# ACCELERATED RED CELL TRANSFUSION FOR SELECTED PATIENTS RECEIVING BLOOD TRANSFUSION AT HOME

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# ACCELERATED RED CELL TRANSFUSION FOR SELECTED PATIENTS RECEIVING BLOOD TRANSFUSION AT HOME

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## DECLARATION

I declare that no material contained in the thesis has been used in any other submission for another academic award.

This thesis is entirely the work of the author.

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# Abstract

**Background:** The Community Intravenous Therapy (CIVT) service gives patients the benefit of receiving IV therapies (including blood transfusion) in their own home, avoiding hospital admission. It is important to ensure this service can be offered to as many patients as possible. If red cell transfusion could be safely performed over a shorter duration (accelerated transfusion), this could theoretically increase the capacity of the service without additional resource. Red cell transfusions are usually administered over a minimum of 90 minutes to a maximum of four hours per unit. It was proposed that one unit could be given in 60 minutes (up to a maximum of 2 units per transfusion episode) to medically selected patients who do not have heart failure or other risk factors for circulatory overload.

**Methods:** Physiological tolerability and safety of accelerated transfusion was evaluated by clinically assessing patients for symptoms and signs of transfusion-associated circulatory overload (TACO) after standard and accelerated rate transfusions. The impact on service capacity and staff resource was evaluated by auditing home transfusion workload data to determine the number of patients who were eligible for accelerated rate transfusion and the potential impact this had on treatment delivery time. Patient and practitioner experiences of accelerated transfusion were evaluated by conducting thematic analysis on semi-structured interviews to assess the acceptability and desirability of service change.

**Results:** When accelerated red cell transfusion was performed on medically selected patients who had been screened for risk factors for circulatory overload, accelerated transfusion appeared to be safe. None of the patients in the study (n=25) developed transfusion associated circulatory overload across 269 accelerated transfusions performed. The mean arterial pressure appeared to statistically significantly increase up to 24 hours after blood transfusion regardless of whether it was infused at a standard or accelerated rate, with the group mean remaining within the normal range (standard rate transfusion: $p = 0.0441$; accelerated rate average across three transfusions: $p = 0.009$). There was no statistically significant difference between pre and post-transfusion mean arterial pressure measurements when standard and accelerated rate transfusions were compared (average across three accelerated rate transfusions: $p = 0.473$), showing that accelerated transfusion itself did not cause an increase in mean arterial pressure above that of standard rate transfusion. A significant proportion of haematology patients (57%, 26/46) were medically eligible for accelerated transfusion, and 49% of total transfusion episodes (224/459) were performed as such. Performing accelerated transfusion on eligible patients could potentially save 105 nursing hours, allowing an additional 35 three hour visits or 26 four hour visits per year. Accelerated transfusion was well received by patients. Positive themes from the data included less time receiving healthcare allowing freedom and time to do other things, improvements in comfort and altruism from knowledge that other patients and the service was benefitting. CIVT practitioners were highly motivated and positive about accelerated transfusion. Themes included satisfaction in seeing positive benefits in

quality of life and social aspects of patient's lives; improved continuity of care, better work scheduling; increased service capacity, job satisfaction; better working conditions and professional autonomy in clinical decision-making.

**Conclusion:** Accelerated red cell transfusion appears to be safe in medically selected patients. It can potentially increase service capacity through efficient use of staff resource whilst maintaining a safe and high quality service. Understanding of patient and practitioner experience suggested that changing the service to offer accelerated transfusion would be both acceptable and desirable.

# Chapter One:

# Introduction

This research study is based upon a service development project at a National Health Service (NHS) Foundation Trust, incorporating the Community Intravenous Therapy Team (CIVT), the Clinical Haematology service, and the Blood Transfusion service within the Laboratory Medicine Department. The first chapter introduces the purpose of the research, the research questions and hypotheses generated, and how these meet the aims and objectives of the research. The chapter concludes with a rationale framework for the research, providing a conceptual synopsis of the introductory chapter.

## Problem Statement

The CIVT Team requires increased capacity to be able to offer intravenous (IV) therapies (including blood transfusion) to more patients at home without impacting on current resources.

In terms of developing the current home transfusion service, two general questions are therefore raised: whilst maintaining or improving the benefits of the service, whether this service may be delivered more efficiently and if so, the options for increasing the efficiency and capacity of the service.

## Statement of Purpose and Research Questions

If red cell transfusion could be safely performed over a shorter duration, this could theoretically increase the capacity of the service without additional

resource. More patients could potentially be treated at home, and the patient would have less intrusion from medical interventions with a shorter home visit, which may also have a positive impact upon patient and practitioner experience. Red cell transfusions are usually administered over a minimum of 90 minutes to a maximum of four hours per unit (BCSH, 2009). It is proposed that one unit can be given in 60 minutes (up to a maximum of 2 units per transfusion episode) to medically selected patients who do not have heart failure or other risk factors for circulatory overload.

The general research question was developed from the literature review in the following chapters and can be defined by asking: whether transfusing two units of red cells over 60 minutes per unit (accelerated transfusion) is safe and could potentially increase CIVT service capacity, while gaining understanding of the patient's and practitioner's experience.

The question can therefore be viewed through the two lenses of physiological tolerability and experiential and organisational acceptability/benefit. This forms the foundation of the multi-methods approach which is discussed further in the Methods chapters.

**Hypotheses**

Based upon the background and impetus for the research supported by existing evidence, the following hypotheses can be developed for the quantitative aspects of the research question:

- $H_1$: Two units of red cells transfused over 60 minutes each can be physiologically tolerated in selected patients ($H_0$ there is no difference in the incidence of Transfusion Associated Circulatory Overload (TACO) between standard and accelerated rate transfusions)
- $H_1$: Implementation of accelerated transfusion could potentially increase CIVT service capacity ($H_0$ Implementation of accelerated transfusion would not potentially increase CIVT service capacity)

The qualitative strand of the study is value-adding and seeks to inductively gain understanding of patient and practitioner experience without *a priori* theories and therefore hypotheses are not appropriate.

**Aims and Objectives of the Research**

The aim of the research was to determine the physiological tolerability of 60 minute per unit red cell [accelerated] transfusions in selected patients. The research also aims to understand the experiential effect of accelerated transfusion on patients and practitioners, and whether there is improvement of service capacity.

The primary objective of the research was to develop and implement this aspect of transfusion practice locally, if the alternative ($H_1$) hypotheses are accepted, and provide evidence for other healthcare organisations to do similar. The secondary objective was to develop and progress existing evidence relating to the recommended rate of transfusion in selected patients, adding to the literature regarding the selection of transfusion rate appropriate to the patient's condition. The study will also contribute to the

literature in the currently under-researched areas of patient and practitioner experience of blood transfusion, and add to the currently small number of qualitative studies in transfusion.

**Rationale and Justification for the Research, and Contribution to Current Knowledge:**

The home transfusion service in the participating NHS Trust is an exemplar of national policy for care delivered closer to home and has received national recognition (Audit Commission, 1999). It is popular both with patients using the service and CIVT practitioners delivering it. The service is well established and has an excellent safety and governance record. Although complex to quantify, there is some evidence this model of service provision is more cost effective than equivalent hospital care (Koepke *et al* 1988; DH, 2009). The exact cost of a blood transfusion for each service model is to some extent academic as each will have different indirect costs for which there will be interdependencies with other unrelated procedures delivered by each of them. There are clear non-economic advantages to the service that persuades the case for continued provision and indeed expansion of home transfusion. This was first endorsed by Rabiner and Telfer (1970) and continues to be important for patients with physical, clinical and social issues to whom hospital day care visits are problematic. Therefore, the alternative perspective to improve the efficiency of the service is to improve capacity, rather than compete on the cost of an individual care episode.

The proposal to improve service capacity by reducing treatment time is constrained by currently limited evidence for safe infusion rates for blood

transfusion, due to a lack of experimentally designed studies in this area of clinical practice. This lack of clarity is further complicated by the paucity of prospective studies of Transfusion Associated Circulatory Overload (TACO) in elective red cell transfusion in stable patients who are not receiving concomitant intravenous (IV) fluids. Previous studies of TACO have been retrospective, sometimes focussed on other types of blood components, non-blood concomitant IV fluids were also sometimes confounding factors, and also involved patients in acute care settings where acute illness could have pre-disposed the patient to fluid overload. It is also difficult to establish the overall incidence of TACO where red cells were independently responsible, due to poor reporting on fluid balance and concomitant fluids in haemovigilance reporting to the UK Haemovigilance Organisation: Serious Hazards of Transfusion (SHOT). This research will generate prospective data on this specific patient group.

The co-morbidity and risk factor themes that have emerged from the SHOT-reported cases of TACO allow for the development of strategies to identify patients who are at risk of circulatory overload. This can be used to inform the development of medical selection criteria to create a framework for the rate and volume of transfusion. This research could potentially contribute new knowledge and evidence for a more refined understanding of safe red cell dosing and infusion-rates and establish a mandate for patient-tailored therapy.

The limited research that exists on patient experience of receiving blood transfusions reports negative responses in terms of the long duration of

treatment. This finding concurs with the anecdotal observations of patients using the service, and staff delivering the service locally, and advocates further research into this area of enquiry. There are no studies on practitioner experience of administering blood transfusions to patients. Research based on qualitative methodology is under-represented in the body of research in transfusion medicine. This study may generate more interest in this approach within this area of practice and demonstrate the benefits of mixed methods research to bring patient-focus to practice change.

The research also respects the external drivers of related national policy: cost-effectiveness and responsible use of resources; patient-centred care and experience; delivery of care closer to home; and national guidance on the co-designing of services with patients. This is further developed in the contextual framework in the following chapter and also justifies the research study.

**Thesis Structure**

The following preparatory chapter forms the contextual framework from which the conceptual framework develops, informing and justifying the methodological approaches. To ensure a clear relationship with the research questions, the methods are presented as three separate chapters which represent the physiological (safety) enquiry, resource and service capacity enquiry, and the patient and practitioner experience enquiry. A similar structure follows with the analytical chapters. The findings from each of the three strands of enquiry then conflate in the concluding chapter to answer the research questions and debate the findings in the light of the limitations

of current evidence on which the research was designed. The discussion also addresses further strengths and limitations of the study and the impact of the research on the future delivery of home transfusion and other IV therapies in the Trust. The influence of the research on the international definition/surveillance diagnosis of TACO and other aspects of transfusion practice, including opportunities for further study are also discussed.

# Chapter Two:
# Literature Review

## Literature Review Strategy

The purpose of the literature review is to identify, appraise, synthesise and analyse published evidence to produce a contextual framework in chapter three, providing background and critique on the current status of research. The thesis is developed in the conceptual framework in chapter four where the literature review supports the development of the arguments formed in the contextual framework chapter.

The type of literature review was determined by considering its aim in the context of the methodological approach. Grant and Booth (2009) proposed a typology of literature reviews which provide a useful tool in determining an appropriate literature review type. The aim of the literature review was determined *a priori*. It was required to pragmatically demonstrate a robust and methodical search process where the quality of the literature identified was appraised for significance, representativeness, reliability, contribution and contemporaneousness. The literature subsequently identified was then used to support arguments for the development of the thesis, emphasising the generation of hypotheses and innovation through critical evaluation. Grant and Booth (2009) characterised review types by assessing them against a *Search, AppraisaL, Synthesis and Analysis* (SALSA) framework.

The aims of the literature review accord most closely with the SALSA characteristics of *The Critical Review* and *Systematised Review.* This was cross-checked with the author's descriptor for both types of review to demonstrate appropriate attribution of review typology. This is summarised in table 2.1 below.

**Table 2.1: Literature Review Typology Evaluation**

| Review Type | Description key words | Search | Appraisal | Synthesis | Analysis |
|---|---|---|---|---|---|
| Review type for this study | Pragmatic, methodical, significance, robust, critical evaluation, theses development, hypotheses, innovation | Identify most significant (pragmatic- may not be comprehensive) | Based on significance, representativeness, contribution, reliability, contemporaneousness | Narrative, conceptual, chronological | What is known, limitations, uncertainty, conceptual, derivative, new theory |
| Critical Review | Extensive, quality, critical evaluation, analysis, conceptual innovation, hypothesis, model | Identify most significant | According to contribution | Narrative, conceptual, chronological | Conceptual, derivative, new theory |
| Systematised Review | Stops short of systematic review, comprehensive, critical | +/- comprehensive | +/- quality assessment | Narrative/ tabular | What is known, limitations, uncertainty |

Adapted from Grant and Booth (2009)

The literature review process for this study aspires to the same aims as the *Critical Review* in that the output of extensive researching and critical evaluation of quality on the value of published work manifests in the synthesis new ideas and hypotheses. However, the limitation of the *Critical Review* is lack of systematisation as the search and appraisal process. The *Systematised Review* provides an attempt at systemisation but acknowledges insufficiencies in meeting the criteria for a *Systematic Review*

such as multiple reviewers and access to all databases and published works. The degree of systemisation may also be limited to parts of the review methodology such as the literature searching method alone. The literature review strategy for this research study combines elements of both *Critical* and *Systematised Review* typologies to demonstrate fulfilment of the literature review aims. This is intended to demonstrate a robust approach using methodical and systematic search and appraisal methods in order to produce output that can present the current status of research while providing critique on limitations and uncertainties, and developing a thesis for the new concept of accelerated transfusion, and its associated hypotheses. The methods applied to this strategy follow below.

## Literature Review Methods

### Sources

The literature search was performed using the National Institute of Health and Care Excellence (NICE) Healthcare Databases Advanced Search (HDAS) using Open Athens account access to allow access to all its available databases. A broad range of databases were required as the research study involved medicine, clinical science, health and social care, psychology, health management and health economics. Of the available databases the following were judged as relevant to the research study, but was accepted as possibly not exhaustive: British Nursing Index (BNI, 1992 to present); Cumulative Index to Nursing and Allied Health Literature (CINAHL, 1981 to present); Excerpta Medica Database (EMBASE, 1974 to present); Health Business Elite (HBE, 1922 to present); Health Management

Information Consortium (HMIC, 1979 to present); Medline (1946 to present); PsycINFO (1806 to present); and PubMed.

It was recognised that relevant sources may not be captured by databases for published works in journals, this included websites, reports, guidelines and comment produced by various organisations. An additional grey literature search was conducted using Google™ and Google Scholar™ search engines. There was also a requirement to hand-search a limited number of sources to address specific complex questions.

**Search Terms and Search Limits**

Search terms were determined by each aspect of the research study title and research questions, and modified according to a trial search in HDAS and Google™ after judging the broad relevance and quantity of the search output and removing duplications. The thesauri of each database were utilised to finesse search key-words. Search terms were limited to the abstract and/or title depending on the number of records returned, and searched in HDAS without date restrictions. The records returned were limited to English language publications and relating to human research studies. The first literature search was first conducted when designing the research study in December 2013 and was repeated in April 2017 when writing the thesis. Table 2.2 below summarises the literature search terms used.

## Table 2.2: Literature Search Terms

| Aspect of title and research question | Sources | Search terms applied |
|---|---|---|
| **Blood transfusion practice** | BNI, CINAHL, EMBASE, Medline, PubMed | ("blood transfusion").ti,ab AND ("history of medicine").ti,ab<br>(transfusion).ti,ab AND (guideline).ti,ab<br>("intravenous therapy").ti,ab AND (standards OR guideline).ti,ab<br>("cost of blood transfusion").ti,ab |
| | Google, Google Scholar | "history of blood transfusion"<br>"transfusion guidelines"<br>"administration of blood"<br>"standards for infusion therapy"<br>"intravenous therapy practice" |
| | Local blood transfusion policy | Hand-search |
| **Rate of blood transfusion Volume/dose of red cells** | BNI, CINAHL, EMBASE, Medline, PubMed | ("blood component").ti,ab AND ("infusion rate").ti,ab<br>("transfusion").ti,ab AND ("body weight").ti,ab) AND ("red cells").ti,ab |
| **Home transfusion** | BNI, CINAHL, EMBASE, Medline, PubMed, HBE, HMIC | ("home transfusion").ti,ab |
| | Local audits and reports | Hand-search |
| **Safety of blood transfusion** | BNI, CINAHL, EMBASE, Medline, PubMed | ("blood transfusion").ti,ab AND (governance).ti,ab<br>(("blood transfusion" AND safety) AND UK).ti |
| | Google, Google Scholar | "transfusion safety UK"<br>"transfusion regulation"<br>"transfusion governance" |
| | Serious Hazards Of Transfusion reports | Hand-search |
| **Transfusion-associated circulatory overload and iatrogenic fluid overload** | BNI, CINAHL, EMBASE, Medline, PubMed | ("pulmonary complications").ti,ab AND ("transfusion").ti,ab<br>("transfusion associated circulatory overload").ti<br>(iatrogenic AND "fluid overload").ti,ab<br>("fluid balance").ti,ab AND ("fluid overload").ti |
| | Clinical medicine text-books | Hand-search |
| **Patient-centred care, co-designing of services in the context of policy and regulation** | BNI, CINAHL, EMBASE, Medline, PubMed, HBE, HMIC | ("healthcare at home").ti,ab<br>(co-designing).ti,ab |
| | Google, Google Scholar | "patient centred care policy"<br>"co-design of healthcare services" |
| **Patient and practitioner experience** | BNI, CINAHL, EMBASE, Medline, PubMed, HBE, HMIC | (transfusion).ti,ab AND ("patient experience").ti,ab<br>(transfusion).ti,ab AND ("lived experience").ti,ab<br>((transfusion AND nurse) AND experience).ti,ab<br>((transfusion AND nurse) AND attitude).ti,ab |
| | Google, Google Scholar | "patient's experience of blood transfusion"<br>"nurse experience of blood transfusion" |

## Appraisal Method

Each title and abstract returned by the HDAS search was evaluated for significance, representativeness, contribution, reliability, and contemporaneousness. The inclusion and exclusion criteria were based on

column 1 of table 2.2 above, favouring recent original articles from high impact journals. Titles and abstracts meeting these criteria were considered eligible and saved outputted into a Microsoft Excel™ file. Records from other sources were evaluated on-screen. This was not a formal systematic review but a degree of rigour was required in the appraisal of the quality of the literature identified from the search. This is represented diagrammatically in figure 2.1 below.

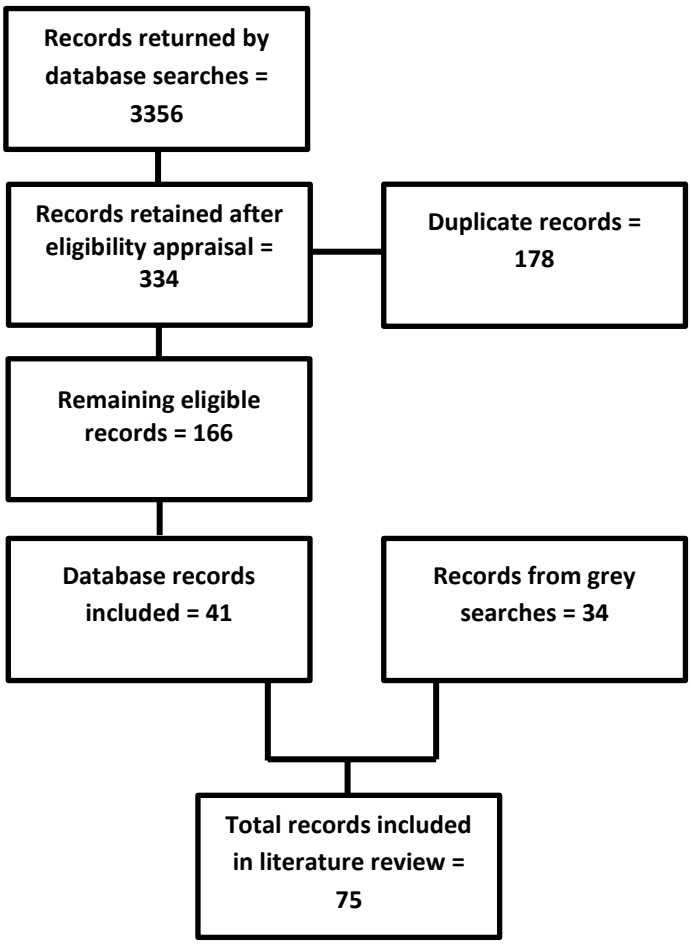



**Figure 2.1: Literature Search Results**

## Synthesis and Analysis

The remaining literature was then used to produce a narrative which critically evaluated the background and current status of research in this area of transfusion medicine and clinical practice, highlighting gaps in current knowledge, limitations and uncertainty, and providing a contextual framework for the research study in chapter three. The synthesis of the published literature collectively provided added value in building arguments to challenge and progress current practice, by supporting the development of new theses and testing of hypotheses presented as a conceptual framework in chapter four.

# Chapter Three:
# Contextual Framework

This chapter is a review of the literature using the strategy described in chapter two. The chapter comprehensively introduces the elements of the thesis title describing the history, safety and clinical practice of blood transfusion, including the development and delivery of home transfusion. The current status of research in this area and the influence of wider healthcare policy are also considered, leading to the development of a contextual framework for the study (figure 3.1, page 41).

## Blood Transfusion in Clinical Practice

This introductory section considers the station of blood transfusion in wider clinical practice and its importance in the provision of elective and emergency healthcare. The regulation and governance of blood transfusion provide practice standards and a means of evaluating the safety of blood transfusion as evidenced by haemovigilance reporting data. The practical aspects of performing blood transfusion and care of patients receiving blood transfusion are also considered in the context of current clinical guidelines. The wider context, safety and practical aspects discussed here provide a descriptive and critical platform from which the contextual framework of the thesis later develops.

## Historic Development of Blood Transfusion

The history of blood transfusion is polarised by momentous achievements and catastrophic failures, on a background of intrigue, rivalry and accusations of murder (Tucker, 2011). The maverick experimenters of the 17th century laid the foundations for modern transfusion medicine. The collateral damage of experimental failures also stalled it for 150 years through hastening the demise of animals and humans alike. This resulted in the practice being outlawed despite being cited in the 1666 Philosophical Transactions of the Royal Society (Royal Society, 1666). By the early 19th century, James Blundell [1791-1878], a medical practitioner, revisited the concept of blood transfusion after witnessing a woman dying from a post-partum haemorrhage (Sturgis, 1942). However, progress in establishing the technique was impeded due to technical difficulties in administering blood, preventing the blood from clotting, and not least, understanding donor-recipient compatibility. The latter problem was solved by Karl Landsteiner's [1868-1943] work on discovery of the ABO human blood group system in 1901 for which he received a Nobel prize in 1930 (Landsteiner, 1930). The 20th century observed an exponential increase in discovery and knowledge in transfusion science and medicine, making transfusion safer for those who needed it. The first UK blood bank was opened in Ipswich in 1937. Organised altruistic blood donation began in a number of regional centres in the United Kingdom (UK), which became critically important in treating casualties of war when the Second World War began a few years later. The National Blood Service was established in 1946. Now known as UK Blood

and Transplant (part of the National Health Service), the organisation collects around 2.1 million blood donations per year (NHSBT, 2014). Transfusion of red cells, plasma and platelets saves, and improves the quality of life for hundreds of thousands of patients in the UK every year. Transfusion of red cells is given for haemorrhage (including trauma), bone marrow failure and other causes of severe anaemia. Major surgery and myelosuppressive chemotherapy would not be an option for patients if red cell transfusion were not possible, and many patients would quickly die from bone marrow failure diseases without regular transfusion support.

Laboratory and clinical practice in blood transfusion is now highly regulated. Modern research and development has yielded solutions to the fundamental barriers based upon experience by the early experimenters such as optimising the storage and administration of blood, compatibility-testing, and screening/testing to improve blood safety. Blood transfusion is a mainstay of current medical and surgical practice, and continuous research and development in every aspect of transfusion practice is essential to refine and finesse knowledge and understanding of this field to improve the safety and utility of this vital therapy.

**The Safety of Blood Transfusion in the UK**

Blood Transfusion is subject to a high level of regulation and governance, to ensure high safety and quality standards. The transfusion clinical process is not directly regulated. The governance of blood transfusion was, until recently, covered by a specific criterion of the NHS Litigation Authority (NHSLA) Standards (NHSLA, 2013), and is now indirectly governed and

regulated by the Care Quality Commission (CQC) and cross-cuts several aspects of the Standards (CQC, 2010). Transfusion Laboratory activities are regulated by the Medicines and Healthcare products Regulatory Agency (MHRA), who inspect facilities under the Blood Safety and Quality Regulations (BSQR, 2005). The MHRA inspect activities relating to the testing, processing, storage and distribution of blood in hospitals. The MHRA also jointly administrate a haemovigilance system, Serious Adverse Blood Reactions and Events (SABRE) with Serious Hazards of Transfusion (SHOT), and hospitals are legally obliged to report to SABRE under the auspices of the regulations. The SABRE gateway allows simultaneous reporting to SHOT and SABRE. Reporting to SHOT is not legally mandated, but the majority of organisations do report to SHOT as this is good governance practice.

In 2016, 100% of NHS organisations participated in SHOT reporting (Bolton-Maggs *et al*, 2017). SHOT has compiled data on transfusion errors, adverse events and reactions since 1996, and publish an annual report with recommendations to improve the safety of transfusion practice. The risks of transfusion can be broadly considered to be procedural errors, pathological reactions and pulmonary complications. The pathological reactions and pulmonary complications may be idiosyncratic and therefore unavoidable, although some may be prevented by improved clinical practice, and were regarded by SHOT as *possibly preventable*. However, the risks caused by procedural error are considered preventable. There were 26 deaths reported in the 2016 report, 8 of which were regarded as *probably* and 15 *possibly*

related to transfusion, and three *definite*. One was in a category regarded as *not preventable* (acute transfusion reaction), 15 were in categories that are regarded as *possibly preventable with improved practice* (haemolytic transfusion reaction and transfusion associated circulatory overload), and 10 were in categories that are regarded as *preventable* (delayed transfusion, and avoidable transfusion). There were a further 122 cases of major morbidity. In context, the risk of death from transfusion is 1.05 per 100,000 blood components issued in 2016, and 4.91 for major morbidity (Bolton-Maggs *et al*, 2017). Blood Transfusion can be considered a low risk for serious harm or death and compares favourably with other medical interventions. For example, the 90 day mortality for a total hip replacement was estimated to be 0.65% (650 in 100,000) (Berstock *et al*, 2014) which is approximately 650 times more than the mortality risk for blood transfusion.

**Intravenous Administration of Blood**

Blood components (including red cells) can be administered by two methods, either gravity infusion or an infusion device. Gravity infusion is a manual technique using an IV administration set specifically for use with blood. The administration set incorporates a 170-200 micron screen filter designed to remove any particulate material present in stored blood. The set is attached to the blood unit via a sterile port. The chamber is filled with blood, and the line is primed. The line is then attached to a cannula sited in a suitable vein in the dorsal aspect of the patient's hand, or in the arm. An indwelling catheter may be used if the patient has had one inserted for other regular intravenous treatments such as chemotherapy.  The volume and rate of the

infusion is prescribed by the medical officer, and the 'drip-rate' is calculated by the practitioner administering the transfusion, using the volume stated on the blood unit label. The volume (ml) to be infused is multiplied by the number or drops in 1ml (typically this is 15 for blood and more for crystalloid fluids which are less viscous than blood, but the manufacturer's instructions should be followed). This value is divided by the number of minutes over which the infusion is to be delivered. This gives the number of drops falling into the drip chamber per minute (Dougherty, 1999). The practitioner adjusts the drip rate accordingly and monitors the infusion to ensure the rate is maintained throughout the transfusion. Alternatively, blood may be administered using an infusion pump that is validated for use with blood components. A specific blood IV administration set must be used that is also compatible with the infusion pump equipment. The pump is programmed to deliver a specified volume (as stated on the blood unit label) over a specified duration, as set by the practitioner in accordance with the prescription. The technique is otherwise identical to gravity infusion in terms of attaching the administration set to the unit, priming and connecting to a cannula in the patient. Infusion pumps have the additional benefit of minimising calculation errors, and will alarm if the flow rate is interrupted. The residual volume of blood remaining in the administration set (and therefore not reaching the patient) is approximately 15ml.

**Volume and Infusion Rate Relationship in Red Cell Transfusion**

The volume of red cell transfusion in the normovolaemic patient is an important consideration in achieving an appropriate haemoglobin increment

in the patient to resolve the symptoms of anaemia. The recommended volume or dose of red cell transfusion in adults is empirical. The NICE guideline for blood transfusion promotes single unit transfusion in non-bleeding patients with review of the patient's symptoms and haemoglobin level after each unit, including recommendations for target post-transfusion haemoglobin level (NICE, 2015). The guideline acknowledges that transfusion-dependent patients require individualised transfusion regimes which may not reflect the standard single unit approach. This relates to the cause of anaemia. Patients with acute and/or reversible anaemia require a single dose of red cells to resolve their symptoms of anaemia and this acts as a buffer until their bone marrow can respond and sustain a physiologically normal haemoglobin level. In contrast to this, patients with bone marrow failure or suppression are transfusion-dependent as the bone marrow cannot contribute to red cell production and therefore repeated transfusions are required to maintain a haemoglobin level that mitigates the symptoms of anaemia. The majority of transfusion-dependent patients receiving regular transfusion receive two units of red cells and have their haemoglobin level checked periodically to inform the frequency of transfusion. All current transfusion guidelines fail to recognise the impact of the compound effect of the size of the adult patient and the variability in the volume of blood units, and how this may affect effective red cell dosing in order to achieve a target haemoglobin level. A dose of 4ml/Kg has been reported to raise the haemoglobin level by 10g/L, but this guidance may only be reliable in a 70Kg adult (Norfolk, 2013). More recently, a red cell dosage calculator was developed showing that a dosage recommendation based on 4ml/Kg

achieved a target haemoglobin level in around 90% of cases. It also demonstrated that the use of actual or estimated body weight in the dose calculation had no effect on predicting achievement of the target haemoglobin level (as a group effect) but may be important to individual patients with extremes of body weight, especially patients with low body weight who may be at risk of circulatory overload (Grey *et al*, 2016).

The current UK guideline recommendation for the duration of red cell transfusion is 90 min to 4 hours per unit (BCSH, 2009). This is based upon opinion from experience in practice (equivalent to grade C, level IV evidence/expert opinion), rather than evidence derived from experimentally designed studies. The American Association of Blood Banks Technical Manual (Roback *et al*, 2008) recommends 150-300ml per hour, while the Australian and New Zealand Society for Blood Transfusion guidelines (2011) recommend the rate of transfusion as 60-180 minutes per unit, unless the patient has heart failure or is at risk of fluid overload. Based upon the shortest recommended infusion time, this is 30 minutes per unit of red cells faster than the current UK guideline recommendation (BCSH, 2009). Aside from general guiding medical principles relating to patients who may not tolerate excessive infusion rates due to co-morbid conditions, there is currently no evidence-based recommendation for a definitive red cell infusion rate for either general application or specific patient groups. General opinion that ‘fast transfusion’ may contribute to circulatory overload is a well-established belief but the evidence for this is lacking (Popovsky, 2009). One study demonstrated a statistically significant relationship between the

duration of transfusion (121 minutes versus 83 minutes average duration) and the development of transfusion-associated circulatory overload in patients receiving a transfusion episode over the shorter period (Andrzejewski, 2012). The significance of this is difficult to evaluate as the data were not analysed as infusion rate in the context of volume transfused.

The patient's body weight not only affects the required dose of red cells to reach a target haemoglobin, but additional variable of variation in individual unit volume which may significantly impact upon the infusion flow rate and overall transfused volume. This may be clinically important particularly in the smaller patient. It has been proposed that by changing practice from a standard 'unit over time' approach to rate of transfusion, in the context of red cell volume/dose and body weight over time (ml/Kg/hr), may finesse the approach to transfusion infusion rates, thereby individualising treatment and improving safety for the smaller adult patient (Grey, 2015). Weight-adjusted infusion rate for red cell transfusion in the context of safe and effective transfusion is under-researched but its importance suggested some time ago (Popovsky, 2009), and could also standardise data for future research.

**Clinical Monitoring of Patients during Blood Transfusion and the Detection of Adverse Events and Reactions**

The British Committee for Standards in Haematology guideline sets out the minimum standards for the administration of blood transfusions, to support the development of standardised local guidelines and practice (BCSH, 2009). The scope of the guideline covers pre-transfusion samples, prescription, collection, and administration of blood components. In common with others,

our NHS Foundation Trust Clinical Transfusion Process policies are based upon this guideline (Bolton NHSFT, 2014). The rationale for the standards relating to administration procedures is the early detection of a pathological reaction, which allows for action to be taken at the earliest opportunity.

The monitoring procedure involves the general observation of the patient to detect any new signs or symptoms such as skin rashes/flushing, pain, discomfort, gastrointestinal upset and specific measurement and recording of vital signs. Acute transfusion reactions are usually easily detected in a conscious adult with appropriate monitoring. They may be less obvious in an unconscious or anaesthetised patient and their detection therefore relies on an appropriate level of clinical monitoring, observation, and care whatever the clinical condition of the patient. The patient's vital signs: temperature, blood pressure, heart rate and respiratory rate are measured and recorded for every blood unit transfused. The respiratory rate is measured by observing and counting the patient's chest movements for one minute (the normal range is 12-20 per minute). Blood pressure and heart rate can be measured automatically using an electronic device. Alternatively, blood pressure can be measured using a manual sphygmomanometer and stethoscope to auscultate the brachial artery (normal blood pressure is between 90/60mmHg and 140/90mmHg) .However, 40% of adults have a blood pressure measuring greater than 140/90, with the proportion increasing with age (NICE, 2011). This complicates the use of blood pressure as a parameter to detect adverse events in blood transfusion. A scale change in blood pressure may be more informative but there is no

specific guidance on this. The heart rate can be measured manually by palpating and counting the radial pulse for one minute (normal is 60-90 beats per minute). Temperature is measured using an infrared tympanum (ear) thermometer in a healthcare setting, as they minimise infection control and prevention risks (normal temperature is around 37$^{o}$C). The BCSH 2009 guideline does not make a recommendation for the routine monitoring of oxygen saturation, however the updated 2018 guideline now recommends monitoring oxygen saturation in patients at risk of TACO (Robinson *et al*, 2018). This may serve as an early warning of respiratory compromise if respiratory rate fails to provide warning.

The first set of measurements is taken prior to the transfusion starting (no more than 60 minutes before the transfusion starts). This is a baseline measurement. The next set of observations is taken 15 minutes after the start of the transfusion. The respiratory rate may not be recorded after the first measurement if there are no signs of reaction. The rationale for the measurement at 15 minutes is to detect severe reactions. Many (but not all) severe reactions such as an ABO incompatible haemolytic transfusion reaction, anaphylaxis and those associated with bacterially contaminated blood *usually* begin within the first 15 minutes. Another set of observations is performed and recorded when the blood unit is completed. Some patients have abnormal vital sign observation values prior to transfusion which relate to their underlying health condition. Indeed, some patients requiring blood transfusion for severe anaemia may have tachycardia, increased respiratory rate, and hypotension detected by their pre-transfusion measurements, as

this is a physiological response to anaemia. The rationale for serial vital sign measurements is the early detection of a reaction which may manifest as outright abnormal measurements, or may become apparent less abruptly as a trend. The National Early Warning Score (NEWS) (RCP, 2012) produces an aggregated score for vital sign observations that identify patients for escalation of care and is therefore also useful for patients receiving blood transfusion in acute care settings and also includes measurement of oxygen saturation.

Complications arising from transfusion and pathological reactions may occur sometime after the transfusion episode has ended. The most common type of late onset acute reaction is fever (febrile transfusion reaction). However, pulmonary, infective and immune type reactions can also occur in the hours following a blood transfusion. Patients should be made aware of this and informed about how to recognise them. Hospital inpatients continue to be observed as part of their ongoing medical care, but patients receiving transfusion as a day case or at home require special consideration. It is good practice to provide information and contact details for patients in case they become unwell after they have left the care of the healthcare practitioner following their transfusion and, where possible, the patient should have a responsible adult with them for at least 2 hours (Green *et al*, 2013). Patients receiving day case or home transfusions in the participating Trust are provided with an information and contact booklet entitled '*Advice for patients receiving blood transfusion as a day case*', which explains transfusion reaction symptoms and signs, and provides 24 hour contact advice.

If a patient develops signs of a reaction, the symptoms and signs are evaluated to determine whether they are related to the patient's underlying condition. If the underlying condition is excluded as a likely cause, and a transfusion reaction is suspected, an assessment is conducted to ascertain whether the reaction is mild, or moderate/severe. Mild reactions are defined as: a fever of less than $39^0$C (or no more than $2^0$C above the baseline measurement, if the baseline was less than $37^0$C) with no other symptoms (i.e. isolated fever); or a mild allergic reaction where there is a rash but no symptoms suggestive of anaphylaxis (such as hypotension, dyspnoea, wheeze or angio-oedema). This type of reaction is treated with the appropriate medication to relieve symptoms such as an anti-pyretic or anti-histamine. There is usually no requirement to stop the transfusion and/or perform diagnostic tests, or report to SHOT/SABRE (MHRA), although the patient will require more frequent vital sign observations performing to ensure the reaction is not worsening.

Moderate/severe reactions may manifest as a high fever greater than $39^0$C, or $2^0$C above the baseline measurement (with or without rigors/chills), significant changes in blood pressure, respiratory rate and heart rate, rash (with additional symptoms), pain, haemoglobin in the urine, or reduced urine output, uncontrolled oozing/bleeding, nausea/vomiting or diarrhoea. These symptoms and signs may occur in isolation or in combination. As with mild reactions, moderate/severe reactions should be evaluated for significance in the context of the patient's underlying condition. A clinical assessment and a range of diagnostic testing is undertaken to ascertain the nature of the

reaction. These reactions must be reported to SHOT and SABRE/MHRA (MHRA, 2010; BCSH, 2012; SHOT, 2014; Bolton NHS FT, 2014). These guidelines and regulatory requirements for detecting adverse events have a *post hoc* focus and there has more recently been interest in pre-emptive approaches to avoid or mitigate adverse reactions. NEWS can facilitate the early response to a deteriorating patient but beyond this, others have sought to identify patients at risk of reaction and this has been particularly evident for pulmonary complications of transfusion. Risk assessment check-lists have been developed (Tseng, 2016; Bolton-Maggs *et al*, 2016) and active electronic surveillance of health records (Clifford *et al*, 2013) to identify patients at risk.

Review of the literature shows that through continuous development, blood transfusion is a safe and effective treatment and a mainstay of wider medical and surgical practice when practised in accordance with its regulation and governance. National transfusion procedural guidelines are well established for the care and monitoring of patients receiving transfusion, but do not account for the problematic nature of blood pressure as parameter for monitoring due to the prevalence of chronic hypertension in the general population. The more personal and anticipatory approach of risk assessment and active surveillance prior to transfusion may further strengthen the clinical guidelines. The literature review highlighted the unsatisfactory status of research on safe infusion rates for red cell transfusion, including the varying guidelines stated globally, and lack of standardisation for what is understood by ‘rate’ transfusion. The lack of evidence for this aspect of the transfusion

process invites a challenge of the perception that ‘faster’ transfusion contributes to circulatory overload.

## Blood Transfusion Service Provision

This section considers the delivery of blood transfusion services to patients, and specifically evaluates the benefits of home transfusion by considering local experience and the wider literature. Issues with current home transfusion provision present a case for change. As an exemplar of patient-centred care, potential changes to home transfusion services are considered in the wider context of national regulation and policy.

### The Location of Blood Transfusion and Out of Hospital Transfusion

Blood transfusions usually take place in a hospital setting. Urgent and emergency transfusions are performed on hospital inpatients in acute care environments such as hospital wards, theatre or specialised units. Additionally, routine transfusions also take place in elective care settings such as day-case units within hospitals. Some hospitals have developed out-of-hospital transfusion services with healthcare facilities outside their organisation, such as Hospices and intermediate care. Provision of transfusion outside a healthcare facility is less common, although has a long history.

Home transfusions were first described in haemophilia patients over 40 years ago by Rabiner and Telfer (1970) who reported significant social benefits and safe outcomes from transfusion of plasma components in the patient’s home. Koepke *et al* (1988) later reported the economic value of home transfusion

as a cost effective alternative to hospital admission for selected patients. Benson *et al* (1998) acknowledged the paucity of information regarding home transfusion practices and surveyed US healthcare providers to gain insight. They found that only 16% of respondents [surveyed in 1994] were involved with the provision of home transfusion services. Whilst the precedent for home transfusion has origins outside the UK, there are very little data in the literature regarding the prevalence or experience of home transfusion practice within the UK. The professional experience of the author of this study perceives the majority of healthcare Trusts across the UK do not provide home transfusion services. More research is required to understand the reasons for this, given that NHS England, the Department of Health and Monitor have endorsed the transformation of services to enable medical care to be delivered closer to home (NHS England, 2014; DH, 2009; Monitor, 2015).

These suggest that both economic and patient experience issues may have a bearing on development of these services. There have been a small number of studies on the financial cost of blood transfusion and where published, these are difficult to interpret and compare due to differences in scope and methodological approaches. Abraham and Sun (2012) published a systematic review which attempted to standardise the results of previous studies in order to estimate the cost of a two-unit red cell transfusion. The cost of a two-unit red cell transfusion was adjusted for historic exchange rates to produce a standardised value. The three UK studies included in the review were reported (in Euros at 2011 rates) as: €969 (Agrawal *et al*, 2006),

€972 (Varney and Guest, 2003) and €672 (Hadjianastassiou *et al*, 2002). There are no studies comparing the costs of hospital versus home transfusions, however the Department of Health produced a Best Practice Guideline in 2009 which cited a case study of home transfusions in South Staffordshire reported their hospital transfusion cost as £500, and that home transfusions were less than half this cost (DH, 2009). The article implies this cost is per transfusion episode however this was not made explicit and does not state the number of units per episode. The differential cost of home and day case transfusion in the participating Trust is difficult to assess. The direct costs are identical (blood products, laboratory compatibility testing and clinical consumables), but the indirect costs (overheads, workforce and pay related costs) are more complex to calculate. This largely depends on the overall indirect costs of each service model, which extends far beyond the provision of blood transfusion alone.

**The Home Transfusion Service**

The Rapid Response Team (now known as the Community IV Therapy (CIVT) Team was formed in 1995 as an extension of district nursing services provided by our Community Healthcare NHS Trust. The team's role was to provide a direct alternative to acute hospital admission, by treating patients in their own home. The types of patients treated by the team included those with acute illnesses, social support issues, physical disabilities, and those with palliative care needs. The service expanded in 1997 to support medical patients with acute care needs, and the delivery of IV (intravenous) therapies including antibiotics, chemotherapy and blood transfusion (Audit

Commission, 1999). The CIVT service is now part of the local NHS Foundation Trust: an integrated care organisation that delivers both community and hospital services to the area.

The origins of the home transfusion service developed from a nurse's concern about the risks and difficulties of transferring a sick patient to hospital from their home for a blood transfusion. The consultant haematologist responsible for the patient's care considered home transfusion as a possible option to improve the patient's experience. The procedure in the home setting had not yet been undertaken by the organisation at that time (1997), but it was acknowledged that such a service could potentially bring benefit to patient care. Recognising both economic and non-economic advantages, a key partnership was set up including the CIVT Team, the Clinical Haematology Team, the Blood Transfusion Laboratory, and patients and their care providers.

The participating Trust was probably one of the first organisations to develop a home transfusion service in the UK, and has been providing home transfusions since the CIVT Team expanded in 1997. The service allows the patient to be treated in their own home, avoiding admission to hospital, which is associated with organisational costs, puts pressure on inpatient bed availability and increases the risk of infection (as a significant number of these patients are immuno-compromised). Elderly, chronically transfused haematology and medical patients are the main users of this service, many of whom have physical and social difficulties accessing hospital-based services. The blood is provided by the Blood Transfusion Laboratory at the

Hospital and the transfusions are administered and monitored by specialist CIVT Team nurses. The service was highly commended in the 1999 Nursing Times National Nursing Awards, and published as a 'good practice' case study by the Audit Commission in 1999 (Audit Commission, 1999). Home transfusion procedures are as rigorous as hospital-based transfusion services.

An audit (unpublished) was performed by the participating NHS Foundation Trust's Haematology Department in 2002, based on 1997-2002 home transfusion data, to evaluate the implementation of the service. The audit reported several advantages stated by staff involved in the service: patients particularly liked the continuity and one-to-one care they received; maintained dignity, comfort and convenience for the patient, but also for their carers who also may have had their own health and mobility issues. There were also organisational advantages reported such as reduction of pressure on inpatient beds and the associated costs of inpatient care, and perceived reduced risk of healthcare-associated infection. Hospital-acquired infection was reported in 6.4% of inpatients in acute care hospitals in 2011(Public Health England, 2016) making avoidance of inpatient admission an important factor for potentially immune-compromised haematology patients who may be vulnerable to infection. Practitioners themselves liked the extended role and the relationships that developed with their regular patients. They generally felt the benefits of working on a single task, which reduced stress and the potential for procedural errors.  A number of disadvantages were also reported by staff in this audit, such as working in unsafe environments

where personal safety was an issue, or where standards of hygiene was below acceptable standards. However, checks and safeguards were in place to identify, avoid or minimise such risks. At the time of the audit (2002), the CIVT Team were administering 130 home transfusions per year. The rate in 2015 was 222 per year which represents a 41% increase in 13 years. Currently, patients are triaged to receive home transfusion because demand for the service outstrips capacity. Fewer priority cases are admitted as day cases either on the Oncology unit or as a day case admission to a medical ward.

Although this has been reported to be an excellent and, anecdotally, popular service to the patient, it requires lengthy one-to-one treatment time, typically four hours for a two unit red cell transfusion (three hours infusion time and one hour for other tasks). In this respect it is a less efficient use of nursing resource than a transfusion delivered as an inpatient, or hospital day case. This prolonged patient contact reduces the overall capacity of the service to deliver transfusions and other IV treatments to other patients requiring the service. The service is currently under pressure to increase its scope and capacity due to policy drivers for out-of-hospital care (NHS England, 2014; DH, 2009; Monitor, 2015), and increasing additional clinical demands. Blood transfusion is only one aspect of the IV services they deliver.

**Patient-Centred Care, Patient Experience and the Co-Designing of Services in the Context of National Policy and Regulation**

The Department of Health and the NHS have established a mandate for patient-centred care and valuing patient experience as a central ideology that penetrates all aspects of their activities, and its foundation is established in various UK legislation and national policies. The formative research in this area was commissioned in 2010 by the Department of Health and NHS Institute for Innovation and Improvement who engaged King's College London and the King's Fund to undertake research on "What matters to patients" (Robert and Cornwell, 2011), with the purpose of developing an evidence base for measuring and improving patient experience. The authors argue a case for methods to improve services and patient experience of healthcare, and strengthening the voice of patients. In February 2012, the NHS National Quality Board (NQB, 2012) defined the NHS Patient Experience Framework, which is based on the Picker Institute framework for patient experience. This framework was identified as a potential framework for defining good patient experience by research funded by the King's Fund and King's College London. The framework outlines evidence-based key elements which are fundamental to patients' experience of NHS Services, and recommends using them to inform service improvement (DH, 2012a). The principles of patient-centred care and patient experience were evident in the 'The Health and Social Care Act' when published later the same year (DH, 2012b). The act legislates for "*a greater voice for patients",* and although this primarily focuses on the collective voice of patients for

application at a commissioning level, it resonates with the philosophies of patient-centred care and patient experience. The NHS Constitution (DH, 2013a) also establishes core values that relate to patient-centred care and patient experience by pledging that patients will be “at the heart of everything the NHS does”, the patient’s right to be involved in changes to services and encourages patients to provide feedback about their experiences. There is also a commitment to best value for tax-payers money and recognising the obligation to effective and sustainable use of finite resources. The NHS Constitution also states the responsibilities of its staff to sustainably improve services by working in partnership with patients, and view services from the standpoint of patients. This is similarly reflected in the ‘Putting Patients First’ NHS England Business Plan for 2013/14-2015/16 (NHS England, 2013b) which sets a patient-centred mandate for the securing of value for money with respect to the NHS England commissioning budget. It aspires to best outcomes for patients and taxpayers through “innovative approaches to service delivery”, “deliver better at lower cost” and “driving quality improvements” (NHS England, 2013b, p. 39). The Department of Health also published best practice guidance for effective clinical and financial engagement in the NHS (DH, 2013b) which correspondingly recognises the need to bring synergy to clinical outcomes and optimum management of financial resources. The guidance was operationalised by the Healthcare Financial Management Association (HMFA) in association with Monitor under the auspices of ‘value-based healthcare’, where ‘value’ is defined as a product of patient-defined outcomes, clinical or experience, and ‘resource’ as opposed to ‘price’. This demonstrates a high level of policy level mandate for

patient-centred healthcare which is a laudable manifesto however it is distanced from actual practice. Although patient-centred care is now widely acknowledged as a fundamental tenet of healthcare provision, it has also been criticised as rhetoric. The 2011/12 Care Quality Commission report on the State of Healthcare in which they reported previous successive reports repeatedly finding fault regarding the lack of patient-centred care, demonstrating the disparity between well-intentioned policy and its translation into actual patient care and experience. The report stated that too much emphasis was placed on task-based rather than patient-centred care, and lack of involvement and planning in how care is delivered. This lack of finesse regarding individual needs was evidenced by the finding that "in too many cases care was not person-centred, people were fitted into services rather than the service being designed and delivered around them" (CQC, 2012, p.72). Bate and Robert (2006) also criticised the rhetoric and gap between 'patient-centred' ideology and actual practice. They went further to develop the patient-centred care philosophy, to propose the role of the patient in the co-designing of services to redress the disconnection between policy and practice. They described this as "experience-based design" (Bate and Robert, 2006, p. 308) utilising patient storytelling as an approach to providing evidence for changing and designing health services around the patient/user, an antidote for the unaccomplished rhetoric of 'patient-centeredness' of service provision and design, and to close the gap between policy and practice. Their approach distinguishes between 'experience' and 'attitudes', the former lending itself to qualitative approaches that can be utilised to design good experiences rather than focusing entirely on good

(task-based) processes which may potentially subtract the value of human experience, and therefore the overall effectiveness and user acceptability of the process or service.

Drawing together the principles of patient-centred care, patient experience and the concept of co-design of services described earlier (Bate and Robert, 2006), the King's Fund launched a toolkit for 'evidence-based co-design' (EBCD), facilitating the operationalisation of research and high level policy. The toolkit emerged from the King's Fund Patient-Centred Care Project in 2011 (King's Fund, 2011) which reports on an EBCD project in which patients using cancer services worked with staff to develop service improvements. Experiences were gathered from patients and staff and 'touch points' (Bate and Robert, 2006 p. 308) or emotionally significant points were identified, that could be used to develop changes that offered patients a better experience of care and the service they used. The approach was inductive and is not based on *a priori* assumptions.

There is now an emerging culture and clear case for harnessing patient insight and feedback, which is a common thread through later policy. In 2013, NHS England published 'Transforming participation in health and care' (NHS England, 2013a), which describes the use of both quantitative and qualitative techniques to accomplish the vision of participatory endeavour in co-designing systems and services.

**Patient and Practitioner Experience of Blood Transfusion**

A literature search did not reveal any research on practitioner experiences of the administration of blood transfusions. To a lesser extent, there is also a paucity of published research on patient experience of the administration of blood transfusion: a literature search revealed only two papers: Fitzgerald *et al* (1999) and Adams and Tolich (2011), highlighting this as an under-researched area of practice. Fitzgerald *et al* (1999) reported on the experience of information-giving regarding blood transfusion and what the patient understood by it. Adams and Tolich (2011) reported on a qualitative study in which every patient responded negatively regarding the duration of the procedure, describing it as “slow”, “tedious” and “lengthy”. This finding concurs with the anecdotal observations of patients and staff using, or delivering, the service locally in our Trust. Qualitative research in transfusion medicine is still unusual despite its advocates (Whittaker, 2006; Arnold and Lane, 2011).

Although home transfusion is not widely implemented, a small number of studies have shown to provide multiple benefits both to the patient and organisations. The desire to provide care closer to home and increasing workload challenges service capacity. Review of national legislation and policy suggests this should influence how change to systems and services are decided and delivered. Specifically this requires a recognition of ‘value for money’ and responsible use of NHS resources, and a participatory approach with patients. The literature review revealed a paucity of studies on patient experience of blood transfusion, suggesting that patients were not

necessarily involved in the way this service is delivered for them. Patients also expressed dissatisfaction with the time taken to receive a transfusion which concurs with local anecdotal experience.

**The Contextual Framework Model**

Blood transfusion is safe and highly regulated, and has allowed important advances in medicine and surgery. The delivery of blood transfusion at home has been shown to have significant economic and social benefits, and is a key IV service delivered by the CIVT Team. The CIVT service is highly valued and has been providing IV services in the patient's home long before DH policy and mandates for care closer to home were established. Unfortunately, demand is now difficult to balance with available capacity. Identifying ways to improve the efficiency and capacity of the service is vital so that it may be offered to more patients, avoiding in-patient admissions.

Achieving this within current resources requires considering the feasibility of shortening treatment time for blood transfusion. The literature review demonstrates the empirical nature of current clinical practice concerning the rate, volume and duration of transfusion in the unexplored context of variable blood unit volume, and weight of adult patients. Consequently, there is currently no available evidence to safely make this change and would require challenging the widely-held view that 'faster' rates of transfusion may contribute to circulatory overload.

Service development changes should continue to respect the patient-centred care philosophy of the CIVT service and of national policy and regulation

through a participatory approach based upon understanding the patient's experience. Current though limited, evidence suggests that patients are frustrated with lengthy infusion times.

The contextual framework model shown below in figure 3.1 illustrates the current benefits of the CIVT service and need for service delivery change in the face of increased demand. It identifies potential efficiencies in increasing capacity by reducing the treatment delivery time, in the context of external forces affecting service development, and the limitations of current available evidence to allow safe change of practice.

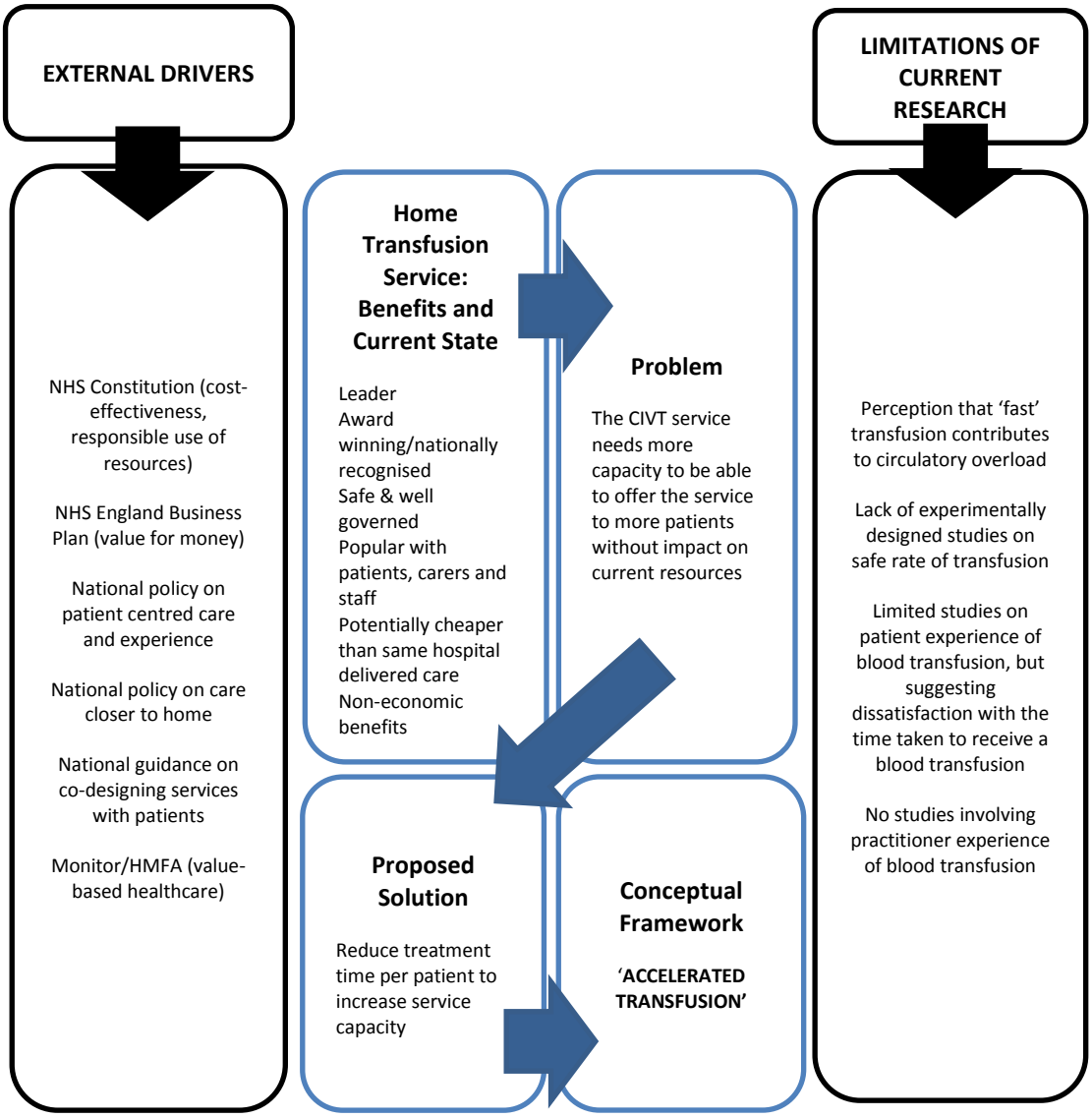



**Figure 3.1: Contextual Framework Model**

**Precis of Thesis Development**

- Home transfusion has a long history and has been shown to offer significant economic and social benefits to both organisations and to patients. The Community Intravenous Therapy (CIVT) Service at the local NHS Trust established a service providing blood transfusions at home many years ago.
- Over the years, the additional pressure of national policy for out-of-hospital care, new and diverse intravenous treatments, and the increased demand for home transfusion outstripped service capacity for this relatively small and highly skilled team.
- Achieving increased capacity within current staff resources relied on finding new and efficient ways of delivering the service, so that it may continue to benefit patients and avoid in-patient admissions.
- One of the variables in the current service model is treatment delivery time per home visit. One of the most time-consuming treatments delivered by the CIVT service is blood transfusion, and there is some evidence in the current literature that patients are frustrated with the length of this treatment.
- This posed the question as to whether the infusion time of a red cell transfusion could be safely reduced in order to gain service capacity and improve patient experience.
- The literature review demonstrated the unstandardized and empirical nature of current clinical practice concerning the rate, volume and

duration of transfusion in the unexplored context of variable blood unit volume, and weight of adult patients.

- Current guidelines on the duration of transfusion is based upon low-level evidence established from experience and expert opinion rather than experimentally designed studies, with global variation in practice
- Weight-adjusted safe rates of transfusion are under-researched but were identified as important some time ago
- There is currently no available evidence to safely make this change and would also challenge the widely-held view that ‘faster’ rates of transfusion may contribute to circulatory overload.
- The primacy of creating efficiencies that focussed on the task and quality of experience as opposed to the number of staff delivering it, respects national policy drivers for service development and change concerning cost-effectiveness, responsible use of resources, and value-based healthcare.
- There is a paucity of research on patient experience of blood transfusion and no research studies on practitioner experience of blood transfusion
- The patient-centred philosophy of the CIVT service and evidence that patients may be dissatisfied with the length of treatment provided a potential mandate to co-design service change with patients and practitioners who use the service.

- This chapter provides the foundation of a conceptual framework that is further developed in the following chapter, where the concept of ‘accelerated-transfusion’ is explored.

# Chapter Four:
# Conceptual Framework

## Purpose and Development of the Conceptual Framework

The conceptual framework model below (figure 4.1) is an evolution of the contextual framework model (figure 3.1) in chapter three, where the concept of accelerated transfusion was proposed as a means to improve CIVT service capacity, while observing the principles of patient-centred care. This chapter forms an argument for the proposal, positioning it within the wider field of research in this area. The chapter also explains the relationship of the conceptual framework to the development of the research question, the research design and methodological approach to answering the research question, and testing of the hypotheses.

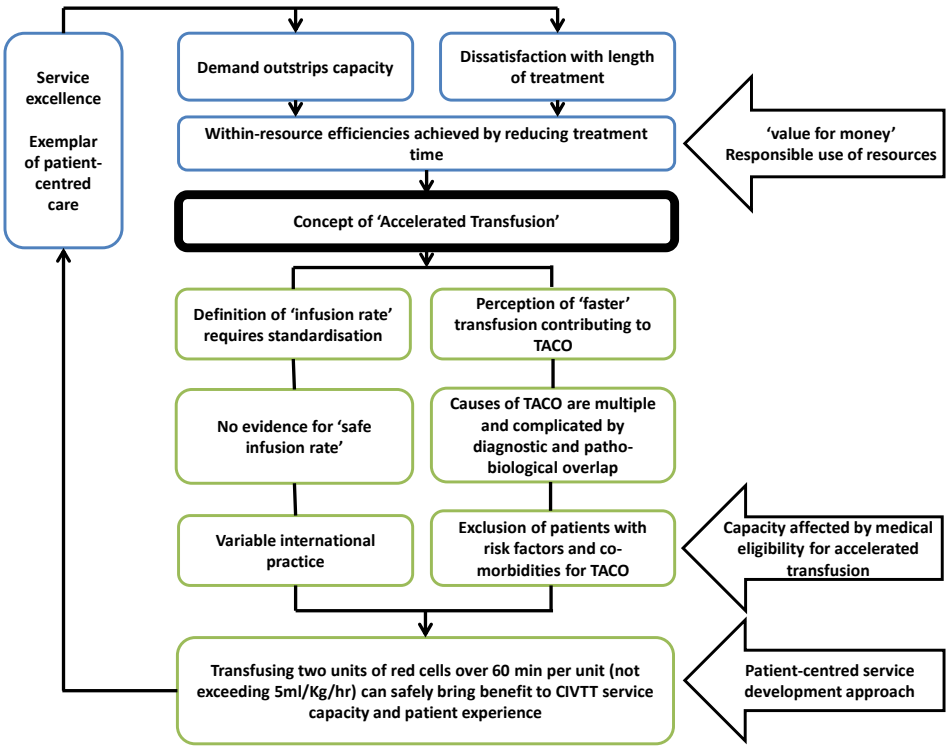



**Figure 4.1: Conceptual Framework Model**

### Conceptual Framework: Addressing the 'Rate' of Transfusion

The ability to safely prescribe red cells for infusion over 60 minutes per unit (instead of 90 minutes per unit) could significantly shorten treatment times. This requires new evidence to be generated for safe standardised infusion rates based upon volume and body weight (ml/Kg/hr). The issue of defining the 'rate' of transfusion was introduced in the previous chapter as current definitions do not take the variables of red cell unit volume and the patient's body weight into account. Current guidance on the duration of transfusion in international standards provide various guidelines and is based upon low-level evidence and is presented as 'red cell unit' over time (BCSH, 2009;

ANZBT, 2011) or as volume over time (AABB, Robeck, 2008). The problematic nature of this can be deconstructed using the following example (figure 4.2). Both patients are on a regular transfusion regime and receive two units of blood per transfusion episode. The frequency of transfusion depends upon the maintenance of their haemoglobin between transfusions.

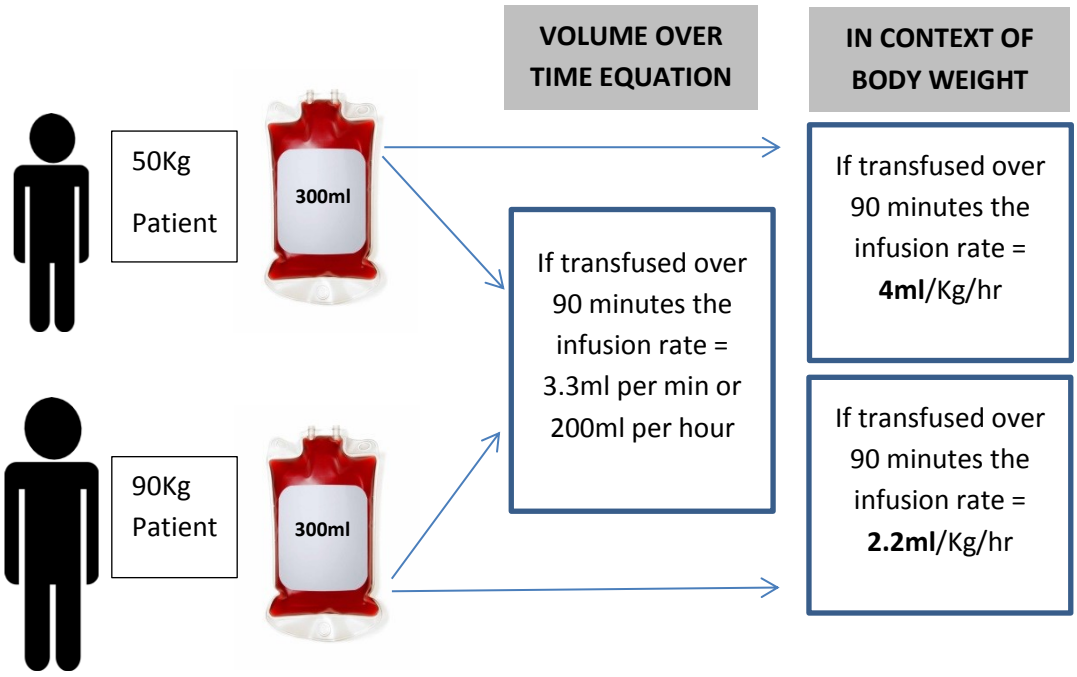



**Figure 4.2: effect of body weight on infusion rate**

Both patients ultimately receive the same volume of blood but the rate of fluid challenge is higher in the smaller patient. The other variable is the volume of the red cell unit. The volume of a UK (NHS Blood and Transplant) red cell unit is 220-340ml, with a mean of 280ml (NHSBT, 2012). The added variable

of patient body weight can produce a significant difference to the infusion rate (figure 4.3).

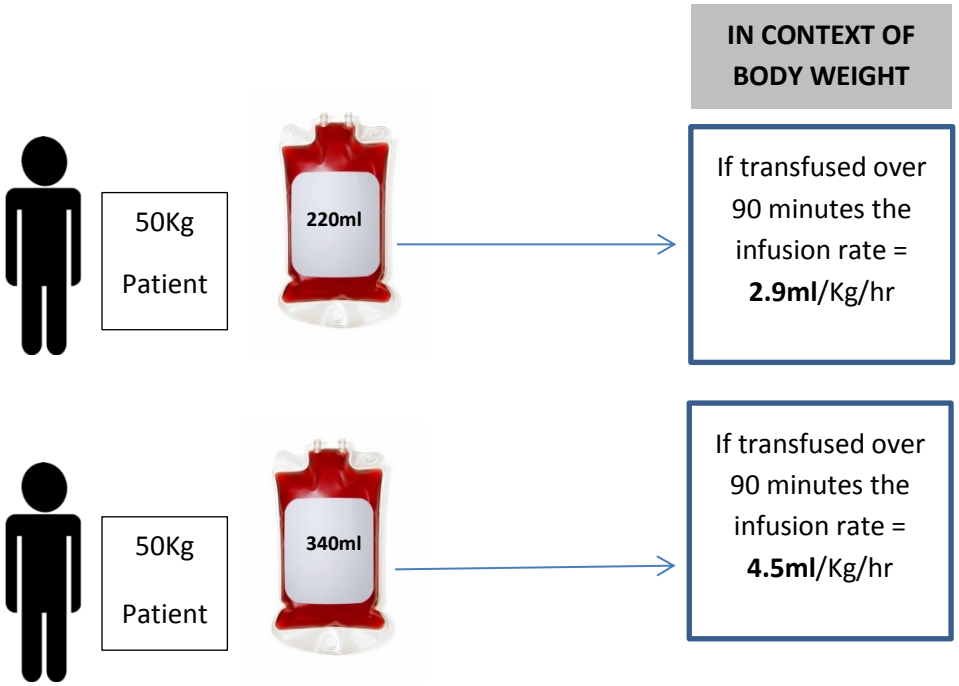



**Figure 4.3: effect of unit volume variability on infusion rate**

Red cell units are not allocated to patients based upon volume or body weight in current practice, and therefore shortening the infusion time to 60 minutes per unit could significantly affect the consequent infusion rate. This may particularly clinically important in the smaller patient with a significantly lower circulating blood volume who may therefore have increased risk of circulatory overload.

**Determining a proposed safe rate of transfusion that would allow two red cell units to be transfused over 60 minutes each**

Notwithstanding the problematic nature of the definition of transfusion 'rate', there is a lack of evidence for a safe rate of transfusion as previously

discussed. There is however some evidence to support the proposition that red cell transfusions can be administered over a shorter duration than is currently endorsed by national UK transfusion guidelines to certain patient groups i.e. those without heart failure or otherwise at risk of fluid overload. The Australian and New Zealand Society for Blood Transfusion guidelines (ANZSBT, 2011) recommend the rate of transfusion as 60-180 minutes per unit (unless the patient has heart failure or is at risk of fluid overload). Based upon the shortest recommended infusion time this is 30 minutes per unit of red cells faster than the current UK guideline recommendation of 90-120 minutes (Robinson *et al*, 2018). However, there is some variability in the volume range of UK and Australian red cell units. The typical volume of an Australian standard red cell unit is 236-282ml, mean 259ml (Australian Red Cross Blood Service, 2012), and the volume of a UK (NHS Blood and Transplant) unit is 220-340ml, mean 280ml (NHSBT, 2012). This must be evaluated in the context of body weight-based infusion rate for the smaller patient.

- 259 ml = mean volume of Australian red cells

Therefore, one unit per hour in a 50Kg adult at 259 ml / 50Kg = **5.2ml/Kg/hr**

- 280 ml = mean volume of UK red cells

Therefore, one unit per hour in a 50Kg adult at 280 ml /50Kg = **5.6ml/Kg/hr**

This suggests that **5ml/Kg/hr** would provide some margin and not exceed the 'Australian' maximum recommended rate of transfusion (60 minutes per unit) when transfusing UK manufactured red cell units. This is only relevant

up to a body weight of 67Kg. At this body weight, the calculated dose to not exceed 5ml/Kg/hr would be 685ml and the combined total of two UK red cell units could not exceed 680ml, which is the maximum possible for two units of UK red cells. Patients weighing greater than 67Kg would therefore not require volume-selected red cells as randomly selected red cell units would not exceed 5ml/Kg/hr in these patients. Conversely, patients weighing less than 67Kg would need to receive volume-selected red cell units to ensure the infusion rate did not exceed 5ml/Kg/hr.

In summary, the definition for the 'rate' of transfusion was unsatisfactory and neglected to consider the impact of the variables of patient body weight and variation in red cell unit volume on the rate of infusion. Expressing the infusion rate as ml/Kg/hr provides standardisation and brings clarity when comparing recommended red cell infusion rates across international guidelines. When adjusting for the variation in red cell unit volume between the UK and Australia, 5ml/Kg/hr appears to be safe in the smaller (50Kg) patient according to the Australian experience of transfusing red cell units over a maximum of 60 minutes per unit. As UK blood units are on average larger than those manufactured in Australia, volume-selected units would be required for patients weighing less than 67Kg in order to receive a unit over 60 minutes without exceeding an infusion rate of 5ml/Kg/hr.

**Challenging the Perception that '*Faster*' Transfusion Contributes to Circulatory Overload**

In agreement with Popovsky (2009), no specific evidence was found in the literature to demonstrate a clear link between the speed of transfusion and

the development of circulatory overload. Although a relationship had later been suggested and investigated (Andrzejewski *et al*, 2012 and 2013) the results of this study were difficult to interpret as the data did not make reference to volumes transfused, referring only to the overall differential duration between each group in the study. There were no studies which compared study groups using standardisation (e.g. ml/Kg/hr) in adults. There have been a small number of studies in paediatric patients with severe chronic anaemia where infusion rates of >1.5ml/Kg/hr (Agrawal *et al*, 2012), 2ml/Kg/hr (Jayabose *et al*, 1993), and 3ml/kg/hr (Olgun *et al*, 2009) were shown to be safe. The physiological differences between paediatric and adult patients may not allow generalisability between these populations, requiring new evidence for safe red cell infusion rates in adults. The other variable to consider when challenging this assertion is the nature of TACO, which is explored in the following sections.

**Defining and Recognising Transfusion-Associated Circulatory Overload (TACO)**

If TACO is suspected to be an adverse consequence of higher rates of transfusion, among other aetiologies, then characterising and defining it is important in giving credence to this proposition, but this has not been without challenges. TACO is one of a triad of pulmonary complications recognised and defined by SHOT, which also includes Transfusion-Related Acute Lung Injury (TRALI) and Transfusion-Associated Dyspnoea (TAD). A universally accepted definition for TACO does not currently exist, but has been broadly regarded by the blood transfusion expert community as an adverse outcome

of transfusion characterised by respiratory distress as a result of pulmonary oedema following infusion of blood components, due to excessive volume and/or infusion rate, and/or when pre-disposing co-morbidities are present (Andrzejewski *et al*, 2013). This can be represented diagrammatically as shown in figure 4.4.

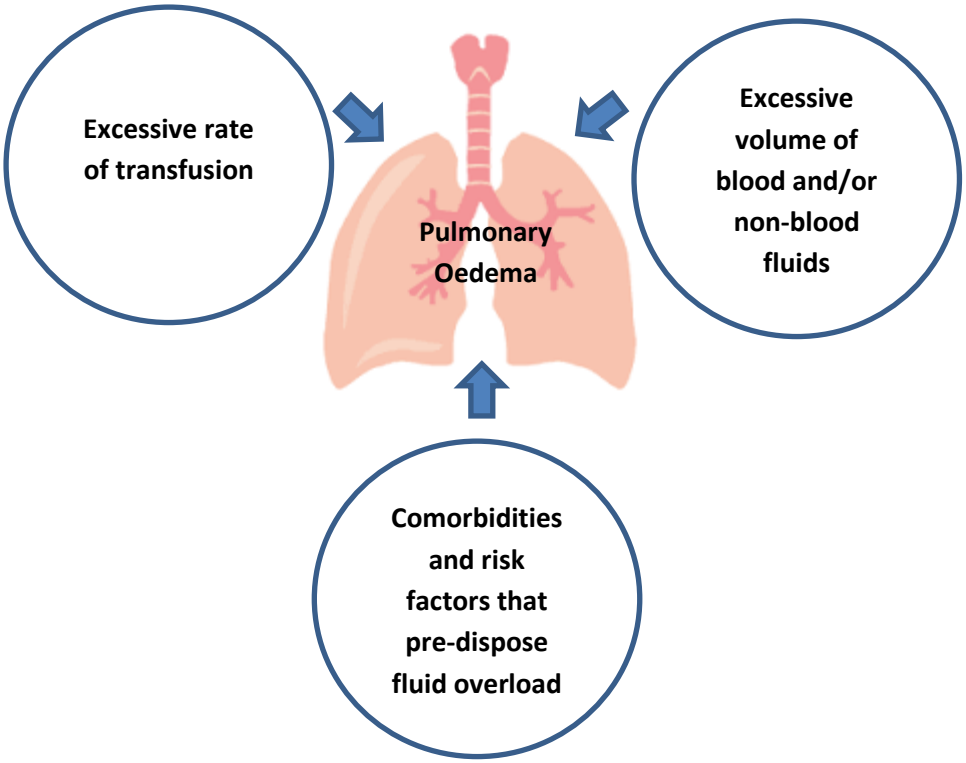



**Figure 4.4: Factors believed to contribute to the development of TACO**

The International Society of Blood Transfusion (ISBT) draft definition (diagnostic assessment criteria) suggests that TACO cases should include at least two primary criteria within 6 hours of transfusion (sometimes up to 12 hours), and acute or worsening respiratory distress must be present. Primary

criteria include acute or worsening pulmonary oedema with bilateral infiltrates, cardiomegaly on imaging and evidence of fluid overload such as positive fluid balance or clinical improvement with diuretics. Alternatively, one primary and two supporting criteria may be present. Supporting criteria may be raised brain natriuretic peptide (BNP) or NT-Pro BNP where the level is greater than 1.5 times the pre-transfusion value, an increase in mean arterial pressure or pulmonary wedge pressure (often with widened pulse pressure), or hypotension in the case of acute cardiac collapse (ISBT, 2014). SHOT assess reported cases for TACO based upon the presence of key clinical features of the condition: acute respiratory distress (in the absence of other specific cause), acute or worsening pulmonary oedema on imaging, evidence of positive fluid balance, evidence of volume intolerance (response to treatment for circulatory overload or evidence of pulmonary oedema on clinical examination). SHOT encourages the reporting of suspected cases even if available information does not meet all of the criteria for TACO, and in suspected cases that have occurred between 6 and 24 hours where there is respiratory distress that improves with treatment for circulatory overload (e.g. diuretics, nitrites and morphine) (Bolton-Maggs *et al*, 2016). Issues with defining and clinically assessing TACO were highlighted in the SHOT report (Bolton-Maggs *et al*, 2016) which drew out a number of problematic areas. Broadly, these included the effect of inter-(expert) assessor variability, lack of inclusivity of some diagnostic approaches, due to lack of routinely available diagnostics or those which may be more suited to a high-care environment, and the presence of confounding clinical factors which may influence the strength of diagnostic certainty. A logic-based application was developed to

calculate the likelihood of TACO based on the presence of weighted symptoms and signs across four diagnostic categories to produce an aggregated score (Bolton-Maggs *et al*, 2016). The application requires further development but may be a useful tool in the future to facilitate reproducible and standardised TACO surveillance diagnosis assessments. International collaboration continues to make incremental steps toward definitional surveillance assessment criteria.

## Pathogenesis and Differential Diagnosis of the Pulmonary Complications of Transfusion

The characterisation of TACO is further frustrated by the complexities of the differential diagnosis of the other pulmonary complications of transfusion, Transfusion-Related Acute Lung Injury (TRALI) and Transfusion-Associated Dyspnoea (TAD), and the proposition that they may not be distinct entities. New theories on the patho-biology of TACO add a further layer of complexity.

TRALI is defined as acute dyspnoea, with hypoxia and bilateral pulmonary infiltrates, during or within 6 hours of transfusion, not due to circulatory overload or other likely causes. TAD brings together a heterogeneous group of cases of acute respiratory distress that do not otherwise match the TRALI or TACO diagnostic criteria, and therefore TAD is a diagnosis of exclusion (SHOT, 2014). The exact pathogenesis of TRALI is not fully understood, but there are thought to be immune and non-immune causes. A two-event model was proposed which requires an initial trigger such as infection, trauma or surgery, followed by a second event where anti-leucocyte antibodies (immune TRALI) or bio-active substances (non-immune TRALI) present in

the blood product are transfused to the patient. This activates neutrophils in the lungs which induce endothelial cell damage and capillary leakage, causing non-cardiogenic pulmonary oedema. More recent studies have demonstrated the formation of neutrophil extracellular DNA traps in response to activation which are injurious to the alveolar tissue of the lung (Thomas *et al*, 2012). This contrasts with the pathogenesis of TACO, in which cardiogenic pulmonary oedema is caused by iatrogenic fluid overload (where the fluid is a blood component).

Fluid overload can be precipitated as a result of any intravenous fluid infusion, and is therefore not limited to blood transfusion. Volume overload (hypervolaemia) has no precise definition but there have been attempts to quantify fluid accumulation and correlate this to clinical outcomes. The percentage of fluid accumulation can be expressed by dividing the cumulative fluid balance (litres) by the patient's baseline body weight (Kg) and multiplying by 100% (Malbrain *et al*, 2014). Fluid overload was identified as greater than 10% increase in fluid accumulation and this was associated with worse outcomes in patients receiving critical care with acute kidney injury (Macedo *et al*, 2010). There are limited data on volume tolerance in humans in non-acute settings, but studies on euvolaemic volunteers (i.e. normal blood volume) suggest that the infusion of 2-3L of isotonic saline will precipitate mild symptoms and signs of fluid overload (Collins *et al*, 1973; Holte *et al*, 2003). However, it is difficult to relate this to red cells to predict tolerance to blood transfusion because red cells are not a crystalloid substance that can be removed by the kidney when present in excess.

Hypervolaemia causes pulmonary oedema due to increased haemodynamic pressure resulting in the over-distension of the left ventricle of the heart, causing increased pulmonary capillary pressure. The increased filtration of fluid out of the capillaries into the interstitial space results in interstitial oedema. Further accumulation of fluid causes cellular disruption and accumulation of fluid in the alveolar spaces (alveolar oedema). The clinical features of pulmonary oedema are dyspnoea, wheeze and crackles (heard by chest auscultation with a stethoscope), and cough (usually productive of blood-tinged frothy sputum), tachycardia, and cyanosis caused by peripheral circulatory shutdown, and raised venous pressure. The chest X-ray shows diffuse haziness due to the accumulation of alveolar fluid. Many of the clinical criteria of TACO relate to the symptoms and signs of pulmonary oedema.

Hilton *et al* (2008) suggest that complications of fluid overload usually arise in the context of co-morbidities that affect the cardio-respiratory system and/or where there is severe inter-current illness. Consequently, patients with pre-existing heart failure are at greater risk of TACO when volume-challenged. However, individuals without co-morbid conditions can also develop pulmonary oedema caused by large volume and/or rapid infusion. The volume and rate of infusion is therefore an important safety consideration for all patients receiving blood transfusions, and particularly significant for those patients with certain co-morbidities or risk factors.

Some authors believe there may be some overlap in the pathogenesis of the pulmonary complications of transfusion. Andrzejewski *et al* (2013), put forward a theory that some cases of TACO may have pro-inflammatory

(immune-based) aspects and may share pathophysiology with non-immune TRALI. They proposed the concept of “barotrauma” (Andrzejewski *et al*, 2013, p.3045) where damage to the vascular endothelium as a result of increased vascular pressure may be the first step in a process leading to pro-inflammatory state and increased vascular permeability.

This challenges the notion that TACO is simply an iatrogenic adverse event singularly relating to pulmonary oedema caused by excessive haemodynamic forces. Indeed, this ambiguity acknowledges the significance and importance of the TAD categorisation. It emphasises the current lack of depth of understanding of the pulmonary complications of transfusion, suggesting a multi-factorial basis in some cases, and the benefit of a flexible reporting criteria to capture cases.

Given the considerable number of similarities of symptoms and signs between TACO, TRALI and TAD, plus the additional theory that the pathogenesis of each may overlap, there may be difficulties in establishing an accurate differential diagnosis. However, this is clinically important from the perspective of medically managing the patient, and for ensuring accurate reporting to SHOT and SABRE/MHRA. Failure to differentiate between TRALI and TACO could lead to the inappropriate use of diuretics in a TRALI case that would increase morbidity/mortality if the patient is already volume depleted. Dyspnoea is common to all pulmonary complications of transfusion, and may also occur in anaphylaxis and otherwise unexplained (uncategorised) complications of transfusion. In the absence of shock, TRALI, TACO and TAD are the likely diagnoses. Stridor and wheeze suggest

an allergic reaction however these signs have been occasionally reported in TACO, which, again, may support the theory for the complex pathogenesis of pulmonary complications. Pulmonary oedema and basal crackles are suggestive of TACO or TRALI, and helps exclude allergy. The differential diagnosis of TRALI and TACO in a patient with dyspnoea as the predominant symptom (where low oxygen saturation and anaphylaxis are excluded), can be evaluated by assessing certain clinical parameters. Some of the criteria relate to the changes in haemodynamics in patients with TACO due to fluid overload. Blood pressure, jugular venous pressure, pulmonary wedge pressure, pulse pressure and mean arterial pressure are often raised in TACO, with abnormal echo-cardiography and cardiomegaly. In contrast, blood pressure is often reduced in TRALI, and jugular venous pressure/pulmonary wedge pressure are normal, with normal echo-cardiography and heart size. Pulmonary oedema can be present in both TRALI and TACO and chest imaging does not always provide clear differentiation. As would be intuitively expected, TACO worsens with fluid load and improves with diuretics whereas the opposite is true for TRALI (Popovsky, 2008; Popovsky, 2010; Kopko and Holland, 1999). These pathophysiological and diagnostic uncertainties create difficulty in confidently attributing either circulatory overload or an idiosyncratic/non-preventable cause for respiratory compromise, which could have occurred independently of the rate of transfusion.

## Epidemiology of TACO

Uncertainty regarding the definition and diagnostic criteria for TACO also impacts upon confidence in quantifying its incidence. A total of 96 cases of TACO were reported to SHOT in 2013. Ninety two cases involved red cell transfusions (Bolton-Maggs *et al*, 2014). Fifty four of these cases were transfusions given in the absence of haemorrhage, and TACO was reported in 28 cases where 2 or fewer units of red cells had been administered. Where data were available, the median duration of the transfusion of the red cell unit was 2.5 (range 1.5-5.0) hours. For all cases of TACO where data were available (n = 93), the onset of symptoms for 51.6% (48/93) was between 0-2 hours, 33.3% (31/93) between 2-6 hours, and between 6-24 hours in 15.1% (14/93) patients. In context, the overall risk of mortality from TACO is 0.56, and risk of major morbidity is 0.72 per 100,000 blood components issued in the UK in 2016 (overall major morbidity for blood transfusion being 4.91 and mortality 1.05) (Bolton-Maggs *et al*, 2017).

Based on SHOT data, TACO is therefore the leading cause of transfusion-related morbidity and mortality, with some authors believing it to be under-reported (Popovsky, 2008; Bolton-Maggs *et al*, 2014). This theme is recited in a number of papers on TACO, but there are few prospective studies that allow for objective quantification of this proposition. Raval *et al* (2013), suggest that passive reporting of TACO underestimates its true incidence, and conducted a prospective study. The retrospective analysis revealed an incidence of 1:5997, but when analysed prospectively, the incidence was much greater at 1:167 platelet units transfused. Li *et al* (2011) demonstrated

a 6% incidence rate in a prospective study of intensive care unit (ICU) patients receiving fresh frozen plasma (FFP), which exceeds the overall incidence reported by SHOT. Narick *et al* (2012) also conducted a prospective study on patients in an acute care or resuscitation setting. An incidence rate of 6.4 per 10,000 units of FFP transfused was observed with prospective analysis, and 147 per 10,000 when analysed retrospectively, was reported. Although these studies support the assertion that TACO is under-reported, these studies were limited to specific patient populations and types of blood component, where concomitant fluids were administered that may have contributed to positive fluid balance. For this reason, the findings are not generalizable and may not be representative of patients receiving elective transfusions of red cells in non-acute settings. There are no specific data on the incidence of TACO in patients receiving red cell transfusion in home or day-care settings.

**Co-Morbidities and Risk Factors for TACO**

Patients with comorbidities and risk factors pre-disposing fluid overload have increased risk of TACO independent of the rate of transfusion. In particular, patients with heart failure are predisposed to pulmonary oedema even before a fluid-challenge is administered. Cardiac failure occurs when the heart is unable to maintain sufficient cardiac output to meet the demands of the body. A number of physiological haemodynamic and neurohormonal mechanisms adapt and compensate, such as vasoconstriction to increase the venous pressure. This leads to sodium and water retention causing raised pulmonary capillary pressure, leading to the leakage of fluid into the alveolar spaces,

resulting in pulmonary oedema. The pathophysiology of fluid overload in heart failure is not fully understood but it is acknowledged that it may be more than a mechanical disorder: Cotter *et al* (2008) proposed that fluid overload in heart failure is caused by the redistribution rather than uniform accumulation of fluid. The cause of this is thought to be linked to vascular constriction in the lung, neurohormonal and inflammatory activation, renal dysfunction and possibly the unwanted effect of some medications. The overall effect of this is the accumulation of redistributed fluid in the body and importantly in the lungs resulting in the development of cardiogenic pulmonary oedema. The pathological processes in existing cardiac failure are exacerbated by further fluid loading from IV fluid administration.

Patients with renal failure are also predisposed to fluid overload. Renal failure is associated with a decreased glomerular filtration rate (GFR) which reduces the capacity of the kidney to excrete sodium. Sodium accumulation causes water retention which leads to expansion of the extracellular volume and oedema. This significantly reduces the patient's capacity to tolerate further fluid loading if administered intravenously, and would considerably increase the risk of pulmonary oedema developing.

Patients develop hypoalbuminaemia for a number of reasons, broadly relating to synthesis or loss of albumin. Conditions associated with hypoalbuminaemia include renal disease with albuminuria, burns, haemorrhage, gastrointestinal losses, liver disease, malnutrition, sepsis, heart failure, inflammatory diseases and haemodilution caused by the administration of intravenous fluids. Albumin has a key role in maintaining

plasma oncotic pressure, and when this is deceases in hypoalbuminaemia, water is lost from the vascular space to the interstitial space. The circulatory volume is then reduced with a fall in cardiac output. The compensatory physiological mechanisms are similar to those seen in heart failure. The extracellular volume then expands and venous pressure increases causing the development of oedema. The increased extracellular volume then predisposes the patient to fluid overload (Kumar and Clark, 1999).

Low body weight has also been associated with the risk of TACO (Bolton-Maggs *et al*, 2014) which is to be expected as smaller individuals have a lower blood volume and therefore require a relatively lower volume of IV fluid to achieve the required level of treatment. Even without co-morbidities, patients with low body weight can only be expected to tolerate excess volume up to a point, beyond which pathological consequences (pulmonary oedema) would ensue.

The presence of one or more co-morbidities that are considered to increase the risk of TACO were reported to SHOT in 58.3% (56/96) of cases, and not reported in 16 cases (Bolton-Maggs *et al*, 2014) . Where body weight data were collected, 5/25 cases had a body weight of 50Kg or less. There is also an association with age and the development of TACO with 63.5% (61/96) being 70 years or over (Bolton-Maggs *et al*, 2014). This may be related to the prevalence of co-morbidities in this group rather than it being an independent risk factor. Unfortunately, fluid balance data were only reported in 28.1% (27/96) of cases, which makes it difficult to determine the proportion of patients who developed TACO from the infusion of blood components alone,

or understand the scale to which blood components (or other fluids) may have contributed to the development of pulmonary oedema. This is a possible source of ambiguity and without more detailed data it is not possible to define the reported incidence of TACO, in terms of blood components being independently responsible for pulmonary complications caused by pulmonary oedema resulting from fluid overload.

Cumulative SHOT data have provided an important insight into risk factors for TACO, which include cardiac failure, renal impairment, hypoalbuminaemia, pre-existing fluid overload, aged more than 70 years and low body weight (Bolton-Maggs *et al*, 2014). Thematic analysis of the 'definite and highly likely' TACO cases reported to SHOT in 2015 revealed that infusion of concomitant fluid during or in the 24 hours prior to transfusion, followed by pre-existing fluid overload and pre-existing cardiac dysfunction were the most significant themes in patients who developed TACO. Other significant but less frequent, themes relating to fluid intolerance were pre-existing pulmonary oedema, low body weight and pre-existing peripheral oedema (Bolton-Maggs *et al*, 2016). All but the fluid management issues are relevant to patients receiving blood transfusions in the non-acute setting (as concomitant fluids are not administered to these patients). The themes emerging from haemovigilance data have provided a useful basis for developing a risk-assessment for patients at risk of TACO (Grey, 2015; Bolton-Maggs *et al*, 2016). This provides a useful tool to exclude patients from accelerated transfusion where the impact of the rate of transfusion on the development of TACO is uncertain. The prevalence of risk factors for

circulatory overload in this population would affect the number of patients eligible for accelerated transfusion, and therefore would need to be evaluated as part of the study.

**Summary**

The study does not seek to demonstrate whether 'faster' rates of infusion contribute to the development of TACO. Having established the lack of evidence for safe rates of transfusion it is prudent to exclude patients who have recognised risks for TACO, where uncertainty remains about whether 'faster' transfusion contributes or not. The debate in this chapter also raises the question of how 'faster rates of transfusion' are meaningfully defined. It is not possible to state what constitutes 'faster transfusion' and evaluate outcomes, without first establishing a standardised method and rate of transfusion that is shown to be as safe as current custom and practice. The rate of 5ml/Kg/hr is only 'accelerated' relative to current practice. This rate of transfusion could in future be regarded as a 'standard' rate of transfusion. It is not possible to determine whether this rate of transfusion is safe in patients with risk factors for TACO without an experimentally designed study.

Revisiting Andrzejewski et al (2013) broad definition of TACO in the context of this study, figure 4.5 illustrates the uncertainties and mitigations.

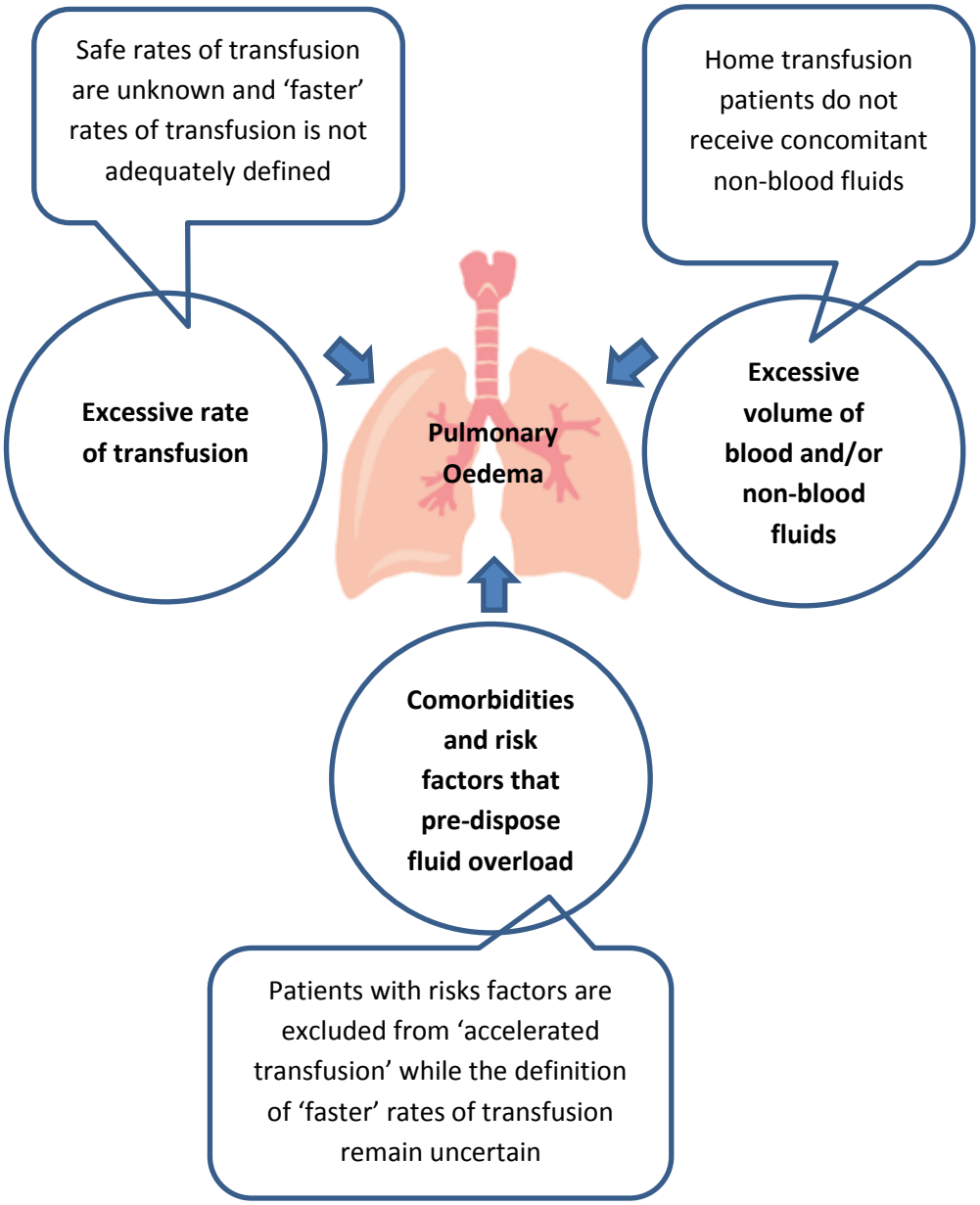



**Figure 4.5: Factors believed to contribute to TACO in the context of 'accelerated transfusion'**

## Conceptual Framework: Development of the Research Question and Hypotheses

The contextual framework described in chapter three (and illustrated in figure 3.1) proposed the concept of accelerated transfusion. The conceptual framework (figure 4.1) is the output of the synthesis of the literature which supports this proposition and from which the following research question and the hypotheses were generated. The original benefits of the CIVT service are patient-focussed care provided at home for those who require it, while protecting inpatient care where it is medically appropriate. These cornerstones remain embedded within the conceptual framework ensuring the research output continues to deliver the intended service philosophy and objectives, with the anticipated benefit of service improvement based on new evidence for practice. The research question can be framed as:

### General Research Question

Whether transfusing two units of red cells over 60 minutes per unit (accelerated transfusion) is safe and could potentially increase CIVT service capacity, while gaining understanding of the patient's and practitioner's experience.

The question can therefore be viewed through the two lenses of physiological tolerability and experiential and organisational acceptability/benefit. This forms the foundation of the multi-methods approach which is discussed further in the Methods chapter.

## Hypotheses

Based upon the background and impetus for the research supported by existing evidence, a number of hypotheses can be developed for the quantitative aspects of the research question:

$H_1$: Two units of red cells transfused over 60 minutes each can be physiologically tolerated in selected patients ($H_0$ there is no difference in the incidence of Transfusion Associated Circulatory Overload (TACO) between standard and accelerated rate transfusions).

$H_1$: Implementation of accelerated transfusion could potentially increase CIVT service capacity ($H_0$ Implementation of accelerated transfusion would not potentially increase CIVT service capacity).

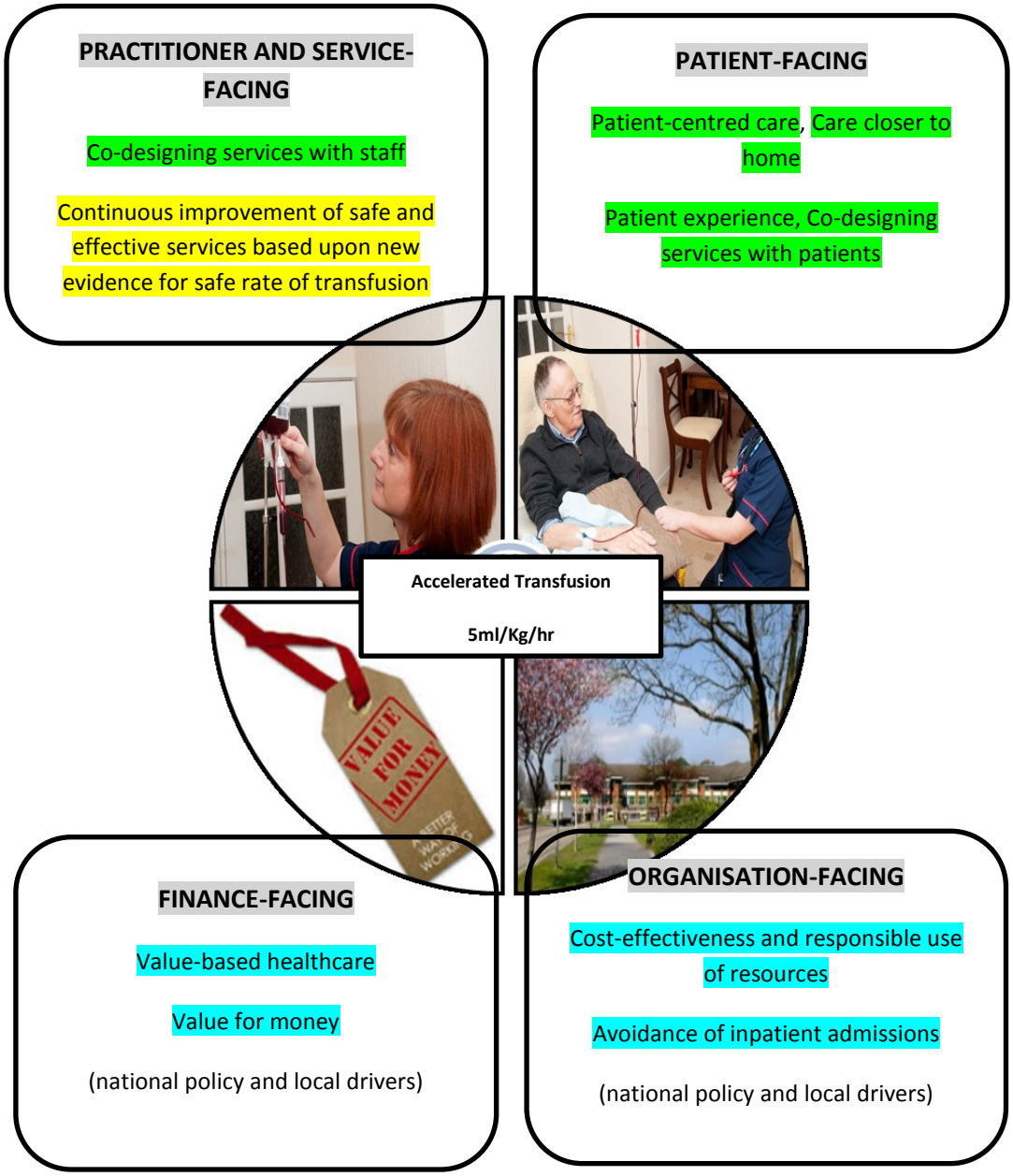
The qualitative strand of the study is value-adding and seeks to inductively gain understanding of patient and practitioner experience without *a priori* theories and therefore hypotheses are not appropriate.

## Contextual Tenets of the Conceptual Framework: Influence on Research Design and Methodological Approach

The conceptual framework model conflates the cornerstones of the existing home transfusion service with the contextual tenets of external (national) policy drivers, patient-centred factors, organisational objectives, and the philosophy of continuous service improvement that rely on the generation of new evidence for practice. The approach and choice of methodology and

underpinning philosophy of each strand of enquiry is also imbued within the framework.

The contextual tenets of the conceptual framework (colour-coded below) inform the methodological approach by establishing three strands of enquiry which require different methodological approaches. Each respective segment can be broadly regarded as: practitioner/service-facing; patient-facing; finance/resource-facing; and organisation-facing (figure 4.5).




Photographs of patients and practitioners taken with formal consent, © of the author's employing organisation

| Key: linkage of contextual tenets of the conceptual framework to strand of enquiry | |
|---|---|
| Physiological/safety enquiry method | |
| Service capacity enquiry method | |
| Patient and Practitioner experience enquiry method | |

**Figure 4.5: Contextual tenets of the conceptual framework informing methodological approach**

Having defined the research question, developed hypotheses from the conceptual framework, it is evident that both ***quantitative*** (physiological tolerability/safety, service capacity), and ***qualitative*** (patient and practitioner experience) elements are embedded within it, and from which the two methodological approaches eventuate. This provides the structure and design of the research and informs the choice of method for each strand of enquiry.

The research design can be identified as a ***multi-methods*** design as each 'strand' can be regarded as an independent enquiry. The quantitative and qualitative phases can potentially be reported separately and do not necessarily relate to each other, or confirm the findings of the other (as would be required to satisfy the definition of a *mixed* methods approach). Morse (2003) proposed three principles for characterising multi-methods research. The first principle defines the theoretical drive (inductive or deductive), the second principle defines the dominance of each method, and the third principle defines the design type (simultaneous or sequential, depending on the temporality of how the methods are conducted). According to Morse's nomenclature, the design of this study can be characterised as a sequential QUANTITATIVE → qualitative study, which indicates a quantitative driven project that is followed by a second qualitative project. The theoretical drive for this research study is predominantly deductive and is experimentally designed to establish the physiological tolerability and resource economics of accelerated transfusion using quantitative methodology. This is followed by a further, self-contained inductive study

designed to provide understanding of patient and practitioner experience using qualitative methods.

Figure 4.6 introduces and summarises the study design and the underpinning philosophy which is described in detail in the following methods chapters.

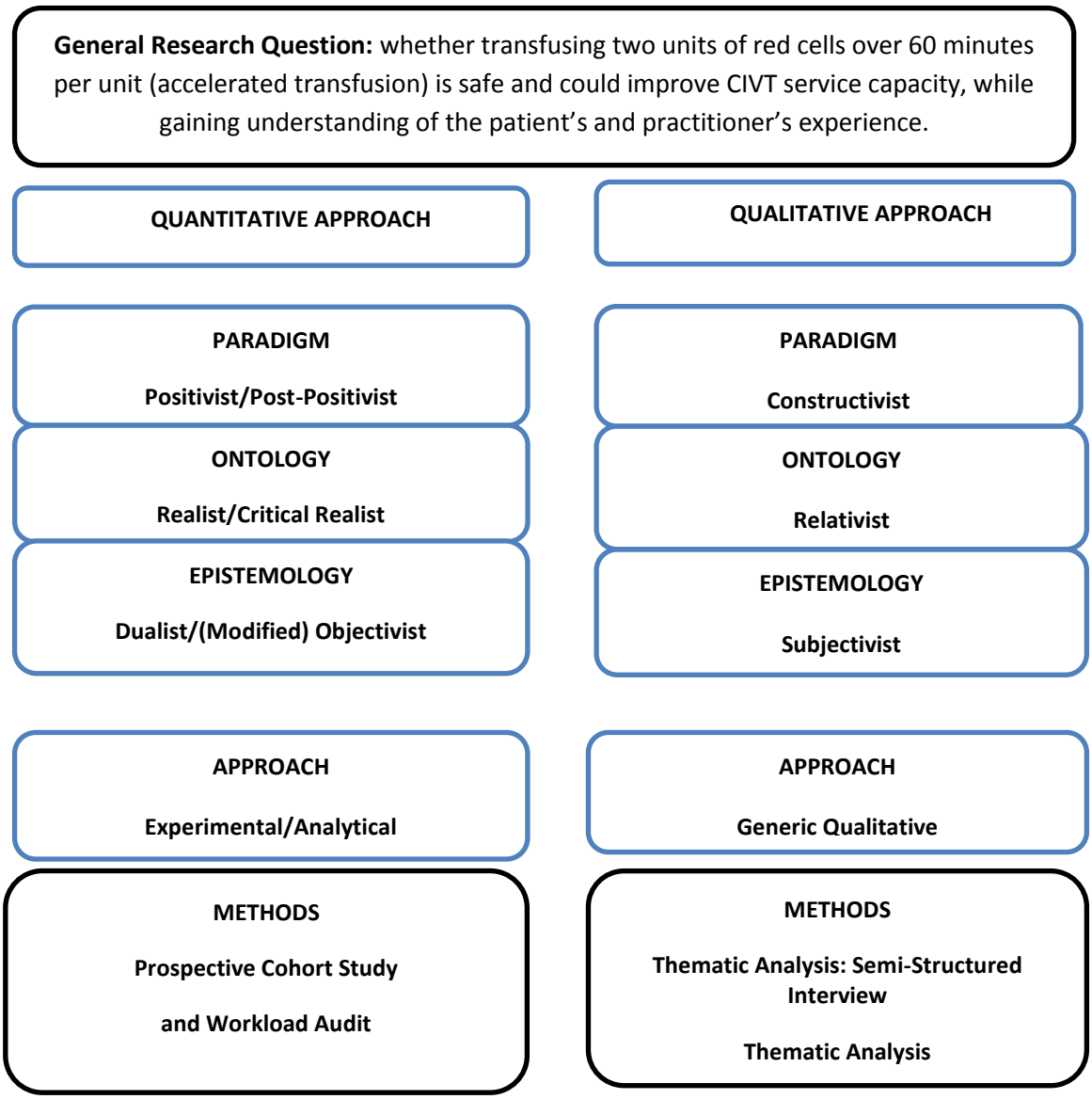



**Figure 4.6: Research Design and Underpinning Philosophy**

**Precis of Thesis Development**

- Red cell transfusions are infused over a maximum of 90 minutes per unit in current practice. The total treatment time for a two unit red cell transfusion was around four hours. The proposal was to reduce this to 60 minutes per unit (accelerated transfusion), in order to reduce the overall treatment time for a two unit red cell transfusion by one hour. In theory this would release time and increase the capacity of the service while reducing the burden of long treatment times for the patient.
- The evidence for current practice is based upon expert opinion and experience as opposed to experimentally designed studies. Unpacking the notion of 'duration' of transfusion raises questions about how this is satisfactorily and meaningfully described.
- The combined variables of patient body weight and red cell unit volume are not taken into account in current practice where it is usual to prescribe a 'unit' over a period of time in adult patients. This results in variations in the determination of the actual infusion rate and may disregard the influence of the individual patient's size.
- The rate of transfusion is not adequately defined in current practice but could be standardised by expressing as ml/Kg/hr
- Derivation of Australia and New Zealand transfusion guidelines support the proposition that 5ml/Kg/hr may be safe which would allow a unit of standard UK red cells to be transfused over 60 minutes per unit. Volume-selected red cells would be required when the patient's

body weight is less than 67Kg to avoid an infusion rate exceeding the proposed value.

- Excessive rate of transfusion is believed to be a cause of Transfusion-Associated Circulatory Overload (TACO) but there is no specific evidence for this, in part due to lack of standardisation of the rate of transfusion and how this has been represented in published studies.
- TACO has aetiologies beyond the rate and volume of transfusion which complicates the contribution of rate of transfusion to the development of TACO, and poses difficulties in its differential diagnosis and epidemiology
- Comorbidities associated with volume intolerance are shown to predispose the development of TACO and may be more important than the rate of transfusion.
- The research question and hypotheses were generated from the conceptual framework
- The contextual tenets of the conceptual framework (patient, practitioner, finance and organisation) inform the methodological approach forming three strands of enquiry requiring both quantitative and qualitative methods described in the following chapters

# Chapter Five:
# Research Ethics, Clinical Governance and Risk Management

This chapter examines the ethical, clinical governance and risk management issues common to all aspects of the study methodology, and forms a foundation for the following methods chapters.

## Ethical approval

Ethical approval for this research was obtained from the National Research Ethics Service (NRES): (REC application reference 14/NW/0229), Manchester Metropolitan University (MMU) research ethics committee and the author's NHS Foundation Trust's Research and Development department. The recruitment did not commence until full approval was obtained from all parties.

## Specific Ethical Considerations

Table 5.1 describes key ethical issues that were identified in the development of the project proposal and explains how they were addressed.

## Table 5.1: Addressing identified ethical issues

| Issue Identified | Action |
|---|---|
| Avoiding coercion to participate | The patient and practitioner received a letter of invitation, information and a response-form which they could read privately and ask for further information if required. The letter explained their right to refuse without consequence or compromising their treatment. The documents were developed in accordance with the "information sheets and consent forms: guidance for researchers and reviewers, NPSA Research Ethics Service (2009). |
| Respecting autonomy and choice | As above. Additionally, the participant was required to consent before each procedure (or interview) with the option to decline at any stage without consequence or compromising their treatment. The document was developed in accordance with the "information sheets and consent forms: guidance for researchers and reviewers, NPSA Research Ethics Service (2009). |
| Ensuring participants are not inconvenienced | No patient was expected to attend a clinic or receive treatment at a time (or frequency) than they otherwise would have done. Patient and practitioner interviews were conducted at a time and place convenient to the participant. |
| Patient safety | The research hypothesis was based upon existing evidence that suggests the proposed intervention is safe for patients who meet the inclusion criteria. The inclusion/exclusion criteria were approved by a consultant cardiologist and consultant haematologist. A pre-transfusion clinical assessment was performed before every transfusion. The transfusions were monitored by a trained and experienced nurse at all times. The patient was provided with post-transfusion contact/care information and also received a visit from a trained healthcare practitioner (24 hours after the transfusion) to perform a post transfusion clinical assessment. In the event of adverse event, a medical officer was to be contacted and there was facility to transfer the patient to hospital. |
| Practitioner Safety | Existing domiciliary and lone-worker organisational policies applied to patient home visits as part of the study. |
| Potential for compromising practitioner professional scope of practice | The research protocol inevitably had some aspects of transfusion practice that did not match current organisational transfusion policy. All practitioners involved in any aspect of the research study were trained to the protocol and this was registered on a training log, ensuring professional standards are respected and appropriate governance applied. |
| Data protection | All participant-identifiable hard copy data generated in the study was kept in a locked filing cabinet in an office that was locked when not in use. All participant-identifiable electronic data was kept on a password protected NHS personal computer. The data was not stored on the hard drive (it was stored on a remote server). Any electronic data that was required to be put on a USB drive was only put on an encrypted device. |
| Confidentiality | Participant data was kept confidential by using a code that could only identify the individual from a single master linkage document that was kept secure. |
| Anonymity | No person-identifiable data will appear in print however participants were made aware that quotations from their interviews may appear in print. This was made clear in participant information and consent document for the interview. |

| | |
|---|---|
| Choice of participant | It is not feasible to answer the research question without home transfusion and CIVT practitioners as participants (no other patient or practitioner group could be used as an alternative). Haematology patients attending the oncology unit for day case transfusion were also invited to participate in order to ensure sufficient participant for the physiological enquiry strand of the research (these patient would normally be eligible for a home transfusion except that their postcode is beyond the scope of the CIVT service geographical reach). These patients were otherwise physiologically similar to the home transfusion patients however they were not be invited for interview (as they had not experienced transfusion at home). There were fewer potential practitioner participants as they are a small clinical team. Established team members were favoured for their greater experience of both types of transfusion. |
| Numbers of participants required | The sample size and power calculation suggested 39 patients were required for the physiological tolerability part of the study (albeit with some limitations). This was not to be exceeded if this number was reached before the expected end of the study. The number of participants for the patient and practitioner part of the study could not be pre-defined and was dependent upon participant willingness to be interviewed. This was nominally set at 10 participants per group for ethics application purposes. |

**Permissions and Liability**

All required permissions were obtained as detailed above prior to the start of the study and recruitment of participants. Legal liability of the sponsor (the author's NHS Foundation Trust) for the management, design and conduct of the research was covered by the NHS indemnity scheme, and this was approved under the auspices of the research ethics and research and development approval process.

**Serious Adverse Events (SAE) and Serious Adverse Reactions (SAR)**

In the event of a SAE or SAR, procedures were in place to investigate and report these appropriately to satisfy both organisational governance and statutory reporting obligations. No additional procedures were required for the purposes of the research study beyond those already in place for blood transfusion SAE and SAR reporting to SHOT and SABRE/MHRA (Serious Adverse Blood Reactions and Events/Medicines and Healthcare products

Regulatory Authority). However, an additional form was generated to record SAEs and SARs specifically in research participants in order to maintain a separate record where required (appendix A).

**Risk Management**

A risk assessment (table 5.2 below) using a '5 x 5' model (NPSA, 2008) was performed on the research protocol. All risks identified were classified as 3 (low risk/green) except for the risk of development of TACO which scored as 4 (moderate risk/yellow). This was based on low likelihood (score 1) but high severity (score 4). However, this was judged as having adequate controls and precautions in place in terms of exclusion criteria, patient monitoring, patient support and follow-up. The protocol was medically reviewed and approved by three consultant haematologists and a cardiologist.

## Table 5.2: Accelerated Transfusion Protocol Risk Assessment

| Hazard Identified | Persons at Risk | How they might be harmed | Existing Controls/Precautions | Likelihood | Severity | Risk Rating |
|---|---|---|---|---|---|---|
| Decision to participate later felt to be wrong decision | Patient<br>Practitioner | Feeling of regret or coercion, stress | Letter of invitation can be read and responded to without pressure or specific time limit. Consent has to be given prior to transfusion or interview with an option to decline without consequences. | 3 | 1 | 3 |
| Development of TACO | Patient | TACO (pulmonary complication of fluid overload) | Medical exclusion criteria approved by consultant medical staff.<br>Pre and post transfusion clinical assessment<br>Patient has contact details and information if unwell and require help | 1 | 4 | 4 |
| Not all healthcare providers aware of patient's participation in study | Patient | Patient may not be appropriately clinically managed if attending hospital for treatment or if develops a complication of transfusion | Patient's GP will receive a letter informing them of their patient's wish to participate and a copy will be placed in the patient's medical notes. | 1 | 3 | 3 |
| Not all healthcare practitioners in the team aware of study related procedures | Patient<br><br>Practitioner | Patient may not be appropriately clinically managed<br>May affect the member of staff's professional registration if performing variations on procedures with no formal training | All staff involved in the study will be trained in the aspects they are involved in (see training log and contents page of protocol) | 1 | 3 | 3 |
| Data protection and confidentiality | Patient<br>Practitioner<br>Organisation | Breach of confidentiality | Forms will be identified using a participant number and the linkage document will be held securely. Completed forms will be stored securely. Electronic files will be on a password protected Trust PC with no hard drive (data on a server). USB sticks are encrypted. | 1 | 3 | 3 |
| Personal safety when visiting a patient's home | Chief Investigator<br>BCIVT practitioners | Assault, other breaches of personal safety and security | The CI will leave details of home visits and expected return times with a colleague. They will have a mobile phone at all times. | 1 | 3 | 3 |

**Research Protocol Training and Responsibilities**

The Chief Investigator and research team were trained in Good Clinical Practice by the NHS Institute for Health Research on ethical and scientific quality standards in clinical research, a mandatory requirement for researchers who take consent and/or are responsible for managing and reporting SAEs or SARs. This is in accordance with the Research Governance Framework for Health and Social Care (DH, 2005). All were committed to two-yearly retraining whilst engaged in research.

All personnel (chief investigator, the clinical haematology team, CIVT staff and transfusion laboratory scientific staff) were trained to the relevant parts of the research protocol according to their role in the study and tasks they were expected to perform, and this was updated with protocol version changes. A delegation of duties log was maintained that described the tasks each individual undertook in the study. Both training and delegation of duties log were updated for staff leaving or joining the organisation during the study period. These records were stored securely in the research site file by the Chief Investigator.

# Chapter Six:
# Strand 1 Methods
# Physiological/Safety Enquiry

This chapter discusses the methods used for the physiological/safety strand of the study which is designed to address whether accelerated transfusion (60 minutes per unit, not exceeding 5ml/Kg/Hr) is associated with a higher incidence of transfusion-associated circulatory overload (TACO) than standard rate transfusion (90 minutes per unit).

**General Research Question**

Whether transfusing two units of red cells over 60 minutes per unit (accelerated transfusion) is safe and could improve CIVT service capacity, while gaining understanding of the patient's and practitioner's experience.

**Hypothesis**

$H_1$: Two units of red cells transfused over 60 minutes each can be physiologically tolerated in selected patients ($H_0$ there is no difference in the incidence of Transfusion Associated Circulatory Overload (TACO) between standard and accelerated rate transfusions).

**Method Aim**

The selected method aims to demonstrate the accelerated transfusion procedure is no worse (in terms of patients developing signs of TACO) than

the current standard rate transfusion procedure. The end point was whether or not the patient developed TACO within 24 hours of the transfusion. This was evaluated using a simple post-transfusion observational assessment of the patient's vital signs. Further analysis of the vital sign observations aimed to demonstrate any statistically significant differences between standard rate and accelerated rate transfusion, in the absence of clinically overt TACO. This was to demonstrate measurable differences physiological response between standard and accelerated rate transfusion.

**Method Design: Rationale and Philosophical Foundations**

An analytical experimental design was considered the most appropriate approach to testing the hypotheses and research question regarding physiological tolerability of accelerated transfusion. A quantitative methodology is appropriate for the objective evaluation of the observed, measurable phenomenon of TACO, and this underpins the philosophical basis of this approach. The positivist/post-positivist paradigm accords with the general tradition and empirical nature of biomedical research as it is based upon objective and measurable phenomena, and concurs with the approach taken to identify and measure TACO in this study. From an ontological perspective, the realist  believes that a physiological "reality" exists that is driven by natural laws, but this is tempered by the critical realist's position that one cannot possibly fully understand or capture its behaviour when fundamentally reality can only be incompletely understood (Guba, 1990). This ontological standpoint acknowledges that the current understanding of TACO and patients at risk is therefore incomplete.

Epistemologically, the modified objectivist's approach taken to identifying and measuring it can only aspire to an approximation based upon previous research that attempts to define the clinical criteria for TACO, and therefore patients who are at risk of developing it. The methodological approach to this study is philosophically defensible, but acknowledges the limitations of knowledge derived from previous research and observations, and of knowledge *per se*.

The design is a prospective cohort crossover study, where the patient acts as their own control. All patients who receive regular two unit red cell transfusions either at home or as a day case on the oncology unit were considered for inclusion. Patients with risk factors for fluid overload were excluded from participating based upon medically assessed exclusion criteria (appendix B). Consenting patients meeting the medical inclusion criteria initially received a standard rate (90 minute per unit) transfusion for their next scheduled transfusion. If this was physiologically tolerated (no signs of TACO), they then proceeded to an accelerated (60 minute per unit) transfusion when they would next normally receive a transfusion, typically two to six weeks later for most patients. Accelerated transfusion was subsequently offered for future transfusions if there had been no signs of TACO and the patient remained medically eligible. This was intended to strengthen the data regarding tolerability of accelerated transfusion, and allow for patient choice.

The rationale for the choice of study design primarily relates to logistic reasons and the physiological nature of the intervention under investigation.

A randomised controlled trial (RCT) would require two groups of patients randomised to either a standard rate or accelerated rate transfusion arm. This would have the advantage of reducing random error relating to physiological variation of individual patients, but would require a relatively large number of participants. As there are a relatively limited number of patients eligible for this study in the time available, the cohort crossover study has the advantage of requiring fewer participants as the patient will act as their own control. However, it is acknowledged that what is gained in convenience may be off-set by the potential for bias to be introduced by studying a smaller group which may not be as representative of the physiological variation in this patient population. Additionally, a two-arm design is usually chosen when the intervention has a potentially permanent effect or requires a significant 'wash out' period. One of the main criticisms of this type of study when reviewed by Mills *et al* (2009) was the distorting effect of carry-over which may affect the outcomes subsequent treatments or interventions. This is not the case with a red cell transfusion, as opposed to drugs, as there are no permanent physiological effects that could bias a subsequent transfusion intervention. A cohort crossover design is therefore scientifically and clinically justifiable and reduces the sample size required.

**Sample Size, Power Calculation and Sampling Strategy**

The aim of the study is effectively to accept the null hypothesis (Blackwelder, 1982): demonstrating the accelerated transfusion procedure is no worse, in terms of patients developing signs of TACO, than the current standard rate transfusion procedure. The study can therefore be defined as a binary

outcome non-inferiority study. There are two possible outcomes (TACO, or no TACO) which are intended to demonstrate that accelerated transfusion is no worse than standard rate transfusions in terms of patients developing signs of TACO.

The sample size and power calculation was determined using a calculator for this type of study provided by Sealed Envelope ™, who offer randomisation services and online databases for clinical trials. Figure 6.1 (page 88) summarises the data used to derive the sample size and power.

**Evidence and Justification for the Sample Size and Power Calculation**

Calculation of the sample size required for the study requires knowledge of the incidence of TACO. The incidence of TACO in the literature focuses on particular patient groups such as ICU patients (Li *et al*, 2011; Rana *et al*, 2006), orthopaedic patients (Popovsky *et al*, 1996), or elderly inpatients in the United states (Menis *et al*, 2012) and the blood components are not limited to red cells (Narick *et al*, 2012). Other studies report wide variation in the incidence of TACO (Murphy *et al*, 2010; Piccin *et al*, 2009; Popovsky, 2006). Therefore this creates a generalisability issue when using data to justify the power/sample size calculation.

The data used in this section were the most contemporaneous data on the reported incidence of TACO, blood issues, and wastage at the time of performing this calculation for the research ethics application. The SHOT 2012 report, relating to 2011 data, states there were 23 cases of Transfusion

Associated Circulatory Overload (TACO) nationally, where up to two units of red cells were implicated (Bolton-Maggs *et al*, 2013, p. 163).

To understand the (SHOT reported) incidence of TACO, denominator data regarding number of units transfused was required from approximately the same period of time. The number of units transfused nationally can be estimated using the Blood Stocks Management Scheme (BSMS) 2011/12 annual report (MacRate (Ed.) and Taylor, 2012). Although less than 100% of hospitals fully participate with providing data, the majority do participate and will provide a realistic estimate of red cell wastage (which will allow a calculation of units actually transfused). This is shown in table 6.1 below.

**Table 6.1: Blood wastage in the UK and Ireland (2011/12)**

| Blood Service | Number of red cell units issued | Wastage % | Estimate of units transfused |
|---|---|---|---|
| **NHS Blood and Transplant** | 1,835,000 | 2.1% | 1,796,465 |
| **Northern Ireland Blood Transfusion Service** | 53,713 | 4.8% | 51,135 |
| **Welsh Blood Service** | 85,620 | 2.6% | 83,394 |
| **Scottish National Blood Transfusion Service** | 188,361 | 0.86% (based upon 6 participant with 270 units of wastage each on average) | 186,741 |
| **Irish Blood Transfusion Service** | 138,080 | Not reported | 138,080 |
| **TOTAL units transfused 2011/12 (estimated)** | | | **2,255,825** |

**The incidence of TACO can therefore be estimated as:**

$$\frac{23^{a}}{2{,}255{,}815^{b}} = 0.0010195\% \text{ (incidence of reported TACO)}$$

[a] cases of TACO reported to SHOT in 2011 involving 2 or fewer red cell units

[b] estimated red cell units transfused in UK and Ireland

Or inversely expressed as:

- 'Successful' transfusions (no TACO reported) = 99.9989805%
- The number of home (2 unit) transfusions in 2 years prescribed by haematology consultants is (01.08.11 to 31.08.13) = 569 (n)
- Number of TACO reports locally in that period = 0
- Local incidence of TACO in home transfusion or day-case patients in 2 years = 0%
- 1/n x 100% = non-inferiority limit (d) = 0.18%

i.e. the estimated period of the data collection phase of the study will be 2 years. One patient developing TACO in that period (increased from zero) would be clinically unacceptable.

A sample size and power calculator provided by Sealed Envelope ™ (www.sealedenvelope.com/power/binary-noninferior) specifically designed for binary outcome non-inferiority studies was used (Sealed Envelope Ltd, 2012).

The results of the sample size calculation (after the significance level, power, and percentage 'success' in the control and experimental group data had

been inputted based upon the calculations above). The calculation shows the sample size required for 80% power (39 patients). This was considered more likely to be achievable than powering to 90% (figure 6.1 below and appendix C).

The results of the 'sample size required' calculation (after the significance level, power, and percentage 'success' in the control and experimental group data had been inputted based upon the calculations above). The above calculation shows the sample size required for 90% power (54 patients). This was considered less likely to be achievable than powering to 80% (appendix C).

These show some agreement with sample sizes calculated from more recent morbidity and mortality data published by SHOT (Bolton-Maggs *et al*, 2016), where the combined mortality and morbidity risk of TACO was stated to be 1.47 per 100,000 blood components issued. This provides a % 'success' rate of 99.99853% and computes a sample size of 57 if powering to 80% or 78 if powering to 90%. However, the comparisons are not identical as the SHOT denominator data is based on all blood components issued, whereas the calculation for the study is based on an estimate of the total number of blood units actually transfused, and is limited to red cells only.

Local data from the participating Trust from 2006/07 to 2015/16 showed an incidence of TACO as 1 per 33,831 red cell units transfused (2 cases in 67,661 red cell units transfused). This provides a % 'success' rate of 99.9970441% and computes a sample size of 113 if powering to 80%. This is based on significantly fewer data than national figures and is easily skewed

as TACO is a relatively rare event, and in addition to this both cases were patients in acute care settings which do not represent the patient group being researched.

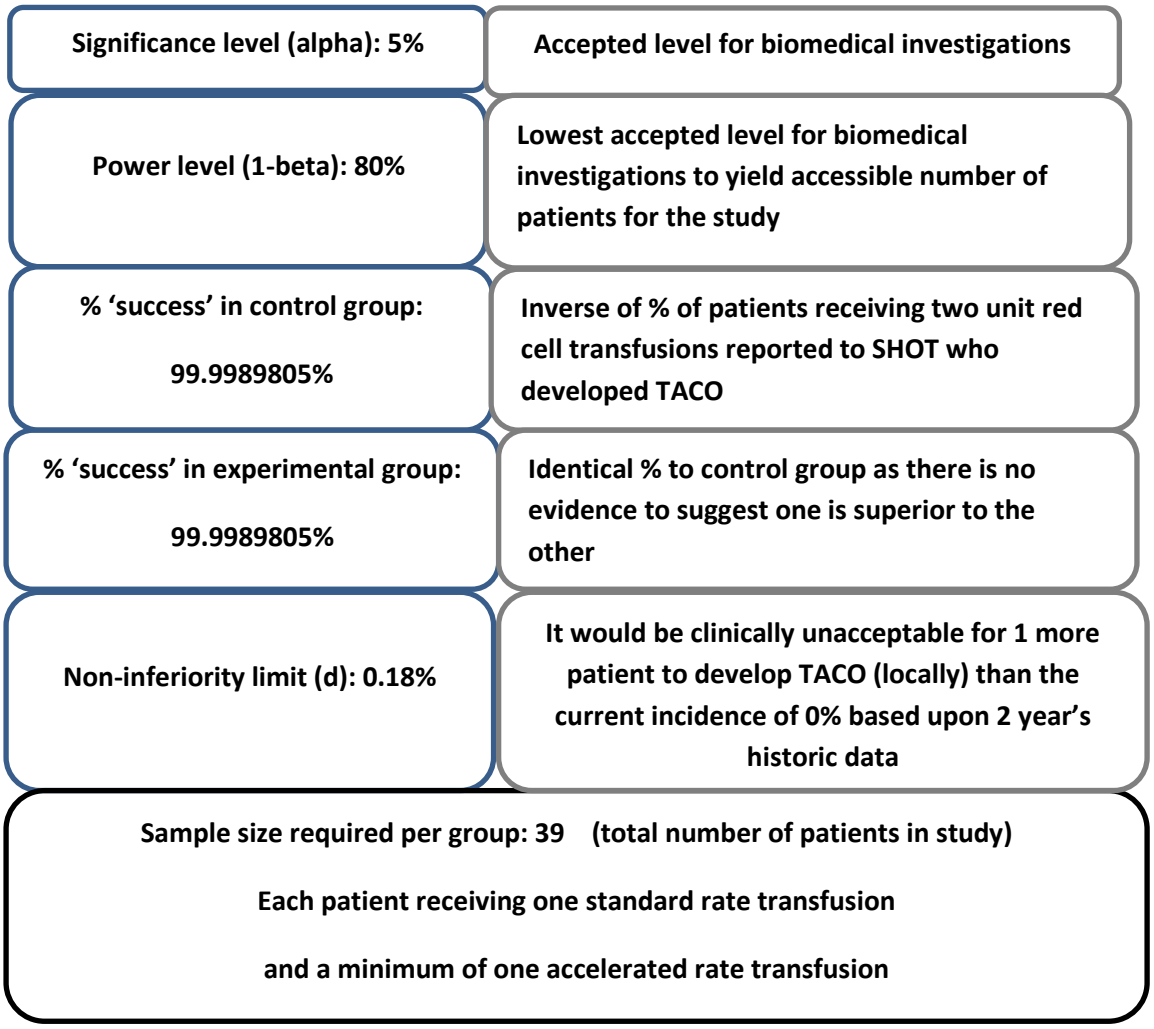



**Figure 6.1: Determination and Justification of Sample Size and Power**

There were a number of important limitations with the data used for the sample size and power calculation, and these are discussed in the concluding chapter. Despite the difficulties and limitations in determining sample size, it was important to address this as far as was practical with the

benefit of all available data and evidence, as this is was a requirement when applying for ethical approval.

### Sampling Strategy

Consecutive non-probability sampling was judged as the most appropriate sampling strategy. The sampling was consecutive in that all consenting patients who fulfilled the medical inclusion criteria were included when they were referred to the Clinical Haematology Team for blood transfusion. This approach ensured the sample size and power were not compromised by excluding eligible patients from an already relatively small group of available patients. The sampling was not random and therefore the data are not generalizable to the general population, however the evidence generated from the study could potentially be applicable to the same population of patients, regardless of the location of transfusion, for example patients who have transfusion at home and/or as a hospital day-case.

### Method Protocol and Rationale

The following sections describe the protocol and rationale for the physiological/safety enquiry methods and are designed to generate evidence for the safety of transfusing two units of red cells over 60 minutes each.

### Patient Selection

Patients were identified from the Clinical Haematology ‘regularly transfused’ patient list, or identified by medical staff when they attended haematology clinic appointments.

Patients were invited to participate either at a usual clinic visit, or were contacted by telephone by Haematology medical/nursing staff if a clinic appointment was not scheduled for the near future. Patients meeting the basic inclusion criteria received a letter of invitation to participate in a) accelerated transfusion, and b) interview about their experience of accelerated transfusion (appendix D). The letter was accompanied by an information sheet (appendix E). Each patient was offered the opportunity to discuss the study further with a healthcare professional involved in the study if they wished. The patient was given instructions to contact the Clinical Haematology office to indicate that they wished to be included in the study. The patient was informed that arrangements would be made to take consent from them which would involve signing a form. Where and who took consent depended upon the patient's usual delivery of care in order to minimise inconvenience to the patient. All healthcare professionals taking consent had Good Clinical Practice training. Consent could be taken by Haematology medical or nursing staff at a subsequent clinic appointment. If the patient did not have a scheduled clinic appointment, the Chief Investigator made arrangements to take consent at the patient's home at a mutually convenient time. In either case, the patient was allowed a period of time to decide that was not less than 24 hours (appendix F). The completed consent forms were retained securely by the Chief Investigator and a copy was placed in the patient's medical notes.

The patients had a range of haematological diagnoses causing anaemia requiring transfusion such as bone marrow failure syndromes and/or on

myelosuppressive therapies. The patients received their transfusions at home or on the Oncology Day Care Unit. Some patients received transfusions in both locations or entirely in one or the other dependent upon their needs and whether their address was within the geographical reach of the CIVT service. All patients were included to maximise participant numbers for the physiological enquiry strand of the study as there was no reason to assume they were not physiologically identical. However, only home transfusion patients were invited for interview about their experience of accelerated transfusion. Patients who fulfilled the following basic inclusion criteria (in the professional opinion of Haematology medical staff) were considered for inclusion and invited to participate. The inclusion criteria are summarised in table 6.2.

**Table 6.2: Inclusion criteria**

| Inclusion Criteria |
|---|
| Expected to receive two or more transfusions over the course of their treatment |
| Receive transfusions at home or on the Oncology Day Care Unit. |
| Have no known co-morbidities that would pre-dispose the patient to fluid overload |
| Judged to have full mental capacity to ensure they could give valid consent |
| Could read and speak English |

Patients who elected to participate in the study were formally assessed by a medical officer from the Clinical Haematology Team against the exclusion criteria below in table 6.3. These criteria were designed to identify patients who may be at risk of fluid overload, based upon the SHOT (2012) report (Bolton-Maggs *et al*, 2013) recommendation, (BCSH guideline (2009) and

addendum (2012)). Patients with heart failure were excluded. This was verified by checking whether an echocardiogram has been performed previously with the Cardiology Department before accepting a patient into the study. All patients with chronic heart failure should have had echocardiography previously performed according to NICE guidelines (NICE, 2010).

The exclusion criteria (table 6.3) also ensured that baseline vital sign measurements did not exceed the criteria for assessing the presence of TACO on the 24 hour post-transfusion assessment. Stage 1 hypertension is defined as greater than 140/90mmHg, however 40% of adults in England have a blood pressure measuring greater than this and not all would necessarily require treatment (NICE, 2011). For this reason, modified stage 2 hypertension criteria (with a slightly lower diastolic threshold) were chosen to define significant hypertension for the study. They were approved by the Haematology Consultant medical staff, and by a Consultant Cardiologist. The patient's body weight was checked and recorded at a scheduled hospital appointment or home visit by the Chief Investigator. This was used for ensuring this aspect of the eligibility criteria was met and was also used for the dose calculation for the red cell prescription.

**Table 6.3: Medical Exclusion Criteria for Accelerated Transfusion**

| | Exclusion Criteria |
|---|---|
| **HISTORY** | Patient has had echocardiography with reported chronic heart failure. Reported as moderate to severe left ventricular dysfunction (ejection fraction <35%). |
| | Severe aortic stenosis |
| | Hypoalbuminaemia (<35g/L) |
| | Low body weight (<50Kg) |
| | Significant renal failure (eGFR <30ml/min) |
| | Significant liver failure (bilirubin >30µmol/L) |
| **EXAMINATION*** | Oedema |
| | Cough, dyspnea and/or respiratory rate >20 breaths per minute |
| | Tachycardia (heart rate >100 beats per minutes) |
| | Un-treated or uncontrolled hypertension (diastolic >95 mmHg, systolic >160 mmHg) |

*checked on pre-transfusion assessment if examination not possible at the time of writing the prescription

Patients who responded indicating they wished to participate in the study were prepared in the following way. The Chief Investigator sent a letter (appendix G) to the patient's General Practitioner informing them of the patient's wish to participate in the study. A copy was also placed in the patient's medical notes.

Each time a patient in the study had red cells prescribed a pre-transfusion checklist was completed to record that the patient still met the medical inclusion criteria (appendix B). The completed document was retained by the Chief Investigator for secure retention in the research site file.

**Requesting and Selecting Red Cell Units: Volume Calculation**

Red cells were requested following the existing procedure in the hospital Trust's Transfusion Clinical Process Policy. Additionally, for the purposes of this study, the required red cell volume was specified on the request form. This was an instruction to the transfusion biomedical scientist in the laboratory to select and provide a specified volume for the patient based on

body weight. This ensured the transfusion rate did not exceed 5ml/Kg/hour. Where the calculation and request form was completed by Haematology nursing staff, it was checked by the prescribing medical officer when completing the prescription.

The rationale for the dosage calculation was derived from the Australian and New Zealand Society for Blood Transfusion guidelines (2011) where the recommended rate of transfusion is stated as 60-180 minutes per unit, unless the patient has heart failure or is otherwise at risk of fluid overload. Based upon the shortest recommended infusion time, this is 30 minutes per unit of red cells faster than the current UK guideline recommendation of 90-240 minutes (BCSH, 2009). However, there is some variability in the volume of UK and Australian red cell units (NHSBT, 2012; Australian Red Cross Blood Service, 2012); this was accounted for in design of the study protocol by standardising the prescribed dose of red cells to 5ml/Kg/hr. Variation between the volume of UK and Australian red cell units was important to consider, as this could introduce bias when developing a thesis based upon non-UK evidence, when the research was conducted using UK manufactured (NHSBT) red cell units. The typical volume of an Australian standard red cell unit is quoted as 236-282 ml (Australian Red Cross Blood Service, 2012). The volume of a UK (NHS Blood & Transplant) standard red cell unit is 220-340 ml (NHSBT, 2012).

In a small (50 Kg) adult this is equivalent to 5.2ml/Kg/hr based upon an average ‘Australian’ unit, and 5.6 ml/Kg/Hr based upon an average UK red

cell unit i.e. the smaller adult is most at risk of TACO with respect to low body weight as a risk factor.

- 259 ml = mean volume of Australian red cells

Therefore, one unit per hour in a 50Kg adult at 259 ml / 50Kg = 5.2ml/Kg/hr

- 280 ml = mean volume of UK red cells

Therefore, one unit per hour in a 50Kg adult at 280 ml /50Kg = 5.6ml/Kg/hr

A 5ml/Kg/hr dose was chosen for ease of calculation and provides a margin that does not exceed the 'Australian' maximum rate of transfusion (60 minutes per unit). This is only relevant up to a body weight of 67Kg. At this body weight, the calculated dose would be 685ml and the combined total of two units would not exceed 680ml, which is the maximum possible for two units of UK red cells. Patients weighing greater than 67Kg would therefore not require volume-selected red cells (table 6.4).

The volume of red cells requested represented the total maximum volume (combined volume of two units) to be supplied by the laboratory, based upon the weight/dose (table 6.4). There was no requirement for the laboratory staff to match the calculated dose, only to ensure the dose was not exceeded.

Table 6.4 describes the red cell volumes for a range of body weights to achieve a 5ml/Kg/hr dose of red cells. An additional amount (15ml) was included to allow for the residual loss in the blood component administration set. The residual volume was determined using saline by decanting and measuring the remaining volume of fluid.

**Table 6.4: Red Cell Dose/Weight Chart**

| Patient's Body Weight (Kg) | Total Volume to Request (ml) |
|---|---|
| 50 (lowest body weight for study inclusion) | 515 |
| 51 | 525 |
| 52 | 535 |
| 53 | 545 |
| 54 | 555 |
| 55 | 565 |
| 56 | 575 |
| 57 | 585 |
| 58 | 595 |
| 59 | 605 |
| 60 | 615 |
| 61 | 625 |
| 62 | 635 |
| 63 | 645 |
| 64 | 655 |
| 65 | 665 |
| 66 | 675 |
| 67 or more | 685<br>2 units will not exceed 680ml in total, which is the total combined maximum possible for 2 units of UK red cells |

Table 6.4 shows whole kilograms for illustration. Actual calculations were accurate to one decimal place and calculated by the formula shown below.

**(Weight (Kg) x 10) + 15 = maximum volume (ml) of red cells to request from laboratory**

The transfusion biomedical scientists selecting blood for patients in the study were instructed and trained that the calculated volume requested by the medical officer did not need to be matched, but must not be exceeded. Two units of red cells were selected from the blood stock fridge. The transfusion biomedical scientist processing the request checked that the combined volume of both of the units as shown on the pack label did not exceed the volume the requester has stated on the transfusion request from. If the patient required selected blood as a special order from the Blood Centre

(e.g. required phenotyped blood, special requirements or required a crossmatch by the reference laboratory due to complex serological issues), the volume requirement was communicated when placing the order. A patient who has special transfusion requirements had their blood ordered following the Online Blood Ordering System (OBOS) laboratory standard operating procedure, ensuring there was an instruction in the 'order notes' in OBOS regarding the required volume to be supplied as calculated and instructed by the medical officer prescribing the blood e.g. "*the 2 units must not exceed a total volume of 615ml*".

If the blood was being crossmatched by the reference laboratory i.e. not the local laboratory, the transfusion biomedical scientist made the reference laboratory scientist aware of the specific volume requirement. Any queries or problems in selecting specified red cell volumes were referred to the Chief Investigator or senior member of staff in the Transfusion laboratory. The arrangements for ordering units of a specific volume was agreed with the Red Cell Immunohaematology Department at the supplying blood Centre, and the NHSBT customer service manager ahead of the study beginning.

**Prescribing Red Cells and Sequence of Transfusion**

The red cells were prescribed on the blood prescription as per usual procedure as stated in the hospital Trust's Transfusion Clinical Process Policy.

The patient's first transfusion was a standard rate (90 minutes per unit). If the standard rate transfusion is tolerated with no signs of TACO, the patient's

second transfusion was an accelerated rate (60 minutes per unit). If this was also tolerated without signs of TACO, subsequent transfusions during the study could also be at the accelerated rate. Figure 6.2 shows the sequence of standard rate and accelerated transfusion.

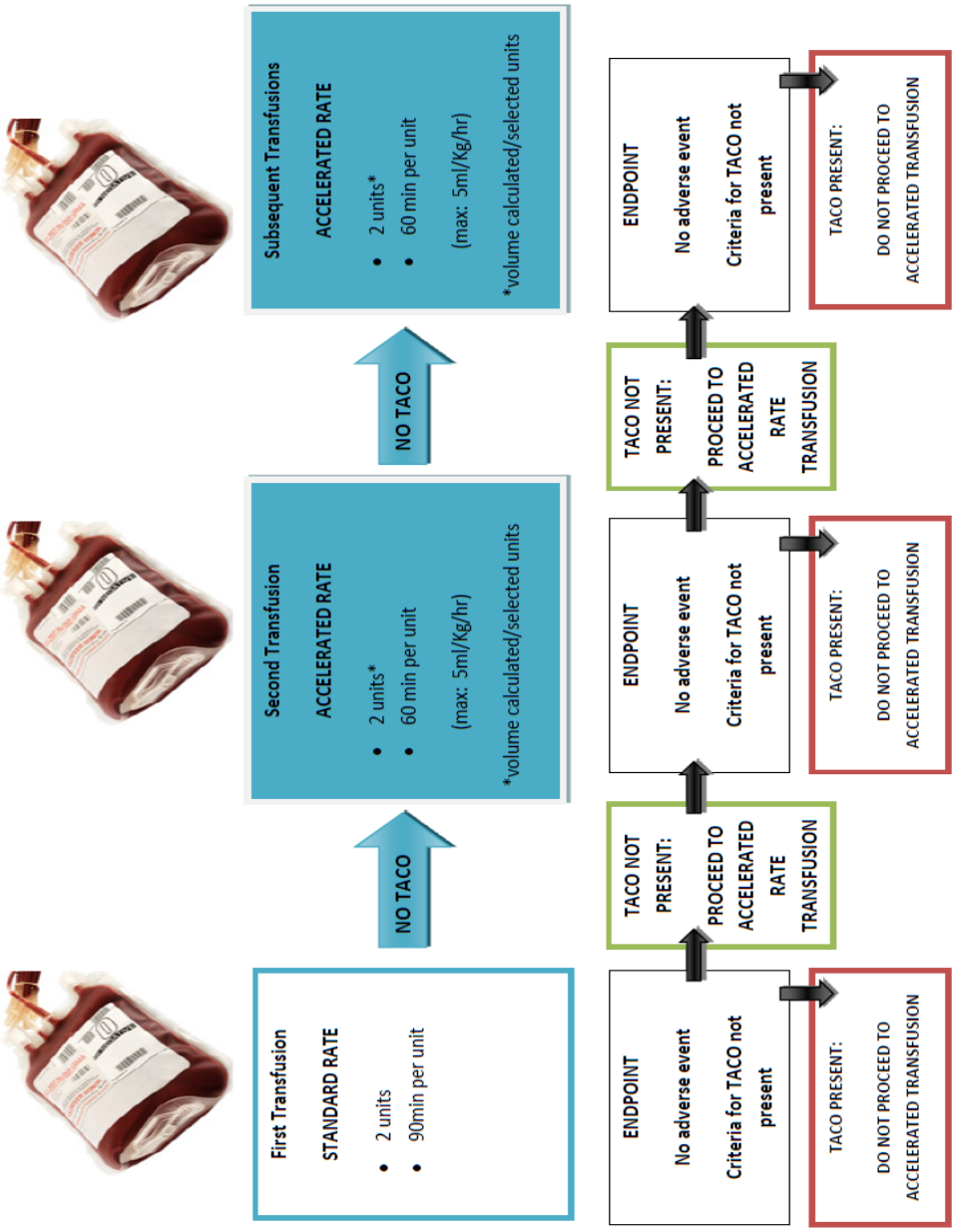



**Figure 6.2: Sequence of Red Cell Transfusion**

### Pre-Transfusion Confirmation of Willingness to Continue in the Study

The patient who has previously consented to participate in the study was required to confirm their willingness to continue before administering any transfusion given as part of the study. The patient had the right to withdraw at any time without giving a reason, or affecting their usual standard of care (DH, 2005). Continued willingness to continue with the study was ascertained verbally with the patient and recorded (appendix H). The form was returned to the Chief Investigator for secure retention in the research site file.

### Pre-Transfusion Clinical Assessment

The purpose of this assessment was to screen the patient to indicate whether there may have been any changes to the medical exclusion criteria assessment made at the time the blood was prescribed. After checking whether the patient was still willing to participate in the study, the vital observations were performed and then recorded on the Pre-Transfusion Assessment form (appendix H). If any of the criteria were not met or the patient did not wish to continue in the study, the transfusion was administered over 90 minutes per unit. In this case the prescription was annotated accordingly by the nurse administering the transfusion. This was also explained to the patient. Any concerns about the patient's condition were reported to a member of the Clinical Haematology medical staff and advice taken. The pre-transfusion assessment form was returned to the chief investigator for secure retention in the research site file.

**Transfusion Procedure**

The transfusion was administered, monitored and documented as described in the hospital Trust's Transfusion Clinical Process Policy for Home Transfusion (as per standard procedure). There were no variations to the standard procedure other than the duration of the transfusion (in the case of accelerated transfusion). The blood was administered by gravity infusion through a blood component administration set.

In order to calculate the drip-rate, the volume (ml) to be infused was multiplied by the number of drops in 1ml (typically this is 15 for blood) however the manufacturer's instructions for the drip-factor were observed. This value was divided by the number of minutes over which the infusion was to be delivered. This gives the number of drops falling into the drip chamber per minute (Dougherty, 1999). Close attention was paid to the progress of the transfusion to ensure it was administered over the prescribed time.

| |
|---|
| Example: volume stated on blood unit label (275ml) x 15 = 4125<br>4125/60 min = 69 drops per minute |

To allow for practical difficulties (especially when using gravity infusion) in meeting the exact infusion durations prescribed (60 or 90 minutes per unit), a +/-10% margin was allowed for the overall duration of the transfusion episode.

| |
|---|
| i.e. Standard rate transfusion: 2 x 90 min = 180 min (162 min – 198 min)<br>Accelerated rate transfusion: 2 x 60 min = 120 min (108 min – 132 min) |

The patient was given a post-transfusion contact booklet (as per standard procedure) to make them aware of signs of adverse reaction and advice on seeking medical help. The Blood Transfusion Clinical Record was returned to Clinical Haematology/Laboratory for validation and archiving as per usual procedure stated in the hospital Trust's Transfusion Clinical Process Policy.

**Post Transfusion Clinical Assessment**

The purpose of the post-transfusion clinical assessment was to determine whether the patient had developed signs of TACO, the study end-point. The International Society of Blood Transfusion draft definition for TACO states that TACO develops within 6 hours of transfusion, but accepts that cases may be observed up to 12 hours after transfusion (ISBT, 2014). The Serious Hazards of Transfusion (Bolton-Maggs *et al*, 2013) criteria state that symptoms and signs usually occur within 6 hours of transfusion, but SHOT also accept suspected cases occurring up to 24 hours after transfusion. Given this considerable variability, the patient was visited at home to have an assessment performed at about 24 hours after the transfusion had ended to allow for this. Given the pressure on CIVT capacity and available nursing hours, this was undertaken by trained support staff and the Chief Investigator. The criteria for the end-point (signs of TACO) were based upon SHOT and some of the ISBT surveillance diagnosis criteria for TACO available at the time of designing the protocol and are summarised in table 6.5. The ISBT draft criteria were updated after the protocol was submitted for ethical approval hence the criteria cited below are not the most recent version.

**Table 6.5: Summary of SHOT and ISBT definition and surveillance diagnosis criteria for TACO**

| **SHOT** (Bolton-Maggs *et al*, 2013) | **ISBT draft definitions** (ISBT, 2014) |
|---|---|
| Any 4 of the following within 6 hours (or up to 24 hours) of transfusion | At least 2 primary criteria, or 1 primary and 2 supporting criteria, within 6-12 hours of transfusion |
| • Acute respiratory distress<br>• Tachycardia<br>• Hypertension<br>• Acute or worsening pulmonary oedema<br>• Evidence of positive fluid balance | **Acute or worsening respiratory distress must be present**<br>**Primary Criteria**<br>• Acute or worsening pulmonary oedema with bilateral infiltrates<br>• Cardiomegaly on imaging<br>• Evidence of fluid overload (positive fluid balance, clinical improvement with diuretics) |
| | **Supporting Criteria**<br>• Raised Brain Natriuretic Peptide (BNP) or NT-Pro BNP greater than 1.5 times the pre-transfusion level<br>• Increase in mean arterial pressure or pulmonary wedge pressure (often with widened pulse pressure), or hypotension in cardiac collapse. |

The ISBT diagnostic criteria are best suited to the patient who has already been identified as acutely unwell with respiratory distress in a high care setting. The SHOT criteria more readily lend themselves to assessing patients in the home environment with simpler clinical measurements and observations. Of the five SHOT criteria, four must be present to suspect TACO although fewer would be accepted for further investigation and reporting purposes in strongly suspected cases. The vital sign

measurements would identify tachycardia, hypertension and tachypnoea. Acute or worsening pulmonary oedema (or overt heart failure) would be evident by the presence of tachypnoea, dyspnoea, cough and peripheral oedema (singularly or in combination). Therefore the 24 hour post-transfusion check-list comprehensively covers the criteria for TACO according to the SHOT surveillance diagnosis. Although these criteria are intended for haemovigilance or surveillance diagnosis as opposed to clinical diagnosis for medical management, they are sufficiently sensitive to identify patients with acute respiratory distress caused by circulatory overload.

The rationale for expected values for vital sign observations is based upon values used in the National Early Warning Score (NEWS) (Royal College of Physicians, 2012). NEWS was devised to promote the assessment of acute illness, the detection of clinical deterioration, and for the initiation of a timely and competent clinical response. NEWS is an aggregate of six physiological parameters (temperature, heart rate, systolic blood pressure, respiratory rate, oxygen saturation, and level of consciousness). A patient can score between 0 and 3 for each parameter (3 indicating higher risk), and the aggregated score triggers defined actions to ensure appropriate monitoring and escalation of care. Although NEWS is intended to be an aggregated score, in this study only some of the vital sign observations are undertaken for the purposes of identifying signs of TACO. A score between 0 – 1 was adopted as a low threshold trigger for each of the vital sign observations recorded. The NEWS score of 0 for systolic blood pressure is equivalent to 111-219 mm Hg, and 12-20 breaths per minute for respiratory rate.

Therefore 219 mmHg was adopted as the upper limit expected for systolic blood pressure, and 20 breaths per minute for respiratory rate. A score of 1 for heart rate is equivalent to 91-110 beats per minute, and a score of 0 is equivalent to 51-90 beats per minute. An upper limit of 100 beats per minute was adopted for the study to indicate tachycardia as 90 beats per minute may have been over-sensitive particularly as some patients have tachycardia due to the physiological effect of anaemia.

The 24 hour post-transfusion clinical check-list below in table 6.6 (appendix I) was designed to detect the relevant symptoms and signs associated with TACO. This was based on the SHOT and ISBT definitions and surveillance diagnosis criteria for TACO shown in table 6.5 and lists the assessment criteria of the 24 hour post-transfusion clinical assessment.

**Table 6.6: The 24 hour post-transfusion clinical assessment**

| Clinical Parameter | Expected Value | Rationale |
|---|---|---|
| Heart rate | Less than 100 beats per minute | To exclude tachycardia |
| Systolic blood pressure | Less than 219mm Hg | To exclude significant hypertension<br>(111-219 = NEWS* score 0) |
| Diastolic blood pressure | No value stated | More useful for monitoring chronic hypertension than acute events* |
| Respiratory rate | Less than 20 breaths per minute | To exclude respiratory distress<br>(12-20 = NEWS* score 0) |
| Presence of cough and/or dyspnoea | Not present | To exclude respiratory distress |
| Presence of peripheral oedema | Not present | May indicate heart failure/fluid overload |
| Any signs of acute illness or adverse event in past 24 hours | Not present | To allow comprehensive assessment of the patient's post-transfusion wellbeing |

*National Early Warning Score (RCP, 2012)

If the patient had any abnormal vital signs or otherwise reported being unwell, the procedure was to report this to the Clinical Haematology medical staff and advice taken. If serious illness was suspected, arrangements would have been made for the patient to go to hospital as per usual procedure stated in our Trust's Transfusion Clinical Process Policy for Home

Transfusion. If Transfusion Associated Circulatory Overload was diagnosed, the procedure required statutory external reporting to SHOT/SABRE (MHRA) as per existing departmental policy/procedures and regulatory requirements by the Chief Investigator. The patient was assessed for *any* Adverse Event (AE) having taken place between the transfusion and the post-transfusion assessment. This required documentation (appendix A) and reporting to Haematology consultant medical staff for causality assessment.

Version 1 of the protocol required a 24 hour post-transfusion assessment after every accelerated transfusion. Some patients in the study found this onerous on their time, and with the benefit of having preliminary data supporting the safety of accelerated transfusion at that point, an application for 'substantial amendment' of the research protocol was made to the NRES committee, which was approved.

After the patient had received three accelerated transfusions without signs of TACO or adverse event, version 2 of the protocol then allowed for the patient to continue to receive accelerated rate transfusions but invited to self-report any post-transfusion symptoms, without the need for a 24 hour post-transfusion check-up. This was discussed with the patient and reference was made to the patient information and contact booklet that had been previously provided and explained. The procedure for patients reporting symptoms, was to contact the Clinical Haematology medical staff, GP out of hours service or the Emergency Department (depending on the time of day), as per guidance in the booklet. If the patient did not wish to self-report, then 24 hour post-transfusion follow-up continued as previous procedure. The post-transfusion

assessment form was returned to the chief investigator for data collection and secure retention in the research site file.

**Data Collection Method**

The pre-prescription check-list (appendix B), the pre-transfusion check-list (appendix H), and the post-transfusion check-list (appendix I) returned to the Chief Investigator were used to obtain and record the required data. The following data set was compiled into a Microsoft Excel™ spreadsheet for later analysis.

<u>All transfusion episodes</u>

- Participant identifier
- Patient characteristics (age, weight, gender, and diagnosis)
- Transfusion type (standard or accelerated)
- Date of transfusion
- Total duration of the transfusion for both units (minutes), and the reason for the transfusion duration not meeting the expected duration (if applicable).
- Presence of symptoms and signs of TACO

Standard rate and first three accelerated rate transfusions

- Pre and post-transfusion respiratory rate
- Pre and post-transfusion heart rate
- Pre and post-transfusion mean arterial pressure* based upon the systolic and diastolic blood pressure recorded.

*MAP = [(2 x diastolic) + systolic] / 3

Diastole counts twice as much as systole because 2/3 of the cardiac cycle is spent in diastole. Usual range: 70-110.

**Data Analysis Methods**

Basic descriptive statistics on the data collected are presented to provide an overview of the data. The analysis was performed using Microsoft Excel™.

The method was required to demonstrate the relative risk of the ratio of the proportions of cases having a positive outcome (developing signs of TACO) in two groups (comparing standard versus accelerated transfusion) in order to accept or reject the null hypothesis (where the is no difference in the incidence of TACO between standard and accelerated rate transfusion). Although the Chi Squared test is designed to test independence by assessing whether paired observations on two variables (expressed in a contingency table), are independent of each other, the assumptions for Chi Squared test were likely to not be met in this study. This test relies on adequate cell counts and it was likely that all counts would be zero (i.e.

patients are not expected to develop signs of TACO).When defining equivalence Wellek (2005) recommends odds ratio (OR) and relative risk (RR) as suitable statistical methods for measuring dissimilarity for binomial two-sample problems, and goes on to state that the exact Fisher-type test for one-sided equivalence provides a satisfactory approach for the analysis of non-inferiority study involving two independent samples of binary data. The data were analyzed using MedCalc™ (www.medcalc.org) simple descriptive statistics expressed as relative risk (RR), odds ratio (OR) with a confidence interval and p value. This statistical method has also been previously applied to non-inferiority studies (Connolly *et al*, 2009).

Differences in physiological response between both types of transfusion were evaluated by performing paired t-tests as set out below.

**a)** Is there a difference between the pre and post transfusion vital sign observations in standard rate transfusion (figure 6.3)?

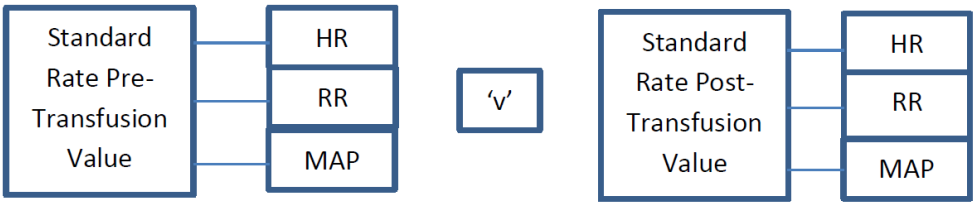



**Fig 6.3: Comparison of pre and post-transfusion vital sign observations in standard rate transfusion**

**b)** Is there a difference between the pre and post transfusion vital sign observations in accelerated transfusion, and is it consistent across three subsequent accelerated transfusions (figure 6.4)?

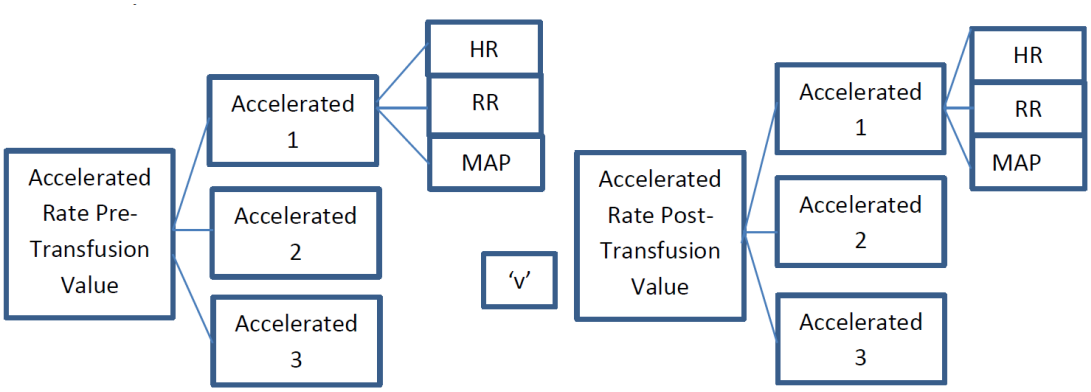



**Fig 6.4: Comparison of pre and post-transfusion vital sign observations in accelerated transfusions**

**c)** Is there a difference in the variance between pre and post transfusion vital sign observation values (pre value – post value), when standard and accelerated rate transfusion is compared (figure 6.5)?

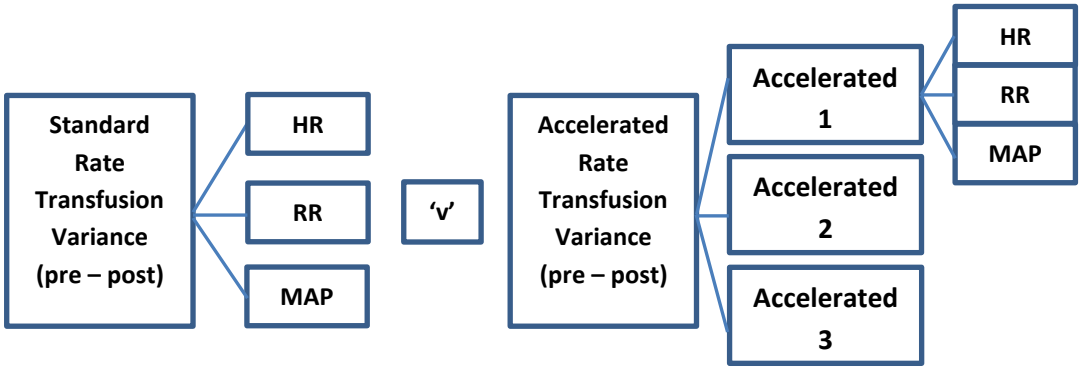



**Fig 6.5: Difference in the variance between pre and post-transfusion vital sign observation values when standard and accelerated transfusion are compared**

**d)** Is there a difference between pre and post transfusion vital sign observation actual values, when standard and accelerated rate transfusion is compared (figure 6.6)?

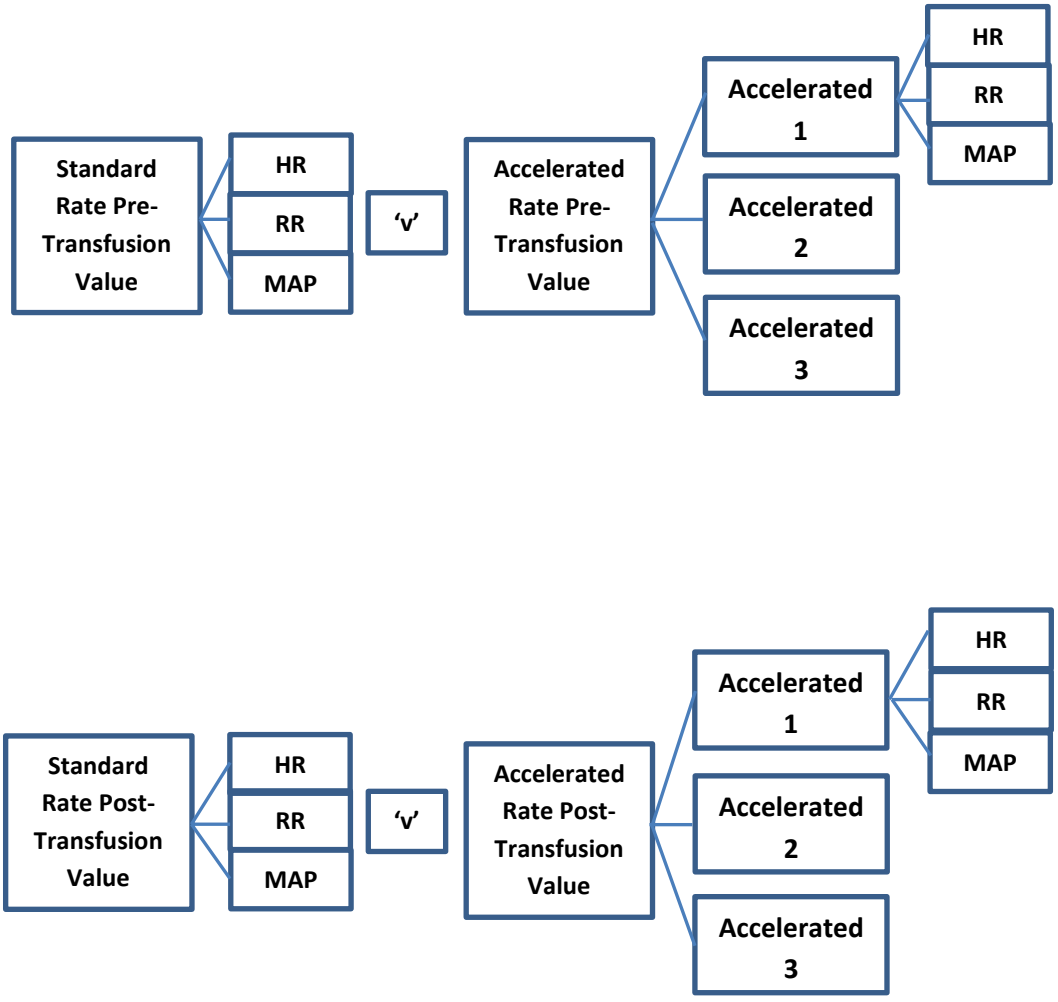



**Fig 6.6: Difference between pre and post transfusion vital sign observation actual values, when standard and accelerated rate transfusion is compared**

**Precis of Thesis Development**

- Quantitative methodology was considered appropriate as TACO (the study end-point) has objective and measurable features
- The underpinning philosophy of the quantitative methodology was considered to be the positivist/post-positivist paradigm, realist ontology, and modified objectivist epistemology
- A prospective cohort cross-over study design was chosen as this requires fewer participants who could act as their own control as there was no 'wash-out' period for blood transfusion. A randomised controlled trial would have reduced random error but required many more participants. The decision was pragmatic and based upon the balance of sample availability/convenience versus potential for bias
- The study can be described as a binary outcome non-inferiority study i.e. TACO or no TACO, and accelerated transfusion is no worse than standard rate transfusion for the development of TACO
- The actual incidence of TACO is debated in the literature and is important for determining sample size and power. The data used was based upon UK haemovigilance data and UK Blood Stocks Management data due to the limitations of individual research studies and of local incidence data
- Patients were excluded from the study based upon risk-factors and comorbidities that predispose circulatory overload. Patients with

baseline examination features or vital sign measurements that would confound features of TACO were also excluded

- Patients weighing <67Kg received volume-selected red cell units to ensure the rate of transfusion did not exceed 5ml/Kg/hr when receiving two units of red cells over 60 minutes each
- Patients had a pre-transfusion clinical check performed to demonstrate continued study eligibility and to ensure there were no features that would pre-dispose or complicate the identification of TACO
- Patients had a post-transfusion clinical check performed to identify the observable/measurable features of TACO (study end-point) that were based upon SHOT/ISBT haemovigilance surveillance diagnosis criteria for TACO
- The data were analysed by calculating the odds ratio (OR) and relative risk (RR) to demonstrate differences between the paired observations for the incidence of TACO in standard and accelerated rate transfusion. Although the Chi squared test is also used for this purpose, it is not mathematically suitable when cell counts are small and values likely to be zero
- Multiple comparisons of vital sign observations were designed to demonstrate differences in physiological response when comparing standard and accelerated rate transfusion using paired t-tests
- The results for this strand of the study are presented in the next chapter

# Chapter Seven:
# Strand 1 Results
# Physiological/Safety Enquiry

**Summary of Patient Characteristics**

Twenty-eight research participants were recruited to the study, but three of these did not contribute data because either their transfusion requirements ceased or they died before a transfusion could take place. Although the majority of eligible patients accepted the invitation to participate in the study, the overall available number in this patient group within the time-frame of the study was inherently small, and fell short of the 39 participants determined by the sample size calculation. It has been argued that reliance on sample size can constrain innovative research (Bacchetti *et al*, 2011), and therefore results based on the sample size obtained in this study still make a useful contribution to knowledge.

The issues presented previously regarding sample size determination are discussed in the concluding chapter. Table 7.1 below summarises the physical characteristics of the research participants.

**Table 7.1: Summary of patient characteristics**

| Patients Characteristics | |
|---|---|
| **Gender** | Male: n=18, Female n=7 |
| **Age (years) at first transfusion in study** | Range: 45 to 83 years<br>(mean = 68.1 years) |
| **Body Weight (Kg) at time of consent** | Range: 59.0Kg to 98.0Kg<br>(mean = 78.1Kg) |
| **Diagnoses** | Myelodysplastic syndrome (n=12)<br>Primary myelofibrosis (n=3)<br>Chronic lymphocytic leukaemia (n=5)<br>Haemolytic anaemia (n=1)<br>Acute myeloid leukaemia (n=3)<br>Acute lymphoblastic leukaemia (n=1) |

## Summary of Transfusion Episodes

Table 7.2 below summarises the duration of transfusions performed in the study. The standard rate transfusion was two red cell units over 90 minutes each +/- 10% (162 to 198 minutes), and accelerated rate transfusion was two red cell units over 60 minutes each +/- 10% (108 to 132 minutes). Accelerated transfusions that were planned but not achieved due to excessive infusion time are also recorded.

**Table 7.2: Summary of transfusion episodes**

| **Transfusion Type** | **Number** | | |
|---|---|---|---|
| **Standard rate transfusions completed** | **25** | | |
| **Transfusion Type** | **Number** | **Duration Range (min)** | **Duration Mean (min)** |
| **Accelerated rate transfusions completed** | **269** | **97 to 132 minutes** | **122.8 min** |
| **Transfusion Type** | **Number (Range)** | | **Number (median)** |
| **Accelerated rate transfusions per patient** | **1-39** | | **9** |
| **Accelerated rate transfusions not achieved** | **39/308 (12.7%)** | **Infusion-related: tissued cannula, positional problems, infusion pump programming, interruptions of flow (n=31)<br>Patient-related: not performed because of the patient's condition or patient declined because post-transfusion follow-up was not convenient (n=8)** | |

## Summary of Transfusion Outcomes

Transfusion outcomes are summarised in figure 7.1 below.

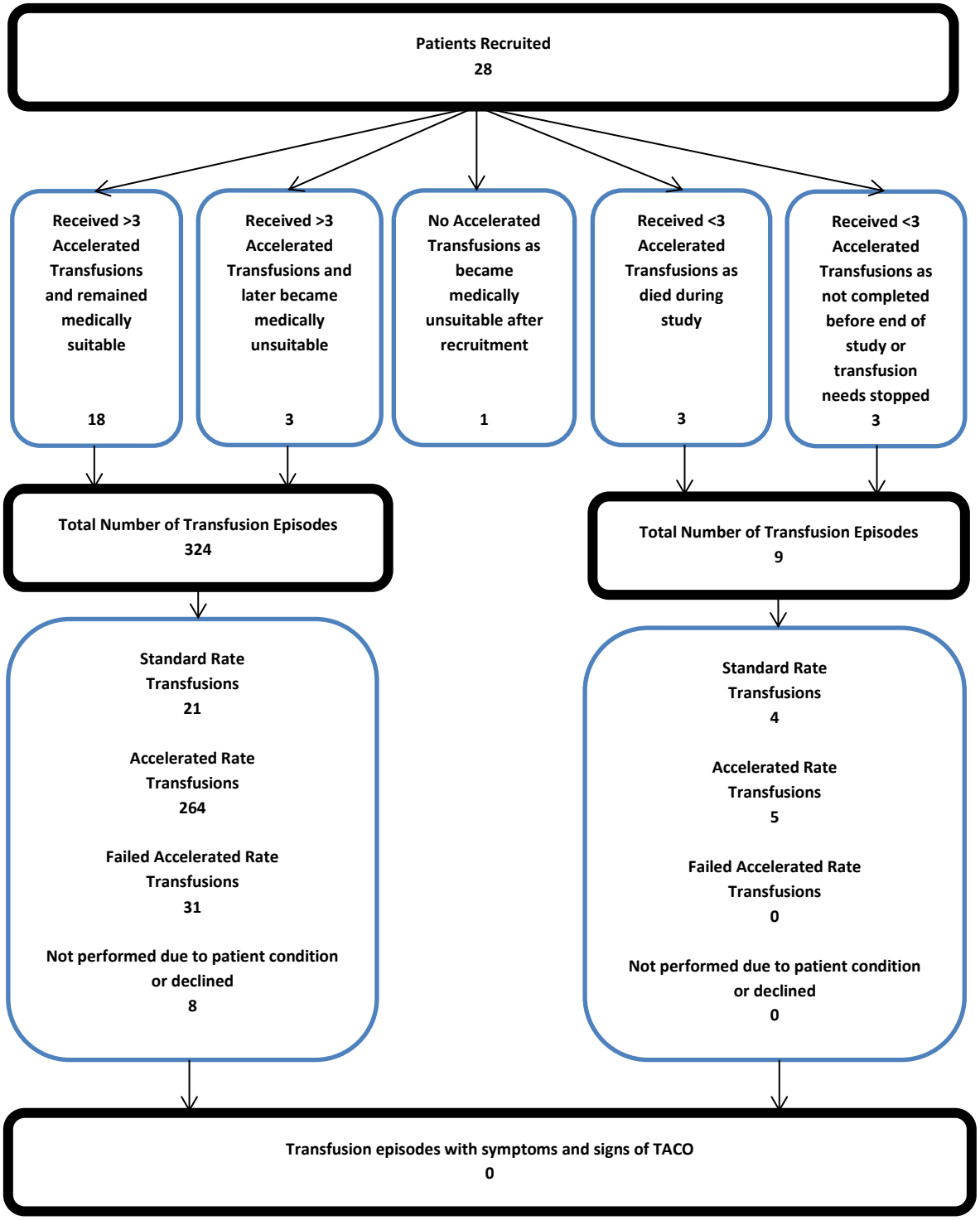



**Figure 7.1: Summary of Transfusion Outcomes**

The transfusion outcomes were analysed by computing the Relative Risk (RR) and Odds Ratio (OR). The RR is the number of times more or less likely TACO will occur in the accelerated transfusion group compared to the standard transfusion (control) group. It is the ratio of absolute risk (AR) for each group, where AR is the probability that and individual will experience TACO over a specified period of time.

**Interpretation of Relative Risk (RR)**

RR = <1.0: less risk of TACO with accelerated transfusion compared to standard rate transfusion

RR = 1.0: identical risk of TACO when comparing accelerated and standard rate transfusion

RR = >1.0: greater risk of TACO with accelerated transfusion compared to standard rate transfusion

The OR is the odds of TACO occurring in the accelerated transfusion group expressed as a proportion of the odds of TACO occurring in the standard transfusion group. When an event is rare (as with TACO) the OR is analogous to the RR.

**Interpretation of Odds Ratio (OR)**

OR = <1.0: less chance of TACO with accelerated transfusion compared to standard rate transfusion

OR = 1.0: identical chance of TACO when comparing accelerated and standard rate transfusion

OR = >1.0: greater chance of TACO with accelerated transfusion compared to standard rate transfusion

The confidence interval (CI) quantifies random error and is an estimate of the range of where the 'real' value lies. If the CI crosses 1.0 then the RR or OR is not significant or informative, as 'no difference' (i.e. 1.0) is contained within the range. The p value informs whether the difference between the two groups is statistically significant which is taken as <0.05 (5%) by convention. As this study seeks to 'prove' the null hypothesis, this can be defined as x% chance of observing a difference as large as observed even if the two populations are identical (the null hypothesis is true).

Table 7.3 below shows the statistical analysis of outcome by patient[a] and demonstrates there is no difference between standard and accelerated rate transfusion for the development of symptoms and signs of TACO (RR = 1.0, OR = 1.0, p =1.0000). Although the confidence intervals (CI) cross 1.0, indicating there is no difference between both groups in the study, the CI are wide meaning the true RR and OR could indicate increased or decreased risk of TACO by accelerated transfusion. However logically decreased risk is not a feasible outcome.

Analysing the outcome data by transfusion episodes[b] reduced the RR and OR to <1.0 which indicates a reduced risk of TACO in the accelerated transfusion group, which again is not logically feasible. It also has the effect of narrowing the CI but this still crosses 1.0 indicating that the RR and OR analyses are not informative.

This type of analysis is difficult to reliably interpret with a small sample size and for rare events when the desired and expected positive/bad outcomes (TACO) for both interventions are expected to be zero.

**Table 7.3: Summary of relative risk (RR) and odds ratio (OR) by patients and transfusion episodes**

| Group | Outcome by Patient[a] | | Outcome by Episodes[b] | |
|---|---|---|---|---|
| **Exposed group: Accelerated transfusion** | **Positive/bad outcome (TACO)** 0 patients | **Negative/good outcome (no TACO)** 25 patients | **Positive/bad outcome (TACO)** 0 transfusion episodes | **Negative/good outcome (no TACO)** 269 transfusion episodes |
| **Control group: Standard transfusion** | **Positive/bad outcome (TACO)** 0 patients | **Negative/good outcome (no TACO)** 25 patients | **Positive/bad outcome (TACO)** 0 transfusion episodes | **Negative/good outcome (no TACO)** 25 transfusion episodes |
| **Relative Risk (RR)** | 1.0000 | | 0.0963 | |
| **95% CI** | 0.0206 to 48.5272 | | 0.0020 to 4.7539 | |
| **z statistic** | 0.000 | | 1.176 | |
| **Significance level** | p = 1.0000 | | P = 0.2394 | |
| **Odds Ratio (OR)** | 1.0000 | | 0.0946 | |
| **95 % CI** | 0.0191 to 52.2205 | | 0.0018 to 4.8700 | |
| **z statistic** | 0.000 | | 1.173 | |
| **Significance level** | p = 1.0000 | | p = 0.2409 | |

This is an inherently difficult study to design with the objective of confidently demonstrating non-inferiority for accelerated rate transfusion due to the unknown true incidence of TACO in this population, and notwithstanding TACO is a relatively rare event. This is discussed further in the concluding chapter.

**Comparison of Pre and Post-Transfusion Vital Sign Observations for Standard Rate and Accelerated Rate Transfusion**

**a)** ***Is there a difference between pre and post transfusion vital sign observations in standard rate transfusions?***

**Table 7.4**: **Comparison of pre and post standard rate transfusion vital sign observations**

| N = 24 | Standard Rate Transfusion | | | | | |
|---|---|---|---|---|---|---|
| | Heart Rate | | Respiratory Rate | | Mean Arterial Pressure | |
| | **Pre** | **Post** | **Pre** | **Post** | **Pre** | **Post** |
| **mean** | 74.38 | 73.08 | 15.42 | 16.04 | 84.63 | 89.88 |
| **SD** | 13.16 | 12.56 | 1.53 | 1.99 | 12.93 | 10.50 |
| **p** | | 0.2407 | | 0.1091 | | 0.0441 |
| **CI** | | -0.93 to 3.51 | | -1.40 to 0.15 | | -10.35 to -0.15 |

There is no statistically significant difference between pre and post - transfusion vital sign observations for heart rate and respiratory rate, but statistical significance is reached for mean arterial pressure due to a small increase in the mean for the group. The increase is well below the pathological range (reference range = 70-110 mmHg) which may be observed in circulatory overload, and therefore may reflect the physiological effects of treated anaemia.

**b)** ***Is there a difference between the pre and post transfusion vital sign observations in accelerated transfusion, and is it consistent across subsequent accelerated transfusions?***

**Table 7.5: Comparison of pre and post accelerated rate transfusion 1 vital sign observations**

| n = 24 | Accelerated Rate Transfusion 1 | | | | | |
|---|---|---|---|---|---|---|
| | Heart Rate | | Respiratory Rate | | Mean Arterial Pressure | |
| | Pre | Post | Pre | Post | Pre | Post |
| mean | 74.25 | 70.83 | 15.38 | 15.38 | 85.63 | 93.00 |
| SD | 11.91 | 12.94 | 1.95 | 2.24 | 12.50 | 12.61 |
| p | | 0.1116 | | 1.0000 | | 0.0036 |
| CI | | -0.86 to 7.69 | | -0.62 to 0.62 | | -12.08 to -2.67 |

**Table 7.6: Comparison of pre and post accelerated rate transfusion 2 vital sign observations**

| n = 20 | Accelerated Rate Transfusion 2 | | | | | |
|---|---|---|---|---|---|---|
| | Heart Rate | | Respiratory Rate | | Mean Arterial Pressure | |
| | Pre | Post | Pre | Post | Pre | Post |
| mean | 73.85 | 71.15 | 15.3 | 15.00 | 82.65 | 90.90 |
| SD | 10.92 | 11.72 | 1.53 | 1.59 | 7.73 | 11.44 |
| p | | 0.0096 | | 0.3793 | | 0.0051 |
| CI | | 0.74 to 4.66 | | -0.40 to 1.00 | | -13.71 to -2.79 |

**Table 7.7: Comparison of pre and post accelerated rate transfusion 3 vital sign observations**

| n = 16 | Accelerated Rate Transfusion 3 | | | | | |
|---|---|---|---|---|---|---|
| | Heart Rate | | Respiratory Rate | | Mean Arterial Pressure | |
| | Pre | Post | Pre | Post | Pre | Post |
| mean | 66.63 | 67.75 | 15.56 | 15.06 | 82.56 | 89.00 |
| SD | 10.02 | 10.39 | 1.26 | 2.08 | 10.68 | 10.17 |
| p | | 0.5996 | | 0.2281 | | 0.0187 |
| CI | | -5.60 to 3.35 | | -0.35 to 1.35 | | -11.64 to -1.23 |

In common with the standard rate transfusion, all three consecutive accelerated transfusions show a consistent statistically significant increase in mean arterial pressure. The possible reasons for this are the same as

described in section (a) above. The second accelerated transfusion also shows a statistically significant decrease in heart rate, but this is not a consistent finding. It does not fall into the pathological range and is a directional change opposite to that expected for circulatory overload.

**c)** ***Is there a difference between the variance between pre and post transfusion vital sign observation values (pre value - post value) when standard and accelerated transfusions are compared?***

**Table 7.8: Comparison of variance between standard and accelerated rate transfusion 1 vital sign observations**

| n = 24 | Heart Rate Variance (pre transfusion – post transfusion value) | | Respiratory Rate Variance (pre transfusion – post transfusion value) | | Mean Arterial Pressure Variance (pre transfusion – post transfusion value) | |
|---|---|---|---|---|---|---|
| | **Std Rate** | **Acc Rate 1** | **Std Rate** | **Acc Rate 1** | **Std Rate** | **Acc Rate 1** |
| **mean** | -0.17 | -3.50 | 0.63 | 0.04 | 5.25 | 8.13 |
| **SD** | 6.03 | 10.06 | 1.84 | 1.52 | 12.08 | 11.3 |
| **p** | | 0.1743 | | 0.1834 | | 0.2449 |
| **CI** | | -1.59 to 8.25 | | -0.30 to 1.46 | | -7.86 to 2.11 |

**Table 7.9: Comparison of variance between standard and accelerated rate transfusion 2 vital sign observations**

| n = 20 | Heart Rate Variance (pre transfusion – post transfusion value) | | Respiratory Rate Variance (pre transfusion – post transfusion value) | | Mean Arterial Pressure Variance (pre transfusion – post transfusion value) | |
|---|---|---|---|---|---|---|
| | **Std Rate** | **Acc Rate 2** | **Std Rate** | **Acc Rate 2** | **Std Rate** | **Acc Rate2** |
| **mean** | 0.45 | -2.90 | 0.65 | -0.30 | 5.05 | 8.25 |
| **SD** | 6.08 | 3.78 | 1.76 | 1.49 | 10.75 | 11.66 |
| **p** | | 0.0827 | | 0.0218 | | 0.3557 |
| **CI** | | -0.48 to 7.18 | | 0.15 to 1.75 | | -10.27 to 3.87 |

**Table 7.10: Comparison of variance between standard and accelerated rate transfusion 3 vital sign observations**

| n = 16 | Heart Rate Variance (pre transfusion – post transfusion value) | | Respiratory Rate Variance (pre transfusion – post transfusion value) | | Mean Arterial Pressure Variance (pre transfusion – post transfusion value) | |
|---|---|---|---|---|---|---|
| | **Std Rate** | **Acc Rate 3** | **Std Rate** | **Acc Rate 3** | **Std Rate** | **Acc Rate 3** |
| **mean** | 1.56 | 1.13 | 0.56 | -0.56 | 4.75 | 5.81 |
| **SD** | 5.77 | 8.39 | 1.71 | 1.67 | 11.61 | 9.70 |
| **p** | | 0.8501 | | 0.0668 | | 0.8189 |
| **CI** | | -4.41 to 5.29 | | -0.09 to 2.34 | | -10.78 to 8.66 |

There are no statistically significant differences in the variance of pre and post-transfusion vital sign observations between standard rate and accelerated rate transfusions 1 and 3. The second accelerated transfusion also shows a statistically significant decrease in respiratory rate, but this is not a consistent finding. It does not fall into the pathological range and is a directional change opposite to that expected for circulatory overload.

**d)** ***Is there a difference between pre and post transfusion vital sign observation actual values when standard and accelerated rate transfusion is compared?***

**Table 7.11: Comparison of standard and accelerated rate pre-transfusion 1 vital sign observations**

| n = 24 | Pre-Transfusion Heart Rate | | Pre Transfusion Respiratory Rate | | Pre-Transfusion Mean Arterial Pressure | |
|---|---|---|---|---|---|---|
| | **Std Rate** | **Acc Rate 1** | **Std Rate** | **Acc Rate 1** | **Std Rate** | **Acc Rate 1** |
| **mean** | 74.38 | 74.25 | 15.42 | 15.38 | 84.63 | 85.63 |
| **SD** | 13.16 | 11.91 | 1.53 | 1.95 | 12.93 | 12.50 |
| **p** | | 0.9569 | | 0.9388 | | 0.6255 |
| **CI** | | -4.61 to 4.86 | | -1.07 to 1.15 | | -5.18 to 3.18 |

**Table 7.12: Comparison of standard and accelerated rate pre-transfusion 2 vital sign observations**

| n = 20 | Pre-Transfusion Heart Rate | | Pre Transfusion Respiratory Rate | | Pre-Transfusion Mean Arterial Pressure | |
|---|---|---|---|---|---|---|
| | Std Rate | Acc Rate 2 | Std Rate | Acc Rate 2 | Std Rate | Acc Rate 2 |
| **mean** | 74.60 | 73.85 | 15.15 | 15.30 | 84.90 | 82.65 |
| **SD** | 13.71 | 10.92 | 1.27 | 1.53 | 12.99 | 7.73 |
| **p** | | 0.7384 | | 0.7481 | | 0.4916 |
| **CI** | | -3.88 to 5.38 | | -1.11 to 0.81 | | -4.47 to 8.97 |

**Table 7.13: Comparison of standard and accelerated rate pre-transfusion 3 vital sign observations**

| n = 16 | Pre-Transfusion Heart Rate | | Pre Transfusion Respiratory Rate | | Pre-Transfusion Mean Arterial Pressure | |
|---|---|---|---|---|---|---|
| | Std Rate | Acc Rate 3 | Std Rate | Acc Rate 3 | Std Rate | Acc Rate 3 |
| **mean** | 72.50 | 66.63 | 15.06 | 15.56 | 84.19 | 82.56 |
| **SD** | 11.82 | 10.02 | 1.18 | 1.26 | 11.35 | 10.68 |
| **p** | | 0.0036 | | 0.1777 | | 0.6553 |
| **CI** | | 2.25 to 9.50 | | -1.25 to 0.25 | | -5.98 to 9.23 |

**Table 7.14: Comparison of standard and accelerated rate post-transfusion 1 vital sign observations**

| n = 24 | Post-Transfusion Heart Rate | | Post-Transfusion Respiratory Rate | | Post-Transfusion Mean Arterial Pressure | |
|---|---|---|---|---|---|---|
| | Std Rate | Acc Rate 1 | Std Rate | Acc Rate 1 | Std Rate | Acc Rate 1 |
| **mean** | 73.08 | 70.83 | 16.04 | 15.38 | 89.88 | 93.00 |
| **SD** | 12.56 | 12.94 | 1.99 | 2.24 | 10.50 | 12.61 |
| **p** | | 0.3398 | | 0.2815 | | 0.104 |
| **CI** | | -2.52 to 7.02 | | -0.56 to 1.90 | | -6.94 to 0.69 |

**Table 7.15: Comparison of standard and accelerated rate post-transfusion 2 vital sign observations**

| n = 20 | Post-Transfusion Heart Rate | | Post-Transfusion Respiratory Rate | | Post-Transfusion Mean Arterial Pressure | |
|---|---|---|---|---|---|---|
| | Std Rate | Acc Rate 2 | Std Rate | Acc Rate 2 | Std Rate | Acc Rate 2 |
| mean | 73.40 | 71.15 | 15.80 | 15.0 | 89.95 | 90.90 |
| SD | 13.49 | 11.72 | 2.02 | 1.59 | 11.37 | 11.34 |
| p | | 0.2963 | | 0.1189 | | 0.5896 |
| CI | | -1.89 to 6.39 | | -0.23 to 1.83 | | -4.57 to 2.67 |

**Table 7.16: Comparison of standard and accelerated rate post-transfusion 3 vital sign observations**

| n = 16 | Post-Transfusion Heart Rate | | Post-Transfusion Respiratory Rate | | Post-Transfusion Mean Arterial Pressure | |
|---|---|---|---|---|---|---|
| | Std Rate | Acc Rate 3 | Std Rate | Acc Rate 3 | Std Rate | Acc Rate 3 |
| mean | 72.00 | 67.75 | 15.63 | 15.06 | 88.94 | 89.00 |
| SD | 12.44 | 10.39 | 2.06 | 2.08 | 9.47 | 10.17 |
| p | | 0.0143 | | 0.3925 | | 0.9839 |
| CI | | 0.98 to 7.52 | | -0.80 to 1.92 | | -6.54 to 6.42 |

There was no statistically significant difference between pre and post transfusion vital sign observation actual values when standard and accelerated rate transfusions 1 and 2 are compared. The third accelerated transfusion also showed a statistically significant decrease in heart rate, but this was not a consistent finding. It does not fall into the pathological range and is a directional change opposite to that expected for circulatory overload. In conclusion, the mean arterial pressure appears to increase up to 24 hours after blood transfusion regardless of whether it was infused at a standard or accelerated rate, with the group mean remaining within the normal range. There is no statistically significant difference between pre and post-

transfusion mean arterial pressure measurements when standard and accelerated rate transfusions are compared, showing that accelerated transfusion itself does not cause an increase in mean arterial pressure above that of standard rate transfusion.

**Precis of New Knowledge**

- Accelerated transfusion (total infusion time for two units is 120 min +/- 10% (108 to 132 minutes) was not always achieved. Accelerated transfusion was not achieved in 12.7% of episodes (39/308). This was due to flow interruptions and infusion pump programming issues in 79.5% (31/39), and the patient declining accelerated rate transfusion in 20.5% (8/39) because they were unwilling to have a follow-up check the following day as part of the study
- Twenty-five patients had standard rate transfusions with a total of 269 accelerated rate transfusions completed in total. There were no cases of TACO detected
- The OR and RR show no statistical difference between standard and accelerated rate ***transfusion by patient***, however there is a wide confidence interval indicating the true risk of TACO from accelerated transfusion could be increased or decreased
- Analysis by ***transfusion episodes*** shows no difference between standard and accelerated rate transfusion and produces a narrower confidence interval

- Choice of statistical method and subsequent analysis and interpretation was frustrated by small available sample size and rare events where the positive outcome (TACO) is expected to be zero for both interventions.
- There was a statistically significant difference between pre and post-transfusion mean arterial pressure (MAP) in standard rate transfusion. The increase was not within the pathological range and may reflect the physiological effect of treated anaemia
- There was a statistically significant difference between pre and post-transfusion mean arterial pressure in accelerated rate transfusion which was consistent across all three accelerated rate transfusions
- There was no consistent difference in variance of pre and post-transfusion vital sign observations when standard and accelerated rate transfusion were compared
- MAP appeared to increase within 24 hours of transfusion regardless of whether the transfusion was infused at a standard or accelerated rate, with the group mean remaining within the normal range
- There was no statistically significant difference between pre and post-transfusion MAP when standard and accelerated transfusion are compared, demonstrating that accelerated transfusion itself does not increase MAP above that of standard rate transfusion

# Chapter Eight:
# Strand 2 Methods
# Service Capacity Enquiry

This chapter discusses the method used for the service capacity strand of the study which is designed to address whether implementation of accelerated transfusion could potentially increase service capacity.

**General Research Question**

Whether transfusing two units of red cells over 60 minutes per unit (accelerated transfusion) is safe and could potentially increase CIVT service capacity, while gaining understanding of the patient's and practitioner's experience.

**Hypothesis**

$H_1$: Implementation of accelerated transfusion could potentially increase CIVT service capacity ($H_0$ Implementation of accelerated transfusion would not potentially increase CIVT service capacity)

**Method Aim**

The selected method aims to demonstrate whether introducing accelerated red cell transfusion for selected patients receiving transfusions at home could have a positive impact upon CIVT service capacity.

## Method Design: Rationale and Philosophical Foundations

A quantitative methodological approach was used to analyse capacity and costs associated with the provision of the CIVT home transfusion service. An analytical method based on workload audit was considered the most appropriate approach to test the hypotheses and research question regarding this aspect of the study. A quantitative methodology is appropriate for the objective evaluation of measurable parameters and this underpins the philosophical basis of this approach. The underpinning philosophy for this approach is described in chapter six regarding the physiological and safety enquiry and is therefore not duplicated in this chapter.

A comparison was made between the current service model (where all transfusions are standard rate), and the developed/future state service model (where a proportion of transfusions are accelerated rate). Data on transfusions performed were collected from the CIVT workload records. Table 8.1 describes the comparison parameters of each service model.

### Table 8.1: Comparators for Resource Analysis

| **Current Service Model** (All Standard Rate Transfusions) | **Future Service Mode** (Proportion Accelerated Rate Transfusions) |
|---|---|
| **Ratio of Standard Rate: Accelerated Rate** (=1.0) | **Ratio of Standard Rate: Accelerated Rate** (=1.?) |
| **Cost of standard rate transfusion** (£ staff pay/annum) | **Cost of accelerated rate transfusion** (£ staff pay/annum) |
| **Time delivering standard rate transfusions** (hours/annum) | **Time delivering accelerated rate transfusions** (hours/annum) |

The rationale for this approach and choice of comparator was to generate data that demonstrates: (i) **costs** associated with each service model (staff pay is the only parameter required for analysis as all other direct and indirect costs remain the same); and (ii) **treatment delivery time** generates data regarding impact upon service capacity. The role of the cost comparator was to demonstrate the relative differences of each service model as opposed to generate an accurate cost. The role of the treatment delivery time comparator was to provide an indicative increase in available treatment time and how this may be used as additional treatment sessions. This provides a practical illustration of how any increase in service capacity may be utilised as well as placing a financial value on it.

**Data Collection Method**

Workload Audit Data Set

Workload data were obtained from the CIVT administrator for each month of the study (July 2014 to November 2016) which detailed the home (red cell) transfusion workload of the team. This was recorded in a Microsoft Exel ™ spreadsheet and data added with respect to the data set shown below in preparation for later analysis.

- Month and year of transfusion
- Patient identifier
- Haematology patient or medical patient (only haematology patients were included in the study)
- Whether the patient was recruited in the study
- Reason for exclusion if the study inclusion criteria were not met

- Assessment of suitability for accelerated transfusion if not participating in the study

Staffing Data

To ensure standardisation, the calculation of staffing costs was based on the mid-point salary scale for a nurse at band 6 which is £30,357 per year, or £15.57 per hour in 2016 based on a 37.5 hour week without shift enhancements. This was the prevailing pay scale at the time of the data collection period (July 2014 to November 2016). This was to avoid bias caused by vacancies and staff incrementing up the pay scale during the duration of the study, and the effect of additional payments for unsocial hours as there were no data available to determine the number of transfusion performed during these shift periods.

**Data Analysis Method**

The data were based on the comparators defined in table 8.1 above. The ratio of standard to accelerated rate transfusions was obtained from the study data, which was dependent upon the final number of eligible patients. The time spent on administering each type of transfusion was calculated using knowledge of the actual time taken to deliver a standard rate transfusion (an average of four hours per visit, as confirmed by the CIVT service manager and nursing staff). An accelerated rate transfusion was determined as the standard rate (time) minus 60 minutes (i.e. 30 minutes x 2 units of red cells). Therefore the average visit time is three hours for an

accelerated rate transfusion. The results were expressed as per annum values and were used to demonstrate any differences in staff resource utilisation. The calculations used to compare resource utilisation for each service model are shown below.

**Current Service Model –**

**All standard rate transfusion**

- Predicted number of home transfusion episodes per year (based on audit data) multiplied by 4 hours (treatment delivery time for standard rate transfusion)

  = **number of hours delivering standard rate home transfusions per year**

- Number of hours per year x £15.57 (standardised hourly rate)

  = **staff costs of delivering standard rate transfusion per year**

**Potential Future Service Model –**

**Proportion of transfusions are at accelerated rate**

- Predicted number of home transfusion episodes per year (based on audit data) multiplied by proportion of accelerated rate transfusions (based on audit data)

  = **number of predicted accelerated rate transfusions per year**

- Predicted number of home transfusion episodes per year (based on audit data) minus number of predicted accelerated rate transfusions per year

  = **number of standard rate transfusions per year**

- Number of predicted accelerated rate transfusion per year multiplied by 3 hours (treatment delivery time for accelerated rate transfusion)

  = **number of hours delivering accelerated rate home transfusions per year**

- Number of hours per year x £15.57 (standardised hourly rate)

  = **staff costs of delivering accelerated rate transfusion per year**

- Number of predicted standard rate transfusion per year multiplied by 4 hours (treatment delivery time for standard rate transfusion)

  = **number of hours delivering standard rate home transfusions per year**

- Number of hours per year x £15.57 (standardised hourly rate)

  = **staff costs of delivering standard rate transfusion per year**

- Treatment delivery time of current service model minus treatment delivery time of potential future service model

  = **number of nursing hours released per year by implementing accelerated transfusion**

- Number of nursing hours released per year by implementing accelerated transfusion divided by 3 or 4

  = **potential number of additional 3 or 4 hour visits available if accelerated transfusion is implemented**

- Number of hours released per year multiplied by £15.57

  = **value of released nursing hours**

These calculations are fully documented in the following results chapter using actual data.

## Precis of Thesis Development

- A quantitative methodological approach based upon audit was considered appropriate to objectively evaluate the effect of accelerated transfusion on CIVT service capacity
- The method was designed to illustrate how any increase in service capacity could be utilised in terms of clinical hours generated and placing a financial value on it with respect to staff resource costs
- A workload audit data set was developed, and staffing data was based upon standardised salary and hours
- The current service model (all standard rate transfusions) was compared to the potential service model (where a proportion was accelerated rate transfusions depending on patient eligibility). The ratio was informed by the audit data and used to determine treatment delivery time and staff costs for each model
- The results for this strand of the study are presented in the next chapter

# Chapter Nine:
# Strand 2 Results
# Service Capacity Enquiry

### Analysis of Patient Eligibility for Accelerated Transfusion

Twenty nine months of home transfusion workload data were analysed (July 2014 to November 2016). Seventy one individual patients (46 haematology patients and 25 medical patients) received home transfusions during that period. Their eligibility for accelerated transfusion in haematology patients is shown below in figure 9.1.

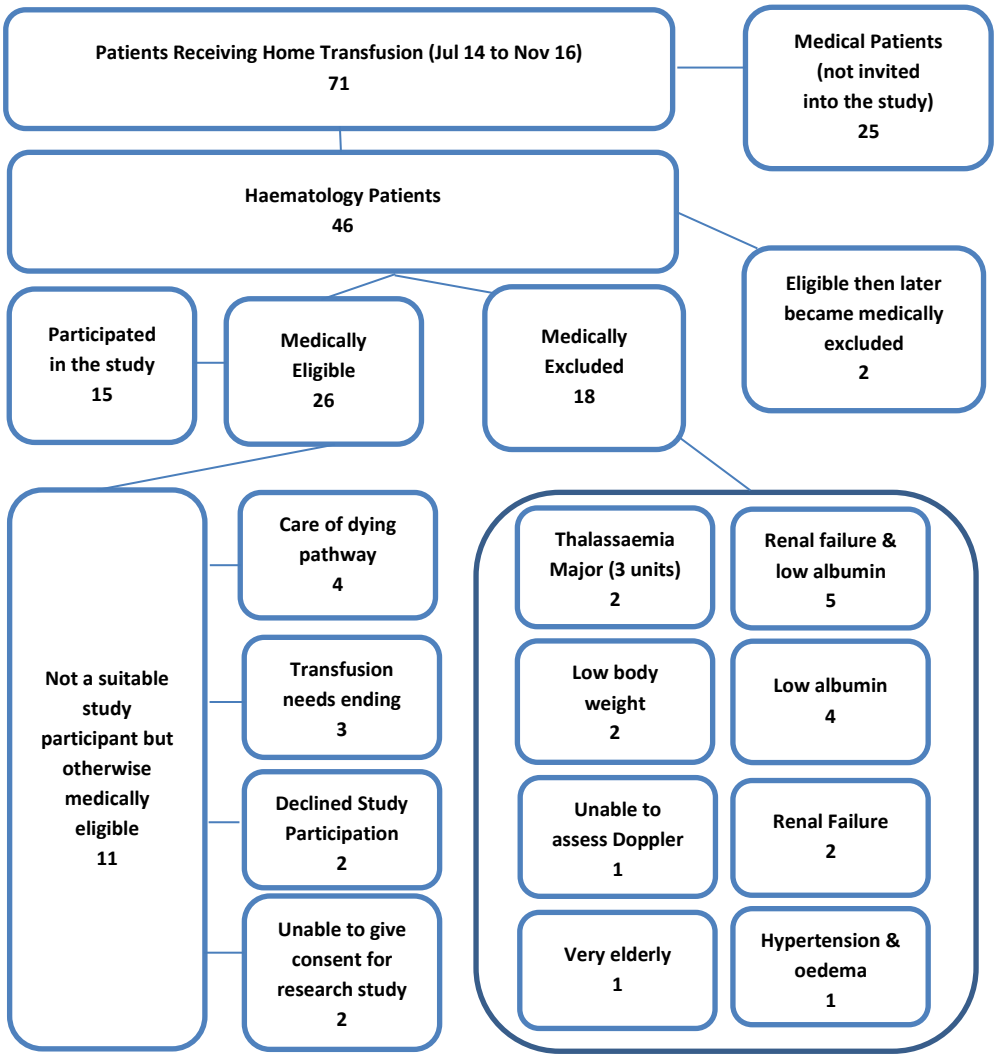



**Figure 9.1: Patient Eligibility for Accelerated Transfusion**

The analysis above shows that 26/46 (57%) of haematology patients fulfilled the medical inclusion criteria for accelerated transfusion. Medical patients receiving home transfusion did not participate in the study but their medical eligibility for accelerated transfusion is theoretically similar, but their requirement for regular transfusion is less intensive.

## Analysis of Accelerated Transfusion Episodes

Twenty nine months of home transfusion workload data were analysed (July 2014 to November 2016). Five hundred and seventeen home red cell transfusions were performed during that period (459 haematology patients and 58 medical patients). Eligibility for accelerated transfusion in haematology patients is shown below in figure 9.2.

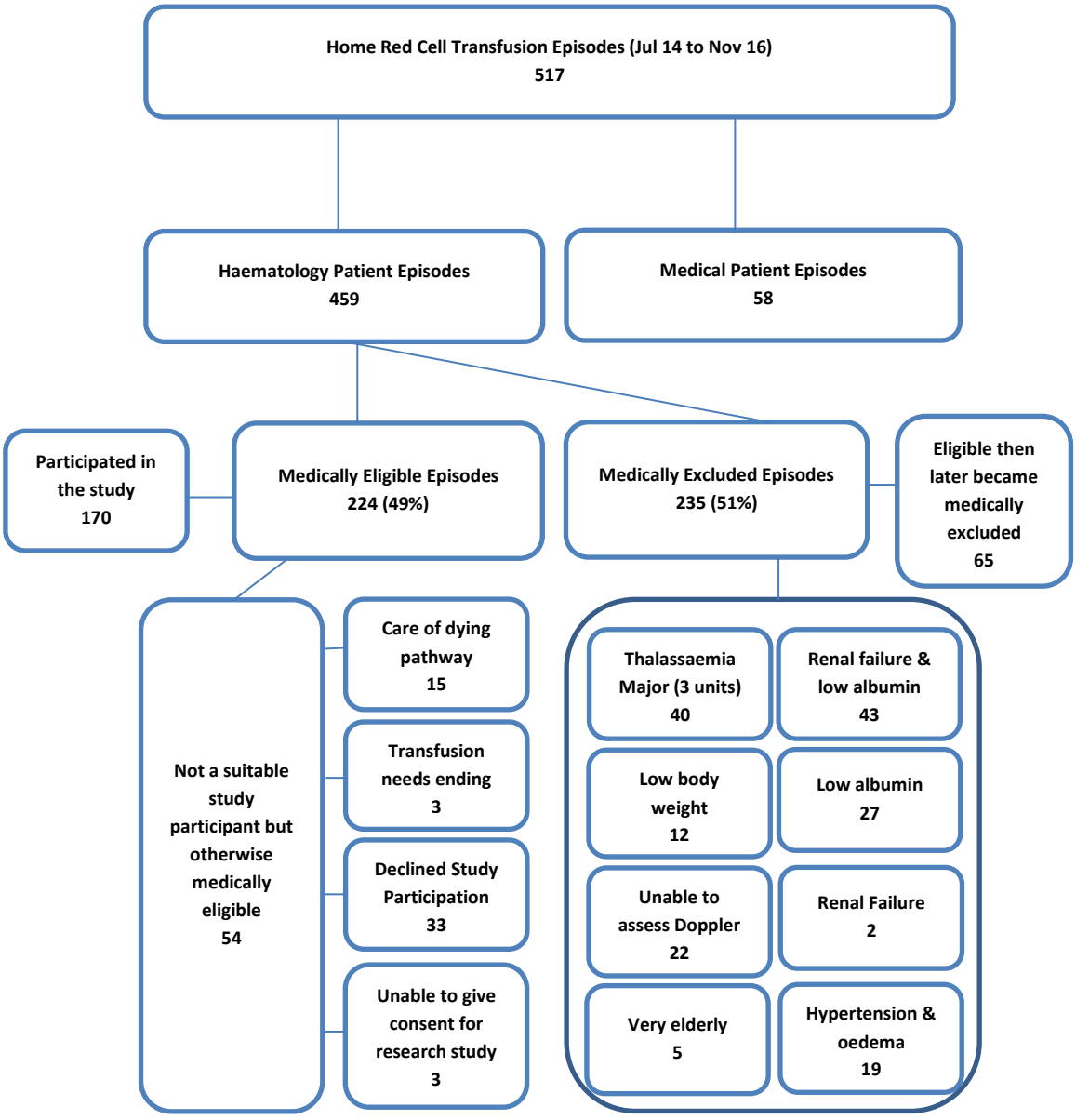



**Figure 9.2: Accelerated Transfusion Episodes**

The analysis above shows that 224/459 (49%) of haematology patient transfusion episodes fulfilled the medical inclusion criteria for accelerated transfusion. Medical patients receiving home transfusion did not participate in the study however their medical eligibility for accelerated transfusion is theoretically similar to haematology patients, but requirement for regular transfusion is less intensive.

## Analysis of the Impact of Accelerated Transfusion on CIVT Service Capacity

### Assumptions

- 215 red cell transfusion episodes are performed per year based upon the workload data (July 2014 to November 2016)
- A standard rate transfusion episode requires a 4 hour home visit
- An accelerated rate transfusion episode requires a 3 hour home visit
- The pay-related cost of a home visit is nominally £15.57 per hour (salary mid-point for a band 6 nurse is £30,357 in 2016 based on a 37.5 hour week without unsocial shift allowance)

### Current Service Model

All transfusions are standard rate

215 episodes per year x 4 hour visits = 860 nursing hours per year

860 x £15.57 = £13,390

### Proposed Future Service Model

A proportion of transfusions (49%) are accelerated rate, based upon the data analysis.

215 x 0.49 = 105 transfusions can be potentially performed as accelerated rate transfusions

105 episodes per year x 3 hour visits = 315 hours (£4,905)

110 episodes per year x 4 hour visits = 440 hours (£6,850)

Totalling 755 nursing hours per year at a cost of (£11,755)

The implementation of accelerated red cell transfusion could potentially save 105 nursing hours per year (£1,635). This is equivalent to 35 extra three hour visits or 26 extra four hour visits, for example.

**Precis of New Knowledge**

- 57% (26/46) of haematology ***patients*** fulfilled the medical inclusion criteria and were therefore eligible for accelerated transfusion
- 49% (224/459) of home ***transfusion episodes*** were eligible to be performed as accelerated rate transfusions.
- If accelerated transfusion was implemented for both haematology and medical patients, service capacity could be increased by 105 nursing hours that could be utilised for additional patient visits whether for transfusion or other IV therapies

# Chapter Ten:

# Strand 3 Methods

# Patient and Practitioner Experience Enquiry

This chapter discusses the method used for the patient and practitioner experience strand of the study which is intended to add value to the overall study by exploring and gaining understanding of experience of accelerated transfusion.

**General Research Question**

Whether transfusing two units of red cells over 60 minutes per unit (accelerated transfusion) is safe and could potentially improve CIVT service capacity, while gaining understanding of the patient's and practitioner's experience.

**Method Aim**

The selected method aims to generate understanding of the experience of administering and receiving accelerated and standard rate transfusions, to address this aspect of the research question. The creation of understanding has implications for the acceptability and desirability of service development and change if accelerated transfusion is implemented into routine practice.

## Method Design: Rationale and Philosophical Foundations

The patients and practitioners who use and deliver the service often develop close relationships with each other which are intensified by the context of the home environment, and often in the presence of life-limiting conditions. Proposed changes to their services must be approached with sensitivity, respecting the tenets of patient-centeredness, the value of understanding personal experience and the benefits of co-design to achieve improved experience of care. A generic qualitative approach was considered appropriate for generating understanding of the patient's and practitioner's experience of accelerated transfusion by exploring their thoughts and feelings. This approach is based upon the use of experience as knowledge, as explained by the individual. Cresswell states that talking directly with people without *a priori* assumptions allows exploration and detailed understanding (Cresswell, 2007). The subjective and individualistic nature of experience requires a philosophical approach based upon the *constructivist* paradigm, where *relativist* ontology acknowledges the person-dependent plurality of 'reality'. If the reality of experience is a mental construction, then epistemologically the *subjectivist* must interact subjectively with the individual to unlock those constructions to ultimately generate knowledge (Guba, 1990). Patient and practitioner research participants were invited to be interviewed (not exceeding 60 minutes as per ethical approval) about their experience of standard rate and accelerated transfusion. The interviews took place in the naturalistic setting of the patient's home where the transfusion took place (or practitioner's workplace) providing a holistic and contextual

setting. This allowed for an inductive/descriptive approach to answer the research question. The semi-structured interview was favoured as a structured interview may constrain dialogue. Structured, pre-determined questions could also make the interview more vulnerable to researcher bias through “asking the wrong questions” as a result of the interviewer’s assumptions or preconceptions (Charmaz, 2001: p.681). Other aspects of researcher bias cannot be completely eliminated but can be controlled through reflexive awareness. This should be balanced with the positive nature of reflexivity which has the potential to enrich the data. This is discussed further below in the context of rigour.

**Rigour in Method Choice and Data Analysis**

Guidelines have been produced in an attempt to provide a quality framework for qualitative researchers (Spencer *et al*., 2003). Whilst acknowledging the existence and influence of government endorsed guidance, the development of a positivistic procedural framework for conducting qualitative research is an epistemological contradiction. A prescriptive approach may not be appropriate to the diverse nature of qualitative research methods as this may in itself begin to define the design of the research (Mays & Pope, 2006), or become a “technical procedure” (Barbour, 2001, p. 1115).

Reliable and valid research is seated in the practical choices, ethical conduct and self-awareness of the researcher. Trustworthiness (rigour) was described by Guba and Lincoln (1985) as having four criteria: credibility (truth value); dependability (neutrality); confirmability (consistency) and transferability (applicability). Applying Guba and Lincoln’s criteria to the

research provides a useful framework to evaluate rigour of the methods and the findings they produce. Ultimately, the reliability and validity of the research is attested by transparently demonstrating appropriate design, systematic data collection, assiduous data analysis, and skilful knowledge translation guided, but not bounded, by Guba and Lincoln's criteria.

**Confirmability** can be assured by observing the National Institute for Health Research principles of Good Clinical Practice (GCP) for research governance which covers both quantitative and qualitative research methods. The Chief Investigator is GCP trained and also experienced in quality management. This ensures high standards in maintaining a robust audit trail of all paper and electronic records generated throughout the data collection and analysis phases of the research process. This also provides a clear description of the rationale and analytical steps of the research-path, providing an auditable record of decision-making steps.

The researcher's station within the research and their potential to influence it is also important to address. This is especially relevant when conducting interviews with research participants where there is an existing relationship or some level of shared experience. Whilst reflexivity has been shown to enrich knowledge from interviews (Finch, 1993), it is also a potential source of bias and criticism regarding reliability and must be carefully managed. Finch's paper is an interesting perspective on reflexive issues encountered in qualitative research. She has been influenced by Ann Oakley's (1981) paper that argues that a researcher cannot subtract one's own values, beliefs and opinions from the research process (i.e. in her case as a feminist). Whether

this is considered bias or enrichment is not easily defined and may be spared scrutiny depending on how it is framed and applied as a research tool. There is an assumption that bias and preconception are undesirable, but it can be argued this is seated in how the notion of 'bias' is constructed. It could be debated that objectivity is regarded as the 'gold standard' in the pursuit of rigorous research and in the absence of objectivity sits subjectivity, and therefore, bias. But, subjectivity lends interpretation, perspective and ideology as part of the human condition, which can both enrich and jeopardise the rigour of qualitative research, and this is moderated by the researcher's reflexive awareness. Objectivity may be incompatible with qualitative research depending on philosophical standpoint, but this is not to say that because qualitative research may be subjective, that ergo it is inherently biased. Malterud (2001) also argued a difference between 'preconception' and 'bias', believing them to be different unless undeclared. Reflexive transparency positions the researcher with a unique perspective where rich and deep understanding may be achieved, as opposed to compromising reliability. Awareness and acknowledgement of subjectivity can therefore enhance the credibility of the research by confining bias, but if uncontrolled risks its detrimental effects on the rigour of research, as diagrammatically presented in figure 10.1. Reflexive transparency can therefore be viewed as a 'check and balance' for reliability. This alternative view may foster deeper understanding between interviewer and interviewee, as well as of the data itself, and bringing confidence to the rigour of the study.

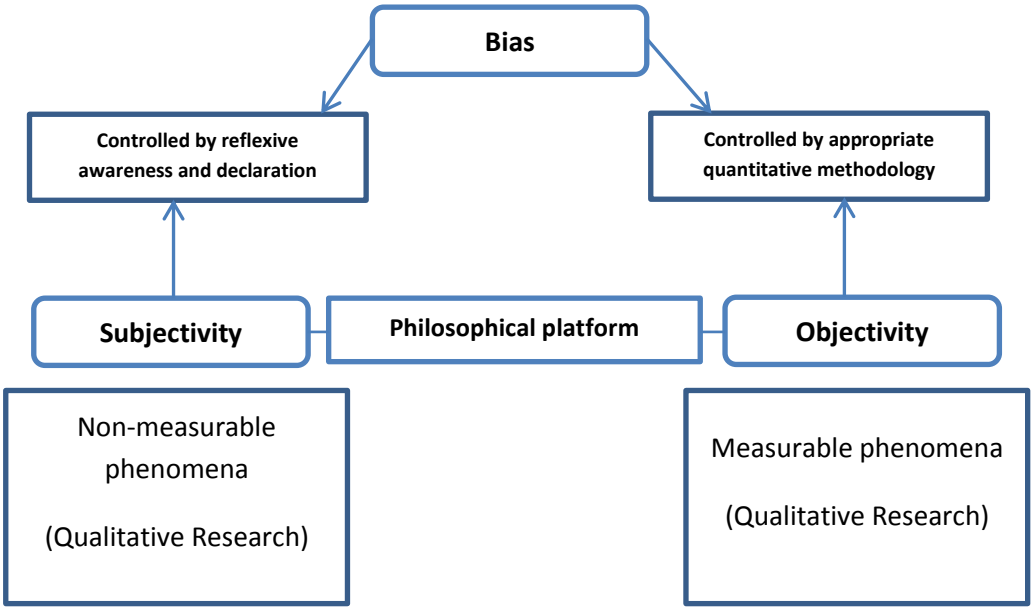



**Figure 10.1: Control of bias: relationship with objectivity and subjectivity**

Table 10.1 below summarises the researcher's declaration of reflexive observations and preconceptions of the research participants. This served as a point of reflexive reference and calibration for conducting the interviews and data analysis, by serving to maintain self-awareness.

**Table 10.1: The Researcher's declaration of reflexive observations and pre-conceptions of research participants.**

| Researcher's Reflexive Observations |
|---|
| The interviewer is closely involved with the delivery and infrastructure of the blood transfusion aspects of the CIVT service. This has benefit of deep understanding of the service but could positively or negatively affect interpretation of what is being said by participants. |
| The interviewer has a desire for the service to succeed and flourish for the benefit of patient care, and job satisfaction of staff and is therefore motivated for a positive outcome which must be moderated to avoid bias. |
| The interviewer has a variable relationship history with the patient. There may have been several previous clinical contacts. The interviewer has professional relationships and regular contact with the CIVT. This may affect the interview dynamic positively or negatively depending upon how it is managed. |
| Insider knowledge tempered with outsider distance may be a good balance to draw the sort of detail that may not be possible if the interviewer was completely neutral (and perhaps with no expertise or experience in blood transfusion). |
| The interviewer's 'insider role' may change the relationship between interviewer and interviewee. This relationship may be seen as a potential source of bi-lateral bias in the interview process, but may also enrich the process (see 'credibility' below). |
| The interviewer is not a professional interviewer: interviewer's perceived negative impact on data quality but this is balanced with the interviewer's professional experience of asking questions and active listening in the medical consultation setting. |
| Knowledge of the Chief Investigator analysing the interviews, and as a small team (even when formally anonymised) the CIVT practitioner's comments would be unlikely to be completely disguised, remaining open to potential for perceived judgement by the researcher with whom they have a working relationship. |
| **Researcher's Pre-Conceptions of Research Participants** |
| All CIVT practitioners are bound to have a more positive experience of accelerated transfusion compared to standard rate. |
| Some patients may prefer the standard rate transfusions experience as they enjoy the social contact but may feel inhibited in articulating this as they feel compelled to endorse accelerated rate transfusions. |
| CIVT practitioners may feel inhibited in articulating any criticisms of the experience of accelerated transfusion directly to the researcher. |

Confidence in **Credibility** may be fostered by the concept of 'prolonged engagement'. Although this perhaps traditionally has more relevance in ethnographic and field research, it also has utility in the context of this study. The Chief Investigator had many years of insight into the service before engaging in the research. The degree of relationship with both patients and practitioner participants could be described as a *peripheral member,* assuming a marginal role*,* using membership typology suggested by Adler and Adler (1987).This provided orientation in the area of research through developing relationships and sharing experiences to achieve shared understanding and co-construction of meaning, at a distance that also allows impartiality. Personal insight not only allows accurate representation of the narrative, but allows reflexive awareness of pre-conceptions and subsequent distortions in the data that may need accounting for in the data analysis. From a participant perspective, relative distance from the researcher may also moderate inhibitions in expressing negative feelings and experiences of accelerated transfusion.

The *aim* of data saturation was to increase the likelihood of obtaining comprehensive themes across the range of participants interviewed. Data saturation was [in this study] defined by failure to identify further codes/themes at the point at which the final data are analysed (based upon Guest *et al*, 2006). The emergence of strong themes provides confidence in the 'truth' of the findings, however this does not detract from the value of lesser occurring themes as significance is not based upon measurement or prevalence (Braun and Clarke 2006).

Identification of contradictory themes was also useful to disclose to demonstrate credibility and unbiased analysis. This can lead to the revision, broadening and confirming of emergent themes from the analysis, and was adopted in the approach to the thematic analysis (Patton, 1999).

**Dependability** may be assured by 'external audit'. Although formal external audit was not part of the method for data collection and analysis, the research was conducted under the supervision of an experienced researcher in qualitative methodology whose role was to provide feedback on drafts of the work relating to the participant interviews and thematic analysis. The effect of interviewer experience on data quality has been studied more frequently in structured or survey interviewing, Fowler and Mangione (1990) being among the first to report the positive effect of interviewer training on data quality. There is less in the literature regarding the effect of the interviewer on semi- or un-structured interviewing, however Fowler (2004) believes that the most difficult skills to acquire in semi-structured interviewing are careful construction of questions and nondirective probing, and that training in this area is profitable when pursuing good data quality. The interviewer had the benefit of professional experience of asking questions and active listening in the medical consultation setting. In agreement with Fowler's guidance, an interview schedule was developed with general open questions and suggestions for probes and prompts (appendix J). It was piloted and modified prior to the actual interviews taking place.

**Transferability** may be achieved by thick description. By describing detail, conclusions may be drawn regarding transferability of the research to other

contexts and scenarios (Lincoln and Guba, 1985). The purpose of the research was to generate experiential understanding to inform practice change in a specific area (home transfusion) and therefore the data were generated from this specific population without the primary intention of producing generalizable evidence. However patients receiving home transfusion also occasionally attend the oncology day unit for blood transfusion and therefore have experience of both settings. Accelerated transfusion could theoretically be offered in the future to patients receiving transfusion as a hospital day-case.

**Sample Size and Sampling Strategy**

The sample size of a qualitative method cannot be pre-determined. Hunter and Brewer (2006) assert that sample characteristics are more important than sample size in qualitative research as the aim is not statistical representativeness, but representativeness of participant experience relating to the research question. Breadth of knowledge is traded for depth, bringing richer data from fewer participants. For this reason purposive non-probability sampling was used, the participants were selected in a non-random fashion based upon their transfusion history. Patients who had been receiving long-term blood transfusion had more experience of standard rate transfusions compared to new patients who may have only received one standard rate transfusion before being recruited into the study. For this reason, the participants who had a longer transfusion history were favoured for interview. This approach may be vulnerable to criticisms of bias if not stated, but returning to Charmaz's point about "asking the wrong question" (Charmaz,

2001: p. 681), it can be argued that careful matching of research participant experience to the research question by asking the correct question in the correct way will avoid the creation of 'false knowledge' and ensure that only relevant knowledge is created. Difficulties with issues of bias also arise from the epistemological dichotomy of 'sample number' in qualitative research. A polarity exists between the positivistic view of numbers in probability sampling, and the constructivist view of richness in non-probability sampling. The aim was data saturation to ensure transferability of emergent themes from which participant numbers could not be predicted *a priori*. Ten participants were judged a reasonable nominal figure for this study in terms of stating participant numbers for the purposes of ethical approval. The final number of participants was also influenced by the availability of participants from inherently small groups, and the point at which data saturation was reached. This decision accords with Wibberley and Price (2012) who also performed a thematic analysis on ten, purposively selected participants for an exploratory-type study. Ultimately, data saturation was aspirational but acknowledged as potentially unachievable on a practical level.

The sample number strategy for this aspect of the study contrasts with the quantitative strand where consecutive non-probability sampling was used. This was to ensure as many eligible patients as possible were recruited from the relatively small eligible population available to meet the calculated sample number. Sufficient quantity of participants was therefore more important to the quantitative aspect of the study than to the qualitative strand

of the study where participant characteristics, as opposed to number, were of greater importance.

**Interview Recruitment Process:**

Patient Invitation, Information and Response

Patients who met the selection criteria for the study received a letter of invitation and a patient participant information sheet (PIS) (appendix D and E). The PIS stated that some patients may be asked to participate in an interview. Patients agreed to being potentially invited for an interview in their study participation consent form however it was made clear they did not have to participate in an interview if they only wished to participate in the accelerated transfusions. Patients who were later selected for interview were contacted by telephone or invited in person at their outpatient clinic visit. Patients were given an opportunity to consider the invitation for interview and reminded that they could decline if they did not wish to participate in this aspect of the study.

Practitioner Invitation, Information and Response

All members of CIVT nursing team were considered for invitation to participate in the interview regarding their personal experience of accelerated transfusion, providing they had administered both standard rate and accelerated transfusions. A letter of invitation to participate was sent to their workplace address (appendix K). The letter was accompanied by an information sheet (appendix L). The practitioner was offered an opportunity

to discuss the study further with the chief investigator if required. A response form and envelope was provided but a telephone response or email was also accepted. The returned consent/response forms were retained securely by the Chief Investigator in the research site file.

**Pre-Interview Preparation and Consent: Patient and Practitioner**

If the patient or practitioner responded indicating that they wished to participate in an interview, contact was made by telephone or in person to arrange a mutually convenient date for the interview to take place. The venue for the interview was the patient's home (for patient interviews), or the practitioner's workplace (for practitioner's interviews). Steps were taken to ensure no inconvenience was incurred to the participant.

Both patients and practitioners agreeing to participate in the interview gave valid consent prior to the interview taking place. The statement on the consent form was read to the patient/practitioner by the person taking consent to ensure understanding (appendix M). The patient/practitioner then signed and dated the consent form. The form was securely retained in the research site file by the Chief Investigator.

**Interview Procedure: Patient and Practitioner**

The interview took place only after the consent statement had been signed. The interview was a semi-structured following the schedule (Appendix J) and the duration, not to exceed 60 minutes. The interview was digitally recorded and saved as an audio file for the purpose of transcribing the narrative

verbatim by a professional transcribing service (www.fingertipstyping.co.uk). The transcripts were quality-checked by comparing the audio file content with the transcript document and auditable amendments made where required.

**Method Choice and Pre-Analytical Considerations**

Thematic analysis (TA) was chosen as a method to understand the patient and practitioner's experience of standard rate and accelerated transfusion. The creation of understanding has implications for the acceptability and desirability of service development and change if accelerated transfusion is implemented into routine practice.

TA is used to identify, analyse and report patterns (themes) in data and may go on to interpret the data. Boyatzis (1998) regarded TA as principal method within the wider field of qualitative analysis, whereas Braun and Clarke (2006) argued only lack of clarity and guidelines prevented it being considered a distinct method. TA was chosen as a method to analyse the data principally because of its flexibility and suitability for early qualitative researchers. Unlike most qualitative methods, TA is not bound by a single theoretical framework and can be applied across a range of approaches to provide detailed and complex insight into the data. The underpinning philosophy described earlier in this chapter places the study approach within the constructivist paradigm. Braun and Clarke (2006) suggest TA may also be considered essentialist, realist or contextualist. This represents another area for researcher reflexivity as it may influence analytical decision-making when seeking to reflect the 'reality' of the research participant's experience. Themes do not 'emerge' from the data, rather they emerge from the

consciousness of the researcher analysing and reporting the data as an active process (Taylor and Ussher, 2001). Therefore the theoretical framework is based upon the researcher's perspective and this must be made clear. Braun and Clarke (2006) argue that TA requires a number of choices, including that must be made explicit, and their account provides a useful framework and is explored in more detail in the following sections.

*Defining a theme*

A theme represents something important in the research question that can be identified as pattern in the data set. It is not bound by prevalence or the concept of 'measurement' in order to assign significance. Semantics used in some studies such as '*many participants*' may indicate prevalence, but actually seek to persuade a case to justify the theme. This contrasts with content analysis which could have been considered as an alternative method for TA in this study, however this is a more deductive and quantitative approach and does not align with the underpinning philosophy embodied within the qualitative methodological approach discussed earlier. In this study, the 'something important' in the research question is the understanding of experience and therefore the initial coding of transcripts focused on participant accounts of feeling or meaning when talking about their experience of accelerated transfusion.

*Rich description versus detailed/limited account*

The study seeks to provide a rich and detailed thematic description of the whole data sets for both patient and practitioner interviews to ensure the

entire dataset for each group are accurately represented. Experience of blood transfusion is an under-researched area where *a priori* assumptions should not be made and therefore the research question is limited to gaining understanding only. A limited account may have been appropriate if there had been a specific research question based upon the finding of previous research studies, such as *should patients have a choice over the infusion rate of their blood transfusion?*

*Inductive versus theoretical TA*

As the analysis is not driven by a specific research question or theory, an inductive approach is appropriate. Themes are linked to the data themselves rather than constraining coding with a pre-developed coding framework based upon a priori assumptions or theories. An inductive approach maximises diversity especially in the absence of prior research in this area.

*Semantic and latent themes*

The level to which the data are analysed is an important consideration. Semantic level analysis is constrained by what is explicitly said, whereas latent analysis adds a further dimension which yields additional information about underlying meaning of what has been said. Latent analysis was expected to yield richer data of patient and practitioner experience in terms of unlocking the sentiment of the patient or practitioner's described experience. The interpretive aspect of this accords with the constructivist paradigm and produces a report that goes beyond basic description. The

data in this study were not deliberately pre-analytically restricted to sematic-level analysis. Latent analysis was also allowed to be considered.

*Returning to epistemology*

Braun and Clarke (2006) argue that TA can be performed in both essesntialist/realist and constructivist paradigms, affecting perspective and outcome. This was discussed in the conceptualisation of the study and has been revisited here in the discussion on choice of analytical method. Although much of the discussion places the approach in the constructivist paradigm much of this debate is centred on the researcher's interpretation of constructivism and the extent to which semantic and latent themes play out in the data analysis. For example, if latent themes are not readily identified, the analysis is based upon language alone. This level of semantic analysis would reflect an essentialist/realist approach. If latent themes are identified, this would reflect a constructivist approach. Either approach determines how *meaning* is theorised. This was more conclusively demarcated after the analysis of the data, allowing epistemological freedom and a more flexible approach but acknowledging reflexive influence of this on the reporting phase.

**Thematic Analysis Procedure**

Braun and Clarke (2006) describe a six-step guide for TA which is intended to be used flexibly, and has procedural similarities to Framework Analysis described by Ritchie and Spencer (1994). While Ritchie and Spencer's method could arguably achieve this, they originally developed their method

for social policy research and had been regarded as better suited to addressing specific research questions or *a priori* theories (Srivastava and Thomson, 2009). As the research question in this study is open-ended and there are no a priori theories to address due to paucity of the literature in this area, an open and exploratory approach was required to gain understanding of the patient's and practitioner's experience of accelerated transfusion. In this setting Framework Analysis did not present itself as the most appropriate choice of analytical method.

The Braun and Clarke (2006) step-wise approach is summarised and adapted for application in this study as described below in table 10.2.

**Table 10.2: Six-step Thematic Analysis Procedure**

| Step | | Procedure |
|---|---|---|
| 1 | **Data Familiarisation** | Professional verbatim transcription of the audio file and quality check audio against transcript including punctuation |
| | | Repeated reading of transcripts |
| | | Consider semantic and latent themes and make notes |
| 2 | **Initial Codes** | Codes are identified as basic segments of data (semantic or latent) without losing context |
| | | Data-driven (as opposed to theory-driven) |
| 3 | **Search for Themes** | Focus on broader level of themes across the codes (combine codes into themes) |
| | | Identification of any sub-themes |
| | | Produce initial thematic map |
| 4 | **Review Themes** | Identification and refinement of candidate themes |
| | | Review at code-level: do all coded extracts in the theme appear coherent. If so, this forms a developed thematic map. If not, do the extracts need to be in a different theme or is the theme wrong? |
| | | Review at data set-level: are the themes valid in relation to the data set? Do they tell a story about the data? |
| 5 | **Define and Name Themes** | Each theme will require a detailed analysis which may be structured by any sub-themes identified |
| | | Each theme should itself tell a story, and a broader story of the whole data set |
| | | Test the theme by being able to describe the scope and content in a few sentences |
| | | Give each theme a concise and informative name and produce a final thematic map |
| 6 | **Report** | Write an analytic narrative using examples from the data to form an argument to address the research question: what is understood about the experience of accelerated transfusion |
| | | This should include interpretive questioning such as: What does the theme mean?, What are the assumptions?, What are the implications – for example on the acceptability/desirability of service model change?, What has caused this?, Why is this expressed/said in this way? |

The patient and practitioner experience enquiries were conducted as two separate thematic analyses on each dataset. This decision was based upon patients and practitioners having separate contexts and perspectives, and the range of potential experience across both types of research participant. A combined analysis of the whole data corpus would not allow separate understanding and may increase complexity of the analysis potentially compromising overall quality.

## Precis of Thesis Development

- A qualitative methodological approach was considered appropriate for generating understanding of patient and practitioner experience of accelerated transfusion and the implications for service change acceptability or desirability
- The method choice is philosophically underpinned by the constructivist paradigm, relativist ontology and subjectivist epistemology at the conceptual level. However, this was challenged when considering epistemology in the context of the analytical process, depending upon whether latent meaning could be identified when conducting the analysis. A definite epistemological standpoint was not committed to ahead of the analytical phase, but was established after coding because of its influence of the following stages of TA
- Lincoln and Guba (1985) criteria for 'trustworthiness' in qualitative research was used as a framework to evaluate rigour in method choice and data analysis
- Methods based upon subjectivist epistemology are not inherently biased because of diametrical opposition to objectivity. Subjectivity can enhance or jeopardise the rigour of qualitative research depending on the effectiveness of the researcher's reflexive awareness
- Semi-structured interviews were favoured over structured interviews as a more descriptive and inductive approach, with the intention of controlling *a priori* assumption, potential for researcher bias and enhancing data quality
- Thematic analysis was used as an inductive method that flexibly aligned with the underpinning philosophy of this stand of the study. It was expected to yield richer understanding on patient and practitioner experience of

accelerated transfusion compared to the more deductive and quantitative method of content analysis

- Pre-analysis considerations, and the six-step analytical procedure were based upon Braun and Clarke (2006)
- The results and finding for this strand of the study are presented in the next chapter

# Chapter Eleven:

# Strand 3 Results

# Patient and Practitioner Experience Enquiry

The aim of this chapter is to firstly introduce and describe the demographic characteristics of the research participants who agreed to be interviewed. The following sections are structured as described in table 10.2 in chapter ten following the six step process of Thematic Analysis (TA) (Braun and Clarke, 2006). The chapter will culminate in a synthesis of the data intended to inform and support the potential implementation of accelerated transfusion as a service development.

**Patient Characteristics**

Five patients agreed to be interviewed about their experience of receiving accelerated blood transfusion. All were male with either primary myelofibrosis (PMF) or myelodysplastic syndrome (MDS). The age range of the participants at the time of the interview was 62 to 78 years (mean 72.2 years, median 73 years). All were transfusion-dependent and on long-term transfusion therapy programmes with a significant history of receiving standard rate transfusion, requiring transfusion every 2 to 4 weeks on average. The number of month's experience of receiving standard rate transfusion prior to receiving accelerated rate transfusion as part of the study was 6 to 51 months (mean 25.2 months, median 27 months). All had

received transfusions primarily at home or occasionally on the hospital oncology unit.

### Practitioner Characteristics

Six practitioners agreed to be interviewed about their experience of delivering accelerated blood transfusion to patients in their homes. Five were experienced female community IV therapy nurses and had significant experience of delivering both standard rate red cell transfusion outside the study and accelerated rate red transfusion as part of the study. One was the service manager who had extensive experience of standard rate transfusion. She had not performed accelerated transfusion in clinical practice in this role, but had experienced the impact on service delivery.

### Step 1: Data Familiarisation

Interview audio files were professionally transcribed *verbatim* and transcripts were then quality checked for accuracy against the original audio file. Member checking was not performed as a commitment relating to the ethics application had been made to reduce burden on the research participants. Although this could theoretically compromise credibility, this is balanced with the benefits of professional transcription and the quality-checking of transcripts against the audio file by a professional who was familiar with the patient and the service. Amendments were made, including punctuation where this would affect intended meaning. Square brackets were added to clarify colloquialisms and preserve context. Audio files and transcripts were repeatedly listened to and read to increase familiarity and immersion in the

data. Informal notes were then made (appendix N), considering semantic and latent themes in order to gain a sense of direction and familiarity with the data in preparation for further analysis.

**Step 2: Initial Coding**

Dialogue concerning consent, preamble and generic closing comments were demarcated in the transcripts to identify these segments as not requiring coding. Using a data-driven, open coding approach the remaining data were coded by highlighting segments of the electronic transcript using the 'comment' feature in Microsoft Word™, taking precautions to ensure context was intact. Coding was guided by the relevant aspect of the research question: *understanding the experience of accelerated transfusion* i.e. what is being said to convey understanding of this experience?, to ensure the scope and focus of decision-making was appropriate. It has been suggested that the coder should ask themselves about "What is going on?, What are people doing?, What is the person saying?, What do these actions and statements take for granted?, How do structure and context serve to support, maintain, impede or change these actions and statements?" (Charmaz 2003: 94-95). Lofland *et al* (2006) suggested that codes should relate to acts, activities, meanings, participation, relationships and settings. Lending from different research traditions, their different approaches to coding were combined in this study to provide useful structure to focus decision-making when coding transcripts and assisting the coder to move from purely descriptive to more analytical codes. Each coded segment of data were then copied and compiled into a Microsoft Excel™ spreadsheet with each code

occupying a separate workbook within the spreadsheet so that text associated each code could be grouped and viewed separately. Table 11.1 below lists the initial codes identified in the patient dataset with a brief definition.

**Table 11.1: Initial codes for patient data**

| Code Name | Definition |
|---|---|
| Personal benefit | Benefits of accelerated transfusion to the patient on a personal level |
| No concerns | No concerns or worries about receiving accelerated transfusions |
| Feel same | Feeling the same after an accelerated transfusion compared to a standard rate transfusion |
| Future | Seeking clarification about the future of accelerated transfusion |
| Makes a difference | Accelerated transfusion has made a difference to the patient in some way |
| Compliance | Putting own wishes aside to help the service |
| Saving time | Identification of time save by accelerated transfusion |
| Restriction | Restrictions the service places upon the patient |
| Ambivalence | Would be happy to have either accelerated or standard rate transfusions |
| Care received | Relationships and interactions with nursing staff delivering blood transfusions |
| Mental discomfort | Mental difficulties experienced when receiving a blood transfusion |
| Active preference | Positive personal preference for either accelerated transfusion |
| Problems (organisational/clinical) | Experiences creating negative or positive feelings either due to organisational factors or clinical factors |
| Family responsibilities | The effect of receiving blood transfusions on responsibilities toward family members |
| Delays/waiting | Episodes of delay or waiting to receive a blood transfusion |
| Social issues | The effect of receiving blood transfusions on social issues |
| Lifestyle | The impact of accelerated transfusion on lifestyle factors |
| Resignation | Feelings of being resigned to problems and difficulties associated with receiving a blood transfusion |
| Lengthiness | The perception of blood transfusion taking too long |
| Convenience | Convenience of shorter blood transfusions |
| Altruism | A point of view about accelerated blood transfusion that identifies benefit for others (patients or service) |
| Physical comfort/Discomfort | Feelings of comfort or discomfort with standard and accelerated rate transfusions |
| Service benefit | Benefits of accelerated transfusion on a service level |
| Flexibility | Flexibility offered by shorter duration transfusions |

Table 11.2 below lists the initial codes identified in the practitioner dataset with a brief definition.

### Table 11.2: Initial codes for practitioner data

| Code Name | Definition |
|---|---|
| Patient benefit | Perceived benefit to the patient from accelerated transfusion |
| Mutual benefit | Accelerated transfusion has both benefit to the patient and the service |
| Service benefit | Accelerated transfusion benefits the CIVT service |
| Service capacity | Accelerated transfusion improves CIVT service capacity |
| Challenging practice | Lack of belief in historic/current practice for duration of transfusion |
| Service capacity pressure | Factors that increase demands for the CIVT service |
| Failing to meet demands | Unable to provide CIVT services as demand outstrips capacity |
| Efficient use of resources | Best use of existing resources (staff time) |
| Social/clinical need conflict | Tension between providing care based upon clinical need and social demands of the patients |
| Patient time impact | Factors that compromise the patient's use of their time |
| Patient preference | Perceived preference of accelerated transfusion by patients |
| Study benefits | Benefits to staff being involved in a research study |
| Flexibility/scheduling | Impact of accelerated transfusion on scheduling work and ability to provide flexibility to patients, or work flexibly |
| Saving time | Performing accelerated transfusion saves time |
| Intruding | Sense of the practitioner intruding in the patient's home or on their time |
| Working conditions | Impact of long home visits on satisfaction with working conditions |
| Clinical knowledge/skills | Application of the practitioner's knowledge and skills |
| Safety | Practitioners believing accelerated transfusion is safe based upon their experience |
| Support | Support practitioners have from the hospital clinical haematology team |
| Autonomy | Practitioner's feelings toward having clinical decision-making autonomy |
| Practitioner preference | Practitioner preference for accelerated transfusion |
| Guarded expectations | Practitioners having moderated expectations about the benefits of accelerated transfusion |
| Time-consuming | Time-consuming nature of the general blood transfusion procedure |
| Job satisfaction | Effect of accelerated transfusion on job satisfaction |
| Selflessness | Practitioners putting patient need first (sometimes above their own), having patient focus |
| Quality | Being able to still provide a quality service over a shorter visit time and heightened awareness of achieving timescales |
| Home transfusion preference | Patient preference for home transfusion (compared to hospital transfusion) |
| Hospital benefit | Perceived benefit to the hospital oncology unit by performing accelerated transfusion |
| Patient continuity | Impact of patient transfusion on allowing the same practitioner to re-visit the patient again the same day |

| | |
|---|---|
| Social impact | Impact of accelerated transfusion on wider social issues for the patient |
| Further investment | Benefit of further investment to maximise the benefits of accelerated transfusion |

### Step 3: Search for Themes

Table 11.3 below summarises the identification of themes from the initial codes in the **patient dataset**

## Table 11.3: Identification of themes in patient dataset

| Code | Sub-Theme 1 | Sub-Theme 2 | Main Theme |
|---|---|---|---|
| Care received | Good standard of care | | General experience of blood transfusion |
| Lengthiness | Frustrations | | |
| Restriction | | | |
| Delays/waiting | | | |
| Resignation | | | |
| Problems (organisational/clinical) | | | |
| Restriction | | | |
| Mental discomfort | Discomfort | | |
| Physical comfort/Discomfort | | | |
| | Makes a physical difference | Personal Benefits | Benefits of accelerated transfusion |
| Convenience | Makes a difference to lifestyle | | |
| Flexibility | | | |
| Social issues | | | |
| Family responsibilities | | | |
| Saving time | | | |
| Service benefits | Service benefits | | |
| Feel same | Reassurance | | Accelerated transfusion in future practice |
| No concerns | | | |
| Active preference | Preference | | |
| Ambivalence | | | |
| Altruism | Thinking of others | | |
| Compliance | | | |
| Future | Future | | |
| **Notes on organisation of themes** | | | |
| Personal benefit | Became sub-theme 2 | | |
| Makes a difference | Became sub-theme 1 and combined with Lifestyle | | |
| Lifestyle | Became sub-theme 1 and combined with Makes a Difference | | |

Table 11.4 below summarises the identification of themes from the initial codes in the **practitioner dataset**.

### Table 11.4: Identification of themes in practitioner dataset

| Code Name | Sub-Theme 1 | Sub-Theme 2 | Main Theme |
|---|---|---|---|
| Guarded expectations | Guarded expectations | | Going forward |
| Safety | Safety | | |
| Further investment | Further investment | | |
| Practitioner preference | Practitioner preference | | Going forward/practitioner benefits |
| Study benefits | Study benefits | | Practitioner benefits |
| Working conditions | Working conditions | | |
| Autonomy | Delivery of role | | |
| Clinical knowledge/skills | Delivery of role | | |
| Support | Delivery of role | | |
| Job satisfaction | Delivery of role | | |
| Challenging practice | Challenging practice | | Problems with current service |
| Failing to meet demands | Capacity | | |
| Service capacity pressure | Capacity | | |
| Time-consuming | Time | | |
| Patient time impact | Time | | Problems with current service/perceived patient benefit |
| Home transfusion preference | Home transfusion preference | | Perceived patient benefit |
| Social impact | Social impact | | |
| Patient benefit | Patient benefit | | |
| Patient preference | Patient preference | | Feelings about patients/perceived patient benefits/ going forward |
| Selflessness | Selflessness | | Feelings about patients |
| Intruding | Intruding | | |
| Social/clinical need conflict | Social/clinical need conflict | | Feelings about patients/shared interests |
| Patient continuity | Patient continuity | | Shared interests |
| Saving time | Saving time | | Shared interests/ service benefits |
| Quality | Quality | | |
| Hospital benefit | Hospital benefit | | |

| | | |
|---|---|---|
| Service capacity | Service capacity | Service benefits |
| Efficient use of resources | Efficient use of resources | |
| Flexibility/scheduling | Flexibility/scheduling | Service benefits/shared interests |
| **Notes on organisation of themes** | | |
| Patient benefit | Became main theme Perceived Patient Benefit | |
| Mutual benefit | Became main theme Shared Interests | |
| Service benefit | Became main theme Service Benefits | |

The themes and inter-dependencies shown in table 11.3 identified from the **patient dataset** illustrated as a hand-drawn initial thematic map shown in figure 11.1 below.

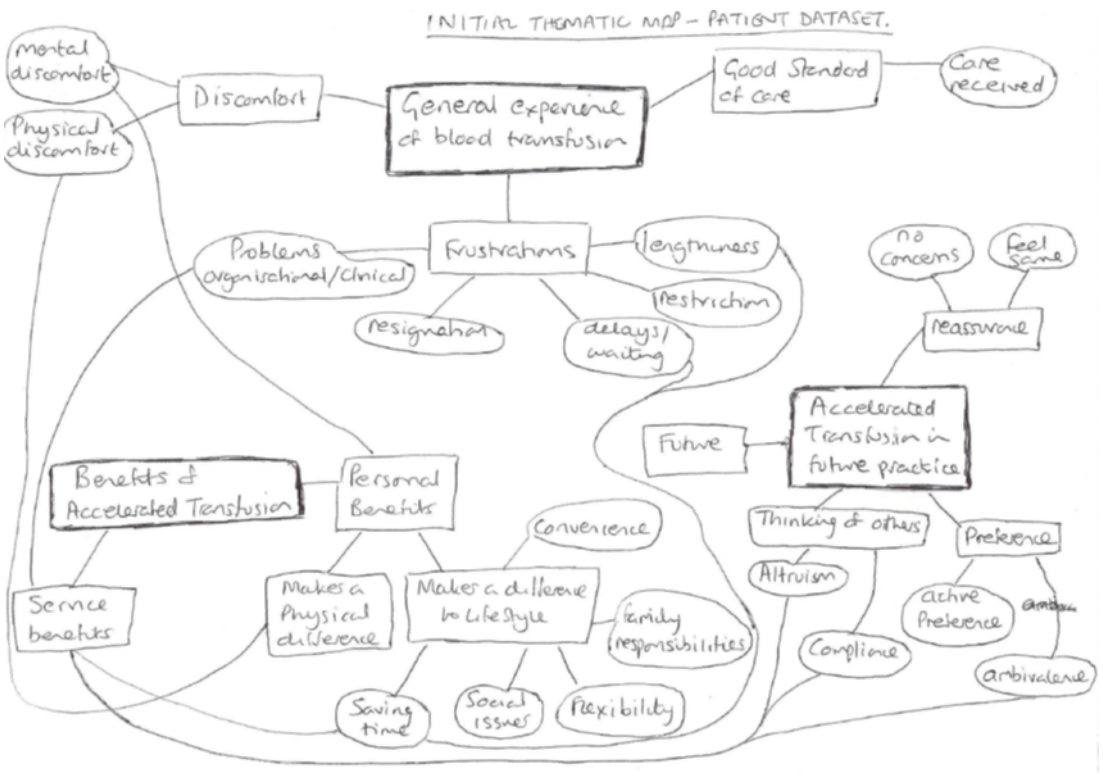



**Figure 11.1: Initial thematic map for patient dataset**

Steps 2 and 3 required an iterative process where codes and themes were tested and re-worked. At the end of this process no new codes or themes were identified when analysing the final patient and practitioner transcripts.

This suggested data saturation had been reached for each dataset as defined earlier.

The themes and inter-dependencies shown in table 11.4 identified from the **practitioner dataset** illustrated as a hand-drawn initial thematic map shown in figure 11.2 below.

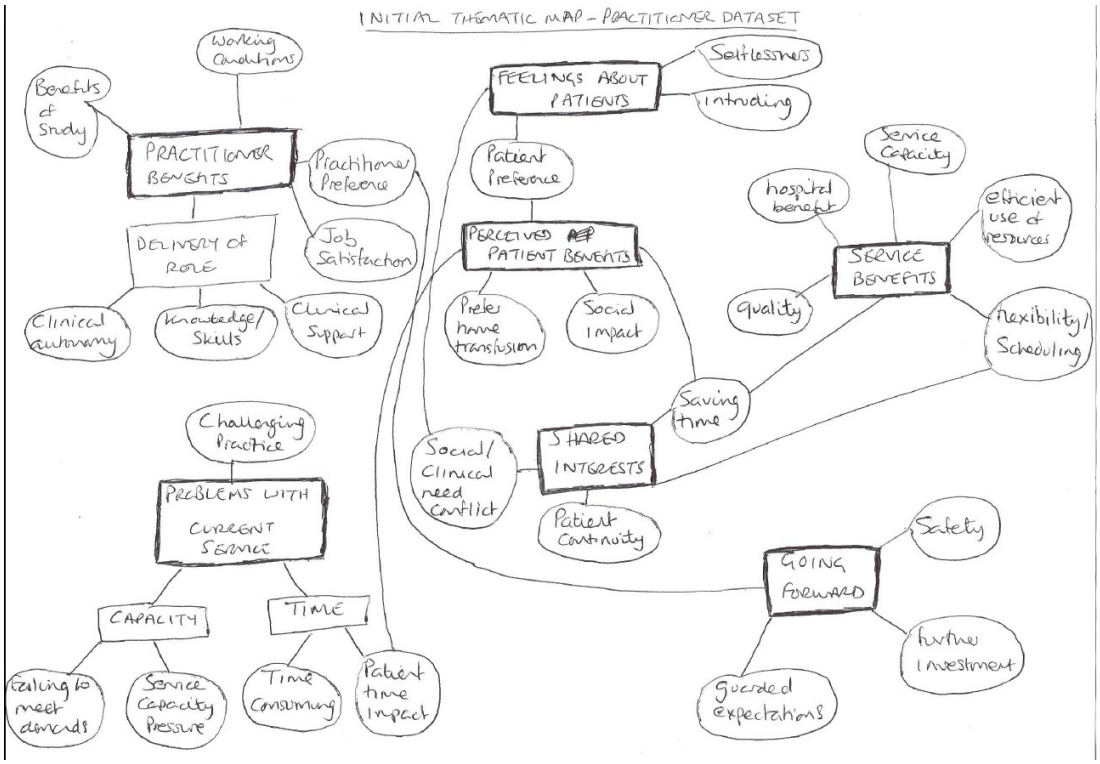



**Figure 11.2: Initial thematic map for practitioner dataset**

### Step 4: Review of Themes

The themes were firstly reviewed at code-level to evaluate whether the codes appeared coherent within their designated theme. The extracts within each code were consolidated into a separate Excel™ spreadsheet workbook by theme. The theme was validated by re-reading the coded extracts at

dataset level (patients and practitioners) to ensure there was a clear story within each theme with respect to understanding the experience of accelerated transfusion for each set of participants. Table 11.5 below summarises the outcome of this procedure.

**Table 11.5: Review of themes**

| Dataset | Coherence of code within theme | Validity of theme within dataset | Summary of Changes |
|---|---|---|---|
| **Patient** | ✓ | ✓ | Simplification of initial thematic maps and renaming of subthemes without material changes to coding. |
| **Practitioner** | ✓ | ✓ | Main themes *Feelings About Patients* and *Perceived Patient Benefits* were combined and renamed *Vicarious Patient Experience*. *Shared Interests* was removed and split between *Vicarious Patient Experience (Social/Clinical Need Tension sub-theme)* and *Service Benefits* (*Continuity* sub-theme was combined into the *Service Delivery sub-theme* ) |

The changes made as a result of this review were used to produce developed hand-drawn thematic maps as shown below in figures 11.3 and 11.4.

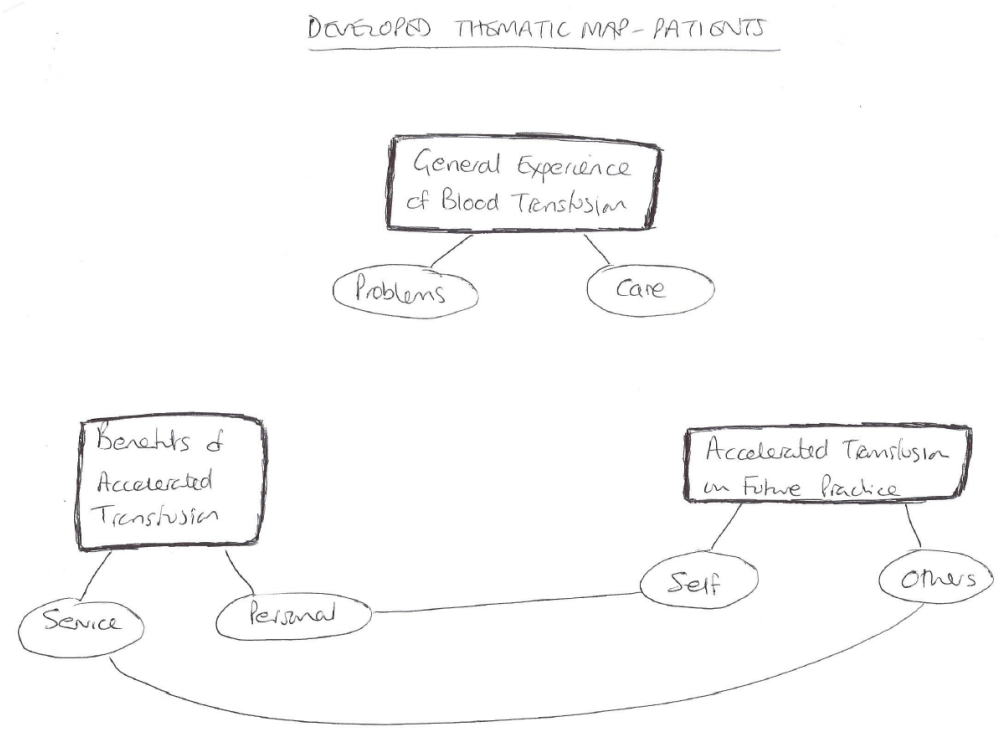



**Figure 11.3: Revised thematic map for patient dataset**

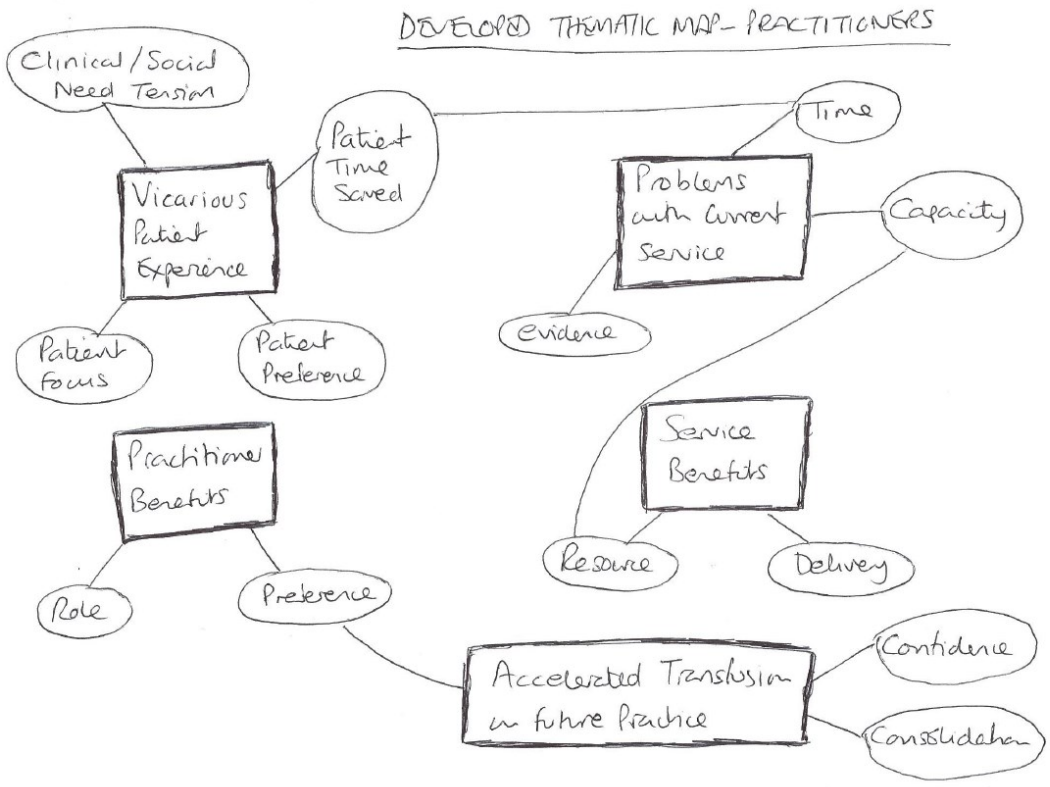



**Figure 11.4: Revised thematic map for patient dataset**

### Step 5: Definition and Naming of Themes

Braun and Clarke (2006) suggest testing each theme by the ability to clearly and concisely describe it in a few sentences. The purpose of this is an assurance check for theme coherency. Table 11.6 below lists the main themes and sub-themes for each dataset with a brief description.

### Table 11.6: Description of themes and sub-themes for each dataset

| Patient Dataset | | |
|---|---|---|
| **Theme** | **Sub-theme** | **Description** |
| **General Experience of Blood Transfusion** | **Care** | Patients both recognise and forgive problems they experience with hospital transfusion – the good experience of care outweighs the problems experienced |
| | **Problems** | Patients experience frustration because of the length of time involved in receiving a transfusion, with an impact on their level of comfort and this is amplified when transfusion is received in the hospital environment. |
| **Benefits of Accelerated Transfusion** | **Personal** | Improved comfort and convenience was experienced to varying degrees and was patient-dependent. The impact of saved time and effect on comfort varied from neutral to highly positive across both home and hospital transfusions. |
| | **Service** | There was patient insight into how accelerated transfusion could benefit delivery of the home transfusion service by increasing efficiency. |
| **Accelerated Transfusion in Future Practice** | **Self** | The patients did not experience a difference in how they felt after accelerated transfusion and this was reassuring to them. Preference for accelerated transfusion ranged between ambivalence to enthusiasm and was dependent upon the patient's personal circumstances. |
| | **Others** | There was a sense of altruism in understanding the potential positive effect on service efficiency above their own needs, but also a sense of reticence to commit to a preference because of a desire to not take advantage. |
| **Practitioner Dataset** | | |
| **Theme** | **Sub-theme** | **Description** |
| **Problems with Current Service** | **Evidence** | Evidence for standard rate transfusion was doubted because of their prior experience, and practitioners indicated that patients shared this view |
| | **Time** | Practitioners experienced frustration with the time-consuming nature of blood transfusion and had concerns about how this impacted on the patient's time. |
| | **Capacity** | Practitioners had experienced challenges with meeting the growing demands of the service due to the volume and diversity of intravenous treatments. They felt the service was under pressure and a duty to ensure resource was being used as effectively as possible. |
| **Vicarious Patient Experience** | **Patient Focus** | Practitioners showed a great deal of empathy and concern for the patient's quality of life and were committed to patient-focussed care to avoid adverse impact on the patient's social issues, time, freedom and comfort. |
| | **Patient Time Saved** | The release of time allowed practitioners to more readily shift the focus for patients from life-limiting illness and contact with healthcare, to 'normal life'. |
| | **Patient Preference** | Patients preferred home compared to hospital transfusion in their experience and they reported that had received positive feedback about accelerated transfusion from patients in terms of preference, satisfaction and popularity. |
| | **Social/Clinical Need Tension** | Practitioners recognised from past experience that some patients may actually prefer longer transfusions because of a desire for company, even if this was not clinically necessary, leading to a tension between balancing the social and clinical care needs of the patient and delivering an efficient service. |

| | | |
|---|---|---|
| **Practitioner Benefits** | **Role** | Accelerated transfusion gave practitioners a sense of increased job satisfaction through the application of their knowledge and skills in well supported autonomous practice for the benefit of the patient. |
| | **Preference** | The experience of accelerated transfusion had led to positive feelings toward implementing it into routine practice. |
| **Service Benefits** | **Resource** | Practitioners felt that the releasing time while performing accelerated transfusion had increased service capacity for blood transfusion and other IV treatments, and avoided hospital admission. Existing resources were being used more efficiently without compromising quality. |
| | **Delivery** | There was improved scheduling of work through the benefit of enhanced flexibility that accelerated transfusion allows, including better patient continuity. Both patients and the service can use time more effectively. |
| **Accelerated Transfusion in Future Practice** | **Confidence** | There was positive practitioner preference for accelerated transfusion and perceived patient preference. Experience of performing accelerated transfusion had affirmed trust in their safety. |
| | **Consolidation** | There was a mixture of guarded expectations for the longer-term impact of accelerated transfusion and the desire to see increased staff resource to maximise its benefit, and an eagerness to implement into routine practice. |

Final theme and sub-theme names were decided by relating the short descriptions shown above to the preliminary name to ensure they support a clear and coherent final thematic map. Final theme and sub-theme names are shown below in table 11.7.

## Table 11.7: Final theme and sub-theme names

| Patient Dataset | | | |
|---|---|---|---|
| **Theme** | **New Theme Name** | **Sub-theme** | **New Sub-Theme Name** |
| General Experience of Blood Transfusion | Patient General Experience of Blood Transfusion | Care | Care Received |
| | | Problems | - |
| Benefits of Accelerated Transfusion | - | Personal | Personal Benefits to Patient |
| | | Service | Service Benefits |
| Accelerated Transfusion in Future Practice | - | Self | Effect on Self (Patient) |
| | | Others | Effect on Others (Service) |
| **Practitioner Dataset** | | | |
| **Theme** | **New Theme Name** | **Sub-theme** | **New Sub-Theme Name** |
| Problems with Current Service | Problems with Current CIVT Service | Evidence | Doubting the Evidence for Safe Infusion Rate |
| | | Time | Time-Consuming Treatment |
| | | Capacity | Service Capacity Pressure |
| Vicarious Patient Experience | Practitioner Perception of Patient Experience | Patient Focus | Patient Needs |
| | | Patient Time Saved | Appropriate Use of Patient Time |
| | | Patient Preference | - |
| | | Social/Clinical Need Tension | - |
| Practitioner Benefits | Practitioner Benefits of Accelerated Transfusion | Role | Role Benefits |
| | | Preference | - |
| Service Benefits | Service Benefits of Accelerated Transfusion | Resource | Resource Benefits |
| | | Delivery | Service Delivery Benefits |
| Accelerated Transfusion in Future Practice | - | Confidence | Confidence in Desirability and Safety |
| | | Consolidation | Consolidation into Routine Practice |

The renamed themes and sub-themes were then transposed into the final thematic maps shown below in figures 11.5 and 11.6.

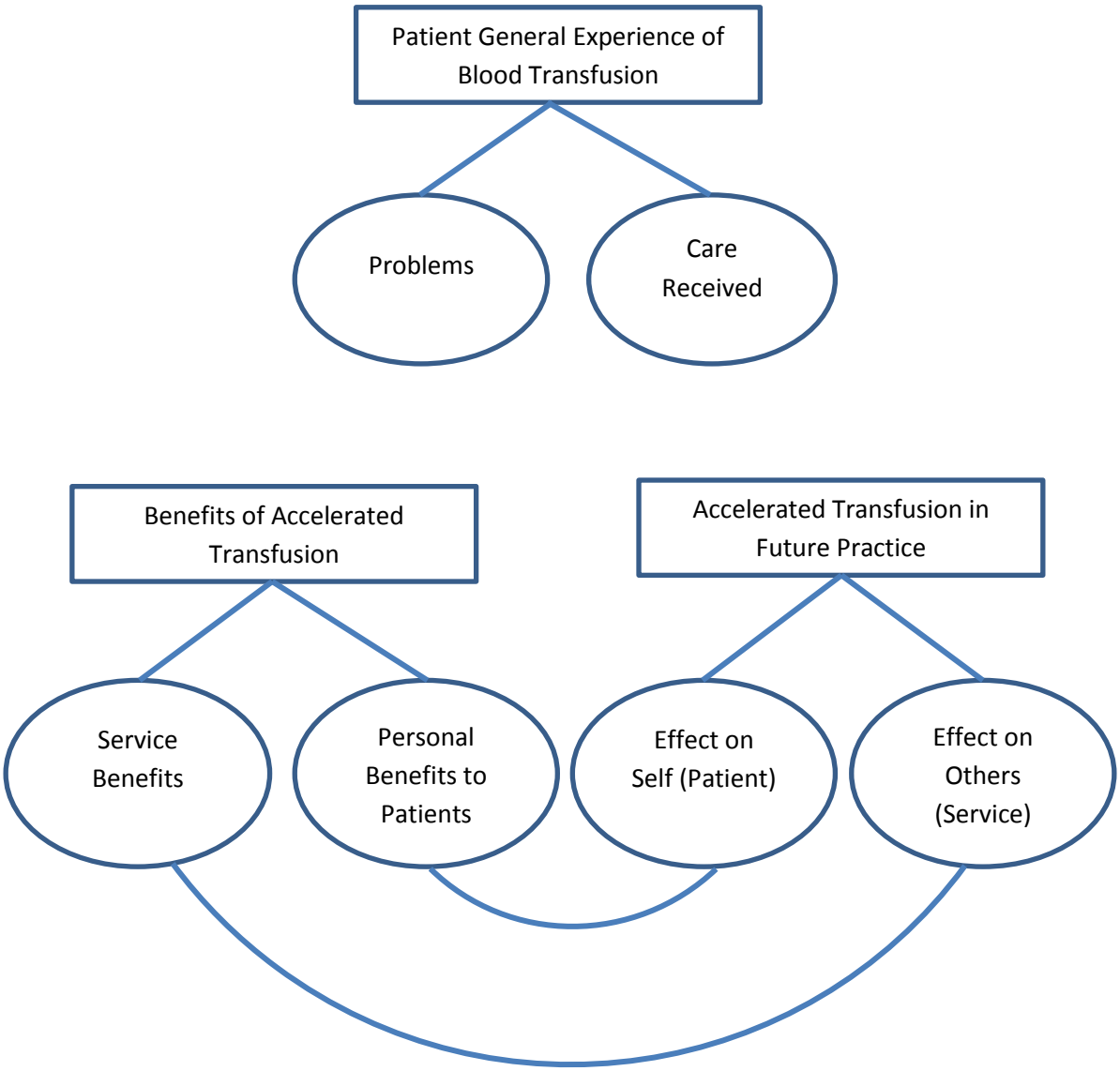



**Figure 11.5: Final thematic map for patient dataset**

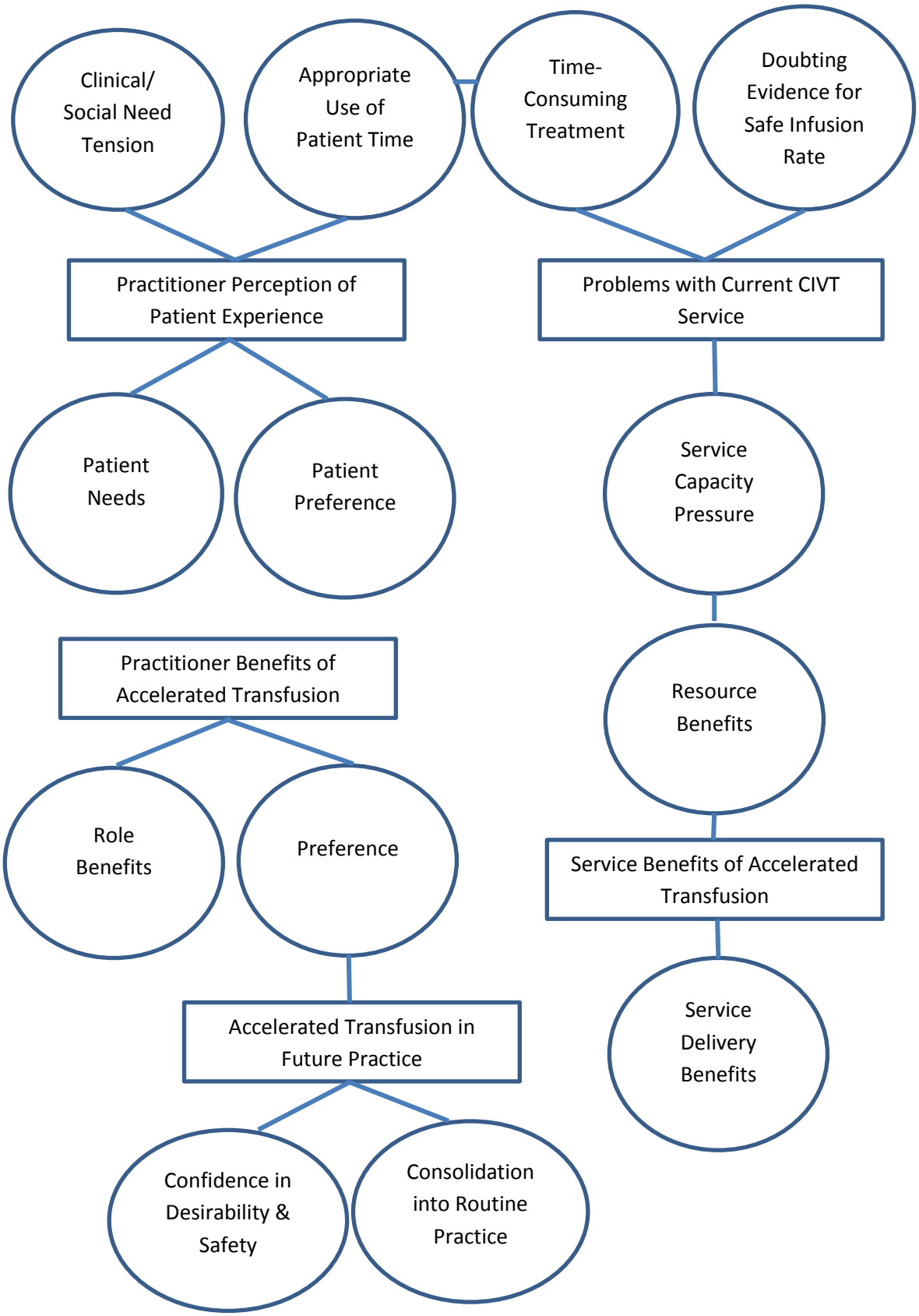



**Figure 11.6: Final thematic map for practitioner dataset**

## Step 6: The Report

The following section is an analytic narrative using examples from the data to address the research question: what is understood about the patient and practitioner's experience of accelerated transfusion? Through exploration of experience, the report addresses the meaning of each theme in the respective datasets whilst considering the implications of the acceptability and desirability of service-model change.

### Patient Dataset

#### The Patient's General Experience of Blood Transfusion

The patients who agreed to be interviewed had a long and frequent experience of receiving blood transfusion as part of the treatment for their haematological condition. All had blood transfusions both on the oncology day unit, and at home from the CIVT team. There was a universal account of frustration and resignation due to problems associated with blood transfusions both inherent to the transfusion process itself and those which were service-related. There was a sense of lowered expectations and resignation to the transfusion process being intrinsically lengthy and this was compounded by infusion problems which sometimes occur unpredictably. It was important to recognise this as a general theme because of the background level of negative feeling toward blood transfusion *per se*, regardless of the duration of the infusion itself. Morris was the most articulate and verbally enthusiastic participant providing the greatest diversity of codes

and themes, and this is reflected by the number of quotations included in the report.

> Morris: *"Before you know it, two hours have gone and you're just starting, type thing, but the best thing I do now is just...it's a day so don't worry about it."*

> Morris: *"I could feel my arm and I knew there was something going wrong with it. As it turned out, she'd missed it completely [vein] and it was going straight in my muscle, and for about three weeks afterwards, I had a totally black arm from there to there. It literally was black. It looked like gangrene arm."*

There was also some questioning of whether the length of transfusion was necessary, as the process of receiving blood is much longer than the donation process.

> Morris: *"As I seem to remember, when I was giving blood, it seemed to be about a 20 to 30 minute process when they took one bag out [of me]…"*

In addition to this, frustration was expressed with the additional restrictions, delays and length of time spent on the hospital oncology unit when home transfusion was not possible.

> Morris: *"It seemed to go on for an awful long time, but then I realised that A, they haven't got blood on the premises so they have to go out every time to get it; even though I'm taking two bags, they can't pick*

*two bags at a time up; they have to do it one at a time. So quite often, because they're very, very busy; I've been in there sometimes in the unit [hospital oncology unit] and they're just parading through. It's like non-stop and you're lucky if there's somewhere to sit even. And they're run off their feet I think, quite often, so you could be there an hour before anything happens."*

Richard: *"It's so busy up there [hospital oncology unit] as well, it really is, it's unbelievable"*

Patients were forgiving of this recognising the workload pressures of the hospital nursing staff. Frustrations with problems experienced on the hospital oncology unit were tempered with expressions of sympathy and gratitude toward the nursing staff for the high standard of care they received in what they observed as difficult circumstances.

Morris: *"I have struggled sometimes, trying to find somewhere to park but once I'm in, everybody's very helpful. I can't believe the attention I'm getting actually. It's great."*

Morris: *"I mean, they're very nice up there, lovely up there, aren't they? You know, they bring sandwiches round and tea, you know, so yes that's not a problem".*

**Benefits of Accelerated Transfusion**

Patients perceived the benefit of accelerated transfusion on two levels: personal benefit, and benefit to the service. Patients were aware that they

sometimes had to attend the hospital oncology unit for their regular blood transfusions because the CIVT team were unable to offer them a home transfusion visit at the time they required their transfusion because of service capacity issues. A connection was made as to how this linked with accelerated transfusion in future practice and the importance on its potential effect on increasing service capacity and is discussed further in the theme on future practice.

> Reginald: *"And they asked me would I go down to help them rather than have it at home because they were a bit short [of staff]…and I had experienced the [oncology unit] prior, when [CIVT] has been busy"*

For some, home transfusion was important to support their ability to perform their carer role.

> Richard: *"They decided that it was best to continue it here [transfusion at home] because of W [grandson to whom he is sole carer]"*

Patients expressed positive feelings and preference for accelerated transfusion, reporting shorter duration transfusions could improve their physical and mental comfort whilst receiving treatment.

> Richard: *"It's just so boring, isn't it [standard rate transfusion]?"*
>
> Reginald: *"…because you did get a little bit uncomfortable because you're sat still, in the two hour one, yeah, it [accelerated rate] improved that a lot"*

Jack: *"Well, to sit here for er, three hours [for standard rate transfusion] is quite a long time really even though I've got a comfortable settee. So, you know, once I've had it done I'm up and walking about just, yeah, my legs are going again 'cause I've quite a bit of problems with my legs so as soon I get exercise a bit, as soon as I've had it really"*

Jeffrey: *"I get my lunch earlier [laughs] [with accelerated] 'Cause it always happens over the sort of lunchtime period 'cause it doesn't start 'til about eleven o'clock so it means I get a late lunch if it's an extended one as opposed to an accelerated one"*

Some stated they could use time saved for other things or expressed satisfaction in not being engaged in healthcare for as long, as well as the freedom and convenience of being able to plan and use their day better.

Reginald: *"That's how I felt personally because sometimes if you tried to arrange things you had to say, because you don't necessarily know what time [the CIVT team] are coming, if they came, say, after half past eleven, I knew then there was nothing I could do afterwards, because by the time everything was over it was a little bit too late. Where on the shorter one [accelerated transfusion] it gave me that more freedom where I thought "right I can do something afterwards, I can nip in town or whatever"*

Reginald: *"I found it then gave you time at the end of the day to actually achieve something [accelerated transfusion]"*

The positive language use when describing accelerated transfusion suggested that patients had felt they had been enduring constraints in their day-to-day life because of the length of the standard transfusion treatment times and this had not only affected them socially but also emotionally.

> Reginald: *"but because I was on the shorter one [accelerated transfusion] this time found it a lot more convenient, and it didn't get you down. You know because in hospital it does take a little bit longer because they've not got both blood bags ready, and I found going to the [oncology unit] a lot, lot easier, same at home"*

Some patients also reported benefits of shorter treatment times when having transfusions in the oncology unit when they were unable to have home transfusions. Although this was not the focus of the study it was an important finding in terms of the potential wider application of accelerated transfusion.

> Reginald: *"Particularly because I had one done in hospital at the [oncology unit] because they [CIVT team] were busy, I found that brilliant because it meant you weren't in the [oncology] unit nowhere near as long"*

Many patients were enthusiastic about the benefits they had experienced from having accelerated transfusions, while others were ambivalent. The degree of benefit experience was variable and largely dependent upon the personal circumstances of the patient.

Jack: *"Er, not really [accelerated transfusion does not make a personal difference], no 'cause I'm retired so I don't do much. I just…I don't do a lot these days"*

This also linked to the theme relating to future practice (and discussed further in the next section).

**Accelerated Transfusion in Future Practice**

The positive feelings and preference expressed for accelerated transfusion suggested that patients would be supportive of introducing this into routine practice. None of the patients reported medical or wellbeing problems with accelerated rate transfusion. Where there was some minor initial concern expressed, the experience of participating in the study was reassuring.

Reginald: *"you were a little bit concerned in the beginning wondering how it would affect you, for the first one or two, but after that when I didn't feel, me personally, I didn't feel any different having it in two hours than what it was when I was having it in three hours. So after that I was quite comfortable with it. And I had no real concerns. It's just that feeling beforehand, you know, thinking is it a bit fast? [Laughter]…And I've had no different feeling than the three hour one"*

Some patients said standard rate transfusion would not necessarily negatively impact them if they had to have standard rate transfusion at home, whereas some were enthusiastic about continuing with accelerated transfusion.

Jeffrey: *"No, I don't think it makes much difference because it's only … we're only talking about an hour at the outside"*

Richard: *"It's just, I don't know… it seems far better, you know. It's brilliant really [accelerated transfusion]"*

This partly related to personal circumstances where shorter duration of treatment would not provide any significant personal benefit (and discussed in the previous theme on benefits of accelerated transfusion), and partly related to the patient's attitude toward the service itself. There was an explicit and implicit sense of altruism in that there was a clear recognition that accelerated transfusion could improve home transfusion service-capacity (and oncology unit processes), and this was important whether or not it benefitted the individual patient.

Jeffrey: *"And, of course, it's an advantage to you, not you personally, but to the community nurses because it means they can treat more patients during the day if you've got an extra hour spare when they're not dealing with the normal transfusion"*

Jeffrey: *"Well, I just think it's better for everybody really, for all the patients as well as the nurses. It means I can think about other people who need the same treatment and everybody benefits then"*

This was also implicit in that some patients reported a lack of 'worthiness' to qualify for home transfusion and communicated a sense of gratefully accepting whatever the service had to offer (a willingness to compliantly fit the service). Despite understanding the potential benefits to home

transfusion service capacity by implementing accelerated transfusion, patients still expressed a self-sacrificing attitude. This may have moderated their willingness in expressing an overt positive preference.

> Morris: *"Hmm, but I think, knowing how much they are run off their feet, you just feel a little bit unfair that you're taking advantage having it at home. Just go in and join the rest of the group"*
>
> Richard: *"I'd choose the hour one [accelerated transfusion] obviously, because it's quicker and, you know, if you had to do the longer one, it wouldn't make any difference"*

## Practitioner Dataset

### Practitioner Perception of Patient Experience

The practitioners expressed their perception of the patient's experience more strongly than the patient's description of their own experience. This vicarious account was given without prompting showing that the practitioner's main concern was delivering care in the best interest of the patient, given that the premise of the interview was to understand the practitioner's experience of accelerated transfusion. The theme comprised of sub-themes relating to preference for accelerated transfusion, patient needs, and appropriate use of the patient's time. The practitioners felt that patients preferred accelerated transfusions as it increased their freedom by shortening the home visit time.

> Rose: *"I think it's just how popular that they are…the accelerated transfusions really. The patients that I've been to see who have*

*experienced both and they are definitely preferring a bit more freedom that we're going to be in for maximum of three hours, rather than four or five hours"*

They felt that saving the patient time was important in allowing them to have more control over their lives and this was an important aspect of delivering holistic care to the patient by recognising their wider, non-clinical needs.

Rose: *"They can schedule things…their own daily schedules as well. The fact that they can go shopping afterwards or beforehand and get everything ready, it is their freedom and that's what the team, I think, always promote anyway. What we want is their quality of life and their treatment because we want them to be empowered"*

Rose: *"It is very focused on them. I mean the blood transfusions at home service always is very patient focused anyway but we can really extend that quality time [due to accelerated transfusion]"*

Appropriate use of patient time was a significant factor. There was a strong desire to help the patient improve their quality of life by the ability to mitigate the negative effects of prolonged contact with healthcare through shortening treatment time with accelerated transfusion.

Erin: *"Yes, you know these people you know they're not older, they're actively involved in the family and they're not able to pick the grandchildren up from school so actually it's a knock on effect on the whole of the family because we're transfusing later on in the afternoon, they're not quite sure what time we're going to finish. So*

*actually they've had to make alternative arrangements and then it's a knock on effect for the whole family, yes so it [shorter treatment time] fits in with their lifestyle a little bit more"*

Rose: *"Obviously when we go and see them it does take up a big part of their day. When they know that we're only going in for that short period [accelerated transfusion] we can usually give them… morning or afternoon. They can get on with their life, they can prepare. They know that we're only going to be there maximum three hours, tops and then we're away. They can get on with their lives and improve their quality of life, really"*

The sense of intrusion on the patient's time and the desire to respect it and use it appropriately also translated into intrusion into the personal setting of the patient's home environment. The practitioners were highly aware that their presence could be seen as an imposition and the time spent in a patient's home should be as short as possible, and that accelerated transfusion supported this.

Cindy: *"Well, you're not like invading their home environment for like a whole day"*

Esther: *"I think it gives patients more satisfaction because we're not in the houses as long"*

This sense of intrusion was made acute by patient's life-limiting conditions, anything that mitigated this would be positive for the patient's experience.

Elizabeth: *"…at the end of the day some of these patients are very unwell and time is a factor for them and they want to fit things in, they've got grandchildren they want to go visiting friends or whatever. So rather than you being there longer they can say well it's only a couple of hours so I can make arrangements to go out in the afternoon because time is a factor for them because a lot of patients are very unwell and they don't know how long they've got left basically… an afternoon to us might mean nothing but to them it means a lot"*

A tension between clinical and social needs was also evident. There was a conflict between delivering clinical care appropriate to service resources whilst providing pastoral aspects of care relating to the social needs of the patient. They felt that a lonely patient may prefer a longer treatment time because of the social benefits of longer contact with the nurse, and this was at odds with comments separately expressed about running the service efficiently.

Elizabeth: *"some patients do like you being there and some patients…don't get a lot of visitors and can't get out so when you go they love it because it's somebody to chat with and discuss. So from that point of view they might feel a little bit, "Oh I wish you was staying a little bit longer."*

**Problems with the Current CIVT Service**

The time-consuming nature of blood transfusion continued into the theme on problems with the current service. There were frustrations about how this impacted upon service capacity as the service was under increasing pressure not only for accepting more home transfusions but also delivering and increased volume and diversity of new or additional intravenous treatments.

> Olivia: *"Just length of treatment really [problems with standard rate transfusion] and capacity in the team, 'cause they could take, kind of, six hours with picking up equipment and taking equipment back again"*
>
> Rose: *"We've got a huge impact with an increased workload with different antibiotics that are coming on at the moment"*

The increased pressure to accept more referrals had caused practitioners to question evidence for safe rates of transfusion.

> Elizabeth: *"Yeah because you're tied up with that transfusion longer [with standard rate transfusion] somebody else is going back in the afternoon to do the afternoon dose of antibiotic because you're still with your patient that's having a transfusion"*
>
> Esther: *"Lengthy, very lengthy"*
>
> Olivia: *"They were too long for the volume of fluid that was being infused [standard rate transfusion]"*

Olivia: *"I think they [patients] couldn't understand why they took so long because there weren't huge volumes of fluid "*

Esther: *"I mean, it used to be four hours at one time. It was four hours, per unit, when I…[inaudible but inferred many years ago]"*

**Service Benefits of Accelerated Transfusion**

The experience of delivering accelerated rate transfusions during the study (i.e. without formal workload analysis) had shown practitioners resource benefits in terms of service capacity in that the time saved could be used to provide additional treatment slots and avoid hospital admission.

Olivia: *"it [accelerated transfusion] frees clinical time up for other treatments that – being shorter, so we can fit more transfusions in a day and more IV other treatments as well. Just because it's not as time-consuming"*

Erin: *"since we've been doing the accelerated transfusions we've now been doing TDS [three times a day] antibiotics so there is, you are able to do your first morning's IV antibiotics at half eight and still get back for their afternoon treatment of antibiotics and do a transfusion in the middle. So it kind of, it works quite well, yes you have got that time"*

Elizabeth: *"perhaps because of staff levels we can only fit one transfusion in we could perhaps now take two patients on one day rather than one which is good for the patients as well because they're*

*getting their transfusions in a timely manner rather than having to wait or to come into hospital when they've not need to come into hospital"*

They also reported service delivery benefits as saving time with accelerated transfusion had allowed better patient continuity and flexibility in staff rostering.

Elizabeth: *"if you've got like patients that are on three times a day [antibiotics] you can manage your time better knowing that you can perhaps do an IV in the morning an IV antibiotic in the morning, your transfusion and perhaps go back in the afternoon as well, so you've got a follow on with your other patients as well with their IV antibiotics"*

**Practitioner Benefits of Accelerated Transfusion**

Practitioners expressed an overwhelming preference for accelerated transfusion where medically possible.

Rose: *"The accelerated transfusion is fantastic and really, really good but like I said we are well aware, as clinicians, that if we need to we can reduce and go back to standard [rate transfusion]"*

Practitioners described benefits to their own role in terms of job satisfaction. They felt a greater sense of autonomy in that accelerated transfusion allowed greater opportunity to exercise clinical skills and judgement while feeling well supported by the clinical haematology team in the hospital.

Erin: *"I do like the aspect that you can deviate as we see fit. So you're going in to do an accelerated transfusion and it's up to our discretion with the patient and we can deviate to a normal transfusion"*

Rose: *"I think as well, the freedom has been as well that as we've gone in and we've assessed patients, and usually we know the patients really, really well, and we can tell as well whether to accelerate or not. There have been incidents where we've said we're not accelerating today and we've gone back to standard transfusion rate. Again, that's probably our knowledge and skill but the flexibility we can have with that as well"*

Erin: *"You know knowing that I've got the support of the haematology team you know I'm their eyes and ears and yes whatever I see is you know they will support me 100% and act on what I've said…I've deviated from it a couple of times when I've been worried about the patients and yes the support that I've received from the haematology staff has you know been faultless"*

There were additional practical benefits to practitioners if less time is spent in the patient's home and this would improve their working conditions. This was expressed discreetly as the connotation was that some patient's homes, although met a basic standard for medical treatment, were not necessarily somewhere they would want to spend more time than needed.

Cindy: *"Erm, well, yeah, because it … I have to say, in some cases you don't want to be in a particular environment any longer than you*

*really need to be. Erm, so that's been a positive for us that we can go in, get the job done and be out a lot sooner"*

Esther: *"Some environments are very good and some are very poor, so with the shorter transfusions, you're not in the houses as long so it's – it does help us [accelerated transfusion]"*

**Accelerated Transfusion In Future Practice**

Practitioner preference for accelerated transfusion extended into views on the future of accelerated transfusion in the CIVT service and a desire to see it continue for both the service and patient benefit.

Rose: *"I think let's just carry on and just keep it going really, and keep the service"*

Olivia: *"I think it would be a definite step back if you went back to the regular [standard rate transfusions]…especially for patients that [had] accelerated [transfusions], they [patients] wouldn't understand the rationale of going back [to standard rate]"*

Practitioners appeared to be reassured, albeit slightly guarded, about the safety of accelerated transfusion and had not experienced any adverse events in clinical practice.

Erin: *"And I personally, I have not had any negative or bad experiences by doing the accelerated transfusion, touch wood, I've not ever had anybody have a, a reaction or a bad effect from it so it's been good"*

*Cindy: "I haven't had a negative experience whilst doing them. So no, it, it seems to work very well for those that I've done anyway"*

Together with their perception of patient preference and service benefit, this contributed to practitioner endorsement of implementing accelerated transfusion into future routine practice without affecting any aspect of service quality.

Esther: *"They still get a quality of service from us, but on a shorter length of time"*

**Precis of New Knowledge: Implications for the Acceptability and Desirability of Service Model Change**

- Both patients and practitioners expressed frustration and dissatisfaction with the general blood transfusion process (especially where this took place in hospital).
- Experience of accelerated transfusion had been positive and alleviated some of the negative experience of standard rate transfusion.
- Patients felt accelerated transfusion was safe and identified benefits to themselves, and/or to others and the wider service, sometimes framed in a desire to obligingly take the service on offer as opposed actively expressing a preference.
- Practitioners felt that shorter treatment time was in the interests of the patient although acknowledging that some patients may actually prefer prolonged visits for social reasons. Interestingly, this was not recounted by patients themselves.
- Practitioners had experienced benefits to the capacity and delivery of the service, and felt increased job satisfaction.
- Practitioners felt their patients gained benefit from accelerated transfusion and that the procedure was safe.
- These findings suggest that both patients and practitioners would support the implementation of accelerated transfusion into routine practice and that change to the proposed service model would be both acceptable and desirable.

# Chapter Twelve:
# Discussion and Conclusion

This concluding chapter revisits the research problem and reviews how it was addressed in the context of the contextual and conceptual framework as described in the introductory chapters. The findings are then summarised and discussed, while critically evaluating the extent to which the research question has been answered and the hypotheses addressed. Specific attention is paid to the strengths and limitations of the study and the impact of the research on contribution to knowledge and clinical practice, with recommendations for clinical practice and further research.

**Problem: The Divergence of CIVT Service Capacity and Demand**

Additional pressure of new and diverse intravenous treatments and the increased demand for home transfusion outstripped service capacity for this relatively small and highly skilled team. Achieving increased capacity within current staff resources relied on finding new and efficient ways of delivering the service, so that it may continue to benefit patients and avoid in-patient admissions. One of the variables in the current service model is treatment delivery time per home visit. This posed the question as to whether red cell transfusion infusion time could be safely reduced, leading to the concept of ‘accelerated transfusion’, and whether this would be acceptable and desirable to patients and practitioners.

## Revisiting the Research Question and Hypotheses

The following research question and hypotheses were developed from the conceptual framework.

### General Research Question

Whether transfusing two units of red cells over 60 minutes per unit (accelerated transfusion) is safe and could potentially increase CIVT service capacity, while gaining understanding of the patient's and practitioner's experience.

### Hypotheses

The following hypotheses were developed for the quantitative aspects of the research question:

- $H_1$: Two units of red cells transfused over 60 minutes each can be physiologically tolerated in selected patients ($H_0$ there is no difference in the incidence of Transfusion Associated Circulatory Overload (TACO) between standard and accelerated rate transfusions). This requires 'proving' the null hypotheses.
- $H_1$: Implementation of accelerated transfusion could potentially increase CIVT service capacity ($H_0$ Implementation of accelerated transfusion would not potentially increase CIVT service capacity).

The qualitative strand of the study was value-adding, seeking to inductively gain understanding of patient and practitioner experience without *a priori* theories and therefore hypotheses were not appropriate.

## Headline Findings

The outcome of the study as a whole suggests that accelerated red cell transfusion (two units not exceeding 5ml/Kg/Hr) does not appear to cause increased harm, could potentially increase the CIVT service capacity, and implementing this service change would be acceptable and desirable to both patients and practitioners. The research question was answered and hypotheses accepted subject to qualification and critique in the following sections.

## Summary and Critical Review of Findings in Relation to the Research Question and Hypotheses

### Safety/Physiological Enquiry

This strand of the study was a prospective cohort study based upon a binary outcome non-inferiority method which sought to demonstrate that accelerated transfusion was no more often associated with TACO than standard rate transfusion. The aim of this strand the study was effectively to accept the null hypothesis by demonstrating the accelerated transfusion procedure is no worse, in terms of patients developing signs of TACO, than the current standard rate transfusion procedure. The study was therefore be defined as a binary outcome non-inferiority study as there were two possible outcomes (TACO, or no TACO). Medical exclusion criteria were developed in order to exclude patients from the study with co-morbid conditions and risk factors that may predispose circulatory overload. These were developed from haemovigilance data where associations had previously been identified

in the literature between patient characteristics and the development of TACO. Each patient had a standard rate transfusion followed by at least one accelerated rate transfusion. A clinical assessment, including vital sign observations, were performed pre-transfusion, and at around 24 hours after the transfusion to assess the patient for signs of TACO.

The target number of participants based upon the sample size calculation was 39 to power the study to 80%. The number of patients recruited (25) fell short of the target but was the maximum achievable in terms of patients agreeing to participate in the study in the time available. The sample size calculation was highly problematic because of issues with the accuracy and representativeness of data used for the calculation. Firstly, TACO may be under-reported to SHOT and/or clinically under-recognised and affects the numerator and therefore estimate of incidence. This is further compounded by very limited and highly variable data in the literature regarding the incidence of TACO and even less in this particular patient group being studied. The number of red cell units transfused nationally was a best estimate. Red cell wastage had to be estimated based upon average wastage data reported by the national Blood Stocks Management Scheme, and this was subtracted from the number of units issued. This affects the accuracy for the denominator data used to estimate the incidence of TACO relating to red cell transfusions where two or fewer units were transfused. Sample size and power calculations based upon data relating to the local incidence of TACO were considered unreliable due to the potential for a relatively rare event skewing fewer denominator data and that the TACO

cases did not represent the population being studied. Despite the difficulties and limitations in determining sample size, it was important to address this as far as was practical with the benefit of all available data and evidence, as this was a requirement when applying for ethical approval. However it is important to state that failure to meet the number of target participants, notwithstanding the limitations of the data used for the calculation, does not allow a judgement to be made about non-inferiority.

Twenty-five patients had standard rate transfusions with a total of 269 accelerated rate transfusions completed in total. Accelerated transfusion (total infusion time for two units is 120 min +/- 10% (108 to 132 minutes) was achieved in 87.3% of transfusion episodes (269/308). No cases of TACO were detected in the study. Outcome by *patient* demonstrated no difference between standard and accelerated rate transfusion for the development of symptoms and signs of TACO (RR = 1.0, OR = 1.0, p =1.0000). Although the confidence intervals (CI) crossed 1.0, indicating there was no difference between both groups in the study, the CI's were wide meaning the true RR and OR could indicate increased or decreased risk of TACO by accelerated transfusion. However logically decreased risk is not a feasible outcome in this study.

Analysing the outcome data by transfusion *episodes* reduced the RR and OR to <1.0 which indicated a reduced risk of TACO in the accelerated transfusion group, which again is not logically feasible. It also had the effect of narrowing the CI but this still crossed 1.0 indicating that the RR and OR analyses are not informative.

This type of analysis is difficult to reliably interpret with a small sample size and for rare events when the desired and expected positive/bad outcomes (TACO) for both interventions are expected to be zero. Computational problems will arise in the case of zero events and the statistical method made an arbitrary correction for this (Pagano & Gauvreau, 2000; Deeks & Higgins, 2010). Such manipulation of the data could have introduced error. This is an inherently difficult study to design with the objective of confidently demonstrating non-inferiority for accelerated rate transfusion due to the unknown true incidence of TACO in this population, and notwithstanding TACO is a relatively rare event as this significantly affects the degree of confidence in the accuracy of the sample size calculation. The approach was theoretically valid but constrained by inherent limitations of the data used for the sample size and power calculation. This could be improved by obtaining more accurate data on the incidence of TACO in stable adult patients receiving red cell transfusion for normovolaemic anaemia. This would need to be a large-scale multi-centre audit. At the time of writing, the National Comparative Audit of TACO is about to be published, however the scope of patients was not limited to stable patients with normovolaemic anaemia or a particular infusion rate, though it may be possible to obtain these data with permission. Statistical significance could be further improved by increasing the size of the study either by continued local data collection on accelerated transfusion outcomes, or by expanding as a multi-site study. This would allow improved comparison of the incidence of TACO in the ‘standard rate’ population compared to the ‘accelerated rate’ population using more numerically balanced data. At the time of writing, the surveillance definition

for TACO is undergoing review and a consensus is expected in the near future. As TACO is the endpoint of the study, universally agreed and validated criteria would also improve the quality of the study.

The conclusion drawn from this study is that accelerated transfusion did not cause harm but was unable to confidently demonstrate non-inferiority to standard rate transfusion. The study does however add credence to 'proof of concept' for 5ml/Kg/hr transfusion in this patient group and could therefore be regarded as a successful pilot study.

Although no cases of TACO were reported, its recognition is partly established by adverse changes to the patient's vital sign observations according to current criteria. Andrzejewski *et al* (2013, p. 3042) proposed TACO as a "multi-phasic spectrum entity" where the condition may be regarded as mild to severe with a commensurate change blood pressure among other parameters. Multi-way comparisons were performed to demonstrate differences between standard and accelerated rate transfusions to explore whether subtle, non-pathological changes occurred which may be an early sign of circulatory overload. There was a statistically significant difference between pre and post-transfusion mean arterial pressure (MAP) in standard rate transfusion ($p = 0.0441$) and the first three accelerated transfusion ($p = 0.0036$ to $0.0187$), however the increase was not within the pathological range. This is in disagreement with Gehrie *et al* (2015) who demonstrated no difference in pre and post transfusion vital sign observations in a large data set, and proposed this could be used for distinguishing benign and pathological changes. However this study

comprised of all types of blood component and was not limited to red cell transfusion in patients with normovolaemic anaemia. There was no consistent difference in variance of pre and post-transfusion vital sign observations when standard and accelerated rate transfusion were compared. The mean arterial pressure (MAP) appeared to increase within 24 hours of transfusion regardless of whether the transfusion was infused at a standard or accelerated rate, with the group mean remaining within the normal physiological range. If the increase in MAP was related to 'early TACO' then there is no evidence that accelerated transfusion causes this more than standard rate transfusion. It may also be speculated that the non-pathological increase is a normal physiological response to treated anaemia or may have been a chance finding in a relatively small patient sample.

**Service Capacity Enquiry**

This strand of the study was based on workload audit and an evaluation of patient eligibility for accelerated transfusion. It was designed to evaluate treatment delivery time of the current and the proposed service models where in the latter a proportion of transfusions could potentially be at an accelerated rate, and how this could potentially affect service capacity. This strand of the study aimed to demonstrate the potential impact of accelerated transfusion on CIVT service capacity. The analysis showed that 57% (26/46) of haematology patients fulfilled the medical inclusion criteria and were therefore eligible for accelerated transfusion, demonstrating that accelerated transfusion could be offered to a significant proportion of patients being transfused at home. 49% (224/459) of home transfusion episodes were

eligible to be performed as accelerated rate transfusions. This percentage depends upon the medical eligibility and intensity of transfusion in individual patients, but nevertheless demonstrates that a significant proportion of the home transfusion workload could be performed as accelerated transfusions. The analysis showed that if accelerated transfusion was implemented for both haematology and medical patients, service capacity could be increased by 105 nursing hours per year. This could potentially be utilised for additional patient visits whether for transfusion or other IV therapies.

The calculated increase in service capacity is an indicative estimate based upon the potential reduction in treatment time and its impact on the overall length of an average visit. This does not illustrate the actual impact of nursing-hours released on service activity as this would depend on how the nursing-hours could be most profitably utilised. For example, if an hour was released by performing an accelerated transfusion in the morning, would this be sufficient time for that practitioner to perform an additional IV treatment later that working day? The dynamics of planning work for a team are more complicated than a simple assessment of treatment time and numbers of patients. Other factors include travel time, skill-mix and patient continuity. To assess the actual impact on service capacity would require a post-implementation audit comparing pre-study capacity and post-implementation capacity. Adjustment would need to be made for confounding factors such as actual total nursing hours available across each of the audit periods, accounting for staffing levels and absences. Standardised productivity pre and post-implementation could then be evaluated by total IV treatments

performed as the numerator) and total nursing hours available as the denominator. The study shows the *potential* for increased capacity based upon demonstration of nursing-hours that could be saved. This strand of the study focussed entirely on impact on capacity from a time-saving perspective. This single-dimension analysis was enriched by the benefit of understanding the practitioner's experience of accelerated transfusion on service delivery, which revealed service benefits beyond time-saving. This is discussed further in the following section.

### Patient and Practitioner Experience Enquiry

This strand of the study sought to explore and gain understanding of the patient's and practitioner's experience of accelerated transfusion by thematic analysis of semi-structured interview transcripts. Both patients and practitioners expressed frustration and dissatisfaction with the general blood transfusion process. This is in agreement with previous limited research on patient's experience of blood transfusion (Weiss Adams and Tolich, 2011). Experience of accelerated transfusion had been positive and alleviated some of the negative experience of standard rate transfusion. Patients felt accelerated transfusion was safe and identified benefits to themselves, and/or to others and the wider service, sometimes framed in a desire to obligingly take the service on offer as opposed to actively expressing a preference. Some patients expressed ambivalence toward accelerated transfusion and this related to their own personal circumstances where a shorter treatment time did not necessarily affect their comfort or use of time. Although a positive personal benefit was not expressed by some patients this

nevertheless indicates that accelerated transfusion is at least acceptable to them in terms of implementing service change. Other patients were highly positive about the benefits of a shorter treatment time. Practitioners felt that shorter treatment time was in the interests of the patient although suggesting that some patients may actually prefer prolonged visits for social reasons. A significant proportion of CIVT patients live alone and/or are elderly. An Age UK evidence review states that loneliness increased with age and is more prevalent among people with long-term health issues (Age UK, 2015), which agrees with CIVT practitioner perceptions. This dichotomy was highlighted by the clinical/social needs tension identified in the thematic analysis, and the problem of how this reconciles with service efficiency. The practitioners were very focussed on providing holistic care but were also passionate about providing the service to all patients who needed it. Interestingly, the issue of extending social contact time with standard rate transfusion was not recounted by patients themselves. This may be allied to the self-sacrificing and altruistic attitudes identified in the thematic analysis. Patients may have felt reticent about exposing non-medical needs knowing other patients or the service may be disadvantaged as a result.

Practitioners had experienced benefits to the capacity (without formal analysis) and delivery of the service. They felt increased job satisfaction through the opportunity for increased clinical autonomy and the benefit of a wider supportive clinical haematology team. Practitioners felt their patients gained benefit from accelerated transfusion and that the procedure was safe. These findings suggested that both patients and practitioners would support

the implementation of accelerated transfusion into routine practice and that change to the proposed service model would be both acceptable and desirable.

The analysis has provided insight to judge and make recommendations regarding desirability and acceptance if implemented into routine practice. The interviews were conducted by the researcher and had the benefit of the interviewer's familiarity with the service, providing shared understanding and the ability to accurately interpret the dialogue. The thematic analysis was undertaken with demonstrable rigour with a clear audit trail of data and decision-making. These were particular strengths of this strand of the study.

## Implications for Practice and Contribution to Knowledge

A number of publications and awards are cited in this section to demonstrate how the study has contributed to practice and knowledge, and are fully listed in appendix O.

### Safety/Physiological Tolerability of Accelerated Transfusion

Although the study was not sufficiently powered to demonstrate non-inferiority to standard rate transfusion, and constrained by uncertainty of the incidence of TACO, it can nevertheless be regarded as a successful pilot study. The transfusion of two units of red cells over an hour each (not exceeding 5ml/Kg/Hr) did not appear to cause harm in this study. The data were reviewed by the research team and a decision was taken to implement accelerated transfusion into routine practice, while continuing to collect and monitor outcome data. A standard operating procedure for accelerated

transfusion is being developed at the time of writing and will append the Trust Blood Transfusion policy. It is not anticipated that the transfusion will be prescribed as ml/Kg/Hr in order to minimise the potential for rate calculation errors. The red cells will continue to be prescribed as unit over time (60 minutes) with special attention paid to patients weighing less than 67Kg where volume-selected units will be obtained to avoid an excessive infusion rate (>5ml/Kg/Hr). Accelerated transfusion will be available to haematology patients who receive transfusion either at home and/or on the oncology day unit if they meet the medical inclusion criteria. The data could be generalisable to any stable adult patient with normovolaemic anaemia also meeting the medical inclusion criteria. It would not be appropriate to extend this to inpatients (whether haematology patients or otherwise) with normovolaemic anaemia where there could be acute inter-current illness and the administration of other intravenous fluids. This situation could potentially add further risks for circulatory overload not accounted for in this study.

The study will change local practice but also adds to the literature and knowledge. The study comprehensively critiques the issues with the current understanding of the ‘rate’ of transfusion and how this can be meaningfully defined. The deconstruction of the ‘rate’ of transfusion has highlighted the significant influence of patient body weight and unit volume on the infusion rate. It persuades a change from ‘unit over time’ to ‘ml/Kg/Hr’ when describing the rate of transfusion. This not only offers a standardised approach which may be useful to future research in this area, but also highlights the benefit of a more personalised approach in the smaller patient

who may be at risk of circulatory overload due to their smaller blood volume. This aspect of the study inspired a project to develop a red cell dosage calculator which predicts the volume of red cells required to meet the target haemoglobin (Hb) level based upon pre-transfusion Hb level and the patient's body weight. The validation work for this project showed that using the patient's body weight to calculate the dose significantly increased the number of patients meeting their target Hb level (Grey *et al*, 2016). The medical exclusion criteria were developed based upon co-morbidities and risk factors that have been previously identified in published haemovigilance data and this study will contribute to validating those observations. The preliminary data from this study was presented as an oral presentation at the International Society of Blood Transfusion Congress in 2015 (Grey, 2015) which focussed on how haemovigilance data for TACO had contributed to developing a framework for patient-tailored rate and volume of transfusion. This original work led to an invitation to join an international working-party for the revision of the haemovigilance definition of TACO (ISBT, 2017) with further opportunities to collaborate and develop this area of research (Bolton-Maggs *et al*, 2017b; Grey *et al*, 2017b) . The author's research interest in TACO also led to an appointment to the Serious Hazards of Transfusion (UK haemovigilance scheme) Working Expert Group, which involves analysing TACO reports from the UK and writing the chapter for the annual report. This has allowed further opportunity to analyse patient comorbidities and risk factors for circulatory overload from TACO reports. Thematic analysis of data in the 2015 report was used to develop a TACO risk assessment tool to assist practitioners at the bedside to identify patients at risk. The use of this

tool became a formal recommendation in the annual report (Bolton-Maggs *et al*, 2016). The following year the annual data were used to validate the tool and with some minor changes it remained a formal recommendation (Bolton-Maggs *et al*, 2017a, Grey *et al* 2017a). The updated tool has a high degree of concordance with the medical exclusion criteria developed for this study which is reassuring when planning for implementation into routine practice, as these criteria will continue to be applied as a safe practice measure. Similar to the SHOT recommendation, medical exclusion criteria for accelerated transfusion is essentially a risk assessment for patients at risk of TACO. This may actually promote the safety of accelerated transfusion above standard rate transfusion because acceptance criteria are a formal pre-requisite for accelerated transfusion. This may more robustly exclude patients at risk of TACO compared to standard practice where pre-transfusion risk assessment may not be performed as rigorously.

### Service Capacity

This aspect of the study provided evidence for the potential for accelerated transfusion to increase CIVT service capacity. As discussed previously, the 'real world' effect can only be evaluated by a pre and post-implementation audit and the positive results of this preliminary assessment provide the impetus for this. The study excluded medical (non-haematology) patients due to logistical difficulties in recruiting them as research participants. Theoretically, accelerated transfusion could be offered to these patients as the findings could be generalisable to this population. In practice some issues may make this less desirable in this patient group. Medical patients

are not subject to the same level of pre-transfusion assessment or consultant-led supervision as haematology patients and the research team felt this would make them unsuitable for accelerated transfusion. Although a significantly smaller patient group, this would still have an impact on service capacity if they could not be included. This could be addressed by the Clinical Haematology team offering a referral service for non-haematology patients who may benefit from accelerated home transfusion, where pre-transfusion assessment could be better controlled. From a wider perspective, this aspect of the study could contribute to the literature on productivity of community services.

### Patient and Practitioner Experience

The insight obtained from the thematic analysis of the interviews provides assurance that implementing this service development would be acceptable and desirable to both patients and practitioners. This aspect of the study adds to the paucity of studies on the general experience of blood transfusion, and specifically to the non-researched area of shorter transfusions in the context of home transfusion. This aspect of the research was recognised with a national award from the Chief Scientific Officer for Engaging Patients and Citizens in Healthcare Science (2017).

## Summary of Recommendations for Clinical Practice

Table 12.1 summarises the recommendations for implementation and future practice.

**Table 12.1: Summary of recommendations for implementation**

| Recommendation | Planned Date |
|---|---|
| A recommendation for implementation into practice has already been made to the Trust Clinical Governance and Quality Committee following approval by the Hospital Transfusion Committee | Approved in July 2017 |
| Develop a referral pathway for non-haematology patients for home transfusion to allow accelerated transfusion in this patient group | Started November 2017 |
| Develop a Trust protocol for accelerated transfusion to append the Trust Transfusion Clinical Process policy and submit for Trust ratification | April 2018 |
| Include accelerated transfusion protocol in Clinical Haematology and CIVT team transfusion mandatory training | April 2018 |
| Commence accelerated transfusion in practice (home transfusion and hospital oncology day unit) | May 2018 |
| Audit patients outcomes of accelerated transfusions | From commencement (ongoing) |
| Perform a pre and post implementation audit of service capacity | 12 months post-implementation |

## Unanswered Questions and Opportunities for Further Research

At this juncture, the actual impact on CIVT service capacity is not known and as previously discussed this will require a pre-study and post-implementation audit to be performed. It would also be of interest to assess the impact of accelerated transfusion on capacity and patient flow efficiency in hospital oncology units.

Similarly, it is not known whether ‘accelerated transfusion’ (not exceeding 5ml/Kg/Hr) is non-inferior to ‘standard rate’ transfusions in terms of patients developing TACO. Post-implementation audit will continue locally but there is also scope for a larger multi-centre study. A larger study could have a similar design, where the patient acts as their own control. Alternatively a larger study would allow randomisation to accelerated or standard rate transfusion. Depending on the number of participants, this design however could lead to unintentional bias due to variation in patient characteristics across each arm of the study. It would also have the disadvantage of fewer accelerated transfusions taking place overall.

The study has also raised the question about the actual contribution of infusion rate of blood to the development of TACO, and whether this is independent of total volume infused and the presence of comorbid conditions and risk factors in the patient. As digital applications become more widespread in healthcare organisations there is now more potential for ‘big data’ analyses. It may now be possible to perform a multiple linear regression on these variables to address this question.

An interesting an unexpected finding in this study was the post-transfusion increase in MAP in both standard rate and accelerated rate transfusion, and the reason for this could only be speculated upon. The study was not designed to investigate this and the finding was based on relatively small numbers. Further contributions to the literature concerning changes to vital signs during and after red cell transfusion in normovolaemic patients from a larger population would be valuable. Beyond this, evidence as to whether the

increase indicates physiological or pathological response would also be required. Brain Natriuretic Peptide (BNP) testing is routinely used for diagnosing and monitoring heart failure and is also been used to support the differential diagnosis of pulmonary complications of transfusion. An increase of 1.5 times the baseline is compatible with TACO, and therefore a pathological increase (Zhou *et al*, 2005). This could be studied by performing serial BNP tests before, during and after transfusion and would indicate stretch of the cardiac muscle in response to volume-loading of the circulation. Assuming a statistically significant increase in MAP is present a concomitant statistically significant (but less marked) increase in BNP may indicate a non-pathological physiological response.

## Dissemination of Findings

Table 12.2 summarises the previous and planned dissemination of findings.

**Table 12.2: Summary of dissemination plan**

| Dissemination Method | Planned Date |
|---|---|
| International Society of Blood Transfusion and International Haemovigilance Network Conference (oral presentation on preliminary data) | June 2015 |
| Chief Scientific Officer's Awards and website (Partnering Patient's and Citizen's in Healthcare Science) | March 2017 |
| Bolton News (newspaper article) | March 2017 |
| Laboratory Medicine News (local newsletter to Trust and local GP's) | March 2017 |
| Trust Clinical Governance & Quality Committee, and Trust Acute Adult Care Division Governance Committee | June 2017 |
| Original research paper to be submitted to the British Journal of Haematology for publication | By Dec 2018 |
| Abstract for the British Society of Haematology Annual Scientific Meeting (oral or poster presentation) | April 2018 |
| Letters to surviving patients to thanks them for their participation as research participants and inform them of the outcome of the study | By April 2018 |

## Concluding Remarks –

### A Practice-Based Problem with a Practice-Based Solution

This study has opened debate about what constitutes a ‘safe’ rate of transfusion and challenged the belief that ‘faster’ rates of transfusion cause circulatory overload independently of pre-disposing comorbid conditions and risk factors. The process of unpacking this dogma has also exposed the inconsistencies and lack of standardisation in the literature and in practice when referring to the ‘rate’ of transfusion, and how this is significantly influenced by the combined effect of patient body weight and volume of blood units. Detailed reassessment and re-articulation of practice has provided new evidence for safely shortening blood transfusion infusion-time in medically selected patients with normovolaemic anaemia. A real-world problem of a resource-limited community-based service, challenged with meeting capacity demands impelled the team to question practice in order to find efficiencies. Having new evidence to change the way blood transfusion is delivered at home has potential to improve CIVT service capacity beyond blood transfusion. Patient-centred care is at the heart of the CIVT service and its individual team members. Importantly, this service development was achieved with the input and endorsement of CIVT practitioners and the patients who benefit from their care.

# References

Abraham, I. and Sun, D. (2012) 'The cost of blood transfusion in Western Europe as estimated from six studies.' *Transfusion Practice*, 52 pp. 1983-1988.

Adams, KW. and Tolich, D. (2011) 'Blood Transfusion: The Patient's Experience.' *American Journal of Nursing*, 111(9) pp. 24-30.

Age UK (2015). Evidence review: Loneliness in later life. https://web1.ageuk.org.uk/Documents/EN-GB/For-professionals/Research/Age_UK_Evidence_Review_on_Loneliness_June_2015.pdf?epslanguage=en-GB?dtrk=true [accessed 18.01.18]

Agrawal, S., Davidson, N., Walker, M., Gibson, S., Lim, C., Morgan, C. and Lowell, W. (2006) 'Assessing the total costs of blood delivery to hospital oncology and haematology patients.' Curr Med Res Opin, 22 pp. 1903-1909.

Agrawal, A., Hsu, E., Quirolo, K., Neumayr, L. and Flori, H. (2012) 'Red blood cell transfusion in paediatric patients with severe chronic anaemia: how slow is necessary?' *Paediatric blood and cancer*, 58(3) pp. 466-468.

Alder, P. and Alder, P. (1987) *Membership roles in field research.* Newbury Park, CA: Sage Publications.

Andrzejewski Jr, C., Popovsky, M., Stec, T., Provencher, J., O'Hearn, L., Visintainer, P. and Steingrub, J. (2012) 'Hemotherapy bedside biovigilance involving vital sign values and characteristics of patients with suspected transfusion reactions associated with fluid challenges: can some cases of transfusion associated circulatory overload have pro-inflammatory aspects?' *Transfusion*, 52(11) pp. 2310-2320.

Andrzejewski, C. J., Casey, M. and Popovsky, M. (2013) 'How we view and approach Transfusion-Associated Circulatory Overload: Pathogenesis, diagnosis, management, mitigation and prevention.' *Transfusion*, 53(3037-3047)

ANZSBT. (2011) Australian and New Zealand Society of Blood Transfusion Ltd and Royal College of Nursing Australia. Guidelines for the administration of blood components. 2nd ed. https://www.anzsbt.org.au/data/documents/guidlines/ANZSBT_Guidelines_Administration_Blood_Products_2ndEd_Dec_2011_Hyperlinks.pdf [accessed 30.11.17]

Arnold, E. and Lane, S. (2011) 'Qualitative Research in Transfusion Medicine.' Transfusion Medicine, 21 pp. 291-300.

Audit Commission (1999) First Assessment. A Review of district nursing services in England and Wales. https://archive.audit-commission.gov.uk/auditcommission/subwebs/publications/studies/studyPDF/1314.pdf (accessed 08.01.15)

Australian Red Cross Blood Service (2012). Blood Component Information. An extension of blood component labels. Circular of information. http://resources.transfusion.com.au/cdm/ref/collection/p16691coll1/id/18 (accessed 12.01.14)

Bacchetti, P., Deaks, S. and McCune, J. (2011) 'Breaking free of sample size dogma to perform innovative translational research.' *Sci Transl Med*, 3(87) p. 24.

Barbour, R.S. (2001) 'Checklists for improving rigour in qualitative research: a case of the tail wagging the dog?' *BMJ,* 332 pp. 1115-1117.

Bate, P. and Robert, G. (2006) 'Experience-based design: from re-designing the system around the patient to co-designing services with the patient.' *Qual Saf Health Care*, 15(5) pp. 307-310.

BCSH. (2009) British Committee for Standards in Haematology Guideline on the Administration of Blood Components (and addendum 2012). http://www.b-s-h.org.uk/media/5152/admin_blood_components-bcsh-05012010.pdf [accessed 30.11.17]

BCSH. (2012) 'Guideline on the investigation and management of acute transfusion reactions. Prepared by the British Committee for Standards in Haematology Blood Transfusion task force.' *Br J Haematol*, 159 pp. 143-153.

Benson, K., Popovsky, MA., Hines, D., Hume, H., Oberman, HA., Glassman, AB., Pisciotto, PT., Thurer, RL., Stehling, L., Anderson, KC. (1998) 'Nationwide survey of home transfusion practices.' *Transfusion*, 38 pp. 90-96.

Berstock, J., Beswick, A., Lengurerrand, E., Whitehouse, M. and Blom, A. (2014) 'Mortality after total hip replacement surgery.' *Bone Joint Research*, 3(6) pp. 175-182.

Blackwelder, W. C. (1982) '"proving the null hypothesis" in clinical trials.' *Controlled Clinical Trials*, 3 pp. 345-353.

Bolton NHSFT (2014) 'Clinical Transfusion Process Policies (Hospital Practice, Home Transfusion, Bolton Hospice).'

Bolton-Maggs, PHB (Ed) and Poles, D. *et al* on behalf of the Serious Hazards of Transfusion Steering Group (2017a) *The 2016 Annual SHOT report (2017)*.

Bolton-Maggs, PHB., Ball, J., Grey, S., Latham, T. and Poles, D. (2017b) 'The changing patterns of pulmonary complications reported to SHOT.' *B J Haem*, 176((suppl. 1)) p. 19.

Bolton-Maggs PHB (Ed) D Poles *et al*. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. (2016) *The 2015 Annual SHOT Report (2016).*

Bolton-Maggs, PHB (Ed), Poles, D., Watt, A., Thomas, D. on behalf of the Serious Hazards of Transfusion Steering Group. (2014) *The 2013 Annual SHOT Report (2014).*

Bolton-Maggs, PHB (Ed), Poles, D., Watt, A., Thomas, D., Cohen, H. on behalf of the Serious Hazard of Transfusion Steering Group. (2013) *The 2012 annual SHOT report (2013).*

Bolton-Maggs, PHB (Ed) and H Cohen on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. (2012) *The 2011 Annual SHOT Report (2012).*

Boyatzis, R. E. (1998) *Transforming qualitative information: thematic analysis and code development.* Thousand Oakes, CA: Sage.

Braun, V. and Clarke, V. (2006) *Using thematic analysis in psychology, Qualitative Research in Psychology.* Vol. 2.

BSQR (2005): Blood Safety and Quality Regulations (SI2005/50 as amended). European Union: https://www.legislation.gov.uk/uksi/2005/50/contents/made [accessed 07.01.15]

Charmaz, K. (2001) 'Qualitative interviewing and grounded theory analysis.' *In* Gubriu, J. and Holstein, J. (eds.) *Handbook of interview research: Context and method*. Thousand Oaks: Sage, p. 681.

Charmaz, K. (2003) 'Grounded Theory.' *In* Smith, J. (ed.) *Qualitative Psychology: A Practical Guide to Research Methods*. London: Sage

Clifford, L., Singh, A., Wilron, G., Toy, P., Gajic, O., Malinchoc, M., Herasevich, V., Pathak, J. and DJ, K. (2013) 'Electronic health record surveillance algorithms facilitate the detection of transfusion-related pulmonary complications.' *Transfusion*, 53(6) pp. 1205-1216.

Collins, J., Cochrane, G., Davies, J. and al, e. (1973) 'Some aspects of pulmonary function after rapid saline infusion in healthy subjects.' *Clin Sci Mol Med*, 45 pp. 407-410.

Connolly, SJ., Ezekowitz, MD., Yusuf, S., Eikelboom, J., Oldgren, J., Parekh, A., Pogue, J., Reilly, PA., Themeles, E., Varrone, J., Wang, S., Alings, M., Xavier, D., Zhu, J., Diaz, R., Lewis, BS., Darius, H., Diener, HC., Joyner, CD., Wallentin, L.; RE-LY Steering Committee and Investigators. (2009) 'Dabigatran versus warfarin in patients with atrial fibrillation.' *N Engl J Med*, 361 pp. 1139-1151.

Cotter, G., Mehra, M., Milo-Cotter, O., Dittrich, H. and Gheorghiade, M. (2008) 'Fluid overload in acute heart failure - re-distribution and other mechanisms beyond fluid accumulation.' *European Journal of Heart Failure*, 10 pp. 165-169.

CQC. (2010) Essential Standards of Quality and Safety.(CQC 2010) https://services.cqc.org.uk/sites/default/files/gac_-_dec_2011_update.pdf [accessed 07.01.15]

CQC. (2012) *Care Quality Commission Report on the state of healthcare and adult social care in England: an overview of key themes in care 2011/12.* http://www.cqc.org.uk/sites/default/files/documents/cqc__soc_201112_final_tag.pdf [accessed 07.01.15]

Cresswell, J. (2007) 'Designing a qualitative study.' *In Qualitative enquiry and research design: choosing among five approaches*. 2nd ed., Thousand Oaks, CA: Sage,

Deeks, J. and Higgins, JPT. (2010) Statistical algorithms in Review Manager 5. https://ims.cochrane.org/revman/documentation/statistical-methods-in-revman-5.pdf [accessed 11.10.17]

DH. (2009) Transforming Community Services. Ambition, action, achievement. Transforming services for acute care closer to home. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215781/dh_124196.pdf [accessed 08.01.15]

DH. (2005) Department of Health. Research governance framework for health and social care. 2nd ed. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/139565/dh_4122427.pdf [accessed 12.11.17]

DH. (2012a) Department of Health. NHS Patient Experience Framework. https://www.gov.uk/government/publications/nhs-patient-experience-framework [accessed 18.01.15]

DH. (2012b) Health and Social Care Act. http://www.legislation.gov.uk/ukpga/2012/7/contents/enacted [accessed 18.01.15]

DH. (2013a) Department of Health. The NHS Constitution. The NHS belongs to us all. https://www.gov.uk/government/publications/the-nhs-constitution-for-england [accessed 08.01.15)]

DH. (2013b) Department of Health. Effective Clinical and Financial Engagement: a Best Practice Guideline for the NHS. https://gov.uk/government/uploads/system/uploads/attachment_data/file/255655/effective_clinical_financial_engagement.pdf [accessed 19.02.15]

Dougherty, L. (1999) *Obtaining peripheral venous access (in: Intravenous Nursing Practice).* Dougherty, L. and Lamb, J. (Eds) Edinburgh: Churchill Livingstone.

Finch, J. (1993) '*It's great to have someone to talk to': ethics and politics of interviewing women.* In: Hammersley, M*. Social Research: Philosophy, Politics and Practice,* Sage Publications CA

Fitzgerald, M. e. a. (1999) 'Blood transfusion from the recipient's perspective.' *J Clin Nurs*, 8(5) pp. 593-600.

Fowler, F. and Mangione, T. (1990) *Standardised survey interviewing. Minimising interviewer-related error.* Newbury Park, CA: Sage Publications.

Fowler, F. J. (2004) 'Interviewer training.' *In* Lewis-Beck, M., Bryman, A. and Futing Liao, T. (Eds.) *The Sage encyclopedia of social science research methods*. Vol. 1. CA: Sage Publications, p. 521.

Gehrie, E., Hendrickson, J. and Tormey, C. (2015) 'Variation in vital signs resulting from blood component administration in adults.' *Transfusion*, 55(8) pp. 1866-1871.

Grant, JM. And Booth, A. (2009) ‘A typology of reviews: an analysis of 14 review types and associated methodologies’. *Health Information and Libraries Journal,* 26, pp.91-108.

Green, J., Pirie, L. and Davidson, A. (2013) Framework for the provision of blood transfusion out of the acute hospital setting. http://hospital.blood.co.uk/media/27199/home_tx_framework_post-shot-2013.pdf [accessed 06.01.15]

Grey, S. (2015) 'Haemovigilance data for transfusion-associated circulatory overload (TACO) provides a framework for informing patient-tailored rate and volume of transfusion.' *Vox Sanguinis*, 109((suppl. 1)) p. 41.

Grey, S., Kinsella, P., Sweeney, K., Steele, A. and Patalappa, C. (2016) 'A red cell dosage calculator could promote single unit red cell transfusion, prevent over-transfusion and reduce red cell usage.' *B J Haem*, 173((suppl. 1)) pp. 158-159.

Grey, S., Poles, D., Fogg, A. Bolton-Maggs, PHB. (2017a) Development of the Serious Hazards Of Transfusion Transfusion-Associated Circulatory Overload Checklist. Transfusion Medicine, 27, Suppl. 2, 44-45

Grey, S., Bolton-Maggs, P., Poles, D., Ball, J. and Lucero, H. (2017b) 'Time to refine transfusion-associated circulatory overload (TACO).' *B J Haem*, 176((suppl. 1)) pp. 137-138.

Guba, E.G. and Lincoln, Y.S. (1985) *Natruralistic Inquiry*. Newbury Park, CA, Sage Publications.

Guba, E.C.(1990) *The Paradigm Dialog.* Newbury Park, CA: Sage Publications.

Guest, G., Bunce, A., and Johnson, L. (2006). How many interviews are enough? An experiement with data saturation and variability. *Field Methods*. 18(1), 59-82.

Hadjianastassiou, V., Virich, G. and Lennox, I. (2002) 'Use of the blood transfusion service in total knee replacement arthroplasty.' *Knee*, 9 pp. 145-148.

Hilton, A., Pellegrino, V. and Scheinkestel, C. (2008) 'Avoiding common problems associated with intravenous fluid therapy.' *Med J Aust*, 189(9) pp. 509-513.

Holte, K., Jensen, P. and Kehlet, H. (2003) 'Physiologic effect of intravenous fluid administration in healthy volunteers.' *Anesth Analg*, 96 pp. 1504-1509.

Hunter, A. and Brewer, J. (2006) Foundations of Multi-methods Research: synthesizing styles. Thousand Oaks, CA: Sage Publications.

ISBT. (2014) Transfusion-associated circulatory overload (TACO) 2014 revision. International Society of Blood Transfusion Working Party on haemovigilance in collaboration with the International Haemovigilance Network. Re-publication of draft (Dec 2014). http://www.isbtweb.org/fileadmin/user_upload_files2015_haemovigilance/TACO_definition_validation_form-Jan2015_haemovigilance.pdf [accessed 31.03.15]

ISBT. (2017) 2017 TACO Revised Reporting Criteria Validation TACO definition revision group: IHN/ISBT haemovigilance working party/AABB [online] http://www.isbtweb.org/working-parties/haemovigilance/ [accessed 01.12.17]

Jayabose, S., Tugal, O., Ruddy, R., Wuest, D. and Ciavarella, D. (1993) 'Transfusion therapy for severe anaemia.' *Am J Paediatr Haematol/Oncol*, 15 pp. 324-327.

Kings Fund (2011) The patient-centred care project. Evaluation report. https://www.kingsfund.org.uk/sites/default/files/field/field_publication_file/patient-centred-care-project-evaluation-aug11.pdf [accessed 18.01.15]

Koepke, MD, Nyman, JA., Koepke, JA. (1988) 'Home blood transfusions: the medical, economic and legal issues surrounding a new treatment procedure.' *J Health Polit Policy Law*, 13

Kopko, P. and Holland, P. (1999) 'Transfusion related acute lung injury.' *Br J Haematol*, 105 pp. 322-329.

Kumar, P. and Clark, M. (1999) *Clinical Medicine.* 4th ed., London: WB Saunders.

Landsteiner, K. (December 11th, 1930) *On individual differences in human blood.* https://www.nobelprize.org/nobel_prizes/medicine/laureates/1930/landsteiner-lecture.pdf [accessed 04.01.17]

Mays, N. and Pope, C. (2006) *'Quality in Qualitative Research*.' In Pope, C. and Mays, N. (eds.) *Qualitative Research in Healthcare*. 3rd ed., Malden, MA: Blackwell Publishing, pp. 32-42.

Li, G., Rachmale, S., Kojicic, M., Shajehan, K., Malinchoc, M., Kor, D. and Gajic, O. (2011) 'Incidence and risk factors for transfusion related circulatory overload among medical intensive care units.' *Transfusion*, 52-2 pp. 338-343.

Lofland, J., Snow, D., Anderson, L. and Lofland, L. (2006) *Analysing Social Settings: A Guide to Qualitative Observation and Anlysis.* Belmont CA: Wadsworth/Thompson.

Mac Rate, E. E. and Taylor, C. (2012) *On behalf of the Blood Stocks Management Scheme (BSMS) Steering Group. The 2011-2012 annual BSMS report.* London: BSMS.

Macedo, E., Bouchard, J. and Soroko, S. e. a. (2010) 'Fluid accumulation, recognition and staging of acute kidney injury in critically ill patients.' *Crit Care*, 14 p. R82.

Malbrain, M., Marik, P., Witters, I., Cordemans, C., Kirkpatrick, A., Roberts, D. and Van Regenmortel, N. (2014) 'Fluid overload, de-resuscitation and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice.' *Anaesthesiology Intensive Therapy*, 46(5) pp. 361-380.

Malterud, K. (2001) 'Qualitative research: standards, challenges and guidelines.' *Lancet*, 358 pp. 483-488.

Menis, M., Anderson, SA., Forshee, RA., McKean, S., Johnson, C., Holness, L., Warnock, R., Gondalia, R., Worrall, CM., Kelman, JA., Ball, R., Izurieta, HS. (2012) 'Transfusion associated circulatory overload among inpatient US elderly as recorded in Medicare administrative databases during 2011.' *Transfusion*, 52((169A)) pp. 0041-1132.

MHRA. (2010) Serious adverse blood reactions and events (SABRE). User guide for mandatory haemovigilance reporting in the UK. Published by the MHRA, the UK competent authority for blood safety and quality. http://www.mhra.gov.uk/home/greoups/dts-aic/documents/websiteresources/con2022529.pdf [accessed 20.01.15]

Mills, E., Chen, A.-W., Wu, P., Vail, A., Guyatt, G. and Altman, D. (2009) 'Design, analysis and presentation of cross-over trials.' *Trials*, 10 p. 27.

Monitor. (2015) Moving healthcare closer to home: summary. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/459400/moving_healthcare_closer_to_home_summary.pdf [accessed 11.11.17]

Morse, J. (2003) 'Principles of mixed methods and multi-method research.' *In* Tashakkori, A. and Teddlie, C. (eds.) *Handbook of mixed methods in social and behavioral research.* Thousand Oaks, CA: SAGE Publications,

Murphy, EL., Kwaan, N., Looney, M., Gajic, O., Hubmayr, R., Gropper, MA., Matthay, MA., Bacchetti, P., Toy, P. (2010) 'Transfusion associated circulatory overload: risk factors and mortality.' *Transfusion*, 50 (127A-128A) pp. 0041-1132.

Narick, C. Triulzi, D. and Yazer, M. (2012) 'Transfusion associated circulatory overload after plasma transfusion.' *Transfusion*, 52(1) pp. 160-165.

NHSBT. (2012) NHSBT portfolio of blood components and guidance for their clinical use. Specification SPN223/5.4 ed. http://hospital.blood.co.uk/media/28748/spn223.pdf [accessed 12.01.14]

NHSBT. (2014) *About Blood*. [Online] http://www.blood.co.uk/about-blood/ [accessed on 26.11.2014]

NHS England (2013a) Transforming participation in health and care. Vol. Publications gateway reference No. 00381. https://www.england.nhs.uk/wp-content/uploads/2013/09/trans-part-hc-guid1.pdf [accessed 18.01.15]

NHS England (2013b) Putting Patients First. The NHS England business plan for 2013/14 - 2015/16. https://www.england.nhs.uk/wp-content/uploads/2013/04/ppf-1314-1516.pdf [accessed 19.02.15]

NHS England (2014) Five year forward plan. https://www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf [accessed 11.11.17]

NHSLA. (2013) NHS Litigation Authority Risk Management Standards 2013-14. http://www.nhsla.com/pages/publications.aspx?library=safety%7cstandards [accessed 07.01.15]

NICE. (2010) Chronic heart failure in adults: management. Clinical Guideline (CG108). https://www.nice.org.uk/guidance/Cg108 [accessed 05.01.17]

NICE. (2011) 'Hypertension: clinical management of primary hypertension in adults. Clinical Guideline CG127.' https://www.nice.org.uk/guidance/cg127 [accessed 05.01.17]

NICE. (2015) 'Blood transfusion' Guideline NG24. https://www.nice.org.uk/guidance/ng24 [accessed 15.12.15]

Norfolk, D. (Ed) (2013) 'Handbook of transfusion medicine'. UK Blood Services, 5th Ed, The Stationary Office, Norwich.

NPSA. (2008) A risk matrix for risk managers. Ref: 0676. http://www.nrls.npsa.nhs.uk/resources/?entryid45=59833&q=0%C2%ACrisk%C2%AC&p=1 [accessed 04.01.17]

NPSA. (2009) National Patient Safety Agency National Research Ethics Service. Information sheets and consent forms. Guidance for researchers and reviewers. version 3.5 (May 2009)

NQB. (2012) Patient Experience Framework. National Quality Board. https://institute.nhs.uk/patient_experience/guide/the_policy_framework.html [accessed 26.11.12]

Oakley, A (1981) 'Interviewing Women: a contradiction in terms.' In Roberts, H (ed.) Doing Feminist Research. London: Routledge and Kegan Paul

Olgun, H., Buyukavci, M., Sepetcigil, O., Karacan, M., Ceviz, N. and Yildirim, Z. (2009) 'Comparison of safety and effectiveness of two different transfusion rates in children with severe anaemia.' *J Paediatr Haematol Oncol*, 31 pp. 843-846.

Pagano, M. and Gauvreau, K. (2000) *Principles of Biostatistics.* 2nd ed., Belmont CA: Brooks and Cole.

Patton, M. (1999) '*Enhancing the quality and credibility of qualitative analysis*.' *Health Serv Res*, 34(5 pt 2) pp. 1189-1208.

Piccin, A., Cronin, M., Murphy, C., Eakins, E., Lawlor, E. (2009) 'Transfusion associated circulatory overload: incidence and risk factors.' *Blood*, 114(22) pp. 0006-4971.

Popovsky, MA., Audet, AM., Andrzejewski C. Jr. (1996) 'Transfusion associated circulatory overload in orthopaedic surgery patients: a multi-institutional study.' Immunohaematology, 12 pp. 87-89.

Popovsky, M. A. (2006) 'Pulmonary consequences of transfusion: transfusion related acute lung injury and transfusion associated circulatory overload.' Transfusion and apheresis science, 34(3) pp. 243-244.

Popovsky, M. (2008) 'Transfusion associated circulatory overload.' *ISBT Science Series*, 3 pp. 166-169.

Popovsky, M. (2009) 'Transfusion-associated circulatory overload: the plot thickens.' *Transfusion*, 49 pp. 2-4.

Popovsky, M. (2010) 'To breathe or not to breathe: that is the question. Pulmonary complications of transfusion.' *Transfusion*, 50 pp. 2057-2062.

Public Health England (2016). Healthcare Associated Infection (HAI): Point Prevalence Survey, England. https://www.gov.uk/government/publications/healthcare-associated-infections-hcai-point-prevalence-survey-england#history [accessed: 22.05.18]

Rabiner, SF and Telfer, MC. (1970) 'Home transfusions for patients with haemophilia A.' *N Engl J Med*, 283 pp. 1011-1015.

Rana, R. e. a. (2006) 'Transfusion related acute lung injury and pulmonary edema in critically ill patients: a retrospective study.' *Transfusion*, 46(9) pp. 1478-1483.

Raval, J., Mazepa, M., Russell, S., Immel, C., Whinna, H. and Park, Y. (2013) 'Passive reporting greatly under-estimates the rate of transfusion associated circulatory overload after platelet transfusion.' *Transfusion*, 53(137A-138A)

RCP (2012) Royal College of Physicians. National Early Warning Score (NEWS). Standardising the assessment of acute illness in the NHS. Report of a Working Party. London: RCP

Ritchie, J. and Spencer, L. (1994) 'Qualitative data analysis for applied policy research.' *In* Burgess, B. a. (ed.) *Analysing Qualitative Data*. London: Routledge, pp. 173-194.

Roback, J., Combs, M., Grossman, B. and Hillyer, C. (2008) Technical Manual. 16th ed., pp. 613-624. Bethesda: American Association of Blood Banks.

Robert, G. and Cornwell, J. (2011) What matters to patients? Policy recommendations. A report for the department of health and NHS Institute for Innovation and Improvement. https://www.institute.nhs.uk/images/Patient_Experience/Final%20Policy%20Report%20pdf%20doc%20january%202012.pdf [accessed 18.01.15]

Robinson, S., Harris, A., Atkinson, S., Atterbury, C., Bolton-Maggs, P., Elliott, C., Hawkins, T., Hazra, E., Howell, C., New, H., Shackleton, T., Shreeve, K., Taylor, C. (2018). The administration of blood components: a British Society for Haematology Guideline. *Transfusion Medicine.* 28, (1). pp. 3-21.

Royal Society (1666) Philosophical Transactions. An advertisement concerning the invention of the transfusion of bloud. Philosophical Transactions. 23-32 ed., Vol. 2, p. 489.

Sealed Envelope Ltd (2012). Power calculator for binary outcome non-inferiority trial. [Online] Available from: https://www.sealedenvelope.com/power/binary-noninferior/ [accessed 22.05.18].

SHOT (2014) Serious Hazards of Transfusion. Definitions of current reporting categories and what to report. http://www.shotuk.org/wp-content/uploads/SHOT-Definitions-Jan-2015.pdf [accessed 20.01.15]

Spencer, L., Richie, J., Lewis, J., Dillon, L. (2003) *Quality in Qualitative Evaluation: a framework for assessing research evidence*. Government chief social researcher's office, Prime Minister's Strategy Unit, Cabinet Office, London

Srivastava, A. and Thomson, S. (2009) 'Framework Analysis: a qualitative methodology for applied policy research.' *JOAAG*, 4(2) pp. 72-79.

Sturgis, C. (1942) 'The history of blood transfusion.' *Bull Med Libr Assoc*, 30(2) pp. 105-112.

Taylor, G. and Ussher, J. (2001) 'Making sense of S&M:  a discourse analytic account.' *Sexualities*, 4(3) pp. 293-314.

Thomas, G., Carbo, C., Curtis, B., Martinod, K., Mazo, I., Schatzberg, D., Cifuni, C., Fuchs, T., Von Andrian, U., Hartwig, J., Aster, R. and Wagner, D. (2012) 'Extracellular DNA traps are associated with the pathogenesis of TRALI in humans and mice.' *Blood*, 119(26) pp. 6335-6343.

Tseng, E., Spradbrow, J., Cao, X., Callum, J. and Lin, Y. (2016) 'An order set and check list improve physician transfusion ordering practices to mitigate the risk of transfusion-associated circulatory overload.' *Transfusion Medicine*, 26(2) pp. 104-110.

Tucker, H. (2011) *Blood Work: a tale of medicine and murder in the scientific revolution.*: WW Norton and Company Inc, New York.

Varney, S. and Guest, J. (2003) 'The annual cost of blood transfusion in the UK.' *Transfusion Medicine*, 13 pp. 205-218.

Welek, S. (2005) 'Statistical methods for the analysis of two-arm non-inferiority trials with binary outcomes.' *Biom J*, 47(1) pp. 48-61.

Whittaker, S. (2006) 'Qualitative Research in Transfusion Medicine: closing the gap.' ISBT Science Series, 1 pp. 133-139.

Wibberley, C. and Price, O. (2012) 'An exploratory study investigating the impact of procedures used to manage patient substance misuse on nurse-patient relationships in a medium secure forensic unit.' *Journal of Psychiatric and Mental Health Nursing*, 19(8) pp. 672-680.

Zhou, L., Giacherio, D., Cooling, L. and Davenport, R. (2005) 'Use of brain natiuretic peptide as a diagnostic marker in the differential diagnosis of transfusion-associated circulatory overload.' *Transfusion*, 45(7) pp. 1056-1063.

# Appendices

# Appendix A:

**ACTION: CHIEF INVESTIGATOR & CONSULTANT HAEMATOLOGIST**

**SAE/SAR REPORT FORM (Document L) version 1: ATS2014/Doc(L) 28.08.14**

| | |
|---|---|
| **Participant Identifier** | |
| **Date of this transfusion (DD-MM-YY)** | |
| **Date of SAE/SAR (DD-MM-YY)** | |
| **What is being reported? (SAE or SAR)** | |

| | | | | | |
|---|---|---|---|---|---|
| **Describe the SAE/SAR** | | | | | |
| **What corrective/preventive action has been taken?** | | | | | |
| **Causality Assessment (Consultant Haematologist)** | **Imputability NA** | **Imputability 0** | **Imputability 1** | **Imputability 2** | **Imputability 3** |
| | Not assessable | Excluded | Possible | Likely | Certain |
| **Rationale for Imputability Score** | | | | | |
| **Is external reporting to SHOT/MHRA required?** | **YES/NO** | **Describe Rationale** | | | |
| | | | | | |
| **For imputability 1-3: Does this SAE/SAR require termination of the study?** | **YES/NO** | **Describe Rationale** | | | |
| | | | | | |
| **Chief Investigator** | Name (PRINT) SHARRAN GREY | | | Date | |
| | Signature | | | | |
| **Consultant Haematologist** | Name (PRINT) | | | | |
| | Signature | | | | |

**RETURN THIS FORM TO SHARRAN GREY AFTER TRANSFUSION (Original Copy in Site File)**

# Appendix B:

**Accelerated Transfusion Pre-Prescription Check-List**

**(Document E) version 1: ATS2014/Doc(E) 28.08.14**

**ACTION: PRESCRIBING MEDICAL OFFICER**

| | |
|---|---|
| **Participant Identifier** | |
| **Date Transfusion to be Given** | |

**I have checked that the patients still complies with the following medical exclusion criteria for accelerated (60 minutes per unit) transfusions:**

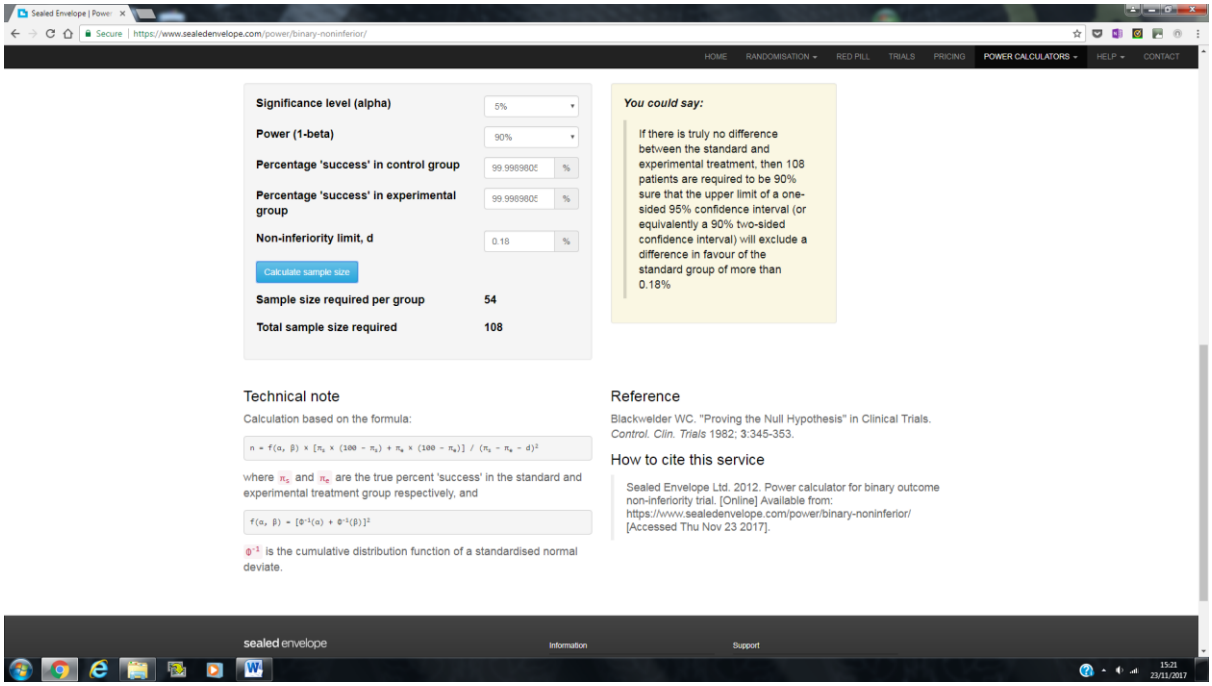
| | **Exclude If** |
|---|---|
| **HISTORY** | Patient has had echocardiography with reported heart failure. Reported moderate to severe left ventricular dysfunction (ejection fraction <35%). All patients with heart failure should have had echocardiography as per NICE guidelines. Check whether an echocardiogram has been performed previously with the Cardiology Department before accepting a patient into the study. |
| | Severe aortic stenosis |
| | Hypoalbuminaemia (<35g/L) |
| | Low body weight (<50Kg) |
| | Significant renal failure (eGFR <30ml/min) |
| | Significant liver failure (bilirubin >µ30mol/L) |
| **EXAMINATION*** | Oedema |
| | Cough, dyspnea and/or respiratory rate >20 breaths per minute |
| | Tachycardia (heart rate >100 beats per minutes) |
| | Un-treated or uncontrolled hypertension (diastolic >95 mmHg, systolic >160 mmHg) |

***Tick box if not able to examine at the time of writing the prescription (to be assessed as part of pre-transfusion clinical assessment** ☐

| | |
|---|---|
| **Name** | |
| **Designation** | |
| **Signature** | |
| **Date** | |

**Place this form with the blood prescription document**
**Return this form to Sharran Grey after the Transfusion (Original to be held in Site File)**

# Appendix C:


Sealed Envelope | Power
Secure | https://www.sealedenvelope.com/power/binary-noninferior/
HOME RANDOMISATION RED PILL TRIALS PRICING POWER CALCULATORS HELP CONTACT
Significance level (alpha) 5%
Power (1-beta) 90%
Percentage 'success' in control group 99.998980
Percentage 'success' in experimental group 99.998980
Non-inferiority limit, d 0.18 %
Calculate sample size
Sample size required per group 54
Total sample size required 108
You could say:
If there is truly no difference between the standard and experimental treatment, then 108 patients are required to be 90% sure that the upper limit of a one-sided 95% confidence interval (or equivalently a 90% two-sided confidence interval) will exclude a difference in favour of the standard group of more than 0.18%
Technical note
Calculation based on the formula:
n = f(α, β) × [π_c × (100 − π_c) + π_e × (100 − π_e)] / (π_c − π_e − d)²
where π_c and π_e are the true percent 'success' in the standard and experimental treatment group respectively, and
f(α, β) = [Φ⁻¹(α) + Φ⁻¹(β)]²
Φ⁻¹ is the cumulative distribution function of a standardised normal deviate.
Reference
Blackwelder WC. "Proving the Null Hypothesis" in Clinical Trials. Control. Clin. Trials 1982; 3:345-353.
How to cite this service
Sealed Envelope Ltd. 2012. Power calculator for binary outcome non-inferiority trial. [Online] Available from: https://www.sealedenvelope.com/power/binary-noninferior/ [Accessed Thu Nov 23 2017].
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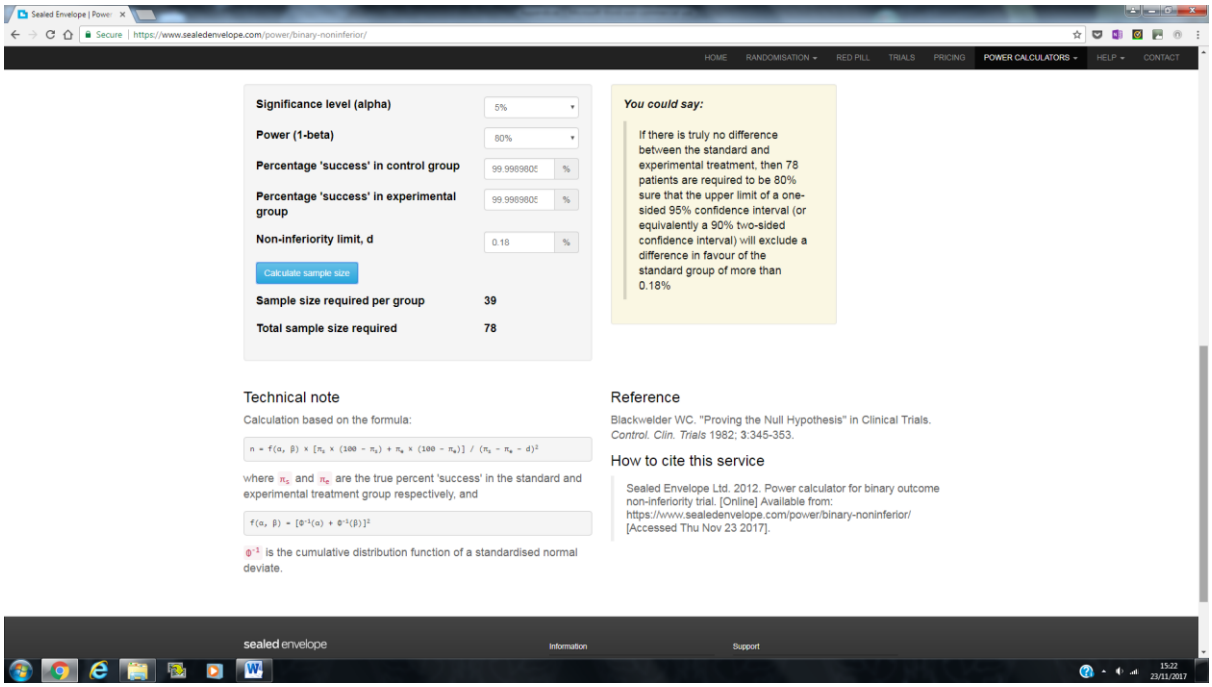
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HOME RANDOMISATION RED PILL TRIALS PRICING POWER CALCULATORS HELP CONTACT
Significance level (alpha) 5%
Power (1-beta) 80%
Percentage 'success' in control group 99.998980
Percentage 'success' in experimental group 99.998980
Non-inferiority limit, d 0.18 %
Calculate sample size
Sample size required per group 39
Total sample size required 78
You could say:
If there is truly no difference between the standard and experimental treatment, then 78 patients are required to be 80% sure that the upper limit of a one-sided 95% confidence interval (or equivalently a 90% two-sided confidence interval) will exclude a difference in favour of the standard group of more than 0.18%
Technical note
Calculation based on the formula:
n = f(α, β) × [π_c × (100 − π_c) + π_e × (100 − π_e)] / (π_c − π_e − d)²
where π_c and π_e are the true percent 'success' in the standard and experimental treatment group respectively, and
f(α, β) = [Φ⁻¹(α) + Φ⁻¹(β)]²
Φ⁻¹ is the cumulative distribution function of a standardised normal deviate.
Reference
Blackwelder WC. "Proving the Null Hypothesis" in Clinical Trials. Control. Clin. Trials 1982; 3:345-353.
How to cite this service
Sealed Envelope Ltd. 2012. Power calculator for binary outcome non-inferiority trial. [Online] Available from: https://www.sealedenvelope.com/power/binary-noninferior/ [Accessed Thu Nov 23 2017].
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# Appendix D:

**PATIENT INVITATION LETTER**
**(Document B1) Version: 2 Ref: ATS2014/Doc(B1) Date 05.05.14**

**Study Title: Accelerated Blood Transfusion**

Dear Sir/Madam,

We would like to invite you to take part in a research study looking at the duration of blood transfusions.

A doctor from our Clinical Haematology Team has recommended blood transfusion as part of the treatment for your condition.

If you are agreeable, we would like to offer you blood transfusion(s) administered over a shorter length of time. If you agree, we would also like to talk to you about your experience of it.

Accompanying this letter, you will have received an information sheet which describes in more detail what this study is about. Please take time to read the leaflet. If you have questions about any aspect of the study your consultant would be happy to answer them. Many thanks for taking the time to read this letter and information sheet.

If we haven't heard from you within 2 weeks, we will telephone you once.

Yours sincerely,

*Haematology Consultant/Specialty Doctor*

# Appendix E:

**(PATIENT) PARTICIPANT INFORMATION SHEET (Document B2)**
**Version: 2 Ref: ATS2014/Doc(B2) Date:05.05.14**

**Study title: Accelerated Blood Transfusion**

## Introduction

You are invited to take part in a research study looking at the duration of blood transfusions. Your doctor has recommended blood transfusion as part of the treatment for your condition.

Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information sheet. Do talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. This leaflet describes what the research is about and what it would involve for you.

**Part 1** tells you about the purpose of the study.
**Part 2** gives you more detailed information about the conduct of the study.

## Background

Red blood cells are made in the bone marrow and carry oxygen around the body. Certain diseases and medications can stop red blood cells being made or destroy them too early. When this happens, anaemia will develop causing tiredness, lethargy and breathlessness. A red blood cell transfusion is a treatment given to correct anaemia. Two bags of red cells are usually given in one treatment over 90 minutes per bag (3 hours in total).

## Part 1

## What is the purpose of the study?

The aim of this study is to see whether the treatment time for red blood cell transfusion (2 bags) can be administered over a shorter period of time, and to understand patient's and nurses experience of it. The study will also evaluate impacts on organisational economics and service capacity.

**Why have I been invited?**

Your doctor has recommended red blood cell transfusions as part of your treatment and thinks you may be medically suitable to receive your blood transfusion over a shorter length of time.

**Do I have to take part?**

It is up to you whether you decide to join the study. You have this information sheet to help you decide and we can also answer any questions you may have. If you agree to take part, we will ask you to sign a consent form. You are free to withdraw at any time without giving a reason. This would not affect the standard of care you would receive.

**What will happen to me if I take part?**

The number and frequency of your blood transfusions will not be affected by participating in the study. You will always receive the same standard of care.

A nurse or member of the haematology team will weigh you so that we can select bags of red cells of a volume that is appropriate to your body weight. This will be done at home at a time convenient to yourself.

**The first blood transfusion** administered in the study will be the standard length of time (over 90 minutes per bag – a total of 3 hours). Your vital sign measurements (blood pressure, heart rate and breathing rate) will be recorded before the transfusion. A member of the team will visit you around 24 hours after the transfusion to check on you, and record your vital signs again.

**The second and subsequent transfusion(s)** administered in the study will be the shorter length of time (over 60 minutes per bag – a total of 2 hours). Your vital sign measurements (blood pressure, heart rate and breathing rate) will be recorded before the transfusion. A member of the team will visit you around 24 hours after the transfusion to check on you, and record your vital signs again.

After you have had some shorter transfusions, we may ask if we can come and talk to you about your experience of it. This will be in the form of a short (no longer than 60 minute) interview that will be recorded on a dictaphone. This will allow us to transcribe what has been said later. You can stop the recording at any time and ask for words to be deleted or rephrased. The recording will not identify you i.e. it will be kept anonymous. The interview will take place on a time and date convenient to yourself. We do not expect you to be asked to do more than one interview, but it is possible that we may ask

for a follow-up interview. You can still take part in the blood transfusion part if you don't wish to be interviewed.

**What will I have to do?**

We will ask you to be at home and available for a check-up around 24 hours after your transfusion, and to take part in one interview at a later date (if you agree). All other aspects of you blood transfusion treatment will remain the same. Participating in this study will not affect any other treatment you may be receiving.

**What are the possible disadvantages of taking part?**

You would have to be available for a small number of additional home visits.

- To be weighed at the beginning of the study
- To have a short check-up the day after your transfusion
- To have one short interview

These visits would be arranged in advance with you for a time that is convenient to yourself and where possible combined with other planned visits.

**What are the side-effects of the treatment received when taking part?**

There are uncommon side-effects of blood transfusion regardless of the duration of the transfusion. These will have been explained to you as part of your regular blood transfusion treatment. You will also have been given the information leaflet "Receiving Blood Transfusion as a Day Case" which tells you about the symptoms of blood transfusion reactions and what to do if you suspect a reaction and need medical help. You should follow this guidance in exactly the same way after receiving a shorter duration blood transfusion.

Any fluid administered into a vein (including blood) could cause 'fluid overload' if given too quickly or if an excessive volume is given. In 2011 there were 33 patients across the UK who were reported to have developed fluid overload after receiving 1-2 units of red cells (out of an estimated 2,255,825 units transfused in the UK). Fluid overload can cause problems with the heart and breathing, and in severe cases can be fatal. The chance of fluid overload developing is minimised by recognising patients who may be at risk of fluid overload and ensuring they receive fluid (and blood) over a length of time appropriate to their condition. The eligibility criteria for participating in this study have been designed to take account of this.

**What are the possible benefits of taking part?**

Having a shorter transfusion will not make your treatment more effective in any way, but it will reduce the amount of time you spend receiving it. We

cannot promise the study will help you, but the information we get from this study may help other people needing regular blood transfusions.

**What happens when the research study stops?**

You will still be offered your blood transfusions as normal. Whether you receive them over a standard or shorter duration will depend upon the overall outcome of the study and your individual response to shorter transfusions.

**What if there is a problem?**

Any complaint about the way in which you have been dealt with in the study or any possible harm you might suffer will be addressed (see part 2 for more details).

**Will my taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are covered in part 2.

This completes part 1. If you are interested and you are considering participation, please read the additional information in part 2 before making a decision

---

**Part 2**

**What if relevant new information becomes available?**

Sometimes we get new information about the administration of blood transfusions. If this happens, the clinical haematology team will tell you and discuss whether or not you should continue in this study. If you decide not to carry on, the team will make arrangements for your usual treatment to continue. If you decide to continue, we may ask you to sign an agreement outlining the discussion.
Or
Your haematology doctor may decide to withdraw you from the study. He/she will discuss the reasons for this with you and arrange for your usual treatment to continue.
Or
If the study is stopped for any other reason, we will tell you and arrange for your usual treatment to continue.

**What will happen if I don't want to carry on with the study?**

If you withdraw from the study we will need to use the data collected on you up to the point at which you withdraw. We would advise you not to withdraw before you have had your check-up after your blood transfusion (as this is in your best interests). We would ask you if we could use the data collected on that visit but if you do not want it to be used then it would be destroyed.

**What if there is a problem?**

**Complaints**

In the first instance we would ask you to report your complaint to any of the following people:

Bolton Community IV Team: 01204 462890
Clinical Haematology Team: 01204 390511
Sharran Grey (Chief/Principal Investigator): 01204 390254

We would aim to address any complaint at this stage. If you feel you need to take the complaint elsewhere or make a more formal complaint, you should contact:

The Patient Advice and Liaison Service (PALS) on by telephone on: 01204 390193. An answer service is available. You can also email PALS: PALS@boltonft.nhs.uk or you can write to them at:

Patient Advice and Liaison Service (PALS)
Bolton NHS Foundation Trust
Minerva Road
Farnworth
Bolton
BL4 0JR

**Harm**

In the event that something goes wrong and you are harmed during the research and this is due to someone's negligence, then you have grounds for a legal action for compensation against Bolton NHS Foundation Trust, but you may have to pay your legal costs. The normal National Health Service complaints procedures will still be available to you.

**Will my taking part in the study be kept confidential?**

Yes. The data relating to the actual blood transfusion part of the study will be recorded on paper and you will be identified by code (not by name). The data

will be: a checklist to say whether you meet certain medical criteria; your vital sign observations before and after the transfusions, and consent forms. This data (which will not identify you) will be transcribed into a file that will be kept on an NHS computer which is password protected. The paper copies will be kept securely on NHS premises. The data relating to the interview (if you agree to take part) will also identify you by code (not by name) however you need to be aware that quotations from the interview may appear in print. This data will be a recording of the interview and will be kept on a computer which is password protected and will not be identifiable as you. The data will only be accessed or viewed by: Bolton Community IV Team, Clinical Haematology Team and the Chief Investigator. All data (paper and computer records) will be securely destroyed at the end of the study (no later than the end of 2018).

**Involvement of the General Practitioner/Family Doctor**

If you agree to participate in this study a letter will be sent to your GP informing them of this for your medical records held by your GP. We will obtain your consent before doing so.

**What will happen to the results of the research study?**

The results will be written into a doctoral thesis about accelerated blood transfusions by the Chief/Principal Investigator. It is likely the results will also be published in a number of medical journals. You will not be identified as a participant. Depending upon the outcome of the research, the Clinical Haematology medical staff may continue to offer and prescribe shorter transfusions for patients who meet the medical criteria. We can inform you of the outcome of the study if you wish.

**Who is organising and funding the research?**

<u>The research is being organised and co-ordinated by</u>:

Sharran Grey (Chief/Principal Investigator)
Consultant Biomedical Scientist (Blood Transfusion Clinical Lead)
Royal Bolton Hospital
Bolton NHS Foundation Trust
BL4 0JR Tel: 01204 390254

<u>The other members of the research team are:</u>

Dr Clare Barnes (Consultant Haematologist), Royal Bolton Hospital
Dr Mark Grey (Consultant Haematologist), Blackpool Victoria Hospital
Dr Yin Thi (Consultant Haematologist), Royal Bolton Hospital
Dr Karen Lipscomb (Consultant Cardiologist), Royal Bolton Hospital

Dr Krystyna Porczynska (Haematology Specialty Doctor), Royal Bolton Hospital
Dr Heyam Hashim (Haematology Specialty Doctor), Royal Bolton Hospital
Mrs Louise Merrick (Haematology Clinical Nurse Specialist), Royal Bolton Hospital
Mrs Joanne Bowman (Haematology Specialist Nurse), Royal Bolton Hospital
Mrs Susan Mikolajewski (Bolton Community IV Team Leader)

No funding has been sought for this research. The only additional equipment required for the study was a patient weighing scale (costing approximately £200) and has been purchased using funds from the Clinical Haematology endowment fund.

**Who has reviewed this study?**

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by:

Research Ethics Committee North West – Preston (14/NW/0229)
Manchester Metropolitan University Research Ethics Committee

This study relates to research protocol document number:
ATS2014/Doc(A)(version 1)

**Further Information and Contact Details**

**General Information about the research**

Bolton Community IV Team: 01204 462890
Clinical Haematology Team: 01204 390511
Sharran Grey (Chief/Principal Investigator): 01204 390254

If you have specific questions (including advice as to whether you should participate), you will be directed to the appropriate member of the team depending on the nature of your question.

If you wish to speak to an independent person outside the research team about participating in this study, you can contact Alison Loftus (Research and Development Co-ordinator) at the Royal Bolton Hospital) on 01204 390390.

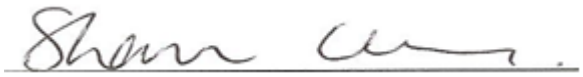
These numbers can also be used if you have any concerns during the study.

Emergency contacts numbers and advice are listed in your ‘receiving blood transfusion as a day case’ booklet.

**What to do next**

If you would like to be a participant in this study, please ring the Clinical Haematology Office on 01204 390511, or inform the doctor/nurse at your next clinic appointment. We will then make arrangements to take your consent to be involved in the study.

Thank you for taking time to consider this study.
Yours Sincerely,



Sharran Grey
Consultant Biomedical Scientist/Blood Transfusion Clinical Lead
(Chief/Principal Investigator)
Royal Bolton Hospital

# Appendix F:

## (PATIENT) PARTICIPANT CONSENT FORM
## (Document B3) Version: 1 Ref: ATS2014/Doc(B3) Date: 12.01.14

**Accelerated Transfusion Study**

| |
|---|
| **Patient (Participant) Study Number:** |
| **Patient's Date of Birth:** |
| **Patient's Initials:** |

| | | Patient Initials |
|---|---|---|
| **1.** | I wish to participate in this study. I confirm that I have read and understood the information sheet (ATS2014/Doc(B2), version number 2). I have had the opportunity to consider the information, ask questions (if any) and have had these answered satisfactorily. | |
| 2. | I understand that my participation is voluntary and I am free to withdraw at any time without giving a reason, without my medical care or legal rights being affected. | |
| 3. | I understand that if I withdraw, the data collected from me up to that point will be used in the study. | |
| 4. | I agree to the storage of my personal information (paper and electronic) for the purposes of this study (until the end of 2018). I understand that any information that could identify me will be kept strictly confidential and that no personal information will be included in the study report or other publication. | |
| 5. | I understand that the relevant sections of my medical notes and data collected in this study may be looked at my individuals from Bolton NHS Foundation Trust, Research Ethics Committees or regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to access my records. | |
| 6. | I agree for a doctor from the Clinical Haematology Team to assess my medical history to check that I am medically suitable to take part in this study, and that he/she may decide in my best interests that I am not suitable for shorter transfusions at some point in the study. | |
| 7. | I agree to my General Practitioner (GP) being informed by letter of my participation in this study | |
| 8. | I understand that the nurse administering my blood transfusion will check my willingness to continue in the study before every transfusion. | |
| 9. | I agree to being invited to be interviewed about my experience of shorter transfusions and that I can decline if I decide later that I do not wish to be interviewed. | |

| Name of Patient | Signature of Patient | Date form Signed |
|---|---|---|
| | | |

| Name of Investigator Taking Consent | Signature of Investigator Taking Consent | Date form Signed |
|---|---|---|
| | | |

(Original copy to be held in Site File 1 Copy in patient's medical notes)

# Appendix G:

## Accelerated Transfusion Study

### Document C Version: 1 Ref: ATS2014/Doc(C) Date: 12.01.14

Dept. Clinical Haematology,

Royal Bolton Hospital,

Bolton. BL4 0JR

Tel: 01204 390511

Dr [GP Name]

[Surgery Address]

Date: xx/xx/xx

Dear Dr [GP Name],

**Re: Patient SURNMAME, First name, date of birth, NHS number, Address**

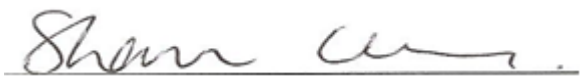
This letter is to inform you that the above named patient has recently agreed to take part in a research study. I am contacting you with this information with the patient's written permission so that you have a record of this for their medical records held by your surgery.

The research is being conducted in the Clinical Haematology Department at the Royal Bolton Hospital and will study accelerated transfusion in selected patients (mainly receiving transfusions at home). Patients will receive their usual two unit blood transfusions over a standard duration (90 minutes per bag), and then over a shorter duration (60 minutes per bag). Some patients will also be invited to take part in an interview to talk about their experiences of having a shorter transfusion.

Patients have been carefully assessed against medical criteria regards predisposition to risk of fluid overload due to co-morbidities, and selected for participation accordingly.

Please contact me, or the Clinical Haematology Team at the Royal Bolton Hospital should you have any further questions.

Yours Sincerely,



Sharran Grey (Chief/Principal Investigator)

Consultant Biomedical Scientist/Blood Transfusion Clinical Lead

Royal Bolton Hospital

# Appendix H:

**ACTION: REGISTERED NURSE PERFORMING TRANSFUSION**

**CONFIRMATION OF WILLINGNESS TO CONTINUE IN STUDY**
**& PRE-TRANSFUSION CLINICAL ASSESSMENT (Document F)**
**Version: 2 Ref: ATS2014/Doc(F) Date: 19.12.14**

| | | | | |
|---|---|---|---|---|
| **Participant Identifier** | | | | |
| **Date of this transfusion (DD-MM-YY)** | | | | |
| **Confirm that the patient is willing to continue in the study** | **YES (circle)** | **NO (circle)** | **Sign** | |
| | | | **Date** | |
| **Assessment Criteria** | **Expected Range** | | **Actual Value** | |
| Heart rate (beats per minutes) | Less than 100/min | | | |
| Blood Pressure (systolic mmHg) | Less than 160 mmHg | | | |
| Blood Pressure (diastolic mmHg) | Less than 95 mmHg | | | |
| Respiratory rate (breaths per minute) | Less than 20/min | | | |
| Cough and/or dyspnoea | Not present | | | |
| Significant Oedema | Not present | | | |
| Red Cell Unit 1 | Start Time | | Stop Time | |
| Red Cell unit 2 | Start Time | | Stop Time | |

If any of the above criteria are not met, or the patient does not want to continue in the study, administer the transfusion over the standard duration of 90 minutes per unit. Annotate the prescription accordingly. If there are any significant concerns about the patient's condition, contact the Clinical Haematology Team for advice (01204 390511).

**Arrangements for Post-Transfusion Check-Up**

| **Check-up not required: Patient accepted invitation to self-report (there have been 3 or more previous accelerated transfusions without adverse event)** | **I have discussed self-reporting with the patient and checked they have an info/contact booklet** | **Tick** | **Initial** |
|---|---|---|---|
| State time agreed with patient for 24 hour post-transfusion check-up | | | |
| State who will be performing the 24 hour post-transfusion check-up | | | |
| Has the person performing the 24 hour post-transfusion check-up been notified and their availability agreed? | | | |
| Practitioner performing above assessment | Name (PRINT) | | |
| | Signature | | |

**RETURN THIS FORM TO SHARRAN GREY AFTER TRANSFUSION (Original Copy in Site File)**

# Appendix I:

**24 HOUR POST-TRANSFUSION CLINICAL ASSESSMENT (Document G) Version: 2 Ref: ATS2014/Doc(G) Date: 19.12.14**

**ACTION: BCIVT NURSE/BCIVT SUPPORT STAFF/CHIEF INVESTIGATOR**

| | | | |
|---|---|---|---|
| **Participant Identifier** | | | |
| **Date of Transfusion** | | **Time Transfusion Ended** | |

| | | |
|---|---|---|
| **Assessment NOT required (3 or more previous accelerated transfusions and patient wishes to self-report)** | | **INITIAL** |
| **Assessment REQUIRED (less than 3 previous accelerated transfusions/patient does not wish to self-report)** | | **INITIAL** |
| **Assessment Criteria** | **Expected Range** | **Actual Value** |
| Heart rate (beats per minutes) | Less than 100/min | |
| Blood Pressure (systolic mmHg) | Less than 219 mmHg | |
| Blood Pressure (diastolic mmHg) | | |
| Respiratory rate (breaths per minute) | Less than 20/min | |
| Cough and/or dyspnoea | Not present (NP) | |
| Significant Oedema | Not present (NP) | |
| Are there any other signs of acute illness? | Not present (NP) | |
| Has there been ANY adverse event in the past 24 hours? | No | |
| Date of this assessment (DD-MM-YY) | | |
| Time of this assessment (24 hour clock) | | |
| Practitioner performing this assessment/completing form | Name (PRINT) | |
| | Signature | |

**If any of the above expected criteria are not met, contact the Clinical Haematology Team for advice (01204 390511 or air call consultant haematologist via switchboard 01204 390390).**

| |
|---|
| **State who has been contacted:** |
| **Date and Time of contact:** |
| **State advice received:** |

If there are any significant concerns about the patient's condition and/or the patient is acutely unwell, arrange for ambulance transfer to hospital.

**RETURN THIS FORM TO SHARRAN GREY (Original to be held in Site File)**

# Appendix J:

**Interview Schedules (Document K) Version: 1 Ref: ATS2014/Doc(K) Date: 12.01.14**

**Patient Interview**

<table>
<tr><th colspan="2">Introduction</th></tr>
<tr><td colspan="2">
<ul>
<li>Start recording and state consent to record has been obtained [consent form must be signed first]</li>
<li>Say why recorded interview is needed (accuracy, nothing left out, can go back)</li>
<li>State the interview reference (research participant identifier X: on [date])</li>
<li>The recording will be anonymous, but may not be confidential (your words may appear in print) and read by others though you won't be identifiable.</li>
<li>Purpose of interview is to gain your views of shorter transfusions. You have been selected because you have received both standard rate and shorter transfusions.</li>
<li>I will ask you some questions – please feel free to reply as you wish. There are no right or wrong answers. I just want your personal opinions and experience.</li>
<li>Feel free to interrupt, ask me to repeat/clarify, or criticise a line of enquiry…</li>
</ul>
</td></tr>
<tr><th colspan="2">Warm-up</th></tr>
<tr><td colspan="2">
<ul>
<li>Is there anything you'd like to ask me before we move on?</li>
<li>I don't have a long list of questions because I want you to be able to tell freely me what you think -think of this more of a 'chat'</li>
</ul>
</td></tr>
<tr><th colspan="2">Main Body</th></tr>
<tr><th>Topic Headings/Key Questions</th><th>Probes and Prompts</th></tr>
<tr><td>Is there anything particular you want to tell me about your experience of receiving standard rate and shorter blood transfusions?<br>Are there any positives or negatives?<br>Do you have a preference?<br>Have I asked you the right questions to understand your views and experience?</td><td>What is your personal view?<br>Can you tell me more about that?<br>What makes you say that?</td></tr>
<tr><th colspan="2">Cool Off</th></tr>
<tr><td colspan="2">
<ul>
<li>Is there anything you would like to add?</li>
<li>Do you think we have missed any important areas?</li>
<li>Is there anything you wish I'd asked?</li>
</ul>
</td></tr>
<tr><th colspan="2">Closing Comments/Closure</th></tr>
<tr><td colspan="2">
<ul>
<li>That brings us to the end of the interview</li>
<li>I will now listen to the recording and transcribe it onto the computer</li>
<li>Would you like a copy of the transcript?</li>
<li>Thanks very much for your time and for agreeing to be interviewed</li>
<li>Collect all notes together as a cue the interview is over</li>
<li>Ensure no further discussion then switch off the recorder</li>
</ul>
</td></tr>
</table>

**Practitioner Interview**

<table>
<tr><th colspan="2">Introduction</th></tr>
<tr><td colspan="2">
<ul>
<li>Start recording and state consent to record has been obtained [consent form must be signed first]</li>
<li>Say why recorded interview is needed (accuracy, nothing left out, can go back)</li>
<li>State the interview reference (research participant identifier X: on [date])</li>
<li>The recording will be anonymous, but may not be confidential (your words may appear in print) and read by others though you won't be identifiable.</li>
<li>Purpose of interview is to gain your views of shorter transfusions. You have been selected because you have administered both standard rate and shorter transfusions.</li>
<li>I will ask you some questions – please feel free to reply as you wish. There are no right or wrong answers. I just want your personal opinions and experience.</li>
<li>Feel free to interrupt, ask me to repeat/clarify, or criticise a line of enquiry…</li>
</ul>
</td></tr>
<tr><th colspan="2">Warm-up</th></tr>
<tr><td colspan="2">
<ul>
<li>Is there anything you'd like to ask me before we move on?</li>
<li>I don't have a long list of questions because I want you to be able to freely tell me what you think – think of this more of a 'chat'</li>
</ul>
</td></tr>
<tr><th colspan="2">Main Body</th></tr>
<tr><th>Topic Headings/Key Questions</th><th>Probes and Prompts</th></tr>
<tr><td>Is there anything particular you want to tell me about your experience of administering standard rate and shorter blood transfusions?<br>Are there any positives or negatives?<br>Do you have a preference?<br>Have I asked you the right questions to understand your views and experience?</td><td>What is your personal view?<br>Can you tell me more about that?<br>What makes you say that?</td></tr>
<tr><th colspan="2">Cool Off</th></tr>
<tr><td colspan="2">
<ul>
<li>Is there anything you would like to add?</li>
<li>Do you think we have missed any important areas?</li>
<li>Is there anything you wish I'd asked?</li>
</ul>
</td></tr>
<tr><th colspan="2">Closing Comments/Closure</th></tr>
<tr><td colspan="2">
<ul>
<li>That brings us to the end of the interview</li>
<li>I will now listen to the recording and transcribe it onto the computer</li>
<li>Would you like a copy of the transcript?</li>
<li>Thanks very much for your time and for agreeing to be interviewed</li>
<li>Collect all notes together as a cue the interview is over</li>
<li>Ensure no further discussion then switch off the recorder</li>
</ul>
</td></tr>
</table>

# Appendix K:

## PRACTITIONER INVITATION LETTER (Document D1)
## Version: 2 Ref: ATS2014/Doc(D1) Date: 05.05.14

### Study Title: Accelerated Blood Transfusion

Dear Sir/Madam,

We would like to invite you to take part in a research study looking at the duration of blood transfusions.

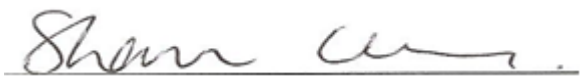
We are currently recruiting selected patients to this study which involves receiving blood transfusion(s) over a shorter length of time. As a practitioner in the Bolton Community IV Team you may administer shorter length transfusions to your patients during the course of this study.

If you agree, we would like to talk to you about your experience of it.

Accompanying this letter, you will have received an information sheet which describes in more detail what this study is about. Please take time to read the leaflet. If you have questions about any aspect of the study I would be happy to answer them. Many thanks for taking the time to read this letter and information sheet.

If I haven't heard from you within 2 weeks, I will telephone you once.

Yours sincerely,



Sharran Grey (Study Chief/Principal Investigator)

Consultant Biomedical Scientist/ Blood Transfusion Clinical Lead
Royal Bolton Hospital

# Appendix L:

## (PRACTITIONER) PARTICIPANT INFORMATION SHEET (Document D2) Version: 2 Ref: ATS2014/Doc(D2) Date: 05.05.14

**Study title: Accelerated Blood Transfusion**

### Introduction

You are invited to take part in a research study looking at the duration of blood transfusions.

Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information sheet. Do talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. This leaflet describes what the research is about and what it would involve for you.

**Part 1** tells you about the purpose of the study.
**Part 2** gives you more detailed information about the conduct of the study.

### Background

Red cell transfusions are administered to patients who have anaemia due to disease and/or medication. For many patients in the study, this will be a long-term treatment. Two bags of red cells are usually given in one treatment over 90 minutes per bag (3 hours in total).

## Part 1

### What is the purpose of the study?

The aim of this study is to see whether the treatment time for red blood cell transfusion (2 units) can be administered over a shorter period of time (60 minutes per unit), and to understand patient's and nurses experience of it. The study will also evaluate impacts on organisational economics and service capacity.

### Why have I been invited?

As a practitioner in the Bolton Community IV Team, you may be administering shorter duration red cell transfusions to your patients over the course of this study.

**Do I have to take part?**

It is up to you whether you decide to join the study. You have this information sheet to help you decide and we can also answer any questions you may have. If you agree to take part, we will ask you to sign a consent form. You are free to withdraw at any time without giving a reason. This would not affect you professionally or the standard of care your patients receive

**What will happen to me if I take part?**

After you have administered some shorter transfusions to your patients, we may ask if we can come and talk to you about your experience of it. This will be in the form of a short (no longer than 60 minute) interview that will be recorded on a dictaphone. This will allow us to transcribe what has been said later. You can stop the recoding at any time and ask for words to be deleted or rephrased. The recording will not identify you i.e. it will be kept anonymous. The interview will take place on a time and date convenient to yourself. We do not expect you to be asked to do more than one interview (but it is possible that you may be asked for a follow-up interview). Interviews will take place during work time.

**What will I have to do?**

If you agree to take part in an interview and you have some experience of administering shorter transfusions, the Chief Investigator will contact you to make arrangements to conduct the interview. This will be on a mutually convenient date and can be done at your workplace or elsewhere if you prefer.

**What are the possible disadvantages of taking part?**

You will be required to find some time for the interview, but any inconvenience should be minimised by arranging this on a convenient date and place. The discussion should not involve anything that is sensitive or emotionally distressing.

**What are the possible benefits of taking part?**

We cannot promise the study will help you personally, but the information we get from this study may help future patients needing regular blood transfusions.

**What if there is a problem?**

Any complaint about the way in which you have been dealt with in the study or any possible harm you might suffer will be addressed (see part 2 for more details).

**Will my taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are covered in part 2.

This completes part 1. If you are interested and you are considering participation, please read the additional information in part 2 before making a decision

---

**Part 2**

**What will happen if I don't want to carry on with the study?**

If you withdraw from the study we would need to use the data collected from you up to the point at which you withdraw.

**What if there is a problem?**

**Complaints**

In the first instance we would ask you to report your complaint to:
Sharran Grey (Chief/Principal Investigator): 01204 390254

We would aim to address any complaint at this stage. If you feel you need to take the complaint elsewhere or make a more formal complaint, you should contact:
Gilbert Wieringa (Laboratory Medicine Clinical Lead) on 01204 390421

**Harm**

If you are harmed during the research and this is due to someone's negligence, then you have grounds for a legal action for compensation against Bolton NHS Foundation Trust, but you may have to pay your legal costs. The normal National Health Service staff complaints procedures will still be available to you.

**Will my taking part in the study be kept confidential?**

Yes. The data relating to the interview will identify you by code (not by name), however you need to be aware that quotations from your interview may appear in print. This data will be a recording of the interview and will be kept on an NHS computer which is password protected. The data will only be accessed or viewed by the Chief Investigator. All data (paper and computer

records) will be securely destroyed at the end of the study (no later than the end of 2018).

**What will happen to the results of the research study?**

The results will be written into a doctoral thesis about accelerated blood transfusions by the Chief Investigator. It is likely the results will also be published in a number of medical journals. You will not be identified as a participant. We can inform you of the outcome of the study if you wish.

**Who is organising and funding the research?**

The research is being organised and co-ordinated by:

Sharran Grey (Chief Investigator)
Consultant Biomedical Scientist (Blood Transfusion Clinical Lead)
Royal Bolton Hospital
Bolton NHS Foundation Trust
BL4 0JR Tel: 01204 390254

The other members of the research team are:

Dr Clare Barnes (Consultant Haematologist), Royal Bolton Hospital
Dr Mark Grey (Consultant Haematologist), Blackpool Victoria Hospital
Dr Yin Thi (Consultant Haematologist), Royal Bolton Hospital
Dr Karen Lipscomb (Consultant Cardiologist), Royal Bolton Hospital
Dr Krystyna Porczynska (Haematology Specialty Doctor), Royal Bolton Hospital
Dr Heyam Hashim (Haematology Specialty Doctor), Royal Bolton Hospital
Mrs Louise Merrick (Haematology Clinical Nurse Specialist), Royal Bolton Hospital
Mrs Joanne Bowman (Haematology Specialist Nurse), Royal Bolton Hospital
Mrs Susan Mikolajewski (Bolton Community IV Team Leader)

No funding has been sought for this research. The only additional equipment required for the study was a patient weighing scale (costing approximately £200) and has been purchased using funds from the Clinical Haematology endowment fund.

**Who has reviewed this study?**

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by:

Research Ethics Committee North West - Preston (14/NW/0229)
Manchester Metropolitan University Research Ethics Committee

This study relates to research protocol document number: ATS2014/Doc(A) (version 1)

**Further Information and Contact Details**

**General Information about the research**

Sharran Grey (Chief/Principal Investigator): 01204 390254

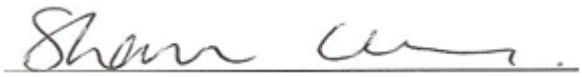
If you wish to speak to an independent person outside the research team about participating in this study, you can contact Alison Loftus (Research and Development Co-ordinator) at the Royal Bolton Hospital) on 01204 390390.

**What to do next**

Please complete the enclosed form to let us know whether you would like to be considered for participation in the study. Please use the pre-paid envelope, or hand deliver to the Haematology Department.

Thank you for taking time to consider this study.

Yours Sincerely,



Sharran Grey

Consultant Biomedical Scientist/Blood Transfusion Clinical Lead
Royal Bolton Hospital

# Appendix M:

## (PATIENT OR PRACTITIONER) PARTICIPANT INTERVIEW CONSENT FORM
## (Document J) Version: 1 Ref: ATS2014/Doc(J) Date: 12.01.14

**Accelerated Transfusion Study**

| |
|---|
| **Participant Study Number:** |
| **Participant's Date of Birth:** |
| **Participant's Initials:** |

| | | **Participant Initials** |
|---|---|---|
| **1.** | I wish to participate in this study. I confirm that I have read and understood the information sheet for patients (ATS2014/Doc(B2), version number 2), **or** information sheet for practitioners (ATS2014/Doc(D2), version number 2). I have had the opportunity to consider the information, ask questions (if any) and have had these answered satisfactorily. | |
| 2. | I understand that my participation is voluntary and I am free to withdraw at any time without giving a reason, without my medical care (for patients) or legal rights being affected. | |
| 3. | I understand that if I withdraw, the data collected from me up to that point will be used in the study. | |
| 4. | I agree to the interview being audio recorded using a digital recorder and stored securely on a computer, and I understand that I will not be personally identified either in the recording itself or files relating to the recording. | |
| 5. | I agree to the storage of my personal information (paper and electronic) for the purposes of this study (until the end of 2018). I understand that any information that could identify me will be kept strictly confidential and that no personal information will be included in the study report or other publication. | |
| 6. | I understand that anything I say will be anonymous but my words may appear in print. | |

| **Name of Participant** | **Signature of Participant** | **Date form Signed** |
|---|---|---|
| | | |

| **Name of Investigator Taking Consent** | **Signature of Investigator Taking Consent** | **Date form Signed** |
|---|---|---|
| | | |

(Original copy to be held in Site File 1 Copy in patient's medical notes if patient)

# Appendix N:

**Patient interview familiarisation notes**

- Frustrations with the additional restrictions, delays and length of time spent on the oncology unit when home transfusion was not possible. Patients were forgiving of this recognising the workload pressures of the hospital nursing staff [semantic and latent]
- Importance of home transfusion as a guardian of a child as hospital attendance would interfere with carer responsibilities [latent]
- Accelerated transfusion would improve the physical and mental comfort of some patients [semantic]
- Positive feelings and preference expressed for accelerated transfusion [semantic]
- Some patients said standard rate transfusion would not necessarily negatively impact them if they had to have standard rate transfusion at home, whereas some were enthusiastic about continuing with accelerated transfusion [semantic]
- No medical or wellbeing problems with accelerated rate transfusion, though there was an initial concern expressed [semantic]
- Using time saved for other things or expressed satisfaction for not being engaged in healthcare for as long [semantic]
- Frustration with infusion problems (not specific to standard or accelerated transfusion) [semantic]
- Resignation to the transfusion process being lengthy and expectations lowered [latent]

- Sense of altruism in ensuring best use of services [semantic and latent]
- Awareness of having to attend the hospital oncology units as the community IV team was over-capacity [semantic]

**Practitioner interview familiarisation notes**

- Perception that patients preferred accelerated transfusion as it was quicker (saving time) and more comfortable, but also a recognition that some patients liked the company afforded by longer transfusions and this may be a factor for lonely patients with an implication that patients may say they are unwell to receive a longer visit. Practitioner comment on enjoying giving more time to patients also [semantic and latent]
- Satisfaction of seeing patient benefit
- Perception that service capacity and flexibility had increased and there was an awareness of the need for best use of resources (especially in a small team and increased service demands) with some expressions of feelings of selfishness because of the focussing on resources [semantic and latent]
- Importance of avoiding hospital admission [semantic]
- Historic opinion that standard rate transfusion was too long for the volume infused contrary to national guidelines and hospital policy especially in the context of very historic transfusion that were over 6 hours. There was a perception that patients also shared these frustrations with the length of transfusion [semantic]

- Improvement in scheduling staff rosters and helping patients by being able to be more specific about arrival time and helping them organise their time better. This had the extra benefit of patient continuity in that time saved could be spent by the same nurse being able to do a follow up on that patient later the same day [semantic]
- Positive impact on scheduling of visits from other agencies and relatives. Less definite scheduling can impact on others [semantic]
- Feeling that long treatments were imposing on patients and specifically this was a factor for patients with life-limiting conditions. Perceived benefit of patients being able to use saved time for leisure and family (and family responsibilities) and that patients gained freedom and also control over their illness [semantic and latent]
- Not having to be in undesirable environments for over-long has positive effect on practitioner comfort [semantic and latent]
- Positive feelings and confidence about professional autonomy/job satisfaction/use of discretion/application of knowledge and skills and the support of clear protocols with clinical back-up. Long-term relationships with patients providing confidence in whether they would be well enough to meet pre-transfusion criteria [semantic]
- No adverse effects of accelerated transfusion [semantic]
- Some uncertainties about how much time could be released as needed more confidence in accelerated transfusion and whether extra time per visit would need to be factored in in case an accelerated transfusion was not possible on the day [semantic]

- Accelerated transfusion provided the same patient-focussed quality of service, albeit over a shorter visit time with some indication of feelings of selfishness for making this point [semantic and latent]
- Feeling conflicted about placing choice in the patient's hands about preferences over transfusion duration. Clinical assessment/practitioner-driven or patient choice (however this would only affect patients with experience of longer transfusions) [semantic and latent]
- Sense of promoting quality of life for patients by increasing their freedom and empowerment. Perceived improvement in patient comfort and the additional benefit of patients being less likely to restrict fluid [semantic]
- Accelerated transfusion increases awareness of the timeframe for transfusion, increasing the challenge of meeting the prescribed infusion time and allowing use of practical skills to achieve this [semantic]

# Appendix O:

## Publications and Presentations

## Awaiting acceptance at the time of thesis submission

Accelerated Red Cell Transfusion for Selected Patients. Grey, S., Roberts, S., Patalappa, C., Lipscomb, K., Hashim, H., Porczynska, K., Merrick, L., Bowman, J., Buckley, K., Sofield, I.

(Submitted for poster or presentation, British Society for Haematology 2018)

A web-app for weight-adjusted red cell dosing: Post-development implementation and clinical effectiveness. Grey, S.L., Farrar, K., Kinsella, P., Roberts, S., Patalappa, C., Davies, S., Ilyas, Z., Littler Adamson, K.
(Submitted for poster or presentation, British Society for Haematology 2018)

## Published

Published abstract and poster: Development of the Serious Hazards Of Transfusion Transfusion-Associated Circulatory Overload Checklist –. BBTS Conference 2017. S. Grey, D. Poles, A. Fogg and P. Bolton-Maggs. Transfusion Medicine (2017), 27, Suppl. 2, 44-45.

Published abstract and oral presentation (presented by colleague): The Changing Pattern of Pulmonary Complications Reported to SHOT. BSH Conference 2017. P. Bolton-Maggs, J. Ball, S. Grey, T. Latham, D. Poles. B J Haem (2017), 176, (suppl. 1), 19.

Published abstract and poster: Time to Refine Transfusion Associated Circulatory Overload (TACO). BSH Conference 2017. S. Grey, P. Bolton-Maggs , D. Poles, J. Ball, H. Lucero. B J Haem (2017), 176, (suppl. 1), 137-138

Published abstract and poster: The Changing Pattern of Pulmonary Complications Reported to SHOT. BBTS Conference 2016. P. Bolton-Maggs, J. Ball, S. Grey, T. Latham, D. Poles. Transfusion Medicine (2016), 26, Suppl. 2, pp 28-29

Published abstract and poster: Time to Refine Transfusion Associated Circulatory Overload (TACO). BBTS Conference 2016. P. Bolton-Maggs , S. Grey, D. Poles, J. Ball, H. Lucero. Transfusion Medicine (2016), 26, Suppl. 2, pp 50.

Poster and published abstract: A red cell dosage calculator could promote single unit red cell transfusion, prevent over-transfusion and reduce red cell usage. ISH/BSH XXXVI World Congress, Glasgow, 2016. S. Grey, P. Kinsella, K. Sweeney, A. Steele, C, Patalappa. B J Haem (2016). 173 (suppl. 1), p. 158-159.

Oral presentation and published abstract: Haemovigilance data for transfusion associated circulatory overload (TACO) provides a framework for informing patient-tailored rate and volume of transfusion. International Society of Blood Transfusion Congress, London (2015). Grey S.L. Vox Sanguinis (2015). 109 (Suppl.1). p. 41

**Scanned copies of publications included at the end of the thesis.**

## Awards

Bolton NHS Foundation Trust Annual Staff Awards for Research and Innovation (Oct, 2015)

Bolton NHS Foundation Trust Annual Staff Awards for Innovation (Transfusing Wisely#1 Team – Red Cell Dosage Calculator Implementation) (Oct, 2016)

2017 NHS England Chief Scientific Officer's Healthcare Science Partnering Patients and Citizen Award: Accelerated Blood Transfusion research project (March, 2017)