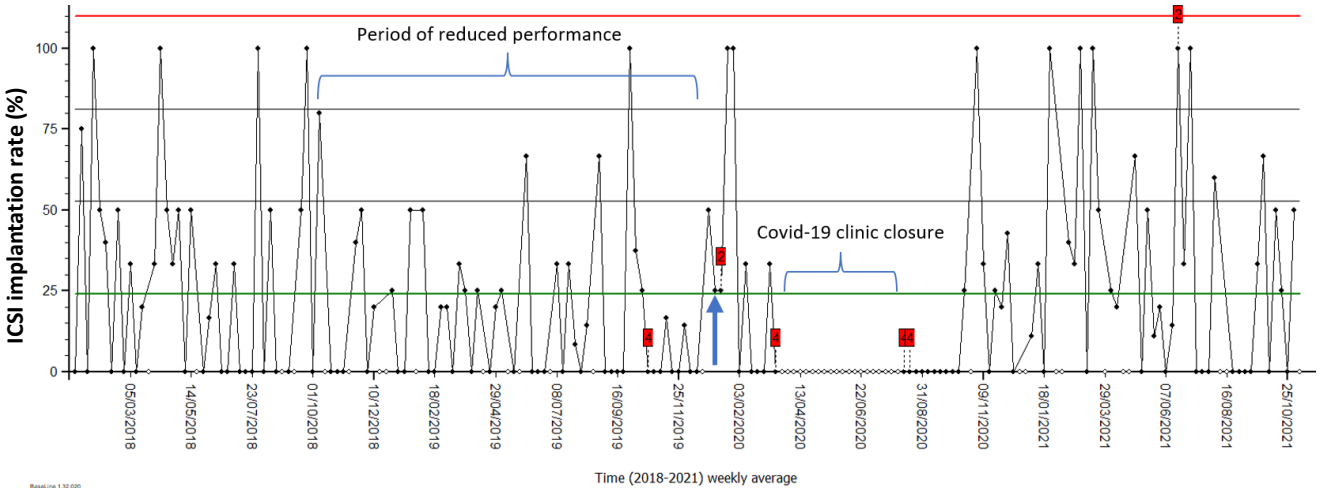


Figure 40 SPC chart of ICSI implantation rate (%) as a weekly average plotted over 4 years. Data show great common cause variation due to the nature of low case numbers each week (many 0% and 100% results of not pregnant/pregnant). The period of poor performance and clinic closure due to the Covid-19 pandemic are marked. The start of the improvement cycle is marked with a blue arrow (6th January 2020). There are 6 signals within the data showing two shifts of good performance and two of poor performance. The data suggest that the closure of the clinic and its recommencement strategy could have had an impact on the success rates during this period. Mean 24.19%.

Figure 41 takes into consideration the period of poor performance and locks the data at the start of the intervention to prognostically see the impact this has on the data. There are 13 signals in the data post intervention that suggest the implantation rate initially improves then gets worse then improves again. The mean implantation rate was 31.04% (01/01/2018-15/10/2018) before the period of poor performance (22/10/2018-30/12/2019), it then dropped to 16.40%. The post intervention period had an improved mean of 26.61% between the time frame of 06/01/2020 to 08/11/2021 reaching the clinic benchmark. Acknowledging the impact of the pandemic and clinic closure on the data by adding another segment gives Figure 42. There are four segments, the first and last are stable with good performance and the middle two are unstable with poor performance. The mean from the last segment, time period from 19/10/2020 to 08/11/2021, of 31.99% implantation rate indicates improvement back to a similar implantation rate in 2018

before the rates dropped. Suggesting that the changes made had resulted in an improvement if you exclude the effects of the pandemic.

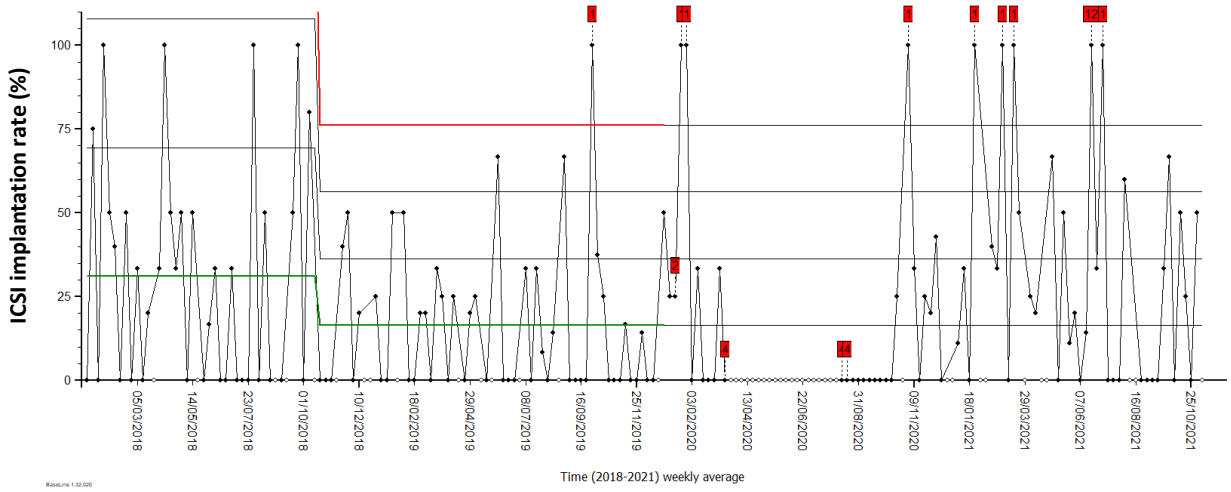


Figure 41 SPC chart of ICSI implantation rate (%) as a weekly average plotted over 4 years. Segment 2 acknowledges the poor performance period that was identified by the clinic from 22/10/2018. The mean drops from 31.04% to 16.40%. The data is then locked at the start of the improvement intervention (6th January 2020). There are 13 signals in the data after the intervention that suggest the implantation rate initially improved then worsened around the period of clinic closure to later improve after October 2020. The mean implantation rate for the post intervention period was 26.61%.

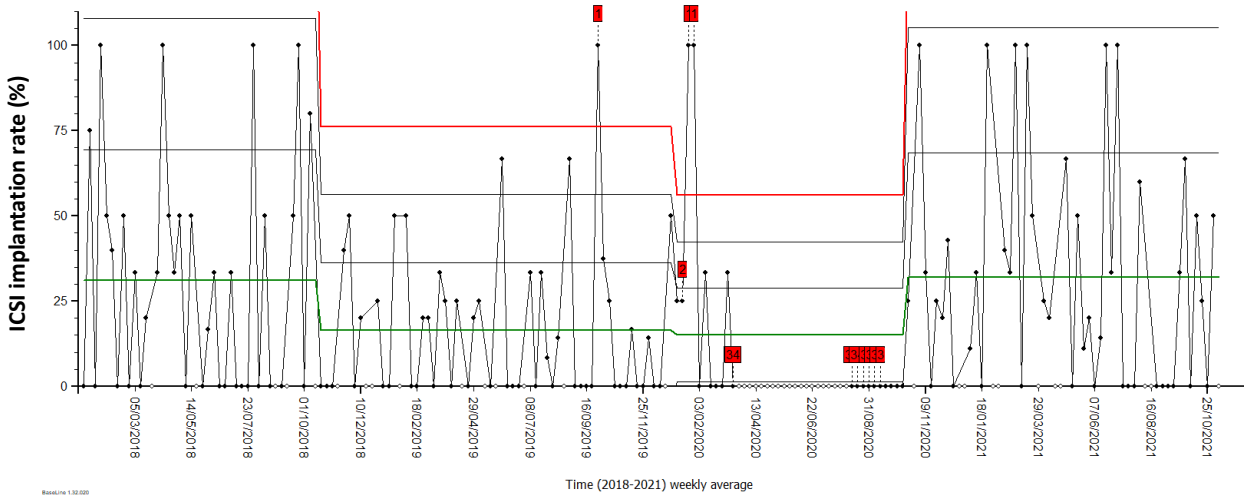


Figure 42 SPC chart of ICSI implantation rate (%) as a weekly average plotted over 4 years. Acknowledging the Covid-19 pandemic impact on success rates following the initial recommencement of cycles by splitting the data into 4 segments. The last segment the period from the 19th October 2020 to November 2021 is stable and has a higher implantation rate mean of 31.99% following two unstable periods of poor performance (means of 16.40% and 15.08% implantation rate). The mean implantation rate appears to have improved and returned to a similar level of performance before the problem period, mean of the first stable segment was 31.04% implantation.

2.3.3 ICSI clinical pregnancy rate per embryo transfer procedure

The clinical pregnancy per embryo transfer procedure was analysed using SPC charts as a 25-case average and also weekly average over time. Figure 43 shows the data from 2017 to 2021 25 case average over time. It demonstrates an identical pattern to the implantation rate with shifts in the data marking the reduction in success rates from points 9-15. No signals in the data between points 3-8 suggests that the better ICSI implantation rate during this period (refer to Figure 34) was likely due to a higher proportion of blastocyst cycles and elective single embryo transfer e.g., fewer double and triple embryo transfers. The mean clinical pregnancy rate for the whole data range was 34.67% which just reaches clinic benchmark of 35%.

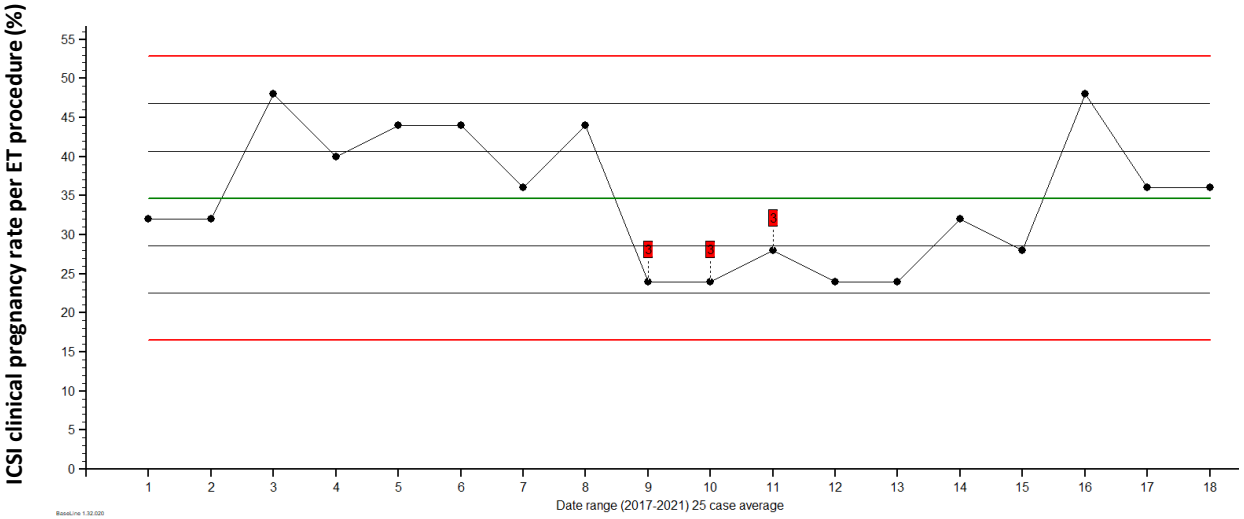


Figure 43 SPC chart of ICSI Clinical pregnancy rate per embryo transfer procedure (%) consecutive 25 case average over a 5-year period. A mean of 34.67% for the whole data period. As significant reduction in pregnancy rate can be seen in the data over 6 points (9-15). Which coincides with the implantation rate data.

The data can be split into appropriate segments to remove the signals and leave segments of stable data. As shown in Figure 44 with the data split at point 9 and locked at the start of the improvement intervention. There are 8 signals in the 5 data points post start of the intervention that indicate a significant shift in the data above the previous mean, suggesting the intervention caused an improvement in clinical pregnancy rate. The mean clinical pregnancy started at 40% between data points 1-8 (Jan 2017-October 2018), reduced to 24.80% between data points 9-13 (Nov 2018-Dec 2019), then following the intervention it increased to 36% during the last 5 data points (Jan 2020-Nov 2021). Splitting the data at point 14 (intervention start) gives 3 segments of stable data (Figure

45). Ideally more data points post intervention are desired to establish if the improvement is sustained and a new baseline has been created.

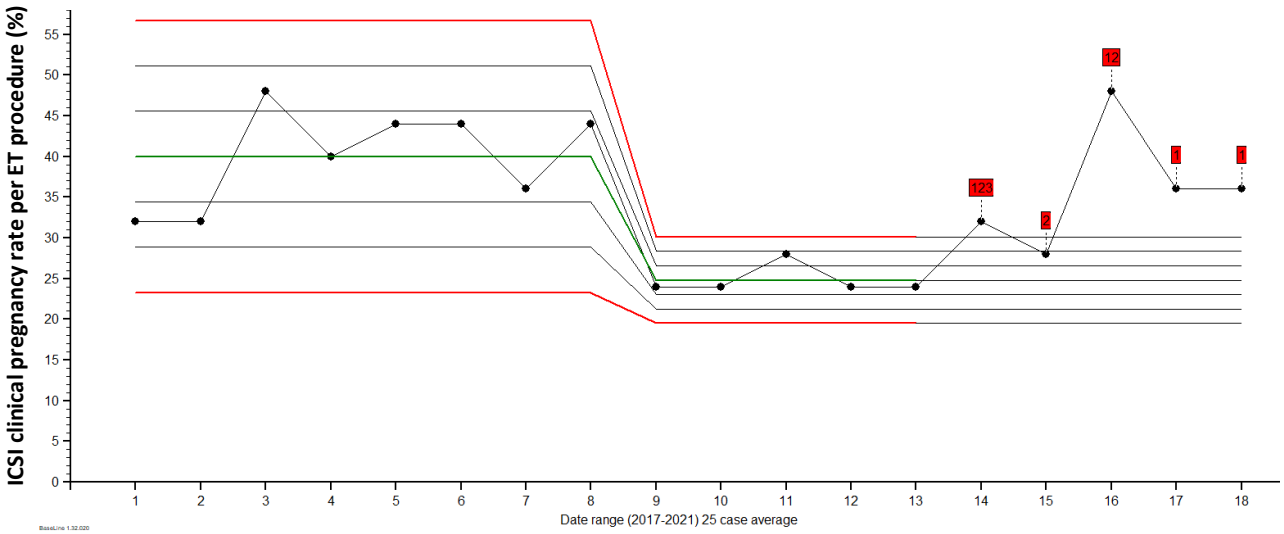


Figure 44 SPC chart of ICSI clinical pregnancy rate per embryo transfer procedure (%) consecutive 25 case average over a 5-year timeline. The data has been split at point 9 to remove signals in the data indicating a reduced pregnancy rate. The data is locked at the start of the intervention for improvement at point 14. The last 5 data points are after the intervention was started and all of them indicate signals of special cause variation, they are all above the previous low mean of 24.8% clinical pregnancy rate during the problem period. They create a new mean of 36% clinical pregnancy rate.

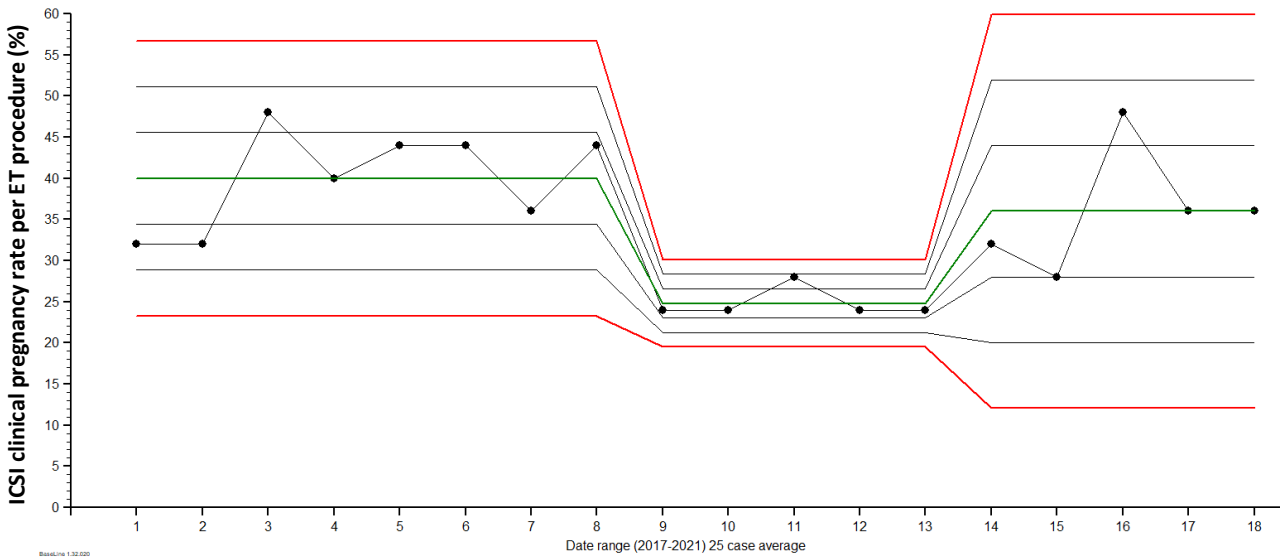


Figure 45 SPC chart of ICSI clinical pregnancy rate per embryo transfer procedure (%) consecutive 25 case average over a 5-year timeline. Data split into 3 stable segments showing the drop and subsequent increase in clinical pregnancy rates following the start of the intervention to a new mean of 36%.

Weekly clinical pregnancy rates were also run on SPC charts to identify additional patterns within the data. The SPC chart shows great common cause variation due to the low numbers of cases each week. Figure 46 shows 5 patterns/shifts in the data. A period

of good success rates early 2018. The dip in success rates late 2018, an improvement in success rates following introduction of the intervention (blue arrow), another dip in rates around the Covid-19 clinic closure and improved rates in 2021. Similar to the patterns seen with implantation rates. The mean clinical pregnancy rate for the whole 4-year period was 30.75%.

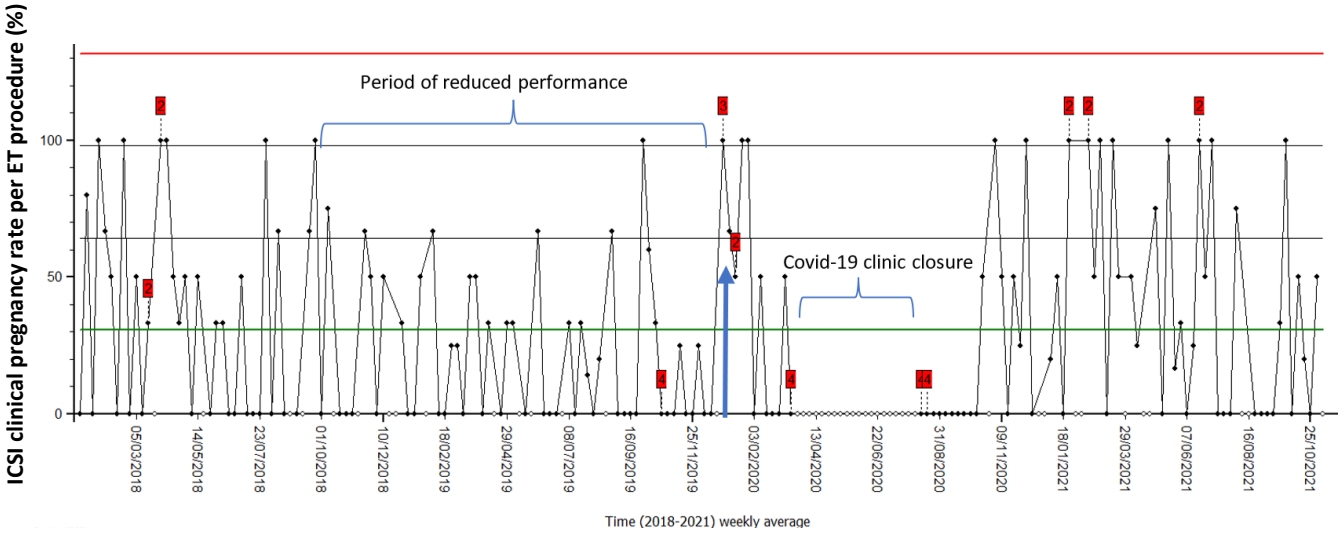


Figure 46 SPC chart of ICSI clinical pregnancy rate per embryo transfer procedure (%) as a weekly average plotted over 4 years. Data show great common cause variation due to the nature of low case numbers each week (many 0% and 100% results of not pregnant/pregnant). The period of poor performance and clinic closure due to the Covid-19 pandemic are marked. The start of the improvement cycle is marked with a blue arrow (6th January 2020). There are 11 signals within the data showing three shifts of good performance and two of poor performance. The data suggest that the closure of the clinic and its recommencement strategy could have had an impact on the success rates during this period. The mean over this whole period was 30.75%.

The period of poor performance is taken into consideration in Figure 47 and the data is locked at the start of the intervention to prognostically see the impact this had on the data for improvement. There are 20 signals in the data post intervention that suggest the implantation rate initially improves, gets worse, then improves again. The mean implantation rate was 37.52% (01/01/2018-15/10/2018) before the period of poor performance (22/10/2018-30/12/2019), it then dropped to 21.59%. The post intervention period had an improved mean of 34.32% between the time frame of 06/01/2020 to 08/11/2021 almost reaching the clinic benchmark. Acknowledging the impact of the pandemic and clinic closure on the data by adding another segment gives us Figure 48. There are four segments, the first and last are stable with good performance and the middle two are unstable with poor performance. The mean clinical pregnancy rate of 41.07% from the last segment, time period from 19/10/2020 to 08/11/2021, shows significant improvement better than the pregnancy rate in 2018 before the rates

dropped. Suggesting that the changes made had resulted in an improvement if you exclude the effects of the pandemic.

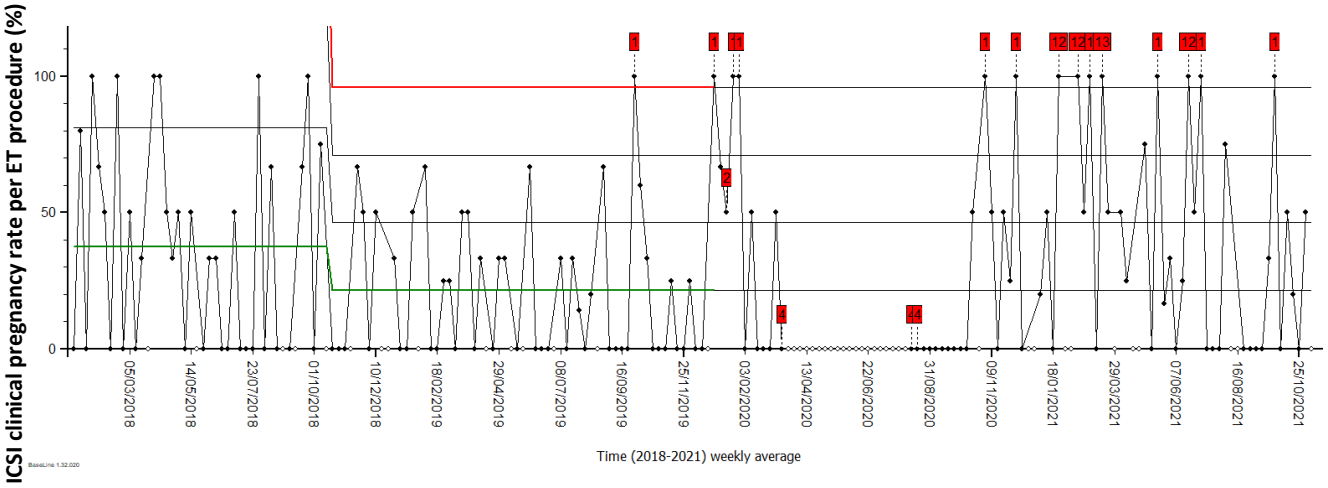


Figure 47 SPC chart of ICSI clinical pregnancy rate per embryo transfer procedure (%) as a weekly average plotted over 4 years. Segment 2 acknowledges the poor performance period that was identified by the clinic from 22/10/2018. The mean drops from 37.52% to 21.59%. The data is then locked at the start of the improvement intervention (6th January 2020). There are two signals of special cause variation within the period of reduced performance that are sporadic good weeks 30th September 2019 (3 ICSI cases, all three pregnant), 30th December 2019 (2 ICSI cases both pregnant, double progesterone intervention was started here). There are 20 signals in the data after the intervention that suggest the pregnancy rate initially improved then worsened around the period of clinic closure to later improve after October 2020. The mean implantation rate for the post intervention period was 34.32%.

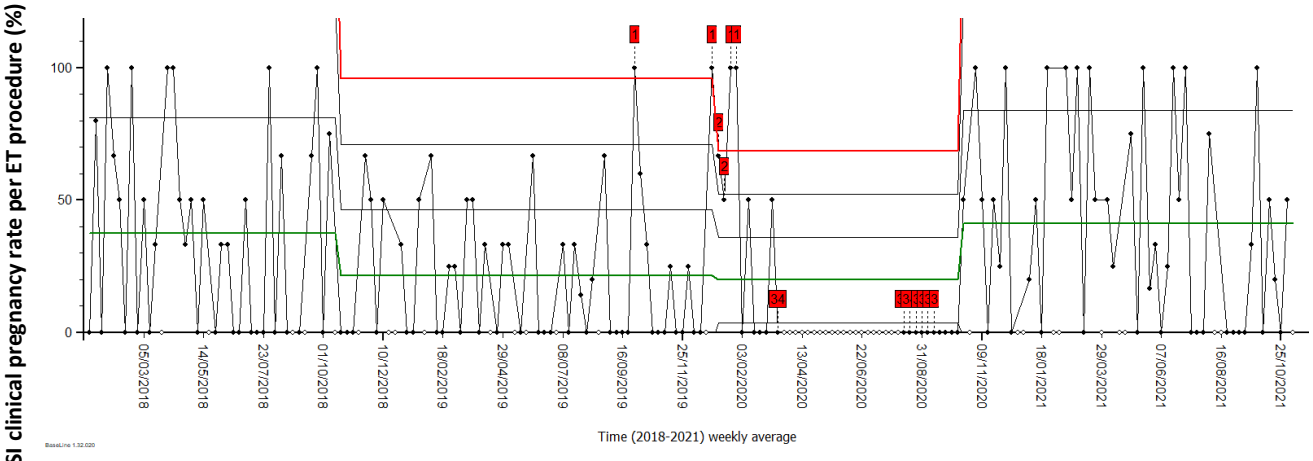


Figure 48 SPC chart of ICSI clinical pregnancy rate per embryo transfer procedure (%) as a weekly average plotted over 4 years. Acknowledging the Covid-19 pandemic impact on success rates following the initial recommencement of cycles by splitting the data into 4 segments. The last segment, the period from the 19th October 2020 to November 2021, is stable and has a higher pregnancy rate, mean of 41.07%, following two unstable periods of poor performance (means of 21.59% and 19.84%). The mean pregnancy rate appears to have improved and returned to a similar level of performance before the problem period, mean of the first stable segment was 37.52% implantation.

2.3.4 Summary of outcome data

Both ICSI implantation rate and clinical pregnancy rate SPC charts demonstrate a period of reduced performance and an improvement following the intervention. The first two data points of the 25-case average are lower and this is likely due to the impact of the Covid-19 pandemic as revealed when the data was plotted as a weekly average. Without the impact of this on the data a bigger improvement may have been seen. More data points should be collected to ascertain whether the improvement is sustained and definitely attributable to the intervention bundle that was introduced.

2.3.5 Process measure results

2.3.6 ICSI damage rate

ICSI damage rate was monitored to determine if the improvement work had an impact on this KPI. This KPI is defined as the proportion of eggs that are damaged during the ICSI injection, or have degenerated by the time of fertilisation assessment on Day 1. Patient mix and stimulation protocols can skew the results but this KPI can be informative of gamete quality and/or operator skill. The clinic's benchmark value for this KPI is <10% as recommended by the ESHRE/Alpha Vienna Consensus. The average damage rate per consecutive 25 cycles over time is show in Figure 49. The data is stable, with no signals, and the mean damage rate over the 5-year period was 6.68% within benchmark however data points 13 (Oct-Dec 2019) and 16 (Dec 2020- May 2021) are periods of high damage rates. Figure 50 shows the data split into three segments; baseline, period of poor ICSI implantation rates and after the intervention was started. There are no signals in the data which is stable throughout and all means are within benchmark <10%.

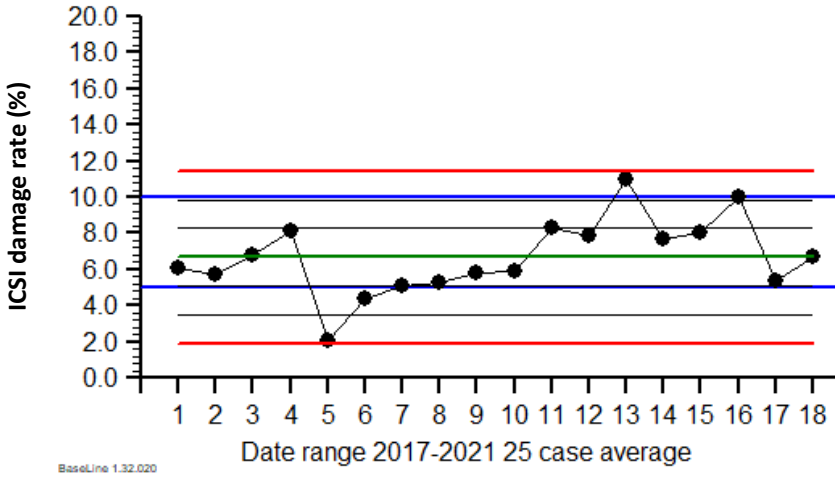


Figure 49 SPC chart of ICSI damage rate (25 consecutive ICSI case average) over 5 years. Mean 6.68% below benchmark. Data stable no signals present.

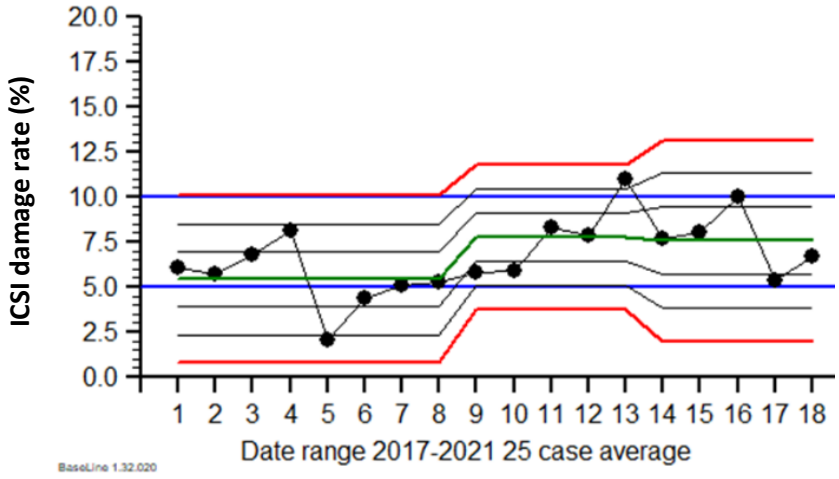


Figure 50 SPC chart of ICSI damage rate (25 consecutive ICSI case average) over 5 years. Split into three segments; baseline (mean 5.43%), period of poor ICSI implantation rate (7.78%) and period after the start of the improvement intervention (mean 7.56%). All means below benchmark. No differences, no signals in the data.

Data plotted as a weekly average is shown in Figure 51. The data is unstable with many signals but the overall mean damage rate of 7.42% is within the benchmark. The triggering of Rule 4 (nine or more points on the same side of the mean) and Rule 3 (four out of five points more than 1 sigma on the same side of the mean) signals starting from the 12/02/2018 for 11 weeks are data points below the mean until 30/04/2018, which suggest a materially significant lower damage rate during this period. A three-week period of high damage rates is indicated by the triggering of Rule 2 (two out of three points more than 2 sigma on the same side of the mean) and Rule 1 (outside the 3 sigma control limits) signals from 17/02/2020 to 02/03/2020. This special cause variation after the intervention was started was investigated, the two weeks in February had only one ICSI case each and the week early March had only 2 ICSI cases. Average damage rate across the 4 cases was 22.73% (10/44 eggs), with an average maternal age of 32 years, 11.25 mean egg number, 45 eggs in total and other KPIs within benchmark (fertilisation rate was 72.73% (32/44), 44/45 eggs mature). One patient achieved a biochemical pregnancy which did not continue. The high damage rate could be due to patient factors or possibly a learning curve with the new ICSI injection procedure.

A single point on the 10/08/2020 triggered Rule 1 (outside the 3 sigma control limits), this was a 50% damage rate caused by only one ICSI case that week with 2 eggs collected from a 42-year-old. Not a concern and expected when plotting weekly averages with low case numbers. This is followed by two 6-week periods of materially significant lower damage rates from 17/08/2020 to 21/09/2020 and 28/06/2021 to 02/08/2021. Indicating improvement. Finally, another Rule 1 was triggered on the 06/09/2021 with a 40% damage rate which was again due to a single ICSI case, a 41-year-old with 5 eggs collected.

Splitting the data after the intervention started gives Figure 52. The mean damage rate increased from 6.18% to 8.99% after the intervention but the data in both segments is unstable and the variation increases despite the ICSI process being more standardised as part of the intervention (consistent practitioner, ICSI rig and micro tools). The increase in damage rate is not meaningful as both Rule 1 signals can be explained by low case/egg numbers. ICSI damage rate does not appear to correlate with implantation rate.

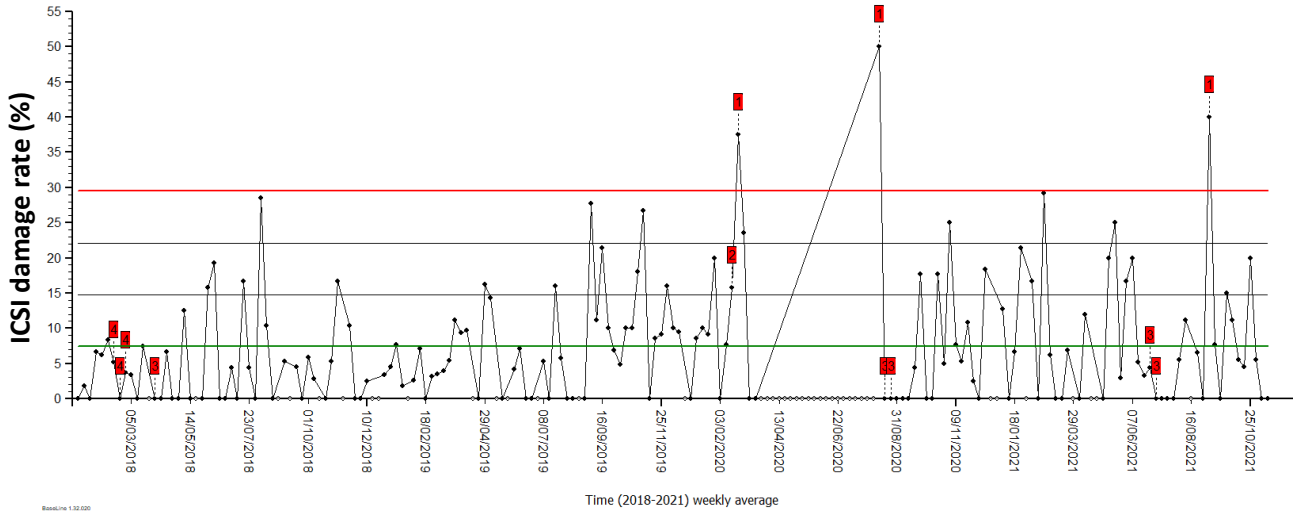


Figure 51 SPC chart of ICSI damage rate as a weekly average over time. Mean damage rate of 7.42% within the benchmark but lots of special cause variation. Some of which were caused by low case and egg numbers for a week, e.g.,10th August 2020 had a weekly average KPI of 50% ICSI damage rate but there was only one ICSI case that week with 2 eggs collected from a 42-year-old.

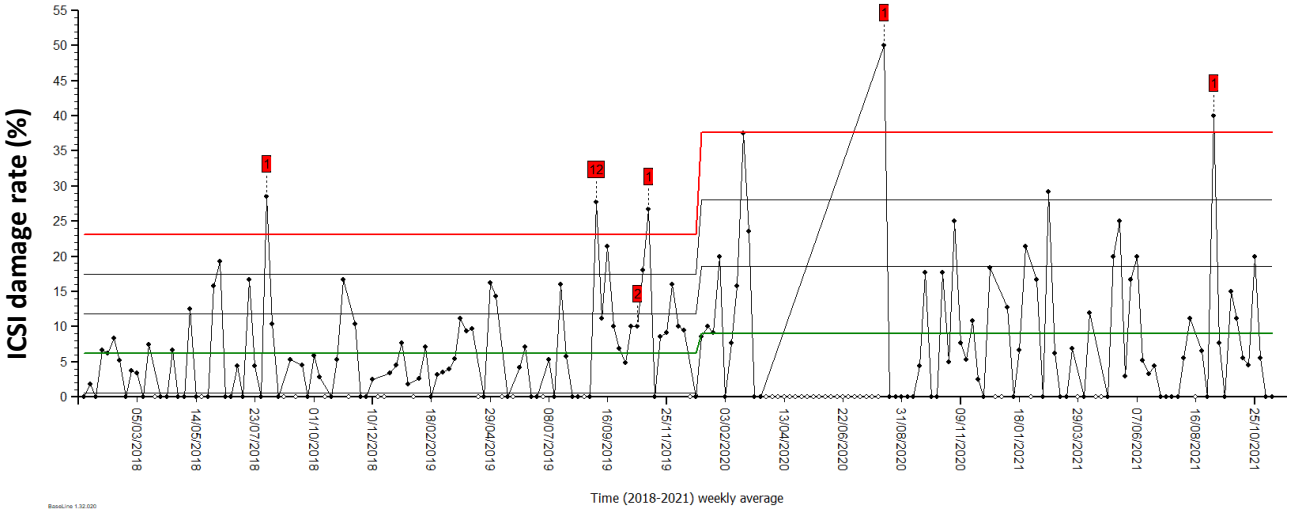


Figure 52 SPC chart of ICSI damage rate as a weekly average over time with data split at the start of the intervention for improvement. The mean increases slightly from 6.18% to 8.99% after the intervention (the two Rule 1 signals can be explained by single cases on these weeks) and there is more common cause variation. Overall damage rate is within benchmark.

2.3.7 ICSI fertilisation rate

ICSI normal fertilisation rate was monitored to determine if the improvement work had an impact on this KPI. With the assumption that changes introduced, strict ICSI injection time of 40-41 hours post HCG trigger and fertilisation check time of 16 hours post injection, would stabilise and improve fertilisation rates. However, the ICSI procedure itself had also changed. The ICSI normal fertilisation rate KPI is defined as the number of fertilised eggs on Day 1 (presence of 2PN and 2PB assessed at 17 ± 1 h post-injection) as a function of all mature eggs injected (ESHRE Special Interest Group of Embryology and Alpha Scientists In Reproductive Medicine, 2017). It is an effective indicator of good laboratory practice, as it is informative of gamete quality and/or operator skill. Usually, it should exclude cycles using surgically retrieved sperm as results may be lower, however due to low ICSI cycle numbers to increase the data set all semen types were included in the SPC charts. The clinic's benchmark value for this KPI is ≥65% as recommended by the ESHRE/Alpha Vienna Consensus. The average fertilisation rate per consecutive 25 cycles over time is show in Figure 53. The data is stable, with no signals, and the mean fertilisation rate over the 5-year period was 68.20% within benchmark, however a poorer performing period from point 9-13 (Nov 2018- Dec 2019) is below the mean. This period

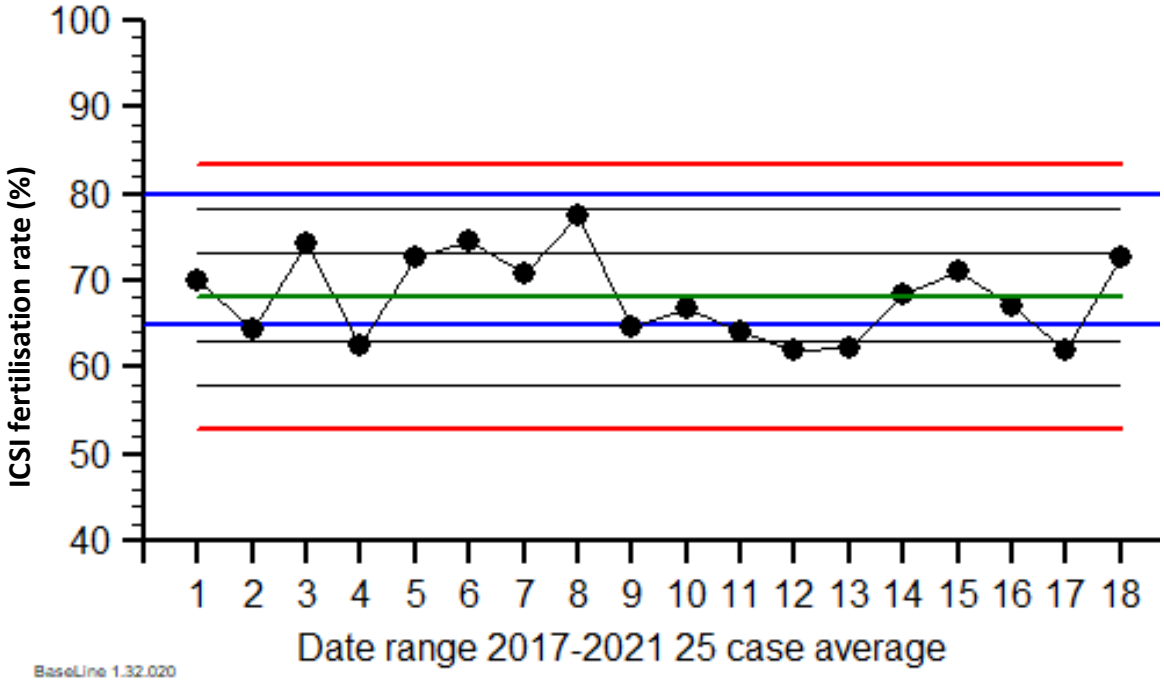


Figure 53 SPC chart of ICSI fertilisation rate (25 consecutive ICSI case average) over 5 years. Mean 68.20%. Data stable no signals present. Blue lines mark the ESHRE/Alpha Vienna Consensus benchmark values for this measure ≥65% & ≥80%. The mean is over the competency value of 65% which is the clinic target.

coincides with the period of poor ICSI implantation rates. Figure 54 shows the data split into three segments; baseline, period of poor ICSI implantation rates, and after the intervention was started. There are no signals in the data which is stable throughout and the mean fertilisation rate drops below benchmark during the period of poor ICSI implantation to 63.95% but increases after the intervention.

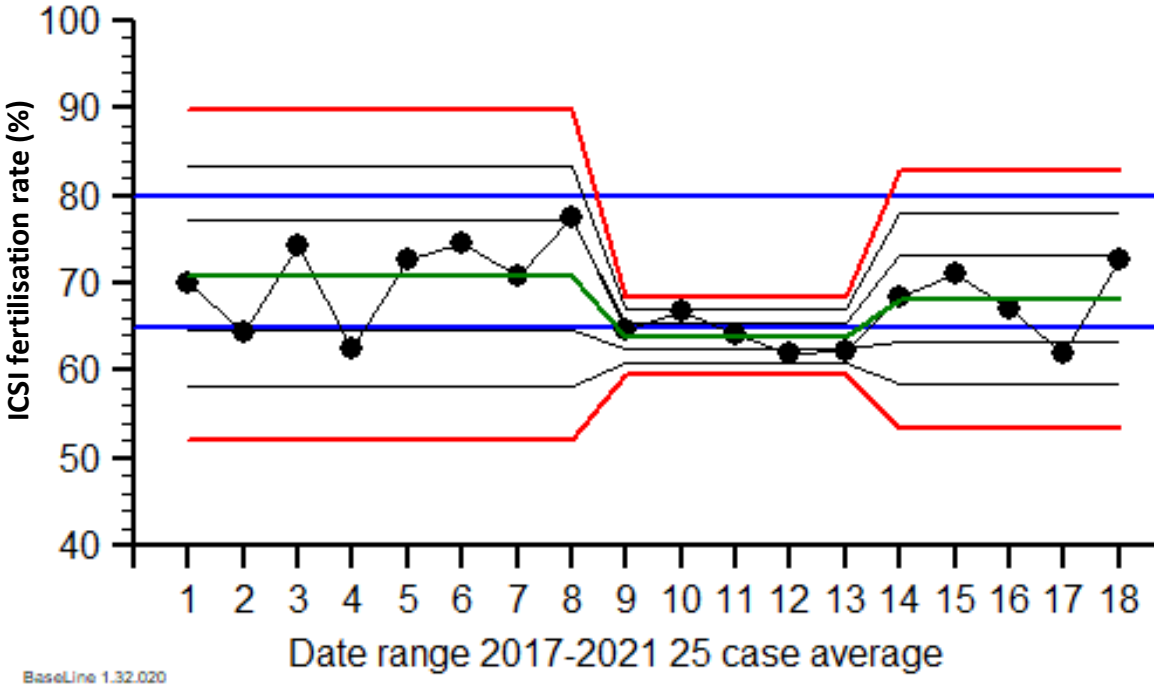


Figure 54 SPC chart of ICSI fertilisation rate (25 consecutive ICSI case average) over 5 years into three segments; baseline (mean 70.84%), period of poor ICSI implantation rate (63.95%) and period after the start of the improvement intervention (mean 68.2%). No differences, no signals but reduced common cause variation during the poor performing period.

Data plotted as a weekly average is shown in Figure 55. The data is unstable with two areas of signals but the overall mean fertilisation rate 67.41% is within benchmark. The first Rule 4 trigger indicates a 9-week period of materially significant good fertilisation rates between 19/02/2018 and 3/04/2018 (mean 78.14%). This is followed by a 10-week period of materially significant lower fertilisation rates (mean 55.33%) between 08/07/2019 to 16/09/2019 (as indicated by the two consecutive Rule 4 signals). This coincides with the period of poor ICSI implantation rates during 2019. Splitting the data after the intervention started gives Figure 56. The mean fertilisation rate increased slightly from 66.96% to 67.98% after the intervention but this was materially insignificant, there are no signals after the intervention and the common cause variation increased. Changes made to the ICSI procedure and fertilisation checks have not negatively affected

the fertilisation rates. Better standardisation of the ICSI procedure and fertilisation checks counterintuitively appears to have increased the variation of average weekly fertilisation rate however this could be an effect of low egg numbers and ICSI cases during some weeks.

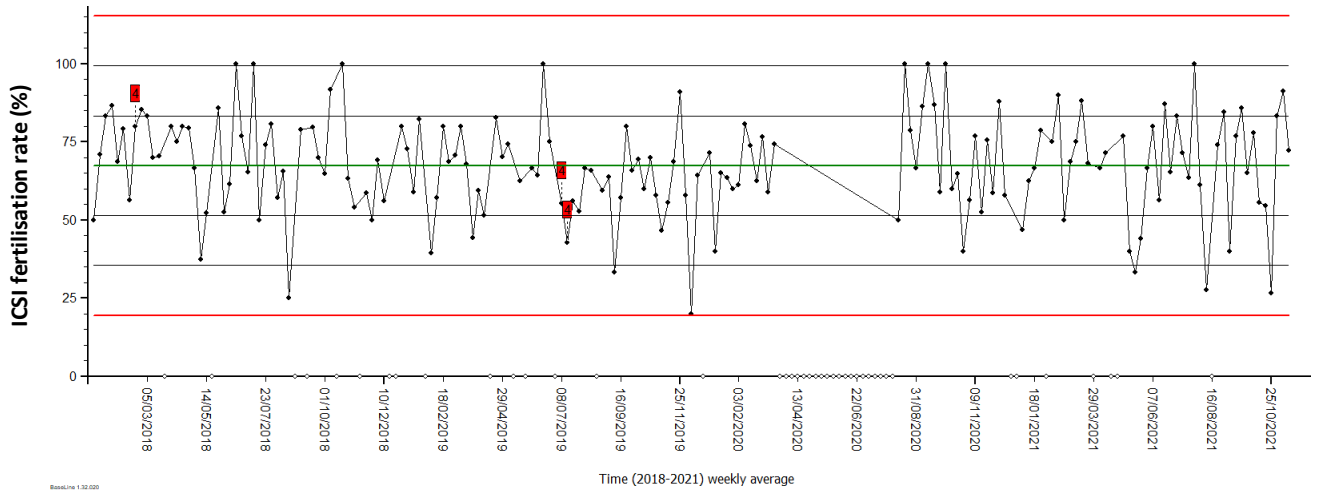


Figure 55 SPC chart of ICSI fertilisation rate as a weekly average over time. Mean damage rate of 67.41% within the benchmark but two areas of special cause variation; good and poor periods of performance. The first trigger of Rule 4 (red flag) indicates a 9-week period of materially significant better fertilisation rates between 19/02/2018 and 3/04/2018 (mean 78.14%). This is followed by a 10-week period of materially significant lower fertilisation rates (mean 55.33%) between 08/07/2019 to 16/09/2019 (as indicated by the two consecutive Rule 4 signals).

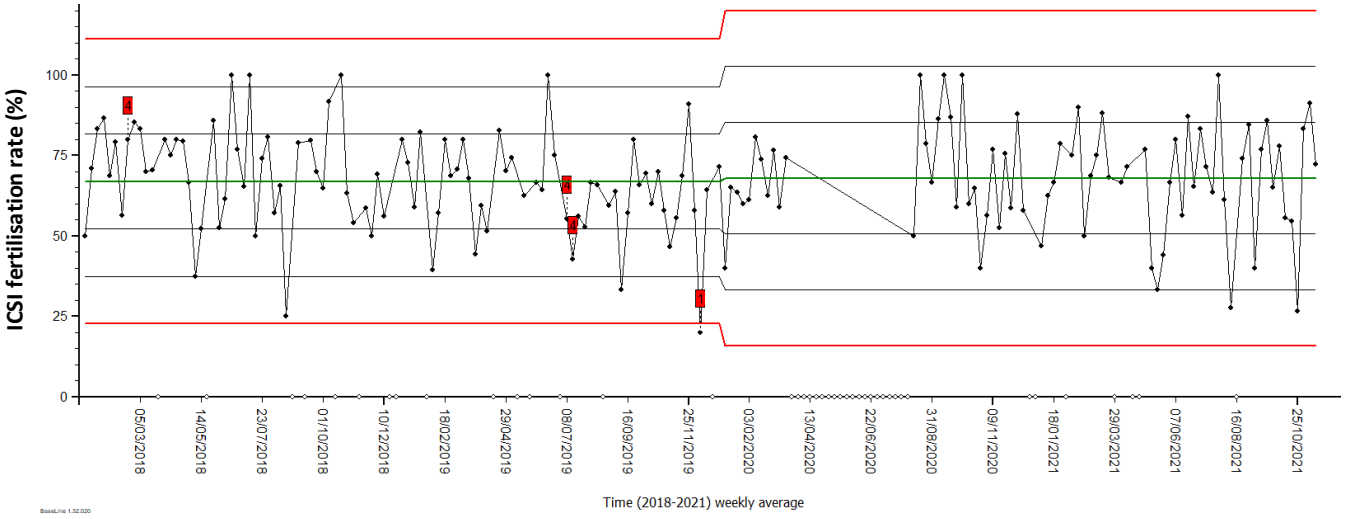


Figure 56 SPC chart of ICSI fertilisation rate as a weekly average over time with data split at the start of the intervention for improvement. The mean increases slightly from 66.96% to 67.98% after the intervention (there are no signals) and there is more common cause variation. Overall fertilisation rate is within benchmark.

2.3.8 ICSI embryo utilisation rate

Embryo utilisation rate was monitored during the project to determine the effect of the intervention on this KPI. There is no agreed benchmark for utilisation as this indicator will vary depending on different clinic protocols and practice but can be defined as the number of embryos (or blastocysts) suitable for transfer or cryopreservation as a function of the number of normally fertilised (2PN) eggs observed on Day 1 (ESHRE Special Interest Group of Embryology and Alpha Scientists In Reproductive Medicine, 2017). A high utilisation rate is an indirect indicator of good embryo quality and higher chance of pregnancy. The clinic benchmark of utilisation rate for blastocyst cycles is >45%. The data was plotted only as a weekly average over time through SPC charts. The mean ICSI blastocyst utilisation rate for the 4-year period was 49.77%, within clinic benchmark (Figure 57). There was one signal from 14/09/2020 to 12/10/2020 which indicates a materially significant increased shift in utilisation rate over this four-week period.

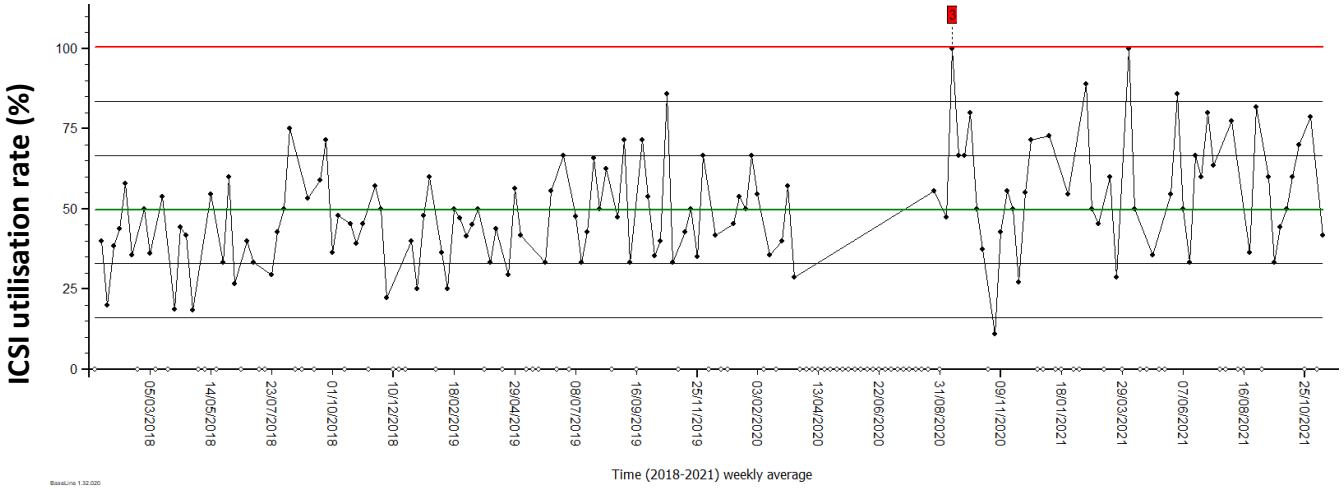


Figure 57 SPC chart of ICSI Blastocyst utilisation rate as a weekly average over 4 years. A mean of 49.77%, above clinic benchmark of >45%. One period of special cause variation is indicated between 14/09/2020 and 12/10/2020, suggesting a shift towards a better utilisation rate.

The start of the intervention and its impact on the utilisation rate is considered by locking the data to give Figure 58, which shows many signals in the data post intervention indicating a materially significant shift towards a higher utilisation rate. The mean utilisation rate increased from 45.33% to 55.89%. Suggesting that more good quality blastocysts were available (frozen and transferred) following the changes made. It is possible that the change of keeping the cumulus cells on for longer and immediate

injection after denudation could be the reasons for better embryo quality and development (Rienzi et al., 1998; Ho et al., 2003; Isiklar et al., 2004). However, when comparing the charts to ICSI implantation rate SPC charts utilisation rate does not appear to correlate well, with periods of poor pregnancy rates having high utilisation rates.

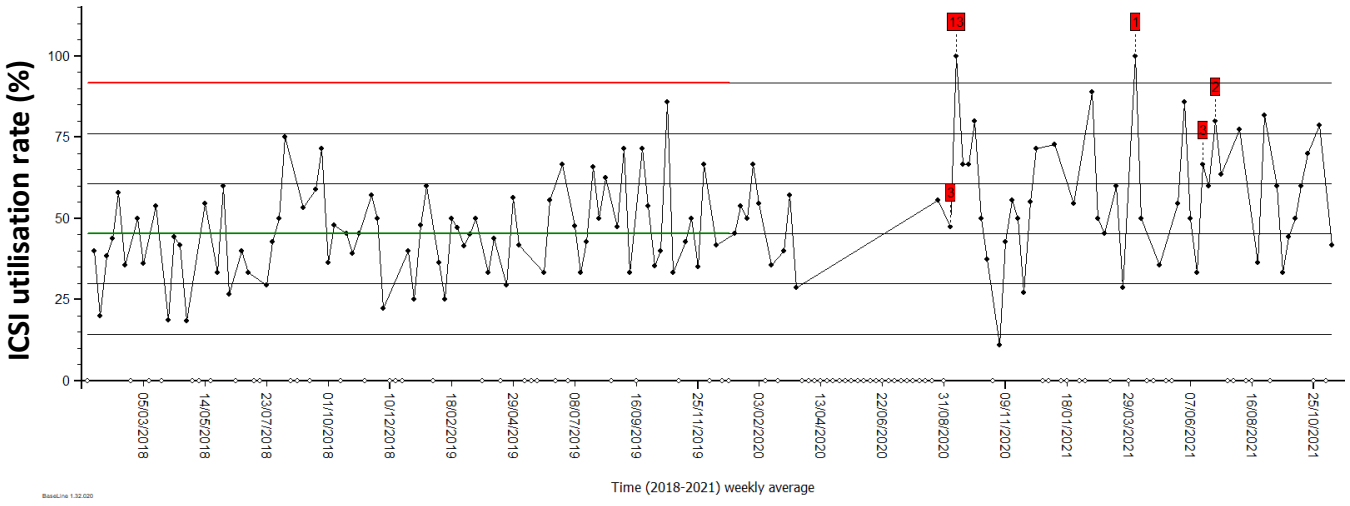


Figure 58 SPC chart of ICSI Blastocyst utilisation rate as a weekly average over 4 years locked at the start of the improvement intervention January 2020. The mean utilisation rate improved from 45.33% to 55.89% (not shown on the chart). There are six signals within the data post intervention which indicates that the utilisation rate has increased.

2.3.9 Summary of process measures

The intervention implemented to improve ICSI implantation rates appears to have had no materially significant effect on the ICSI damage rate nor fertilisation rate. Although the mean damage rate appears to have increased slightly and there were periods of weekly averages with higher damage rates possibly due to changes made to the procedure or patient factors. The mean fertilisation rate increased slightly. The period of poor ICSI implantation rates showed reduced fertilisation rates and increased damage. The pattern of ICSI blastocyst embryo utilisation rate did not correlate with ICSI success rates but improved following the intervention, higher proportions of good quality blastocysts were available.

2.3.10 Balancing measure results

2.3.11 ICSI blastocyst cycle percentage

The proportion of the clinic's fresh ICSI blastocysts cycles was monitored over the 5-year period (consecutive 25 ICSI case average) (Figure 59). Changes in laboratory and clinical practice could also have had an impact on the ICSI success rates and vice versa. The mean blastocyst cycle rate over the whole period was 58.51%. In 2017 the majority of fresh treatment cycles were cleavage stage embryo transfers. The popularity and demand for extended culture to the blastocyst stage and blastocyst stage transfer increased. Towards the end of 2017 (data point 5) the blastocyst percentage increases from 40% to 68%. The clinic made changes to its egg collection days in order to offer blastocyst culture to all patients in 2018, resulting in a steady rise to its highest at 80% between February and July 2019 (data points 10 and 11). The percentage then drops down in 2020/2021. The SPC chart (Figure 59) shows 14 signals within the data of special cause variation which shows the difference between the percentage of blastocyst cycles in 2017 compared to 2018/2019 due to the change in clinic policy to push more patients towards blastocyst culture. Removing the signals by splitting the data gives Figure 60, three segments of stable data show that the percentage of blastocyst cycles increased from mean 25.00% in 2017 to 73.50% in 2018/2019 and drops to 60.86% following the improvement work in 2020/2021. The clinic's extended culture criteria has become more lenient in the most recent years to enable more patients to try to get to blastocyst transfer than previously, therefore the drop in ICSI blastocyst transfers is not due to clinic practice but is more likely a result of patient factors (higher maternal age, lower egg numbers, fewer embryos available). The ICSI implantation rate seems to have improved post intervention despite a reduction in the number of blastocyst transfers.

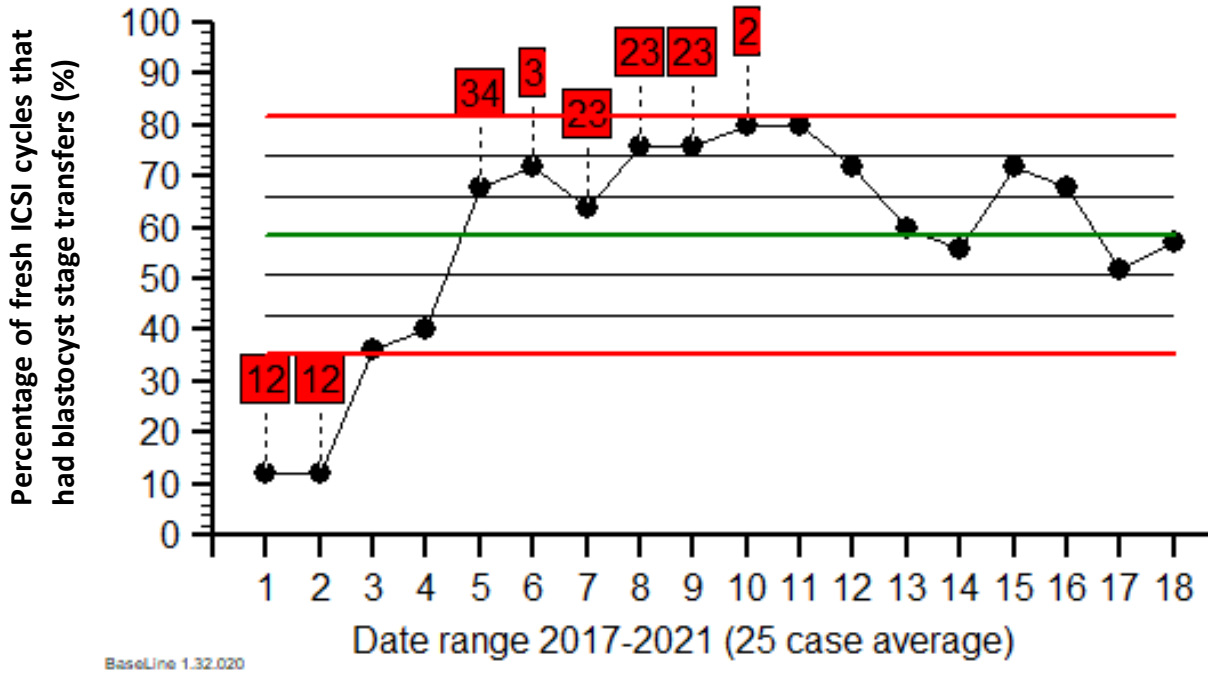


Figure 59 SPC chart of the percentage of fresh ICSI blastocyst transfers (consecutive 25 ICSI case average) over 5 years. 14 separate special cause signals triggering SPC rules within the data demonstrate an increase in the percentage of fresh ICSI blastocysts transfers from 2017 to 2018/19. During this time the clinic made changes to its practice to enable all patients to have the option of blastocyst culture and transfer. It is therefore unsurprising that the number of blastocyst transfers increased dramatically.

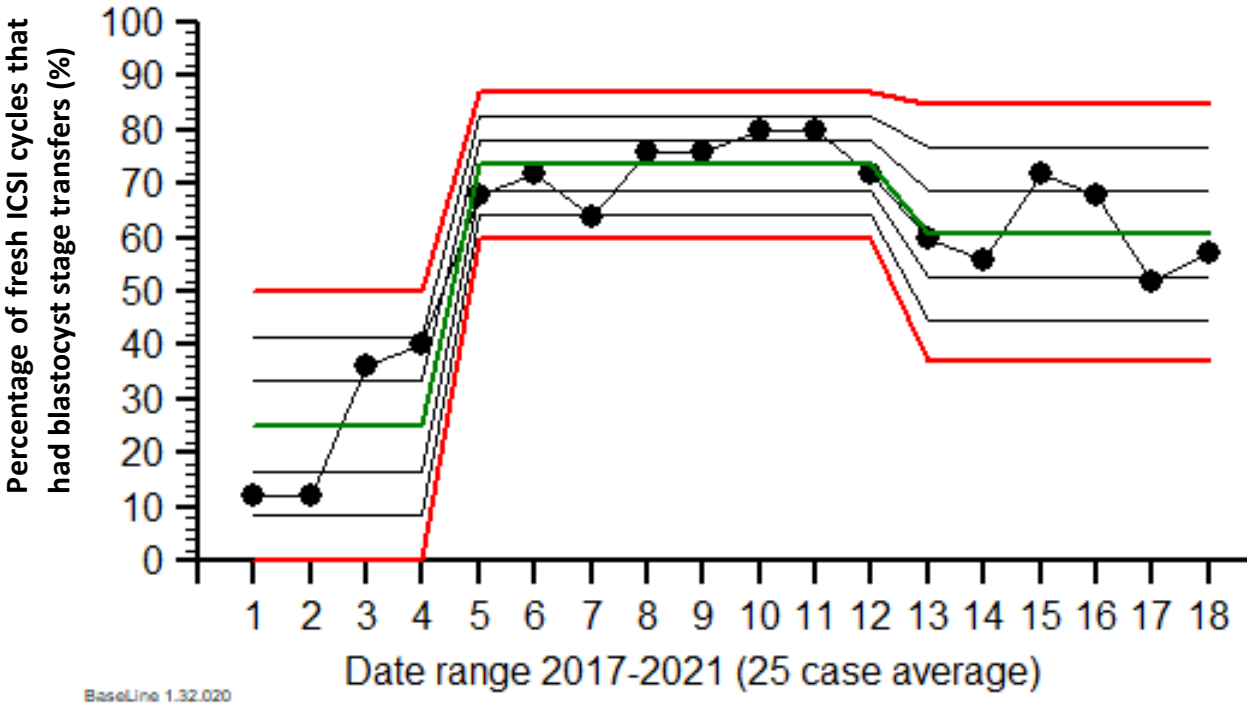


Figure 60 SPC chart of the percentage of fresh ICSI blastocyst transfers (consecutive 25 ICSI case average) over 5 years. Data split to remove signals and stabilise data. The mean percentage of blastocyst transfers was 25% in 2017 (first segment), increases to 73.50% 2018/19 (second segment), and decreases following the intervention to 60.86% 2020/21 (third segment).

2.3.12 Proportion of mature eggs at ICSI

The proportion of mature eggs at ICSI is a performance indicator that is not influenced by laboratory practice but can indicate the effectiveness of ovarian stimulation and the competence of eggs coming into the laboratory. This can affect the performance of the laboratory KPIs. Higher proportions of either immature or post-mature eggs can result from changes in the ovarian stimulation or triggering, as indicated by any instability with this indicator. It is defined as the proportion of eggs that have nuclear maturity at the time of injection and the expected range is 75–90% (ESHRE Special Interest Group of Embryology and Alpha Scientists In Reproductive Medicine, 2017). Part of the improvement intervention included changes to the triggering protocols and follicle aspiration practice therefore this indicator was monitored over time to understand any resulting impact. Individual HCG trigger times were introduced to ensure all IVF cases had egg collections at 36 hours post trigger, all ICSI cases 37 hours post trigger, and no egg collections would commence <36 hours post injection. A new Cook suction pump replaced aging equipment in February 2020 and follicular flushing during egg collections was reduced to as little as possible (consultants' discretion/case dependent). Cumulus cells were now left until just before ICSI with injection straight after egg denudation a change which could help to improve the egg maturity.

The proportion of mature eggs at ICSI over a 5-year period is shown in Figure 61. The mean for this period was within benchmark at 82.23%. The data is stable with no special cause variation detected. The data is split at the start of the improvement intervention in Figure 62. Once again, the data is stable with no signals and both means within benchmark, however there is a trend of reduced proportion of mature eggs post intervention with all 5 data points being below the original baseline mean. Further data and monitoring would be required to establish whether this trend is significant. The mean drops from 83.73% to 78.34%. The reduction in mature eggs at ICSI since changes were made is rather counterintuitive, tightening up on timings for triggers, egg collections and leaving cumulus cells on eggs for longer should optimise the clinic's ability to obtain more mature eggs at injection. It is more likely that the changes made to clinical practice as a result of the Covid-19 pandemic for 2020/21 limiting the clinic to a single egg collection

day a week due to restricted theatre use, and the resulting reduced flexibility with ovarian stimulation and trigger could be influencing this performance indicator.

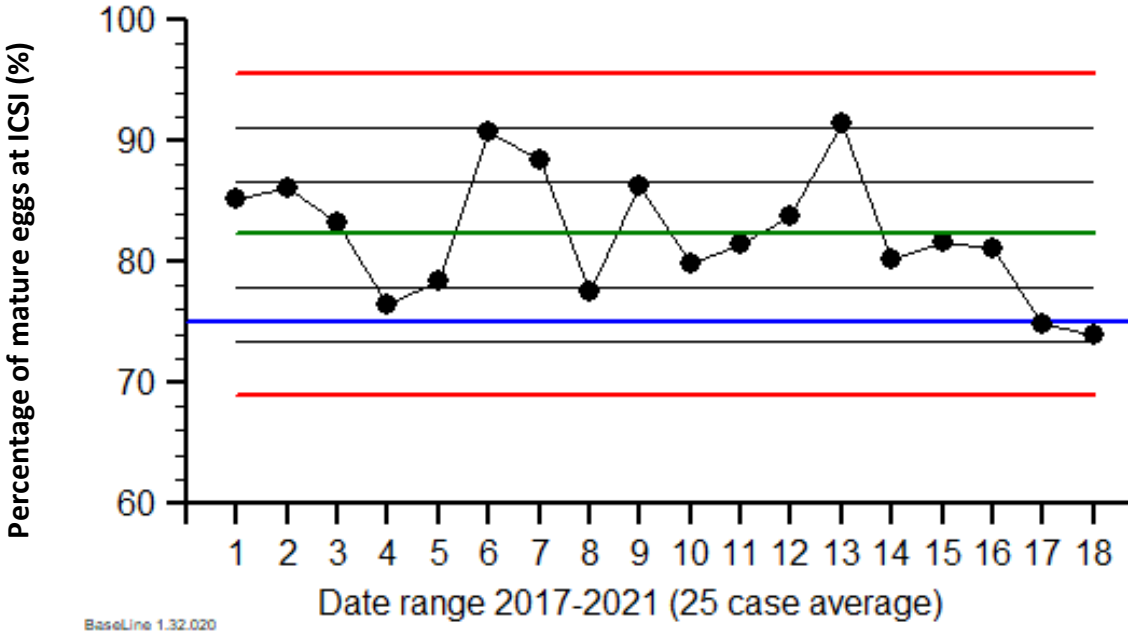


Figure 61 SPC chart of the proportion of mature eggs/oocytes at ICSI (25 consecutive case average over 5 years). The mean for this period is 82.23%, data is stable with no special cause variation and within benchmark (blue line at 75%). The last two data points drop below the benchmark, a time period of May 2021 to November 2021.

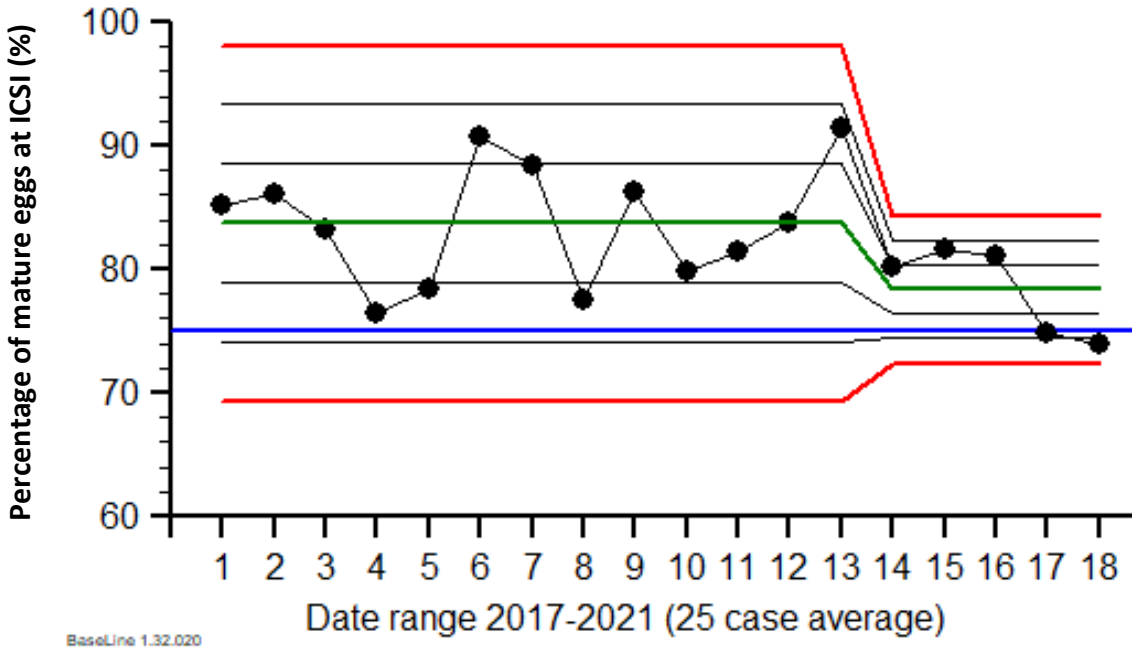


Figure 62 SPC chart of the proportion of mature eggs/oocytes at ICSI (25 consecutive case average over 5 years). The data is split at the start of the improvement intervention. There is a downward trend in the data following the changes made towards a lower proportion of mature eggs available for ICSI. The last 5 data points are all below the baseline mean. More data is required to determine whether this drop is significant. The mean drops from 83.73% to 78.34%, with the last two data points dropping below the benchmark.

2.3.13 Average number of eggs collected for ICSI cases

The number of eggs available for ICSI will have an influence on the success rates with reduced egg numbers being associated with a lower chance of extended culture, blastocyst transfer, embryo freezing, and pregnancy. Too many eggs will also affect success rates with more elective freezing of all embryos (no fresh embryo transfer to reduce the risk of OHSS) of better responders or good prognosis patients changing the patient mix and skewing the data. The clinic aims for a reasonable egg number of between 6-18 eggs (there is no defined benchmark for egg number). The egg number could be influencing the SPC charts of outcome and process measures above and it is possible that the changes of the intervention regarding egg collection could have an impact on the number of eggs collected. New equipment was introduced in February 2020 (Cook suction pump) and August 2020 (Unica enclosed cabinet).

Figure 63 shows the average number of eggs collected for ICSI over 5 years, the data is stable with no special cause variation and a mean egg number of 10.87 eggs, a reasonable number. Figure 64 shows the same data but split after the start of the improvement intervention to show any relationships between egg number and the changes made. The number of eggs collected reduces following the intervention dropping from a mean egg number of 11.27 to 9.83. More data points are required to determine whether this drop is significant. Considering the higher immaturity rate for this period also the clinic is doing well to achieve better implantation and clinical pregnancy rates post intervention despite fewer mature eggs being available. The mean egg numbers are reasonable and not a concern, the reduction in egg numbers could be due to the changes made or the patient mix during this period (maternal age (excludes data from women ≥40), FSH dose, low ovarian reserve, poor responders).

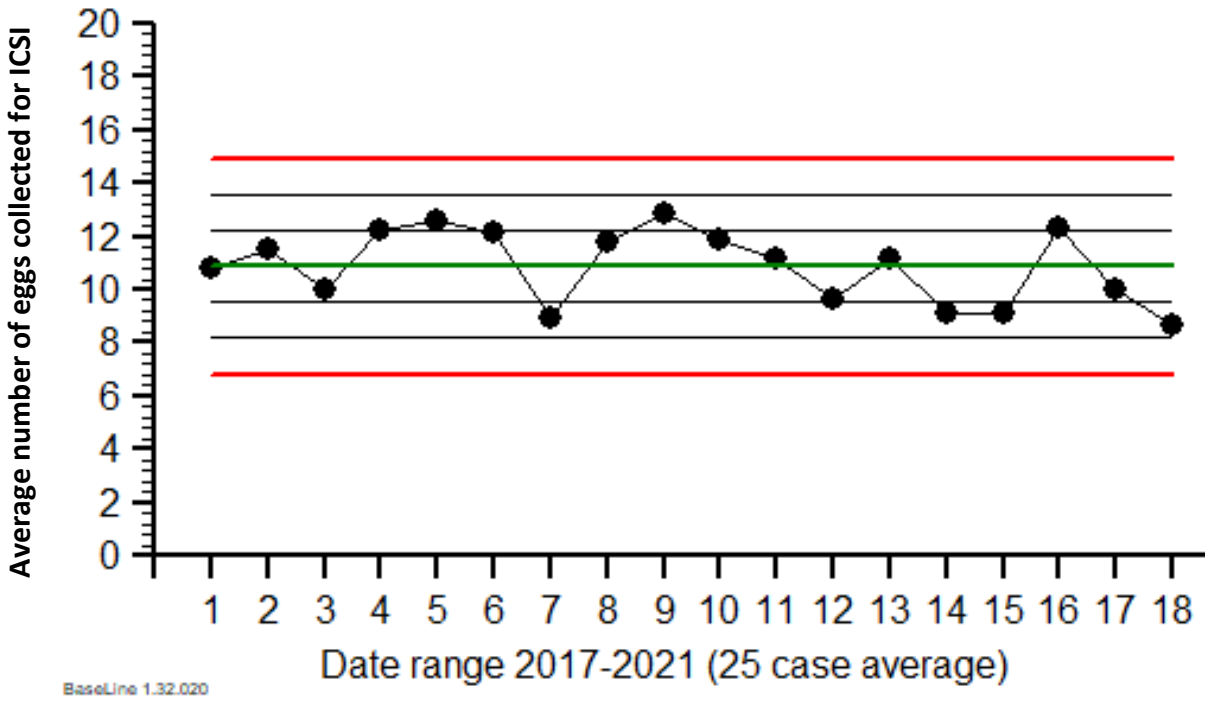


Figure 63 SPC chart of the average number of eggs collected for ICSI over 5 years (25 case average). Mean of 10.87 eggs. Data is stable, no special cause variation observed.

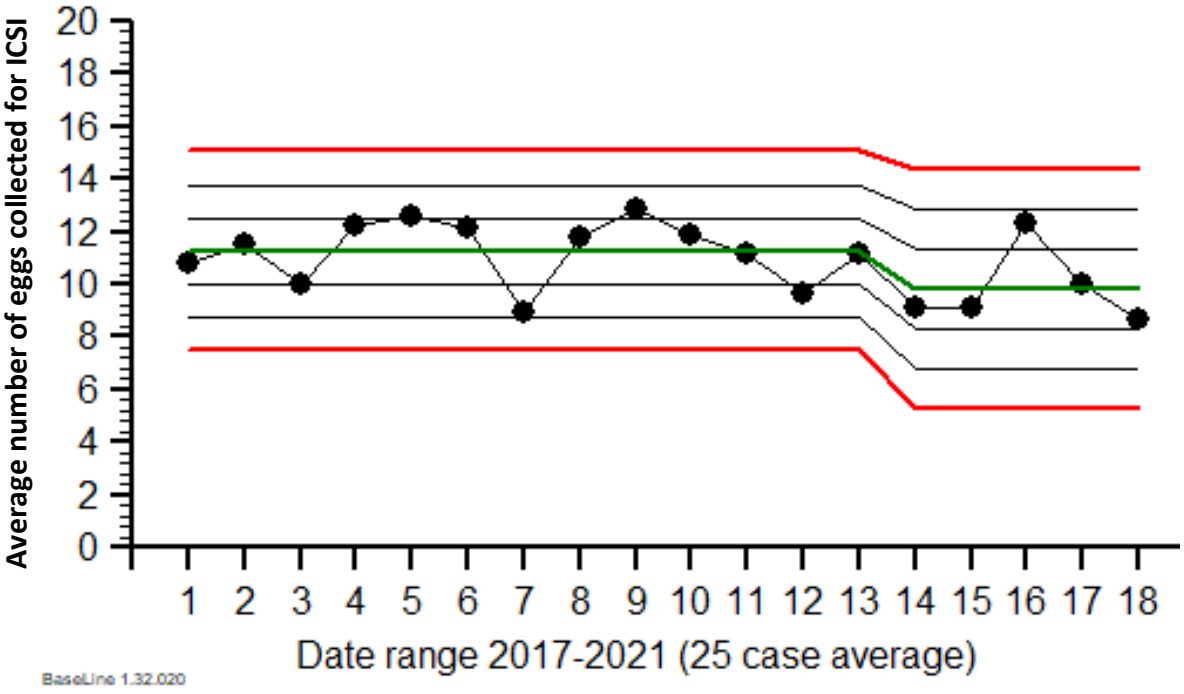


Figure 64 SPC chart of the average number of eggs collected for ICSI over 5 years (25 case average). Data split at the start of the improvement intervention. The mean egg number drops from 11.27 to 9.83 eggs. More data points would be required to establish if reduction in egg numbers is significant.

Egg numbers for ICSI was also monitored as a weekly average to determine any further patterns within the data, and is shown in Figure 65. Weekly data included all ICSI cases regardless of maternal age (only excludes ICSI/IVF splits). The mean egg number for this 4-year period was 10.36. There are two areas of special cause variation within the data. Two triggers of Rule 4 indicate a 10-week period (10 data points one side of the mean) between 24/02/2020 and 14/09/2020 shift in the data of materially significant lower egg numbers than usual during this period. The mean number of eggs collected for ICSI dropped to 6.2. This could partly be due to patient factors of those patients prioritised on the waiting list for when fertility treatment could resume (higher maternal age, lower ovarian reserve, poor prognostic patients). This in turn can offer an explanation for why the first couple of data points after the improvement intervention change had higher ICSI damage rates and did not see an improvement with the implantation rate. Replacing aged equipment (suction pump in February 2020 and Unica hood August 2020) coincides with this period of reduced egg numbers. However, the mean egg number increased to 10.62 between 21/09/2020 and 15/11/2021 (period of stable data) when this equipment was still in use so this transient 10-week reduction is more likely due to patient factors. The second single data point triggering Rule 1 (outside the 3 sigma control limits) at the week of 26/10/2020 can be explained by only one ICSI case that week being a 25 year old with 25 eggs collected.

Splitting the data at the start of the improvement intervention in Figure 66 does not remove the signal of reduced egg numbers over 10 weeks. This reduction does not persist beyond the 21/09/2020 therefore is unlikely to be as a result of the intervention changes made to egg collection but more likely due to patient factors during this period.

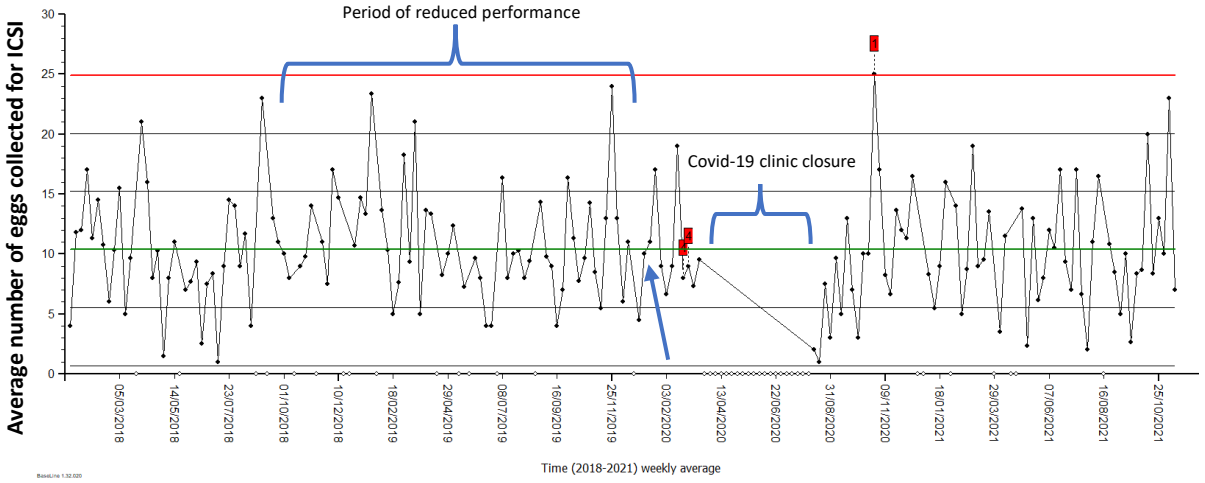


Figure 65 SPC chart of the average number of eggs collected for ICSI as a weekly average over 4 years. Mean of 10.36 eggs. The period of reduced ICSI implantation rate does not show any signals for reduced egg number that could perhaps have affecting the success rates. The start of the intervention for improvement is marked by the blue arrow. The period of clinic closure due to the Covid-19 pandemic is marked end of march 2020 to August 2020. There are two areas of special cause variation; a 10-week period from 24/02/2020 of reduced egg numbers, and a single data point at week 26/10/2020 (outside the 3 sigma control limits) due to a single ICSI case of 25 eggs.

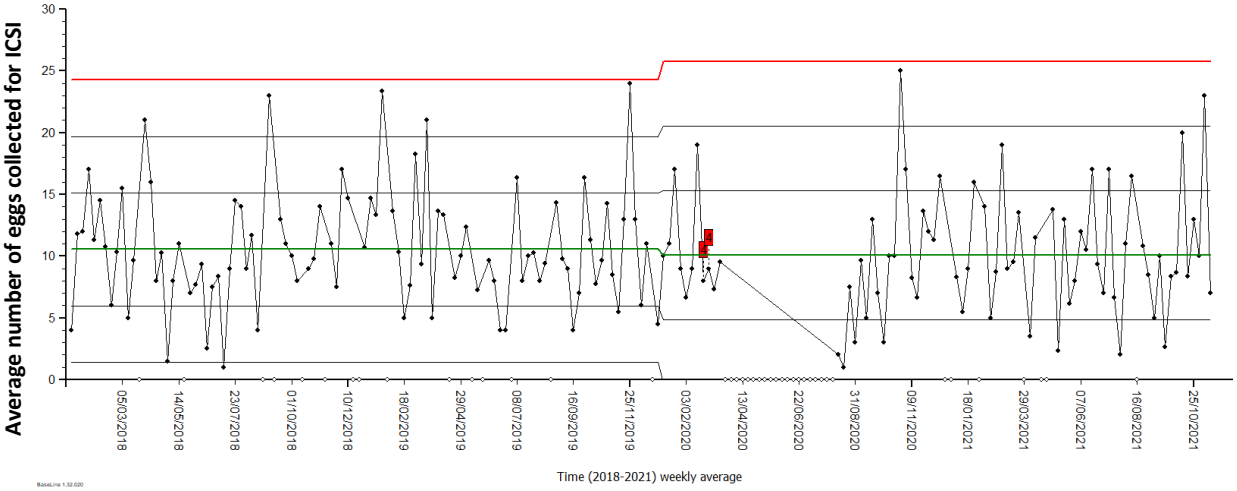


Figure 66 SPC chart of the average number of eggs collected for ICSI as a weekly average over 4 years. The data are split at the start of the intervention January 2020. The mean number of eggs drops slightly from 10.56 to 10.10, the 10-week period of special cause variation persists from the 24/02/2020 this period appears to have reduced egg numbers. It is unlikely as a result of the changes of intervention as it does not persist. New equipment was implemented during February and August 2020.

2.3.14 Average maternal age ICSI cases

Maternal age has a significant impact on the chances of pregnancy. Periods of higher average maternal age would reduce the clinical pregnancy and implantation rate, especially as more than one embryo is commonly transferred in women >37 years old. Maternal age as a 25 consecutive ICSI case average over 5 years (excluding women ≥40 years) and weekly average maternal age of ICSI patients (all ages but excluding ICSI/IVF splits) was monitored using SPC charts. The intervention would have no influence over maternal age but it is likely that maternal age could be influencing all of the SPC charts above. Figure 67 shows maternal age plotted over 5 years with a mean of 33.25, data is stable with no signals which is not unexpected as this data excluded patients ≥40 years to help reduce the variation when looking at outcome data. Figure 68 shows the same data but split at the start of the intervention showing slightly higher maternal age (mean increased from 32.94 to 34.08).

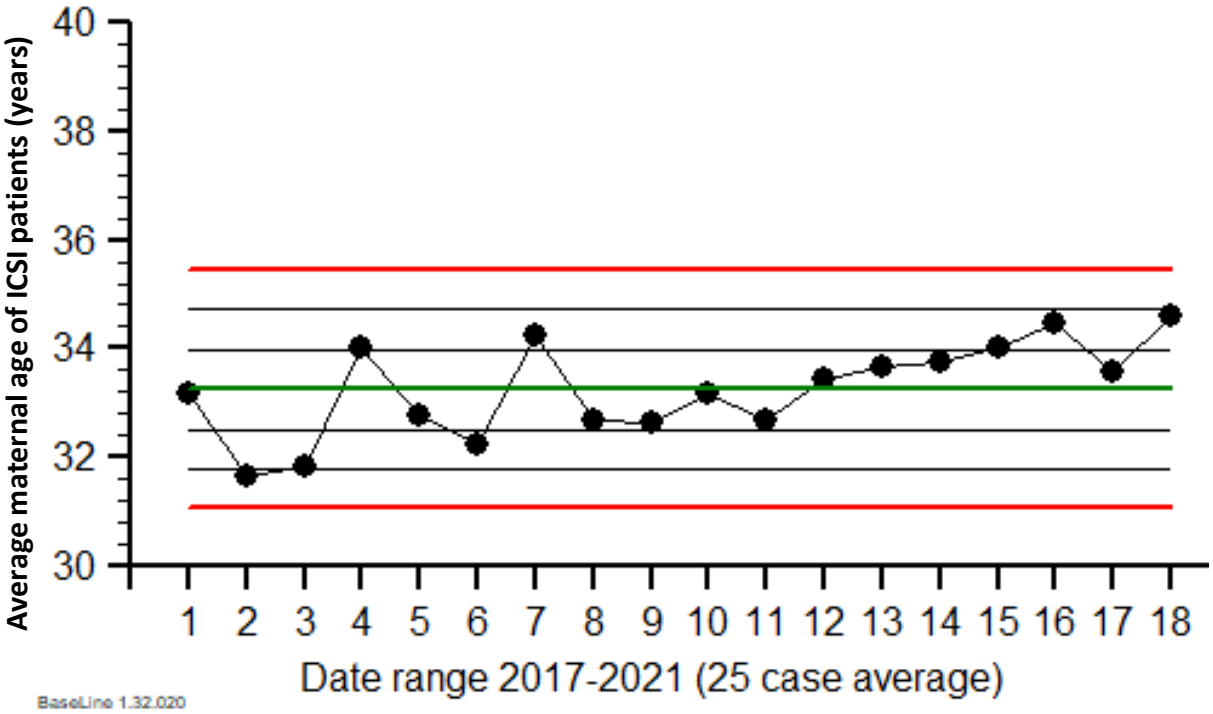


Figure 67 SPC chart of the average maternal age of ICSI patients (25 consecutive case average over 5 years, excluding women ≥40). The data is stable with no special cause variation and mean of 33.35.

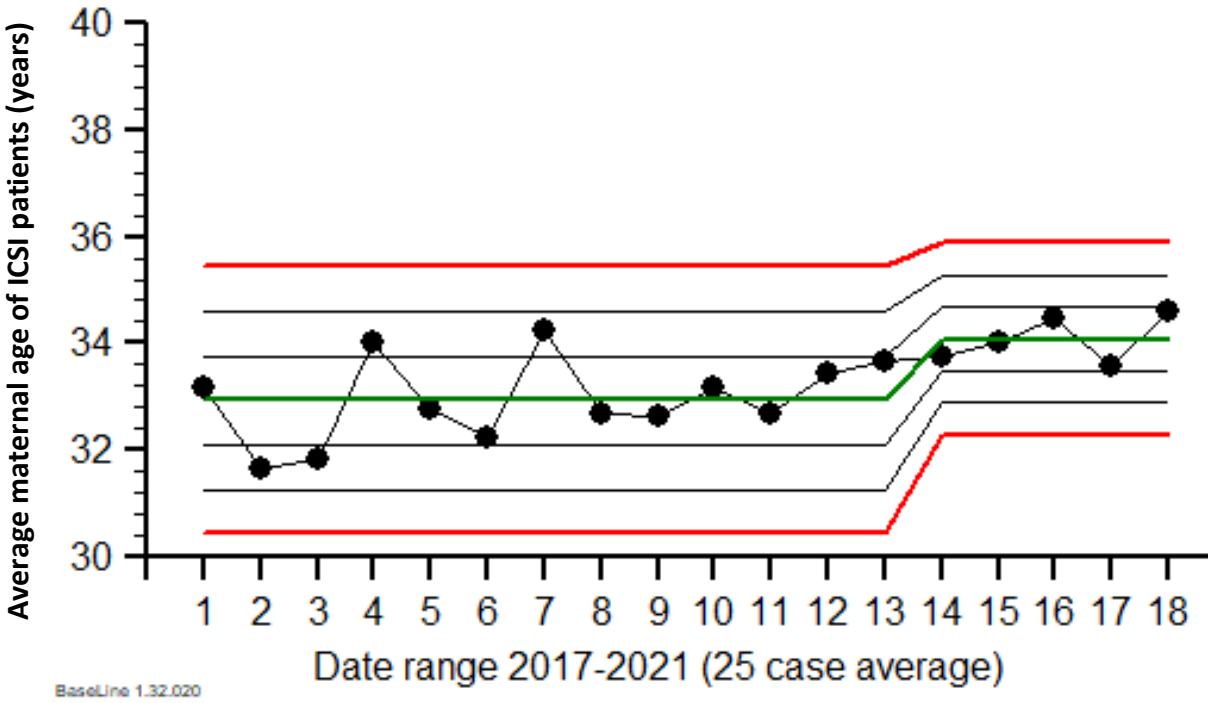


Figure 68 SPC chart of the average maternal age of ICSI patients (25 consecutive case average over 5 years). The data is split at the start of the improvement intervention, both data segments are stable with no special cause variation and the mean maternal age increases slightly from 32.94 to 34.08.

When looking at weekly average maternal age over 4 years (data including all maternal ages) the data is not stable and there is special cause variation (Figure 69). Three signals are identified in the data range with a mean maternal age of 34.4 years for the four-year period. A trigger of Rule 4 at the start of the chart shows a 9-week period (01/01/2018 to 26/02/2018) with materially significant below average maternal age with relatively young patients having ICSI. This period coincides with an excellent implantation rate of 34.21%. There are no signals within the period of poor ICSI implantation (2018/2019) therefore perhaps maternal age was not a factor. A trigger of Rule 3 between 10/08/2020 to 07/09/2020 reveals a 5-week period following treatment recommencing after the pandemic closure with materially significant above average maternal age. Likely due to the clinic's recommencement strategy and prioritising patients on its waiting list patients who were most effected by the closure and delay (age criteria funding expiration, advanced maternal age, reduced ovarian reserve, poor prognosis patients). This period coincides with a period of poor pregnancy rate. Finally, there is a single data point (triggering Rule 1) at 16/10/2020 due to only one ICSI patient this week who was 25 years old. Splitting the data at the start of the intervention does not remove any signals nor

create any more, the data remains unstable, the mean maternal age increases from 33.95 to 34.98 post intervention (Figure 70).

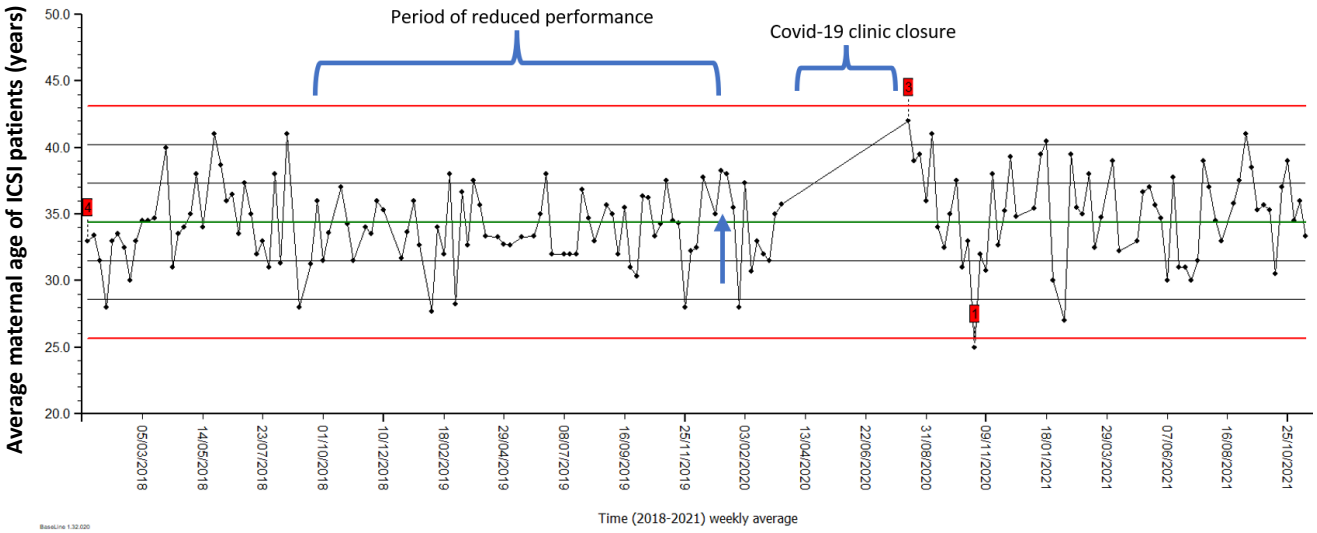


Figure 69 SPC chart of weekly average maternal age of ICSI patients (all ages excluding ICSI/IVF split cases over 4 years). There are three signals in the data, a 9-week period January/February 2018 of materially significant younger than average patients. The period of poor success rates shows no special cause variation therefore maternal age did not play a role. The start of the intervention is marked with a blue arrow (January 2020). The Covid-19 pandemic clinic closure is marked from March 2020-August 2020. There is a 5-week period when treatment first recommences following the closure with materially significant older than average patients having ICSI treatment. This was due to the clinic's recommencement strategy and prioritisation of patients on its waiting list. This very likely had an impact on success rates and provides some explanation for the lower ICSI success rates following recommencement of treatment. A single data point in October 2020 triggering a Rule 1 signal was due to low case numbers (only 1 ICSI

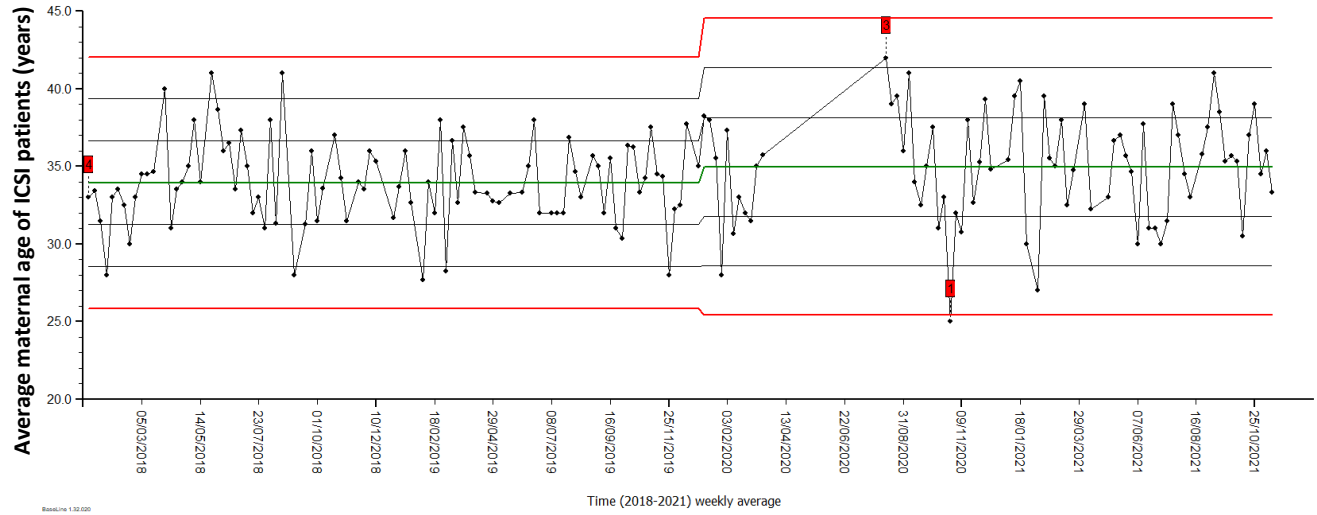


Figure 70 SPC chart of weekly average maternal age of ICSI patients (all ages excluding ICSI/IVF split cases over 4 years). The data is split at the start of the intervention. Both data segments remain unstable (signals remain). The mean maternal age increases slightly post intervention (increase from 33.95 to 34.98).

2.3.15 Summary of balancing measures

The proportion of ICSI blastocyst transfers dramatically increased in 2018/19 due to a change in clinic practice to offer extended culture to all patients. The number of blastocyst transfers drops in 2020/21, despite a more lenient extended culture criteria introduced in 2021, with more patients having cleavage stage transfers after the improvement intervention. However, this does not affect the ICSI implantation rate which remains improved despite fewer blastocyst transfers.

The average number of eggs for ICSI and egg maturity are both reduced post intervention whilst the maternal age is slightly increased. This may explain why a higher proportion of patients had a cleavage stage transfer. The period around the clinic closure due the pandemic had lower eggs numbers and higher maternal age which may have influenced the reduction in ICSI implantation rates following the start of the improvement work. The implantation rate initially improved following the changes but then dipped from February 2020 to October 2020 before improving again.

Balancing measures have provided important information to a complex system helping to inform how the system's performance has changed over time and providing possible explanations. Monitoring the measures as weekly averages displaying variation over time helped to identify and interpret patterns that might otherwise have been missed e.g., egg numbers and maternal age.

2.3.16 Additional background data

IVF case data was also monitored on SPC charts to provide additional information about the system (data not shown). A similar pattern of reduced egg numbers and higher maternal age following clinic recommencement of treatment was apparent. The reduction in ICSI egg numbers and implantation rates in February 2020 following replacement of the egg collection suction pump was not observed with IVF cases. This suggests that the new equipment was not the cause.

Excellent frozen embryo transfer (FET) success rates indicate that the ICSI embryos created during the period of poor fresh ICSI cycle implantation rates were not compromised (22/10/2018 to 30/12/2019). Suggesting the original clinic ICSI processes were producing embryos with good potential for pregnancy but perhaps the fresh endometrium was not optimal for implantation. Success rates are show per date of embryo freezing and thawing (Table 11), all implantation rates are well within benchmark. There were many more ICSI FET cycles using embryos frozen in 2019 because more patients were coming back for a frozen cycle after having an unsuccessful fresh cycle.

Table 11 Frozen embryo transfer success rates

Frozen success rates (vitrified embryos by date of thawing)

Year	Number of FET ICSI cases	Clinical pregnancy rate per Embryo Transfer (%)	Implantation rate (%)
2019	44	45.45	40.00
2020	42	45.24	40.38
2021	50	42.00	34.92

Frozen success rates (vitrified embryos by date of freeze)

Year	Number of FET ICSI cases	Clinical pregnancy rate per Embryo Transfer (%)	Implantation rate (%)
2018	15	53.33	53.33
2019	69	42.03	36.05
2020	27	51.85	45.45
2021	15	42.86	37.50

2.3.17 Impact of Covid-19 pandemic

The pandemic, clinic closure and recommencement strategy had an impact on many of the KPI measures as already mentioned. Additionally, there was a change of practice to a more cautious approach to ovarian stimulation and elective freeze all (FAE) cycles which may have had an impact on the post intervention success rates. This was an important part of the clinic's recommencement strategy to reduce the chance of patients being admitted to hospitals with OHSS and placing an additional strain on the NHS during the pandemic. The number of FAE cycles had increased in 2020/2021 (Table 12), these patients would most likely be the clinic's better prognosis patients (younger women who are good responders to stimulation) who are then removed from the fresh ICSI cycle data by not having an embryo transfer and therefore skewing the data.

Table 12 Number of elective FAE cycles over 4 years at the clinic. FAE cycles due to risk of OHSS only (excludes polyps, endometrial issues, fertility preservation)

year	Number of fresh cycles	Number of FAE	Proportion of FAE cycles
2018	223	14	6.3%
2019	296	10	3.4%
2020	166	15	9.0%
2021	229	23	10.0%

2.3.18 Summary of results

The aim of this QI project was to increase the ICSI implantation rates to benchmark as soon as possible (clinic's benchmark of combined maternal ages (<40 years) of at least >35% clinical pregnancy per embryo transfer and >25% implantation rate for fresh ICSI cycles). ICSI implantation rate and clinical pregnancy rate SPC charts demonstrated a period of reduced performance and an improvement following the intervention. When looking at data as a 25-case average, the 5 data points following the intervention for improvement (Jan 2020-Nov 2021) gave a mean implantation rate of 26.61% and mean clinical pregnancy rate per embryo transfer of 36%, both measures reaching clinic benchmark. The first two data points following the intervention are lower and this is likely due to the impact of the Covid-19 pandemic as revealed when the data was plotted as a weekly average. Without the impact of this on the data a larger improvement may have been seen. More data points should be collected to ascertain whether the improvement is sustained and definitely attributable to the intervention bundle that was introduced. It is not possible to determine which of the changes made had the most effect on the outcomes. The intervention implemented to improve ICSI implantation rates appears to have had no meaningful effect on the ICSI damage rate nor fertilisation rate. Although the mean damage rate appears to have increased slightly and there were periods of weekly averages with higher damage rates possibly due to changes made to the procedure or patient factors. The mean fertilisation rate increased slightly. The period of poor ICSI implantation rates showed reduced fertilisation rates and increased damage. The pattern of ICSI blastocyst embryo utilisation rate did not correlate with ICSI success rates but improved following the intervention, higher proportions of good quality blastocysts were available.

Balancing measures provided important additional information which suggest an explanation for the delayed improvement of ICSI implantation rate following the changes made in January 2020. Due to prioritising patients most impacted by the delay to treatment when the clinic reopened fewer eggs were collected and maternal age appeared higher. The number of mature eggs for ICSI has dropped since the intervention started.

The intervention changes made have been embedded into the clinic's clinical practice.

Results Chapter 3

Supporting fertility patients using quality improvement methods for continuous improvement and possible marginal gains.

The MFI and system behaviour charts were applied to identify areas for improvement within the clinic's patient support. This was a prospective study. Many QI tools were used including SPC charts (BaseLine© SAASoft), PDSA, and cause and effect diagram. Measurements included standard clinic patient feedback data and new measures to the clinic, cumulative pregnancy rates, counselling uptake, and patient discontinuation rates. A number changes were implemented as part of an improvement cycle with the aim to see marginal gains within patient support. The clinic already had good patient feedback. By gaining a better understanding of its patient's emotional support needs the clinic could better support patients to continue treatment and for all patients to receive exceptional care. The data set was interrupted by the Covid-19 pandemic when the clinic was shut from March 2020 until August 2020.

Results chapter 3.1 Background

Infertility and burden of fertility treatment can be incredibly difficult and distressing for patients, leading to an increased risk of developing symptoms of psychological distress. With the average birth rate per embryo transferred at 24% in 2018 (HFEA, 2021) the reality is that many fertility patients will suffer multiple failed treatment cycles and some will never achieve their parenthood dreams. Due to the burden of fertility treatment and chance of failure is it critical that fertility clinics support patients throughout their treatment journey and provide patients with a 'good' experience irrespective of treatment outcome.

In the UK three quarters (75%) of fertility patients say they were satisfied with their fertility treatment overall (HFEA, 2018c), therefore 25% felt treatment was unsatisfactory. In 2017, 54,760 patients underwent 75,425 treatments in the UK, that's approximately 13,500 people per year dissatisfied with how the fertility sector treated them (HFEA, 2019b). As a sector this should be much better and fertility clinics should aim for an

exceptional experience for all patients with the majority being very or extremely satisfied with their care.

The HFEA (Human Fertilisation and Embryology Authority) regulates the fertility sector in the UK and provides a Code of Practice (CoP) for clinics to follow. An update of the CoP in 2018 included new guidance to help strengthen support to patients by staff at all levels, in every clinic. The HFEA aimed to improve patient emotional experience and raise standards of patient care by proposing that all clinics set out a policy outlining how patients, donors and their partners will receive appropriate psychosocial support from all staff before, during and after treatment. Many clinics already do an excellent job in supporting their patients, but there is always room for improvement. The HFEA proposed a patient emotional support pathway to provide examples of good practice in patient emotional support which could be explored, tailored, and refined by individual clinic teams.

In 2018 a fertility clinic with consistently good feedback from patients assessed whether more could be done to improve patient support further. As a small clinic, patients tend to see the same staff throughout treatment and can build a good rapport with staff, the clinic prides itself on its patient centered care and this is reflected in its patient feedback. The vision at Salisbury NHS Foundation Trust is to deliver safe and compassionate healthcare to our patients. It is our aim to provide “An Outstanding Experience for Every Patient” across the organisation. An outstanding patient experience means exceeding patient expectations. Patient satisfaction questionnaire feedback (data from 51 patients from April - Nov 2018) highlighted three areas which do not receive 80% or higher within the ‘excellent’ field. These are support group/literature provided, awareness of independent counselling, and support offered with regards to treatment outcome. Historically, patients have commented on these questionnaire forms that a call within the two-week wait (2WW) would be helpful, however the team has always considered that for other patients this would not be appropriate and so did not take this further. In 2018 the clinic saw three cycles cancelled due to severe anxiety on the day of surgery (egg collection and surgical sperm retrieval) or personal/relational issues (FET cycle). These were unusual occurrences but perhaps the clinic could do more to identify those patients

who might need or would benefit from additional psychological support before treatment.

QI PDSA cycles would be used to improve the support of patients coming through the centre following the MFI. The main aim was to improve the standard patient feedback to >80% within the 'excellent' field (highest score of '5') for areas covering counselling, coordination, and support by 2021. The centre wishes to also have no further cases where patients ceased treatment on the day of treatment, due to stress or anxiety related reasons. A QoL screening process for patients would be considered alongside implementation of an innovative self-administered psychological intervention.

Infertility can lead to stress, anxiety, depression, and the breakdown of relationships (Fertility Fairness, 2016). When fertility treatment is provided it is emotionally and physically burdensome (Boivin & Takefman, 1995). Unsuccessful treatment, egg retrieval, the 14 days of waiting for the result of the treatment and having a pregnancy test are the most stressful aspects of fertility treatment (Boivin & Takefman, 1995). Evidence suggests fertility patients have an increased risk of developing symptoms of psychological distress, depression and anxiety despite them having no previous record of mental health issues in their medical history (Klemetti et al., 2010). The Impact of Fertility Problems (2016) survey highlighted that 90% of respondents reported feeling depressed; 42% suicidal; nearly 50% reported on average feeling out of control, frustrated, and worried most of the time; with 70% reporting some detrimental effect on their relationship with their partner (Payne & van den Akker, 2016). The fertility clinics' obligations for and the importance of offering counselling and emotional support to fertility patients has never been more crucial and has been highlighted in the recent HFEA CoP (9th eds HFEA, 2019a). The Covid-19 pandemic and fertility clinic closures resulting in delay of fertility treatment has further compounded psychological distress for infertility patients (Lawson et al., 2021; Boivin et al., 2020), a focus on improving patient support has never been more pertinent. Birth rates are important, but patients' emotional needs should not be overlooked by fertility clinics.

There is good evidence to show a positive association between the experience of patients and improved outcomes and patient safety (HFEA, 2018c), therefore improving the experience of the patient should improve the chances of a successful outcome. The main

drivers of patient satisfaction, according to the 2018 HFEA National Patient Survey, are the interest shown in you as a person, the quality of counselling (for those that receive it), and the coordination and administration of treatment. Clinic staff have a huge impact on patients receiving a positive experience (HFEA, 2018c). Perhaps more could be done to enhance patient satisfaction which in turn may indirectly improve treatment outcomes.

The negative feelings patients experience through infertility and its treatment impact on the patient's overall life satisfaction and well-being, chance of success, and ability to continue with treatment (Boivin et al., 2011). Therefore, there is a need for QoL to be addressed by clinics. Validated QoL questionnaires specifically for fertility patients are available which may enable clinics to measure and take into account the QoL of the patients coming through their doors. The questionnaires serve as a way to identify and address risk factors for poor adjustment to infertility or its treatment, and addressing patients QoL could lead to improved patient outcomes and experience. Available validated questionnaires include; QPP-IVF (Holter et al., 2014b) quality of care from patient's perspective specific to IVF treatments and validated in Sweden, FertiQol (Boivin et al., 2011) internationally validated instrument to measure QoL in individuals experiencing fertility problems, or HADS (hospital anxiety and depression scale) (Zigmond & Snaith, 1983). However, assessment of QoL of fertility patients as part of clinical practice has yet to be adopted in the UK.

Fertility success rates can be influenced by patient disengagement with treatment. It has been showed that 22% of patients discontinue their treatment primarily for psychological reasons, despite a good prognosis and the ability to cover the treatment's cost (Gameiro et al., 2013b). The experience of a failed treatment cycle can discourage patients re-engagement with treatment (Gameiro et al., 2012). This discontinuation of fertility treatment, before the most clinically effective number of cycles have been completed (3 full cycles) (NICE, 2013), is associated with a 15% lower pregnancy rate (Gameiro et al., 2013b). Therefore, if patients were supported to undertake the optimum number of treatment cycles, through reducing the psychological burden of treatment, then cumulative clinical pregnancy and live birth rates would improve.

It is not clear whether a better uptake of counselling services would encourage greater treatment adherence. At licensed UK fertility clinics counselling is offered to all patients

before, during or after fertility treatment, both in a written information pack, and during consultations. However, studies have shown that just 67% of couples actually recall being offered counselling and only 20% take up the offer and attend a counselling appointment (Rajkhowa et al., 2006). This is similar to the experience of previous researchers (Boivin, 1997; Hammerberg et al., 2001) and indicates that despite patients expressing an interest in taking up counselling, the actual take-up rate is low. More could be done to try to encourage patients to utilise this resource offered by clinics. When increasing the take-up rate, it is also important to ensure the quality of counselling that is offered, which is a main driver of patient satisfaction of those who had an appointment (HFEA 2018).

It has been suggested that there could be a link between increased psychological distress and reduced pregnancy rates (Boivin, 2003; Boivin & Schmidt, 2005). Several studies have investigated the efficacy of psychological interventions on psychological distress and fertility treatment outcomes, but the results are inconclusive (Frederiksen et al., 2015). A more recent metanalysis by Katyal et al. (2021) based on 15 studies found a positive association (RR = 1.12, CI= (1.01;1.24), p = 0.033) between psychosocial intervention to improve mental health and pregnancy rate, which supports the general hypothesis that mental health affects the ability to achieve pregnancy, at least for women and couples in ART treatment.

One intervention that has been shown to reduce stress and increase pregnancy rates is the Mind/Body Programme for Infertility (Domar et al., 2000; 2011). This 10-week group programme involves cognitive behaviour therapy, relaxation training, lifestyle changes, journaling, self-awareness, and social support components. A recent randomised controlled prospective pilot study included an online version of the mind/body programme (Clifton et al., 2020) something more cost effective and easily integrated within clinical practice. The internet-based intervention group showed significant reduction in anxiety and depression, and a higher pregnancy rate however a larger sample size and more stringent methodological considerations are needed to replicate and confirm the findings. Internet-based mind/body interventions when available could change the way fertility treatment is provided. Providing an easy screening and monitoring tool to identify distressed patients and then offering a convenient, effective, and affordable intervention to support them.

Simpler, more cost effective, self-administered psychological interventions have been developed that can easily be integrated into the clinic setting as they require little staff time. These take-home tools can be used by patients as and when they are needed to manage the demands of treatment thereby potentially improving their overall QoL during treatment (Domar et al., 2015). The period of greatest distress for many IVF patients is the wait between embryo transfer and the pregnancy test (Boivin & Lancastle, 2010). If the cycle is not successful this distress not only decreases the QoL for patients but might also lead patients to decide to drop out of treatment. The cognitive coping and relaxation intervention (CCRI) has been shown to improve QoL and reduce anxiety, whilst it appears to reduce treatment discontinuation rates by 67%, this was not significant and it did not increase pregnancy rates (Domar et al., 2015). The Positive Reappraisal Coping Intervention (PRCI) encourages a form of coping that helps patients take account of positive aspects of unpredictable and uncontrollable stressful situations, like medical waiting periods, and was designed to help patients cope during the 2WW. It has been shown to make the stress of the waiting period seem more tolerable rather than taking away the negative emotions that waiting produces and had no effect on treatment outcome. However, patients deemed the PRCI to be acceptable, practical and they perceived a psychological benefit to its use (Ockhuijsen et al., 2014) and it can be easily offered within a clinical setting.

Understanding the impact of psychological distress and treatment burden on our patients, the team sought to find a sustainable low-cost intervention that was tailored to the areas of improvement identified at the clinic.

The MDT already provide excellent support to its patients as evidenced in our patient feedback. However continuous improvement could still be made in different areas to get a better understanding of our patients' QoL and how the clinic could better support them, possibly leading to an accumulation of marginal gains. Some preliminary data gathering and monitoring was used to inform the QI PDSA cycles. Initial data collections focused on the clinic's standard patient satisfaction questionnaire feedback results, an offer of a call during the 2WW, and the uptake of counselling. Factors for consideration which might influence patient support are shown in the fishbone diagram (Figure 71).

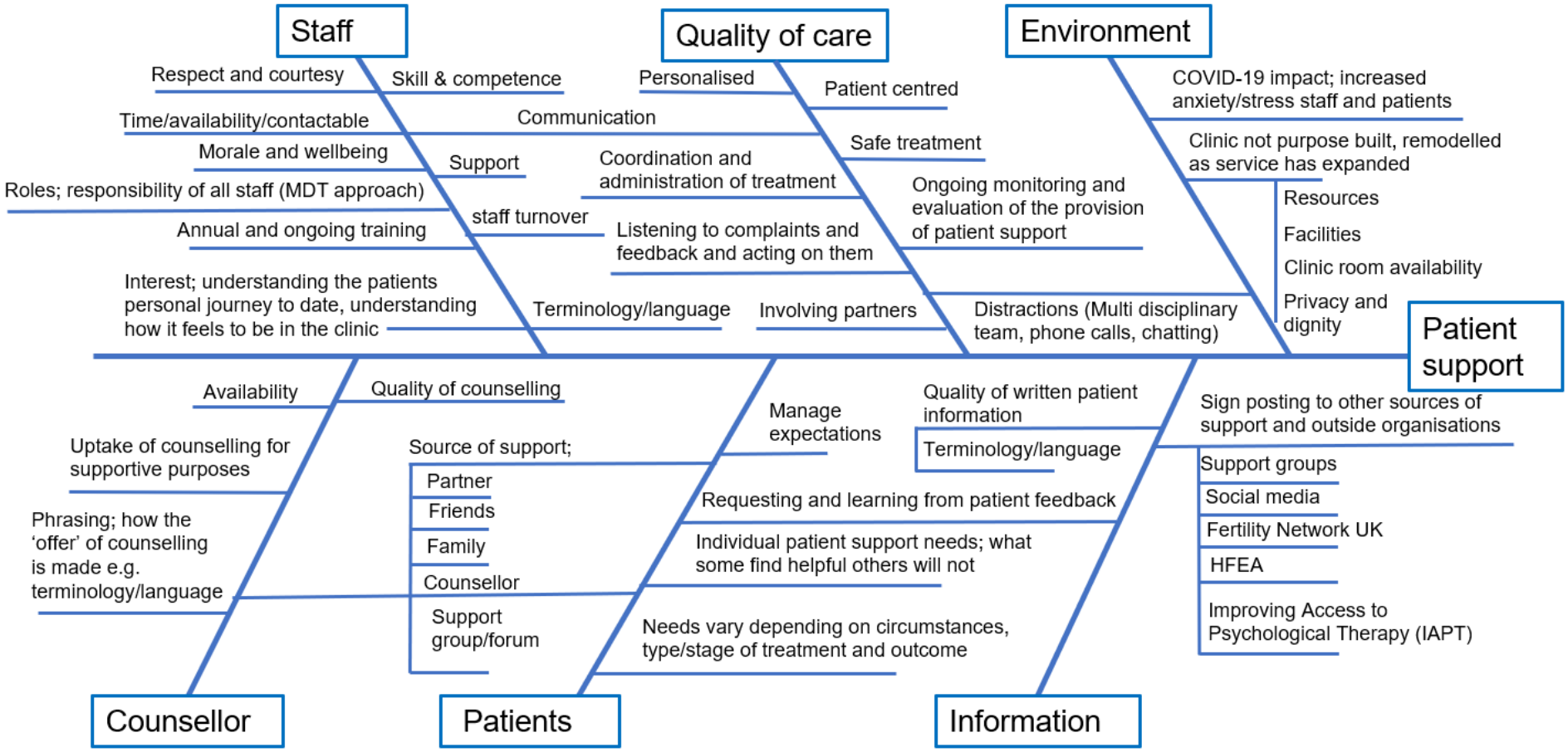


Figure 71 Fishbone diagram of factors that influence patient support

The patient satisfaction questionnaire (Appendix 16) covers a range of questions related to the entire treatment pathway from initial consultations to embryo transfer, patients and partners can separately indicate their response using a 1-5 Likert scale (1= unsatisfactory, 2= Poor, 3= Average, 4= Good and 5= excellent). Questionnaires are given at embryo transfer and brought back to the clinic when the patient attends for pregnancy blood test. A review of patient satisfaction feedback data from 51 patients from April-November 2018 highlighted three areas which do not receive 80% or higher within the 'excellent' field. These were support group/literature provided, awareness of independent counselling, and support offered with regards to treatment outcome.

Historically, a minority of patients have commented on the patient satisfaction questionnaires that a call within the 2WW would be helpful. The team has always considered that a blanket policy to call all patients during the wait for pregnancy test would not be appropriate for everyone. It was also assumed that to offer a call would increase the nurse's workload considerably. The current process assumes that patients would and do call if they have concerns during the waiting period and these are often due to bleeding. The clinic undertook a period of monitoring to establish how many calls were received from patients within their 2WW. During a 6-month period from 21st of January 2019 to 26th July 2019 there were 215 embryo transfers and 33 calls to the clinic, 25 of which were regarding bleeding/pain (79%), 6 regarding stress or anxiety/worry about treatment outcome (18%), and 1 regarding questions about the luteal support (3%). Assuming the same patient did not call multiple times roughly 15% (33/215) of patients called the main office during the 2WW to speak to a nurse about their concerns. It is possible that more patients called in but a record was not made as it relied on the nurses documenting phone calls during this time frame. The laboratory staff asked 6 patients on day-6 whether they would like a call in the waiting period to gain a "snapshot" of patient take-up rate. Of these patients 3 declined saying they prefer to call the clinic if needed, 3 accepted the offer. Those wanting a call had a medical background, one could not be contacted despite many attempts and the two that were spoken to fed back that that they found contact from the clinic helpful for emotional support. Additional feedback would be sought during the improvement project and a self-administered psychological intervention would also be introduced.

The clinic does not currently monitor patient's uptake of counselling, cumulative pregnancy rates or patient discontinuation rates. This additional information would help the clinic to gain a better understanding of the burden of treatment patients experience, whether improvement is needed, and evaluate what could be done differently to better support patients. The improvement work would include evaluating the normal rates for the current system and attempt to see the impact of improvement interventions on these measures. The clinic would wish to decrease its patient discontinuation rate and time to pregnancy whilst increasing the cumulative pregnancy rate and uptake of counselling.

In 2018 the clinic saw three planned cycles cancelled due to severe anxiety on the day of surgery (egg collection and surgical sperm retrieval) or personal/relational issues (FET cycle). These were unusual occurrences but perhaps the clinic could do more to identify those patients who might need or would benefit from additional psychological support before treatment. The team would hope to have no adverse events such as these following the improvement work and aimed to implement a screening process to help identify patients who might require additional support or signposting prior to or during treatment planning.

Supporting patients is the responsibility of all clinic staff however the nursing team and counsellor have a larger role and impact, therefore their input into any changes for improvement was critical. The project team consisted of the author as a representative of the laboratory staff and main project driver, with the perspectives of the clinical team, administrative team, and counsellor consulted as the PDSA cycles evolved. Any changes made would have a direct impact on the administrative team, clinical team, and counsellor so it was important to get them involved and engaged with the project.

Prior to any introduction of patient screening or psychological interventions it was important to address any staff concerns and skills. Clinic staff have a huge impact on patients receiving a positive experience (HFEA, 2018c), staff morale, wellbeing, skills and competence will have a big effect on how well patients feel emotionally supported through treatment. This is supported by Gameiro et al, (2013a) who suggest that avoiding negative patient–staff interactions through training staff in communication/interaction skills helps deliver optimal fertility treatment by reducing patient vulnerability and psychological distress. The team felt it was important to offer staff support and training

therefore a fertility clinic tailored psychological assessment skills training session would be delivered by the clinic's independent counsellor based on the Clinical Psychology departments training offered by the Trust. Update sessions would follow with staff aware that they can approach the counsellor with any concerns they might have.

The team wished to implement a patient QoL questionnaire to help identity patients requiring additional support at the start and post treatment. The Hospital Anxiety and Depression scale was chosen after seeking advice from the Trust's Clinical Psychology department, clinic counsellor, and clinic staff because it was perceived to be more acceptable to patients (less detailed questions asked compared to the other two options) and the Trust was already using HADs clinically in other departments e.g., Clinical Psychology, Maternity departments. Assumed benefits of implementing the HADs include; inexpensive intervention, early identification of patients not coping with the negative feelings and burden of treatment, and action by clinic to help those patients requiring additional support, thereby may increase emotional QoL of patients, which may help patients to stay in treatment. Also, the forms themselves explicitly bring to the forefront the psychological distress of infertility and enable conversations to occur that otherwise might not. This emphasises the importance of counselling and sources of support at the very start of treatment to both patients and staff. However, there is a chance that patients may not engage or complete the questionnaire, and it may increase the workload of the clinic counsellor. To safely implement the HADs forms within clinical practice a procedure, flow chart, patient information and consent forms were created. This would ensure all staff knew what was expected, there was patient choice to complete the forms, returned forms were scored in a timely manner and returned to the medical notes, and that any borderline or clinical scores were actioned. The increased workload for staff would be monitored. The independent clinic counsellor and the Trust's Clinical Psychology department were consulted to ensure safe delivery of the patient support QI aspects of the project.

Once the HAD form process was established within the clinic successfully the team planned to next introduce the PRCI to patients at embryo transfer. This simpler, cost effective, self-administered psychological intervention could help patients to better cope during the 2WW for treatment outcome. Patients often ask at embryo transfer if there is

anything they can do during the 2WW to improve their chance of success and/or manage the waiting period. It was perceived by the team that being able to offer something evidenced based that could help would be beneficial to some patients. The PRCI would be tested for a short period and patients would be given a separate feedback form to provide specific feedback on the usefulness of the PRCI. Once again, the clinical team would be consulted on how and when this could be offered to patients because the clinical team would be responsible for briefly explaining to patients what the PRCI is and how it could be helpful. This would need to be managed carefully as clinical fellows briefly joining the team may not be aware. Patient feedback would determine whether the PRCI is valued by patients and whether the clinic will continue to offer it.

The introduction of the offer of a call within the 2WW would also be trialled for a short period with additional patient feedback being requested and reviewed to determine whether this is valued by our patients and worthwhile change of process.

Staff and patient feedback and complaints would be monitored throughout the project and acted upon.

The series of interventions that the team planned to implement to improve the quality of patient support delivered by the clinic are shown in the driver diagram (Figure 72).

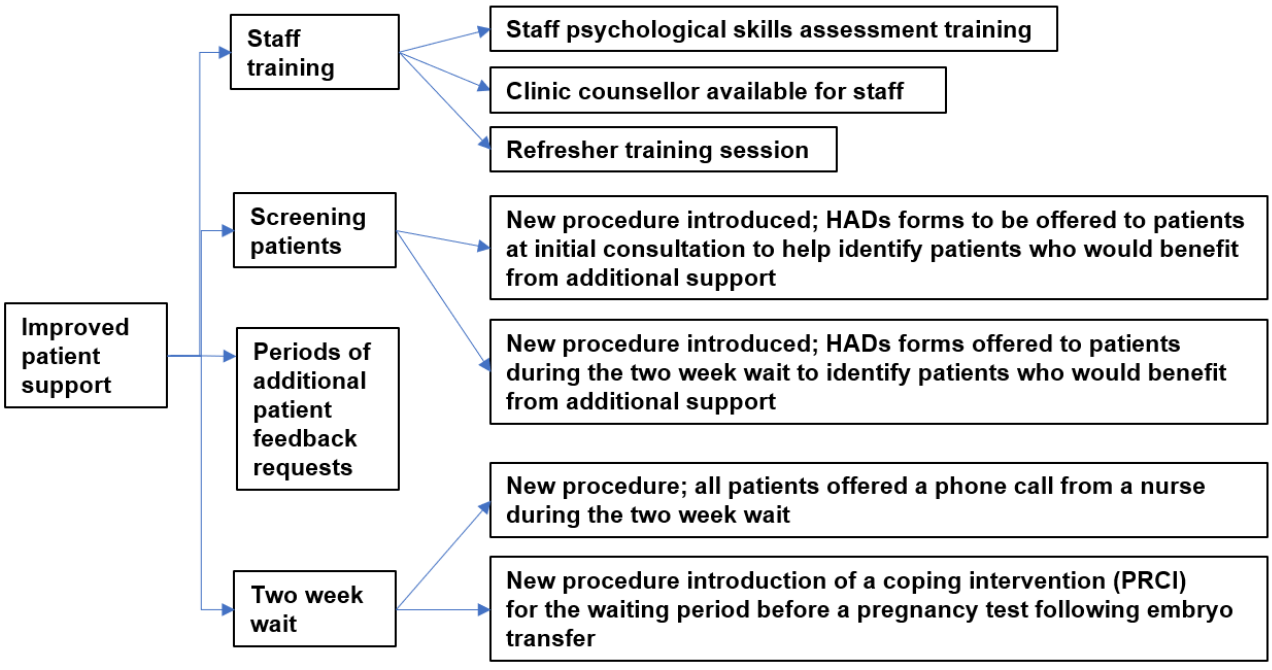


Figure 72 Driver diagram for patient support

The changes made would be sustained by having a lead person responsible for the project, delivering regular meetings and updates of the team with progress and data, and regularly asking for and listening to any feedback from the team members effected e.g., nurses, administration team and counsellor.

The teams SMART aim was to improve patient support so that standard patient feedback reached >80% within the 'excellent' field by the end of the project.

Results chapter 3.2 Method

During the project five PDSA test cycles were undertaken. The main measures include; continuous monitoring of standard patient feedback questionnaire responses throughout the QI project, continuous monitoring of HADs scores once routinely offered, patient discontinuation rates, cumulative clinical pregnancy rate, time to pregnancy rates, additional patient feedback questionaries, counsellor availability, uptake of supportive counselling, staff/patient complaints, and adverse events.

A list of measures selected for the improvement project are listed in Table 13.

PDSA 1: Psychological skills training for all staff within the MDT. Patient support is the responsibility of the entire team not just the clinic counsellor. The team are already skilled at supporting patients and do so well, however with the intended introduction of the HADs intervention specific psychological skills training was offered to reduce any anxiety or concerns that staff might have around the project. Junior members of the team could also benefit from the training session. The training session was offered in April 2020, staff completed a pre and post training feedback form to establish the effectiveness of the training and to gauge staff confidence regarding patient psychological support.

PDSA 2: Introduction of the HADs questionnaire to all new patients at the start of treatment and all patients after embryo transfer. Commenced 5th October 2020. The QI team would monitor the increased workload generated from this for the counsellor and the number of patients that required action from the clinical team e.g., signposting or counselling. This would be reported at regular intervals with the team. The only patient

feedback regarding the HAD form during the project was a patient concerned that treatment might be denied due to a raised score and advice to book an appointment with the counsellor. This was acted on and the letter template was changed to make it clear that this was not the case. This intervention was assumed to help the clinic better identify

Table 13 List of improvement project measures, their definitions and benchmarks.

Measure		Definition	Benchmark %
Outcome	Patient satisfaction questionnaires	Score of 5 on patient satisfaction feedback forms for the awareness of the offer of counselling, support group/literature provided, and support offered with regards to treatment outcome, plus three other areas regarding support	>80% scoring 5 as a monthly average
Outcome	HAD scores for patient anxiety and depression at initial consultation and following embryo transfer	Scores from 0-21 Anxiety Scores from 0-21 Depression	0-7 normal range 8-10 borderline range 11-21 clinical range
Outcome	Additional patient feedback questionnaires	Additional 'snapshot' surveys of patients during improvement project. Pre and post intervention.	n/a
Outcome	Adverse events	Number of planned cycles that are cancelled on the day of treatment due to stress/anxiety/burden of treatment	0
Outcome	Time to pregnancy within 6-months of primary outcome of 1st egg collection	All women ≤37 1st cycle cumulative pregnancy rate 6-month follow up. Pre and post intervention periods.	?
Process	Treatment discontinuation within 6-months of primary outcome of egg collection	Number of patients dropped out of treatment following an unsuccessful attempt. Pre and post intervention. Exclusion criteria women ≥38 years old, 0 or 1 egg collected, no embryo transfer, patients who achieved a clinical pregnancy following embryo transfer.	<20%
Process	Uptake of supportive counselling	Number of patients that attended a supportive counselling session/ number of egg collections and frozen transfers in a specified period pre and post intervention.	>20%
Balancing	Counsellor availability	Number of available counselling appointment slots booked per month over time.	n/a
Balancing	Staff feedback and patient complaints	Staff asked for feedback throughout the project and complaints monitored and action.	n/a

those patients that needed more support and to ensure they were signposted to the counsellor or support sources outside the clinic. Perhaps preventing any adverse events of patient planned for treatment abandoning due to anxiety, emotional or relational issues. Patients would hopefully feel better supported leading to marginal improvements of the clinic's standard feedback results and it was also assumed that more patients might stay in treatment following an unsuccessful cycle possibly resulting in an improved time to pregnancy or cumulative pregnancy rates. The clinic's discontinuation rates and time to pregnancy would be monitored pre and post intervention to assess where there was an improvement. HAD scores would also be monitored continuously over the project.

PDSA 3: An additional patient satisfaction questionnaire based on support during and following treatment was given out over 4 weeks to establish a baseline of how the clinic was doing after implementing the HADs. Patients are already asked for feedback on the clinic's standard form, a lot of paper forms are given, the team did not wish to overwhelm patients with paperwork and feedback requests for an extended period of time so a 4-week snapshot was used. This included 27 patients from the 9th of March 2021 to the 14th of April 2021. This additional patient feedback questionnaire was created by the QI lead with input from the lead consultant and counsellor. The questions were based on the HFEA patient survey (2018). Please refer to Appendix 5. Outcomes from this feedback suggested the clinic could do more for patients during the 2WW and the majority of patients wished to have a call in the 2WW.

PDSA 4: In response to patient feedback an offer of a call from a nurse during the 2WW was introduced on the 21st of April 2021. The nursing team was consulted to determine the best process ensuring all patients are offered, good records are kept of those wanting a call, and calls are made. Poor record keeping could result in missed calls and not meeting patients' expectations leading to poor patient satisfaction. The team had to ensure we delivered what was offered as not doing what we say we would do is worse than not offering any calls at all. A record sheet was created which would be passed to the nursing team. At first the lab team completed the form because patients received a call from the lab on day-6 of a fresh cycle to inform them about the fate of remaining embryos and it was helpful to share the workload across the team. However as not all patients having a fresh embryo transfer had embryos for extended culture to day-6 and

some embryo transfer lists having frozen cycles also, it became apparent that some patients were being missed off the list and others were being asked twice if they would like a call. To remove these errors and issues with handover between staff the nursing team then took full responsibility for completing the forms at embryo transfer as one nurse looks after each transfer list. Additional feedback questionnaires were once again given out at embryo transfer for a 4-week period while phone calls were being offered (10/05/2021- 02/06/2021) to determine whether patient satisfaction improved. This improvement work increased the workload of the nurses as expected but they were engaged with the project and happy to continue because they could see an improvement in patient feedback. The process was embedded into practice and was sustained throughout the project.

PDSA 5: On the 30th of June 2021 the clinic implemented use of the self-administered psychological intervention PRCI to all patients after both fresh and frozen embryo transfer. Patients would be given a separate envelope labelled with PRCI containing the A4 leaflet from Cardiff University so the rationale is clear (Lancastle, 2006; Lancastle and Boivin, 2008) and a small laminated card containing the 10 statements for patients to use however they find helpful. Patients might take a picture of it and keep on their phone, or stick to the fridge or bulletin board or place inside a wallet. The most important thing was to be certain that patients read the explanatory leaflet and were signposted to it. Prior to offering to patients the whole fertility team was advised of the start date, and were sent a copy of what patients would be given, alongside published evidence which supports its use and rationale. A copy was laminated and placed on the nurses' station for reference. Staff were given an opportunity to ask questions and make suggestions for improvements to the process of implementing the intervention. The project was received well by the team and gained some interest, especially from clinical fellows rotating through the fertility clinic. The QI lead would ensure sufficient envelops were ready and given to the clinical team ahead of all embryo transfer lists. The clinical team, consultant or nurse performing the embryo transfer, would be responsible for briefly explaining what was in the envelope and that it could help during the waiting period, a standard phrase was suggested. An additional patient feedback form was created, based on published papers looking at the effectiveness of the PRCI and reviewed by the clinic counsellor and consultant in charge prior to use, to capture patient feedback on the usefulness of the

intervention. The QI lead would monitor the number of patients offered the PRCI and collect the feedback questionnaires returned to the clinic.

A study flow table (Table 14) displays the 5 phase changes that occurred over time by working group involvement. The project was affected by the Covid-19 pandemic as the clinic was forced to close from mid-March 2020 until recommencing frozen treatment cycles in June 2020 and fresh treatment cycle in August 2020. The pandemic would likely have its own impact on patient QoL and ability to cope with the burden of fertility treatment when offered. Patient anxiety and stress due to delay of fertility treatment caused by clinic closures has been evidenced to further compound psychological distress for infertility patients (Lawson et al., 2021; Boivin et al., 2020). To recommence treatment safely following the pandemic many changes were made to procedures to reduce footfall in the clinic. Consent and counselling appointments were delivered by video conferencing or phone calls, and not face to face. Some patients preferred this for convenience but staff and other patients felt it was harder to build a rapport. This would likely have an impact on the patient satisfaction feedback.

Table 14 Study flow table

	Summary of working group improvement efforts by phase of implementation					
	Interventions by working groups					
Phase / PDSA	**Date completed**	**Counsellor**	**Laboratory team**	**Administrative team**	**Clinical team**	**QI lead**
1	April 2020	Deliver a fertility clinic tailored psychological assessment skills training session	To attend training and update when required with counsellor	To attend training and update when required with counsellor	To attend training and update when required with counsellor	To organise training session, attend and gather feedback
2	5th October 2020	• Available for staff and patients • Consulted regarding forms and process	To be aware of HADs processes	To be aware of HADs processes, send HADs forms to new patients, ensure HADs forms present in the notes for post embryo transfer, place returned HADs forms to tray in office	To be aware of new HADs process and signpost patients with borderline/clinical scores	• Regularly review and inform team about project • Score all HADs forms and ensure borderline/clinical scores are actioned • Monitor form return rate, additional workload created, and patient/staff feedback
3	March/ April 2021	• To be aware of change implemented • To review and provide feedback on new patient feedback questionnaire	• To be aware of change • To offer calls from the nursing team and record	To be aware of change implemented	• To be aware of change • To offer calls from the nursing team and record • Call patients during the two-week wait • Provide feedback	• Regularly review and inform team about project • Ask for staff feedback • Collect and monitor • Create additional feedback questionnaire with team feedback, give to patients, collect data and feedback to team
4	21st April 2021	To be aware of change implemented	To be aware of change	To be aware of change implemented	• To offer calls from the nursing team and record • Call patients during the two-week wait • Provide feedback	• Regularly review and inform team about project • Ask for staff feedback • Collect and monitor record sheets after calls made • Create additional feedback questionnaire with team feedback, give to patients, collect data and feedback to team
5	30th June 2021	• To be aware of change • To review and provide feedback on new patient feedback questionnaire	To be aware of change	To be aware of change implemented	• To be aware of change • To have some understanding of the PRCI • To give PRCI to patients and briefly inform them what it is	• Regularly review and inform team about project • Ask for staff feedback • Keep a record of who was offered the PRCI • Create additional feedback questionnaire with team feedback, give to patients, collect data and feedback to team
Covid-19 pandemic: nationwide fertility sector closure, fresh cycles stopped from March 27th until 14th August 2020						

Results chapter 3.3 Results

3.3.1 Standard patient feedback

Patient satisfaction scores for 6 areas were monitored and plotted over time using SPC charts. The standard questionnaires ask patients to score the quality of services provided by the clinic using a Likert scale from 1-5 (1= Unsatisfactory, 2= Poor, 3= Average, 4= Good and 5= Excellent). Areas chosen as measures for the improvement work included;

A. Support groups and literature provided at initial consultation
B. The awareness of independent counselling at initial consultation
C. Information provided regarding embryo transfer procedure and treatment outcome on embryo transfer day
D. Support offered with regards to treatment outcome post treatment
E. Did you feel involved in the decisions about your care?
F. Did you feel supported by staff throughout your treatment journey?

The monthly Likert scale average was plotted over time based on the date the form was competed. This would be two weeks after embryo transfer when patients complete these forms and return to the clinic therefore there is an inherent delay in the data with regard to any improvement changes made based on embryo transfer date. Data from January 2019 to January 2022 is included in all SPC charts except for F in which data collection started when the questionnaire was updated in October 2019. Patient satisfaction questionnaire feedback (data from 51 patients from April - November 2018) highlighted three areas which do not receive ≥80% within the '5=excellent' field and were a focus for improvement work these were; A, B and D. The other areas were chosen because they relate to the drivers of patient satisfaction identified by the 2018 HFEA National Patient Survey i.e., the interest shown in you as a person, and the coordination and administration of treatment.

The Covid-19 pandemic may have had an impact on this data. The clinic closed from the end of March 2020 recommencing frozen cycles in July 2020 and fresh cycles in August 2020. Hence why there is no feedback for June 2020, and April/May 2020 represents feedback from very low numbers of fertility preservation patients only. There were many

other changes made to processes and procedures to prevent the spread of the virus and reduce footfall within the clinic. Initial consultations, counselling and nursing consultations were provided online only via video conferencing platform 'Attend anywhere'. This would undoubtably influence patient feedback and could lead to reduced patient satisfaction as the rapport built from face-to-face appointments may be compromised by screens and technological issues. Mask wearing may also impact on communication between staff and patients. The patient feedback data is displayed below.

A. Support groups and literature provided at initial consultation

Patients have always been given literature and information regarding support before initial consultation and provide feedback regarding this to the clinic. This feedback was monitored to determine whether the introduction of the HADs screening improved the patients' awareness of support groups and literature. The data is shown in Figure 73. The data flips between 3.0 (average) and 5.0 (excellent) with peaks and troughs of common cause variation. The data is split from October 2020 when the HADs forms were implemented within the clinic. The mean drops slightly from 4.45 to 4.32. The data in both segments is stable with no special cause variation observed. The HADs implementation had no effect on this aspect of patient feedback, however overall, the average feedback rating did not dip below 4.0 'good' post implementation of the HADs.

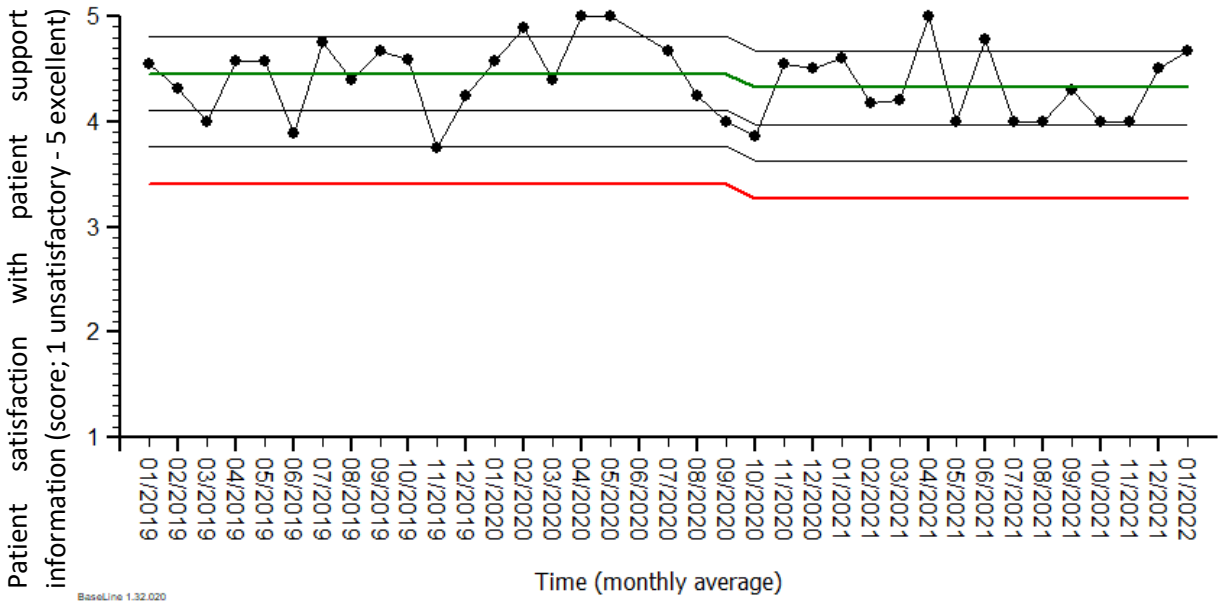


Figure 73 SPC chart of patient's satisfaction score for support information provided as a monthly average. Data is split at the implementation of the HADs forms in October 2020. Pre HADs mean = 4.45 Post HADs mean = 4.32. The data is stable with no special cause variation. Satisfaction scores are still overall good but not excellent.

The percentage of patients scoring this aspect '5=excellent' did not improve and is still under the >80% target, in the period before HADs the average was 62% and after implementation of the HADs it reduced to 54% (Appendix 13).

B. The awareness of independent counselling at initial consultation

Patients have always been offered counselling at initial consultation and are provided with literature and information of how to access it. This feedback was monitored to determine whether the introduction of the HADs screening improved the patients' awareness of independent counselling. The data is shown in Figure 74. The data flips between 4.0 (good) and 5.0 (excellent) with peaks and troughs of common cause variation. The data is split from October 2020 when the HADs forms were implemented within the clinic. The mean drops slightly from 4.68 to 4.60 and the data in both segments is stable with no special cause variation observed nor reduction in common cause variation. The HADs implementation had no effect on this aspect of patient feedback, however reassuringly the average feedback rating did not dip below 4.0 'good' throughout. The percentage of patients scoring this aspect '5=excellent' did not improve and is still under the >80% target, in the period before HADs the average was 77% and after implementation of the HADs it reduced to 74% (Appendix 13).

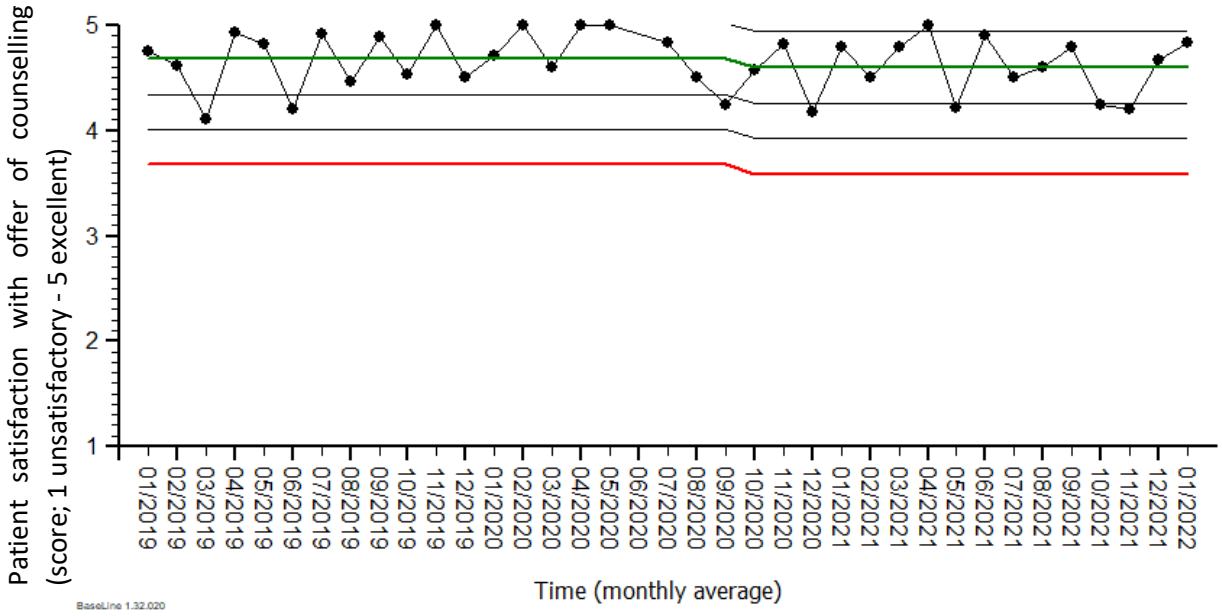


Figure 74 SPC chart of patient's satisfaction score for the offer of counselling as a monthly average. Data is split at the implementation of the HADs forms in October 2020. Pre HADs mean = 4.68 Post HADs ean = 4.60. The data is stable with no special cause variation. Satisfaction scores are still overall good but not excellent.

C. Information provided regarding embryo transfer procedure and treatment outcome on embryo transfer day

Patients are supported by the laboratory team, consultants, and nursing team on the day of embryo transfer and are provided with written patient information. This feedback was monitored to determine whether the introduction of staff training, the HADs screening, offer of a call in the 2WW and offer of PRCI improved patients' satisfaction on embryo transfer day. The data is shown in Figure 75. The data flips between 4.0 (good) and 5.0 (excellent) with peaks and troughs of common cause variation. The data is split from April 2020 when the first improvement PDSA cycle commenced with staff training. The mean remains consistent (4.91 to 4.90) and the data is stable with no special cause variation observed. Common cause variation is reduced following the improvement work which suggest less variation with patient feedback and more patients scoring higher. However, the feedback has not shown materially significant improvement due to the changes made. The percentage of patients scoring this aspect of care '5=excellent' was historically higher than >80% and this continues throughout the period of the project, prior to improvement work the average was 91% and after implementation of the changes it increased slightly to 92% (Appendix 13).

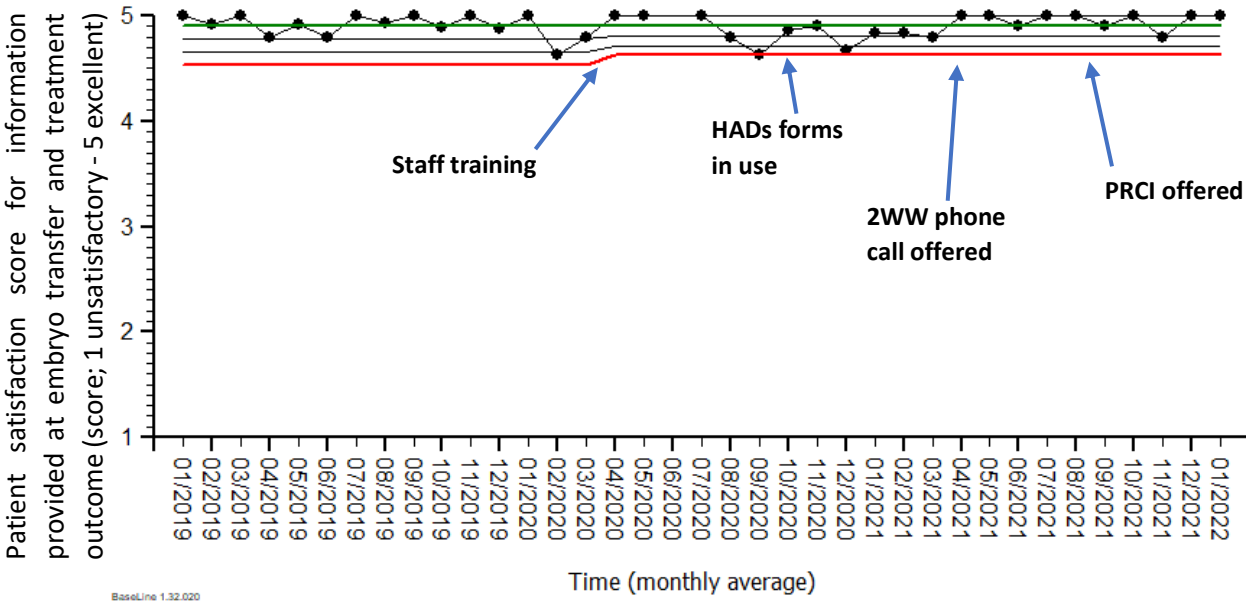


Figure 75 SPC chart of patient's satisfaction score for the information provided at embryo transfer and treatment outcome as a monthly average. Data is split at the implementation of the first phase of improvement staff training in April 2020. Pre intervention mean = 4.91 Post intervention mean = 4.90. The data is stable with no special cause variation. Satisfaction scores are overall excellent throughout. The PDSA improvement cycles are indicated at their various starting points, none appear to have any meaningful influence over the data however the common cause variation has reduced post intervention period.

D. Support offered with regards to treatment outcome post treatment

Patients are supported by the nursing team on the day of treatment outcome with a phone call giving the result and offering the next steps and support. This feedback was monitored to determine whether the introduction of staff training, the HADs screening, offer of a call in the 2WW, and offer of PRCI improved patients' satisfaction with regards to support at treatment outcome. The data is shown in SPC chart below (Figure 76).

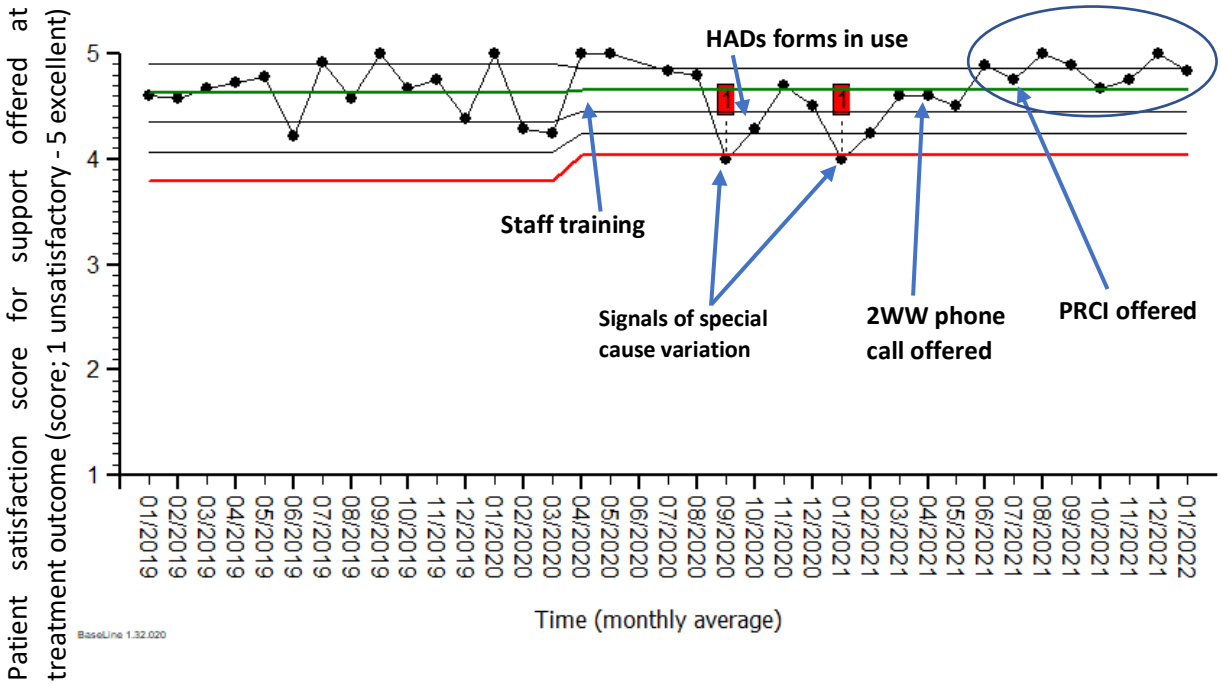


Figure 76 SPC chart of patient's satisfaction score for support offered at treatment outcome as a monthly average. Data is split at the implementation of the first phase of improvement staff training in April 2020. Pre intervention mean = 4.63 Post intervention mean = 4.66. The data is stable pre intervention but there are two points of special cause variation in September 2020 and January 2021 with materially significant lower patient feedback. Satisfaction scores are otherwise overall good/excellent throughout. The PDSA improvement cycles are indicated at their various starting points, none appear to have any influence over the data however the common cause variation has reduced post intervention period and the last 8 data points from June 2021 are all one side of the mean. Suggesting that if the next data point is also above the mean the patient satisfaction score may have improved due to the combination of the offer of a call in the 2WW and the PRCI.

The data flips between 4.0 (good) and 5.0 (excellent) with peaks and troughs of common cause variation. The data is split from April 2020 when the first improvement PDSA cycle commenced with staff training. The mean remains consistent throughout (4.63 to 4.66) and the data is stable before the improvement work. Common cause variation is reduced following the improvement work which suggest less variation with patient feedback and more patients scoring higher. With the exception of two special cause variation signals

during the improvement work, September 2020 and January 2021, with a lower monthly average feedback rating of 4.0 or 'good'. In September 2020 there were 7 patient ratings with 3/7 giving an 'average' score of 3.0 and in January 2021 there were 6 patient ratings with 2/6 giving an 'average' score of 3.0 which brought down the average for the month. No particular reason could be identified for this slight drop. Overall, the feedback has not improved due to the changes made but a pattern of 8 data points above the mean at the end of the data set may indicate a significant shift of improved patient feedback but more data is required (at least 9 data points one side of the mean) possibly as a result of offering the PRCI. The percentage of patients scoring this aspect '5=excellent' did not improve and is still under the >80% target, and this continues throughout the period of the project, prior to improvement work the average was 73% and after implementation of the changes it increased slightly to 75% (Appendix 13). The last 10 data points have a mean of 81% which suggests the 2WW calls and PRCI offer might have had more of an impact on improving patient feedback but further data is required. Covid-19 shutdown and recommencement changes alongside the winter in 2020 could have had an impact on the patient feedback during this time.

E. Did you feel involved in the decisions about your care?

Involving patients in decisions about their treatment is an important driver of patient satisfaction related to the interest shown in you as a person. Personalising patient treatment based on clinical history and respecting patient's wishes is key. This aspect of feedback was monitored as a background measure to establish whether the many changes to procedures due to Covid-19 had an impact on this important driver of treatment satisfaction e.g., reduced face-to-face appointments. The data is shown in Figure 77. The data flips between 4.0 (good) and 5.0 (excellent) with peaks and troughs of common cause variation but no special cause variation or patterns can be observed. The mean patient score was 4.85 with on average 87% of patients giving a score of 5 'excellent'. This suggests that the Covid-19 pandemic lockdowns, procedural changes made to recommence treatment safely, and winter pressures did not impact on patients' satisfaction with being involved in decisions about their fertility treatment.

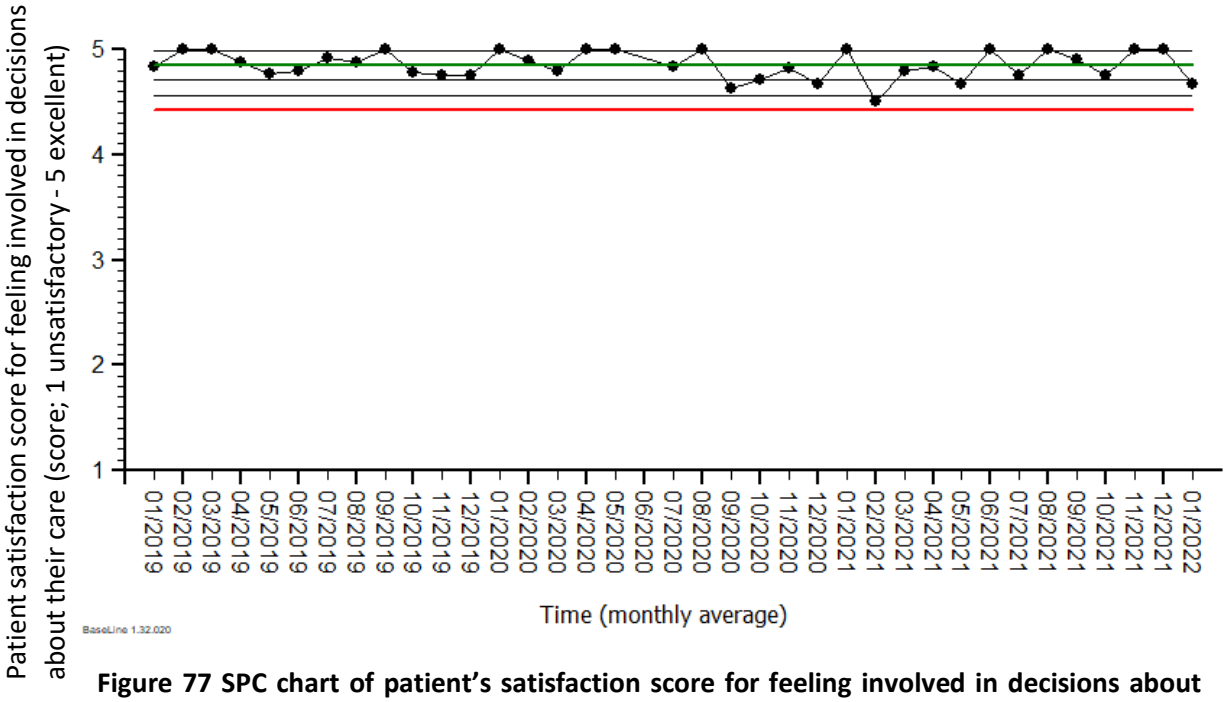


Figure 77 SPC chart of patient's satisfaction score for feeling involved in decisions about their care as a monthly average. There are no splits in the data as it is a background measure. The mean score is 4.85, 'excellent'. The data is stable with no special cause variation. Satisfaction scores are overall excellent throughout.

F. Did you feel supported by staff throughout your treatment journey?

Patients are supported by the whole MDT throughout the patient's journey, this question was added to the clinic's standard questionnaire in October 2019. Therefore, this measure has a shorter baseline period during the project prior to the PDSA improvement changes and there is an insufficient baseline to split the data at the start of the improvement work. The data is shown in the Figure 78. The data flips between 4.33 (good) and the maximum score of 5.0 (excellent) and shows a single special cause variation signal of below average patient satisfaction in October 2021. With an average of 4.38 for this month the patients still felt the service was 'good' but not 'excellent' (67% of them gave a score of 5 'excellent'). There were only three patient feedback forms returned for this month and one patient scored a 3 'average'. The mean satisfaction score for the whole time period was 4.85. Overall, for the period of the project the mean percentage of patients giving an 'excellent' score of 5 for satisfaction with feeling supported throughout treatment was 89% which is very good. A marginal gain in this feedback due to the changes made cannot be seen but the clinic will continue to monitor this measure going forward.

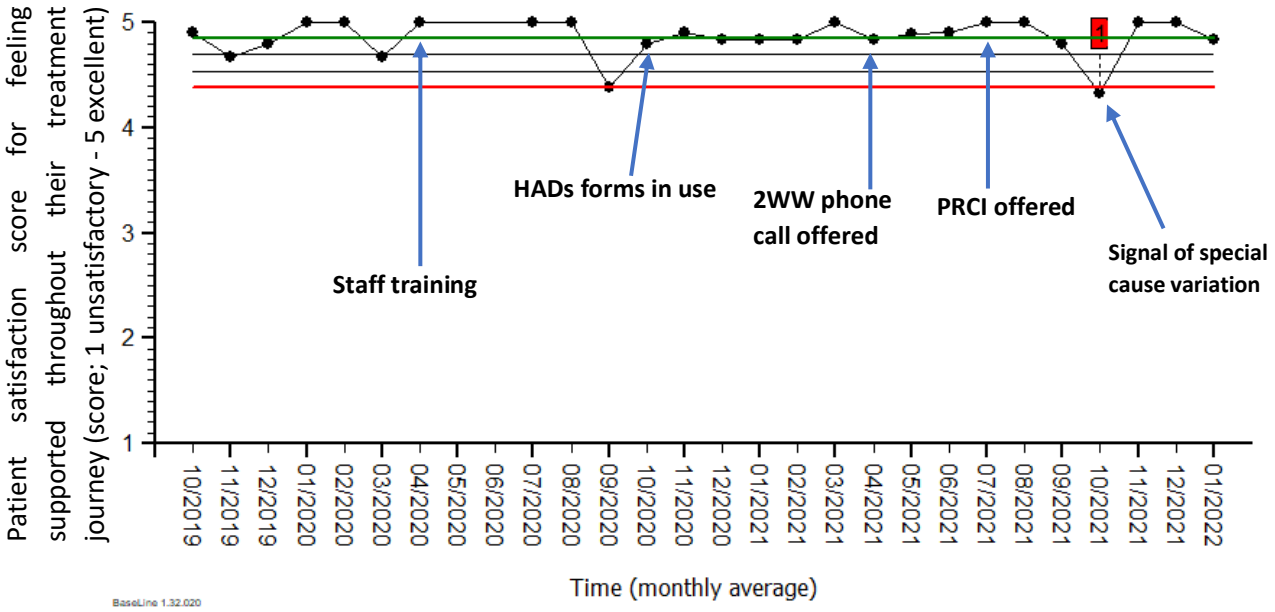


Figure 78 SPC chart of patient's satisfaction score for feeling supported throughout their treatment as a monthly average. The mean patient score was 4.85 'excellent'. The data is not stable with one special cause variation in October 2021 due to one patient scoring a '3'. Satisfaction scores are overall excellent throughout. The PDSA improvement cycles are indicated at their various starting points, none appear to have any significant influence on the data.

If the special cause variation of October 2021 due to one patient rating a 3 is excluded the SPC shows reduced common cause variation for the other months following implementation of the HADs forms in October 2020 (Figure 79). The majority of patients are very satisfied with the support they received throughout treatment.

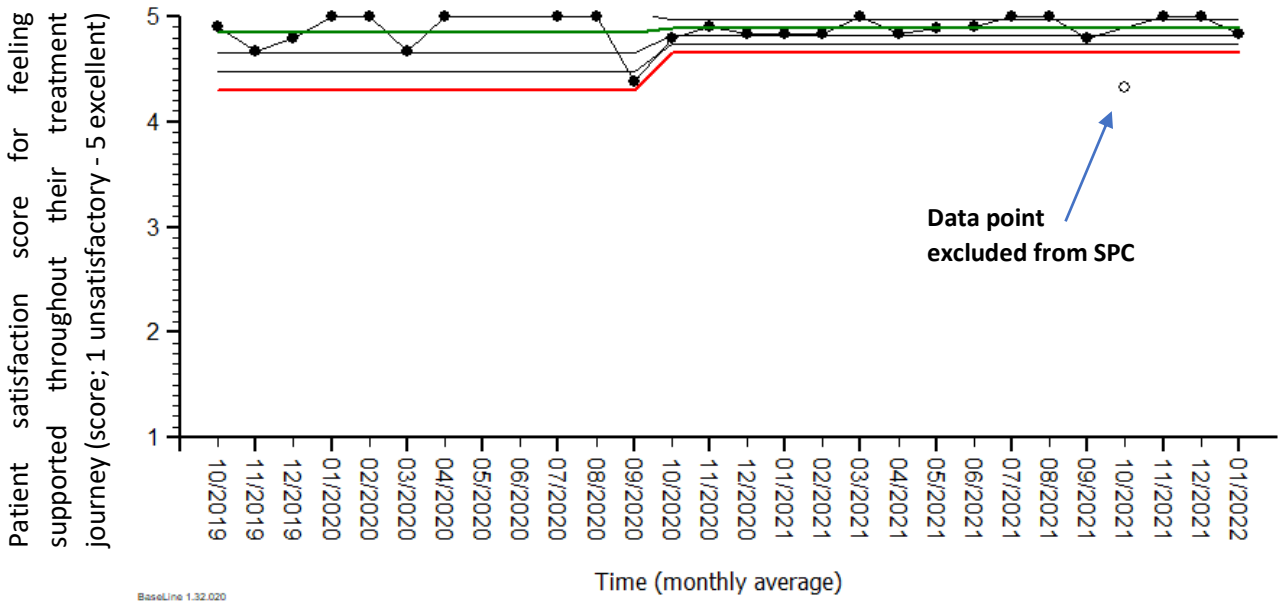


Figure 79 SPS chart of patient's satisfaction score for feeling supported throughout their treatment as a monthly average (excluding the month of October 2021 with one patient scoring a '3' average). Data split following the start of the implementation of HADs forms. The common cause variation is reduced indicating that more patients are consistently rating the clinic as '5' 'excellent' for being supported throughout treatment. The mean increases slightly from 4.84 to 4.89.

3.3.2 Adverse events

Since 2018 there have been no cases of cancelled treatment cycles prior to the day of treatment or on the day of treatment due to anxiety, emotional or relational issues. One case presented which was picked up by the team in 2021. A couple experiencing great distress following a failed first cycle and family bereavement putting a strain on the relationship. Throughout treatment planning the couple were open about their anxiety of going through another failed attempt and the team supported the couple with multiple counselling sessions and coping strategies. The couple went ahead with egg collection and embryo culture as planned but made a decision to delay embryo transfer. The embryos were frozen as per their request. Embryos were later thawed and transferred in a successful cycle when the couple were ready to go through the 2WW following embryo transfer. The clinic staff did exceptionally well to manage the case.

No other cases occurred and now 100% of patients at initial consultation and post embryo transfer are offered to complete the HADs form as a way of screening patients to identify those who might need additional support.

3.3.3 Effectiveness of staff training

A three-hour psychological skills training session was delivered to staff by the clinic's counsellor in April 2020. The training session covered both fertility patients and patients referred for fertility preservation due to a cancer diagnosis or gender dysphoria. Staff members were asked to complete a pre and post training questionnaire. All staff who attended the session showed an improvement in their confidence to assess and support patients exhibiting psychological distress as shown in Figure 80. The biggest improvement in staff confidence following the training session was regarding using specific screening tools to detect psychological problems in patients (question 3). Therefore, this session was effective at addressing and alleviating concerns that staff had about the anticipated induction of the HADs form to clinical practice. It gave staff the chance to ask questions and know what to do if they are concerned about a particular patient. The counsellor was very clear that staff could go to her for support and advice. It was reassuring to see that staff already felt confident about discussing concerns about a patient's psychological distress with other members of the team (question 7), the team already support each

other well in this respect. The average score for all questions asked was above 5, still room for improvement but confidence should grow throughout the project and with annual training and support. A 10th question gave staff the option to list any main concerns they had, if any, about discussing psychological issues with patients, comments pre training included;

- "*That I won't know what to say or I'll say something that makes it worse*" Lab
- "*Not knowing specific places to signpost to i.e., procedure. Saying the wrong thing to the patient*" Lab
- "*Lack of training, unsure how to manage the situation, worried make things worse*" Lab
- "*Knowing how much involvement the patient needs from us - often feel unsatisfied with the emotional support I offer (limited time to spend with them etc). But also, unsure whether these patients want to come here and divulge feelings to us or whether they just want to come here and concentrate on their fertility treatment. Their treatment is squeezed in quickly to complete before chemotherapy etc, so we don't get to know them like we perhaps would other patients*" Nurse

Following the training session, the concerns which remained were:

- "*How to properly address whether any psychological issues are purely a result of shock or a symptom of more long-lasting anxiety/depression*" Lab
- "*Think confidence will increase with experience. Following the talk I feel more confident re sign-posting alerting GP if risk ect*" Lab
- "*Missing signs which might have a negative impact on patients. Also jumping to conclusions or coming across patronizing*" Lab
- "*Not knowing whether I am saying the right thing*" Admin
- "*Feeling of wanting to share everything right there and then + make patient feel better*!" Nurse
- "*Ensuring I am providing the best information that the patient deserves*" Admin

There was still some anxiety around processes and what to do/say. The counsellor was consulted by the QI team to create a flow chart for the HADs process alongside patient information leaflets for additional emotional support, support groups, signposting and what the HADs score means. Training staff in communication/interaction skills has been

recommended by Gameiro et al (2013a) to minimise patient, treatment, and clinic sources of burden, in order to provide enhanced delivery of treatment for patients and staff.

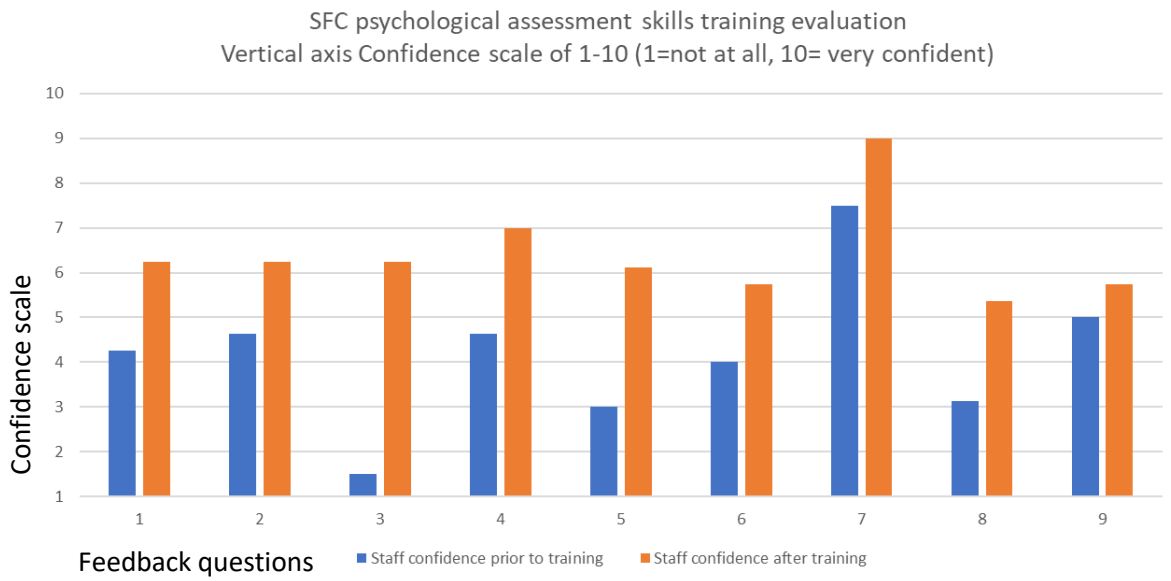


Figure 80 Effectiveness of Psychological assessment skills training delivered to staff of the clinic. The confidence questionnaire included 9 questions with an ordinal scale of 1-10 (1 being not at all confident and 10 being very confident). A 10th question gave staff the option to write down any main concerns they had, if any, about discussing psychological issues with patients. The average score for the whole MDT is shown above. (n = 8 staff members completed the feedback forms (4 laboratory staff, 2 nurses, 2 administrators)).

Question 1. How confident do you feel about discussing psychological problems with patients with health problems?

Question 2. How confident do you feel about your ability to elicit worries or concerns from patients?

Question 3. How confident do you feel about using specific screening tools to detect psychological problems in patients?

Question 4. How confident o you feel about your ability to recognize symptoms of psychological disorders (e.g., depression) in patients?

Question 5. How confident do you feel about your ability to manage a patient who is describing symptoms of psychological distress?

Question 6. How confident do you feel about providing information to patients about how to manage their psychological distress?

Question 7. How confident do you feel about discussing concerns about a patient's psychological distress with other members of your team?

Question 8. How confident do you feel discussing suicide with patients and families?

Question 9. How confident do you feel about managing your own feelings when dealing with

3.3.4 HADs

The HADs forms were offered to patients at initial consultation and during the 2WW from the week commencing the 5th of October 2020. Consent forms, patient information and flowcharts can be found in Appendix 4. The data below covers the start of offering the HADs to the end of the QI work January 2022. However, the clinic maintained the procedures into clinical practice and continued to offer the HADs at initial consultation and following embryo transfer. Patients were informed to complete the HADs forms at home (on day 10 of the 2WW) and bring back to the clinic. During the study period 941 HADs forms were offered to patients (513 at initial consultation and 428 following embryo transfer). In total 478 completed forms were returned to the clinic for scoring. Patients at initial consultation had a good response rate with 392 forms returned (return rate of 76.4%). Post embryo transfer patients had a much lower response rate 86 forms returned (20.1%). Due to the time between treatment planning and embryo transfer and low post treatment response rate only 15 patients completed a HADs form at the start and end of treatment during the project. Some returned HADs forms could not be scored because they were not fully completed by the patient, these were excluded from the data analysis.

HADs patient scores following the pandemic is novel and is displayed as raw data and average scores over time.

The distribution of HAD scores at initial consultation and post treatment are shown in the box-Whisker plots (Figure 81). All patients show higher levels of anxiety than depression. As would be expected both anxiety and depression score increase post treatment. There are a number of outliers in each group but the majority of patients scored within the normal range (0-7).

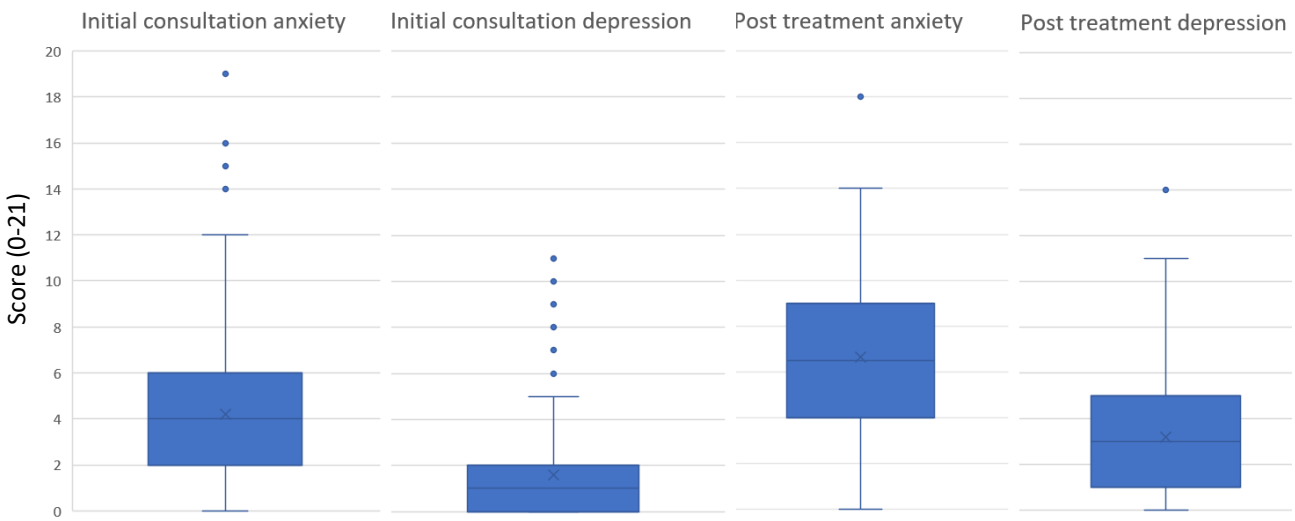
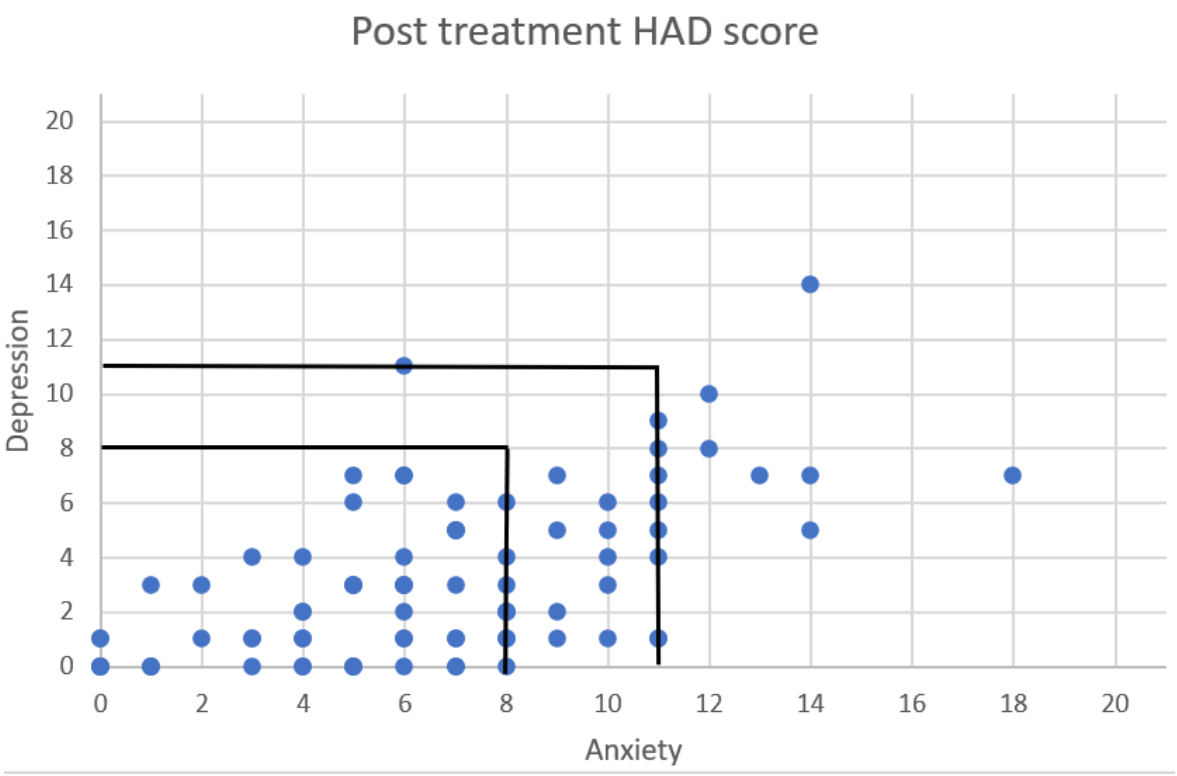


Figure 81 Box Whisker plots of HAD score distributions for anxiety and depression both at initial consultation and following embryo transfer. The mean scores were within the normal range (0-7) and are as follows;
Anxiety at initial consultation = 4.2,
Depression at initial consultation = 1.6,
Data set included scores from completed HADs forms from 389 patients at initial consultation (3 HADs forms could not be scored as they were incomplete and were excluded from the Box Whisker plots)
Anxiety post treatment = 6.7,
Depression post treatment = 3.2,
Data set included scores from completed HADs forms from 84 patients post treatment (2 HADs forms could not be scored as they were incomplete and were excluded from the Box Whisker plots)
All groups had some patients with scores within the borderline (8-10) and clinical range (11-21) which required action from the clinic.

Patients who returned a HADs forms with a borderline score or higher for either anxiety or depression were contacted either by phone or letter to offer support. In total 61 patients (61/392=15.6%) at initial consultation and 36 patients following embryo transfer (36/86= 41.9%) required action from the clinical team due to a borderline or higher score. In most cases a standard letter was posted to patients regarding sources of support and counselling and most patients with raised scores following embryo transfer were booked for a follow-up appointment or counselling appointment.

Combined anxiety and depression scores for both patient groups are shown in Figure 82. The pattern of cases within the borderline and clinical range of the HAD score can be seen.



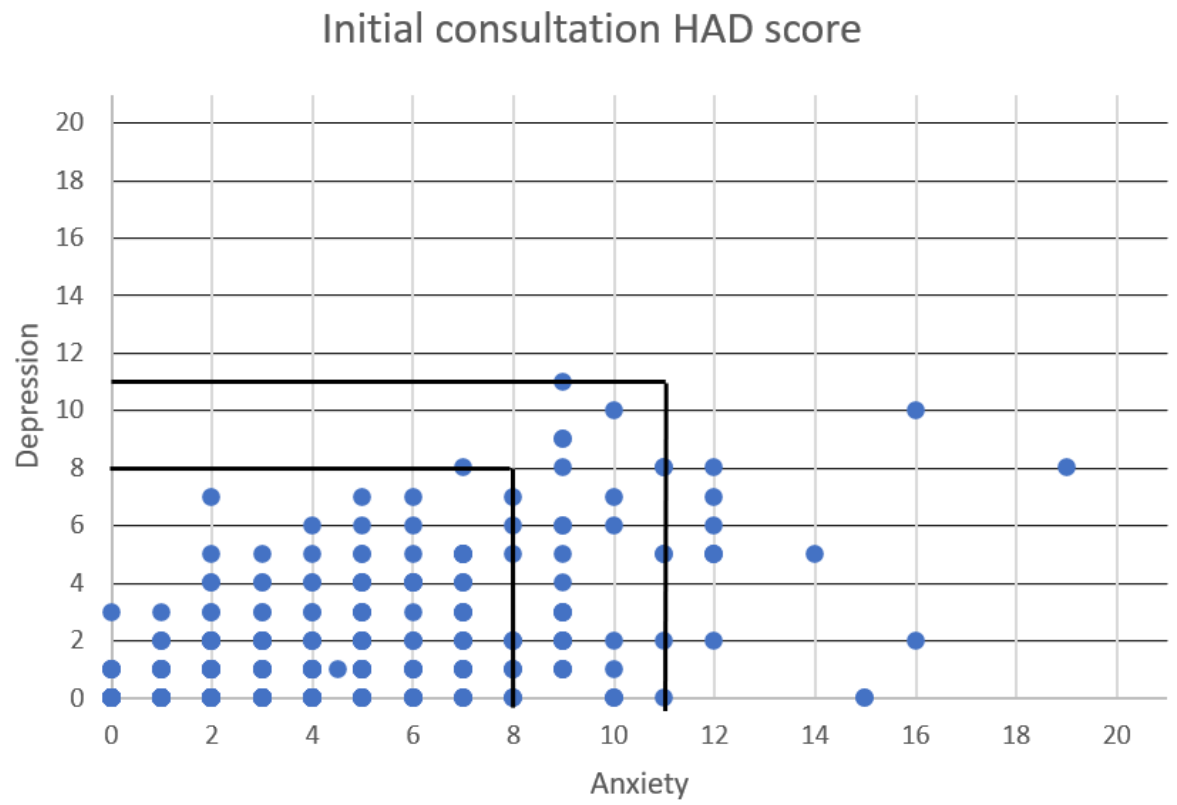


Figure 82 Combined HAD scores for patients at initial consultation and post embryo transfer. Some patients had a score above 7 for either anxiety or depression which required action by the clinical team. In total 61 patients at initial consultation (61/392= 15.6%) and 36 patients following embryo transfer (36/86= 41.9%) required action from the team due to a raised score, borderline (8-10) or higher (clinical range 11-21) (marked by the black lines). (n = 84 completed HADs forms post treatment and n = 389 completed HADs forms at initial consultation)

As the HAD score for fertility patients is novel in routine clinical practice the data was also plotted over time on SPC charts to assess any pattern on the variation seen possibly due to the effects of winter and/or the lockdowns during the Covid-19 pandemic. The data for patients at initial consultation is stable throughout the project and no patterns can be identified (Figures 83 & 84). The mean scores were 4.19 for anxiety and 1.52 for depression, both within the normal range.

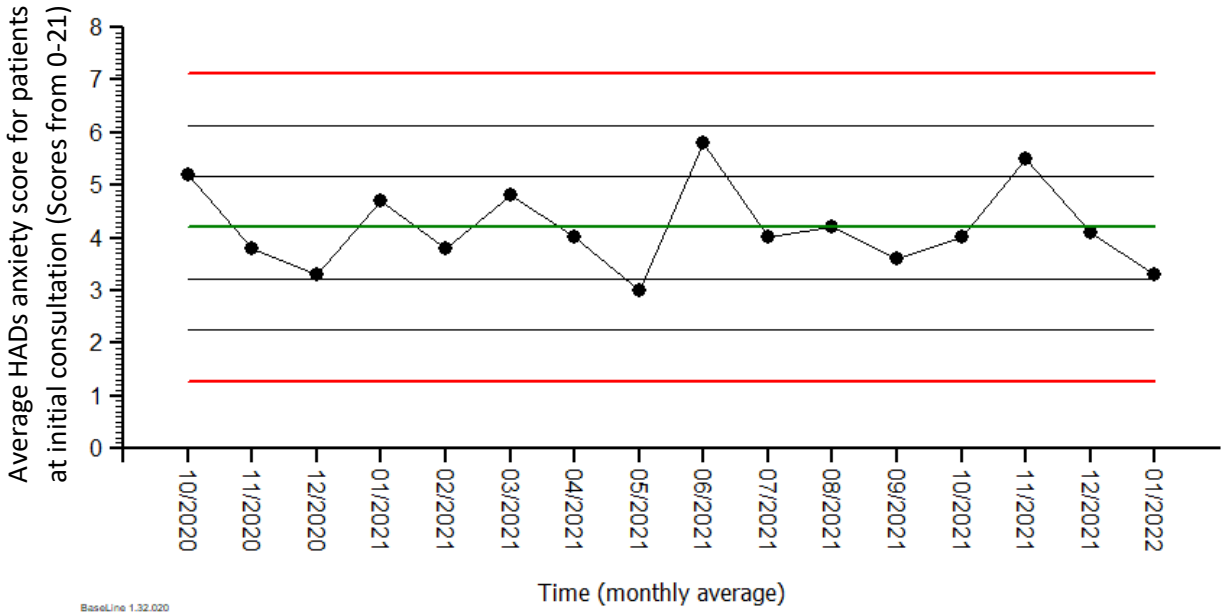


Figure 83 SPC chart of HAD anxiety scores of patients at initial consultation as a monthly average over time. The data is stable with no special cause variation. The mean score for anxiety was 4.19 well within the normal range (<8).

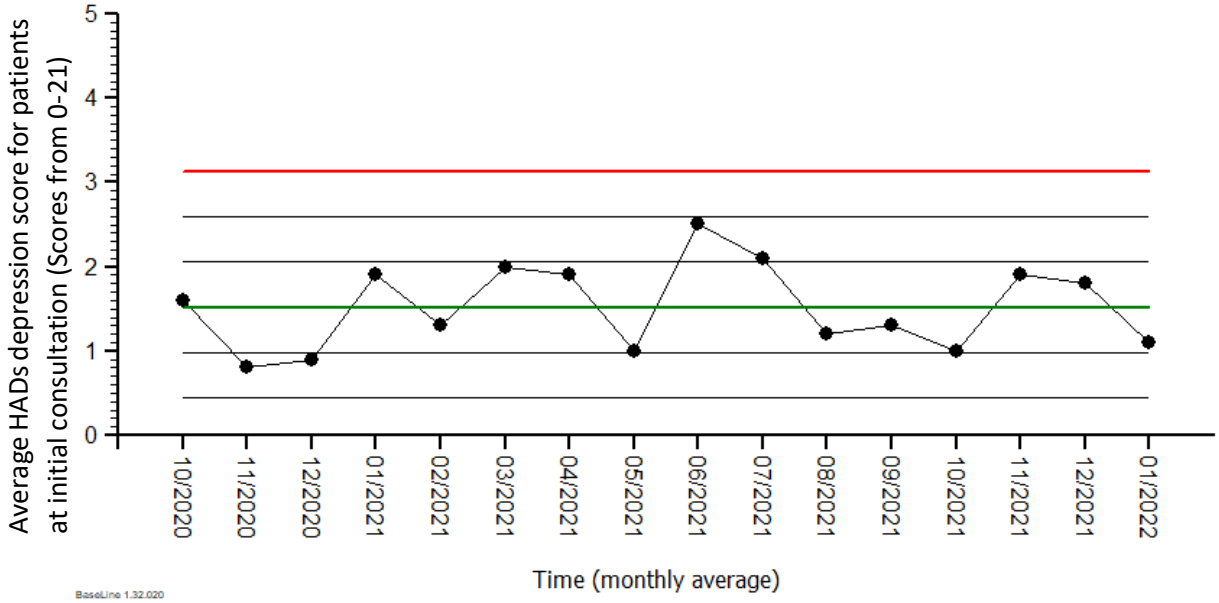


Figure 84 SPC chart of HAD depression scores of patients at initial consultation as a monthly average over time. The data is stable with no special cause variation. The mean score for anxiety was 1.52 well within the normal range (<8).

Post embryo transfer data was also plotted as a monthly average over time to assess any improvement since offering the PRCI in June 2021 (Figures 85 & 86). The data has shown

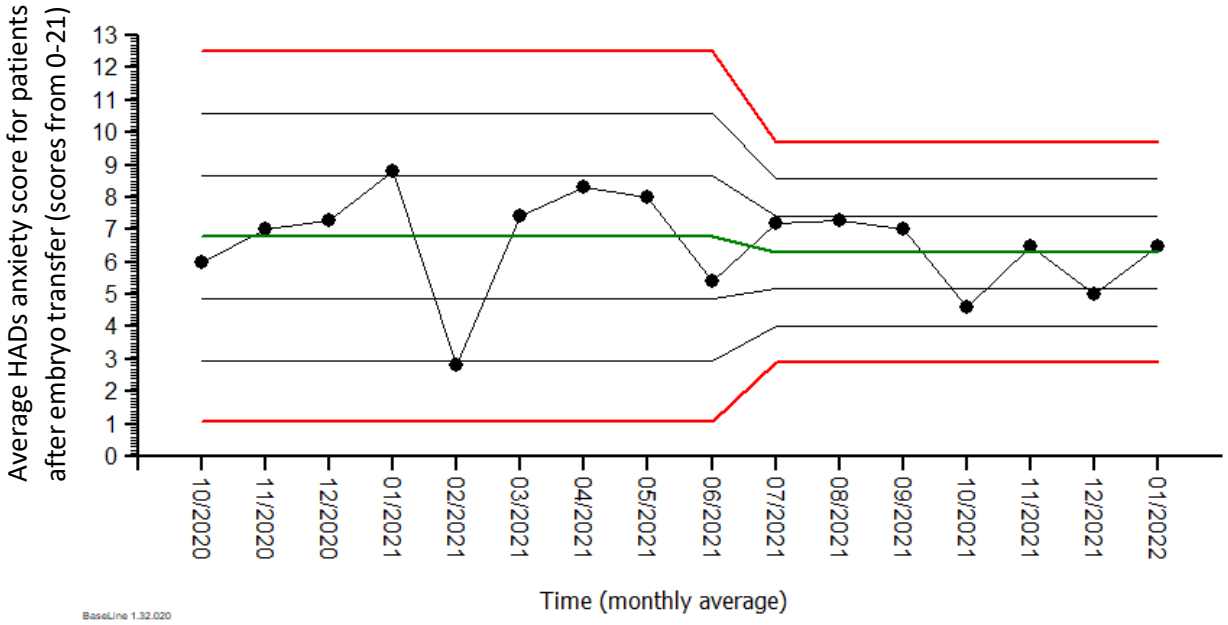


Figure 85 SPC chart of HAD anxiety scores of patients after embryo transfer as a monthly average over time. The data is stable with no special cause variation. The data is split at the start of the next phase of improvement work, offer of PRCI at the end of June 2021. The mean score for anxiety decreased slightly from 6.78 to 6.30 following the intervention. Both data segments are just within the normal range (<8). The common cause variation decreases greatly following the offer of the PRCI.

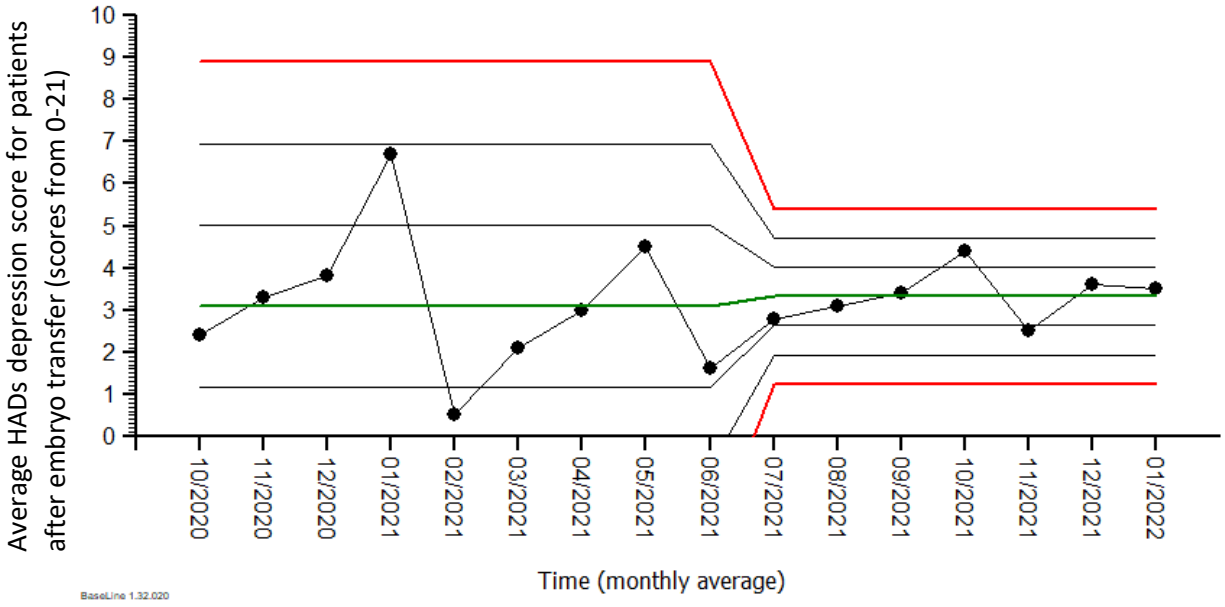


Figure 86 SPC chart of HAD depression scores of patients after embryo transfer as a monthly average over time. The data is stable with no special cause variation. The data is split at the start of the next phase of improvement work, offer of PRCI at the end of June 2021. The mean score for depression increased slightly from 3.10 to 3.33 following the intervention. Both data segments are within the normal range (<8). The common cause variation decreases greatly following the offer of the PRCI.

that common cause variation reduces for both anxiety and depression post treatment after implementation of offering the PRCI. No patterns or special cause variation can be seen. The mean anxiety score decreased slightly from 6.78 to 6.30 and the mean depression score increased slightly from 3.10 to 3.33. These are both materially insignificant changes and all mean scores were within the normal range for the HAD scores.

Of the returned forms, 15 patients returned a HADs form both at initial consultation and post embryo transfer. The mean anxiety and depression scores can be seen in the Figure 87 and 88. The numbers are small but a trend is seen of increased anxiety and depression levels post treatment. Similar to findings of Ockhuijsen et al, (2014) who showed anxiety and depression levels were significantly higher during the waiting period (day 10 post embryo transfer) compared to just before. The 15 patients split into pre and post implementation of the offer of PRCI is shown below for interest. The data set if far too small to show any significance but the clinic will continue to collect post embryo transfer HAD scores to build the data set. On initial glance the group who did not have the PRCI offered maintain the pattern of increased anxiety post embryo transfer however the group offered the PRCI did not show an increased anxiety level. More data is needed but it appears to support the evidence that the PRCI is associated with reduced symptoms of anxiety during the waiting period (Ockhuijsen et al., 2014). The group offered the PRCI appear to show a trend of a larger increase in the depression score. Ockhuijsen et al, (2014) highlighted depression scores are significantly affected by the time that the HADs was completed, demonstrating that during the waiting period and 6 months following the waiting period depression scores increased. Depressive symptoms are tied to the perceived or actual outcomes of imminent events (Lazarus & Folkman 1984). Therefore, it is understandable for depression scores to be higher during the waiting period, compared to initial consultation, when patients may have experienced poor prognosis symptoms prior to treatment outcome e.g., started bleeding before pregnancy test. It is not clear why the post PRCI group would have slightly higher, though not significant, depression levels than the group not offered the PRCI. Ockhuijsen et al, (2014) acknowledged that the PRCI had no effect on depression levels and is perhaps not optimised to reduce symptoms of depression.

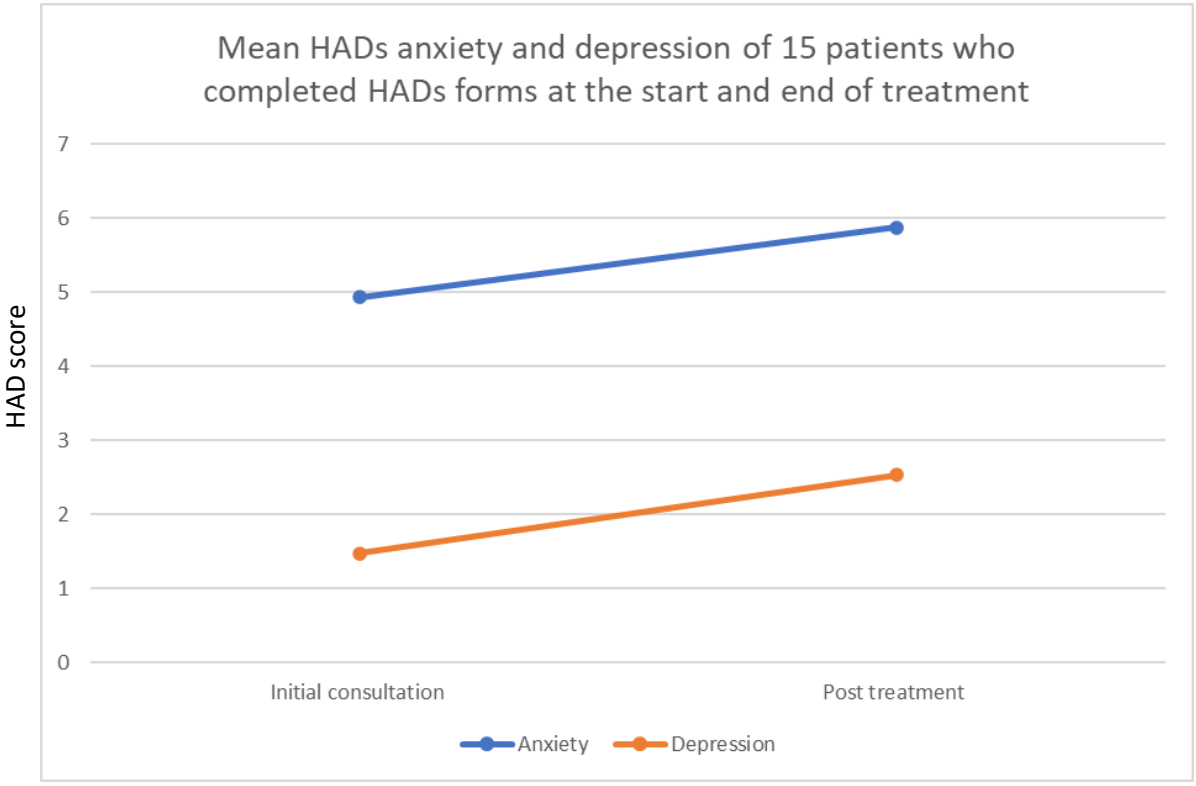


Figure 87 Graph showing mean HADs anxiety and depression scores of 15 patients at the start and end of treatment. Both increase post embryo transfer as expected.

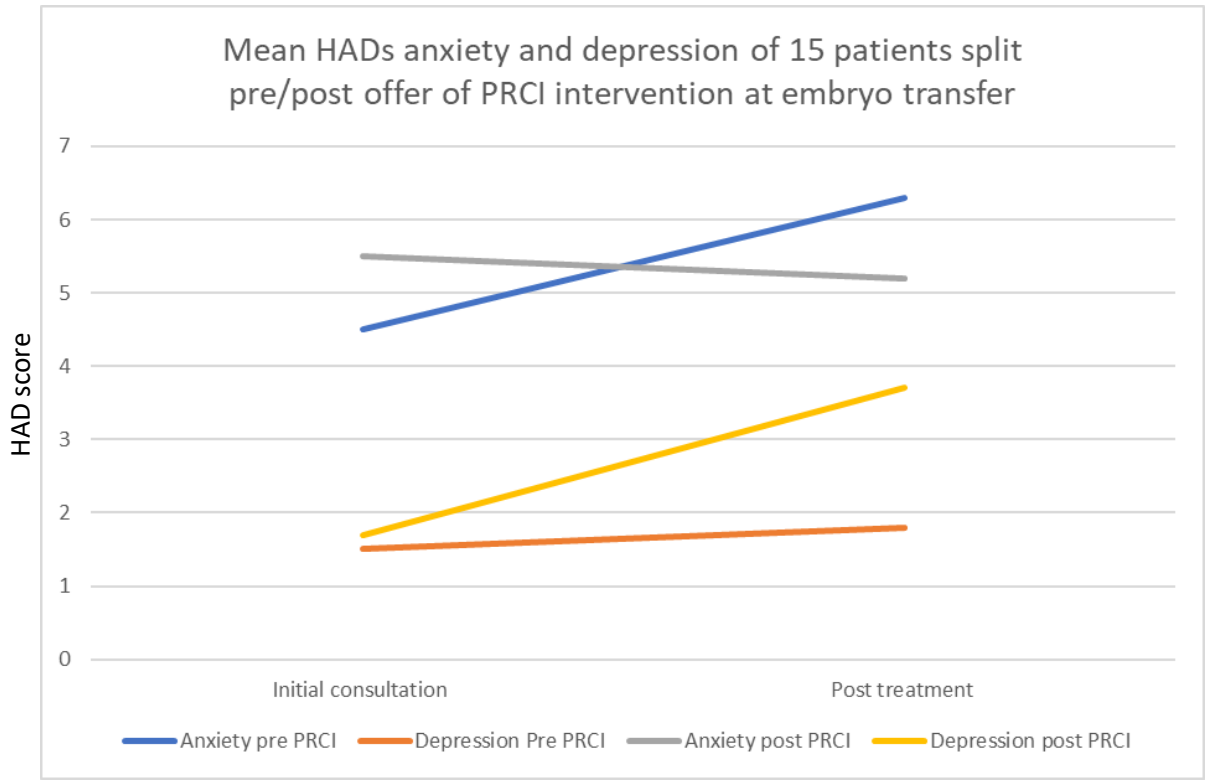


Figure 88 Graph showing mean HADs anxiety and depression scores of 15 patients at the start and end of treatment, before the implementation of the PRCI offer (pre PRCI) and after (post PRCI). The 15 patients are split into a pre PRCI offer (n= 9) and a post PRCI offer (n=6). The pre PRCI offer group shows the same pattern of increased anxiety and depression scores post embryo transfer however the PRCI group anxiety score did not increase.

3.3.5 Counselling availability and uptake

Counselling at the clinic is delivered by one independent counsellor during a weekly clinic of three appointment slots. The number of counselling appointments booked and type of counselling delivered was monitored during the period of the improvement work in order to determine if the introduction of HADs forms and QoL monitoring increased the workload of the counsellor, with more patients taking up the offer of counselling for support during treatment. More patients taking up the offer of counselling for supportive purposes would be beneficial, to help them stay in treatment, but if the clinic cannot keep up with the demand this would not provide good quality counselling if patients must wait for an appointment. The data is shown in the Figure 89. The Covid-19 pandemic would have had an impact on this data, the clinic was closed mid-March 2020 to July 2020, patients could access counselling sessions but these were delivered by telephone or video conferencing. The number of patients having fertility treatment in the first half on 2020 was lower than normal due to the closure. Following the Covid-19 pandemic and the introduction of HADs forms and screening to the clinic procedures the number of counselling sessions booked increased from roughly 45-55 every 6 months in 2019/2020 to 70-77 in 2021. The number of counselling appointments for supportive purposes also

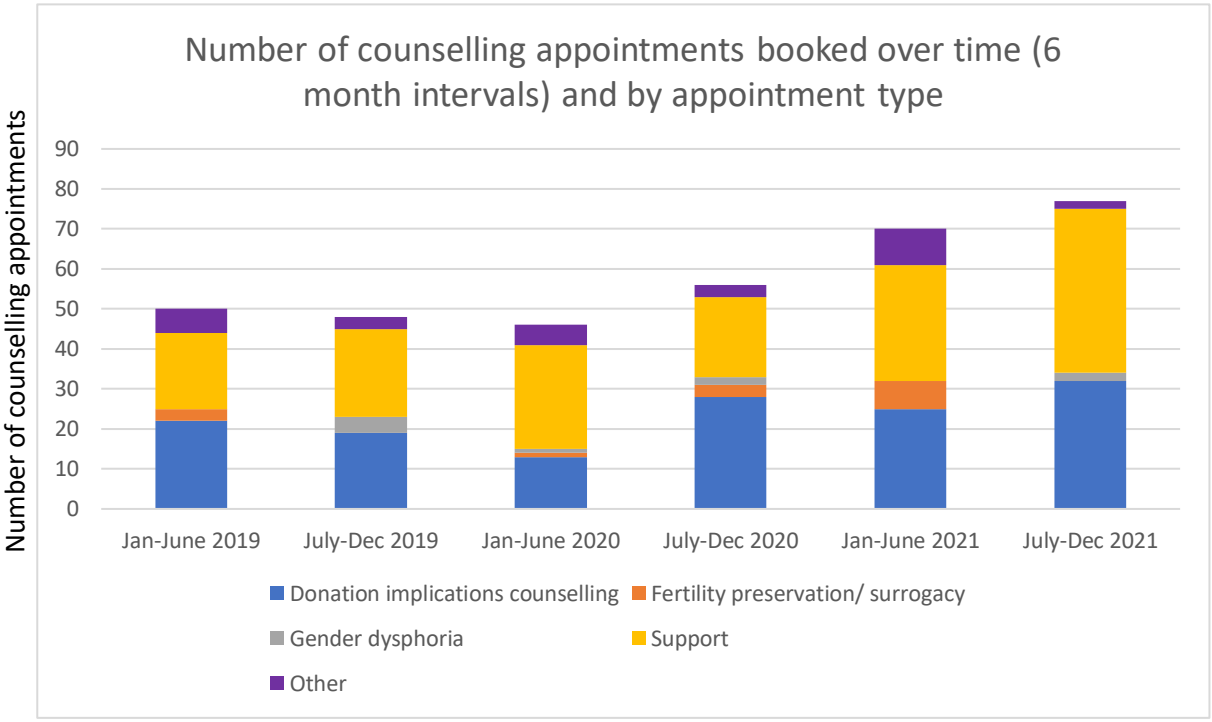


Figure 89 The number of counselling sessions booked over time and by type. The utilisation of clinic counselling slots has increased over time for both supportive and implications counselling purposes.

increased in 2021 (roughly 30-40 every 6 months) compared to 2019/2020 (roughly 20-25 every 6 months). However, as a percentage of overall counselling appointments, supportive counselling sessions remained consistent over the years, roughly between 35% and 56%, with the highest proportion of supportive sessions being taken in 2020 during the time of clinic closure (Figure 90). Due to the increased demand for counselling in early 2021, from March 2021 an additional counselling slot was added every other week to increase capacity and minimise long waits for counselling appointments. Even with the additional appointments almost all counselling slots are utilised.

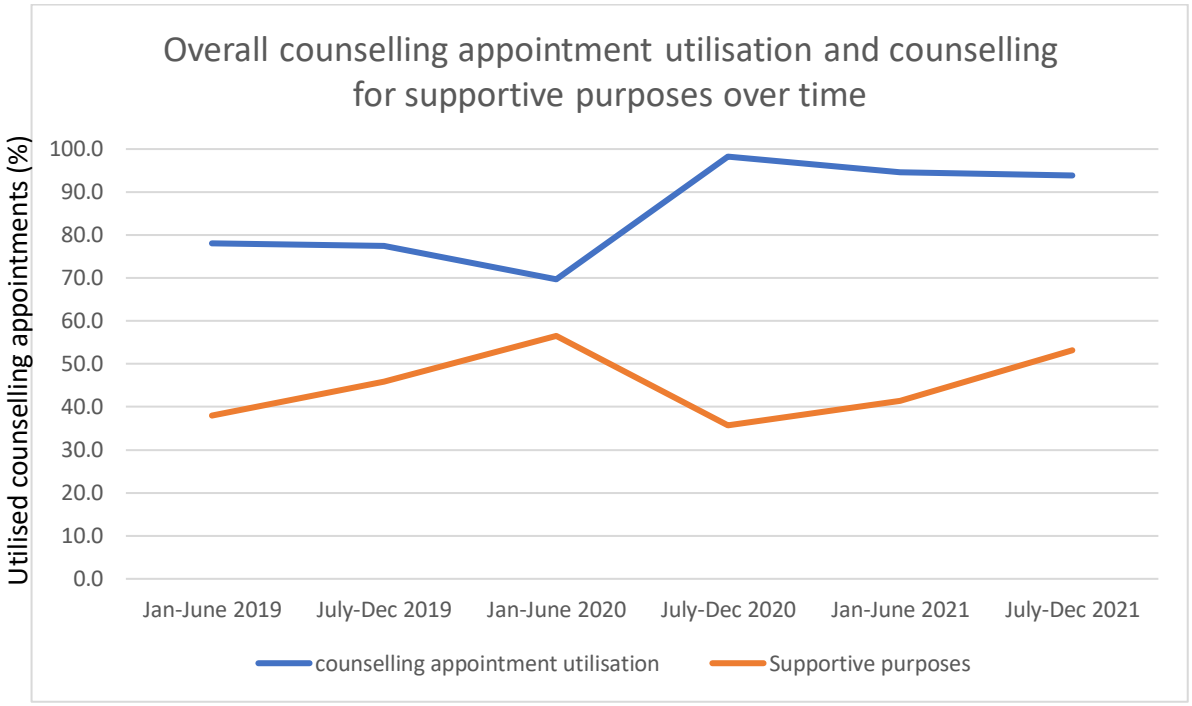


Figure 90 Counselling utilisation and the percentage of appointments for supportive purposes over time. Even with the addition of extra counselling appointments from March 2021 almost all sessions are utilised since July 2020. The highest proportion of sessions booked for supportive purposes was during the period of clinic closure in early 2020 due to Covid-19.

The clinic has never monitored the number of patients who attend counselling for supportive purposes. Patients are all entitled to up to three counselling sessions as part of their IVF treatment regardless of funding source. The uptake rate was evaluated for a 6-month time period, from January to June, for two different time periods, 2019 before any changes to patient support were introduced and 2021. To determine whether more patients booked counselling sessions post introduction of the HADs forms than previously. It is also possible that the stress of the pandemic may also influence the number of patients seeking counselling. An aim of the project was to gain a better

understanding of how our patients utilise the counselling service offered and to perhaps increase the uptake rate of counselling. With the assumption that this might reduce the burden of treatment and help them to continue treatment following any failed attempts. Patients seeking treatment with surrogacy or donated gametes/embryos were excluded from this data set as it is compulsory at the clinic to attend for implications counselling. Data shown in Table 15.

Table 15 Uptake of supportive counselling

Time period	Uptake rate of supportive counselling		
Jan 2019 – June 2019 Pre improvement work	Fresh cycles	24/125 = 19.20%	43/205 = 20.98%
	Frozen cycles	19/80 = 23.75%	
Jan 2021- June 2021 Post HADs implementation	Fresh cycles	24/88 = 27.27%	35/143 = 24.48%
	Frozen cycles	11/55 = 20.00%	
			Pearson Chi-Square *P*= 0.441

The number of patients that take up the offer and attend a counselling appointment at the clinic is in line with published studies describing a low take up rate of just 20% (Rajkhowa et al., 2006; Boivin, 1997; Hammerberg et al., 2001). The percentage of patients that took up counselling during their treatment increased following implementation of the HADs forms from 20.98% to 24.48% but this was not significant. Implementation of the HADs and Covid-19 pandemic does not appear to increase the number of patients taking up supportive counselling in this 6-month period.

3.3.6 Additional feedback and two-week wait calls

Additional patient feedback post HADs implementation but prior to offering a call during the 2WW is shown in Figure 91. This data was collected for 4 weeks and questionnaire forms were given to 27 patients following embryo transfer. Just 7 forms were returned to the clinic, a response rate of 26% missing a larger group of our patient population who did not respond. The results of the questionnaire were summarised and shared with the team at a team meeting.

Comments from patients regarding support and suggested improvements:

"Some of the health professionals were better than others when asking "how are you?" and digging a bit deeper to really check you're ok", "Knowing I could contact the fertility centre during the 2ww was enough support for me" and "*The two-week wait is harder than any other part. A little more contact would be good"*

Similar to historical clinic feedback some patients thought a call in the 2WW would be helpful while others did not. The questionnaire focused on areas highlighted by the HFEA patient survey (2018) as important drivers of patient satisfaction. Full results can be found in Appendix 14, a summary of the overall response for each section is shown in pie charts below. Reassuringly the majority of patients felt happy with their care. Only one area was highlighted by one patient who was dissatisfied with 'being seen by the same healthcare professionals throughout your treatment'. All patients were either very satisfied or satisfied with their most recent treatment cycle.

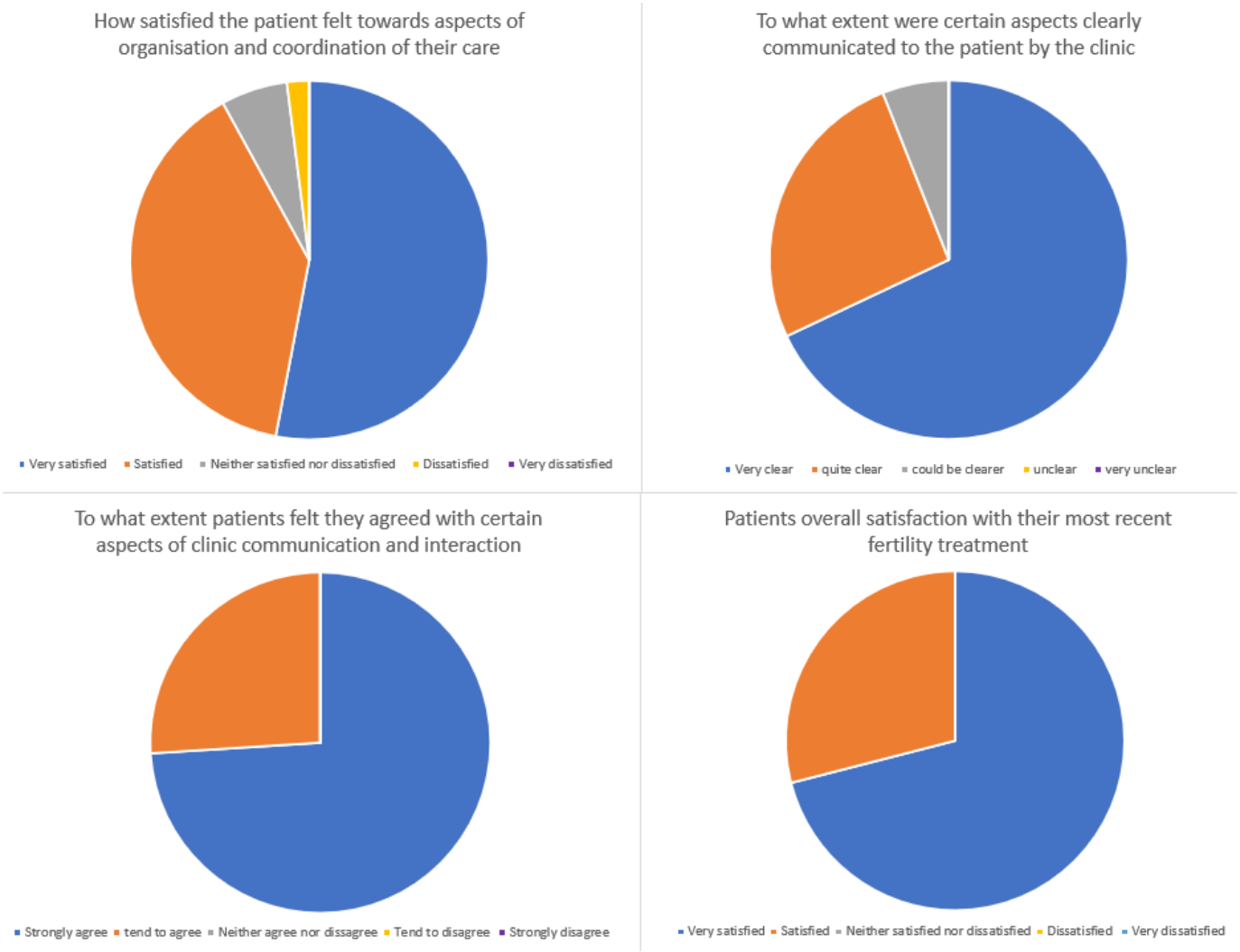


Figure 91 Overall patient satisfaction responses during the 9th of March 2021 to the 14th of April 2021 following implementation of the HADs. (n = 7 patients).

Patients were asked what emotional support they had received which was helpful. All respondents (7/7) said they found support from their partner, 57% (4/7) said they found support from friends or family members, 14% (1/7) said they found support from an online support forum (such as fertility friends, Fertility UK, Fertility network UK), 14% (1/7) said they found support from the receptionist/admin team, 57% (4/7) said they found support from the nurses, 14% (1/7) said they found support from the embryologists, 43% (3/7) said they found support from the doctors/consultants. Importantly no patients felt that they did not receive any helpful support. Respondents did not find emotional support from; support groups that met in person, telephone helplines, counsellors found separately from the clinic, or the clinic's counsellor (however 0/7 actually had a counselling appointment). When asked about counselling at the clinic 6/7 (86%) patients remembered receiving information about how to access counselling (one patient could not recall) and 0/7 patients accessed counselling sessions at the clinic.

Patients were asked what the clinic could do to better support its patients, results shown in Table 16.

Table 16 Results from additional patient feedback questionnaire regarding support March/April 2021.

What could we do better to best support our patients?	
The centre manages patient expectations well during treatment	4/7= Strongly agree 57% 7/7 = Strongly agree + tend to agree 100%
The centre always ensures privacy and dignity during scans, tests and treatments	6/7 = Strongly agree 86% 7/7 = Strongly agree + tend to agree 100%
The centre allows sufficient time for patients to absorb new information	4/7= Strongly agree 57% 7/7 = Strongly agree + tend to agree 100%
The centre provides information on possible physical and emotional symptoms **(one patient neither agreed nor disagreed)**	4/7= Strongly agree 57% 6/7 = Strongly agree + tend to agree **86%**
I would like the centre to phone me halfway through the 'two-week wait' **(one patient neither agreed nor disagreed, one patient tend to disagree)**	1/7= Strongly agree 14% 5/7 = Strongly agree + tend to agree **71%**
I felt supported during the 'two-week wait' and was able to speak to the centre if I needed to **(two patients neither agreed nor disagreed and one patient tended to disagree)**	3/7= Strongly agree 43% 4/7 = Strongly agree + tend to agree **57%**
I was offered counselling at the time of my pregnancy result **(only 4 patients responded to this question) (one patient neither agreed nor disagreed)**	2/4= Strongly agree 50% 3/4 = Strongly agree + tend to agree **75%**
I would like the centre to phone me a week after any pregnancy result (**only 6 patients responded to this question) (three patients neither agreed nor disagreed) (one patient tended to disagree)**	1/6= Strongly agree 17% 2/6 = Strongly agree + tend to agree **33%**
I felt supported by the centre throughout treatment	4/7= Strongly agree 57% 7/7 = Strongly agree + tend to agree 100%
The centre could do more to help patients cope during the 'two-week wait' **(5 patients neither agreed nor disagreed, one patient strongly disagreed)**	**0/7= Strongly agree 0%** 1/7 = Strongly agree + tend to agree **14%**

Overall, most (71%) of patients agreed they would like a phone call in the 2WW (only one patient tended to disagree with this and another did not feel strongly either way). Disappointingly only 57% of patients felt supported during the 2WW, with two patients neither agreeing nor disagreeing and one patient tended to disagree. Clearly more could be done by the clinic to improve this. Overall patients did not want a phone call a week after pregnancy result (67%) and reassuringly all respondents felt supported by the clinic throughout their treatment. Most respondents neither agreed nor disagreed that the clinic could do more to help patients cope during the 2WW.

To conclude this section, the response rate was low but still informative for a PDSA cycle. The feedback was overall very good, 100% of patients felt supported by the clinic throughout treatment, and 100% were either very satisfied or satisfied with their recent treatment. Reassuringly no patients felt that they did not receive any helpful support. However only 57% felt supported during the 2WW, most sat on the fence as to whether they thought SFC could do more to help patients cope. The feedback highlights areas for improvement work.

Areas for consideration for improvement:

- Continuity of care (being seen by the same healthcare professionals throughout your treatment).
- Consider implementing a call (or a clear consistent offer of a phone call) during the 2WW. As most (71%) patients agreed they would like a phone call in the 2WW, but one patient tended to disagree with this but not strongly.
- Most patients neither agreed nor disagreed that the centre could do more to help patients cope during the two-week wait. Only 57% of patients felt supported during the 2WW. Perhaps implementation of the PRCI could help address this.

In response to patient feedback an offer of a call from a nurse during the 2WW was introduced on the 21st April 2021. Additional feedback questionnaires were once again given out at embryo transfer for a 4-week period while phone calls were being offered (10/05/2021- 02/06/2021) to determine whether patient satisfaction improved. Questionnaire forms were given out to 27 patients again and 8 were returned to the clinic (30% response rate). The results of the questionnaire were summarised and shared with the team at a team meeting.

Comments from patients regarding support and suggested improvements were very positive:

"*During our IVF treatment the service received was excellent. Unfortunately, on our first cycle this was not successful, however the support received from staff members was incredible. Even during Covid they allowed my husband to attend to support me. On our second cycle I was kept fully up to date and informed of the progress made*.", "*Always very organised, never worried about chasing up or scheduling. Never a wait for long/ever in the waiting room- very happy!", "The staff were always there to listen. They never rushed any of my appointments and would ensure I was ok prior to leaving.", "A very friendly, lovely bunch!*", and "*During our two week wait I felt I was able to call the clinic at any time for guidance. Although I felt I was asking many questions I was always reassured I could call at any time*."

Full questionnaire results can be found in Appendix 14, a summary of the overall response for each section is shown in pie charts (Figure 92). Reassuringly the majority of patients felt happy with their care and improvement can been seen in all areas compared to the last survey in March 2021. There were no areas where patients were unhappy or dissatisfied with their care.

Patients were asked what emotional support they had received which was helpful. Of the respondents 75% said they (6/8) said they found support from their partner, 75% (6/8) said they found support from friends or family members, 13% (1/8) said they found support from an online support forum (such as fertility friends, Fertility UK, Fertility network UK), 76% (6/8) said they found support from the nurses, 38% (3/8) said they found support from the embryologists, 38% (3/8) said they found support from the doctors/consultants. Importantly no patients felt that they did not receive any helpful support. Respondents did not find emotional support from; receptionist/admin team, support groups that met in person, telephone helplines, counsellors found separately from the clinic, or the clinic's counsellor (0/8 actually had a counselling appointment). When asked about counselling at the clinic all (8/8) patients remembered receiving information about how to access counselling, though none of them actually accessed counselling sessions at the clinic. It is reassuring that 100 % of patients could recall the offer of counselling.

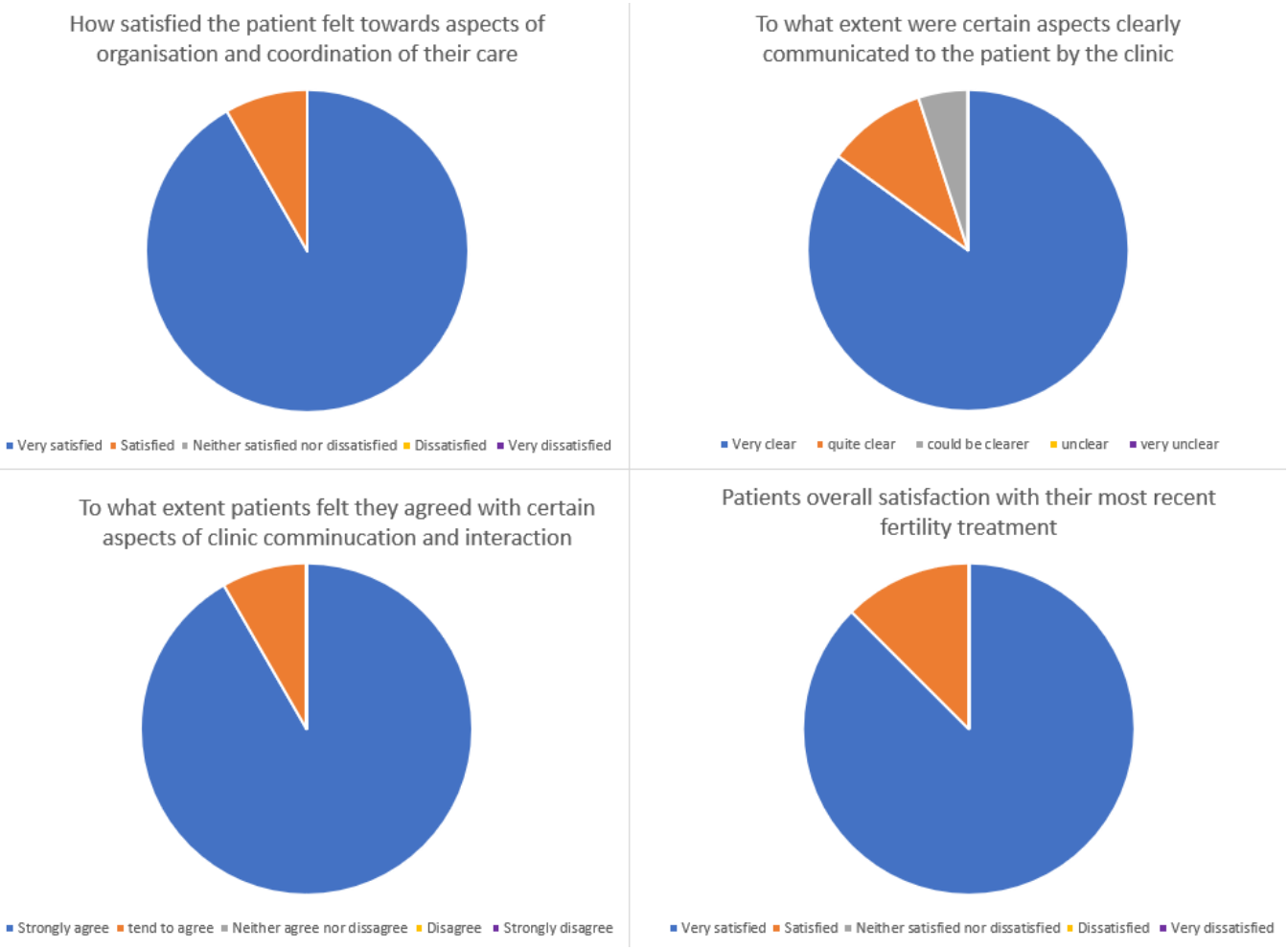


Figure 92 Overall patient satisfaction responses during the 10th of May to the 2nd of June 2021 following implementation of the HADs and 2WW calls. (n=8 patients).

Patients were asked what the clinic could do to better support its patients, results shown in Table 17. Once again improvement can be seen in many areas compared to the last survey.

Since implementing the offer of calls the number of patients who agreed they would like a phone call in the 2WW has reduced from 71% to 43%. However, since explicitly offering the calls 100% of patients now agreed they felt supported during the 2WW, compared to 57% in the previous survey. A great improvement. Overall half of patients stated they would like a phone call a week after pregnancy result, something the clinic could consider implementing. Once again, all respondents felt supported by the clinic throughout treatment but now 100% felt they strongly agreed. No respondents thought that the clinic could do more to help them during the 2WW. This has completely switched around after implementing the explicit 2WW call offer at embryo transfer.

Table 17 Results from additional patient feedback questionnaire regarding support Ma/June 2021

What could we do better to best support our patients?	
The centre manages patient expectations well during treatment	7/8= Strongly agree 88% Improved by 31% 8/8 = Strongly agree + tend to agree 100% No change
The centre always ensures privacy and dignity during scans, tests and treatments	8/8 = Strongly agree 100% Improved by 14% 8/8 = Strongly agree + tend to agree 100% No change
The centre allows sufficient time for patients to absorb new information	7/8= Strongly agree 88% Improved by 31% 8/8 = Strongly agree + tend to agree 100% No change
The centre provides information on possible physical and emotional symptoms	6/8= Strongly agree 75% Improved by 18% 8/8 = Strongly agree + tend to agree 100% Improved by 14%
I would like the centre to phone me halfway through the 'two-week wait' **(three patients neither agreed nor disagreed, one patient tends to disagree, One patient did not answer)**	3/7= Strongly agree 43% Up by 29% 3/7 = Strongly agree + tend to agree 43% **Down by 28%**
I felt supported during the 'two-week wait' and was able to speak to the centre if I needed to **(All patents agreed)**	5/8= Strongly agree 63% Improved by 20% 8/8 = Strongly agree + tend to agree 100% **Improved by 43%**
I was offered counselling at the time of my pregnancy result **(only 4 patients responded to this question) (one patient neither agreed nor disagreed).** (Perhaps this question is not well phrased as patients may have filled in the form prior to being told their result).	1/4= Strongly agree 25% Down by 25% 3/4 = Strongly agree + tend to agree **75%** **No change**
I would like the centre to phone me a week after any pregnancy result **(One patient did not answer) (three patients neither agreed nor disagreed)**	1/7= Strongly agree 14% Down by 3% 4/7 = Strongly agree + tend to agree 57% up by 24%
I felt supported by the centre throughout treatment **All patients strongly agreed to this**	8/8= Strongly agree 100% **Improved by 43%** 8/8 = Strongly agree + tend to agree 100% No change
The centre could do more to help patients cope during the 'two-week wait' **(one patient did not answer)** **No patients agree that the centre could do more**	**0/7= Strongly agree 0% (no change)** 0/7 = Strongly agree + tend to agree 0% Down by **14%** 3/7= Neither agree nor disagree 43% Down by 28% 3/7= Tend to disagree 43% Up by 43% 1/7= Strongly disagree 14% No change

To conclude this section, the response rate was low but still informative for a PDSA cycle. The feedback was overall very good, 100% of patients felt supported by the clinic throughout treatment, 100% were either very satisfied or satisfied with their recent treatment. Reassuringly no patients felt that they did not receive any helpful support. A big improvement seen is that now 100% (up from 57%) felt supported during the 2WW, and none agreed that the clinic could do more for them during this time. Improvements

were also seen across the board for all questions asked, with more patients selecting strongly agree. All patient recalled being offered counselling and how to access.

This time no patients were dissatisfied with 'being seen by the same healthcare professionals throughout your treatment' which was identified in the last feedback as requiring improvement.

This positive feedback was communicated to the team and helped staff morale, engagement and commitment to the implemented change of offering calls. It increased their workload but they were happy to continue as they could see the difference it was making to patients. The clinic continued to offer the 2WW calls as patients appeared to really appreciate it and the feedback indicates we are supporting our patients well during this stressful period.

The number of patients who accepted the offer of a call during the 2WW was monitored to get an understanding of the impact this work has on the nurse's time. The data is shown below.

Table 18 The offer of a call from the nursing team during the two-week wait.

Month	Number of patients having embryo transfer	Number of patients who would like a call	Number of patients that were uncontactable	Uptake rate	non-contact rate
Apr-21	11	7	0	**64%**	**0%**
May-21	26	14	3	**54%**	**21%**
Jun-21	28	17	2	**61%**	**12%**
Jul-21	19	15	3	**79%**	**20%**
Aug-21	26	19	1	**73%**	**5%**
Sep-21	27	19	4	**70%**	**21%**
Oct-21	27	15	1	**56%**	**7%**
Nov-21	29	23	6	**79%**	**26%**
Dec-21	27	20	3	**74%**	**15%**
Total	**220**	**149**	**23**	**68%**	**15%**

In total 220 patients have been asked if they would like a call during the 2WW since the 21st of April 2021 and 68% of them accepted the offer. This is a fairly substantial increase of workload for the nurses to take on varying from 7 to 23 calls each month, roughly 4-5 calls a week. Prior to the introduction of the offer to call the nursing team took 33 calls

from patients waiting for treatment outcome during a 6-month period from 21st of January 2019 to 26th July 2019 that's roughly 1.4 calls a week. These incoming calls may have now reduced with the introduction of a call from the team however the nursing workload has increased. This is made worse by patients not being available to answer the phone resulting in the nurses having to try multiple times or leave messages to call back. The team could not contact 15% of patients who requested a call.

This improvement work increased the workload of the nurses as expected but they were engaged with the project and happy to continue because they could see an improvement in patient feedback. The process was embedded into practice and was sustained throughout the project and beyond.

3.3.7 Positive Reappraisal Coping Intervention (PRCI)

Following on from the feedback in the section above the PRCI would be introduced to patients following embryo transfer from the 30th of June 2021. An additional patient feedback questionnaire accompanied the psychological intervention and patients were encouraged to return the feedback form regardless of whether they used the PRCI or not. This questionnaire is shown in Appendix 7. Of the 169 patients who were given an envelope containing the PRCI information after embryo transfer just 28 forms were returned to the clinic. There is a high nonresponse bias (83.4%) and it is not clear how many patients might have used the PRCI and not returned the feedback form. However, for a period of time all patients were at least given the option to use the coping intervention technique to manage their worries during the waiting period and this was the part of the improvement intervention. Of the patients that provided feedback on the PRCI the majority did not use it and gave a reason why. No patients used the PRCI intervention at least twice a day as advised in the A4 leaflet provided by Cardiff University. Figure 93 illustrates how the patients who responded used the PRCI that was offered.

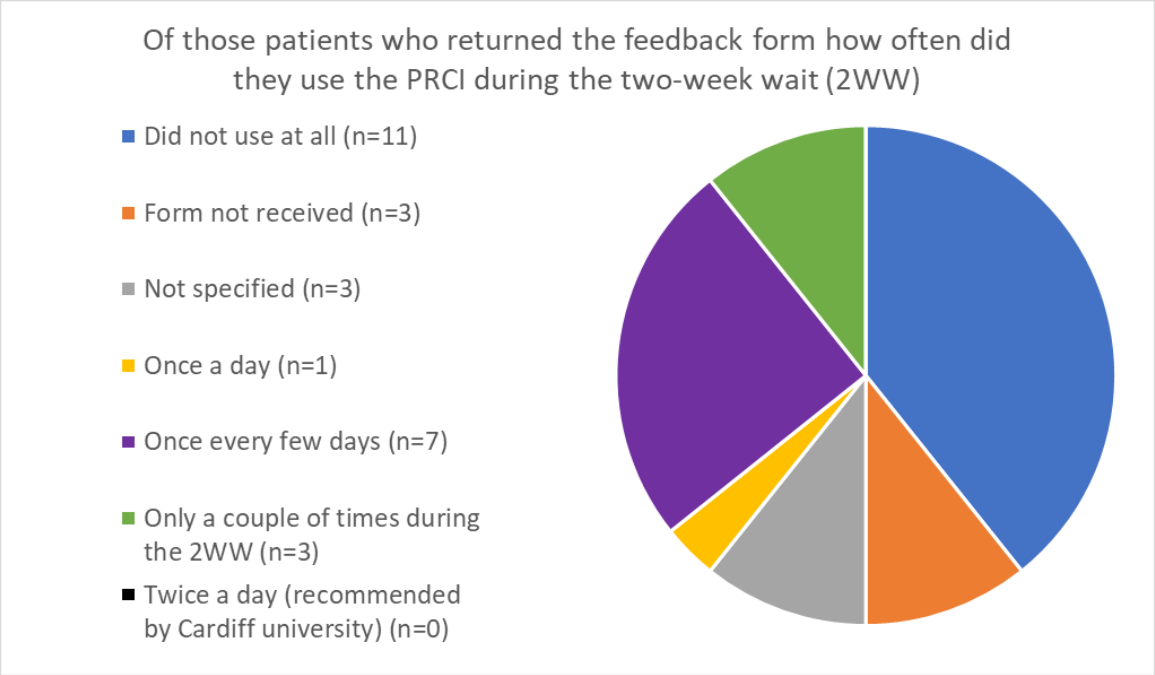


Figure 93 How was the PRCI used by the patients who returned the feedback form. (n = 28 patients).

Of the patients who returned feedback and used the PRCI to some extent 16 provided a rating for how much they agreed with statements about the ease of use and perceived benefit of the PRCI. Data shown in Figures 94 and 95. On average the feedback was positive with all means above 4.0 so to some extent patients felt the PRCI was easy to use and helpful, all but two patients would want to use the PRCI again and would recommend it to others during the 2WW. Only one did not find reading the PRCI statements helpful in some way. This small data set reflects the studies of Lancastle & Boivin (2008) and Ockhuijen et al, (2014) that demonstrate the use of the PRCI is feasible in the IVF context and was perceived by patients as an acceptable intervention to help reduce the strain of waiting for pregnancy test results during fertility treatment. The majority of patients who stated they did not use the PRCI had already been through their first IVF attempt and had either already learnt how to cope or they tried not to get emotionally involved during the 2WW. Others stated they did not use it because they felt treatment would work, or they were already well supported and/or had made plans to look forward to or kept busy at work during the 2WW. One patient had forgotten, a few were not made aware of the PRCI. Those who used the PRCI to some extent left comments;

'*Can I please add that the PRT was a brilliant idea but nothing changed my nerves because it's my third attempt so no criticism of the form itself*', '*A lot of this is within my daily*

approach and practice e.g., meditation', *'I think is a really good technique its basically my lifestyle so for me it's just more than what I do, I am sure is really helpful for many people. First one was so difficult for me. This time I am more relaxed. I have hope, faith. I know the treatment better less stress but super tired'*, and '*Thank you for the card it was really useful and a conversation starter. We used it when either of us was feeling low rather than each am/pm as felt we were too repetitive with our answers this frequently*'.

As this low-cost self-help psychological coping intervention was felt to be useful to some patients going forward the clinic decided to offer the PRCI at embryo transfer as an option for patients to take away only if they wish (would no longer be given as part of the embryo transfer information pack). Forms and cards would be made available in the treatment room for patients to look at and take away with them.

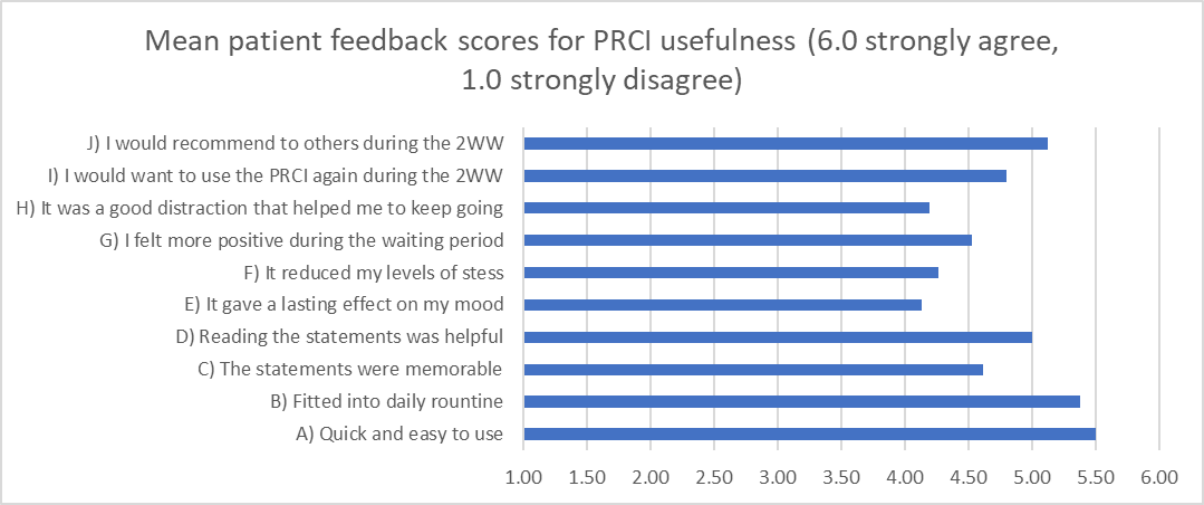


Figure 94 Patient feedback scores for the usefulness of the PRCI and listed questions (n=16 patients).

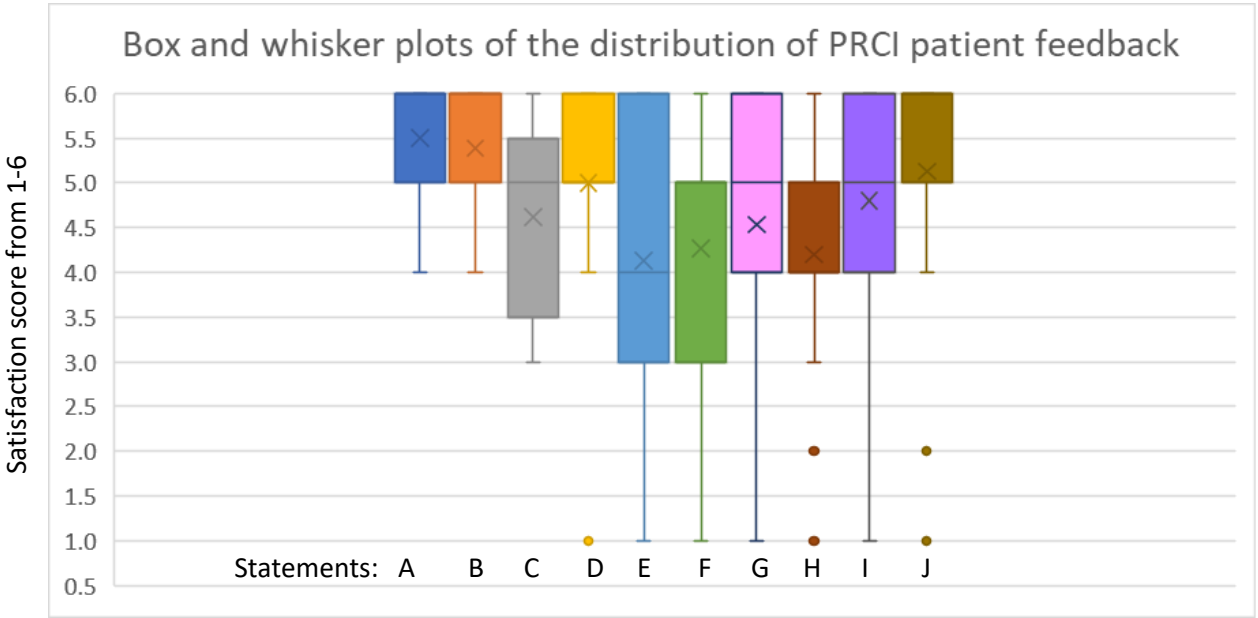


Figure 95 Box and whisker plots of the same data showing the distribution of scores. Very few patients scored a low score of 1 or 2 and were outliers. (n=16 patients).

3.3.8 Patient discontinuation rates

The clinic has never monitored its treatment discontinuation rates, like many clinics and published studies the focus is on KPIs per egg collection or embryo transfer procedure, and not cumulative pregnancy rates. As part of the improvement project there was an assumption that improving patient support might help to reduce the burden of treatment and keep patients in treatment. This would see an improvement in the discontinuation rate, possibly decreasing time to pregnancy. Data was retrospectively collected from two time periods before and after the implementation of the HADs forms in October 2020. Troude et al, (2014) identified characteristics of couples who discontinued IVF treatment showing that older women, women with duration of infertility >5 years or medical factors associated with impaired chance of successful IVF, with female factor or unexplained infertility, with 0 or 1 oocyte retrieved and no embryo transfer during the first IVF were more likely to discontinue treatment early. To reduce the effect of poor prognosis patient groups on the results the following criteria was used to generate a list of egg collections within a time period for follow up. Inclusion criteria; maternal age of <38 years, >1 egg collected, had a fresh embryo transfer, and did not have a clinical pregnancy confirmed by scan at 7 weeks. Unfortunately, infertility type and duration were not recorded and could not be excluded. The follow-up of the patients was 6-months from the primary outcome of the egg collection that occurred within the selected time period. Patients going on to have treatment elsewhere and treatment interruptions due to recommendation by clinician (e.g., polyp removal) cannot be excluded and would be assumed to be discontinued treatment. The data is shown in Table 19.

The patient discontinuation rate reduced in the time period from October 2020 to September 2021 following implementation of the HADs forms. It is unlikely that the lockdowns and Covid-19 influenced these results because although the clinic shut down from March 2020 and reopened in July/August 2020 there were many cases from 2018 and 2019 who had plenty of time to return to the clinic for further treatment within 6 months from the egg collection. Almost two thirds of cases (n=134) had an egg collection before July 2019 and would not have been affected by the clinic closure. More patients return for further treatment cycles withing 6 months of egg collection following the introduction of the HADs forms in October 2020 but this was not significant. This is

despite the additional stress from the Covid-19 pandemic lockdowns in November 2020 and January-May 2021. A complex interplay of factors will influence a couple's decision to delay or discontinue treatment. Gameiro et al, (2012) systematic review suggested patients discontinue treatment because they choose to postpone it, due to its physical and psychological burden, to relational and personal problems, to moral/ethical objections and/or fear of negative health effects of treatment and organisational/clinic problems. Perhaps the changes made to procedures within the clinic and psychological skills assessment training for staff during the improvement work has led to marginal gains with patient support. Staff and processes are better equipped to ensure that patients receive support to meet the demands of treatment, that they have all the necessary treatment-related information and the opportunity to discuss their values, express their concerns and have their treatment misconceptions addressed, ultimately helping them to return to the clinic for further treatment attempts. The clinic will continue to monitor the discontinuation rates with a 1-year follow-up of patients to increase the data set and assess whether a significant improvement is seen. Many patients did return for more treatment beyond 6 months in both time periods following two unsuccessful cycles but this could not be included in the analysis due to insufficient time to follow-up post HADs group.

Table 19 Patient discontinuation rates pre and post HADs implementation.

Time period	**January 2018 to September 2020 pre HADs**	**October 2020 to September 2021 post HADs**
Number of cases having egg collection within this time period with an unsuccessful attempt	205	68
Number of those cases undertaken another cycle within 6 months of egg collection	106	40 (includes 1x FAE, 1x awaiting scan outcome)
Clinical pregnancy rate per embryo transfer of the repeated attempt	43/106 = 40.6%	15/38= 39.5%
Discontinuation rate following failed cycle*	99/205 = 48.3%	28/68 = 41.2%
Number of cases with two failed attempts following egg collection	63	28
Number of those cases undertaken yet another cycle within 6 months of egg collection	0	0
Clinical pregnancy rate per embryo transfer of the repeated attempt	n/a	n/a
Discontinuation rate following 2nd failed cycle	63/63 = 100%	28/28 = 100%

Not statistically significant *Pearson Chi-Square P= 0.308

3.3.9 Time to pregnancy and conservative cumulative clinical pregnancy rates

The clinic has never monitored its cumulative pregnancy rates, all KPIs focus on success per single cycle or embryo transfer. Cumulative live birth rate is generally perceived to be the preferred reporting system for fertility, however an international consensus on how this statistic is calculated, reported and interpreted is lacking (Maheshwari et al., 2015). It is interesting to establish a baseline for the clinic's cumulative pregnancy rate and time to pregnancy, and see if the changes made to improve patient support have helped patients with the burden of treatment enabling them to return for more than one cycle, quicker, and have a better chance of a clinical pregnancy. Data was collected from two time periods before and after the implementation of the HADs forms in October 2020. Patients included in the data set were under 38 years old and undergoing their first egg collection between the time periods of January 2019 to Sept 2020 and October 2020 to September 2021. This would allow a 6-month follow-up of the patients from the primary outcome of their first egg collection that occurred within the selected time period. Conservative cumulative clinical pregnancy rates were calculated by dividing the number of women achieving a clinical pregnancy within a predetermined number of cycles, by the total number of women starting treatment. One method described by Maheshwari et al, (2015) for cumulative live birth rates.

The data for both time periods is shown in Table 20. There were no 3rd cycles within 6 months of the first egg collection for both time periods.

The cumulative pregnancy rate was higher for the post HADs group but this was not significant. This was despite the Covid-19 second wave and November and January-May 2021 lockdowns and limited egg collection lists for the clinic in 2021 due pressures on Trust theatres. The clinic will continue to monitor this data and follow the patients up to 1 year to increase the data set. When the same data is plotted by Kaplan-Meier survival analysis the time to pregnancy can be seen (Figure 96). The differences seen are not significant (P= 0.372) but in the post HADs time period (group 2) 50% of the patients achieve a clinical pregnancy faster at 4 months following first egg collection compared to the pre HADs time period (group 1) of 5 months. An interesting trend that perhaps 6 more months of follow up might help confirm any significant improvement.

Table 20 Patient conservative cumulative clinical pregnancy rates pre and post HADs implementation.

Pre HADs January 2019 to September 2020	Cycle 1	Cycle 2
Number of women entering treatment (egg collection within this date range)	192	82
No. of women with a clinical pregnancy at scan	62	38
Clinical pregnancy rate per cycle	62/192 = 32.29%	38/82 = 46.34%
Cumulative clinical pregnancy rate	32.29%	(62+38)/192 = 52.08% *
Post HADs October 2020 to September 2021	Cycle 1	Cycle 2
Number of women entering treatment (egg collection within this date range)	114 (excludes 1x awaiting scan outcome)	54
No. of women with a clinical pregnancy at scan	37	29
Clinical pregnancy rate per cycle	37/114 = 32.46%	29/54 = 53.70%
Cumulative clinical pregnancy rate *	32.46%	(37+29)/114 = 57.89%*

Not statistically significant * Pearson Chi-Square *P* = 0.365

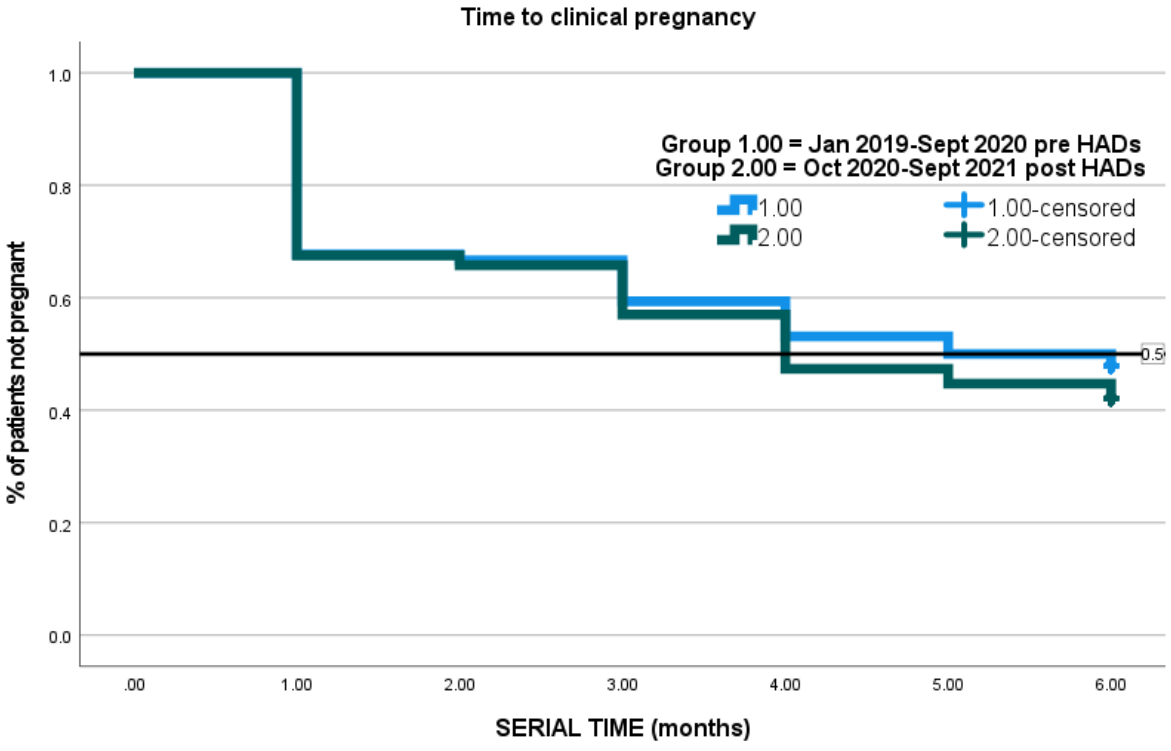


Figure 96 Kaplan-Meier curve generated by SPSS for time to pregnancy plot over a 6-month study period. By 6 months 47.9% of patients in group 1 have yet to achieve a clinical pregnancy (Mean group 1 = 3.969 months, Median = 5 months), compared to 42.1% of patients in group 2 (Mean group 1 = 3.825 months, Median = 4 months). Group 2 reached 50% pregnancy quicker at 4 months compared to 5 for group 1.

3.3.10 Staff feedback and patient complaints

Staff were encouraged to engage with the project and provide any feedback to the QI team for improvement. Most feedback was positive. The only changes suggested by staff was the responsibility of the offer of the 2WW calls record sheet switching from the lab to the nursing team. This came from the nursing team who were happy to take on the extra work to ensure it was accurate and no patients were missed. Patient complaints are addressed at the clinic's team meetings and none referred directly to patient support offered by the clinic and the QI project. The counsellor feedback that the completed HADs forms recorded in the patients' medical notes were beneficial to counselling sessions and believed that a few patients, booked for supportive counselling because of a raised HADs score, were averted from a potential psychiatric crisis due to early support and intervention.

3.3.11 Summary of results

Small changes were implemented in order to create marginal gains in patient satisfaction feedback, up-take of supportive counselling, cumulative pregnancy rates, and discontinuation rates. Patient satisfaction feedback remained consistent but less variation was observed following interventions for improvement. More patients took up supportive counselling sessions post intervention but this was not significant. The improvement work may have helped to decrease patient discontinuation rates, time to pregnancy and increase cumulative pregnancy rates but this was not significant and a further 6-month study period would be helpful for these long-term measures.

Use of quality improvement tools and undertaking PDSA cycles as a team helped the clinic to better understand the emotional support needs of our patients and equipped staff to make changes for improvement. Although no significant improvements were observed as a direct result of the interventions trialled all measures were maintained or appear to improve despite further compounded psychological distress for infertility patients from the Covid-19 pandemic and clinic closures.

Chapter 5. Discussion

5.1 Embryo culture

Focussing on process metrics the intervention has reduced the number of door openings of incubators 3 and 5 and this is irrespective of the number of cases and eggs collected on the day. It has also reduced the number of practitioner 'paces' taken during procedures when carrying dishes around the laboratory with associated benefits of reduced procedure length, reduced exposure of ICSI eggs to suboptimal conditions and reduced risk of an incident in the laboratory. As expected, there was great variation in much of the data collected for this project and this was all common cause variation. The only special cause variation observed occurred when looking at the incubator gas data. Incubator 3 on the 5th week 07/03/2018 had exceptional range from the lowest to the highest readings measured between 8am and 4pm, investigating reasons for this it became apparent that ambient water was added to incubator 3 (humidified incubator) in the morning when it had no embryos/eggs within it to top up the supply. Interestingly this did not affect the temperature of the incubator as much as it affected the carbon dioxide and oxygen levels. Reassuringly patients with eggs incubated within incubator 3 that afternoon all became pregnant. This demonstrates how averages of data can hide information about a system.

This project relied on the engagement of the whole laboratory team to implement the changes in the action plan. It is possible that the measurements used within this project could be subjected to other causes of variation not controlled for or monitored as a balancing metric. For example, the batch number of all consumables used in each treatment cycle, how well patients adhered to their drug regimes, practitioner variation during procedures and adherence to the intervention of fewer dishes out of the incubator at one time. Frydman et al, (2004) demonstrate how continuous changes prevent critical overview of the team's assisted reproduction techniques, it is difficult to link outcomes to individual processes within the IVF system because of great variation that is difficult to control for (Frydman et al., 2004).

Timescale limitations to plan and carrying out the project, alongside weekly metric data collection and the delay in longer term outcome measures of IVF meant that this PDSA cycle was longer than usual. Due to these challenges an intervention bundle within one PDSA or several simultaneous PDSA (ACT, 2018) were tested in the hope that they would have a 'marginal gain' effect on the culture stability. It is acknowledged that it may be

difficult to attribute any improvements made to an individual intervention. One metric collected was documenting how often the incubator doors were opened in a day by marking a sheet of paper attached to each door. This was not a perfect measurement because it relies on people remembering to do it and it may be subject to the Hawthorne effect because practitioners were aware of the observations being made (NHS Wales, 2010). The practitioners may have improved an aspect of their behaviour, such as making an effort to avoid opening the doors, simply because they were being observed experimentally (NHS Wales, 2010). Use of an A3 to capture the progress of the project for the team was very straightforward and nicely illustrated the potential gains from the work being done by the team and fuelled further engagement.

Due to the intervention bundle the frequency of incubator door openings was reduced by 36%. The distance oocytes travelled within the laboratory was reduced by 22% and each culture dish was out approximately 15.5 seconds less during procedures. This resulted in a 9% reduction in the time that oocytes spent outside of optimum incubator culture conditions and removed approximately 9.5 'paces' taken by practitioners during procedures. The daily fluctuation of incubator O_2/CO_2 gas levels showed materially significant reduction. No meaningful change was seen with incubator temperature fluctuation. Outcome measures of fertilisation rate, embryo utilisation rate, implantation rate, and live birth rate remained consistent. This work resulted in improvement in the culture system workflow by refining processes, without impacting on clinical results and at no extra cost to the clinic.

The project aim to reduce culture disruption was met but this did not lead to improvement in measurable outcome measures e.g. live birth rate.

The project was continued to run past September but further changes were made to processes when a new box type incubator was installed (Incubator 1) underneath the MIRI incubators and used to equilibrate dishes. Negating the need to bring dishes from incubator 4 to the benchtop incubators before use.

The lab team learnt from the project experience, which highlighted the value of QI for continuously driving better ways of doing things and encouraging a mindset of QI, enabling staff to suggest and make changes to the way of working. A QI movement

beginning to gain momentum within the IVF centre. A focus on performance improvement within the laboratory (e.g., temperature monitoring/mapping, fewer dishes out at one time, reducing door openings) may have influenced practitioners' behaviour and encouraged best practice and adherence to standard operating protocols.

It is important to disseminate any learning from QI, even is unsuccessful, so that our profession can benefit from understanding how industrial manufacturing principles can be applied to fertility clinics to drive continuous quality improvement. It would be assumed that in a larger IVF clinic with higher throughput of cycles this type of performance improvement may lead to even greater and more significant rewards.

To conclude, clinic staff engaged with the project that emphasised the importance of QI within the laboratory. This work resulted in improvement in the culture system workflow by refining processes, without impacting on clinical results. Team exploration of QI principles was a valuable learning experience encouraging a mindset of continuous QI and accelerated performance improvement within the IVF laboratory.

5.2 ICSI

The clinic was able to detect a drop in its fresh ICSI implantation rates through monitoring KPI's. Due to the low cycle volumes at the clinic the trend was picked up over an extended time period. The clinics clinical and laboratory team used a series of quality improvement tools, root cause analysis, literature review, and input from an external review to identify potential problems with the fresh ICSI pathway and protocols, developing interventions that addressed these areas for improvement. Several recommended changes, supported by evidence, were identified, and assumed to deliver improvement in the fresh ICSI success rates. The project highlighted the difficulty of IVF clinics with low cycle volumes to sensitively monitor KPI's in a timely and responsive way. The very nature of delayed outcomes with confirmation of a pregnancy many weeks after an ICSI cycle and the need to accumulate sufficient data to be confident of any patterns/concerns means small clinics could be less responsive to any problems or may even be too reactive to false positives.

Due to the urgency and commitment of the clinic to improve its fresh ICSI success rates many changes were made at the same time. Ideally it would have helped identify the more effective interventions by having many PDSA cycles and changing only one thing each time. This approach was not selected because of the inherent delay in outcome data with fertility and low cycle numbers meaning that the clinic could go on for many months without seeing any improvement, something that the team were not prepared to do. Therefore, a bundle of changes was implemented together based on best practice and an external review. This felt more ethical, responsive, and low risk as none of the interventions were expected to reduce performance. However, this approach was more expensive as some interventions (e.g., purchase of new equipment and increased progesterone dose) had an associated increased cost to the clinic and this 'bundle' approach would complicate attribution of improvement to specific changes made.

The improvement project was affected by the Covid-19 pandemic, which cut short a promising improvement trend in fresh ICSI success rates in the first quarter of 2020. Additional changes to the service and procedures were required in response to the pandemic when the clinic reopened for fresh cycles in August 2020 to enable treatment to resume safely during the Covid-19 emergency whilst maintaining compliance with the

Government's current requirements. This affected the initial fresh cycle results in many ways including theatre use, staff and patient wellbeing, the prioritization of patients on the waiting list, and a more cautious approach to OHSS. It was reasonable to prioritise patients in whom delay is most likely to significantly affect the outcome of treatment (ARCS, 2020). Many poor prognostic patients at special risk include those with a low ovarian reserve, advanced age and those facing extirpative pelvic surgery (for instance due to severe endometriosis or bilateral ovarian cysts). This patient group prioritisation strategy and the increase in FAE cycles for the best prognosis group likely had an effect on clinic success rates following recommencement of treatment.

Balancing measures provided important information to a complex system helping to inform how the system's performance changed over time and provided possible explanations. Monitoring the KPI measures as weekly averages displaying variation over time helped to identify and interpret patterns that might otherwise have been missed e.g., egg numbers and maternal age. It is hard to detect relatively small changes with SPC, perhaps the use of more statistical tests on the data set could have provided further information to the study.

Although an improvement was observed during this study it required a longer amount of time to show this on an SPC chart, due to the shutdown period and reduced activity of a small IVF clinic which already had low fresh cycle volumes. An increase in FAE cycles reduced the fresh cycle data further. The improvement work was not as responsive as was desired. The statistical KPI monitoring system demonstrated by the current study may be more effective at identifying KPI shifts in larger clinics with higher cycle volumes.

There is no agreed optimal protocol for ICSI and processes vary from clinic to clinic (Simopoulou et al., 2016). A much-needed ICSI best practice paper is due for publication this year. The clinic's clinical and laboratory team used a series of QI tools, root cause analysis, literature review, and input from an external review to identify potential problems with the fresh ICSI pathway and protocols, developing interventions that addressed these areas, for improvement. Implementation of the interventions improved the fresh ICSI pregnancy rates but the Covid-19 pandemic and treatment recommencement in 2020 had an impact of the improvement work. Extended time was

required to ensure sufficient data was available to establish if the interventions resulted in an improvement, making the improvement work less responsive than desired.

Although performance has significantly increased and has been successfully recovered above benchmark threshold, the QI team did not manage to get to the root cause of the initial dip in ICSI implantation rate which triggered and motivated the QI work. The situation required fast action and it was more responsive and ethical to implement a bundle of interventions aimed at addressing all possible causal factors, based on best practice and an external review, for patient care.

The changes made and continued improvement has been sustained within the clinic with no drift in protocols. This was possible due to a small team with excellent engagement and commitment from all staff. The clinic will continue to closely monitor the KPIs, more data points on the SPC charts would help to demonstrate whether this significant improvement is sustained due to the changes made.

It is worthwhile disseminating this root cause analysis and improvement work to the assisted conception field as there are limited published reports where embryology KPIs are tracked following defined and controlled laboratory or clinical changes (Hammond & Morbeck, 2019).

This project could be more effective within a larger clinic with higher cycle volumes. Interventions made within this project may not be effective or suitable within other clinics due to each clinic's unique patient population and ways of managing workloads. Each clinic would need to be informed by its own data analysis on the optimal ICSI procedure.

The next steps for the clinic to continuously improve its fresh ICSI cycle success rates and to increase capacity would be, to provide more flexibility to egg collection days having two theatre lists back when the Trust allows, and to review procedures again when the ICSI best practice paper is published later this year.

5.3 Patient support

Due to the burden of fertility treatment and the high chance of failure per treatment cycle it is critical that clinics support patients throughout their treatment journey and provide patients with a 'good' experience irrespective of treatment outcome (HFEA, 2018C; Gameiro et al., 2013a). Evidence suggests fertility patients have an increased risk of developing symptoms of psychological distress, depression and anxiety despite them having no previous record of mental health issues in their medical history (Klemetti et al., 2010). The Covid-19 pandemic and clinic closures resulting in delay of fertility treatment has further compounded patients' psychological distress (Lawson et al., 2021; Boivin et al., 2020). There is a positive association between the experience of patients and improved outcomes and patient safety (HFEA, 2018c), and a need for QoL to be addressed by clinics (Boivin et al., 2011; Gameiro et al., 2013a). Validated QoL questionnaires are available to serve as a way to identify and address risk factors for poor adjustment to infertility or its treatment, and addressing patients QoL could lead to improved patient outcomes and experience (Boivin et al., 2011). However, assessment of QoL of fertility patients as part of clinical practice has yet to be adopted. This is the first QI UK study to implement the HADs questionnaire as part of clinical practice as a way of screening patients, addressing patient QoL and providing a measure for QI. The HADs data for patients at initial consultation and post embryo transfer during the pandemic in a clinical setting is novel and reassuring to see that the majority of patients scores fell within the normal range for anxiety and depression. The numbers are small but a trend was seen of increased anxiety and depression levels post embryo transfer, supporting the findings of Ockhuijsen et al, (2014) who showed anxiety and depression levels were significantly higher during the waiting period (day 10 post embryo transfer) compared to just before. Following implementation of the HADs there were no adverse events of cancelled cycles on the day of treatment due to anxiety and distress. One of the main aims of the project.

Gameiro et al, (2013b) demonstrated that 22% of patients discontinue their treatment primarily for psychological reasons, despite a good prognosis and the ability to cover the treatment's cost. The experience of a failed treatment cycle can discourage patients re-engagement with treatment (Gameiro et al., 2012). This treatment discontinuation before

the most cost and clinically effective number of cycles have been completed (3 full cycles) (NICE, 2013), is associated with a 15% lower pregnancy rate (Gameiro et al., 2013b). The cumulative effect of three complete cycles increases the chances of a successful pregnancy up to 45–53% for women <40 years old (NICE, 2013). Therefore, if patients were supported to undertake the optimum number of treatment cycles, through reducing the psychological burden of treatment, then more patients would achieve a live birth. However, many fertility clinics do not measure patient discontinuation rates or focus on performance indicators beyond the denominator of a single cycle of embryo transfer or egg collection. Treatment is usually discussed on a cycle-by-cycle basis with patients, possibly leading to mismanaged patient expectations of a single cycle of IVF. This QI study looked at the impact of improvement interventions on patient discontinuation and cumulative pregnancy rates. In doing so the study encouraged the clinic to gain an understanding of what these rates were for our patient population and how this relates to the burden of treatment and the patient experience. Although no significant changes were identified, the clinic's discontinuation rates showed a reduced trend following implementation of the HADs forms, and cumulative clinical pregnancy rates appeared to improve with a quicker time to pregnancy. This was despite the complexities and interference of the pandemic on the results.

It is not clear whether a better uptake of counselling services would reduce patient discontinuation. Studies have shown that only 20% take up the offer and attend a counselling appointment (Rajkhowa et al., 2006; Boivin, 1997; Hammerberg et al., 2001) despite patients expressing an interest in taking up counselling, the actual take-up rate is low. The number of patients booking a counselling session increased following the HADs implementation to the point that additional sessions had to be provided by the centre but it is not clear whether this was caused by the introduction of the HADs forms or as a result of the pandemic and delays in access to treatment. The study identified the clinic's supportive counselling uptake rate was in line with published studies and increased slightly after implementing the HADs, but this was not materially significant.

Many studies suggest a link between mental health, psychological interventions and pregnancy rate (Boivin, 2003; Frederiksen et al., 2015; Katyal et al., 2021). Simpler, more cost effective, self-administered psychological interventions have been developed that

can easily be integrated into the clinic setting as they require little staff time. Yet very few UK clinics offer such interventions as part of clinical practice. This study provides further evidence to support the findings of Ockhuijsen et al, (2014) and Lancastle & Boivin (2008) that the PRCI could prevent an increase in anxiety during the waiting period for treatment outcome, is perceived by patients to be acceptable, practical, and there was some psychological benefit to its use. This study demonstrates the ease of use of the PRCI within a clinical setting to those patients who want to use it, at no cost to the clinic. More data is required to evaluate its impact on clinical pregnancy and discontinuation rate. Take-home tools such as the PRCI can be used by patients as and when they are needed, to manage the demands of treatment thereby potentially improving their ability to endure the challenges of treatment, maintaining QoL, and helping them to return for a second or third attempt. More data is required but the common cause variation for average HADs anxiety and depression score for patients post embryo transfer decreases following the implementation of the offer of the PRCI, resulting in less fluctuation of scores following its introduction. The HADs data also appears to support the evidence that the PRCI is associated with reduced symptoms of anxiety during the waiting period (Ockhuijsen et al., 2014) but more data is required.

The project did not see any significant improvement in the chosen measures and the main aim to increase standard patient feedback to >80% within the 'excellent' field was not achieved for some measures. Other measures were already providing excellent feedback and were perhaps not sensitive enough to any of the improvement changes. Feedback was assessed as a monthly average rather than weekly due to insufficient numbers of returned forms. It is important to note that the many changes made to clinical practice in response to the pandemic did not appear to reduce patient satisfaction, with all measures maintained at an average patient's satisfaction score of at least '4' or 'good'.

The strengths of this project were the engagement with staff and patients. Staff training, regular meetings, and updates kept staff interested and involved. The snap shot patient surveys proved a helpful way to understand our patients needs during the 2WW, evidenced the basis for changes for improvement, and adjust feelings and assumptions about what patients actually want. Despite a low response rate to the survey, any

feedback is better than making assumptions and low numbers are not a concern with PDSA cycles where the idea is to test changes in some small way, even a single patient, and then build from there. It was a real success to implement the offer of a call within the 2WW despite the additional workload this created for the nurses, and patients truly appreciated it. The process was sustained and continues without the input from the QI lead.

What would have made the project better might possibly have been the use of real-time customer feedback kiosks, electronic feedback platforms or online patient surveys sent following appointments. This might have been more sensitive to monitor the impact of changes and track trends instead of relying on paper forms which patients must return. This was looked into by the QI lead but was not possible to implement in good time for the project baseline data collection and was not pursued. In future it would be helpful to have real-time feedback for small QI cycles.

The biggest limitation for this project was the large nonresponse bias due to poor response rates with paper feedback forms for standard patient feedback, HADs forms post treatment, and PRCI feedback. It is possible that the respondent data used in the project does not fully represent the breadth and depth of the clinic's patient population. A large nonresponse bias would influence the reliability and validity of survey study findings. The main project measures were questions from the standard clinic feedback form so it relied on patients completing these forms and returning them to the clinic. The response rate for these forms remained consistent following changes for improvement with the baseline data for the project. However historically there is a proportion of our patient population that we cannot be sure of their experience of treatment and whether anything could be improved as they do not return any feedback forms.

Another limitation was the completion of HADs forms away from the clinic and not in person. Ideally for better accuracy HADs forms should be completed on the spot with a healthcare practitioner to get the patient's immediate reaction to each item rather than allowing time and a long thought-out response. The original project plan was for the HADs forms to be complete by patients while they wait for their appointment in reception, the forms could then be scored and addressed at their appointment. This was not possible due to the requirement to limit patients waiting in reception for social

distancing reasons. The solution was to post out the forms and ask patients to return them at their next appointment. This method had a surprisingly good response rate for patients at initial consultation but not following embryo transfer. The post embryo transfer forms which were returned often varied by which day the form was completed by the patient, some did not follow the instruction to complete the form on day 10 of the 2WW and instead completed straight after the embryo transfer procedure.

The PRCI feedback had a high nonresponse bias possibly because there was too much paperwork given to patients at embryo transfer appointment which could have overwhelmed patients. An online feedback survey might have had a better response but the clinic does not use a patient portal nor does it regularly communicate with patients by email. No patients used the PRCI as frequently as recommended by Cardiff University, despite the A4 leaflet instructing them of how best to use the coping technique. There were also some communication issues with the team offering the PRCI to patients, with the offer not being explicit enough, patients did not know what they were given, or in some cases were not actually given an envelope with the PRCI. This was made worse by staff sickness of the QI lead.

It is likely that the Covid-19 pandemic had an impact on the project results. More patients would be suffering from anxiety or depression, finding treatment hard, and increasing the demand for counselling. Therefore, an increase in counselling uptake may not be solely due to implementation of the HADs forms but due to the stresses of the pandemic and delays to treatment. The increased demand for counselling at the clinic caused a waiting list and eventually additional clinic counselling hours were enabled. The timing of the pandemic and lockdowns is unfortunate in that it occurred around the same time of the testing of changes for improvements to patient support. The recommencement of treatment following the shutdown period required many changes to clinic procedures which would impact on staff and patient satisfaction with how services were delivered. For example, the nurses disliked consenting patients via video conferencing due to many technical issues and difficulty building a rapport with patients. Many patients found treatment especially hard due to partners not being able to attend all appointments and procedures.

Some measures were not sensitive enough to show significant marginal gains in patient support. The clinic's standard patient feedback has always been very good for most areas, therefore there was very little common cause variation for most SPC charts beyond the 4.0 'good' rating. Resulting in very narrow control limits. It is very difficult to get 100% of patients scoring 'excellent' which might have been required to improve significantly from 'good'. It is challenging to obtain significant improvement in an already excellent performing clinic. If the clinic in the study had a poor baseline data set for patient satisfaction scores the project might have demonstrated significant improvement due to the interventions implemented. It is also hard to detect relatively small changes with SPC, perhaps the use of more statistical tests on the data set could have provided further information to the study.

The clinic maintained good patient satisfactions scores despite the effects of changes to the service due to the pandemic which may have reduced patients' satisfaction. Therefore, although little improvement was seen in patient satisfaction scores perhaps the staff training and QoL screening process helped to maintain patient satisfaction scores. Gameiro et al, (2013a) suggest that optimal fertility treatment should include a way of minimising the psychological burden of ART and enhancing the delivery of treatment for patients and staff, by tackling patient vulnerability through implementation of pre-treatment evidence-based screening for psychological distress and avoiding negative patient–staff interactions through training staff in communication/interaction skills.

The nature of some of the aims with longer-term measures (patient discontinuation rates and cumulative pregnancy rates) and time limitations of the project meant that the data analysis was limited to a 6-month follow-up and the improvements seen were not significant. The clinic will continue to monitor this data and follow-up patients for a year to establish whether any improvements were made. However, the clinic now has an understanding of its general patient discontinuation rate, cumulative pregnancy rate, and supportive counselling take-up rate.

QI work to improve patient feedback would be easily replicated in a larger clinic and might yield better improvements to a larger clinic with more patients coming through the doors and more patient feedback which could be analysed as a weekly average over time.

This would be more sensitive to changes and help identify and track trends hidden by larger averages and lower numbers. Larger clinics would likely have paperless processes and different ways of managing patient treatment, support and feedback, with use of online consent platforms and patient portals. Easier ways of gaining real-time feedback with better response rates than relying on paper forms which patients must return. A project such as this would certainly be more beneficial and might demonstrate significant improvement for a clinic which does not already have excellent patient feedback. Some aspects of this study would not be replicable in other fertility clinics. Clinics with large case numbers and patient portals would likely not offer a phone call to patients in the 2WW as this would likely not be feasible to staff and would have additional cost. More likely that these clinics would send out automated SMS messages of support and offer to call the clinic if needed, keeping in touch with their patients by alternative means.

The changes implemented in the project have been embedded into clinical practice and sustained. This was possible due to a small MDT and great staff engagement and ownership of the improvement work. It may not be so easily sustained in a larger clinic or with staff turnover. The clinic will continue with HADs screening at initial consultation as it makes the offer of counselling more explicit and serve as a way to identify and address risk factors for poor adjustment to infertility or its treatment, highlighting to the team patients that might require extra time and/or support throughout treatment. Thereby addressing patients QoL hopefully improving patient experience, satisfaction and outcomes. The clinic will continue offering the HADs at embryo transfer for a few more months to increase the data set of patients with pre and post treatment HADs scores to establish if the reduction in anxiety symptoms is sustained. Then the clinic will cease HADs at post treatment eventually due to the poor response rate. All patients are expected to have raised anxiety during the wait for treatment outcome and all are offered counselling and follow-up appointments when told their results, therefore the benefit of a screening process is lost during this part of treatment. The clinic will continue to offer the PRCI to patients at embryo transfer but this will not be given to all patients as standard but offered instead. Patients who would like to take one of the forms and would like to try it are free to take one from the treatment room.

This QI work will continue with further monitoring of the chosen measures to establish if any significant improvements could be attributed to the changes made to patient support, including follow-up of patient outcomes and discontinuation rates for a further 6 months. Going forward with any additional QI work more sensitive feedback measures would be useful, the clinic will push for more patient feedback and encourage a better response rate so that we can reduce the nonresponse bias of our standard patient questionnaires. The clinic will also explore the use of real-time customer feedback kiosks, electronic feedback platforms or online patient surveys. The next aspect for improvement of patient experience and support would be a focus on re-framing treatment to be a multi-cycle process for both patients and fertility clinic staff. As suggested by Harrison et al, (2021) a multi-cycle approach could empower patients and clinicians to discuss treatment expectations realistically and agree treatment plans that take account of the high likelihood of cycle failure in addition to the treatment decisions that may need to be made when a cycle fails. This approach could help clinics to support patients to come back for repeat attempts following failed cycles to help more patients achieve their parenthood goals.

With two out of three patients' enduring the distress of a failed IVF cycle and 25% of fertility patients rating their experience of treatment within the UK fertility sector as unsatisfactory, further studies regarding attempts to improve the emotional support of fertility patient are needed. The pandemic and fertility sector closure resulting in delay of fertility treatment has further compounded psychological distress of our patients. A focus on improving patient support has never been more pertinent.

5.4 General discussion

The MFI was a helpful approach to planning the processes involved in this QI project. It is important to conduct investigations prior to starting the use of PDSA to ensure that the 'problem' is correctly understood and framed (Reed & Card, 2016). Many QI tools were utilised in each result chapter to this effect. The primary effect of MFI is to enhance learning and accelerate improvement assuming that multiple cycles of testing change ideas are performed in small teams (IHI.org, 2018). This was certainly achieved during the study. An understanding of the SQUIRE guidelines for reporting quality improvement project was important for focusing the project design, write up and reporting of this study.

The literature review indicates that it is unclear if there is a wide-reaching understanding of how to apply QI science to effect change within the assisted conception field. Possibly because it is hard to measure improvement in IVF due to so many variables which are often out of the clinic's control (Frydman et al., 2004), inherent delays in outcomes, a culture of accepting new technologies without a solid evidence base (Harper et al., 2017), multiple competing clinical research and clinical demands, and there might be need for more expertise in this domain. A dearth of publications of QI work, especially compliant with the SQUIRE Guidelines, may serve as a reflection of this gap. In order to ensure optimal patient care for fertility patients, it is essential to support QI work and cultivate improvement culture.

The PDSA cycle presents a pragmatic scientific method for iterative development and testing of improvement changes in complex healthcare systems (Taylor et al., 2014; Moen & Norman, 2004). The four stages mirror the scientific experimental method (Speroff & O'Connor, 2004) of formulating a hypothesis, collecting data to test this hypothesis, analysing and interpreting the results, and making inferences to iterate the hypothesis. Measures involved are often different from those of typical research measurement, for instance, the focus is on the day-to-day work and the new knowledge that can be found (Crowl et al., 2015). By focusing on small tests and measuring impact of change, improvement is seen faster within an organisation, compared with use of a typical research measurement (Crowl et al., 2015). The effectiveness of PDSA as a method for improvement depends on correct application and compliance with its underlying

principles; iterative cycles, initial small-scale testing, prediction-based testing of change, use of data over time, and documentation (Taylor et al., 2014). All results chapters applied PDSA with prediction-based testing of change and use of regular data over time at monthly or more frequent intervals enabling the impact of changes to be tracked within a 'live' system. However, results chapter 1 did not use iterative cycles. Results chapters 1 and 2 combined a number of change concepts as an intervention 'bundle' that were trialled simultaneously due to time constraints. Bunching together interventions makes it impossible to determine their individual impact on the project outcome, and this knowledge would help future projects prioritise their time (Sena et al., 2022; Parks et al., 2017). However, Parks et al. (2017) suggest that no single intervention had a significant impact on their study outcome in isolation, but improvement was gradually seen over time as more interventions were trialled and implemented. Therefore, for significant improvement to be seen in certain studies a multitargeted and sustained approach could be required, and that individual initiatives in isolation are unlikely to be successful (Parks, et al., 2017). Results chapter 3 was more compliant with PDSA principles of iterative cycles and small-scale testing of individual changes over time. The offer of the call within the 2WW and offering the PRCI seemed to have the most impact on certain patient feedback data.

The study included balancing measures to determine any unintended consequences, in order to ensure that the QI intervention improves care and does not create new problems, as recommended by Wong & Sullivan (2016). These measures also served to provide more information about the complex IVF system helping to decipher patterns in outcome and process measures.

Results chapters 1 and 2 are examples of how averages can hide information about a system (Savage, 2002). By plotting data in more frequent intervals (weekly) and not combining incubator data special cause variation was picked up that would otherwise have been missed.

Although improvement could not be attributed to changes made in all results chapters e.g., the main aim of increasing patient satisfaction scores was not met, well-conducted QI interventions that do not achieve their intended outcomes are still important and worthwhile for dissemination (Wong & Sullivan, 2016).

Another aim of the project was to improve the clinic's stock control by removing waste from the processes. Repeated attempts were made using lean 5S to tidy and introduction of Kanban cards as a way of managing inventory. Attempts were unsuccessful because of the impact of Brexit and unavailability of certain products following the pandemic, meaning that the clinic had to stockpile consumables and switch to alternative products due to supply chain disruptions and a global shortage of resin. The QI team will make further attempts to address this niggle which effects the entire MDT.

The study aimed to address a difficult problem within assisted conception of how fertility clinics can improve the chances of a live birth, help patients to stay in treatment, and lessen the psychological burden associated with infertility and fertility treatment despite increased operational costs and limited financial resources. The application of QI strategies conceived from manufacturing should lead to learning and improvement of fertility clinics without additional costs. When considering the '3 wins'; patients (service quality), staff (workload, stress), and organisation (performance, cost, regulation) (Dodds, 2007) the study achieved marginal gains for the patients and organisation. But some interventions increased costs to the clinic e.g., 2WW calls increasing nurse's workload, replacing old equipment, and increasing the progesterone dose. Replacing old equipment is a necessary cost of running a service and should be budgeted for. Better temperature control through new heated stages and enclosed Unica cabinet would intuitively help to improve success rates as eggs are extremely sensitive to physical and chemical stress (Simpaolous et al., 2016; Pickering et al., 1988). The clinic cannot be certain of any benefit from the additional cost of doubling the progesterone dose but calls during the 2WW did improve patient satisfaction at this small clinic.

All of the interventions trialled during this study were implemented into routine practice to ensure any marginal gains would be sustained. Including a key member of each of the MDT disciplines in the project team significantly helped with sustainability of this study as part of routine clinical practice even after the project had finished. The 2WW calls is an excellent example of this. Having a core team of staff invested in the improvement effort, looking out for areas for improvement, empowered to make changes and acknowledging that they can make a difference to the day-to-day work, made this study possible. A similar finding to published studies staff buy-in to the improvement work was vital to the

success of the QI project (Sena et al., 2022; Parks et al., 2017; Poksinska et al., 2017). Taking this work to a larger group of people or clinic requires clarity in describing why a change is needed and the benefits that have been realised from the change on a small scale (Crowl et al., 2015). Challenges to recreating this study in another clinic might include difficulty in creating time to conduct tests of change, staff turnover, staff engagement, clinic culture, and changing or competing priorities (Reed & Card, 2016). However larger clinics with higher cycle numbers could see a larger improvement through implementing QI principles and benefit more from their application.

Comparing baseline data to the data collected after a change has been implemented can have disadvantages related to interpretation of the results if an unrelated change occurs during the time a change is made (Crowl et al., 2015). Unfortunately for results chapters 2 and 3 both were impacted by the Covid-19 pandemic with the clinic closure occurring just before or after the intervention for improvement was started. The many procedural and policy changes made to continue treatment safely would have impacted on the measures of both chapters. Perhaps a more significant improvement might have been seen otherwise. It was reassuring to see that success rates still improved and patient satisfaction did not reduce following the pandemic.

Chapter 6. Conclusion

This project increased our understanding of how QI principles conceived from the manufacturing industry can be applied within an IVF service, identifying any barriers and enablers along the way, and that their application can lead to incremental improvement of a clinic's performance in terms of both outcomes (success rates) and quality of care. Continuous improvement of service performance, whether clinical outcomes or patient support, is in line with the aims and strategies of the sectors regulator the HFEA and the NHS.

The current study demonstrated application of PDSA cycles and behaviour charts to evaluate improvement interventions, and provides a novel report of QoL assessment and use of an innovative self-administered psychological intervention during routine clinical practice. Embryo culture disruption was reduced and patient support remained good despite the effects of the Covid-19 pandemic. The QI principles were used to successfully troubleshoot a reduction in a KPI and bring results back within benchmark value.

Any research based in an ART setting needs advanced and innovative methods to analyse clinic outcome data. Underpinning the project is the ability to interrogate the clinic's data collection and analysis tool, the KPI and patient feedback. This is how many research topics have been addressed historically in the reproductive science field, sometimes subject to major criticism due to confounding variables and low numbers. However, the project also selected areas to study which can provide valid outcomes within the constraints of the clinical setting, e.g., rapid quality improvement cycles. PDSA is useful as it's a pragmatic scientific method for testing changes in complex systems and fertility is certainly very complex (Moen & Norman 2006).

The application of QI principles is not just about use of tools, it is a culture of continuous improvement. The project has emphasised the importance of continual improvement and empowered clinic staff to make changes, turning them into problem solvers that take ownership of improvement activities and work every day to streamline processes (Poksinska et al., 2017). A QI approach would not work without engagement from the team using it and supportive leadership (Kaplan et al., 2014; Dodds, 2007).

Over the 4 years of the study the clinic has seen streamlining of processes, replacement of ageing equipment, an increase in success rates, and a strong focus on patient support. Marginal gains from each area when combined result in better clinic performance. This research project has had a direct impact on the patients of the clinic with a better chance of a successful cycle and a good treatment experience regardless of outcome. Therefore, the fertility sector can benefit from the application of QI principles and this might be more effective, gleaning greater improvements, in larger fertility clinics with higher case numbers. Further research is encouraged to validate the effectiveness of the application of QI principles within different clinic settings, and more studies from the sector should be published using the SQUIRE guidelines.

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Appendices

Appendix 1.

Details of literature search strategy for incrementalism within healthcare or assisted reproduction (utilising the Trust library).

Resources searched: *Medline, EMBASE, HBE, HMIC, PubMed.*

Search terms used: *"marginal gain*", "incremental gain*", "incremental improvement*"*

Searching for the specific terms above in title and abstract resulted in many results but attempts to restrict them by healthcare terms i.e. clinical science, fertility etc did not produce any meaningful results. Therefore, the original search was limited to the appearance of the terms in the title only, using the logic that if the article was seriously addressing these topics they would be referred to in the title. There are very few articles in the five medical databases on this topic.

Appendix 2.

Details of literature search terms used for QI and assisted reproduction literature review (utilising the Trust library resource)

#	Database	Search term
1	Medline	(fertili*).ti,ab
2	Medline	INFERTILITY/
3	Medline	FERTILITY/
4	Medline	(infertil*).ti,ab
5	Medline	("assisted reproduct*").ti,ab
6	Medline	"REPRODUCTIVE TECHNIQUES, ASSISTED"/
7	Medline	("clinical embryology").ti,ab
8	Medline	(embryology).ti,ab
9	Medline	EMBRYOLOGY/
10	Medline	("reproductive science").ti,ab
11	Medline	(ivf).ti,ab
12	Medline	("in vitro fertilisation").ti,ab
13	Medline	("in vitro fertilization").ti,ab
14	Medline	"SPERM INJECTIONS, INTRACYTOPLASMIC"/
15	Medline	"FERTILIZATION IN VITRO"/
16	Medline	("fertilization in vitro").ti,ab
17	Medline	("fertilisation in vitro").ti,ab
18	Medline	("assisted conception").ti,ab
19	Medline	(1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18)
20	Medline	(subfertil*).ti,ab
21	Medline	(19 OR 20)
22	Medline	(quality).ti,ab
23	Medline	("quality improve*").ti,ab
24	Medline	"QUALITY IMPROVEMENT"/
25	Medline	("lean think*").ti,ab
26	Medline	"QUALITY CONTROL"/
27	Medline	"TOTAL QUALITY MANAGEMENT"/
28	Medline	"QUALITY ASSURANCE, HEALTH CARE"/
29	Medline	("six sigma").ti,ab
30	Medline	(pdsa).ti,ab
31	Medline	("plan do study act").ti,ab
32	Medline	("process map*").ti,ab
33	Medline	("systems thinking*").ti,ab
34	Medline	"SYSTEMS ANALYSIS"/
35	Medline	("systems analysis").ti,ab
36	Medline	("lean principle*").ti,ab
37	Medline	(22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36)
38	Medline	(21 AND 37)
39	Medline	(23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36)
40	Medline	(21 AND 39)
41	Medline	[Languages English]

42	EMBASE	("clinical embryology").ti,ab
43	EMBASE	EMBRYOLOGY/
44	EMBASE	(embryology).ti,ab
45	EMBASE	("assisted reproduction*").ti,ab
46	EMBASE	"INFERTILITY, MALE"/
47	EMBASE	"INFERTILITY, FEMALE"/
48	EMBASE	"IN VITRO FERTILIZATION"/
49	EMBASE	"ARTIFICIAL INSEMINATION"/
50	EMBASE	"INFERTILITY THERAPY"/
51	EMBASE	(infertility).ti,ab
52	EMBASE	(ivf).ti,ab
53	EMBASE	("in vitro fertilisation").ti,ab
54	EMBASE	("in vitro fertilization").ti,ab
55	EMBASE	("reproductive science*").ti,ab
56	EMBASE	("assisted conception").ti,ab
57	EMBASE	"INTRACYTOPLASMIC SPERM INJECTION"/
58	EMBASE	("fertilisation in vitro").ti,ab
59	EMBASE	("fertilization in vitro").ti,ab
60	EMBASE	(42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59)
61	EMBASE	(quality).ti,ab
62	EMBASE	"TOTAL QUALITY MANAGEMENT"/
63	EMBASE	"QUALITY CONTROL"/
64	EMBASE	"QUALITY CONTROL PROCEDURES"/
65	EMBASE	("quality improvement").ti,ab
66	EMBASE	("lean thinking*").ti,ab
67	EMBASE	("six sigma*").ti,ab
68	EMBASE	(pdsa).ti,ab
69	EMBASE	("plan do study act").ti,ab
70	EMBASE	("process map*").ti,ab
71	EMBASE	("systems thinking*").ti,ab
72	EMBASE	("lean principles*").ti,ab
73	EMBASE	("systems analysis").ti,ab
74	EMBASE	"SYSTEM ANALYSIS"/
75	EMBASE	("system analysis").ti,ab
76	EMBASE	(61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75)
77	EMBASE	(62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75)
78	EMBASE	(60 AND 77)
79	EMBASE	[English language]
80	BMJ Quality and safety	(19 OR 20)
81	Implementation science	(19 OR 20)

Appendix 3.

Ethical approval of project

Ethos approval letter

29/01/2020

Project Title: INCREMENTAL GAINS WITHIN AN ASSISTED CONCEPTION SERVICE – UTILIZING EVIDENCED BASED QUALITY IMPROVEMENT STRATEGIES IN A NOVEL SETTING

EthOS Reference Number: 12242

Ethical Opinion

Dear Emma Woodland,

The above application was reviewed by the Research Ethics and Governance Team and on the 29/01/2020, was certified as a service evaluation. The certification is in place until the end of your project and is based on the documentation submitted with your application.

Application Documents

Document Type	File Name	Date	Version
Additional Documentation	Literature review C1 final version	17/03/2019	1
Ethical Approval Letter	HRA form for C2 project	05/12/2019	1
Ethical Approval Application Form	Trust approval of project	10/12/2019	1
Ethical Approval Supporting Information	RE Advice HSST student	24/01/2020	1

Conditions of certification

The Research Ethics and Governance Team would like to highlight the following conditions

Adherence to Manchester Metropolitan University's Policies and procedures

This ethical approval is conditional on adherence to Manchester Metropolitan University's Policies, Procedures, guidance and Standard Operating procedures. These can be found on the Manchester Metropolitan University Research Ethics and Governance webpages.

Amendments

If you wish to make a change to this approved application, you will be required to submit an amendment in accordance with Salisbury NHS Foundation Trust guidelines, and inform Manchester Metropolitan University of the change. Please contact the Research Ethics and Governance team for advice around how to do this.

We wish you every success with your project.

Research Ethics and Governance Team

HRA form

Go straight to content.

MRC Medical Research Council

NHS Health Research Authority

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

Working title: Incremental gains within an assisted conception service – utilizing evidenced based quality improvement strategies in a novel setting

IRAS Project ID (if available):

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the HRA to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at HRA.Queries@nhs.net.

For more information please visit the Defining Research table.

Follow this link to start again.

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BELL, Louise (SALISBURY NHS FOUNDATION TRUST)
Mon 09/12/2019 12:45

Mark as unread

To: WOODLAND, Emma (SALISBURY NHS FOUNDATION TRUST);

You replied on 09/12/2019 16:15.

Hi Emma

I am sorry it has taken so long to respond. I can confirm that we do not consider your study to be research and therefore formal review by the R&D department/Trust is not necessary. Please be aware there is guidance on service evaluation and all other Trust policies (for example information governance) must be followed. Good luck with your project.

Best wishes

Louise Bell

Louise Bell
Research Manager
Salisbury NHS Foundation Trust

Research & Development
Block 26
Salisbury NHS Foundation Trust
Salisbury District Hospital
Odstock Rd
Salisbury
SP2 8BJ

Direct: 01722 425026 Extension (internal): 2026

Appendix 4.

HADs process documents (consent, patient information sheets, clinic flow chart).

HADs patient information and consent

Salisbury Fertility Centre

We feel it is important not only to look after the physical aspects of fertility treatment, but also the emotional elements and the impact it may be having on you.

The questionnaire you have been given enables us to do just that. It is called 'The HAD Scale' which assesses anxiety and depression, it involves 'ticking boxes' and takes about 5 minutes to complete. Please read each statement and tick the box beside the reply that is closest to how you have been feeling in the past week. There are no right or wrong answers. Do not spend too much time on any statement; it is important to not take too long over you replies: your immediate is best. Please check you have answered all the questions.

Once completed please return the questionnaire to the Fertility centre by post alongside your patient registration forms or treatment feedback questionnaire form, alternatively hand in to a member of staff at your next appointment. The result will be analysed and filed within your medical notes. If the result for anxiety and/or depression is high, then we will discuss with you some options in order to help you with this.

The scale is intended to help us to provide the most comprehensive fertility service we can for our patients, but if you would prefer not to complete it, then just let a member of staff know, as it is not compulsory to fill it in. Please return any completed and uncompleted forms to the centre.

The Salisbury Fertility Centre Team, Salisbury District Hospital.

HAD Scale

Patient name: .....

Patient Date of birth:.....

Date completed: .....

Patient ID label

Office use only

Treatment type: FET IVF/ICSI IUI

Stage of treatment: Initial post

This questionnaire is designed to help your doctor to know how you feel. Read each item and place a tick in the box opposite the reply which comes closest to how you have been feeling in the past week. Tick the box beside the reply that is closest to how you have been feeling in the past week. Don't take too long over you replies: your immediate reaction to each item is more important.

Tick only one box in each section

I feel tense or 'wound up':

Most of the time	
A lot of the time	
From time to time (occ.)	
Not at all	

I feel as if I am slowed down:

Nearly all the time	
Very often	
Sometimes	
Not at all	

I still enjoy the things I used to enjoy:

Definitely as much	
Not quite as much	
Only a little	
Hardly at all	

I get a sort of frightened feeling like 'butterflies' in my stomach:

Not at all	
Occasionally	
Quite often	
Very often	

I get a sort of frightened feeling as if something awful is about to happen:

Very definitely and quite badly	
Yes, but not too badly	
A little, but it doesn't worry me	
Not at all	

I have lost interest in my appearance:

Definitely	
I don't take so much care as I should	
I may not take quite as much care	
I take just as much care as ever	

I can laugh and see the funny side of things:

As much as I always could	
Not quite so much now	
Definitely not so much now	
Not at all	

I feel restless as if I have to be on the move:

Very much indeed	
Quite a lot	
Not very much	
Not at all	

Worrying thoughts go through my mind:

A great deal of time	
A lot of time	
From time to time, but not often	
Only occasionally	

I look forward with enjoyment to things:

As much as I ever did	
Rather less than I used to	
Definitely less than I used to	
Hardly at all	

I feel cheerful:

Not at all	
Not often	
Sometimes	
Most of the time	

I get sudden feelings of panic:

Very often indeed	
Quite often	
Not very often	
Not at all	

I can sit at ease and feel relaxed:

Definitely	
Usually	
Not often	
Not at all	

I can enjoy a good book or radio or TV programme:

Often	
Sometimes	
Not often	
Very seldom	

Do not write below this line

A:_____ D:_____

How to process the HAD scale questionnaire

- At patient registration for initial consultation patients are given the HADs form and HADs consent/info form alongside the CD, and registration forms. They return the HADs forms back to SFC alongside the registration and CD forms (completed or not). Patients and partners are given a form each. When posting HADs forms out at patient registration please tick the patient SFC number book with a tick to indicate HADS has been sent (so we can gauge the response rate).
- Patients are also given HADs at ET/FET/IUI/DI alongside the patient feedback questionnaire and are informed to complete on day 10 of the waiting period and return the form to SFC alongside their feedback form.
- Once forms are received back at SFC a member of the team analyses the HADs score. Convert the tick to a score from 0-3. HADs forms are to be filed in the patients blue medical notes.
- Total the score for Anxiety (left hand column) and Depression (right hand column) separately and record clearly at the bottom of each HADS form.

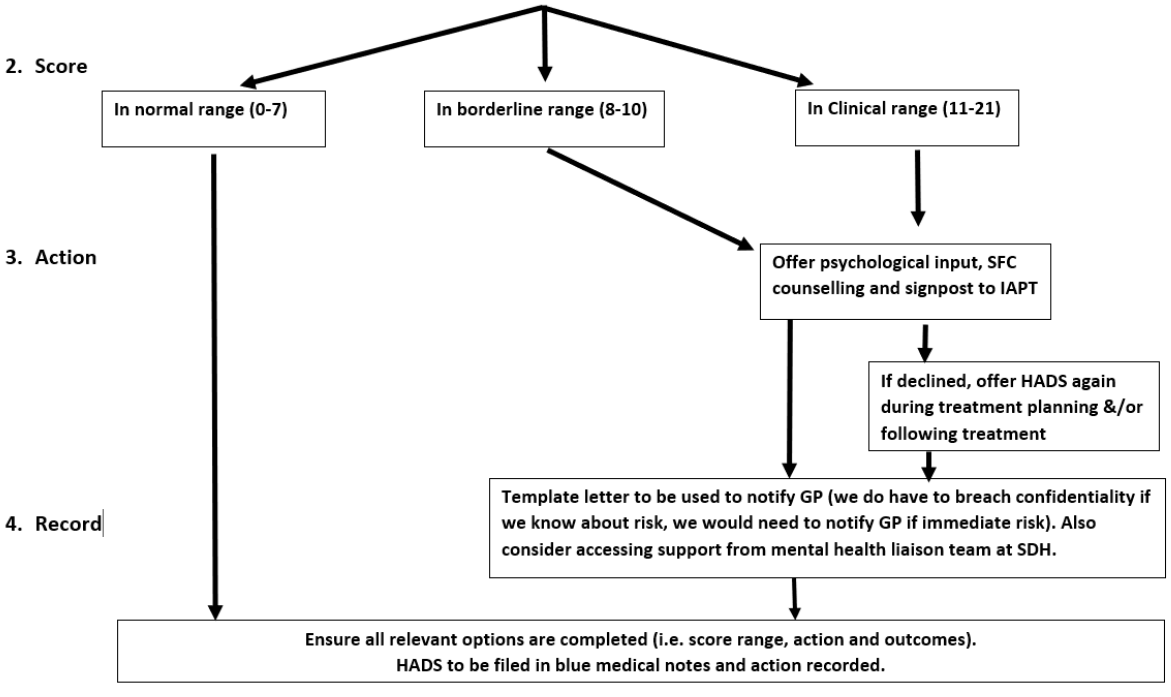
Total score: Depression (D) _____ Anxiety (A) _____

	Score	Result	Action required
1	0-7	= Normal	Inform patient. Treatment continues as planned with offer of counselling.
2	8-10	= borderline	Inform patient. Explain options for patient for additional support. Referral to fertility counsellor or GP or local IAPT service, give patient information leaflet. Treatment continues at planned with offer of support and counselling.
3	11-21	= Clinical	Inform patient. Explain options for patient for additional support. Referral to fertility counsellor or GP or local IAPT service, give patient information leaflet. Seek advice from counsellor regarding continuing treatment as planned or delay.

- Prepare HADs score for consultation/follow-up including score result and patient information. **Any clinical results should be actioned straight away by the clinical team (do not wait for next appointment).**
- Securely store all HADs forms within the blue medical notes for the patient.
- If clinically significant result clinician or nurse to document within blue medical notes including any advice for self-referral for additional support that was discussed.

Fertility HADs pathway

1. **ALL patients and partners (if applicable) to be asked to complete a HADS at the start of treatment pathway and at the end of the cycle (day 10 of two week wait). SFC can therefore support patients before, during and following treatment and identify those patients who may need additional supportive counselling or who may be at risk.**



What does my HAD scale result mean?

Based on your responses to questions within the HAD scale questionnaire, you are experiencing symptoms seen in people with anxiety and/or depression but only an experienced health professional can tell for sure as your HADs result is not a diagnosis.

If you have been feeling depressed for more than a few weeks or your anxiety is affecting your daily life we strongly advise you to consider booking an appointment with our independent counsellor at Salisbury Fertility Centre, or booking an appointment with your GP or self-referral to your local IAPT (Improving Access to Psychological Therapies) programme. You can do this through visiting this website: https://www.nhs.uk/service-search/find-a-psychological-therapies-service/ you need to be registered with a GP to get talking therapies on the NHS.

It may be helpful for you to talk to our independent counsellor before starting your fertility treatment, during and/or following treatment. Please contact us to arrange this.

Local IAPT programmes:

IAPT programme	Address	Contact
Steps 2 Wellbeing (Southampton)	3rd Floor, Grenville House Nelson Gate, Southampton Hampshire SO15 1GX	Tel: 0800 612 7000
iTalk	Black Horse House 3rd Floor, 8-10 Leigh Road Eastleigh, Hampshire SO50 9FH	Tel: 02380 383 920
Steps 2 Wellbeing (Poole, Purbeck and East Dorset)	Bearwood Neigbourhood Centre 325 King John Avenue Bearwood, Bournemouth Dorset BH11 9TF	Tel: 0300 123 1120
Steps 2 Wellbeing (Bournemouth and Christchurch)	16-18 Tower Road Bournemouth, Dorset BH1 4LB	Tel: 0300 7900 542
Wiltshire IAPT	Lodge 3 Devizes, Wiltshire SN10 5DS	Tel: 01380 731335
St Mary's Hospital	St. Mary's Hospital Parkhurst Road Newport, Isle of Wight PO30 5TG	Tel: 01983 822099

Additional sources of help, support and information

If you want to talk to someone right away, the **mental health helpline** page has a list of organisations you can call for immediate help. This can be accessed here: https://www.nhs.uk/conditions/stress-anxiety-depression/mental-health-helplines/

The NHS Moodzone offers practical advice, interactive tools, videos and audio guides to help you feel mentally and emotionally better. Please see https://www.nhs.uk/conditions/stress-anxiety-depression/

If you have had thoughts of self-harming or are feeling suicidal, contact someone you can trust immediately, such as a GP (we have a duty to notify your GP or mental health liaison team if we are concerned about any immediate risk).

Appendix 5.

Additional patient feedback questionnaire based on the 2018 HFEA National Patient Survey (HFEA, 2018c)

How are we doing at SFC? We would love your feedback.

We aim to continuously improve our service and ensure patients receive the best quality care throughout their fertility journey. To do this we seek and greatly value any patient feedback about our service. As part of a quality improvement project we would be very grateful if you could take the time to complete this additional patient survey questionnaire and return it to the centre, alongside our standard patient questionnaire. You do not have to complete this additional form if you do not wish to and if you choose to complete it you can remain anonymous if you wish.

Information gathered from this questionnaire will help to inform and direct future quality improvement work at our centre.

We wish you the very best of luck following your treatment cycle and hope that you feel supported during your wait for treatment outcome. Please do not hesitate to contact us during this time.

The Salisbury Fertility Centre Team, Salisbury District Hospital.

Name: _____

(If you would like us to respond to your feedback please write your name above so that we can contact you)

Patient or Partner (please circle)

Date completed: _____

We would be very grateful if you could please answer the following questions.

How satisfied or dissatisfied were you with these aspects of organisation and coordination? (Please circle)	
With the coordination/administration of the treatment	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
That the number of separate days you/your partner had to attend for treatment was kept to a minimum	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
With the length of time between your appointments	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
With flexibility of appointment times and dates	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
With time spent in waiting rooms on the day of your appointments	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
Being seen by the same healthcare professionals throughout your treatment	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
That you could contact a named person at the clinic	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
If you have any comments or experiences you would like to share about the coordination of treatment please write them here.	

To what extent would you agree or disagree with the following aspects of communication and interaction… (please circle)	
I felt comfortable asking questions to healthcare professionals	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I felt involved in decisions about my treatment	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I felt heard and listened to	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I had appropriate time with the healthcare professional during my appointments	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I felt able to state concerns or complaints at any time	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree

I felt able to provide feedback at any time	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree

If you have any comments about your experiences with our team of health professionals please write them here.

To what extent, if at all, were each of the following aspects clearly communicated to you by the clinic? (Please circle)

The consent forms for treatment	very clear / quite clear / could be clearer / unclear / very unclear
A treatment plan (information about what happens and when)	very clear / quite clear / could be clearer / unclear / very unclear
What to do if there are medical issues or emergencies	very clear / quite clear / could be clearer / unclear / very unclear
The chances of success	very clear / quite clear / could be clearer / unclear / very unclear
The health risks of treatment such as side effects	very clear / quite clear / could be clearer / unclear / very unclear

From which, if any, of the following did you or your partner receive emotional support that was helpful? Please tick all that apply.

- ☐ Your partner
- ☐ Friends or family members
- ☐ An online support forum, such as fertility friends, Fertility UK, Fertility network UK
- ☐ A counsellor you found separately from the centre
- ☐ The centres counsellor
- ☐ Centre receptionist / admin team
- ☐ Centre nurses
- ☐ Centre embryologists
- ☐ Centre doctors/consultants
- ☐ A support group that met in person
- ☐ Telephone helpline
- ☐ Other
- ☐ None of the above, did not receive any helpful support

Do you remember receiving information about how to access counselling? Please circle	Yes / No / Can't recall
Did you access counselling sessions with our centre's independent counsellor? Please circle	Yes / No
If yes to the above question, did you find this helpful during your treatment journey? Please circle	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree

If you have any comments or experiences you would like to share about counselling or support at Salisbury fertility centre please write in here.

What could we do better to best support our patients? (please circle)	
The centre manages patient expectations well during treatment	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
The centre always ensures privacy and dignity during scans, tests and treatments	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
The centre allows sufficient time for patients to absorb new information	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
The centre provides information on possible physical and emotional symptoms	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I would like the centre to phone me halfway through the 'two week wait'	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I felt supported during the 'two week wait' and was able to speak to the centre if I needed to	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I was offered counselling at the time of my pregnancy result	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I would like the centre to phone me a week after any pregnancy result	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
I felt supported by the centre throughout treatment	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
The centre could do more to help patients cope during the 'two week wait'	strongly agree / tend to agree / Neither agree nor disagree / tend to disagree / strongly disagree
If you have any comments or suggestions of how we can continuously improve the support we provide, before, during or after treatment please write in here.	

How satisfied or dissatisfied were you with aspects of respect and dignity? (please circle)	
How safe you / your partner felt during treatment	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
The respect and courtesy you were shown	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
The dignity you /your partner were shown during treatment	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
The clinic environment	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
The interest shown in you as a person.	very satisfied / satisfied / Neither satisfied nor dissatisfied / dissatisfied / very dissatisfied
Overall, how satisfied/dissatisfied were you with the most recent fertility treatment you had?	very satisfied / satisfied / neither satisfied or dissatisfied / dissatisfied / very dissatisfied

Appendix 6.

PRCI A4 leaflet given to patients (Lancastle, 2006; Lancastle and Boivin, 2008)

Coping with the IVF waiting period

When you are waiting to take the pregnancy test after your IVF embryo transfer you may often find yourself thinking about whether you are pregnant or not. You might also find yourself frequently checking for physical signs to tell whether you are pregnant or not. You may find that this intense focus on the result of treatment makes you feel nervous and worried. Patients often ask us for suggestions about how to deal with these intrusive and persistent thoughts. This leaflet describes a technique you can use to manage your worries during the IVF waiting period.

The Positive Reappraisal Technique

All situations involve some good aspects and some bad aspects and the aspects we pay attention to often determines how good or bad we feel.

Thinking more about the positive aspects of a difficult situation and dwelling less on problems or uncertainties about the future helps people feel better. This is especially true during the challenges of the IVF waiting period when there is not much a person can do to influence the outcome of treatment.

The positive reappraisal technique can help you manage your worries by encouraging you to think positively about the situation you are currently experiencing. In the context of fertility treatment, the positive reappraisal technique involves actively thinking about any positive aspects of *infertility or fertility treatment itself*.

Thinking about the positive aspects of a difficult situation does not mean pretending that everything is wonderful when you do not feel it is or thinking that you will definitely get pregnant when you feel unsure or ignoring all the negative aspects of a difficult situation. What it *does* mean is choosing to take account of good aspects alongside the more negative aspects of the situation, and reminding yourself that even very challenging situations have some positive elements. Taking the positive aspects into account will help you feel better during the two-week waiting period.

The positive aspects of the waiting period will differ depending on your personal circumstances. Some people might focus on appreciating the support or kindness that friends or family have shown them during fertility treatment. Others might think about the ways in which their relationship with their partner is stronger now because of this shared experience. These are the sort of benefits that women going through IVF have shared with us in the past. You may be able to think of other examples which are personally important to you.

What do you consider to be some positive aspects of this situation?

_____

_____

_____

_____

1

To help people use the positive reappraisal technique we designed a card that contains ten different ways of thinking positively. The statements are general and do not refer to any one specific positive aspect because we know that different people will have different ideas about what is or isn't positive. This small card can be put in a purse or a pocket so you can remind yourself of the positive reappraisal technique whenever and wherever you feel the need.

You should read the statements and think about how each statement applies to you personally. For example, what could you do to make yourself feel positive? What do you feel you have learnt from this experience? Think about the parts of your experience of infertility or fertility treatment that have led to something positive or some benefit, or that help you to carry on even when the situation gets really difficult.

We suggest that you read the card twice a day, once in the morning and once at night, and then any other time you feel the need.

As with any new way of thinking and behaving, it can take time for the positive reappraisal technique to become second nature. Thinking differently can feel strange and unnatural at first. However, practice will help so try and persevere. You should find the technique easier the more you practice it and you should then find that you are not dwelling so much on thoughts that worry and upset you.

Positive Reappraisal Coping Intervention (PRCI)

During this experience I will:

1. Try to do something that makes me feel positive
2. See things positively
3. Look on the bright side of things
4. Make the best of the situation
5. Try to think more about the positive things in my life
6. Focus on the positive aspects of the situation
7. Find something good in what is happening
8. Try to do something meaningful
9. Focus on the benefits and not just the difficulties
10. Learn from the experience

This tool was developed during the PhD studies of Deborah Lancastle (Lancastle, 2006, Cardiff University) supervised by Jacky Boivin. Where PRCI is used please cite: Lancastle D, Boivin J (2008). Feasibility, acceptability and benefits of a self-administered positive reappraisal coping intervention (PRCI) card for medical waiting periods. Human Reproduction, 23, 2299–2307.

Appendix 7.

PRCI Feedback form

Salisbury
FERTILITY CENTRE

Tel: 01722 417224
Email: sft.sfc@nhs.net
www.salisburyfertilitycentre.nhs.uk

NHS
Salisbury
NHS Foundation Trust

The Positive Reappraisal Technique

Salisbury fertility Centre aims to continuously improve the experience of our patients during their time with us. We understand that the two week wait following embryo transfer can be a very anxious time for patients and we do get asked by patients is there is anything that can help during this time.

Your consultant at embryo transfer has given you a leaflet regarding **The Positive Reappraisal Technique**, with 10 statements, and also a laminated card. This intervention was developed by Cardiff University to help patients cope during the two week waiting period.

It is not compulsory for you to use this technique during your wait, you may find it helpful or you may not.

We would like to understand how useful this is to our patients and whether we should provide it as an option for all of our patients in the future. Therefore, we would be incredibly grateful for your feedback. We would like to know if the intervention helped you during the two week wait and whether it was easy to use. It's also very helpful for us to know the reasons for patients that decided not to use it.

Therefore, even if you choose not to use the positive reappraisal technique, we would be very grateful if you could kindly complete the feedback form below and please return to Salisbury fertility centre with your other feedback forms and the HADs form.

If you have any questions please do not hesitate to contact a member of the team.

Patient Positive Reappraisal Technique evaluation form (PLEASE CIRCLE YOUR ANSWERS)

Date of your embryo transfer: _____

Patient name:_____ **Date form completed:** _____

How often did you use it? Twice a day / once a day / once every few days /

only a couple of times during the two week wait / I did not use it at all

If you did not use The Positive Reappraisal Technique please could you provide feedback as to the reasons for not using?

.....

.....

.....

On a scale of 1-6 (1 being low and 6 being high) how would you rate The Positive Reappraisal Technique for.....	☹	😐	☺
Ease of use			
It was quick and easy to use	**1 2 3 4 5 6**		
It fitted into my daily routine	**1 2 3 4 5 6**		
The statements were memorable	**1 2 3 4 5 6**		
Perceived benefit			
I found reading the statements helpful	**1 2 3 4 5 6**		
Reading the statements gave lasting effects on my mood	**1 2 3 4 5 6**		
Reading the statements reduced my levels of stress	**1 2 3 4 5 6**		
I felt more positive during the waiting period	**1 2 3 4 5 6**		
It was a good distraction that helped me to keep going	**1 2 3 4 5 6**		
I would want to use the Positive Reappraisal Technique again during the two week wait	**1 2 3 4 5 6**		
I would recommend it to others during the two week wait	**1 2 3 4 5 6**		

Many thanks from the Salisbury Fertility Centre Team, Salisbury District Hospital.

Appendix 8.

The context of the C2 research project within the wider content of the whole DClinSci.

Doctor of Clinical Science (DClinSci) Programme overview (Details taken from MMU 2019/2020 student handbook (MMU (Manchetser Metropolitan University), 2019/2020)

The Higher Specialist Scientific Training (HSST) DClinSci is a five-year, practice-based education and training programme supported by an underpinning part-time professional doctorate and Medical Royal College qualifications. The academic component of HSST is known as the DClinSci a Research Degree meeting QAA Level 8 criteria and FQ-EHEA for doctoral degrees. The overall structure is illustrated in the HSST Doctoral Training Programme High-Level Framework diagram below. The Professional Doctorate comprises 540 credits (of which a minimum of 360 credits must be at Doctoral level (Level 8 in QAA National Framework)) split across the three sections of the programme, which can be summarised as:

- Section A: Leadership and Professional Development (120 credits)
- Section B: Specialist Scientific and Clinical Programme (150 credit)
- Section C: Research, Development and Innovation (270 Credits)

Students in the life sciences (***including Reproductive Science***) complete:

- Section A (Delivered by the Alliance Manchester Business School, University of Manchester at Level 7) [*120 credits*],

University of Manchester
Level 7

Core Units				
Unit Code	Occurrence[1]	Status - Pre/Co-requisites - Excluded units	Unit Title	No of credits
6ACP7160	9	None	A1: Professionalism and Professional Development in the Healthcare Environment	30
6ACP7161	9	None	A2: Theoretical Foundations of Leadership	20
6ACP7162	9	None	A3: Personal and Professional Development to Enhance Performance	30
6ACP7163	9	None	A4: Leadership & Quality Improvement in the Clinical and Scientific Environment	20
6ACP7164	9	None	A5: Research and innovation in health and social care	20

- Specialty Specific Section B (Section B3 below –Discipline-Specific Specialist Clinical and Scientific Units) [*150 credits*] Students currently demonstrate the attainment of Section B3 unit learning outcomes by passing Part 1 of the Fellowship Examination of the Royal College of Pathologists (FRCPath, part 1) in the corresponding discipline.

Reproductive Science: The following Level 8 units will be taken by candidates specialising in reproductive science according to the high level curriculum overview as shown in Section H.

Core Units				
Code	Occurrence	Status - Pre/Co-requisites - Excluded units	Unit Title	No of credits
6ACP8044	9	None	Underpinning the Practice of Reproductive Science	30
6ACP8045	9	None	Specialist Practice of Reproductive Science: Presentation and Management of Infertility	30
6ACP8046	9	None	Specialist clinical skills: Effective Communication	30
6ACP8047	9	None	Specialist Practice of Reproductive Science	30
6ACP8048	9	None	Specialist Practice in Cryobiology	30

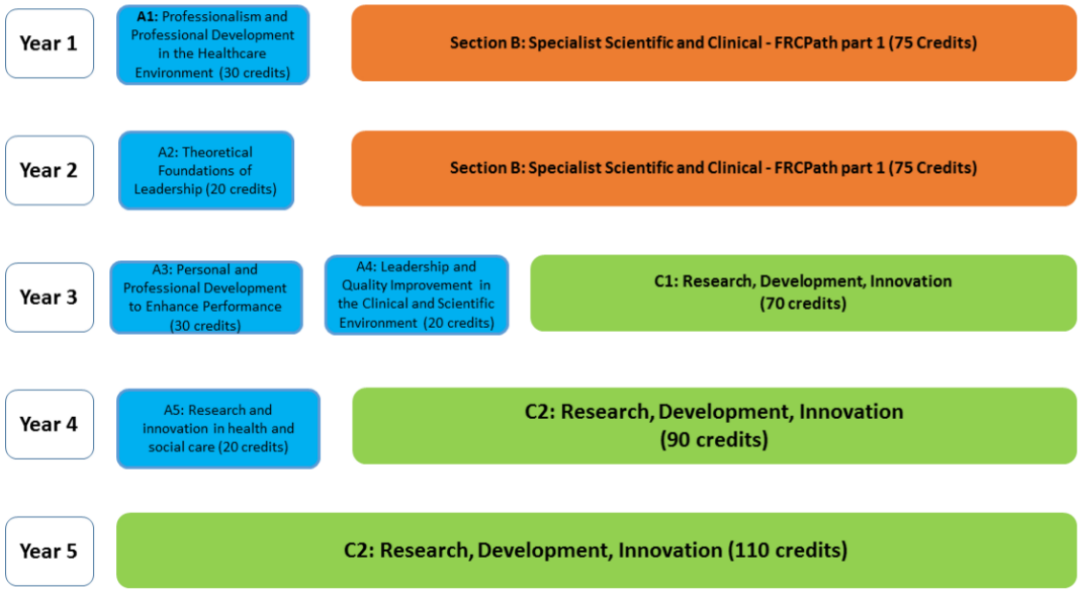
- Section C – Research, Development and Innovation [*270 credits*]. The doctoral thesis element is focused to the candidate's discipline. All units are at Level 8.

Section C: Research, Development and Innovation Units

Core Units				
Code	Occurrence[2]	Status - Pre/Co-requisites - Excluded units	Unit Title	No of credits
6ACP8024	9	None	C1: Doctoral Research and Innovation in Clinical Science – Preparing the Proposal	70
6ACP8025	9	None	C2: Research Project	200

Final Exit Award following completion of Sections A, B and C: **Doctor of Clinical Science (DClinSci);**
Interim Exit Award for non-completion of the Doctoral Thesis: **Master of Philosophy.**

Life Sciences



Patient Public Involvement

Valuing patient feedback and experience is an important aspect of the training that HSST healthcare professionals receive. Lay representatives are an equal partner in trainee education and are involved in assessment, curriculum development and sharing their story as part of a teaching session. The academic component of the DClinSci reflects

elements of the NHS Constitution and the Duty of Candour throughout the teaching using a variety of methods (eg. Case studies, news articles, self-reflection, direct patient interaction). During the Research component (Section C) trainees will be expected to address and clearly communicate how their research impacts on patients and the patient pathway (including delivering an assessed lay presentation to scientific examiners and lay representatives (C1 assessment)).

Appendix 9.

Evidence of completion of HSST Section A

FW: HSST: Your final Section A marks have been ratified by the Exam Board

From: PG Dip [mailto:PGDip@manchester.ac.uk]
Sent: 28 November 2018 14:39
To: Emma Woodland
Subject: HSST: Your final Section A marks have been ratified by the Exam Board

Dear HSST Trainee,

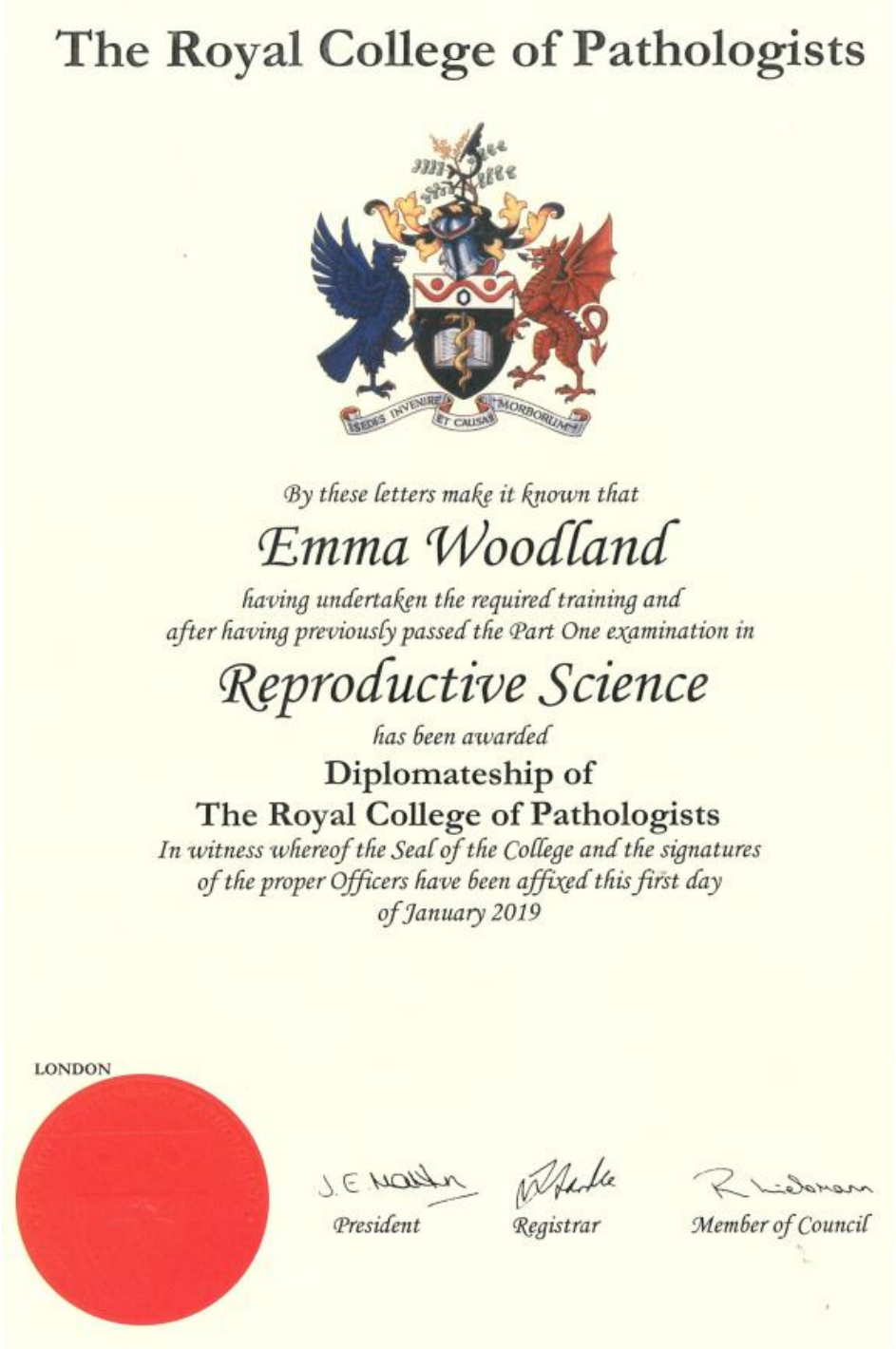
Congratulations! Your final Section A marks, as detailed in the attached document, have been ratified by the Exam Board. You are therefore awarded 120 credits at Post Graduate level, to be put towards the award of DClinSci.

Very best wishes,
Akvile

Akvile Birgelyte | Programme Manager | Section A (PGDip) - Higher Specialist Scientist Training Programme
Alliance Manchester Business School | The University of Manchester | G.035 Dover Street | Manchester M13 9PL |

Appendix 10.

Evidence of completion of HSST section B FRCPath part 1 and part 2 exams



The Royal College of Pathologists

By these letters make it known that

Emma Woodland

having undertaken the required training and
after having previously passed the Part One examination in

Reproductive Science

has been awarded

Diplomateship of
The Royal College of Pathologists

In witness whereof the Seal of the College and the signatures
of the proper Officers have been affixed this first day
of January 2019

LONDON

President *Registrar* *Member of Council*

The Royal College of Pathologists
Pathology: the science behind the cure

College Reference Number: 20007537

Candidate Number: **A276**

Emma Woodland

20 November 2020

Dear Miss Woodland,

FRCPath Part 2 Practical and Oral Examination in Reproductive Science – Autumn 2020

I am pleased to inform you that you have satisfied the Examiners in the Part 2 Examination.

However, as you are aware, you are not yet eligible to become a Fellow of The Royal College of Pathologists as your Part 2 Project has not yet been approved.

We look forward to receiving the project in due course. If you have any queries about your project, please contact exams@rcpath.org.

Congratulations on your success in this examination.

Yours sincerely

Dr Sanjiv Manek
Clinical Director of Examinations

RE: HSST research proforma update please

Flag for follow up.

You replied on Mon 1/4/2021 4:43 PM

Alison Mackay <Alison.Mackay@rcpath.org>
Mon 1/4/2021 3:42 PM
To: WOODLAND, Emma (SALISBURY NHS FOUNDATION TRUST)
Cc: Michael Carroll <Michael.Carroll@mmu.ac.uk>; 'Mark Slevin' <M.A.Slevin@mmu.ac.uk>

Emma Woodland (002) Appr...
461 KB

Dear Emma,

Thank you for your email.

I'm sorry you've not had a response. I had passed your original email on to Mark Slevin at MMU (copied in), as your project proposal was approved and sent back to MMU by the College in August 2020. This should have been passed on to you by MMU.

Please find the approval attached.

Once you've completed the HSST programme (i.e. the full project), you'll be eligible for Fellowship – we'll be notified at that stage by MAHSE.

Kind regards,
Allie

Alison Mackay
Pronouns: she/her
Senior Examinations Coordinator
The Royal College of Pathologists
6 Alie Street
London
E1 8QT
T: 020 7451 6793

Appendix 11.

Results chapter 1 data collection sheets

w/c _____2018 Ambient lab temp: _____ ◦C

ICSI RI temp ICSI dish: _____◦C ICSI N temp ICSI dish: _____ ◦C

MARs Hood temp (5 drop dish under light lid off): _____ ◦C N24 Hood temp: _____◦C

Average maternal age: _____ any exclusions: _____

Number of fresh EC total: _____ Number of eggs total: _____ Number of embryos: _____

Number of blastocysts: _____ Number frozen: _____ Number transferred: _____

Number of Fresh ETs: _____ Number of Frozen's in incs 3/5 tues/weds: _____

Number of staff in: Tues_____ Weds: _____

Inc 3 door openings tues/weds: _____ Inc 5 door openings tues/weds: _____

Blastulation rate (early blast to graded blast only up to day 6): _____

Number of FH: _____ Number of Live births: _____

Utilisation rate: IMPLANTATION RATE: LIVE BIRTH RATE/embryos transferred:

Appendix 12.

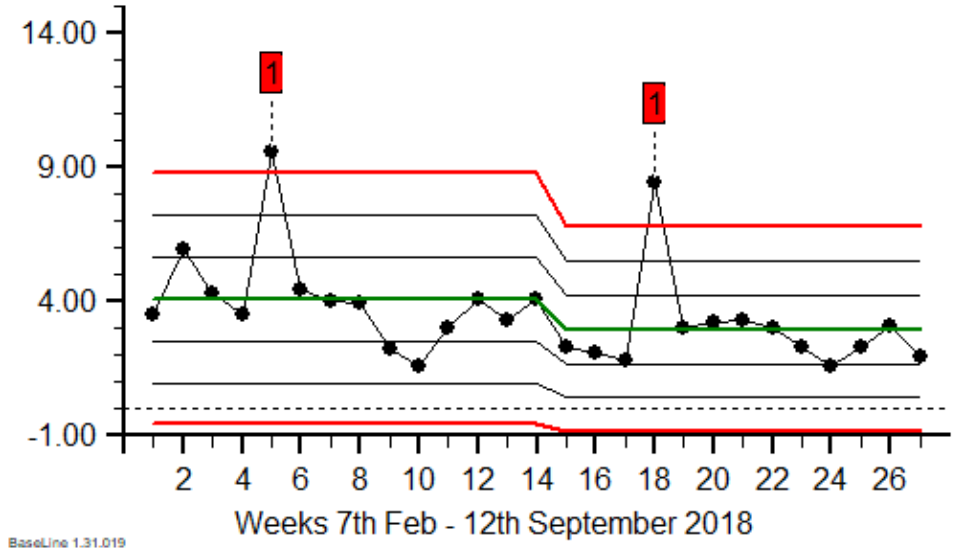
Results chapter 1 additional data

Averages of data can hide patterns that would otherwise be picked up. Averages of incubator 3 and 5 level changes were used for the report analysis but each incubator was also looked at individually for this reason, see below.

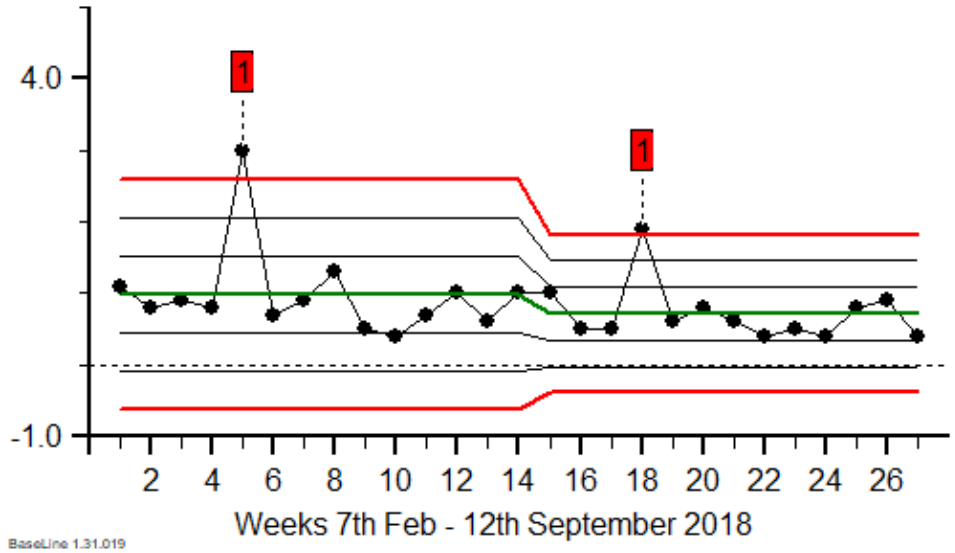
Incubator	Parameter	Pre intervention mean variation	Post intervention mean variation	Triggering SPC rules
3	CO_2	0.979	0.715	**Yes**
3	O_2	4.100	2.946	**Yes**
3	Temperature	1.379	1.862	No
5	CO_2	1.136	0.862	**Yes**
5	O_2	3.493	3.108	No
5	Temperature	0.671	0.700	No

SPC charts for incubator 3 data only, oxygen and carbon dioxide level variation observed within the day on a Wednesday. Special cause variation signals picked up on week 5 pre intervention 7th March 2018 caused by incubator 3 water levels being topped up on this day (no eggs/embryos were within the incubator at the time of this event), and week 18 post intervention 4th July 2018 caused by large egg numbers resulting in more door openings for incubator 3 (49 eggs, 3 patient cases within incubator 3, 24 door openings of incubator 3). These two special cause variation signals were not present on the SPC chart for temperature of incubator 3. Incubator 5 was not affected by the events did not show any special cause variation (data not shown). When incubator 5 data was plotted individually no improvement was seen in the stability of the oxygen levels and temperature post intervention, an improvement was seen in carbon dioxide level stability.

Incubator 3 oxygen level variation



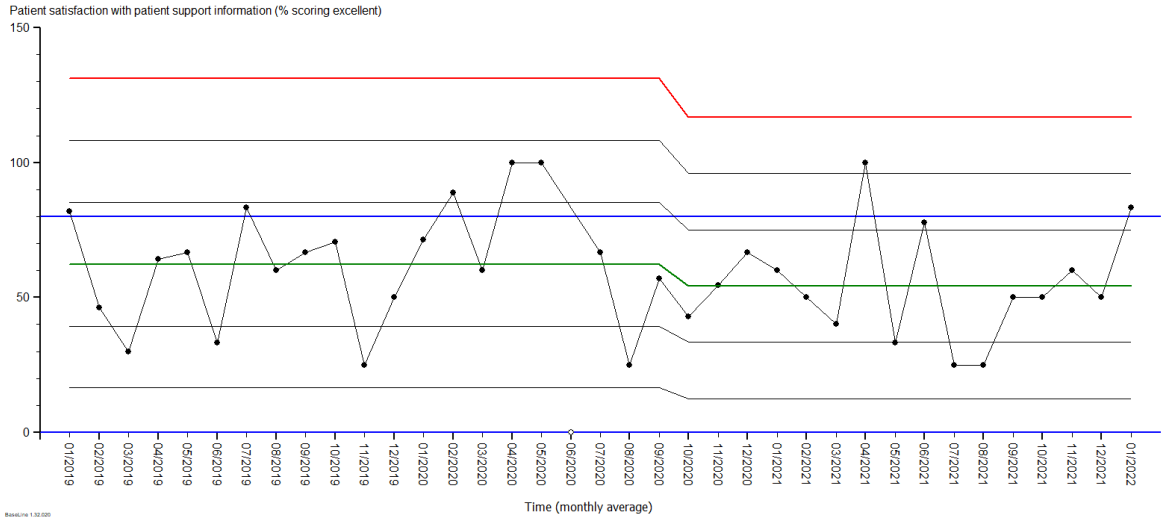
Incubator 3 carbon dioxide level variation



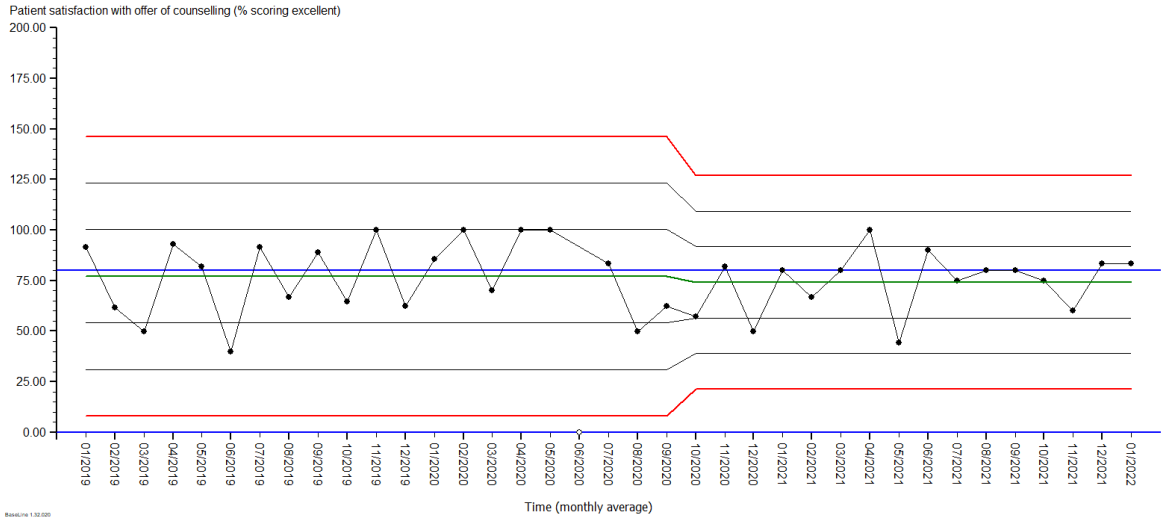
Appendix 13.

Results Chapter 3 SPC charts showing standard patient feedback data over time as a percentage of patients rating the clinic '5' or 'excellent'.

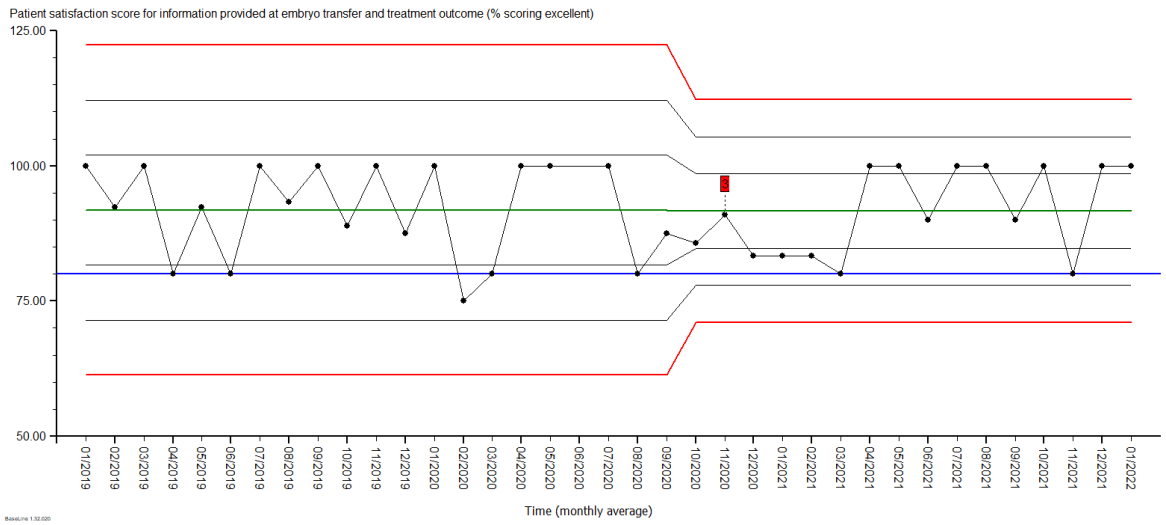
A



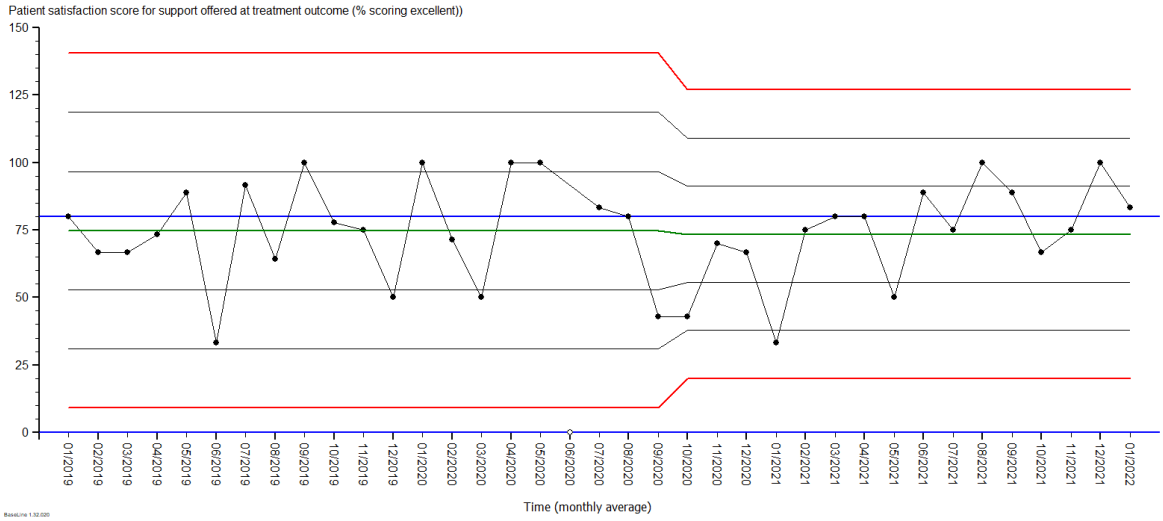
B



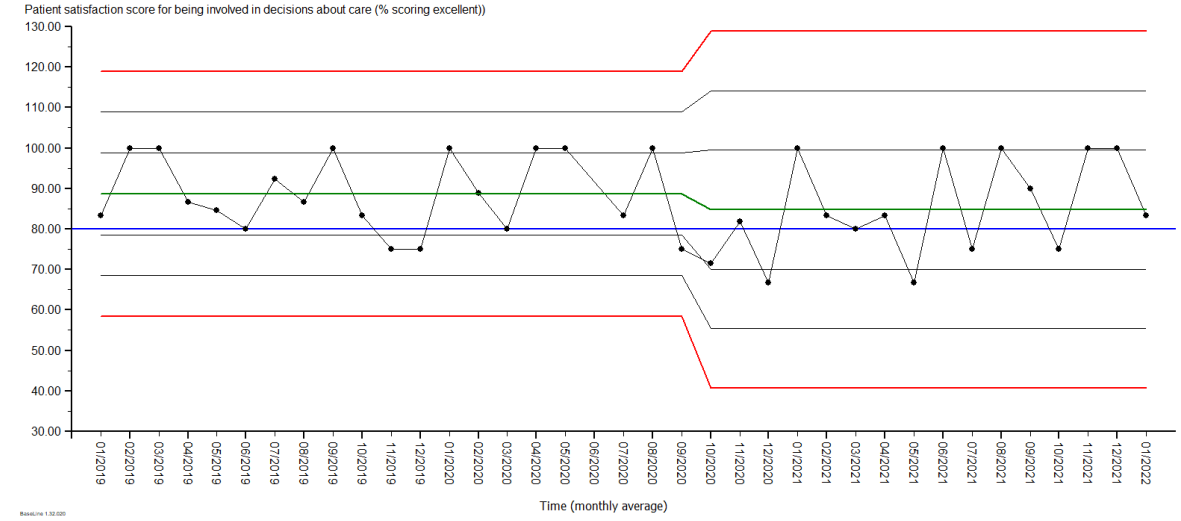
C



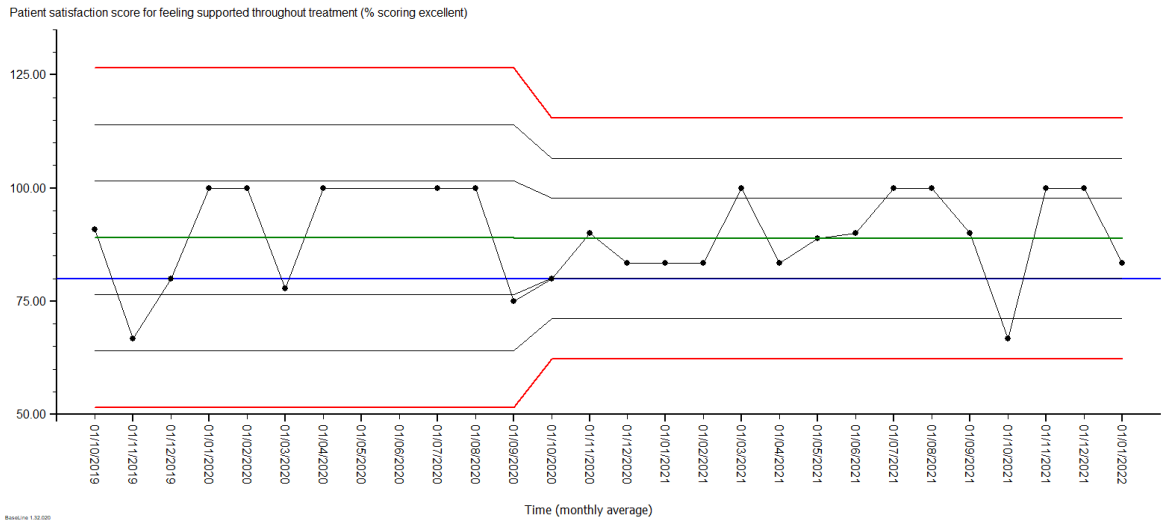
D


Patient satisfaction score for support offered at treatment outcome (% scoring excellent))
150
125
100
75
50
25
0
01/2019 02/2019 03/2019 04/2019 05/2019 06/2019 07/2019 08/2019 09/2019 10/2019 11/2019 12/2019 01/2020 02/2020 03/2020 04/2020 05/2020 06/2020 07/2020 08/2020 09/2020 10/2020 11/2020 12/2020 01/2021 02/2021 03/2021 04/2021 05/2021 06/2021 07/2021 08/2021 09/2021 10/2021 11/2021 12/2021 01/2022
Time (monthly average)

E


Patient satisfaction score for being involved in decisions about care (% scoring excellent))
130.00
120.00
110.00
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
01/2019 02/2019 03/2019 04/2019 05/2019 06/2019 07/2019 08/2019 09/2019 10/2019 11/2019 12/2019 01/2020 02/2020 03/2020 04/2020 05/2020 06/2020 07/2020 08/2020 09/2020 10/2020 11/2020 12/2020 01/2021 02/2021 03/2021 04/2021 05/2021 06/2021 07/2021 08/2021 09/2021 10/2021 11/2021 12/2021 01/2022
Time (monthly average)

F


Patient satisfaction score for feeling supported throughout treatment (% scoring excellent)
125.00
100.00
75.00
50.00
01/10/2019 01/11/2019 01/12/2019 01/01/2020 01/02/2020 01/03/2020 01/04/2020 01/05/2020 01/06/2020 01/07/2020 01/08/2020 01/09/2020 01/10/2020 01/11/2020 01/12/2020 01/01/2021 01/02/2021 01/03/2021 01/04/2021 01/05/2021 01/06/2021 01/07/2021 01/08/2021 01/09/2021 01/10/2021 01/11/2021 01/12/2021 01/10/2022
Time (monthly average)

Appendix 14.

Results chapter 3 full results of additional patient feedback questionnaires

Additional SFC feedback form for QI and support March- April 2021

How satisfied or dissatisfied were you with these aspects of organisation and coordination?	
With the coordination/administration of the treatment	6/7= very satisfied 86% 7/7= Very sat + satisfied 100%
That the number of separate days you/your partner had to attend for treatment was kept to a minimum	5/7= very satisfied 71% 7/7 = Very sat + satisfied 100%
With the length of time between your appointments	3/7= very satisfied 43% 7/7 = Very sat + satisfied 100%
With flexibility of appointment times and dates **(one patient neither satisfied or dissatisfied)**	3/7= very satisfied 43% 6/7 = Very sat + satisfied **86%**
With time spent in waiting rooms on the day of your appointments	2/7= very satisfied 29% 7/7 = Very sat + satisfied 100%
Being seen by the same healthcare professionals throughout your treatment **(one patient dissatisfied with this)**	4/7= very satisfied 57% 6/7 = Very sat + satisfied **86%**
That you could contact a named person at the clinic **(two patients neither satisfied or dissatisfied)**	3/7= very satisfied 43% 5/7 = Very sat + satisfied **71%**
Overall for this section Very satisfied = 53% Satisfied = 39% Neither satisfied nor dissatisfied = 6% Dissatisfied = 2%	

To what extent would you agree or disagree with the following aspects of communication and interaction…	
I felt comfortable asking questions to healthcare professionals	7/7= Strongly agree 100% 7/7 = Strongly agree + tend to agree 100%
I felt involved in decisions about my treatment	5/7= Strongly agree 71% 7/7 = Strongly agree + tend to agree 100%
I felt heard and listened to	5/7= Strongly agree 71% 7/7 = Strongly agree + tend to agree 100%
I had appropriate time with the healthcare professional during my appointments	5/7= Strongly agree 71% 7/7 = Strongly agree + tend to agree 100%
I felt able to state concerns or complaints at any time	5/7= Strongly agree 71% 7/7 = Strongly agree + tend to agree 100%
I felt able to provide feedback at any time	4/7= Strongly agree 57% 7/7 = Strongly agree + tend to agree 100%

To what extent, if at all, were each of the following aspects clearly communicated to you by the clinic?	
The consent forms for treatment	5/7= very clear 71% 7/7= very clear + quite clear 100%
A treatment plan (information about what happens and when)	5/7= very clear 71% 7/7= very clear + quite clear 100%
What to do if there are medical issues or emergencies	5/7= very clear 71% 7/7= very clear + quite clear 100%
The chances of success **(two patients thought this could be clearer)**	4/7= very clear 57% 5/7= very clear + quite clear **71%**
The health risks of treatment such as side effects	5/7= very clear 71% 7/7= very clear + quite clear 100%

How satisfied or dissatisfied were you with aspects of respect and dignity?	
How safe you / your partner felt during treatment	7/7= very satisfied 100% 7/7= Very satisfied + satisfied 100%
The respect and courtesy you were shown	7/7= very satisfied 100% 7/7= Very satisfied + satisfied 100%
The dignity you /your partner were shown during treatment	7/7= very satisfied 100% 7/7= Very satisfied + satisfied 100%
The clinic environment	5/7= very satisfied 71% 7/7= Very satisfied + satisfied 100%
The interest shown in you as a person.	5/7= very satisfied 71% 7/7= Very satisfied + satisfied 100%
Overall, how satisfied/dissatisfied were you with the most recent fertility treatment you had?	5/7= very satisfied 71% 7/7= Very satisfied + satisfied 100%

Additional SFC feedback form for QI and support May- June 2021

How satisfied or dissatisfied were you with these aspects of organisation and coordination?	
With the coordination/administration of the treatment	8/8= very satisfied 100% Improved by 14% 8/8= Very sat + satisfied 100% No change
That the number of separate days you/your partner had to attend for treatment was kept to a minimum	7/8 = very satisfied 88% Improved by 17% 8/8 = Very sat + satisfied 100% No change
With the length of time between your appointments	6/8 = very satisfied 75% Improved by 32% 8/8 = Very sat + satisfied 100% No change
With flexibility of appointment times and dates **(same as last feedback review, one patient neither satisfied or dissatisfied)**	5/8 = very satisfied 63% Improved by 20% 7/8 = Very sat + satisfied 88% **Improved by 2%**
With time spent in waiting rooms on the day of your appointments	6/8= very satisfied 75% Improved by 46% 8/8 = Very sat + satisfied 100% No change
Being seen by the same healthcare professionals throughout your treatment **(No patients dissatisfied with this)**	7/8= very satisfied 88% Improved by 31% 8/8 = Very sat + satisfied 100% Improved by 14%
That you could contact a named person at the clinic **(No patients neither satisfied or dissatisfied)**	7/8= very satisfied 88% Improved by 45% 8/8 = Very sat + satisfied 100% Improved by 29%
Overall for this section Very satisfied = 82% (up from 53%) Satisfied = 16% (down from 39%) Neither satisfied nor dissatisfied = 2% (down from 6%) Dissatisfied = 0% (down from 2%) No patients very dissatisfied	

To what extent would you agree or disagree with the following aspects of communication and interaction…	
I felt comfortable asking questions to healthcare professionals	8/8= Strongly agree 100% 8/8 = Strongly agree + tend to agree 100% No change
I felt involved in decisions about my treatment	7/8= Strongly agree 88% Improved by 17% 8/8 = Strongly agree + tend to agree 100% No change
I felt heard and listened to	8/8= Strongly agree 100% Improved by 29% 8/8 = Strongly agree + tend to agree 100% No change
I had appropriate time with the healthcare professional during my appointments	7/8= Strongly agree 88% Improved by 17% 8/8 = Strongly agree + tend to agree 100% No change
I felt able to state concerns or complaints at any time	7/8= Strongly agree 88% Improved by 17% 8/8 = Strongly agree + tend to agree 100% No change
I felt able to provide feedback at any time	7/8= Strongly agree 88% Improved by 31% 7/7 = Strongly agree + tend to agree 100% No change

To what extent, if at all, were each of the following aspects clearly communicated to you by the clinic?	
The consent forms for treatment	7/8= very clear 88% Improved by 17% 8/8= very clear + quite clear 100% No change
A treatment plan (information about what happens and when)	8/8= very clear 100% Improved by 29% 8/8= very clear + quite clear 100% No change
What to do if there are medical issues or emergencies	8/8= very clear 100% Improved by 29% 8/8= very clear + quite clear 100% No change
The chances of success **(one patient thought this could be clearer (compared to two last time)**	4/8= very clear 50% Down by 7% 7/8= very clear + quite clear 88% **Improved by 17%**
The health risks of treatment such as side effects One patient thought this could be clearer	7/8= very clear 88% Improved by 17% 7/8= very clear + quite clear 88% Down by 12%

How satisfied or dissatisfied were you with aspects of respect and dignity?	
How safe you / your partner felt during treatment	8/8= very satisfied 100% 8/8= Very satisfied + satisfied 100% No change
The respect and courtesy you were shown	8/8= very satisfied 100% 8/8= Very satisfied + satisfied 100% No change
The dignity you /your partner were shown during treatment	8/8= very satisfied 100% 8/8= Very satisfied + satisfied 100% No change
The clinic environment	7/8= very satisfied 88% Improved by 17% 8/8= Very satisfied + satisfied 100% No change
The interest shown in you as a person.	7/8= very satisfied 88% Improved by 17% 8/8= Very satisfied + satisfied 100% No change
Overall, how satisfied/dissatisfied were you with the most recent fertility treatment you had?	7/8= very satisfied 88% Improved by 17% 8/8= Very satisfied + satisfied 100% No change

Appendix 15.

Baseline rules for SPC charts (assignable/special cause variation or red flags/signals)

Four Western Electric Rules for Assignable Cause Variation are used for the Ind Charts in this study.

Note: These were designed for approximately normally distributed data where the mean and median are similar.

Rule#1 - One point more than 3 sigma from the mean.

Rule#2 - Two out of three points more than 2 sigma on the same side of the mean.

Rule#3 - Four out of five points more than 1 sigma on the same side of the mean.

Rule#4 - Nine or more points on the same side of the mean.

Other Signal Detection Rules NOT used in Baseline include:

Six or more points steadily increasing or decreasing.

Eight points in a row with no points less than 1 sigma from the mean.

Fourteen points on a row alternating up and down.

Fifteen points in a row less than 1 sigma either side of the mean.

Appendix 16.

Standard clinic patent feedback form

Tel: 01722 417224
Email: sft.sfc@nhs.net
www.salisburyfertilitycentre.nhs.uk

NHS Salisbury NHS Foundation Trust

Salisbury Fertility Centre – Patient Questionnaire

At Salisbury Fertility Centre (SFC) we aim to provide an excellent service and choice of fertility treatments to all patients. We would appreciate it if you would take the time to complete this questionnaire as fully as possible. Patient feedback at all stages of treatment is vital for us to improve/enhance our service. Please be aware that any comments you make may be included on the SFC website and/or our Facebook page. You would remain anonymous. You can also rate our clinic and share your experience by visiting the HFEA website at hfea.gov.uk.

Please ring the number that represents your comments on the quality of services provided at Salisbury Fertility Centre. Many thanks for your time.

Please add any further comments in the space provided.

5 = Excellent
4 = Good
3 = Average
2 = Poor
1 = Unsatisfactory

☹ 1 2 3 4 5 ☺

1. CONSULTATION	**PATIENT**	**PARTNER** (if applicable)
a) Communication and written information provided about treatments available.	1 2 3 4 5	1 2 3 4 5
b) Ease of obtaining blood test and semen analysis results	1 2 3 4 5	1 2 3 4 5
c) Support groups/literature provided	1 2 3 4 5	1 2 3 4 5
d) Satisfaction with conclusion of consultation and plan	1 2 3 4 5	1 2 3 4 5
e) Awareness of independent counselling	1 2 3 4 5	1 2 3 4 5
2. TREATMENT CYCLE		
a) Ease of contacting suitable members of SFC for information and answering questions	1 2 3 4 5	1 2 3 4 5
3. EGG RECOVERY (❑ tick if not applicable)		
a) Service provided by Day Surgery staff	1 2 3 4 5	1 2 3 4 5
b) Duration of stay	1 2 3 4 5	1 2 3 4 5
c) Information provided on day of egg recovery	1 2 3 4 5	1 2 3 4 5
d) Facilities provided by day surgery unit	1 2 3 4 5	1 2 3 4 5
4. SEMEN SAMPLE PRODUCTION (❑ tick if not applicable)		
a) Comfort of "the room"	1 2 3 4 5	1 2 3 4 5
b) Privacy of "the room"	1 2 3 4 5	1 2 3 4 5
c) Information on test results	1 2 3 4 5	1 2 3 4 5
5. DAY FOLLOWING EGG COLLECTION (❑ tick if not applicable)		
a) Level of communication with SFC	1 2 3 4 5	1 2 3 4 5
b) Support and advice provided by SFC	1 2 3 4 5	1 2 3 4 5

Salisbury FERTILITY CENTRE
Tel: 01722 417224
Email: sft.sfc@nhs.net
www.salisburyfertilitycentre.nhs.uk
NHS Salisbury NHS Foundation Trust

☹ 1 2 3 4 5 ☺

6. EMBRYO TRANSFER DAY (❑ tick if not applicable)		
a) Duration & comfort of embryo transfer procedure	1 2 3 4 5	1 2 3 4 5
b) Information provided regarding embryo transfer procedure and treatment outcome	1 2 3 4 5	1 2 3 4 5
7. POST TREATMENT		
a) Information regarding post treatment	1 2 3 4 5	1 2 3 4 5
b) Support offered with regards to treatment outcome	1 2 3 4 5	1 2 3 4 5
c) Follow up communication with SFC and future plan of action	1 2 3 4 5	1 2 3 4 5
8. OVERALL		
a) Did you feel involved in the decisions about your care?	1 2 3 4 5	1 2 3 4 5
b) Were the staff available to talk about concerns?	1 2 3 4 5	1 2 3 4 5
c) Did you both have privacy when discussing treatment options?	1 2 3 4 5	1 2 3 4 5
d) Did you feel supported by staff throughout your treatment journey?	1 2 3 4 5	1 2 3 4 5
e) Did you find it easy to access the service?	1 2 3 4 5	1 2 3 4 5
f) Did you know who to contact if you were worried about a condition or any part of your treatment	1 2 3 4 5	1 2 3 4 5
g) Were you informed about the medication you were taking?	1 2 3 4 5	1 2 3 4 5
h) If you had friends or family requiring similar treatment, how likely are you to recommend SFC?	1 2 3 4 5	1 2 3 4 5
i) Did you use the SFC website at any stage in your treatment?	Yes / No	Yes / No
j) If yes, how useful did you find the website? *Any specific comments about the website can be left below.*	1 2 3 4 5	1 2 3 4 5

9. COMMENTS OR SUGGESTIONS

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Rate our clinic and share your experience by visiting the HFEA website (hfea.gov.uk) and selecting Salisbury Fertility Centre

Scan me

If you include your name then we can to reply to your comments. You may remain anonymous if you would prefer. Thank you for your help. Best wishes from the SFC team.

Name **Date**

Appendix 17

Attempt to utilise 5S to declutter and reorganise the Fertility centres stock cupboard for a more efficient working environment which reduces risk of possible disruption to service delivery.

Before 5S exercise

After 5S (blue labels added to shelves and product location chart created)