Safely shortening the duration of hospitalisation in children and young people with febrile neutropenia

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Abstract

Febrile neutropenia is the commonest life-threatening complication of treatment for children with cancer. Though the majority of children have no significant complications associated with its occurrence, current management includes intravenous antibiotics and in-patient care. Reduced therapy regimes for children at low risk of complications may have benefits for families and the National Health Service.

This thesis aimed to answer two main questions: In children and young people with low risk febrile neutropenia, are reduced therapy regimes safe, effective and acceptable to key stakeholders? What factors are involved in decision-making about acceptability of early discharge regimes?

Given the complexity of the research problem, the work utilised a mixed methods approach, selecting appropriate methodologies for each aspect of the problem and then combining results to provide a nuanced consideration of this multifaceted topic. Three sequential phases were performed, each informing and developing the next, whilst simultaneously allowing deeper interpretation of findings in earlier phases. Phase one, a quantitative systematic review, provided safety and treatment failure rates relating to reduced therapy regimes, whilst phase two, a qualitative synthesis, presented an interpretive account of experiences of early discharge. Phase three involved a focus group study exploring experiences and perceptions of key stakeholders involved in febrile neutropenia care in the United Kingdom.

Following mixing of phases in both design and interpretation stages, the thesis found that reductions in therapy are associated with increased readmission rates, but not increased risk of serious adverse events. It exposed the previously underestimated harms of febrile neutropenia admissions and the paternalistic nature of decision making.

Increasing shared decision making through discussing risks, developing mutual trust and negotiating control is necessary to achieve individualised treatment and improve experiences for stakeholders. The thesis outlines aspirations for future care of these children and young people and proposes various actions to achieve these goals.

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Author's declaration

I confirm that this thesis is a presentation of original work and I am the sole author. As reported in the acknowledgements, Jemma Cleminson performed double-checking of references and data extractions of both the systematic review and the qualitative synthesis. I also received technical assistance in undertaking the searching of electronic databases for both of these reviews. This thesis has not previously been submitted for an award at this University or elsewhere. Where information has been derived from other sources, they have been appropriately acknowledged and full references have been provided.

The following papers have been published from the work described in this thesis:

1. Protocol for a systematic review of reductions in therapy for children with low-risk febrile neutropenia. Morgan JE, Stewart L and Phillips RS. Syst Rev. 2014 Oct 21;3:119. doi: 10.1186/2046-4053-3-119.

2. Systematic review of reduced therapy regimens for children with low risk febrile neutropenia. Morgan JE, Cleminson J, Atkin K, Stewart LA and Phillips RS. Support Care Cancer. 2016 Jun;24(6):2651-60

Chapter 1: Febrile neutropenia: history, current research priorities and overview of thesis

Febrile neutropenia is the commonest complication of therapy in children with cancer.(1) Its current treatment involves hospital admission and antibiotic administration, with considerable associated burden to patients, families and the healthcare service. For children at low risk of serious complications of their febrile neutropenia, it has been suggested that reducing treatment to allow children to be at home may be an appropriate course of action that results in significant physical, social, psychological and financial benefits. However, many steps towards achieving this goal have yet to be clarified, including the time at which discharge should occur and the acceptability of these approaches to patients, families and healthcare professionals. This thesis intends to synthesise existing evidence and provide additional primary data to explore these issues, so as to inform the design of future services for children with cancer in the UK.

This chapter serves as an introduction to the thesis. I present some of the key concepts relating to febrile neutropenia, provide a brief history of the research within this area and outline the current issues surrounding the management of febrile neutropenia in children and young people with cancer in the UK. I then clearly define the research problem and describe the overarching methodology for this thesis. I provide both a written and pictorial representation of the structure of the thesis and outline how the research problem will be addressed.

What is febrile neutropenia?

To begin this chapter, it is important to understand what febrile neutropenia is and its clinical impact in childhood cancer. Neutrophils are the most common type of white blood cells. They play a vital part in cell-mediated immunity by engulfing and destroying infecting micro-organisms. Neutropenia describes a reduced number of neutrophils in the blood. The precise definition of neutropenia is varied, with some definitions giving a value of greater than two standard deviations below the population mean, whilst others, including current National Institute for Health and Care Excellence (NICE) guidelines, use a level of $0.5x10^9$ cells per millilitre.(2) Neutropenia can occur for many reasons, including congenital conditions, aplastic anaemia, autoimmune disease, viral infections and medications (see Box 1). In patients with cancer, neutropenia occurs for two main reasons. First, the infiltration of bone marrow with disease results in insufficient production of cells and hence low levels of circulating neutrophils. Secondly, the treatment of malignancy, including chemotherapy and radiotherapy, can have a

myelosuppressive effect. Indeed, neutropenia occurs most commonly in cancer patients following chemotherapeutic interventions.

Patients with neutropenia are at risk of infection with bacteria, viruses and fungi, each of which pose a different risk to the patient. Children with cancer are often already at increased risk of infections due to other effects of their disease or treatment. There may be inadequate skin and mucosal barrier protection due to mucositis and the presence of indwelling medical devices, particularly central venous access catheters or 'lines'. Normal body flora is disrupted by the frequent administration of antimicrobial agents. The malignancy and its treatment may also affect other aspects of the immune system, causing hypogammoglobulinaemia and impaired immune cellular function, resulting in decreased cell numbers and reduced activity.(3,4)

Box 1 Causes of Neutropenia (2)

Isolated:

- Congenital: Kostmann's syndrome
- Acquired: Drug-related (Anti-inflammatory drugs, antibiotics, anticonvulsants, antithyroids, hypoglycaemics, phenothiazines, psychotropics, antidepressants, miscellaneous)
- Benign: racial or familial
- Cyclical
- Immune: autoimmune, Systemic Lupus Erythematosus, Felty's syndrome, Hypersensitivity, Anaphylaxis
- Large granular lymphocytic leukaemia
- Infections: viral, fulminant bacterial

General Pancytopenia

- Bone marrow aplasia (congenital, idiopathic acquired, ionizing radiation, chemical-induced, drug-related, viral)
- Acute leukaemia, myelodysplasia, myeloma
- Infiltration with tumour
- Megaloblastic anaemia
- Paroxysmal nocturnal haemoglobinuria

Febrile neutropenia, which is seen in all causes of neutropenia (see Box 1), describes the presence of a fever in a person with a low neutrophil count. Fever may occur in a neutropenic patient for many reasons, including administration of certain medications (particularly chemotherapeutics), blood products, allergic or inflammatory reactions and due to the malignancy itself. However the most concerning reason for raised temperature is the presence of an infection, and therefore febrile neutropenia is usually considered to be due to infection unless proven otherwise. For the remainder of this work, the phrase 'febrile neutropenia' will be used to describe this condition

exclusively in patients receiving treatment for haematological and oncological disorders, the patients who most commonly present with febrile neutropenia.

Febrile neutropenia is the commonest life-threatening complication of treatment of children with cancer.(1) It occurs in around a third of episodes of neutropenia, at a rate of 0.75 episodes per 30 days of neutropenia and 0.15 per month of chemotherapy exposure time.(5,6) Certain groups of children are at greater risk of developing febrile neutropenia, depending on their disease and its treatment. Around 3% of children with cancer will die of an infection during their treatment.(1,7) Other potential septic complications of a febrile neutropenic episode include bacteraemia, significant bacterial infections, and medical complications (such as hypotension, altered mental state, and renal dysfunction). It can also require intensive care input and lead to delays in further treatment of the child's malignancy.(8,9) However, many episodes of febrile neutropenia in children have no significant sequelae, and up to 50% of episodes have no clinically or microbiologically defined infection.(9,10)

History of febrile neutropenia

Febrile neutropenia was first recognised as a significant medical problem in the 1950s, when the initial treatments for leukaemia were being developed.(11) In those early years of chemotherapy, febrile neutropenia posed a significant risk to the patients being treated, with up to 70% of deaths of children with cancer being due to infections.(12) However, as penicillins were introduced to practice in the early 1960s, outcomes improved.

In 1966, Bodey et al noted that the risk of infection, and indeed infection-related mortality, in cancer patients was related to the degree of neutropenia.(13) At around the same time, Curtin and Marshall recognised the importance of rapid recognition of febrile neutropenia and initiation of early antimicrobial therapy in improving patient outcomes.(14) Over the next ten years, protocols were developed for early empirical[1] treatment with antibiotics in febrile neutropenia. These protocols involved prolonged inpatient stays for intravenous antibiotics whilst fever and neutropenia persisted, but resulted in a significant reduction in mortality related to neutropenic sepsis.(11)

The next period of febrile neutropenia history focused on development of improved antibiotic schedules, with cover for the bacteria Pseudomonas resulting in a further significant decline in

[1] Empirical treatment, in this setting, refers to the use of antibiotics before a specific organism has been identified, thus the antimicrobial selected is chosen for its ability to cover the most frequent and most serious infections seen in this population.

mortality. Furthermore, prophylaxis against certain infections, including *Pneumocystis jiroveci* (previously *Pneumocystis carinii*), was recommended for selected patients.(15)

In the early days of managing febrile neutropenia, patients were kept in hospital on intravenous antibiotics for the duration of both their fever and their neutropenia.(16,17) Over time, it was recognised that it was safe to discontinue antibiotics and discharge patients if they were afebrile, with no other signs of infection, despite ongoing neutropenia.(9,17,18) In current practice, the majority of children with febrile neutropenia will be discharged without resolution of their neutropenia, the only significant exceptions to this are those children with certain haematological malignancies for whom the risk following discharge is particularly high. These include children with Acute Myeloid Leukaemia (AML) and Infant Acute Lymphoblastic Leukaemia (ALL).

This work into improving the clinical management of febrile neutropenia, has continued such that the risk of death from infection in children with cancer has fallen from the original 70% to around 3%.(1,7,12) Given this significant improvement in mortality, febrile neutropenia research has developed in various directions.

I will now explore the two main current areas of research that are relevant to this thesis: (i) risk stratification and (ii) the reduction of therapy for patients at low risk of septic complications of their febrile neutropenia.

Risk stratification in febrile neutropenia

Risk stratification is the process of categorising patients according to their risk of developing a disease or complication of treatment. Clinicians can then adjust their management based on these categories and provide more personalised care, by instigating more intensive monitoring, investigation and treatment for high risk patients, and reducing therapy, with its associated side effects, in low risk patients. In haematology and oncology services, risk stratification was first considered following the observation that a large number of patients with febrile neutropenia have no significant sequelae of the condition, whilst a much smaller number are at high risk of medical complications including organ failure and death.

Various risk stratification models have been developed in adult haematology and oncology. The first model created by Talcott in 1988 defined as low risk those who presented as outpatients, with no co-morbidities and with controlled cancer.(19) In 2000, the Multinational Association for Supportive Care in Cancer (MASCC) developed a scoring system that reduced the misclassification rate and had increased sensitivity compared to the Talcott score, although this came at the

expense of reduced specificity[2] (Table 1).(20) The MASCC score has been validated on a number of occasions and has been recommended as the most appropriate risk index score for adults with febrile neutropenia.(21)

Table 1 - The MASCC score (score ≥21 identifies low risk patients) (20)

Characteristic	Weight
Burden of illness: no or mild symptoms	5
No hypotension	5
No Chronic Obstructive Pulmonary Disease	4
Solid tumour or no previous fungal infection	4
No dehydration	3
Burden of illness: moderate symptoms	3
Outpatient status	3
Age <60 years	2

Unfortunately, these adult risk scores cannot be applied to paediatric, teenage and young adult patients.(22) The spectrum of malignancy seen in paediatric and young adult practice is different to that seen in older adults and children often have fewer co-morbidities than their adult counterparts. Therefore, they receive different therapeutic regimes for their cancer, often including more intensive myelosuppressive agents. Consequently, children tend to have more prolonged and profound periods of neutropenia, with the accompanying increased risk of infection. Furthermore, the spectrum of infections that children are susceptible to is different to the adult population, with children being more likely to develop streptococcal illnesses and affected less frequently by staphylococcal infections.(23) Finally, children have a different physiological response to infection, being more prone to high temperatures (above 39°C) and experience hypotension as a much later sign of circulatory abnormalities. In addition to this, some of the specific criteria in the MASCC score are not helpful in differentiating children with febrile

[2] Sensitivity refers to the ability of a test (or risk stratification tool) to accurately detect people with the disease, in this case high risk febrile neutropenia. Specificity describes the test's ability to accurately identify those people without the disease, in this case those who do not have high risk febrile neutropenia - those with low risk disease.

neutropenia. Age stratification to under or over 60 years of age is not relevant, whilst Chronic Obstructive Pulmonary Disease (COPD) is not seen in children and young people.

Given the inapplicability of adult risk scores, attempts have been made to create risk stratification tools specifically for use in paediatrics.(24–27) Over 23 different paediatric risk stratification tools have been described in the literature.(10) Each of these rules is defined by different criteria of fever and neutropenia, and is designed for different patient groups, for example outpatient only compared with all patients, and no stem cell therapies compared with all patients. In various combinations, they have used criteria such as the underlying diagnosis, the intensity of recent chemotherapy, profound neutropenia ($<0.1 \times 10^9/L$), thrombocytopenia (platelet count <50g/L), comorbidities and expected duration of neutropenia to identify those at the highest risk of adverse events.

The utility of these tools has been investigated in a systematic review and meta-analysis carried out by Phillips et al in 2010 and updated in 2012.(8,10) Validation studies for each of the six tools evaluated were found to have higher misclassification rates than the studies initially introducing the tools. This is to be expected given that the rule has been created from a particular cohort with individual characteristics, some of which are different in the validation population and reduce the tool's accuracy. Almost all tools will be less accurate in a validation population compared to the groups they were developed on. The important issue is the degree of difference and whether the use of the tool in different populations still provides clinically meaningful information.

Particular challenges in the development of Clinical Decision Rules include having sufficient sensitivity to identify those patients at high risk of significant complications, alongside appropriate specificity to identify enough patients as low risk to enable clinically important numbers of patients to be treated on a reduced therapy protocol. Furthermore, Clinical Decision Rules need to be simple, quick and easy to apply regularly to patients in day-to-day clinical work. They need to be applicable to the specific population they serve, such that different rules may be need for different geographical areas. On-going work by the Predicting Infectious Complications of Neutropenic sepsis In Children with Cancer (PICNICC) collaboration, using Individual Patient Data meta-analysis to develop a more accurate Risk Prediction Rule, aims to resolve some of the challenges mentioned above and to provide clinicians with further guidance.(28) So far, this collaboration has designed a risk prediction model including malignancy type, temperature, a clinical assessment as 'severely unwell', haemoglobin, white cell count and absolute monocyte count which appears accurate but requires further investigation to confirm its use in the clinical environment.(29)

Reduced therapy regimens

As mortality from febrile neutropenia continues to fall and risk stratification tools become more reliable, researchers have begun to focus on the safe reduction of treatment for patients who are believed to be at low risk of developing septic complications of febrile neutropenia.(1) Approaches to reducing treatment focus on either reducing the duration of hospitalisation or reducing the duration of intravenous antibiotic administration. Studies focusing on location of treatment can be split into those that aim for early discharge, wherein the child or young person spends some time as an inpatient before being discharged at a point earlier in the treatment course than for standard treatment, and those that aim for entirely outpatient therapy, where the child spends no time in hospital following the initial assessment and diagnosis of febrile neutropenia. Similarly, studies tackling the route of administration may either give a period of intravenous antibiotics that is shorter than standard treatment (sometimes followed by a period of oral antibiotics) or aim to treat the episode of febrile neutropenia entirely with oral antibiotics, thus completely avoiding intravenous administration. As yet, there has been no assessment of the most appropriate time to reduce therapy, either through early discharge or switching from IV to oral antibiotics. Very few studies have investigated a strategy in which patients identified as low risk are observed without any antimicrobials given.(30)

Reducing treatment for low-risk febrile neutropenia has a number of potential benefits. Firstly, patients and their families may prefer to be at home during treatment for chronic conditions.(31) This is reflected in national policy documents that advocate care as close to home as possible for children and young people wherever this is safe and achievable.(32,33) Within the realms of febrile neutropenia care, adult studies have found that outpatient treatment protocols results in improved quality of life.(25)

Interestingly however, paediatric studies have found that healthcare professionals tend to assess child and parents' quality of life during inpatient stays as worse than the parents do, and also overestimate the improvement in quality of life associated with going home.(35) Indeed, parents have been found to predict that their own quality of life would not improve if given oral antibiotics for their child to have at home instead of an inpatient stay.(35) Therefore, care needs to be taken before assuming that reduced therapy options are what patients and their families would prefer. Attitudes to reductions in therapy are further explored later within this chapter and are a key focus of the thesis as a whole.

A further suggested benefit of alternative strategies for managing febrile neutropenia is that there is a theoretical reduction in the risk of hospital acquired infections as a result of reduced contact with the healthcare environment. Indeed, a recent Children's Oncology Group review of

infections in children with Acute Myeloid Leukaemia found that hospitalisation of neutropenic children did not reduce their risk of infection related mortality but did increase their risk of Clostridium difficile infection.(36)

Finally, from a health service point of view, reductions in hospital stay significantly reduce the costs of providing care. This reduction has been reported to be between £3500 and £7000 per episode of febrile neutropenia, depending on the regimes used for comparison and the country in which the research was performed.(37,38) However, there is some evidence that this reduction in costs to the service is partially transferred to the patient.(39) For families, having a child at home receiving treatment for febrile neutropenia, may result in additional costs, including time away from work and transport to and from the hospital for frequent reviews of progress.

The NICE Guidelines

In 2010 the National Institute for Clinical Excellence (NICE) set up a guideline development group for febrile neutropenia. They were tasked to develop a guideline for the prevention and management of febrile neutropenia, to include all adult and paediatric patients with febrile neutropenia related to treatment for cancer.

NICE Clinical Guideline 151 "Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients", published in 2012, was the results of the development group's work. It clearly defines febrile neutropenia (for which the term "neutropenic sepsis" is used throughout the guideline) as a neutrophil count of $<0.5 \times 10^9$/L with either a temperature >38°C or symptoms or signs consistent with clinically significant sepsis. The guidance advises that patients should be risk stratified within the first day of hospital admission using a validated risk scoring system. For paediatric patients, the modified Alexander rule is advised (see Box 2). Treatment should then be tailored according to this risk assessment. The following recommendation is particularly relevant to this thesis:

> *"Consider outpatient antibiotic therapy for patients with confirmed neutropenic sepsis and a low risk of developing septic complications, taking into account the patient's social and clinical circumstances and discussing with them the need to return to hospital promptly if a problem develops."(21)*

The guideline proved to be controversial in the paediatric oncology community for a number of reasons.(21) These can be split into two main areas. The first is the argument that 'children are not little adults' and therefore should not be included within the same guidelines as adult patients. However, this concern can be contended by the fact that although only around 1.2% of patients with cancer within the UK are diagnosed under the age of 24 years, around 50% of the

evidence for the NICE guideline comes from this age group. Thus paediatric and young adult patients are significantly overrepresented within CG151 and the evidence that is provided in children is generally consistent with adult data.(21) Having said this, the numbers of children included in the analyses is still relatively small and so some experts have been cautious about the guideline recommendations.

Box 2 - Modified Alexander Rule

Risk factors excluding from low risk protocol:

Admission and 48 h assessment

- Age
  - <1 year
- Associated medical conditions requiring hospitalisation
  - Shock or compensated shock
  - Haemorrhage
  - Dehydration
  - Metabolic instability
  - Altered mental status
  - Pneumonitis
  - Mucositis (unable to tolerate oral fluids or requiring IV analgesia)
  - Respiratory distress/compromise
  - Perirectal or other soft tissue abscess
  - Rigors
  - Irritability/meningism
  - Organ failure
- Cancer associated co-morbidities
  - ALL at diagnosis/relapse <28 d
  - ALL not in remission >28 d
  - AML
  - Infant ALL
  - Intensive B-NHL protocols
  - Haemopoietic stem cell transplant
  - Sequential high dose chemotherapy with PBSC rescue
- History
  - Intensive care admission during last FN episode
  - Non adherence (social concerns or patient)
  - Inability to tolerate oral antibiotics

48 h Assessment only

- Positive blood culture result at 48 h
- ANC < 0.1×10^9/L at 48 h
- Child not clinically well at 48 h (clinician judgement)

ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; B-NHL, B cell non-Hodgkins lymphoma; BMT, bone marrow transplant; PBSC, peripheral blood stem cells; and ANC, absolute neutrophil count.

The second main cause of controversy within the NICE guidelines is that, although the majority of the guidelines are consistent with current adult practices, they do not reflect practice in most

paediatric haematology and oncology centres.(39–41) This juxtaposition of current practice with the new guidelines has induced a degree of concern.

UK service structure and current management for paediatric febrile neutropenia

In the UK, children and young people with cancer are treated within highly specialised multidisciplinary teams. Upon diagnosis, children are transferred to one of the Principal Treatment Centres (PTCs) where further investigations are performed and their initial treatment is commenced (see Figure 1). Some children receive all their treatment in their PTC, whilst others may be managed using shared care between the PTC and a Paediatric Oncology Shared Cared Unit (POSCU) located closer to the child's home. The role of shared care centres and the services they provide varies depending on regional design.

Due to the absence of national or international Clinical Practice Guidelines for febrile neutropenia until recently, the management varies widely across the UK.(40,42) A national audit of febrile neutropenia practices was performed in 2012, prior to the introduction of NICE guidelines, and again in 2015, three years after the guidelines were published, to establish current management and to describe areas where the guidelines were not adhered to.(31,32) The initial survey included 21 centres and the follow-up included 45 (of which 14 were principal treatment centres). In 2015, only 49% of centres used the NICE guideline definition of febrile neutropenia (temperature $\geq 38^{\circ}C$ on one occasion and neutrophil count of $<0.5 \times 10^{9}/L$).(21)

In each audit, just 42% of centres routinely risk stratified patients, and thus many children at low risk of septic complications of their febrile neutropenia are managed similarly to those at high risk of septic shock, intensive care admission or death. Those centres using risk stratification generally used the modified Alexander rule outlined in the NICE guidelines (see Box 2). In the 2012 audit, all UK centres managed children and young people with at least 48 hours of inpatient care and used intravenous antibiotics for the empirical treatment of febrile neutropenia.(40) The duration of admission was not clearly documented within the 2015 audit but intravenous antibiotics were used throughout.

From these data, it can be seen that UK practice does not currently comply with the NICE guidelines. Some of the potential reasons for this have been explored above but others will be expanded in the following subsections about attitudes to reductions in therapy and change management.

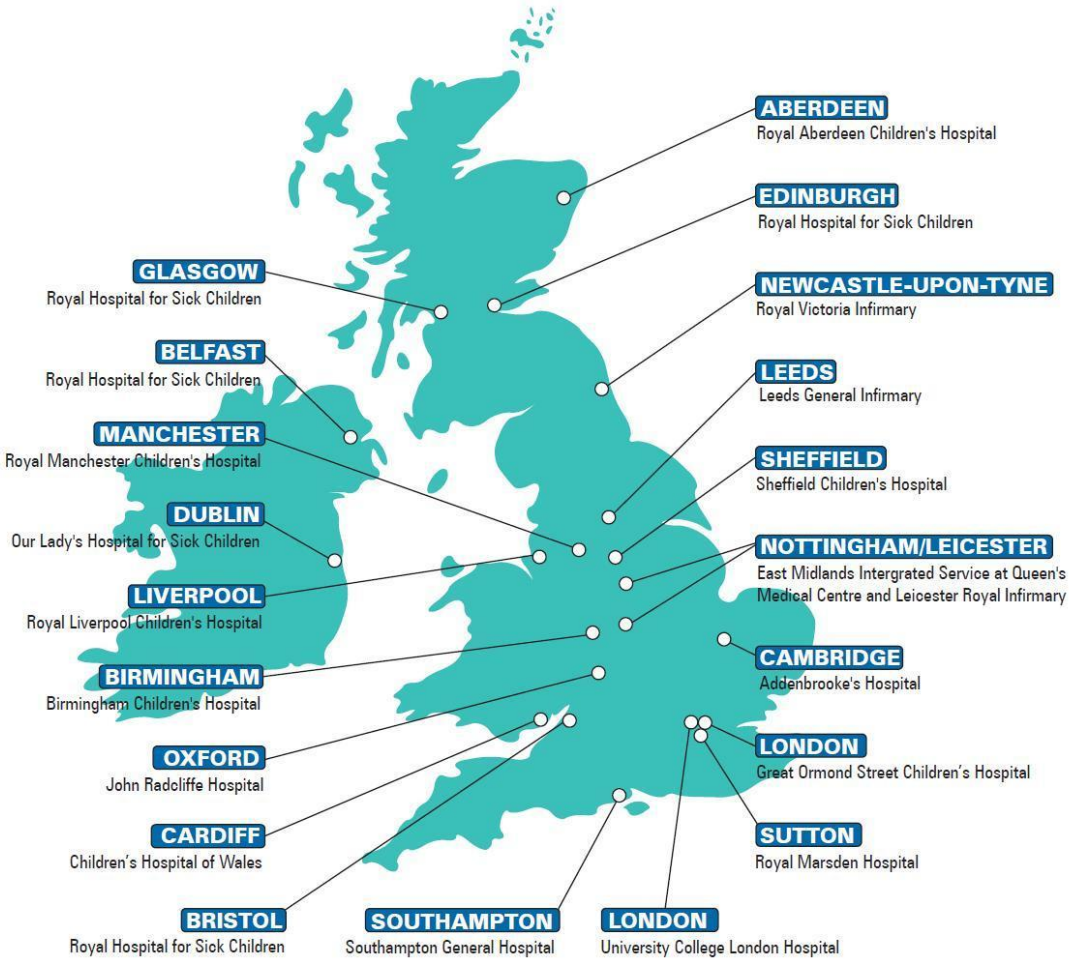


Figure 1 - Location of UK Principal Treatment Centres for Paediatric Haematology and Oncology (43)

A systematic review into why physicians do not follow guidelines suggested that the main barriers were related to physician knowledge, attitudes and behaviour.(44) When related to the current NICE guidelines, the main barriers may be attitudinal, such that physicians are concerned about the potential risks of this strategy and its applicability to children and young adults. There may also be concerns regarding the practicalities of providing such a service and the challenges in establishing this given current NHS financial difficulties.

Attitudes to reductions in therapy

Ever since reduction in the intensity of febrile neutropenia therapy was suggested, studies have been performed to assess the attitudes of healthcare users and providers to this approach. The research has been illuminating to those in the field. In adult febrile neutropenia, where the practice of outpatient treatment or early discharge with oral antibiotics has been commonplace for some time,(45) these strategies are acceptable to most adult cancer patients and seem to

improve health-related quality of life, although attitudes obviously vary between individual patients.(46)

However, in paediatric haematology and oncology, the findings have been somewhat different. Whilst it might be expected that families would prefer to be together in their own homes with more control over their surroundings, the work so far has varied in its findings. Some studies whose main intentions were to establish the efficacy of alternative treatment strategies also examined patient preferences and almost universally report high satisfaction with these approaches.(47,48)

However, in a more specific attitudinal study Cheng et al found that only around a half of families would take up a reduced therapy option, and inpatient therapy is often preferred.(46) Furthermore, work by Sung et al established that this preference persisted even when the risk of significant deterioration (death or intensive care admission) was equal between the groups treated at home or in hospital.(35) This was despite an increase in the anticipated Health Related Quality of Life with outpatient therapy including initial admission followed by early discharge.(46) More recently, Sung et al have aimed to identify what aspects of an outpatient therapy schedule might be most acceptable to families and found that a requirement for frequent clinic attendance and a high probability of readmission was likely to be a barrier to early discharge approaches.(49)

This body of research has found a degree of disparity between groups regarding acceptance of outpatient regimes. Parents seem less keen for their children to be treated at home than the healthcare professionals involved in providing care. Children and young people also appear to be more keen to be out of hospital than their parents and are willing to accept a higher frequency of clinic visits and higher readmission risk in order to achieve this.(49)

Current evidence has identified certain characteristics that make families more likely to prefer outpatient care. These include less fear or anxiety about febrile neutropenia, parents with higher income and higher education, and those who assessed their child as having higher current Health Related Quality of Life.(35,46) However, it should be recognised that all of this research into the attitudes of children, families and healthcare professionals has been performed by a single research group, within a single centre in Toronto, Canada. Thus further information is required from other centres and settings, to explore whether these results apply to other populations, and also to identify other features that might influence the attitudes of key stakeholders.

The negative attitudes of families towards reductions in therapy could be reflected in poor recruitment to trials of early outpatient therapy. For example, in the Swiss Paediatric Oncology Group (SPOG) 2003 FN study a third of patients who were eligible to take part refused consent, although the reasons for this were not fully explored.(17) Rates of consent to paediatric

haematology and oncology trials are usually very high and thus this rate of refusal is noteworthy.(53) Whether low recruitment rates are particularly prevalent in reduced therapy trials for febrile neutropenia has not been investigated.

The issue of non-participation in cancer trials in general has been explored by Cox and McGarry, who found a variety of reasons why patients do not participate in trials.(50) In particular, they identified that patients may not be offered trial participation by their doctors, despite being eligible for entry; they may find the burden of participation too demanding; or they may distrust the idea of participating in medical research. These reasons may also be relevant to febrile neutropenia studies. However, there may be additional or different concepts that are relevant to any poor recruitment to reduced therapy febrile neutropenia trials. I will further explore the issues of choice and decision-making that relate to this thesis, within chapter 2.

The problem addressed by this thesis

Febrile neutropenia is a common problem within paediatric haematology and oncology. Reduced therapy regimens may provide benefits to both patients (including increased quality of life and reductions in hospital acquired infections) and the health service (including cost savings and reduced bed pressures), when there is a low risk of septic complications. As outlined in the earlier sections of this chapter, further information is required about the safety and efficacy of these regimens, and specifically, how these change according to the timing of reductions. There also remain a number of unresolved issues regarding attitudes towards early discharge in patients with low risk febrile neutropenia, particularly in identifying barriers and facilitators to acceptance of early discharge as a treatment strategy. The factors used in this decision making process need to be considered and the methods people use to balance the benefits and challenges of early discharge explored. Furthermore, investigation of any differences in acceptance between young people, their parents and the professionals caring for them, and how these might be aligned, is needed so as to provide an acceptable service for all.

Aims of the thesis

Box 3 – Main research questions for thesis

In children and young people with low risk febrile neutropenia, are reduced therapy regimes (particularly early discharge) safe, effective and acceptable to key stakeholders?

What factors are involved in decision-making about acceptability of early discharge regimes?

The main aim of this thesis is to further investigate the issues surrounding the reduction in

therapy for children and young people with low risk febrile neutropenia (see Box 3 for main research questions). In particular, it will aim to establish the safety, adequacy and treatment failure rates of various reduced therapy strategies in the face of new research evidence. It focuses specifically on the issue of the timing of reductions in therapy, that is the point in the care pathway at which the child or young person moves from inpatient to outpatient care or from intravenous to oral antibiotic administration. These data are essential to inform decisions about care strategies and aim to allow discussions which are based on the best current available evidence when designing and providing care.

The work then investigates the attitudes of those involved in strategies involving early patient discharge in various hospital settings. This aims to provide wide-ranging information about the experiences of early discharge and potential barriers and facilitators to the provision of these services for children and young people. Finally the views of key stakeholders, specifically about early discharge in paediatric febrile neutropenia, have been sought. These provide a nuanced account of the perceptions of various strategies proposed for this group of patients. It conveys the voice of patients, parents and healthcare professionals from multiple institutions in the UK, in order to provide health care service providers and policy makers with information on how best to address these issues, and how to structure future services for children and young people with febrile neutropenia.

Mixed methods applied to this research

The complexity of the research problem, rooted in clinical practice, that this thesis addresses and the varied nature of its component aims, required a mixed methods approach. I drew on both quantitative and qualitative research paradigms selecting of the most appropriate methodologies for each aspect of the research problem, and then combining these results to achieve a more nuanced consideration and deeper understanding of this multifaceted topic. Mixed methods research is a relatively new concept, which allows for the exploration of complex problems by examining them using different perspectives, and thus providing a more holistic study of the various interacting aspects of the situation.(51) The triangulation of results constructs a detailed account of the subject of the research, in this case reduced therapy in paediatric febrile neutropenia. Using this methodology enables the inclusion of both quantitative and qualitative data, methods and modes of thought, so as to provide a deeper, clearer and more nuanced understanding of the research problem and its potential solutions. This is particularly applicable in areas where there are both quantitative and qualitative facets to the research problem – as in paediatric low risk febrile neutropenia, where there are questions about risks of certain outcomes alongside those about experiences, perceptions and attitudes.(52) Using a mixed methods

approach and selecting the most appropriate methodology for each of these components should ensure that the research problem is extensively explored and the research questions are answered, whilst overcoming some of the limitations of each of the individual included methodologies.(53)

However, challenges arise in mixed methods research when the underlying epistemological and ontological beliefs of these quantitative and qualitative paradigms are in opposition.(53) The resolution of these potential disagreements occurs when focus is placed on the problem to be addressed and the strengths and weakness of each methodology used are acknowledged. The results may then be combined to best utilise each methodology and the conclusions outlined while explicitly recognising these issues.(54) Mixed methods research is particularly suited to a pragmatic philosophy, as is often seen in health sciences, and for this project allows for the most appropriate exploration of the research problem with the intention of providing a clinically informative and practically useful outcome for all involved in paediatric haematology and oncology services.(53,55,56)

The following section of the chapter details the way in which the thesis has been structured and how the methodology has been applied to the research problem.

Structure of thesis

The work undertaken for this thesis was carried out as three sequential research phases. Each addressed different aspects of the research problem and used appropriate methods to tackle specific research questions.. The earlier phases provided data and theory to inform and develop the design of later phases, the contribution of which is discussed at the beginning of each of the relevant chapters. The later phases then helped to expand and explore issues identified at earlier points, allowing deeper interpretation of findings in earlier phases. This is discussed further within relevant chapters reporting these phases, and the translating of works together is further described within the conclusions in Chapter 9. Phases 1 and 2 are both systematic reviews of the earlier literature, seeking to combine pre-existing research evidence and generate new knowledge within the findings. Phase 3 is an exploratory piece of primary research that seeks to build on the two syntheses and to generate further data to expand upon the earlier work and to provide new insight to the research problem. The phases were performed chronologically in sequence with some overlap between phases 1 and 2, such that the final analysis of phase 1 occurred at the same time as the design and searching for phase 2. The analyses of both phases 1 and 2 were completed before the design of phase 3, which was informed by both pieces as outlined in Chapter 4. The three phases of the thesis are outlined narratively below and pictorially in Figure 2.

Phase 1 - Systematic review of reduced therapy regimens for children with low-risk febrile neutropenia

This phase involved the synthesis of quantitative data within the existing literature to define the safety, adequacy and treatment failure rates of oral antibiotics and outpatient management for low-risk paediatric febrile neutropenia. Standard systematic review and meta-analysis methodologies were applied, with thorough searching of the literature, screening of identified references, and data extraction and quality assessment of included studies. Data were combined in meta-analyses and subgroup and sensitivity analyses undertaken. The results provide detailed information regarding the outcomes of various treatment strategies for febrile neutropenia and, in particular, explore the effect of timing of reductions in therapy on the rates of treatment failure in paediatric febrile neutropenia, which has not previously been examined. Furthermore, this review specifically collected data on rates of refusal to consent to studies of reduced therapy for children with low risk febrile neutropenia so as to begin to explore the issues surrounding acceptance of reduced therapies. The findings of this phase, particularly the refusal to consent data, contribute to the design of both the qualitative synthesis and primary study, as discussed in Chapters 3 and 5. The safety and treatment failure rates also formed part of the topic guide for discussion within the qualitative study in phase 3.

Phase 2 - Experiences of early discharge, with a focus on paediatric febrile neutropenia: a meta-ethnography

The second phase of the study was a systematic review of the qualitative literature describing experiences of early discharge, aiming to explore concerns raised in Phase 1 that reductions in therapy might not be acceptable to key stakeholders. This was an original approach to considering this research problem and uses a relatively new methodology to explore the issues in a unique way. It used structured searching of literature, with screening of all identified references to obtain evidence in the area of paediatric febrile neutropenia. As that evidence was sparse, it also drew on experiences of early discharge in adults with febrile neutropenia and children with other chronic conditions. The quality of data was assessed and used to inform the analysis which followed an adapted version of Noblit and Hare's phases of meta-ethnography.(57) The work aimed to triangulate experiences from patients with those of their parents or carers, and their healthcare professionals. It considered the process of decision making and the factors influencing the choices made, as well as features of early discharge strategies that could improve the experiences of participants. The synthesis allowed the development of higher level themes and the identification of potentially relevant theories, as well as the description of significant gaps in current knowledge. These were then explored and expanded through Phase 3, where the

qualitative study findings were translated back into the qualitative synthesis results within Chapter 8.

Throughout the thesis, this phase of the work is referred to as the qualitative synthesis so as to provide clarity and to help distinguish between this phase and that of the quantitative systematic review already described. It should be noted that both pieces of research use standardised systematic review methodology and rigorous scientific methods; the differences in terminology simply aim to reduce confusion over the pieces of work being referred to. Thus "systematic review" will be used to refer to phase 1 of the work and "qualitative synthesis" to phase 2.

Phase 3 – A multi-centre focus group study of experiences and perceptions of early discharge in paediatric low-risk febrile neutropenia involving patients, parents and healthcare professionals

The final phase of the work used a qualitative study designed to further investigate the experience and perceptions of early discharge strategies within the UK, and provide original data relevant to this area of paediatric supportive care. In particular, the views of patients, parents and healthcare professionals were sought in an exploration of the triadic nature of this problem. For each stakeholder group, focus groups discussions allowed the examination of how decisions are made and the identification of barriers and facilitators to acceptance of outpatient care. Using multiple centres enabled the recognition of the influence of the centre's structure, culture and current treatment strategy on the perceptions of different models of care. This study drew on the knowledge gained from, and the safety and treatment failure rates quantified in, Phase 1 to inform participants of risk and benefits of various treatment strategies. It also aimed to scrutinise and develop the theory created in Phase 2 of the project. A detailed account of how the findings of phases 1 and 2 were incorporated into the qualitative study is provided in chapter 5. This phase then provides further interpretation to the earlier findings of phase 1 and 2, as described in Chapters 8 and 9.

The final conclusions section of this thesis further translates the findings from all three phases of the work in order to address holistically the original problem and to explore possible explanations for findings. The original contributions of this thesis to the field are clearly outlined and I reflect on the process of performing the work, with a particular focus on how this influences the application of the results. The potential implications for current policy and practice are also detailed and various options for further development within the field of paediatric low risk febrile neutropenia are presented with the aim of further progressing service design and improving experience for these children and young people.

Summary

Within this chapter, I have introduced the concept of febrile neutropenia, as a common complication of treatment for childhood cancer. I have explored the history of its management within the UK and how this has now resulted in standard care for paediatric patients being a 48 hour inpatient admission for intravenous antibiotics. Two broad areas of current research have been introduced – the risk stratification of episodes of febrile neutropenia in children, and the potential for reduced therapy regimes in children at low risk of septic complications. This second area of research is supported by current NICE guidelines which suggest that outpatient treatment should be considered for low risk episodes, but the safety and efficacy of these approaches in children and the attitudes of key stakeholders in this area have yet to be fully explored.(21) This thesis therefore addresses the issues of safety and efficacy in relation to the timing of reduced therapy in children, and explores the experiences and perceptions of early discharge in febrile neutropenia from the perspectives of patients, parents and healthcare professionals. I have decided to use a mixed methods approach in recognition of the multi-faceted nature of the research and its pragmatic aims. I have outlined the three phases of the thesis and provided a brief summary of what each of these involve, including the original findings that they contribute to the field. The following chapter introduces many of the concepts lying behind the qualitative work and further sets the scene for the work within this thesis.

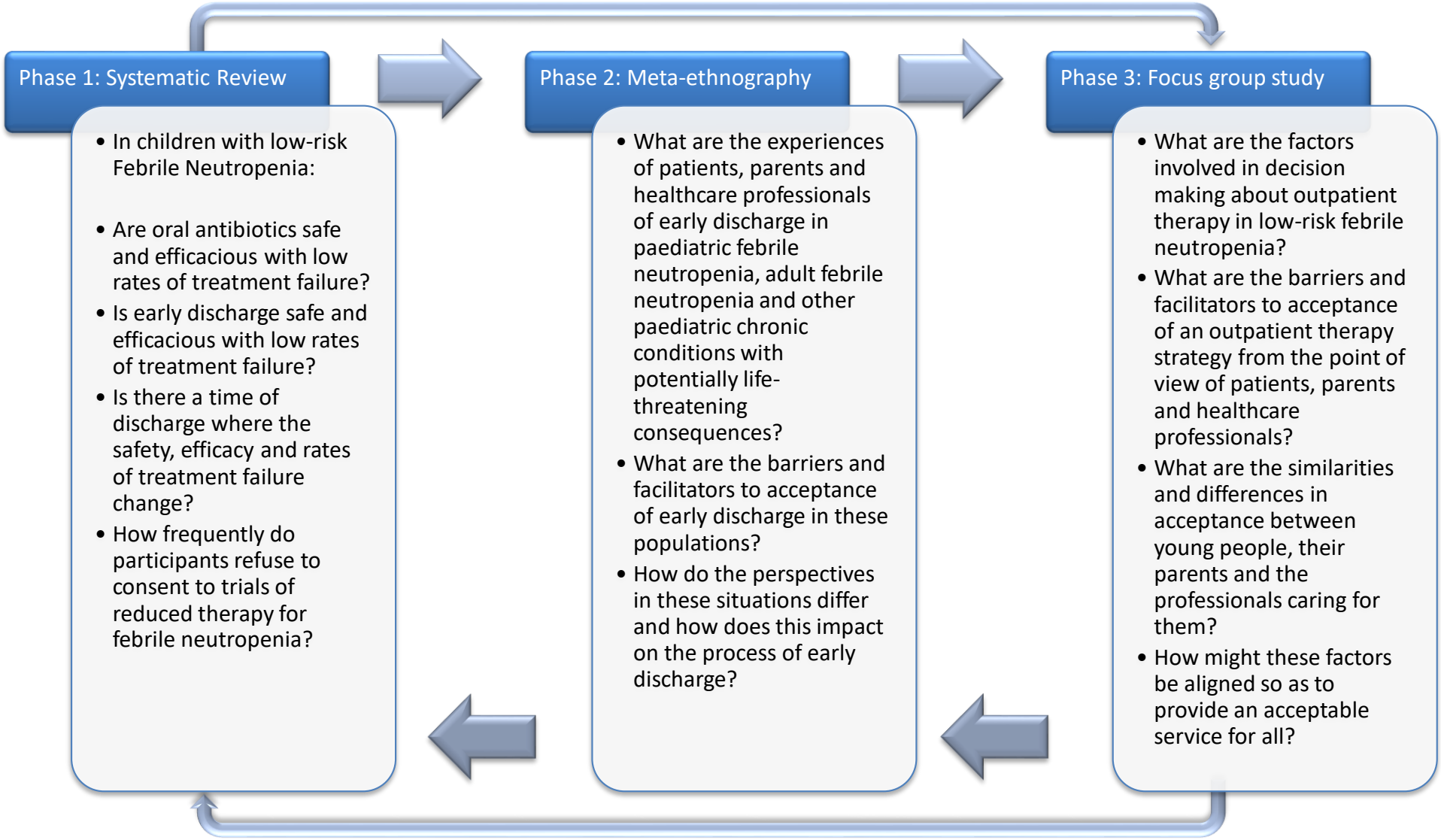


Figure 2 - Overview of Thesis (Research questions for each Phase outlined within each box), upper arrows indicate mixing at design phase whilst lower arrows demonstrate mixing in interpretation.

Chapter 2: Choice and decision making in paediatric practice

Introduction

This chapter aims to provide an overview of some of the issues involved in exploring attitudes towards early discharge that are relevant to all phases of the thesis. It is a contextual discussion of some of the surrounding literature, providing further background to the thesis, and to the debates that will be discussed in later chapters. It also outlines many of the underlying tenets of the thesis, particularly in relation to the value of young people's voices and the challenges of healthcare decision making in this population. Leading on from these general discussion points, I will then perform a more conventional and focused qualitative synthesis, scoping the primary literature surrounding early discharge in Chapter 4.

This chapter first covers the areas of child and young person choice and participation in healthcare decisions and in research, specifically outlining the importance of allowing children and young people their own voice within these areas. This forms the basis of the rationale for including the views of young people in the following sections of this thesis. It then moves on to cover the challenges of triadic consultations and therefore decision making when children, young people, parents and healthcare professionals are making choices together about care. This informs the approach to the focus group discussions, including the analysis of this work. It also underpins the discussion of how the findings of this thesis may apply to clinical practice and to areas of future research.

Finally this chapter discusses decision making processes in general and in relation to clinical trials. Consideration is given to the fact that giving or obtaining consent is part of a decision making process about specific treatment options, whether as part of standard medical care or within the structure of a trial. By introducing relevant concepts and theories, it aims to explore the use of consent rates to trials in the systematic review as a proxy marker for attitudes to reduced therapy regimes and begins to examine areas relevant to following chapters. This is consistent with the overarching objective of the thesis to explore wide-ranging issues surrounding the acceptance of early discharge in paediatric febrile neutropenia and to identify potential barriers and facilitators to the provision of these services for children and young people.

Children and young people's choice and participation

The issue of patient choice is much discussed and politicised, and is at risk of becoming a tokenistic catch-phrase used for political impact, but divorced from service provision. There is argument about whether patients truly can make choices about healthcare in the same way as

they would when making consumer choices. The experience of healthcare, and particularly children's cancer, is somewhat different to a classical consumer choice.(58) Families often have little experience of the options being offered, the potential benefits and associated risks are considerably greater, the uncertainty more difficult to understand and there may not be repeated opportunities to get it 'right'. Furthermore, there is generally no option to defer or avoid making a choice, as may occur in consumer situations. Even when doctors become patients, the challenges in making these 'choices' are great.

Acknowledging these issues and constraints, but recognising the importance of allowing autonomy, national and international guidance states that healthcare professionals should endeavour to involve patients, and their relatives, in their care; be this in small choices such as where an intravenous cannula should be placed, in the greater decisions of their individual care (for example, when to stop treatment with curative intent) or in how services are designed and delivered:

> *'You must listen to patients, take account of their views, and respond honestly to their questions.'(59)*

Historically, these concepts applied only to adults with capacity, but over time as the social construction of childhood has changed, children have been given a greater voice in their own care. Healthcare providers are guided by Article 12 of the United Nations Convention on the Rights of the Child:

> *'States Parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child.'(60)*

In agreement with this, Professor Terence Stephenson, previous president of the Royal College of Paediatrics and Child Health, succinctly captured the professional dedication to seek the opinions of paediatric patients:

> *'We do a great injustice to children and young people when, as a society, we fail to listen to their views, take on board their perspectives and value their contribution in shaping child health services.'(61)*

However, there are a number of challenges to allowing children to be heard. Firstly, the opinions of children are often obtained from a proxy; that is the opinions of the parents are sought as a reflection of their child's and taken to be a true representation of that child's thoughts. There is now a considerable body of evidence that this approach does not capture the views of children

accurately.(62) Furthermore, there is a distinct risk of double silencing, in that the views of the child are not heard directly, and the parent fails to express their own views through trying to represent the child.(63) Thus neither voice is clearly heard.

Secondly, there may be a paternalistic view of the abilities of children to participate in making choices, with both parents and healthcare professionals feeling that children and young people lack cognitive and emotional skills to contribute, particularly to choices that are more complex or those with greater consequences.(105,107–109) Thus children may be listened to but restricted from making overt choices about their care.

Despite these challenges and despite later in this chapter questioning the extent to which people can exercise choice, it is imperative that society maintains a commitment to hearing children's voices and involving them in their healthcare as far as possible. All healthcare decisions ought to be made in partnership between a healthcare professional and the patient, or in the case of paediatrics, between the child or young person, their parents and the healthcare professional, wherever the patient has the capacity to participate in the decision. Interestingly, alongside this moral imperative to include all stakeholders in decision making, there is also evidence that decisions made by groups are generally better than those taken by individuals:

> *'…on average, groups outperform individuals on such tasks [making important decisions], although group decisions frequently do not measure up either to the decisions made by their most capable individual members or to statistical aggregates of individual decisions… In other words, while groups tend to make better decisions than individuals, on average those decisions are often are not as good as they theoretically might be.'* (67)

In the case of low risk febrile neutropenia, there are distinct power differentials within this group. Healthcare professionals may be seen to hold the most intrinsic power in this situation – they hold responsibility for the inpatient beds and therefore can theoretically decline a patient stay in hospital. Furthermore, they hold social power in which society confers greater control over decision making to professionals than to their clients. At the same time, decision making about children and young people almost exclusively takes place within families, and their surrounding communities, such that parents hold considerable power over their children, even as they become young adults with a degree of their own autonomy. Thus the child or young person might feel that their own contributions to these decisions are minimised or even completely excluded. Parental impact, and that of wider society, on young people's choices should not be ignored, as choices are rarely exercised in isolation. Parents play a key role in supporting young people to

develop the skills required to make competent decisions.(68) This is discussed further in the following section of this chapter.

Further research is needed into how healthcare decisions for children and young people can be best supported so as to allow contributions from all stakeholders to be heard and valued. Healthcare professionals may make efforts to share information and knowledge with young people and their families so as to reduce the power differential and allow for decisions to be more equally shared. This concept of shared decision making will be discussed further later in this chapter and in Chapters 8 and 9. Linked with these considerations about involving young people in healthcare choices, this chapter now considers the triadic nature of paediatric consultations and the challenges of communication and decision making within this structure.

Triadic consultations

In paediatric practice, the issue of shared decision making is complicated by the three-way consultations involved, in which young people, their parents and the health care team may all have different views, values and choices when it comes to a healthcare decision. It is essential to consider how these triadic relationships function and how differences are negotiated, in order to be able to understand how they might influence the issue of reduced therapy in paediatric low risk febrile neutropenia, helping to both explain the findings of previous research and to inform the analysis and interpretation of the primary research performed within this thesis.

The dynamics of these complex triadic consultations have been explored by Tates and Meeuwesen.(65) Perhaps most interesting from a professional's point of view is the finding that the child's contribution to a consultation was mostly controlled by the parent, with large proportions of questions that had been directed to the child being interrupted and answered by the parent. Although these issues may have improved over time as society has become less paternalistic, other strategies could also improve the child's participation in discussions, including their own determination to contribute and the persistence of the professional in directing discussion towards the child.(65,69) It is worth noting that for some children this may be because they prefer to use their parents to indirectly communicate with the professionals and this preference should be accepted provided it is the patient's choice.(70)

When considering the involvement of children and young people in health care discussions, it is also worth noting the different conversational styles that professionals tend to use when addressing them compared to their parents. Doctors have a tendency to be more effective when conversing with children, using softer tones and limiting discussions to obtaining information.(65) Although the communication skills used with children and young people must be adapted to

enable them to engage in the consultation, it is essential that this change in consultation style does not diminish the value of the opinions of the child or young person nor limit their ability to participate in decision making as far as they are able. Close attention to the developmental stage of the child or young person may facilitate the greatest degree of involvement possible.

The challenges of maintaining a balanced triadic consultation are perhaps even greater in the setting of paediatric oncology than those settings where the majority of this work has been completed. Parents of children with cancer have significant levels of health anxiety and this degree of concern may create an emotional or psychological need to control more of the discussions, and also decisions regarding care. Parents may wish to protect their child from the more distressing aspects of a diagnosis or a decision to be made and thus choose not to involve them in the information sharing discussions about their disease.(71) Furthermore, the complexity and potential consequences of the choices to be made may cause both parents and professionals to limit the involvement of children and young people in decision making, for fear of them making a 'wrong' decision.

Despite this, it is important to note that conflicts within triadic decision making are relatively uncommon.(72) Generally, decisions can be reached which all parties are happy with. There may be many reasons for this frequency in consensus. The first is that young people tend to learn their decision making processes from their parents. They observe the attribution of weight to various factors, along with the attitudes of their parents towards risk.(68) Young people also tend to have similar health knowledge and beliefs to their parents. As such, they are likely to come to similar decisions to their parents as this is the model of decision making they are most exposed to. Secondly, young people develop their confidence and perceived self-efficacy in healthcare decision making from the observation of their parents and through the feedback given to them by their parents and healthcare professionals. They may seek the approval of parents and healthcare professionals when making decisions as they are still negotiating this relatively new task. It is not surprising then that they chose similar decisions to the more dominant adults within the consultation. Thirdly, parents, young people and healthcare professionals frequently herald from similar cultures. Thus the influence of the predominant culture on each factor within the decision making process is likely to be similar and therefore result in more unified conclusions. The normative values and assumptions of the culture result in an unspoken pressure to reach a certain decision - for example to prioritise a child's physical health over the psychological and social wellbeing of other family members.(73)

The infrequency of conflict within triadic decision making means that when this does occur it is a particularly difficult scenario. The challenges of reconciling these differences are familiar to healthcare professionals dealing with this age-group. However, although communication training

and conflict resolution skills are increasingly being taught within both undergraduate and postgraduate healthcare professional training, the particular challenges related to adolescent decision making (including the various stages of adolescent cognitive development) and methods for supporting shared decision making within triadic consultants are rarely covered. Professionals may struggle to harmonise decisions in the absence of specific guidance and within the often high-pressure and time-critical setting of many healthcare decisions in paediatric haematology and oncology services.

Having considered the challenging nature of triadic consultations and of decision making within them, this chapter now moves to more of the psychological and sociological theories surrounding healthcare decision making, aiming to highlight features that are specifically relevant to decisions surrounding early discharge in paediatric low risk febrile neutropenia.

Decision making theories

An understanding of healthcare decision making theories enables the exploration of attitudes surrounding reductions in therapy for low risk febrile neutropenia. Alongside identifying the attitudes stakeholders have towards different strategies, it is vital to understand how patients, families and healthcare professionals come to the decisions that they make in this area. Furthermore, exploring how these decisions differ between family members, and between families and healthcare professionals, might enable further understanding of the specific reasons for agreeing to or declining reduced therapy options and thus help to address the research problem outlined in Chapter 1. This section of the chapter considers how people negotiate decisions, within their own decision making processes, within family relationships and within healthcare consultations.

One of the earliest works about healthcare decision making is found in the Health Belief Model (**Error! Reference source not found.**).(74) First described in the 1950s by social psychologists R osenstock, Hochbaum and Kegels, the Health Belief Model describes how a person's health care decisions, and actions, are influenced by four main perceptions. (74) These are their perceived susceptibility to the specific condition, the perceived severity of the condition (both physical and social), the perceived benefits of a decision or behaviour, and the perceived barriers to that decision or behaviour. Furthermore, a 'cue to action' or prompt is required to stimulate the person to make the decision or action. All of these factors may be influenced by demographic and sociological variables.

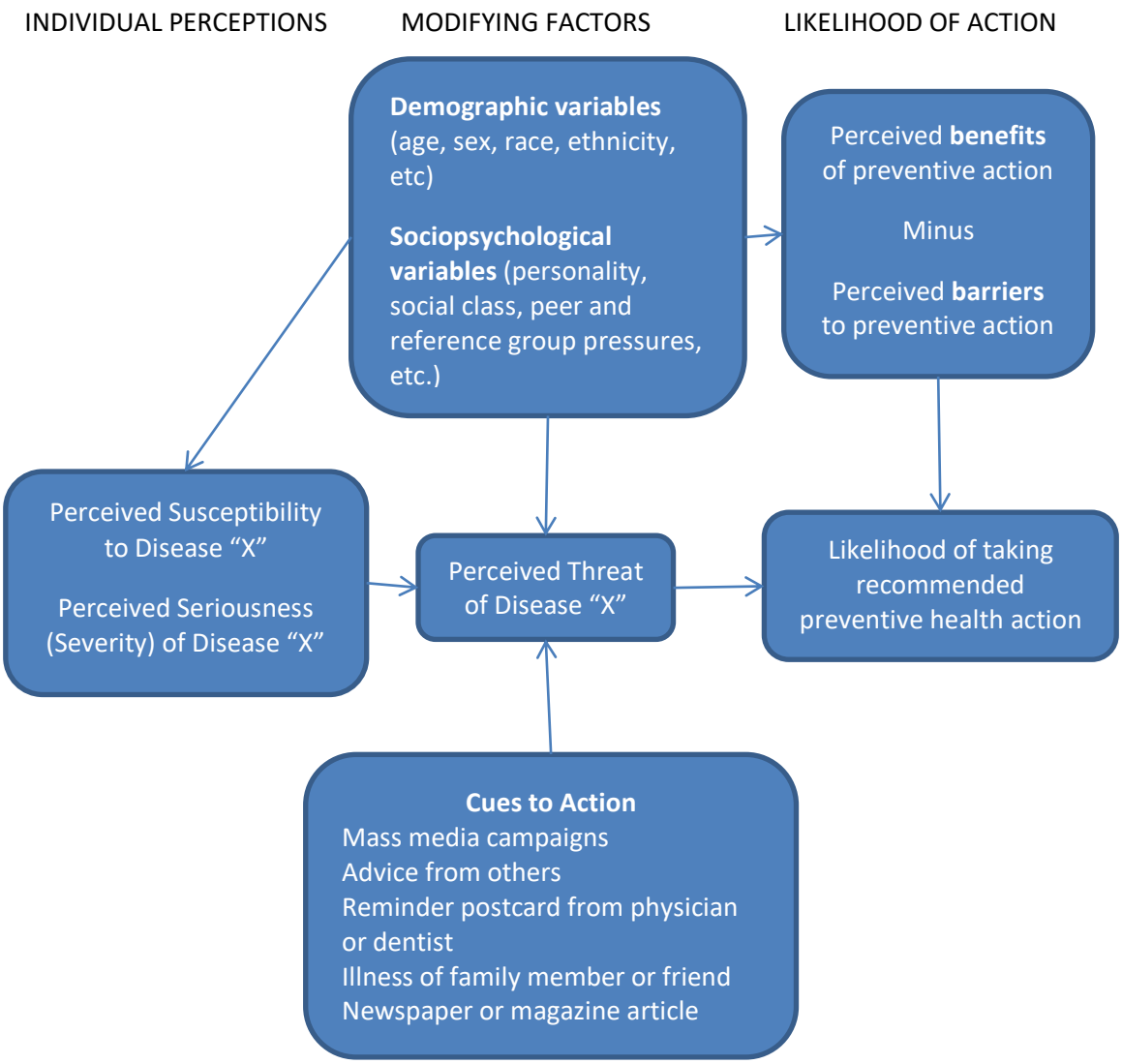


Figure 3 The Health Belief Model

The Health Belief Model is a simplified way of considering health care decision making, focusing mainly on screening or disease prevention actions, although it can be transferred to almost any decision making situation. The importance of perceptions in the model is key. Most healthcare decisions are made in situations of uncertainty, where although events may occur with a predictable probability, it is not possible to know whether, for this particular person in this situation, the event will occur. (67) Decision making may therefore be influenced by the communication of this uncertainty between members of the consultation, and attitudes towards risk within the decision making person or group.

Similarly, consideration must be given to the ways in which different stakeholders may view health conditions. Specifically, research has found that those who have experience of a health condition, for example those who have previously experienced cancer, often consider the quality of life in this condition to be higher than those who have no experience of it. (67) Healthcare professionals will generally assign a value between these two groups. This may be particularly

important for low risk febrile neutropenia – patients with no experience of low risk febrile neutropenia may be less likely to opt for an early discharge option than those who have been admitted for previous episodes, particularly if those episodes have not resulted in serious adverse events. Furthermore, patients who have experienced an early discharge strategy may be more likely to value this option again and thus have a more positive perception of this course of action. Healthcare professionals may have a more moderate view, influenced by both their experience of poor outcomes in febrile neutropenia and by their day-to-day contact with patients who suffer no significant septic complications.

The Health Belief Model, although a useful way to consider the basics of decision making, is perhaps overly reductive as a theory. Decisions are rarely made in such a rationalist and autonomous fashion, and may be shaped by inaccurate perceptions, social factors, and normative values and assumptions.

Consideration of challenges to accurate perceptions is vital when exploring the process of decision making and considering the Health Belief Model. Cognitive biases describe the influences of various heuristics that result in systematic deviations from rational reasoning.(75) In the setting of febrile neutropenia, both professionals and families may be contending with multiple cognitive biases, including availability bias (where frequency assessments are based on ease of recall of their occurrence), loss aversion (where losses hold more weight within decision making than equivalent gains), status quo bias (where people prefer the current situation over changes), and anchoring (where there is persistence in thinking dependent upon the initial information available).(75,76) Perhaps most significant in terms of reductions in therapy is that of omission bias, whereby any harm (eg intensive care admission) that occurs to a child from committing to change to an early discharge strategy is felt more keenly than harms that occur due to omitting to change.(76) Healthcare professionals have been found to be at particular risk of employing biases and heuristics, due to the benefits in speed and accuracy that these cognitive strategies often bestow.(76)

The Health Belief Model also fails to recognise that healthcare decisions are invariably made within the confines of social, economic, cultural and historical contexts, such that the choice is constrained by various factors acting upon the patient and those around them.(77,78) The influences of gender, race, power, family structure, social views on age on both patient and healthcare professional decision making have been clearly described in the literature, but are not acknowledged by the Health Belief Model.(62,68,77,79)

Working alongside these social influences, normative values and assumptions about appropriate responses to health challenges may greatly impact on the choices offered and made. For parents

who are making healthcare decisions about their children, a key influence in the decision making process is often the concept of doing what a 'good parent' would do. The 'good parent' in the literature is represented in a similar way across varied populations and appears to be socially defined.(73,80) Three key features within this literature that are particularly relevant to health care decision making are that the 'good parent' makes *"informed, unselfish decisions in the child's best interest", "tries to prevent suffering and protect health"* and *"teaches the child to make good choices…".*(80) The decisions made by parents are therefore constrained by the societal pressures to be a 'good parent'.

In the case of healthcare professional decision making, staff are governed by various professionally enshrined ethical principles. The four pillars of medical ethics described by Beauchamp and Childress of beneficence, non-maleficence, justice and autonomy are taught explicitly within professional curricula and also implicitly during the apprenticeship of new colleagues into the healthcare service. (81) Beneficence describes the importance of working for the benefit of the patient and non-maleficence compels clinicians to work to minimise the harms to patients of treatment.

Meanwhile, the importance of allowing patients to make their own decisions, within their own beliefs, even if these contrast with those of their healthcare team is captured in the ethical pillar of autonomy. The role of autonomy for children and young people, where they have the capacity to contribute to decisions about their own healthcare, has already been discussed within this chapter. Those involved in service design must consider that families might choose different options to healthcare professionals and service providers. The extent to which practitioners should encourage patients to take particular options and therefore limit autonomy is debateable. Within the classical model of informed decision making, the patient is given information regarding the various options available to them, and is then the primary decision maker. However, within a shared decision making model, the healthcare professional and patient might share the information about various options, along with their values and preferences, so as to come to a decision together. From this concept stems the GMC advice:

> *"The doctor may recommend a particular option which they believe to be best for the patient, but they must not put pressure on the patient to accept their advice."(82)*

The issues surrounding shared decision making will be discussed further later in this thesis.

Finally, when contemplating the normative values within healthcare professional decision making, the fairness of healthcare decisions, also known as justice, should be considered. Patients are considered to have a 'right' to receive similar care to other patients in their situation, regardless of cost, and consideration should be given to the distribution of healthcare through the

community. This feature of medical decision making is focused less on the direct care of the individual patient and so may not feature so strongly in the choices made by families. However, clinicians making decisions are often also thinking about the impact of their decisions at a societal level. They may be making decisions for whole groups of patients, based on the costs of various treatment options, the potential outcomes and resource constraints within the specific department and within the health service as a whole; decisions about individual patients take place against a backdrop of wider healthcare decisions.

For low risk febrile neutropenia, physicians may be thinking about how a patient in hospital may be located in a bed space that could be needed for another child who is also the clinician's patient or may be receiving nursing and medical staff time which might otherwise be used differently. Balancing these health care service costs and benefits alongside the advantages and disadvantages for the individual patient makes the decision about whether to implement an early discharge even more complex. This may, in part, account for differences in the choices made by healthcare professionals compared with patients and families when it comes to the issues surrounding early discharge for paediatric low risk febrile neutropenia.

When people choose to let a healthcare professional make a choice for them, it ought to be noted that this should also be considered an active decision. It requires a degree of trust in the professional involved, and as such professionals have a responsibility to obtain as much information about the patient's preferences, goals and values as possible and to communicate their rationale for the chosen course. This feature of decision making has been eloquently captured by Atul Gawande, who writes:

> *"The new orthodoxy about patient autonomy has a hard time acknowledging an awkward truth: patients frequently don't want the freedom that we've given them. That is, they're glad to have their autonomy respected, but the exercise of that autonomy means being able to relinquish it."(19)*

Younger patients and those with higher educational levels are more likely to want to be involved in medical decision making, whilst gender also plays a role. (67) Female patients are more likely to wish to be involved in the decision making process. Furthermore, patients tend to prefer to make simpler medical decisions, with a tendency to relinquish the decision to professionals if it requires a higher degree of medical proficiency. (67) Thus, families may not wish to be involved in decisions about which chemotherapeutic agents to use for their child's primary diagnosis, but may want to contribute to the decision surrounding treatment of low risk febrile neutropenia. The desire to be involved in some decisions, and not others, requires frequent checking and negotiation by healthcare professionals.(83,84) This reflects the dynamic nature of medical

decision making, in which conditions may change frequently, and where individuals may feel more or less willing to participate in decision making based on their physical, psychological or social situation.

Finally, relating to the theories of decision making, it is important to consider the issue of 'option setting' in which practitioners make choices about what options they offer to patients, whether this is treatment options or an invitation to participate in trials. This process precedes that of decision making and may limit the ability to participate in decisions by reducing the choices offered to patients. The range of options offered may be influenced by local policy, the professional's knowledge of the various options, organisational constraints, the professional's sense of duty and responsibility and assumptions made on the behalf of the patient about their values and preferences.(85) Importantly, the judgements made about interest and capability may exclude participants from disadvantaged social groups, including the very young or very old and those from ethnic minority and lower social economic backgrounds from participation in treatment options or research studies which they might otherwise have chosen. (85–87)

Assessment of decision making

Having explored these theories and the various influences on decision making, two main areas need discussion. First, how can 'good' decision making be defined and identified, and second, how should research assess decision making in healthcare.

The assessment of decision making in clinical practice traditionally takes an individualistic approach, assessing only the patient themselves. Within this context, healthcare professionals are encouraged to assess the process of the patient's decision making, through the assessment of capacity, rather than assessing the option chosen or the outcome related to that choice. Thus a patient may chose an option that the healthcare professional may not feel is the 'best' option, but provided the patient can show that they understand the relevant information, can retain it long enough to make the decision, can weigh the information and communicate their decision then that decision is considered to be medically 'good'.(88)

Again this traditional approach may seem overly simplistic. Defining a good decision as informed decision making alone, or autonomous choice, neglects the psychological and social complexities of decision making as discussed earlier in this chapter. Furthermore, the opinions of various stakeholders about whether a decision was 'good' may vary over time. Thus a decision that was 'good' when first diagnosed with a chronic condition may no longer be a 'good' decision later in the course of that disease. Within the context of termination of pregnancy, the strength of feeling

about whether a decision was ‘good’ or not has been shown to reduce over time, suggesting that the emotional intensity of decision making diminishes with distance from the event.(89)

Practically, there are two main methodologies used to assess decision making in healthcare research. The first, sited within the quantitative paradigm, uses utility assessments to provide numerical assessments of decisions and the worth that participants place on various effects. These methods include discrete choice experiments, threshold techniques or utility analyses (using visual analogue scales, willingness to pay or time trade off methods). (46,90) They aim to define the features of a decision, which, if changed in a certain way, might alter the choices made. Participants may be asked to assign a worth to a feature in terms of time or of money. These methods have been used in numerous studies to explore many important aspects of attitudes to reductions in therapy for febrile neutropenia and present them in a quantitative manner that fits with the current medical paradigm.(35,46,49) For example, Sung et al determined that requirements for significant outpatient attendance (more often than thrice weekly) or a readmission rate of greater than 7.5% would be a barrier to most families eligible for such care. (49)

However, there are some limitations to this approach, particularly in the fact that it limits the participants to the options provided by the researchers and that it provides a relatively superficial account of the features involved in a decision. In particular, probability trade-off methods have not been proven to be an accurate method for assessing group decision making or in service development issues, whilst utility assessment is difficult in transient states such as febrile neutropenia where the worth given maybe less varied than for more chronic conditions. (67) Finally, utility assessment and trade-off methodologies can be quite cognitively demanding and require a level of development which may be challenging to comprehend for children and young people who have yet to acquire skills in abstract thinking.

In the second main methodology for assessing decision making, qualitative techniques may complement these utility based assessments by helping to answer other difficult clinical questions about the decision making process. Thick qualitative material may provide details about the process of weighing up decisions and balancing the various risks and benefits involved in a decision. They can provide depth to quantitative methodologies by expanding on the rationale for certain choices in specific situations, allowing for a more comprehensive understanding of the social and cultural contextual influences on a decision. Qualitative methods may also allow the assessment of the negotiations between various members in decisions made by groups and may address the influence of additional social and cultural factors through these observations of decision making process.

Decision making in clinical trials

Having identified and reviewed various theoretical aspects of medical decision making as well as considering how to assess the choices made, this section now explores two main aspects of decision making in clinical trials. As discussed briefly in Chapter 1, there are a number of reasons why participants may choose not to participate in clinical trials, this section aims to discuss these more broadly. This is important to the thesis given that the rates of consent to studies of reduced therapy regimens for febrile neutropenia are explored in Chapter 3 as a proxy marker for attitudes to early discharge regimes. However, rates of consent may be partly due to factors which are specific to decision making in clinical trials, rather than a reflection of a particular treatment approach. Thus this section of this chapter will consider the issue of decision making in clinical trials separate to that used in other clinical decisions, and will highlight issues which are particularly relevant when considering consent to clinical trials. It adds to the thesis both by informing these explorations in Chapter 3, but also through providing discussions of aspects of consent relevant to the qualitative study in phase 3 and to the research implications discussed in Chapter 9. The first aspect of decision making I will explore in this section is the legal and ethical aspects of informed decision making in clinical trials, particularly those involving children, and the second is the factors involved when individuals choose to be part of a clinical trial.

The main legal process involved in decision making for clinical trials is that of consent. The majority of clinical trials will require a written record signed by the participant confirming they are happy to participate in the study. Often this signature is referred to as 'consent'. However, the term actually refers to making a decision to allow the researchers to perform the study on the participant. It is not a 'one-off' event, at which the participant puts pen to paper; instead it is a process, involving a two-way flow of information about the study, the requirements, the patient's role and the effects on them, as well as their own thoughts and considerations about the research. The importance of this as an ethical construct is outlined clearly by the General Medical Council and in Good Clinical Practice principles, which are underpinned by the Declaration of Helsinki, the Nuremberg Code and other laws and directives.(26–29)

The process of consent is somewhat different when considering children, and becomes particularly complex when dealing with adolescents and young adults. For very young children, who are unable to contribute to discussions, their parents, or legal guardians, are responsible for making decisions relating to their care. For medical decisions, the age of capacity is set at 16 years.(88) Once you have turned sixteen, you are considered competent and able to make your own decisions in any medical or research setting, supported by your family and healthcare professionals.

For children who are able to voice an opinion about a decision but who are younger than sixteen, the guidance surrounding consent differs between clinical decision making and that involved in trial participation. In the clinical setting, if a patient is younger than sixteen, they may be considered able to consent if they show capacity, that is they can understand the treatments offered, including the risks and benefits, retain this information, weigh up their options and then communicate that decision.(88,95) This 'Gillick competence' is decision and situation specific. For example, a relatively young child may be able to decide whether they want anaesthetic cream or cryogesic spray to help with the pain of venepuncture, but is unlikely to be able to make a decision about chemotherapy options. It should be noted that decisions by Gillick competent young people to refuse treatment may be overruled by the consent of a parent. Furthermore, clinicians can struggle to apply the guidance regarding the assessment of Gillick, being influenced by their own opinions and by the complexity of this judgement:

> *"In practice, judgements of competency go beyond semantics or straightforward applications of legal rules; such judgements reflect social considerations and societal biases as much as they reflect matters of law and medicine."(95,96)*

In contrast to this, the rules regarding consent to participation in clinical trials are somewhat different. In general, parental consent would be considered to be required for the involvement of all young people under the age of sixteen, even if the child is competent to make their own decisions.(91) Furthermore, in the case of research, the young person's refusal to assent to participate is given more weight, and is less likely to be overruled than within decisions about standard medical practice.

Choosing to be part of a clinical trial can be a difficult decision for patients. They often have the choice of standard treatment, for which the risks and benefits have been more clearly defined and the healthcare professionals caring for them often have more experience with, or a new treatment, which may, or may not, have better benefits or fewer risks than the conventional option. The challenge of dealing with uncertainty, both in the effects of a new treatment and in the process of randomisation to treatment, compounds the dilemma, which is often posed at a time when patients are already trying to absorb news of a diagnosis or adjust to deterioration in their condition.

Alongside this, research has found that patients and families can find consenting to trials of reduced therapy even more difficult than randomisation of intensification or substitution trials. Tulstrup et al found that parents of adolescents were more likely to consent to reductions in therapy compared with parents of younger children, and this may reflect the involvement of young people in these decisions.(97) This suggests that parents find it harder to consent to

reductions in therapy than adolescents do and is worthy of consideration within the later phases of this thesis. This is further supported by evidence that parents chose to take less risks for their children than competent adults or adolescents would chose for themselves.(49)

Summary

This chapter has highlighted some of the issues surrounding involving young people in choices within healthcare and research settings as well as the challenges of triadic consultations. Relevant concepts and theories, including the Health Belief Model and cognitive biases in decision making, have been explored. Some of the complexities of medical decision making and how this may be assessed have been discussed, particularly in relation to involving children and young people in healthcare decision making. This background research further contextualises and provides the grounding for the thesis, particularly the qualitative synthesis of experiences of early discharge and the subsequent focus group discussion study. Many of the concepts outlined in this chapter will be referred to again, where relevant, in the following phases of the work.

Chapter 3: Systematic review and meta-analysis of reduced therapy regimens for children with low risk febrile neutropenia

Introduction and rationale

In this first empirical chapter of the thesis, I report the systematic review of reduced therapy regimens, including early discharge, outpatient care and oral antibiotics, for children with low risk febrile neutropenia. I aim to address the safety, efficacy and rates of treatment failure for each regimen, whilst considering the role of timing of treatment change upon each of these outcomes. This provides a robust and up-to-date synthesis of current quantitative evidence in the field, so as to inform key stakeholders about the different options for care, whilst also providing the data for discussion within the focus group study performed in Phase 3 of the thesis. This chapter also provides initial data about the issue of attitudes to reduced therapy regimens as consideration of the rates of consent to studies included within the systematic review provides a crude measure of perceptions of early discharge and oral antibiotics. This will be assessed further in phases two and three of the thesis, through the synthesis of current qualitative evidence and the performance of the focus group discussion study.

As discussed in Chapter 1, reduced therapy regimens for managing children and young people with low risk febrile neutropenia may provide benefits to both patients (including increased quality of life and reductions in hospital acquired infections) and the health service (including cost savings and reduced pressure on hospital beds).(34,36–38) However, any reduction in therapy must be both safe and effective to justify a change from current practice.

A previous systematic review conducted by Manji et al considered two aspects of the reduction of therapy.(98) It compared outpatient treatment with inpatient treatment, and oral antibiotics with intra-venous (IV) therapy. They included only low-risk patients as defined by individual study protocols, recognising that this is a heterogeneous group.

The review found that treatment failure, defined as persistence, recurrence or worsening of fever/infecting organisms, new infections, any modification of antibiotics, readmission, or death during study drug treatment, was as likely to occur in inpatients compared with outpatients and that inpatients were more likely to have alterations made to their antibiotic regimens. Within the included studies, two low risk patients died – they had both been treated as inpatients. The authors found no increase in medical complications with oral therapy. In particular, there were no deaths, and no increase in readmission to hospital or in treatment failure, including the need to modify the antibiotic regime, for patients receiving oral therapy.

Although this review provided essential information about the broad concepts of outpatient and oral therapy for febrile neutropenia, it involved combining data from very different groups and thus lost some of the more nuanced information from the original trials. This is particularly important when considering timing of discharge as further information is required to know precisely when discharge should be advised.

Meanwhile, a recent Cochrane review focused mainly on adults with febrile neutropenia and found that oral therapy was an acceptable alternative to intravenous antibiotics.(99) A subgroup analysis of paediatric studies found no difference in treatment failure rates within this population, although this included exclusively randomised controlled trials, of which there were only 8 identified in children. Furthermore, it examined the impact of oral antibiotics alone, without consideration of the role of location of treatment.

Finally, neither review included non-English studies despite the presence of very active research groups in this field based in South America. In addition to these limitations, I was aware that important further work had since emerged in this area. In particular, one trial had looked specifically at early step-down from intravenous antibiotics given as an inpatient to oral outpatient treatment within 22 hours of presentation with febrile neutropenia.(17)

Given all of these issues and the high likelihood of identifying other new and relevant studies, I decided that a new systematic review should be performed. This review had more focused aims than previous reviews, particularly in defining the most appropriate time of discharge in these patients, and had a new and more thorough search strategy. It also included studies using observational methods, and aimed to provide further depth and clarity to the findings of prior works.

Methodology

Systematic review is an established methodology used to identify, evaluate and summarise the research evidence in a specific area. It involves a structured, pre-planned and considered approach to identify relevant research studies. In systematic reviews of effectiveness, as described in this phase of the thesis, attempts are made to identify as many relevant studies as possible, to critically assess them and combine their results in a way that is informative to the intended audience.(100) This method aims to reduce the biases inherent in a narrative review through consideration of all available research evidence relevant to the research question.(101)

Where appropriate, meta-analysis of quantitative results provides a more precise estimate of an intervention's effectiveness, given the power provided by increased events.(100,101) Furthermore, by exploring differences between subgroups of studies, further research questions

can be answered beyond the original studies' objectives. For this systematic review, the use of meta-analysis provides estimates of the safety, efficacy and treatment failure rates of the various treatment regimens for febrile neutropenia. As these estimates are more specific, robust and precise than those previously available, they inform both the subsequent chapters of this thesis and future clinical decision making.

Aims and objectives

This systematic review aimed to provide an up-to-date and robust assessment of the role of the route of antibiotic administration and the location of treatment in the management of low-risk febrile neutropenia in children being treated for cancer. It aimed to define the overall success (or failure) of each treatment regime in resolving an episode of febrile neutropenia without complications. Furthermore, I aimed to explore both safety and efficacy for each potential regime. In particular, I investigated the timing of discharge (before 24 hours, 24-48 hours or after 48 hours), including the role of entirely outpatient treatment.

Finally, considering that there may be concern regarding reduction of therapy from patients, their parents and the healthcare professionals caring for them, this systematic review collected data on rates of declined consent, where this was reported, as a way of gaining insight to the potential acceptability of these approaches. The precise research questions for this review are outlined in Box 4.

Box 4 - Research Questions

In children with low risk febrile neutropenia:

1. Are oral antibiotics safe and efficacious with low rates of treatment failure?
2. Is early discharge safe and efficacious with low rates of treatment failure?
3. Is there a time where the safety, efficacy and rates of treatment failure change?
4. How frequently do participants refuse to consent to trials of reduced therapy for febrile neutropenia?

Methods

A protocol for this review was developed, registered on PROSPERO (CRD 42014005817) and published, prior to commencing the work.(102) This chapter is presented in accordance with PRISMA guidelines.(103)

Searches

Electronic searches of MEDLINE, MEDLINE in-Process & Other non-Indexed Citations, EMBASE, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL via the Cochrane Library), Literature Latinoamericana y del Caribe en Ciencias de la Salud (LILACS), Health Technology Assessment Database (HTA) and Database of Abstracts of Reviews of Effects (DARE) were performed. The search strategy focused on febrile neutropenia and the interventions of antibiotics and early discharge, whilst using a paediatric filter. Published and unpublished studies were sought and no date or language filters were applied. The latter is important given I suspected that there would be a number of studies that had been performed in Spain, Portugal and South America as these areas have been active in research into paediatric supportive care. The full database search strategy is provided in Appendix 3.1.

Conference proceedings of the RCPCH (Royal College of Paediatrics and Child Health), SIOP (International Society of Paediatric Oncology), ASPHO (American Society of Paediatric Haematology/Oncology), ASCO (American Society of Clinical Oncology) and ICAAC (Interscience Conference on Antimicrobial Agents and Chemotherapy) meetings were searched for relevant abstracts. Reference lists of included articles and relevant systematic reviews were also reviewed. Authors of relevant studies and prominent clinicians within the field were contacted seeking further studies.

Study selection

I screened the title and abstract of all studies for inclusion. A second reviewer (JC) independently screened a sample of 1000 of the titles and abstracts. The kappa statistic for agreement was calculated and showed good agreement between reviewers (k = 0.69, 95% confidence interval 0.59-0.79). Full text was obtained for all potential articles of interest. All full texts were assessed for eligibility by two reviewers (myself and JC). Disagreements were resolved by consensus, or referred to a third reviewer (RSP, 5 studies referred).

Inclusion and Exclusion criteria

Studies were included if they met the criteria shown in Box 5.

Study design:

I anticipated, given the previous reviews, that the number of RCTs in this area would be small. I believe there is clinical value in knowing the absolute numbers of patients experiencing failures in safety and adequacy. Therefore, I derived information from both prospective observational cohorts and the separate arms of RCTs to determine these estimates, and to provide observations on different treatment groups within a range of studies. Quasi-randomised trials would have been

eligible for inclusion provided the methods of allocation to treatment groups were clearly described.

Retrospective studies were excluded, as were studies that enrolled participants ≥24 hours after initial empiric treatment.

Box 5 - Inclusion criteria

Study Design: Randomised Controlled Trials, Quasi-Randomised Controlled Trials and prospective observational cohorts

Population: Aged <18 years with low-risk fever and neutropenia secondary to treatment for cancer, or results available for this subgroup

Interventions: one or more of

- Location of treatment – inpatient, outpatient, or initial inpatient with early discharge to outpatient
- Route of antibiotic administration – intravenous, oral or intravenous with switch to oral (IVOST)

Outcomes: one or more of

- Treatment failure at 30 days- persistence, worsening or recurrence of fever/infecting organisms, modification of antibiotics, new infections, re-admission, admission to critical care services or death during treatment.
- Safety - medical complications, defined as admission to critical care services or death.
- Adequacy - resolution of the episode without change in antibiotic or location of the patient.

Population:

Children or young adults (aged less than 18 years) who attended paediatric services with fever and neutropenia secondary to treatment for cancer and who were assessed to be at low risk of medical complications.

Studies that enrolled only children and studies in which the majority (defined as > 80%) of patients were less than 18 years old, even if those patients are not reported separately were included. This reflects the fact that some paediatric studies may include a small number of young adults who have malignancies and physiology similar to the paediatric cohort being investigated and who are therefore treated within Teenage and Young Adult services by paediatricians. Such

studies designed for the paediatric group that have recruited small numbers of young adults do not generally recruit from the older adult population, in which the causes and outcomes of febrile neutropenia are likely to be different. Studies of adults which report data for patients less than 18 years old were included, if outcome data for children were reported separately. Studies which included > 20% of adult populations and those which included mixed age populations with no details on age distribution were excluded.

There were no eligibility restrictions concerning the definitions of fever and neutropenia or the stratification rule used. Studies of multiple risk groups were included, if data for low risk patients (as defined by study protocols) could be extracted separately.

Interventions and comparators:

I was aware that studies had included a variety of treatment regimens, including inpatient IV therapy, outpatient IV therapy and oral outpatient therapy.(98) This created a challenge as there are two components to the comparison – the route of administration of the antibiotics (IV or oral) and the location of the patient's treatment (outpatient or inpatient) – which could be correlated in individual studies. In particular, oral antibiotics and outpatient treatment are likely to be used together and I appreciated that it might be difficult to establish whether any differences in outcome are related to the route, the location of treatment, or both. The considerable intermeshing of these two issues within the literature justified the use of a single review to attempt to address the various options in reduction of therapy to these patients.

To be included a study had to have investigated the location of treatment or route of administration of antibiotics. Prospective single arm studies had to examine these features of the regime as the primary aim of the study. Studies examining different antibiotics given by the same route and in the same location were excluded.

For the purpose of this review, outpatient care was defined as discharge within 8 hours of presentation. Justification for using an eight-hour cut-off is a practical one. The time taken to review a patient, ensure they are eligible for outpatient treatment and then prescribe and obtain any medications to take home may be up to eight hours. Any period longer than this could reasonably be called admission to hospital. The timing of discharge was grouped into outpatient (admission of less than 8 hours), <24 hours, 24-48hrs, >48 hours and entirely inpatient treatment. Early discharge is used to refer to all categories except entirely inpatient treatment, unless otherwise specified.

Where patients received a single dose of IV antibiotics followed by a course of oral antibiotics, this was considered to be an entirely oral course. This was to allow for studies in which IV antibiotics are administered whilst awaiting the results of blood tests to confirm low risk status, but once the

patient was identified as low risk, they were started on oral antibiotics. The timing of switch to oral antibiotics was grouped into entirely oral (as described above), <24 hours, 24-48hrs, >48 hours and entirely intravenous treatment. The phrase 'any oral therapy regimen' is used to refer to all categories except entirely intravenous treatment, unless otherwise specified.

Outcomes:

For the purpose of this review, the three primary outcomes were treatment failure, safety and adequacy. The definitions of these outcomes are given in Box 5. These outcomes were used because they are likely to provide the information that patients and clinicians combine when making decisions about choice of care, thus they are the most clinically relevant outcomes for those involved in planning and delivering paediatric haematology and oncology services. Multinational guidelines have recommended that the primary outcome of studies into febrile neutropenia should be a composite measure, hence the use of treatment failure (persistence, worsening or recurrence of fever/infecting organisms, antibiotic modification, new infections, re-admission, admission to critical care or death) as an outcome.(104) Meanwhile, knowledge about the safety of a strategy is essential to be able to consider its use at all, whilst information about adequacy would allow services to plan appropriately for potential re-admissions or changes in treatment associated with changing to a new low risk strategy.

To be included a study had to have recorded and provided data for one or more of the primary outcomes.

Data extraction and Quality assessment

Data were extracted by myself and independently checked by a second researcher (JC). This included information related to the aims, design, inclusion and exclusion criteria, and definitions used by the study, as well as the participants, interventions and all outcomes described by the study and included in the pre-defined outcomes of the systematic review (Appendix 3.2). This was performed using Microsoft Word forms and then exported into Excel before being converted into CSV files for use in the R environment. Risk of bias was assessed using the Cochrane risk of bias tool for controlled trials and the NICE prognostic studies tool for observational cohorts.(101,105)

Analysis

The study characteristics and quality assessments were described narratively and represented in tabular form. For each outcome, study level data were combined with a random-effects model using the DerSimonian & Laird estimator using metafor within the R programming environment.(106) Comparative analyses of randomised controlled trials were performed and expressed in odds ratios. Safety and adequacy outcomes were explored using data derived from

single arm studies and from the individual arms of comparative studies. Weighted averages are presented for each outcome.

Subgroup analyses related to timing of discharge, risk stratification tool used and timing of risk assessment were planned to assess the role of these features in relation to the safety, efficacy and failure rates of the various treatment regimens. Sensitivity analyses were used to explore potential areas of heterogeneity. For the purpose of sensitivity analyses, as the studies used a variety of methods of risk stratification, the risk tools were grouped into more or less stringent tools. The more stringent tools generally required a period of observation after presentation, and excluded very young patients, patients following bone marrow transplant (BMT) or with leukaemia (except ALL on maintenance), those with a neutrophil count $<0.1x10^9$/L and patients with respiratory symptoms. Less stringent rules all had only two or three exclusion criteria that were not restrictive. For example, a less stringent rule might exclude patients with signs of sepsis and those with social concerns such as no reliable caregiver, but allow the inclusion of all other patients, regardless of age, underlying diagnosis and neutrophil count.

Heterogeneity was examined using χ^2 tests, the I^2 and tau^2 statistics and by visual inspection of forest plots. I^2 represents a quantitative assessment of the degree of statistical heterogeneity beyond that expected by chance. Meanwhile tau^2 provides an estimate of the between-study variance. The risk of publication bias was explored using contour-enhanced funnel plots and Harbord and Peters tests.

Results

A flow diagram for study selection is provided in Figure 4. 2370 titles and abstracts were assessed and 112 full text articles retrieved. 80 full text articles were excluded as they failed to meet the inclusion criteria. (Appendix 3.3.) Five conference abstracts were identified through searching proceedings and a further study through reference searching of included articles.

Of the 37 included studies, 12 are RCTs, including a total of 1291 episodes of febrile neutropenia.(17,107–118)
One further RCT was identified, but was not included in the RCT analyses as it compared early discharge on oral antibiotics with early discharge on an oral placebo. However, the individual arms of this trial have been included in the analyses of the observational cohorts. No quasi-randomised trials were identified by the searches. The demographics of included studies are given in Table 2 and the study interventions and definitions are outlined in Table 3.

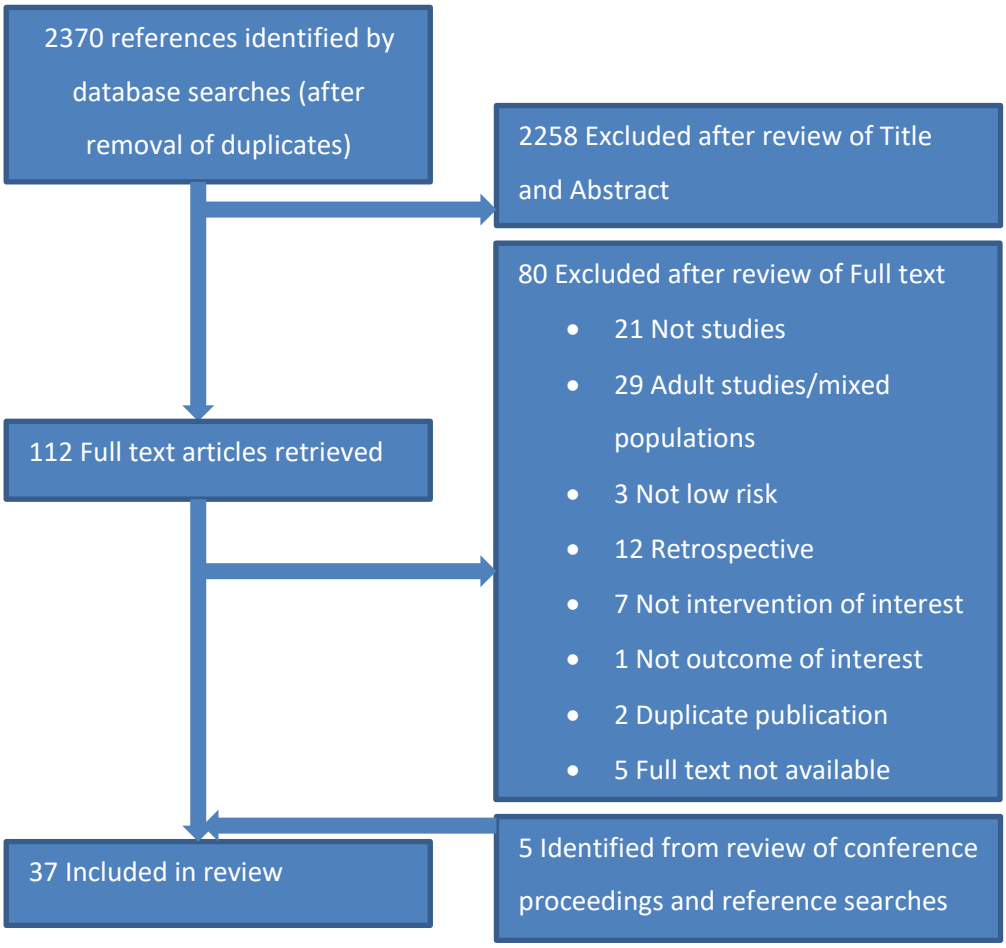


Figure 4 - Flow diagram for study selection

Table 2 - Demographics of included studies

Study	Design	Language	Country	Number of episodes (patients)	Age Mean ± SD (years)	Gender (M:F)	Diseases	Bacter-aemias	Notes
Randomised Controlled Trials									
Brack et al, 2012(17)	RCT	English	Switzerland	61 (52)	Experimental group 4 <4yo, 9 age 4-7.99 yrs, 8 age 8-11.99yrs, 6 ≥12yo; Standard group 9 <4yo, 10 age 4-7.99 yrs, 6 age 8-11.99yrs, 9 ≥12yo	26:35	31 leukaemia, 7 brain tumours, 23 solid tumours	5	
Cagol et al, 2009(107)	RCT	Portuguese	Brazil	91 (58)	7.74±4.55	57:34	7 leukaemia, 1 lymphoma, 50 solid tumours	8	
Gupta et al, 2009(108)	RCT	English	India	119 (82)	not given (1.4-19.0)*	67:21	41 leukaemia, 82 non-leukaemia	5	Diseases include 4 episodes excluded from analysis
Mullen et al, 1999(110)	RCT	English	USA	73 (41)	9.7±4.3	Not given	22 leukaemia, 51 non-leukaemia	4	

Table 2 - Demographics of included studies

Orme et al, 2014(111)	RCT	English	Australia	37 (27)	6.38 +/-3.87	17:20	22 ALL, 15 solid tumours	3	
Paganini et al, 2000 (114)	RCT	English	Argentina	154 (128)	5.13 (0.67-16.67)†	68:86	80 leukaemia, 8 lymphoma, 66 solid tumours	0	
Paganini et al, 2001 (113)	RCT	English	Argentina	93 (87)	Not given (0.92-15.83)*	50:43	38 leukaemia, 4 lymphoma, 51 solid tumours	1	
Paganini et al, 2003 (112)	RCT	English	Argentina	177 (135)	7.5 (1.6-15.8)*	Not given	104 leukaemia, 8 lymphoma, 65 solid tumours	Unclear	
Petrilli et al, 2000 (115)	RCT	English	Brazil	116 (70)	9.8(3-20)†	45:25	6 lymphoma, 132 solid tumours	1	Diseases include 22 episodes excluded from analysis
Santolaya et al, 2004(116)	RCT	English	Chile	149 (107)	5.02±0.66	69:80	67 leukaemia/lymphoma, 82 solid tumour	3	
Shenep et al, 2001(117)	RCT	English	USA	200 (156)	Not given (1.3-19.0)*	94:106	124 leukaemia, 76 solid tumours	NR	

Table 2 - Demographics of included studies

Varan et al, 2005(118)	RCT	English	Turkey	21(18)	9(3.5-17)*	Not given	lymphoma and solid tumours only	Not given	Conference Abstract
Prospective Observational Cohorts									
Abbas et al, 2003 (119)	POC	English	Saudi Arabia	68 (64)	4.7±3.2	33:35	All ALL	12	
Aquino et al, 2000(120)	POC	English	USA	45 (32)	6.5 (2-20)†	24:21	31 leukaemia/lymphoma, 14 solid tumours	2	
Bash et al, 1994 Group A(18)	POC	English	USA	70 (NA)	Not given	Not given	52 haematological malignancy, 22 solid tumours	NR	Diseases include patients later excluded from analysis
Bash et al, 1994 Group B(18)	POC	English	USA	8 (NA)	Not given	Not given	52 haematological malignancy, 22 solid tumours	NR	Diseases include patients later excluded from analysis
Dommett et al, 2009 Group A(121)	POC	English	UK	143 (NA)	5.58 (0.08-17.5)*	Not given	Not given	NR	age at first recorded FN admission

Table 2 - Demographics of included studies

Dommett et al, 2009 Group B(121)	POC	English	UK	18 (NA)	5.58 (0.08-17.5)*	Not given	Not given	NR	age at first recorded FN admission
Doyle et al, 1996(122)	POC	English	Canada	79(NA)	Not given	Not given	Not given	NR	Conference Abstract
Fernandez et al, 2012(123)	POC	English	Spain	5(5)	9.58 (not given)*	Not given	Not given	Not given	Conference Abstract
Kaplinsky et al, 1994(124)	POC	English	Israel	50 (NA)	Not given	Not given	16 leukaemia, 9 lymphoma, 20 solid tumours	2	
Karthaus et al, 2000(125)	POC	English	Germany	75 (NA)	Not given (0.5-15)*	45:29 (1 no data)	39 leukaemia, 3 lymphoma, 33 solid tumours	19	
Klaassen et al, 2000 Group A (109)	RCT	English	Canada	37 (NA)	4.9 (not given)*	16:21	24 leukaemia, 2 lymphoma, 11 solid tumours	NR	(antibiotic arm)
Klaassen et al, 2000 Group B (109)	RCT	English	Canada	36 (NA)	4.3 (not given)*	14:22	24 leukaemia, 3 lymphoma, 9 solid tumours	NR	(placebo arm)
Lau et al, 1994(126)	POC	English	Canada	23 (21)	6.81 ± 5.17	Not given	8 leukaemia, 3 lymphoma, 12 solid tumours	NR	

Table 2 - Demographics of included studies

Malik, 1997(127)	POC	English	Pakistan	91 (75)	9.2±4.3	49:42	19 leukaemia, 25 NHL, 47 other solid tumours	0	
Miedema et al, 2012(128)	POC	English	The Netherlands	47 (NA)	Not given	Not given	Not given	3	Conference Abstract
Mustafa et al, 1996 (37)	POC	English	USA	19 (19)	7.5 (2-15)†	12:7	13 leukaemia/lymphoma, 6 solid tumour	0	
Paganini et al, 2001(129)	POC	Spanish	Argentina	247 (215)	5.33 (0.67-16.67)*	118:129	118 leukaemia, 12 lymphoma, 117 solid tumours	Not given	
Paganini, 2000(130)	POC	Spanish	Argentina	101 (91)	5.42 (0.75-18.33)*	60:41	53 leukaemia, 6 lymphoma 42 solid tumours	Not given	
Paganini, 2003(131)	POC	Spanish	Argentina	127 (90)	6.2 (0.58-17.92)*	64:26	62 leukaemia, 8 lymphoma, 57 solid tumours	Not given	
Park et al, 2003(132)	POC	English	USA	30 (26)	8.2 ±3.5	17:13	19 leukaemia, 4 lymphoma, 3 solid tumours	NR	
Petrilli et al, 2007(133)	POC	English	Brazil	201 (108)	10.8 (3-21)†	70:38	12 leukaemia, 12 lymphoma, 84 solid tumours	4	
Phillips et al, 2006(134)	POC	English	UK	281(NA)	Not given	Not given	Not given	NR	Conference Abstract
Preis et al, 1993(135)	POC	English	Germany	64 (42)	9 (1-22)*	21:21	29 systemic disease, 13 solid tumours	0	

Table 2 - Demographics of included studies

Quezada et al, 2007(136)	POC	English	USA	59 (NA)	9.4 (2-21)†	Not given	80 non-haematological malignancies. 25 hematologic malignancies.	4	Demographics include patients later excluded from protocol
Sari et al, 2007(137)	POC	English	Turkey	44(19)	Not given	Not given	All solid tumours	1	Conference Abstract
Shrestha et al, 2009(138)	POC	English	Nepal	54 (54)	7.2 (2-14)†	22:32	40 haematological, 14 solid tumours	Not given	
Tordecilla et al, 1998 (139)	POC	Spanish	Chile	NA (77)	Not given	Not given	Not given	NR	
Wiernikowski et al, 1991 (140)	POC	English	Canada	22 (13)	Not given	Not given	Not given	10	

Key: *median (range), †mean (range), ‡ - Italicised data has been calculated by combining data from two arms. NR - bacteraemia was exclusion criteria for study therefore not relevant,

Table 3 - Study interventions and definitions

Study	Location(s)	Timing of discharge	Route(s)	Timing of antibiotic change	Antibiotics	Risk Tool	Fever definition	Neutropenia definition
Randomised Controlled Trials								
Brack et al, 2012 (17)	Early discharge Inpatient	9-24 hours NA	Oral IV	NA NA	ciprofloxacin + amoxicillin not given	More stringent	Compound	<0.5 x109/L
Cagol et al, 2009 (107)	Inpatient Inpatient	NA NA	Oral IV	NA NA	ciprofloxacin, co-amoxiclav +oral/IV placebos cefipime + oral placebo	Less stringent	Low-grade Compound	<1.0 x109/L
Gupta et al, 2009 (108)	Outpatient Outpatient	NA NA	Oral IV	NA NA	ofloxacin-clavulanate ceftriaxone	More stringent	Compound	<0.5 x109/L
Mullen et al, 1999 (110)	Early discharge Early discharge	3-16hours 3-16 hours	IV Oral	NA NA	ceftazidime ceftriaxone	More stringent	Compound	<0.5 x109/L or falling
Orme et al, 2014 (111)	Inpatient Outpatient	NA 4 hours	IV IV	NA NA	cefipime cefipime	Less stringent	Compound	<0.5 x109/L
Paganini et al, 2003 (112)	Outpatient Outpatient	NA NA	IVOST IV	24 hours NA	ceftriaxone + amikacin, then ciprofloxacin ceftriaxone + amikacin	More stringent	Compound	<0.5 x109/L or falling

Table 4 - Study interventions and definitions

Paganini et al, 2001 (113)	Early discharge Early discharge	72 hours 72 hours	IVOST IVOST	24 hours 72 hours	ceftriaxone+ amikacin, then ciprofloxacin ceftriaxone + amikacin, then cefixime	More stringent	Compound	<0.5 x109/L or falling
Paganini et al, 2000 (114)	Early discharge Early discharge	72 hours 72 hours	IVOST IV	72 hours NA	ceftriaxone + amikacin, then cefixime ceftriaxone + amikacin	More stringent	Compound	<0.5 x109/L or falling
Petrilli et al, 2000 (115)	Outpatient Outpatient	NA NA	IV Oral	NA NA	ceftriaxone ciprofloxacin	More stringent	Low-grade Compound	<0.5 x109/L or falling
Santolaya et al, 2004 (116)	Outpatient Inpatient	NA NA	IVOST IVOST	72 hours 72 hours	ceftriaxone + teicoplanin, then cefuroxime ceftriaxone +teicoplanin, then cefuroxime	More stringent	Compound	<0.5 x109/L
Shenep et al, 2001 (117)	Inpatient Inpatient	NA NA	IVOST IV	48 hours NA	vancomycin + tobramycin/ticarcillin or ceftazidime, then cefixime vancomycin + tobramycin/ticarcillin or ceftazidime	More stringent	Compound	<0.5 x109/L
Varan et al, 2005 (118)	Early discharge Early discharge	48 hours 48 hours	IVOST IVOST	48 hours 48 hours	cefepime then cefixime cefepime then ciprofloxacin + co-amoxiclav	Not given	Not given	Not given

Table 5 - Study interventions and definitions

Prospective Observational cohorts								
Abbas et al, 2003 (119)	Outpatient	NA	IV	NA	ceftriaxone +amikacin	Less stringent	Compound	<0.25-1.0 x109/L
Aquino et al, 2000 (120)	Outpatient	NA	Oral	NA	ciprofloxacin	More stringent	Compound	<0.5 x109/L
Bash et al, 1994 Group A (18)	Early discharge	48 hours	IV then stop	48 hours	ceftazidime, then oral abx if indicated	More stringent	Compound	<0.5 x109/L
Bash et al, 1994 Group B (18)	Early discharge	48 hours	IV then stop	48 hours	ceftazidime, then oral abx if indicated	More stringent	Compound	<0.5 x109/L
Dommett et al, 2009 Group A (121)	Early discharge	48 hours	IVOST	48 hours	piperacillin/tazobactam + gentamycin, then co-amoxiclav	More stringent	Compound	<1.0 x109/L
Dommett et al, 2009 Group B (121)	Early discharge	48 hours	IVOST	48 hours	piperacillin/tazobactam + gentamycin, then co-amoxiclav	More stringent	Compound	<1.0 x109/L
Doyle et al, 1996 (122)	Early discharge	24 hours	IVOST	24 hours	IV regime not given, then cefixime and flucloxacillin	More stringent	>38°C	Not given
Fernandez et al, 2012 (123)	Early discharge	48 hours	IVOST	48 hours	Not given	More stringent	Not given	Not given
Kaplinsky et al, 1994 (124)	Outpatient	NA	IV	NA	ceftriaxone	Less stringent	Compound	<0.5 x109/L

Table 6 - Study interventions and definitions

Karthaus et al, 2000 (125)	Outpatient	NA	IV	NA	ceftriaxone	Less stringent	≥38.5°C	<0.5 x109/L or falling
Klaassen et al, 2000 Group A (109)	Early discharge	48 hours	IVOST	48 hours	piperacillin + gentamycin then cloxacillin + cefixime	More stringent	Compound	<0.5 x109/L
Klaassen et al, 2000 Group B (109)	Early discharge	48 hours	IV then stop	48 hours	piperacillin + gentamycin, then placebo	More stringent	Compound	<0.5 x109/L
Lau et al, 1994 (126)	12 inpatient, 11 outpatient	72 hours	IVOST	72 hours	ticarcillin + gentamycin, then cefixime + cloxacillin	Not given	?	Not given
Malik, 1997 (127)	Outpatient	NA	Oral	NA	ofloxacin	Less stringent	Compound	<0.5 x109/L or falling
Miedema et al, 2012 (128)	Early discharge	12 hours	Nil	NA	NA	Less stringent	?	Not given
Mustafa et al, 1996 (37)	Outpatient	NA	IV	NA	ceftriaxone	Less stringent	?	<0.5 x109/L
Paganini et al, 2001 (129)	Early discharge	72 hours	IVOST	72 hours	ceftriaxone + amikacin, then cefixime	More stringent	>38°C	<0.5 x109/L
Paganini, 2000 (130)	Outpatient	NA	IVOST	24 hours	ceftriaxone then ciprofloxacin	More stringent	>38°C	<0.5 x109/L

Table 7 - Study interventions and definitions

Paganini, 2003 (131)	Early discharge	24 hours	IVOST	24 hours	ceftriaxone + amikacin, then cefixime or ciprofloxacin	More stringent	>38°C	<0.5 x109/L
Park et al, 2003 (132)	Early discharge	48 hours	IVOST	48 hours	ceftazidime then ciprofloxacin +amoxicillin	More stringent	Compound	<0.2 x109/L
Petrilli et al, 2007 (133)	Outpatient	NA	Oral	NA	gatifloxacin	More stringent	Low-grade Compound	<0.5 x109/L or falling
Phillips et al, 2006 (134)	Early discharge	48 hours	IVOST	48 hours	piperacillin/tazobactam + tobramycin, then ciprofloxacin	Not given	Compound	<1.0 x109/L
Preis et al, 1993 (135)	Outpatient	NA	IV	NA	ceftriaxone	More stringent	>38.5°C	<1.0 x109/L
Quezada et al, 2007 (136)	Early discharge	24 hours	IVOST	24 hours	cefepime then ciprofloxacin + azithromycin	More stringent	Compound	<0.5 x109/L or falling
Sari et al, 2007 (137)	Mostly inpatient	NA	IVOST	48 hours	cefepime or cefaperazone/sulbactam then co-amoxiclav + ciprofloxacin	Not given	Not given	Not given
Shrestha et al, 2009 (138)	Inpatient	NA	Oral	NA	ofloxacin/amoxy-clav	More stringent	Compound	<0.25-1.0 x109/L
Tordecilla et al, 1998 (139)	Early discharge	96 hours	IVOST	96 hours	cloxacillin, amikacin, cefoperazone	More stringent	Compound	<0.5 x109/L

Table 8 - Study interventions and definitions

Wiernikowski et al, 1991 (140)	Early discharge	48 hours	IV	NA	multiple	More stringent	?	Not given

Key: IV- Intravenous, IVOST – Intravenous to Oral Switch of Therapy, NA – not applicable, ? - definition unclear or not given,

Twenty-four observational cohorts are included, describing 26 separate treatment cohorts, including a total of 1914 episodes of febrile neutropenia. (37,119–141) Two of these cohorts have been split into two arms, as in each case the patients they describe form two distinct risk or treatment groups.

In total, this review describes 3205 episodes of paediatric low risk febrile neutropenia.

Six of the included studies (one randomised controlled trial, five prospective single arm studies) were identified as conference abstracts only.

Within the RCTs, three directly compared different locations of treatment and eight examined the route of administration of antibiotics. Twenty three observational cohorts examined outpatient treatment or early discharge and 18 explored oral antibiotics or IVOST regimes.

Multiple different risk stratification tools were used by the included studies; the majority of which were unnamed and un-validated. The tools were grouped as described within the Methods section. Twenty-five studies used more stringent tools and eight used less stringent tools. Four studies did not describe their risk stratification tool in enough detail to allow classification of the tool.

Risk of bias

All but one of the RCTs showed a moderate risk of bias as participants and outcome assessors were not blinded to the intervention received. It is worth noting that it is not possible to blind participants to the location of their treatment. Furthermore, some of the outcomes included in this review are unlikely to be affected by this lack of blinding, including admission to critical care services or death. Other outcomes, particularly treatment failure, have been specifically selected to examine pragmatic issues, which are as closely related to standard clinical practices as possible, and hence the outcomes of unblinded studies are informative in these situations. Other than the issue of blinding, the RCTs were generally at low risk of bias, as were the prospective observational cohorts (see Appendix 3.4).

Adequacy

No studies explored the concept of adequacy outwith the definition of treatment failure. The timing of the final aspect of risk stratification universally matched the timing of discharge and hence planned subgroup analyses of the timing of risk stratification were not performed.

Safety

There were two deaths within the data from the RCTs (12 studies, 1291 episodes).(14–26) One child died of an adenovirus infection on day 10 of treatment. The second died of a Pseudomonas

aeruginosa infection after an acute deterioration on day 3 (notably, this child was well until day 3 and had negative blood cultures on admission). Both patients were treated entirely with intravenous inpatient therapy. A further two safety events were identified in the observational cohorts (total 2663 episodes, 42 arms). (3,14–33,35–37,39–44,46–50) These two patients were admitted to intensive care; one with pneumonia and one with diarrhoea causing hypotension. Neither patient died. Both had been treated with oral therapy as outpatients from presentation. Therefore, the proportion of low risk episodes which resulted in intensive care or death was 0.1% (95% confidence interval (95%CI) 0.03-0.3%).

Treatment failure

Three RCTs (including 247 episodes of febrile neutropenia) compared the risk of treatment failure between inpatient and outpatient treatment, including discharge up to 48 hours after admission. (17,111,116) The odds ratio for failure with outpatient treatment was 0.98 (95% CI 0.44-2.19, I^2=0%, tau^2=0, Figure 5), providing no clear evidence of a difference in failure rates between these treatment settings. There were insufficient trials for subgroup analyses.

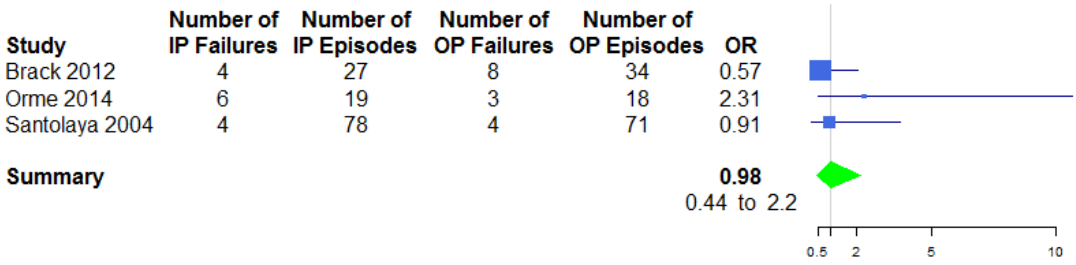


Figure 5 - Forest plot of odds ratios for treatment failure in studies comparing inpatient versus outpatient treatment for paediatric low risk febrile neutropenia

Eight RCTs (including 930 episodes of febrile neutropenia) compared the risk of treatment failure between intravenous and oral therapies, including change to oral medications up to 48 hours after presentation. (14–16,18,20,22,23,25) The odds ratio for failure with oral treatment was 1.05 (95% CI 0.74-1.48 I^2=0%, tau^2=0, Figure 6), which also provides no clear evidence of difference between the two approaches. Again, there were insufficient trials for subgroup analyses.

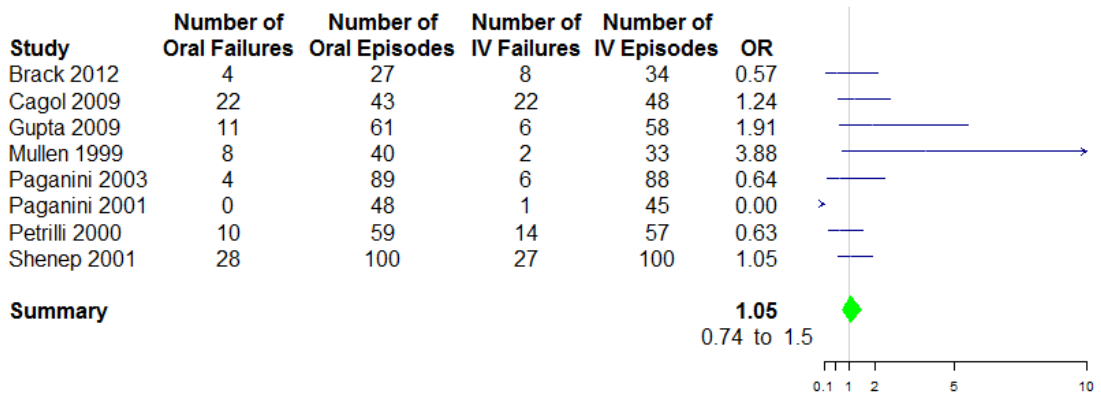


Figure 6 - Forest plot of odds ratios for treatment failure in studies comparing intravenous versus oral antibiotics for paediatric low risk febrile neutropenia

The RCT data for reduced therapy options suggests that the odds of treatment failure are similar for both reduced therapy and conventional regimes. However, the confidence intervals are wide, suggesting uncertainty about this issue. I therefore went on to explore the rates of treatment failure for data derived from the observational cohorts combined with the individual arms of the RCTs.

Within these data, 42 prospective arms (including 2619 episodes of febrile neutropenia) in which patients were treated on any outpatient or early discharge regimen were included. (3,14,16–24,26–37,39–43,46,49,50)

The estimated rate of failure using these approaches was 11.2% (95% CI 9.7-12.8%, I^2 = 77 %) and included patients treated on any outpatient or early discharge regimen. Given the significant clinical and statistical heterogeneity in this group, this combined estimate suggests there are features of an early discharge strategy which will alter the risk of treatment failure. I therefore proceeded to analyse these as subgroups split by timing of discharge. Upon further investigation of the timing of discharge, for studies of patients treated entirely as outpatients, the treatment failure rate was 14% (95% CI 9.7% -19%, I^2 = 82%,

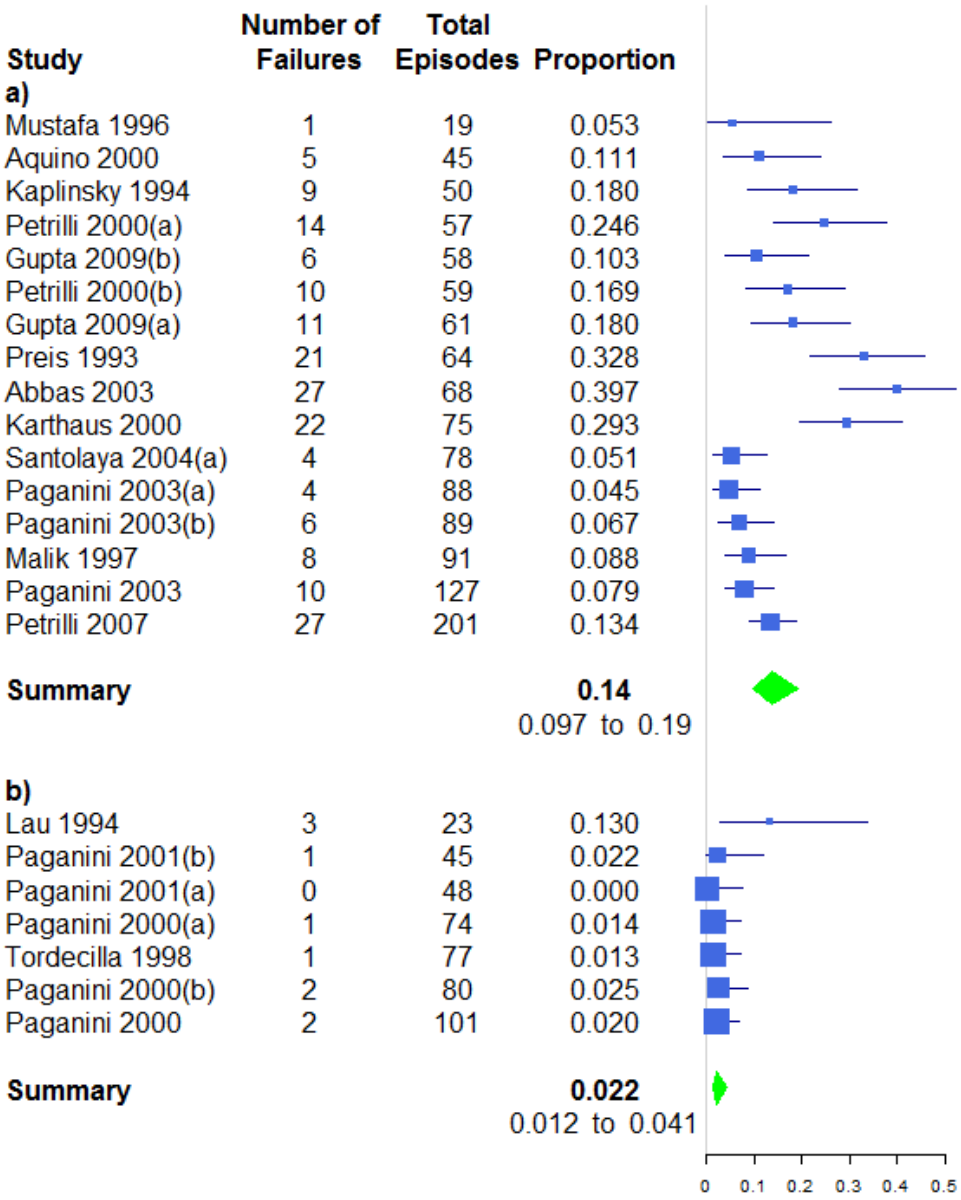


Figure 7a). The rate of treatment failure for studies including patients receiving early discharge after 48 hours was 2.2% (95% CI 1.2-4.1%, I^2 = 0%,

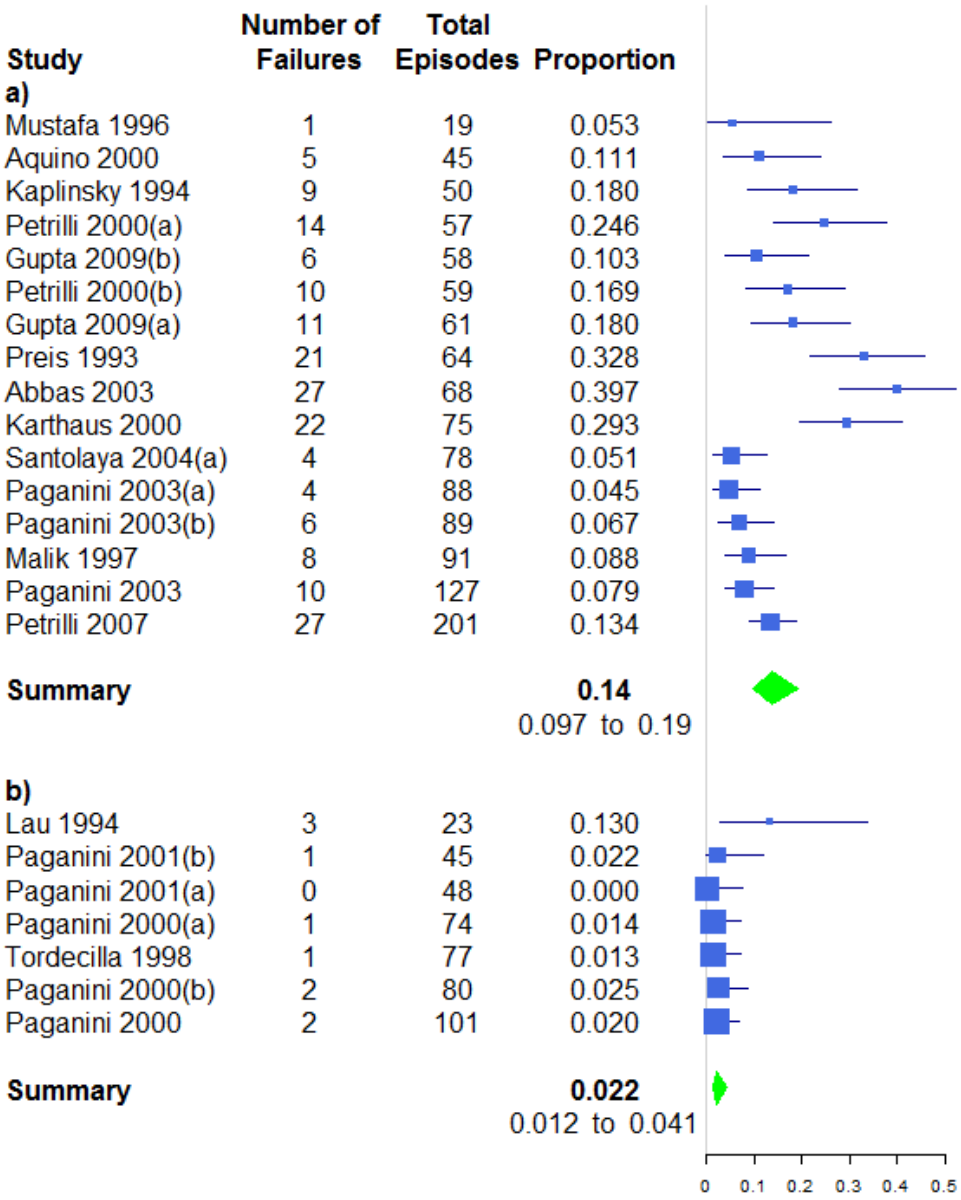


Figure 7b).

34 cohorts (from observational cohort studies and the individual arms of the RCTs, including 2251 episodes of febrile neutropenia) were included in the assessment of treatment failures following any oral therapy regimen. (14–26,28–32,35,36,39–43,46–49) The estimated rate of failure using this approach was 10.5% (95% CI 8.9-12.3%, I^2 = 78%). Due to high heterogeneity in this composite analysis, we again proceeded to subgroup analysis based on timing of change to oral antibiotics. The rate of failure for those receiving oral antibiotics after 48 hours of intravenous administration was 3.4% (95% CI 2-5.7%, I^2 = 11%) and for patients treated entirely with oral antibiotics the rates of treatment failure were 17% (95% CI 12-25%, I^2 = 75%).

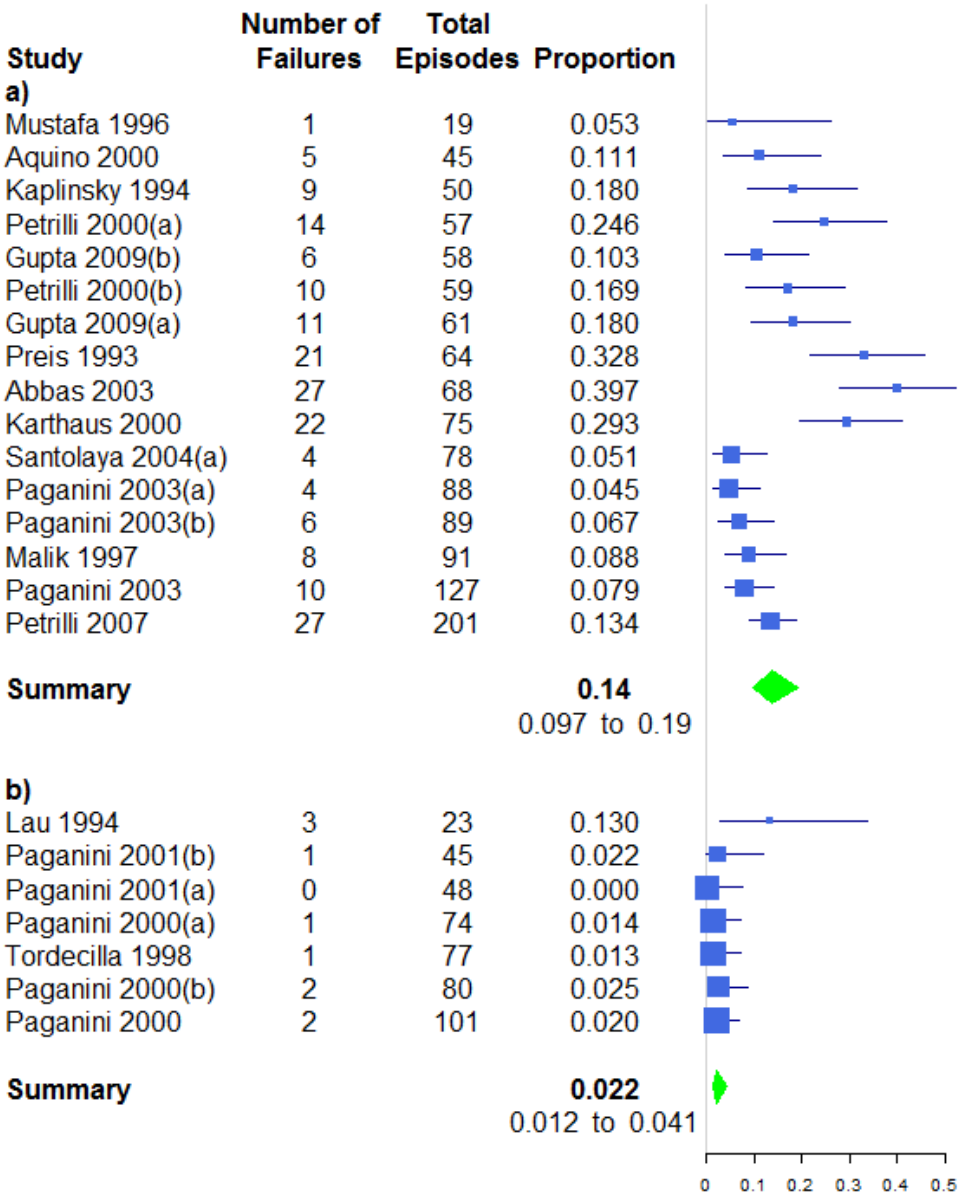


Figure 7 - Forest plots of rates of treatment failure in a) patients treated entirely as outpatients and b) patients discharged early after at least 48 hours of inpatient care

Re-admission

The examination of readmission data within the RCTs comparing location is not possible, given that one arm of each trial were kept as inpatients and therefore were unable to be readmitted. For the RCTs related to route of administration of antibiotics, two studies treated all patients as inpatients and therefore do not provide readmission data. One study treated one arm as inpatients and one as

outpatients and therefore was also not included in the readmission data. This left 5 studies (including 578 episodes of febrile neutropenia) comparing the effect of route of antibiotic administration on the rates of readmission. The odds ratio for readmission with oral treatment was 1.65 (95% 0.76-3.58, I^2= 0%, tau^2=0, Figure 8), which also provides evidence of no clear difference between the two approaches. There were insufficient trials for subgroup analyses.

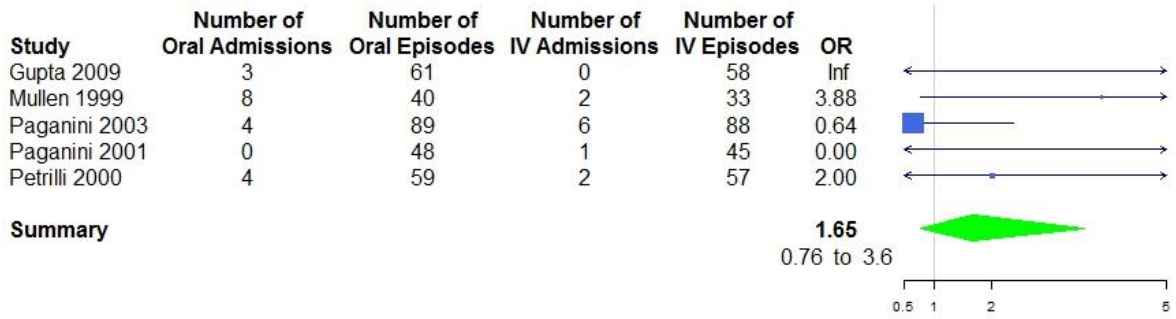


Figure 8 - Forest plot of odds ratios for readmission in studies comparing intravenous versus oral antibiotics for paediatric low risk febrile neutropenia

43 observational cohorts were included in the assessment of re-admissions following outpatient treatment or early discharge. The estimate of risk of re-admission in studies using this approach was 8.8% (confidence interval 7.4-10.3%, I^2 = 85%). The rate of re-admission for trials of patients treated entirely as outpatients it was 8.6% (confidence interval 5.4% -14%, I^2 = 85%,

Figure 9a) and for those of patients receiving early discharge after 48 hours was 2% (confidence interval 1-3.8%, I^2 = 0%,

Figure 9b).

30 observational cohorts were included in the assessment of re-admissions following oral therapy regimens. The estimate of risk of re-admission in studies using this approach was 7.4% (95% CI 6.2-8.8%, I^2 = 80%). For studies of patients treated entirely with oral antibiotics the rate of re-admission was 10% (95% CI 7% -14%, I^2 = 26%).The rate of re-admission for studies of patients receiving oral antibiotics after 48 hours of intravenous administration was 2.8% (95% CI 1.5-4.9%, I^2 = 0%).

Sensitivity analyses

The rates of the outcome measures were unaffected by the use of full text articles alone, fixed effect meta-analysis or location of the study. Given the similarities in risk of bias between studies, it was not possible to assess whether the quality of study affected rates of the outcome measures. There is

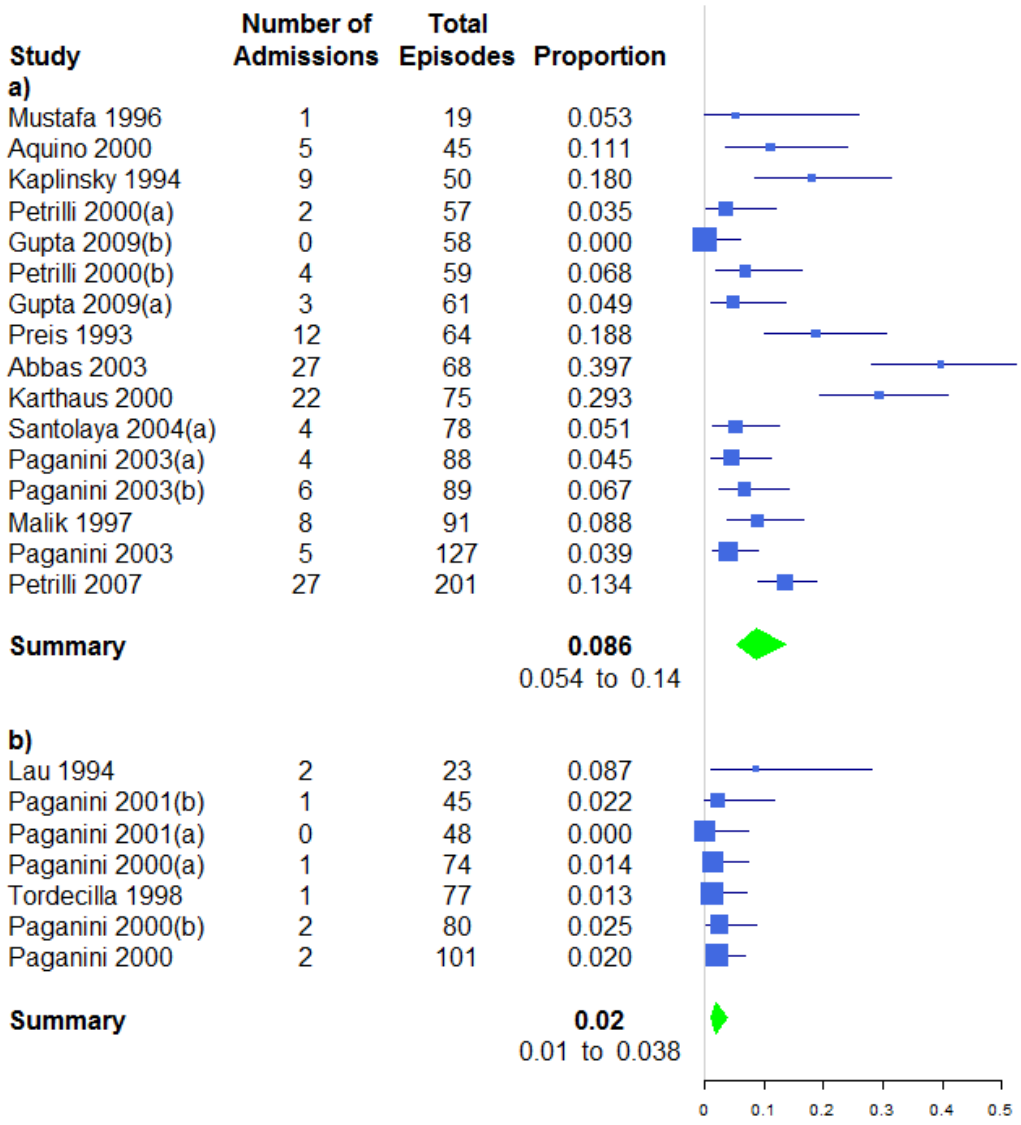
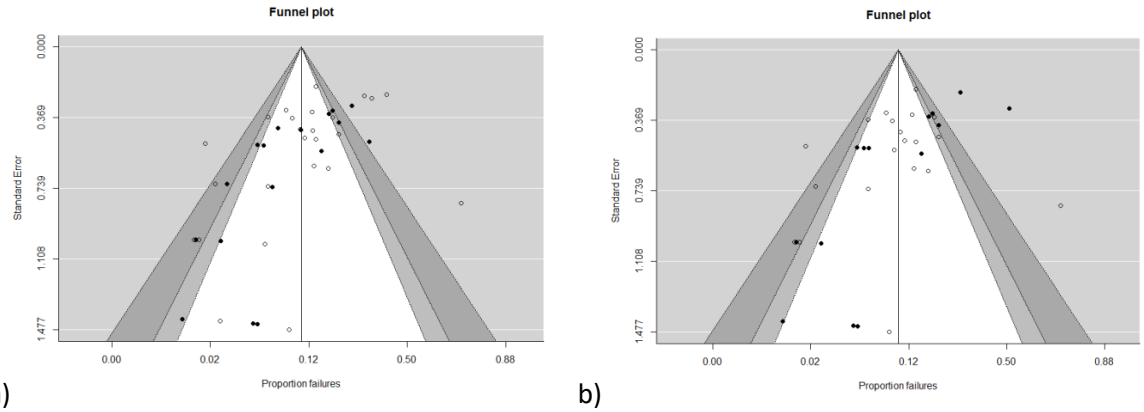


Figure 9 - Forest plots of rates of readmission in a) patients treated entirely as outpatients and b) patients discharged early after at least 48 hours of inpatient care

a suggestion that using a more stringent risk stratification tool reduces the rates of treatment failure, as might be expected given the features used in risk tools. When considering location of treatment, studies using the most stringent risk tools report failure rates of 7% (95% CI 4.7-10.3%, I^2 = 82%) compared with failure rates of 19.1% (95% CI 11.7-29.6%, I^2 = 77%) in studies with the least stringent risk tools. Similarly, regarding the route of administration of antibiotics, studies using the most stringent risk tools reported failure rates of 7.8% (95% CI 5.2-11.6%, I^2 = 85%). There were only two studies exploring the route of administration of antibiotics and using less stringent tool. These found a failure rate between 8.8% and 51%.

Publication bias

As the meta-analyses that provided the estimates of rates of treatment failure included the largest numbers of studies, I assessed publication bias primarily using these studies. When examining the studies which reported patients receiving early discharge or outpatient care, Peters test did not reveal evidence of heterogeneity (p=0.21) whilst Harbord's test suggested that publication bias might be present (p<0.001). Examination of the contour enhanced funnel plot (Figure 9a) reveals that there is a wide spread of proportion of failures in studies with small standard error, but that in studies with a larger standard error, few evidenced high levels of treatment failure. This pattern does not differ between RCTs and observational cohorts. In the arms relating to oral antibiotic regimens, both Harbord and Peters tests suggest publication bias (p= 0.06 and 0.004 respectively), whilst the funnel plot (Figure 10b) presents a similar picture to that of location.



a) b)

Figure 10 Contour-enhanced funnel plots[3] for treatment failure in a) early discharge or entirely outpatient treatment and b) any oral antibiotic regimens. Solid dots represent data from RCTs, open dots represent data from prospective observational cohorts

Refusal to consent

10 studies provided data on refusals to participate (see Table 4).(17,110,111,116,117,122,126,132,136,140) The data provided were very heterogeneous and thus

[3] Contour-enhanced funnel plots provide a visual means for assessing the risk of small study bias.(100,101) This scatter graph of the standard error, a close proxy for the size of the study, against the outcome of interest, allows the examination of any areas where studies would be expected to exist but are not present within the identified literature. The underlying premise is that by chance 95% of relevant studies, if all published, should lie within contours plotted on the graph and studies with a smaller standard error will generally lie closer to the estimate effect than those with a larger standard error. If particular sections of the scatter graph do not include any studies, it may be suspected that studies which have found results in this area have not been published, either through researcher choice or due to bias within the publication system. These are generally smaller studies and so researchers should also consider whether the scatter seen is actually due to differences in effect between smaller and larger studies in the area of interest.

not amenable to meta-analysis. However the data can be conceptually grouped into the issues of refusal to enrol in a study and refusal to confirm consent following enrolment (in study designs when enrolment takes place prior to episodes of febrile neutropenia with further consent sought at the time of presentation with an episode).

Study	**Concept described**	**Number of instances where parents refused consent**	**Number of instances where physicians refused consent**	**Total number of eligible patients**	**Notes**
Brack et al, 2012 (17)	Enrolment	25	NA	93	
Doyle et al, 1996 (122)	Enrolment	5	NA	84	
Lau et al, 1994 (126)	Enrolment	5	NA	29	
Mullen et al, 1999 (110)	Enrolment	12	13	66	
Park et al, 2003 (132)	Enrolment	9	NA	39	Includes inability to take oral antibiotics
Quezada et al, 2007 (136)	Enrolment	3	9	34	First year of study only
Santolaya et al, 2004 (116)	Enrolment	2	NA	151	
Shenep et al, 2001 (117)	Enrolment	86	NA	286	
Orme et al, 2014 (111)	Confirmation following enrolment	6	7	50	
Quezada et al, 2007 (136)	Confirmation following enrolment	8	Included with parental refusal	67	

Wiernikowski et al, 1991(140)	Confirmation following enrolment	2	NA	24	

Table 9 - Refusal to consent data

Eight studies looked at failure to consent to enrolment in the study. They found that 147 of 760 patients (19.3%, range 1.3-30.1%) who were eligible for enrolment refused to participate. Two of these studies also included data on episodes that were not enrolled as the physician was uninterested or not willing for the patient to take part. These found that in 19.6-26.5% of otherwise eligible episodes the treating physician chose not to enrol the patient in the study.

Three studies provided data on confirmation of consent following enrolment. One looked at physicians' attitudes and found that in 7 (14%) of 50 otherwise eligible episodes, the oncologist decided not to include the patient in the study. Two studies examined parental confirmation and found refusal of 8.3-12% of eligible episodes. Finally, one study did not separate parental and physician refusal to confirm consent, but found that 8 (12%) of 67 episodes in enrolled patients were not included due to the preference of the physician or family.

Discussion

Outpatient therapy and oral antibiotics are safe treatment options for paediatric low risk febrile neutropenia. The episodes included in this review had a very low risk of death or admission to critical care services. Furthermore, for the few adverse events observed, there was no obvious association between their occurrence and the route or location of treatment. Remaining as an inpatient receiving intravenous antibiotics did not prevent all deaths within this group. This illustrates the importance of recognising that low risk febrile neutropenia is not 'no risk febrile neutropenia'.

The overall rates of treatment failure are also low. Studies that moved patients from a more intensive regimen to a reduced therapy option at 24 or 48 hours had lower rates of treatment failure than those who were treated entirely on reduced regimes. Although these data are from separate observational cohorts and therefore it is not appropriate to statistically compare groups, the trend would seem clinically plausible. The results of this study indicate that outcomes are different for those treated as outpatients to those discharged at 48 hours. I therefore suggest that the combined estimate of treatment failure rates is not a clinically useful figure as it describes a very heterogeneous group, and that instead rates for each group be used separately to inform the design of future services. It should be noted, however, that all treatment regimens achieved a high success

rate (over 83%) and therefore the rates of treatment failure may be considered acceptable in any group.

For some studies, the reasons for re-admission, and therefore treatment failure, were clearly reported. In others, they were unclear or not documented. Where provided, the indications were variable, such that failure rate recorded within studies is driven by the components of the definition of treatment failure. For example, in some studies, a single repeated fever after reduction in therapy would be defined and counted as a treatment failure. This does not necessarily describe an unwell child and may not be of concern to either parents or clinicians. Additionally, where a child is on a reduced regime, there may be a tendency for physicians to increase therapy more rapidly than for children where standard, more familiar, treatment is already ongoing. Thus, the estimates of treatment failures within this review may be higher than the rates of clinically meaningful deterioration for children on reduced therapy regimens, and this effect is likely to be more strongly accentuated in those who receive reduced therapy regimens earlier in their episode of febrile neutropenia.

In the exploration of treatment failure in relation to the timing of discharge, it should also be noted that a substantial proportion of the data is from one group (Paganini et al). Most data about discharge after at least 48 hours of inpatient care are provided by this group. Along with this, the studies examining patients treated entirely as outpatients seem to be grouped within the forest plot into two distinct areas. Studies with smaller numbers of episodes have more variable failure rates compared to those with more episodes. Interestingly, the treatment failure rates in larger studies seem to be lower than for smaller studies, however, again the Paganini group provide much of these data. Therefore, it is unclear whether these differences are due to variations in treatment failure at the various time points or whether they are instead due to the impact of this group's definitions and approaches.

This review has shown a small study effect in the literature regarding paediatric low risk febrile neutropenia. A small study effect could be reasonably expected in this area. Small studies are likely to be produced by groups for whom the process of treating children with oral antibiotics or as on an outpatient basis is a new concept. These teams may be more concerned about the introduction of these techniques and therefore be more cautious about re-admission and changes in antibiotics. This would result in higher rates of treatment failure. Meanwhile, groups who have become more comfortable with these regimens may attempt studies including larger number of febrile neutropenic episodes. Simultaneously, they are more likely to be tolerant of minor changes in a child's condition without recommending a change in treatment approach. Thus, familiarity with a

regimen results in reduced treatment failure and the conduct of larger trials to evidence this. If this mechanism were to be correct, it could also be potentially reassuring for those considering introducing reduced therapy regimens to their services. It could be predicted that there would be an initial high rate of treatment failure followed by a gradual reduction in failures as clinicians and families become familiar with the new service.

Another issue which must be discussed is that of the influence of risk stratification tools. There was significant heterogeneity between the tools used to assess whether participants were low risk. However, there was a suggestion within the sensitivity analyses that the stringency of the risk tool affects the likelihood of treatment failure. This is unsurprising given that some of the most stringent tools required a child to have a blood culture which was negative at 48 hours and at least 24 hours without a fever before they were eligible to be low risk. This therefore excluded the use of an immediate reduced therapy regimen, and thus avoided many of the issues surrounding treatment failure that I have previously discussed. Thus the finding that a more stringent risk stratification tool results in low rates of treatment failure may actually represent the fact that a longer time to discharge leads to less treatment failure. It should be noted however that the four safety events occurred in studies that used relatively stringent risk tools.

The sheer variety in the antibiotics used for paediatric febrile neutropenia adds complexity to this review. Both the previous work by Manji et al and the recent NICE guideline found numerous different antibiotic regimes studied, in both adult and paediatric protocols.(21,98) It is worth noting however that although the specific antibiotics used are varied, the microbiological coverage of these antibiotics is certainly less so. Thus, differences between regimes are more likely to be related to the route of administration, including absorption and dosing, than the specific antibiotic used.

When considered alongside the results of the two previous reviews by the Cochrane group and Manji et al, the work in this phase of the thesis reinforces the conclusion that reduced therapy can be safely achieved in children with low risk febrile neutropenia.(98,99) However, these treatment failure rates contrast with those of Manji et al.(98) The previous review had found that treatment failure was more likely in patients treated as inpatients than those who received outpatient care. This review has found that the rate of treatment failure was higher in the group who were treated as outpatients earlier in their course. This difference in results is likely to be due to the differences in inclusion criteria for the two reviews, resulting in the comparison of different inpatient regimens. In particular Manji chose to examine all initial treatment regimens for febrile neutropenia, and thus included RCTs comparing inpatient IV treatment regimens with other inpatient IV treatment regimens. These studies are likely to be designed to be more sensitive at detecting certain treatment

failures, such as changes in antibiotics, and therefore may detect a greater number of failures that the trials that I have included in this review. This may account for the differences of findings between the reviews. Meanwhile, the Cochrane review by Vidal et al found similar rates of failure for intravenous and oral regimens as this review.(99)

There are high rates of refusal to participate in trials of these regimens, which relate to both families and physicians. In many areas of research, a refusal to consent rate of up to 30% may not be considered problematic. However, in the context of children's cancer where high recruitment rates are generally seen, this rate of refusal is noteworthy.(143) Refusal to consent to enrolment was generally greater than refusal to confirm consent following enrolment. This may be due to the fact that participants who have committed to the study by consenting to enrol are already likely to have considered many aspects of the research and have decided that these are acceptable prior to presenting with febrile neutropenia. They are prepared for the possibility of randomisation when attending the hospital and so are less likely to decline. In addition to this, once committed to a decision, people tend not to change their minds due to a sunk-cost effect, where the effort put into considering and agreeing to the study means they are more likely to continue with their original decision to prevent 'wastage' of their invested effort.

In studies that examined the number of refusals by physicians, these were similar to or greater than the refusals by parents. This may reflect physician refusal as a proxy for parents, or alternatively may represent uncertainty amongst physicians about the safety or efficacy of reduced therapy. No studies provided data on why families and physicians refused to participate, but two discussed potential issues. They used anecdotal evidence to describe practical issues as a potential barrier to participation for families, whilst a perceived lack of safety may be an issue for both families and physicians considering reduced therapy options.

Strengths and limitations

The main strength of this work is in the examination of a large amount of data. The RCTs are few, and although they suggest that reduced therapy regimens are safe, the additional consideration of observational cohort data provides further support for these strategies. The inclusion of a large number of episodes also allows the consideration of the issue of timing in early discharge so as to inform service development in this area.

The main limitation within this work is its inability to completely define the features of a low risk strategy that result in the lowest rates of treatment failure. This is mostly due to the considerable heterogeneity within the literature, with regards to the inclusion criteria and interventions used. In

particular, I was unable to fully explore the influence of various risk stratification tools, as a large number of tools were used by the studies and thus sensitivity analysis could only be performed using broad groups.

Summary

This systematic review has shown that reduced therapy regimens for paediatric low risk febrile neutropenia are safe and have low rates of treatment failure. The adverse events observed seem to occur regardless of the route or location of treatment. The risk of treatment failure seemed to be higher when reduced intensity therapies were used immediately after assessment, with lower rates observed when these were introduced after 48 hours. However, both rates might be considered acceptable given the potential benefits of early discharge. The high rates of refusal to participate in trials of these regimens, by both families and physicians, suggest that key stakeholders may be uncertain about adopting these regimens and this requires further investigation. In the next phase of the thesis, the qualitative synthesis (Chapter 4) will explore the existing qualitative literature surrounding early discharge, drawing on evidence from relevant fields, so as to begin to understand the possible reasons for these low rates of consent and to identify barriers and facilitators to implementation of these strategies in the futures.

Chapter 4: Experiences of early discharge, with a focus on paediatric febrile neutropenia: a meta-ethnography

Introduction and rationale

The systematic review in Chapter 3 raised concerns that reduced therapy, particularly outpatient treatment, may not be acceptable to patients, their parents or the health care professionals providing for them.(144) Within this chapter of the thesis, I now report the qualitative synthesis of experiences of early discharge, focused on paediatric febrile neutropenia, which forms the second phase of the thesis.

Performing a qualitative synthesis alongside the systematic review of effectiveness draws on one of the key strengths of this methodology, which is its ability to contextualise the results of quantitative reviews.(145–147) Thus the qualitative synthesis provides analytical depth and further nuanced interpretations to the consent rates found in the studies in the systematic review recounted in Chapter 3. It also provides an extensive exploration of the qualitative literature surrounding paediatric low risk febrile neutropenia, in a structured systematic way, to inform and prepare for the primary qualitative study performed in phase three.

This synthesis of primary qualitative work provides an in depth narrative of the different perspectives of those involved in early discharge services, focusing specifically on paediatric febrile neutropenia. The thorough exploration of the existing literature outlines the issues that may act as barriers or facilitators to acceptance of outpatient therapy for different groups. The resultant account provides sufficient insight to allow the development of a subsequent overarching theory outlining the factors influencing the acceptance of early discharge in febrile neutropenia, and the features of services that might make them more successful from the perspectives of different stakeholders. Thus, the findings from the qualitative synthesis complement the findings from the systematic review of effectiveness and help to inform those designing commissioning and implementing services.

The qualitative synthesis aimed to explore perceived experiences and understanding of early discharge, with a focus on paediatric febrile neutropenia and from the viewpoint of patients, their family carers and healthcare professionals. I anticipated, and the preliminary literature searches confirmed, that the subject-specific qualitative material available would not be of sufficient volume to perform an in-depth exploration of potential barriers and facilitators, or the differences in perspectives between patients, their parents and their healthcare professionals.

To account for this, I expanded the review to consider other qualitative material that might reasonably inform theories about the experience of early discharge in paediatric febrile neutropenia. I, therefore, explored the literature surrounding experiences of early discharge in two additional areas (Figure 11). The first area of exploration was adult febrile neutropenia, where many of the concerns related to complications of febrile neutropenia and experiences of oncological services might be similar. For example, patients, their carers and healthcare professionals may feel particularly anxious about early discharge with febrile neutropenia because of previous bad experiences with severe infections, or because of education about the potential severity of an episode of febrile neutropenia. The second area of exploration was other paediatric chronic conditions with life-threatening consequences, where there may be similar social implications of early discharge strategies. For example, parents may struggle with the practicalities of taking a child home, including giving medications or attending frequent follow-up appointments, or feel anxious about the responsibility of caring for their child during an acute exacerbation of illness.

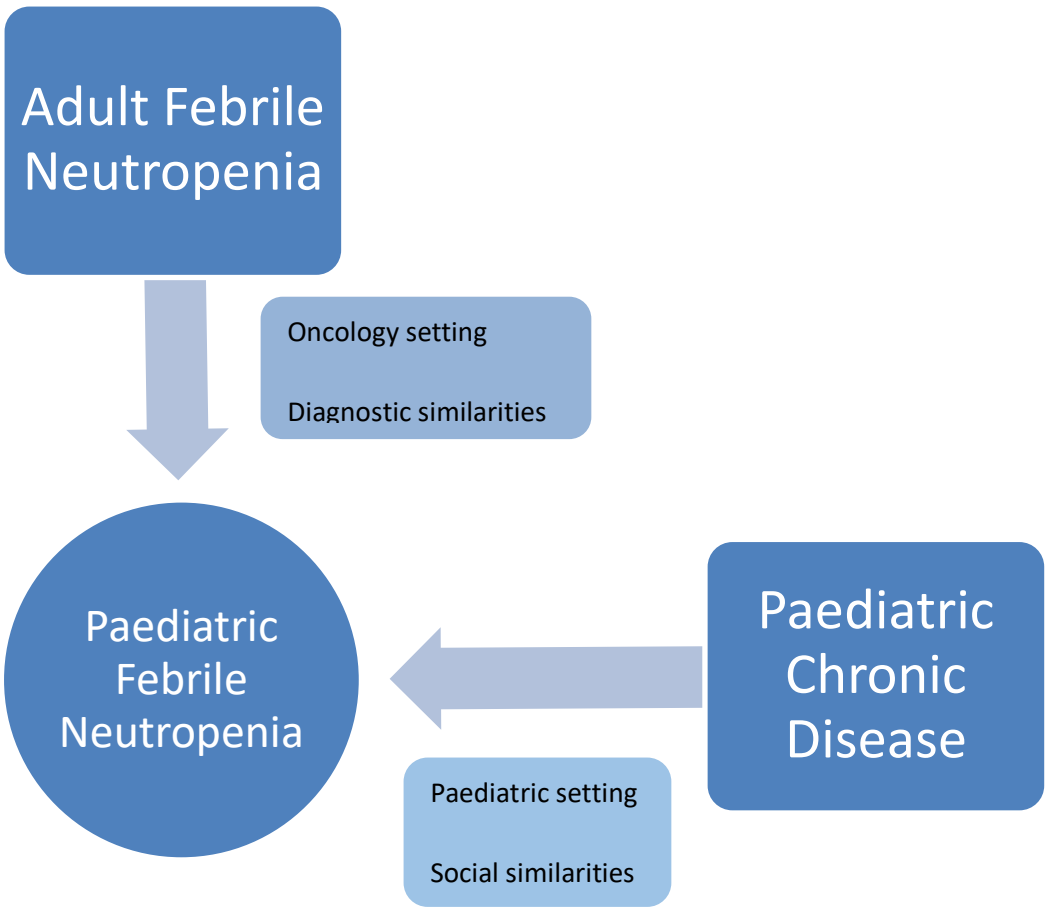


Figure 11 - Interactions of different topic areas for synthesis

Aims and objectives

This synthesis aimed to explore perceived experiences and understanding of early discharge, with a focus on paediatric febrile neutropenia. I aimed to explore how these concepts differ between groups and how they form barriers and facilitators to acceptance of early discharge. In particular, I focused on the views of patients, their carers, and the healthcare professionals providing services to them. The specific research questions for this qualitative synthesis are outlined in Box 6. Following the assessment of this broad and more contextual literature, I aimed to develop higher level theory about the experience of early discharge in paediatric febrile neutropenia and the factors which influence the acceptance of this as a management strategy. This synthesis seeks to contextualise some of the findings from the systematic review in Chapter 3 and has fed into the qualitative study described in Chapters 5-8.

Box 6 - Research Questions

1. What are the experiences and perceptions of patients, parents and healthcare professionals of early discharge in paediatric febrile neutropenia?
2. What are the experiences and perceptions of patients, carers and healthcare professionals of early discharge in adult febrile neutropenia?
3. What are the experiences and perceptions of patients, parents and healthcare professionals of early discharge in other paediatric chronic conditions with potentially life-threatening consequences?
4. What are the barriers and facilitators to acceptance of early discharge in these populations?
5. How do the perspectives in these situations differ and how does this impact on the process of early discharge?

Methods

A protocol for this synthesis was developed and registered prior to commencing this work (PROSPERO CRD 42014013084). This chapter is reported in accordance with ENTREQ (Enhancing transparency in reporting the synthesis of qualitative research) guidelines.(148)

Methodology

Although quantitative synthesis in the form of systematic reviews, with meta-analyses as a significant subgroup, has become an established concept for those involved in health research, similar methodology in the qualitative paradigm has only been developed more recently. (145–147) When considered, qualitative synthesis clearly has great potential to benefit the health sciences, not just through increasing the numbers of patients involved thus giving more confidence in the

conclusions drawn (as for quantitative synthesis), but also in allowing the development of higher level theories and further analysis of complex constructs. Finally, just as in quantitative synthesis, it can be used to identify key gaps in the literature so as to guide future research endeavours.

Selecting the most appropriate method for qualitative synthesis is challenging and depends on a number of components, including the research question, its intended output (to inform theory, practice or policy), the underlying epistemological beliefs of the researchers carrying out the synthesis, and those of the studies which are to be included within the review.

I considered using a number of different approaches.(147) A thematic analysis would perhaps be the most recognisable to a clinical audience, and might provide results which are most accessible to an audience already versed in quantitative systematic reviews. Thematic analysis provides a clear description of the evidence available and allows assessment of current gaps in the literature. However, this methodology may not provide as much depth as more interpretive approaches and has less use when integrating more varied forms of qualitative research, as I anticipated would be present in this review.

At the more interpretative end of the spectrum of qualitative synthesis methodologies, critical interpretative synthesis provides an inductive process of adding studies where necessary, intending primarily to create new theory. I decided this was not the most appropriate methodology for this research, given the intention to both describe the current literature base and to create new theoretical considerations. Furthermore, I aimed to combine and compare the results with the quantitative systematic review, which would be less straight-forward with critical interpretative synthesis. This methodology is also less accessible to clinicians and therefore less likely to have an impact on the intended audience.

Ultimately, I chose to use meta-ethnography to perform this qualitative synthesis. This methodology was first described by Noblit and Hare in 1988.(146) Although initially used to combine only ethnographic studies, it is now used to synthesise many different theoretical and methodological approaches. This pragmatic approach sits well with the overarching philosophy of this thesis, and was likely to yield the highest volume of included studies when there may be minimal good quality literature. Furthermore, the mixing of different theoretical and methodological approaches is especially consistent with the mixed methods nature of the thesis, which performs a similar technique with the different phases of the work.

Another benefit of meta-ethnography is that although it aims to describe the various themes in the studies included, it also aims to translate those concepts into each other and thus create higher-level

theory, which may be more generalizable. It was this balance between descriptive and interpretative approaches that was my primary reason for selecting a meta-ethnographic approach. The constant comparison of the similarities and differences in studies and their findings is particularly applicable to my work, as the literature selected provides both overarching themes and interesting contrasts in perceptions of early discharge in different contexts. By using this interpretive approach, I aimed to inductively produce a model of experiences and understanding of early discharge.

Searches

Electronic searches of MEDLINE, CINAHL, EMBASE, British Nursing Index and PsychInfo were performed. A full search strategy is provided in Appendix 4.1. As eligible studies were likely to be poorly indexed and I was searching particularly for theoretical richness, I used a CLUSTER approach to searching.(8) This involved using key reports as nodes from which to explore the literature, in a systematic and explicit way. The CLUSTER searches are outlined in Appendix 4.3. The reference lists of all included and relevant excluded papers were also searched. All authors were contacted to request details of any other work that they were aware of in this area.

Study selection

I screened the title and abstract of all studies for inclusion. A second reviewer (JC) independently screened a sample of 1000 of the titles and abstracts. The kappa statistic for agreement was calculated and showed acceptable agreement (k = 0.44, confidence interval 0.04-0.85). Full texts were obtained for all potential articles of interest and assessed for eligibility by two reviewers (myself and JC) using a standardised study eligibility form. Disagreements were resolved by consensus or referred to a third reviewer (KA).

Inclusion and exclusion criteria

Studies were eligible for inclusion if they met all of the following criteria:

Study design

All studies using qualitative methodology were eligible for inclusion, including but not limited to ethnography, phenomenology, and grounded theory. Studies that used qualitative methods but which did state an explicit methodology were also eligible to be included, provided that they presented qualitative data. This included, but was not limited to, studies using focus group discussions, interview studies and observational studies. Similarly, mixed methods studies were eligible for inclusion if they provided sufficient qualitative data.

Study Participants

Patients, their parents/carers, healthcare professionals, commissioners and/or policy makers.

Topic of Interest

Early discharge from hospital, defined by the study. There had to be details of the difference between early discharge and routine care, although routine care could be described with reference to a historical group.

Context (any of)

a) Paediatric febrile neutropenia

b) Adult febrile neutropenia

c) Other paediatric chronic conditions with life-threatening consequences. This could include, but was not limited to, asthma, diabetes mellitus, inborn errors of metabolism and neurodegenerative conditions at risk of respiratory exacerbations.

Outcome of Interest

Experiences or perceptions (where early discharge had not been experienced).

Exclusions

i) Studies of early discharge in the neonatal period of healthy term newborns or babies following admission to neonatal critical care services were not included.

These studies were excluded as they describe a very different context to that of febrile neutropenia. New parents are likely to describe different experiences and concerns compared to those with a previously well child who is now suffering from a life-threatening illness. Furthermore, the design of services in neonatal care is unique, particularly in relation to community-based follow-up and therefore is not comparable to that of febrile neutropenia.

ii) Studies of early discharge from psychiatric services were excluded.

Again, these studies describe a different service to that provided for paediatric haematology and oncology patients. Psychiatric services are more likely to used phased discharge processes and have ongoing community care. Furthermore, the disease processes described, although life threatening, have few other similarities to paediatric febrile neutropenia and, as such, are likely to result in very different experiences for patients, parents and healthcare professionals.

iii) Studies exclusively using methods to quantitatively define preferences were excluded. These could have used Visual Analogue Scores, Time Trade Off analyses, Willingness-to-Pay or other methods. Studies that used one or more of these methods but also provided qualitative data were eligible for inclusion in the review.

iv) Studies using a survey design were not included, unless they also provided qualitative data using another method.

Language

Studies were limited to those written in the English language for three reasons. Firstly, these were most likely to reflect the cultural experiences of the group in which I planned to apply the results, that is paediatric haematology and oncology patients with febrile neutropenia in the UK. Secondly, the benefit of qualitative research is to allow participants to express their experiences and perceptions, the clarity of which could be lost through translation and thus the results of the synthesis may less accurately capture the views of participants. And finally, I speak only English and therefore the decision to exclude non-English papers also represented a pragmatic approach.

Data extraction and quality assessment

General study data was extracted using a standardised data extraction form. Data extraction was performed by myself and checked by JC. All studies were assessed for quality using the Qualitative Assessment and Review Instrument (QARI) tool, a 10 point critical appraisal tool developed by the Joanna Briggs Institute for use in qualitative syntheses.(149) The criteria assessed by the QARI tool are demonstrated in Appendix 4.4.

Analysis

The analysis followed an adapted version of Noblit and Hare's phases of meta-ethnography using ATLAS.ti software (**Error! Reference source not found.**).(57) The adaptation, developed by Flemming e t al, is a simplification of the methodology described by Noblit and Hare that removes three stages originally described (Getting started, Deciding what is relevant to the initial interest, and Expressing the synthesis).(57,146) This adapted version also provides a more concise description of the phases. In practice, this adapted version is of little difference from the originally described methodology. The review was an iterative process, driven by the studies identified through the systematic searches. Qualitative data from the reports were transferred to ATLAS.ti software and read repeatedly to ensure full understanding. The context was fully explored and study content thematically coded for key findings. Review by supervisors ensured accuracy of coding (Phase 1 of meta-ethnography).

Codes were compared, grouped and translated to provide the initial level of synthesis and reviewed at meetings with supervisors.(Phases 2-3) This process confirmed that the codes and findings showed little evidence of stark contradiction between studies, meaning a refutational synthesis was not appropriate. However, the studies were not completely similar, showing differences between different social and clinical settings, rendering a reciprocal approach inappropriate. Instead I used a 'line of argument' synthesis, drawing on both the similarities and differences between studies to form the overarching synthesis. (Phases 2-4)The resulting account was then further explored and compared to identify a small number of higher theoretical constructs and to create the lines of argument (Phase 4).

Box 7- Phases of meta-ethnography (10)

Phase 1: Reading the studies

- Studies are read to develop an understanding of their position and context before being compared with others. Repeated re-reading of studies to identify key findings.

Phase 2: Determining how studies are related

- Determining the relationships between individual studies by compiling a list of the key findings in each study and comparing them with those from other studies. If findings are oppositional, a refutational synthesis should be undertaken.

Phase 3: Translating the studies into one another

- Determining the similarities and differences of key findings in one study with those in other studies and translating them into one another. The translations represent a reduced account of all studies. (First level of synthesis)

Phase 4: Synthesizing translations

- Identification of translations developed in phase 3, which encompass each other and can be further synthesized. Expressed as 'line of argument'. (Second level of synthesis)

An example of this process can be seen in the discussion of resources as an influence on decision making. Repeated reading of the studies identified their key findings, noting specifics such as social support from grandparents, finances and parental abilities to provide care (phase 1). Comparing these across studies identified the similarities and differences between groups in different studies that are discussed in detail in pages 105-6 (phase 2). In Phase 3 these ideas were then brought together within the reduced concept of resources, and in Phase 4 this concept was recognised to sit within the overarching theme of *Complexities of decision making and influences on this.*

I aimed to explore the broader context and implications of each study. I considered the role of health service design and how this might influence the experience of early discharge, as well as social, cultural and economic structures and patient factors that could contribute to certain themes. I looked for patterning of the data for themes that suggested how different groups of participants might perceive similar experiences and how these perceptions could influence acceptance of services.

Specifically, the broader literature was explored for themes that might provide concepts and theory that can be translated to the context of paediatric febrile neutropenia. In reports of studies of adult febrile neutropenia, I expressly looked for themes related to aspects of the febrile neutropenia diagnosis and the experiences of oncological services that might influence perceptions of early discharge. Meanwhile, in studies of experiences in chronic childhood conditions, I explicitly examined the data for the influences of social circumstances and care in the paediatric setting as potentially transferrable concepts.

The conceptual contribution of each report was explored in relation to the final theory, so as to more explicitly demonstrate the similarities and differences between studies. Furthermore, I considered the complex issue of quality within qualitative research, and aimed to integrate the findings of the quality assessment within the analysis. In particular, I evaluated whether studies which appeared to be of higher quality contributed concepts to the final theory that were not evident within poorer quality studies and whether specific quality attributes explained any differences. This is consistent with the iterative and reflexive approach which characterises qualitative methodologies.

I also examined the literature base to establish how it is conceptually organised and to identify any particular dominance in regards to geography, professional interest and theoretical standpoints. Furthermore, I sought to identify areas where the body of research is incomplete, with a view to indicating potential future areas for exploration. The strengths and limitations of the synthesis process were explicitly explored adding reflexivity to the review.

Results

Study details

A flow diagram for study selection is provided in Figure 12. 4275 titles and abstracts were assessed and 50 full text articles retrieved. 46 full text articles were excluded as they failed to meet the inclusion criteria. Appendix 4.2 outlines the reasons for exclusion for each study. Thus four studies were included from the database searches. One further study was included from the reference list of

an excluded paper that was relevant to the topic of interest. Three studies were included from searching the reference lists of included papers. No further studies were identified by contacting authors of the included papers. CLUSTER searching of three key papers identified 538 records of which one paper was included in the synthesis (see Appendix 4.3).

In total, nine papers were included in the synthesis (see Most studies included parents or caregivers within the participant group. Three studies explicitly explored the views of children, with another briefly discussing a single child's comment. A total of twenty-six children had been interviewed across the studies. Where the age of children was given, the majority were aged 5-12 years, with one 13 year old and one 14 year old also interviewed. All studies involving children used interviews, some augmented with drawing techniques. Notably, the literature included very few teenagers or young adults, and no focus group discussions with children or young people. One study researched the views of adult patients. Three of the studies involved healthcare professionals in some manner, mostly nursing staff and general practitioners. No studies considered the views of commissioners or policy makers in this area.

Generally the studies gave few details of the social and environmental surroundings of the participants (including housing, local amenities, income banding, ethnicity, socio-economic status, and educational level). Tatman et al, however, gave in depth details of the context within which their participants lived, including ethnicity, employment status, housing situation and family structure and support. (150)

Table 10 for included study details). These were published between 1977 and 2011. Two thirds were performed within the United Kingdom, with the remaining from North America. Those who described the funding provided had received academic support only.

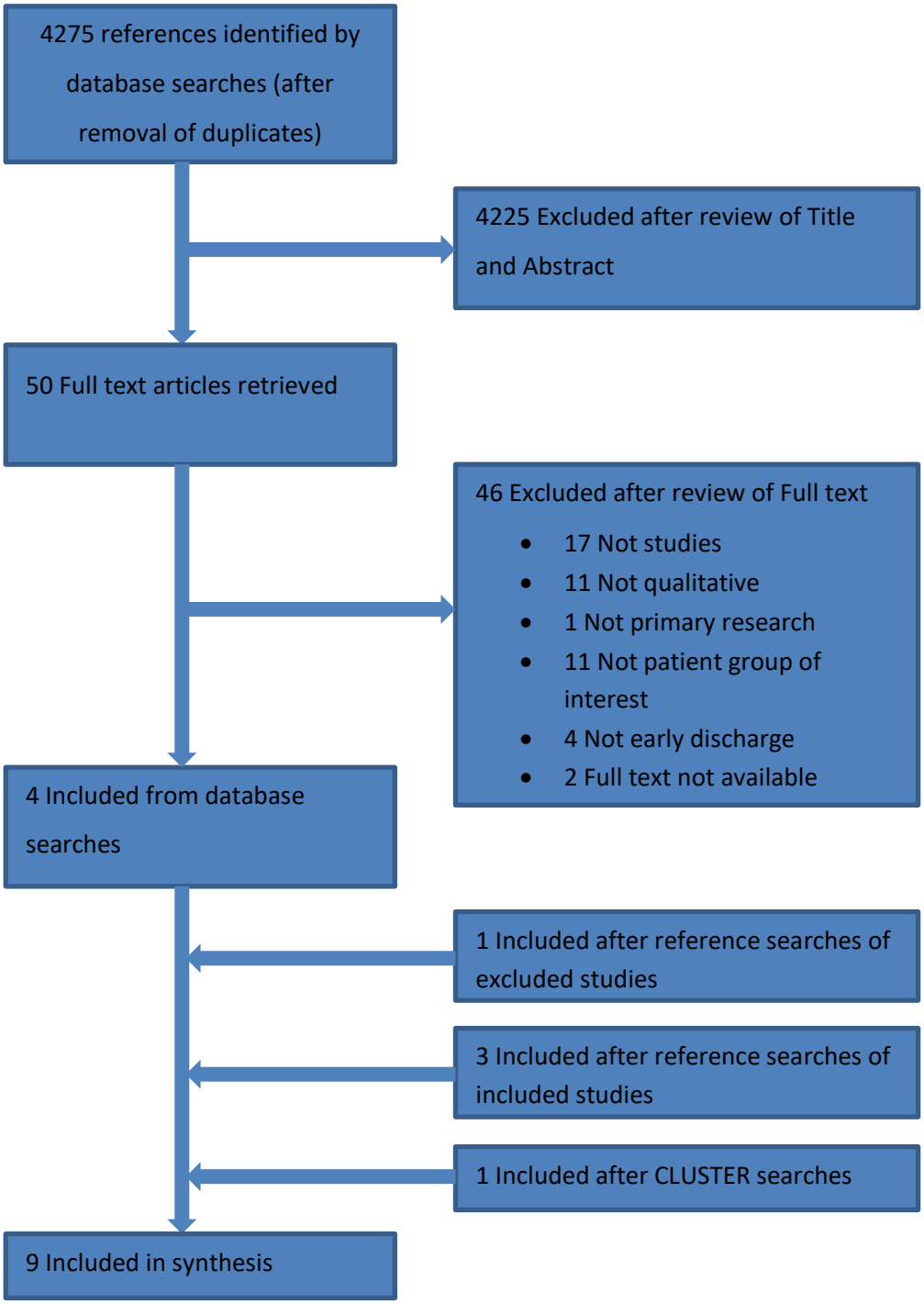


Figure 12 - Flow diagram for study selection

Within the included reports, one study was specific to the area of paediatric febrile neutropenia. One study did not specify the context, although the paper refers to 'caregivers' which suggests an adult setting. The remainder of the studies focused on children with conditions other than febrile neutropenia, although one did include patients undergoing haematopoietic stem cell transplantation. Therefore, the majority of the literature relates to paediatric patients and their parents, as such, the findings rely mostly upon studies with participants from this background. The main methodology used was of semi-structured interviews, sometimes alongside other methodologies as part of an overarching research project. One study reported observational ethnographic methods and one used focus group discussions.

Most studies included parents or caregivers within the participant group. Three studies explicitly explored the views of children, with another briefly discussing a single child's comment. A total of twenty-six children had been interviewed across the studies. Where the age of children was given, the majority were aged 5-12 years, with one 13 year old and one 14 year old also interviewed. All studies involving children used interviews, some augmented with drawing techniques. Notably, the literature included very few teenagers or young adults, and no focus group discussions with children or young people. One study researched the views of adult patients. Three of the studies involved healthcare professionals in some manner, mostly nursing staff and general practitioners. No studies considered the views of commissioners or policy makers in this area.

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Table 10 - Included study details

Study	Country of origin	Methods	Phenomenon of interest	Setting	Population	Methods of Analysis
Diorio et al, 2011 (151)	Canada	Interview	Parent preferences for treatment of febrile neutropenia and the key drivers of parental decision making	Paediatric Febrile Neutropenia	155 parents	Thematic analysis
Freund and Siegel, 1986 (152)	USA	Observations through practice	Global issues of readjustment that may occur in any family with a child undergoing the transplant procedure. Notably also – the psychosocial concerns faced by the patient and the family in the transition from the hospital to the home environment	Paediatric Bone Marrow Transplantation	83 patients, of whom 56 had leukaemia, 13 had aplastic anaemia and 14 had SCID	Thematic analysis
Fuji et al, 2013 (153)	USA	Focus Group Discussions	Perceptions of care transitions, their role within the process, barriers to effective care transitions, and strategies to overcome these barriers	Unclear	18 patients and/or caregivers, 13 hospital-based providers, 7 non-physician community providers	Content analysis

Table 5 - Included study details

Hally et al, 1977 (154)	UK	Multi-methods – quantitative data, interviews, questionnaires	Describe a home nursing scheme	Paediatric home nursing scheme	53 (of 61 eligible) families, 18 GPs from six practices and number of nurses unclear (?4)	Descriptive
Sartain et al, 2000 (155)	UK	Semi-structured interviews, augmented with drawing techniques for children	To explore children's parents' and health professionals' experience of childhood chronic illness	Other paediatric chronic condition with potentially life-threatening exacerbations	6 children, 10 parents, and one healthcare professional associated with each family	Grounded theory
Sartain et al, 2001 (156)	UK	Structured and semi-structured interviews.	Experiences of hospital and home care	Hospital at home service	11 children age 5-12 (6 hospital care, 5 hospital at home). Parents – 20 in hospital care, 20 in hospital at home.	Content analysis

Table 5 - Included study details

Smith and Daughtrey, 2000 (157)	UK	Semi-structured interviews	To identify any gaps in nursing services for acutely sick children and their families following discharge, and to suggest ways to improve integration and communication between hospital and primary care to facilitate a `seamless web of care' for families.	Children's ward in medium sized DGH with both medical and surgical patients	20 parents who had needed help/support from a health care professional in the first 48 hours following discharge	'Burnard's (1991) method for analysing interview transcripts in qualitative research'
Tatman et al, 1992 (150)	UK	Semi-structured interviews and questionnaires	Views of parents and GPs of a paediatric home care service	Other paediatric chronic condition with potentially life-threatening exacerbations	46 parents of 47 children. In depth detail of the families' social context given within paper.	Descriptive analysis
While, 1992 (158)	UK	Semi-structured interviews	Experiences of hospitalization and home care	Other paediatric chronic condition with potentially life-threatening exacerbations	9 children, number of adults unclear-suggestion of 40 but not clearly stated	Content analysis

Quality assessments

When assessed using the QARI tool, the quality of the included studies was variable (see Appendix 4.4). The theoretical premises on which the studies were based were rarely described, nor was their impact on the methodologies used acknowledged. Indeed only Sartain et al gave a clear theoretical basis to their work, which then obviously flowed from this starting point.(155) The remaining studies were largely descriptive in nature. Another clear omission through all the included papers was the lack of reflexive consideration of the influence of the researchers' own values and attitudes on the work they were performing. However, generally the methods of data collection, analysis and interpretation seemed appropriate to the research problem posed and the participants' voice seemed to be communicated well through this process. The overall conclusions drawn by most of the papers seemed to be clearly demonstrated within the data and its analysis, with obvious lines of argument seen through the reports.

Analysis

During my work on this meta-ethnography, it became apparent that the overarching experience of early discharge is that the decision making involved is complex and difficult. This experience may be influenced by various common factors, including fear, timing and resources. From this challenging background, I identified two clear and distinct themes. First, participants struggled with some of the practical aspects of their treatment regimens, namely those of childcare, finances and attendance at follow-up. Second, I explored the social and emotional issues raised during early discharge, particularly those of social benefits and isolation, although relational and environmental issues were also raised. Linking these two themes, participants noted the importance of continuity of care and the need for information if they accepted early discharge strategies. This theme represents the opinions of participants within the included studies who expressed possible changes to strategies that would circumvent some of the practical challenges they faced and alleviate some of the feelings of isolation experienced.

This overarching theory of the meta-ethnography is represented in **Error! Reference source not found.**, whilst supporting evidence for all themes is given in Table 11.

Table 11 - Themes and Subthemes with supporting evidence

Themes and Subthemes	Sample Evidence
Practical Logistics	
• Child care	*"The more kids you have the harder it is to be in hospital."*(151) "It [home nursing] also avoided special arrangements for other siblings and the disruption entailed in visiting the hospital."(154)
• Finances	"six parents (30%) commented on the financial cost of staying in hospital with their children. Extra expenditure included meals for parents, telephone calls, and buying things (such as toys and magazines) to keep their child preoccupied"(156) *"…we saved a fortune, when you're in hospital you spend more money than you ever dream you will, so we didn't have all that expense, which was good again."* (156) "The respondents also felt that time and money had been saved and, in particular, they referred to savings as regards travelling to hospital."(158) "Parents reported that the cost of fuel, parking, and meals necessary during clinic visits were higher than the cost of staying in hospital for several days" (151)
• Follow-up	*"The nurse comes once a day but we have to come back three times a week. That's not good."* (151) *"Forget it, I'll just stay in the hospital if I have to be here every day."*(151)

Table 12 - Themes and Subthemes with supporting evidence

Social and Emotional Issues

• Social benefits and isolation	See Table 16
• Normal social relationships	**"…I missed going to school and playing with my friends..."**(155) **"I don't get to see half of my friends because I was in hospital. I miss out on loads of stuff at school"** (155) "Just over half of the children interviewed said that it was nice to remain at home with the family…"(158)
• Environmental influences	**"there was a lot of things that I missed from home that I had, so the things at home that I can play with and amuse myself but I haven't got at the hospital"**(155) "Stephen tried to minimize the disruption actively by taking his own duvet into hospital and by setting up his computer games in hospital" (155) *"you may as well be at home where you've got your creature comforts, you've got your own bed…"*(156) *"We would have definitely preferred to have been at home, and I think when you're in your own surroundings, it's far better, it makes a difference."* (156) *"I can still look after him at home and in your own environment really, and plus for X he's in his own surroundings, he doesn't like change, he's got his own toys around, he's got his own bed and things like that, so it's benefited him and it's also benefited us"* (156) "one parent (parent 21) stated that home care allowed the child to have 'decent' meals

Table 13 - Themes and Subthemes with supporting evidence

	and enabled him to do what he wanted with all his toys available for play…"(158)
• Staff experiences	"Separation anxiety and a reluctance to give up the care of the child are frequent manifestations experienced by staff during the period the family is preparing to take the child home."(152) "it is important for them to learn that the child is home, well cared for, and recovering satisfactorily" (152) "The staff must be assisted to acknowledge feelings of loss and to resolve them so as not to complicate the process of transition for the patient and family" (152)
Continuity of care	**"it might be a nice thing if the hospitals would call to ask, 'How is everything going? . . . Do you have any questions?"**(153) "The feelings of anxiety and isolation following discharge were exacerbated if parents did not have a named person to contact when they needed reassurance and specific advice."(157) *"I would have felt happier if I had had a point of contact at the hospital because obviously they were familiar with him. They knew what had been wrong with him"* (157) *"The nurses who visit are never just "in and out"; they have always had time to stop and talk and have always been incredibly supportive."*(158)
Need for information	"While definitive answers may not be possible, the provision of at least a tentative

Table 14 - Themes and Subthemes with supporting evidence

	timetable would provide patients and families with a framework that enables them to begin to plan for the future."(152) "Nurses described needing notice for advance planning to evaluate and reinforce medication and aftercare education, reconcile medications for discharge with pharmacists and physicians, complete and verify understanding of patient discharge teaching, and provide transfer information to staff at the receiving agency."(153) "Patients described the need for additional education and follow-up post-discharge."(153) *"I would have just liked them to talk to me a bit more and explain what to do if she has another fit, because I still don't know what to do."* (157) "… the general practitioner wrote: "The home care team largely communicated fairly well, but as I had little information from the hospital as to the overall plan I found dealing with arising problems difficult."(150)
Complex decision making and influences on this • Fear	*"[It's a] hard [decision] because my child likes being home but as a parent I feel scared [at home]."*(151) "Parents were also concerned about children contracting infections either from other children at home or from other children during clinic visits, while they are neutropenic. Interestingly,

Table 15 - Themes and Subthemes with supporting evidence

	very few parents mentioned concerns about nosocomial infections during hospital admissions" (151) "The child too may feel anxious about the parents' capacity to keep the child "well" at home"(152) "Resuming total responsibility for their recovering child once at home produced inordinate amounts of stress and anxiety to the interviewed parents, not least because they felt isolated from any professional support."(157)
• Timing	*"Part of me wants early discharge, but I remember the last time ending up in ICU."*(151) *"You've caught me at a good time, when my son's health is good ... if it was a worse time maybe my answers would have been different."* (151)
• Resources	*"Two years ago, hospital is the only one I would have considered, but we've become much more confident in our ability to administer medication."*(151) *"The more you can do in hospital, the more you want to do at home"*(158) *"…we had to disrupt other people to help us, get like his parents to help us get there and bring things for me, money for food and that."* (156)

Key: black – words of report author(s), *blue* – words of parents, **red** – words of children

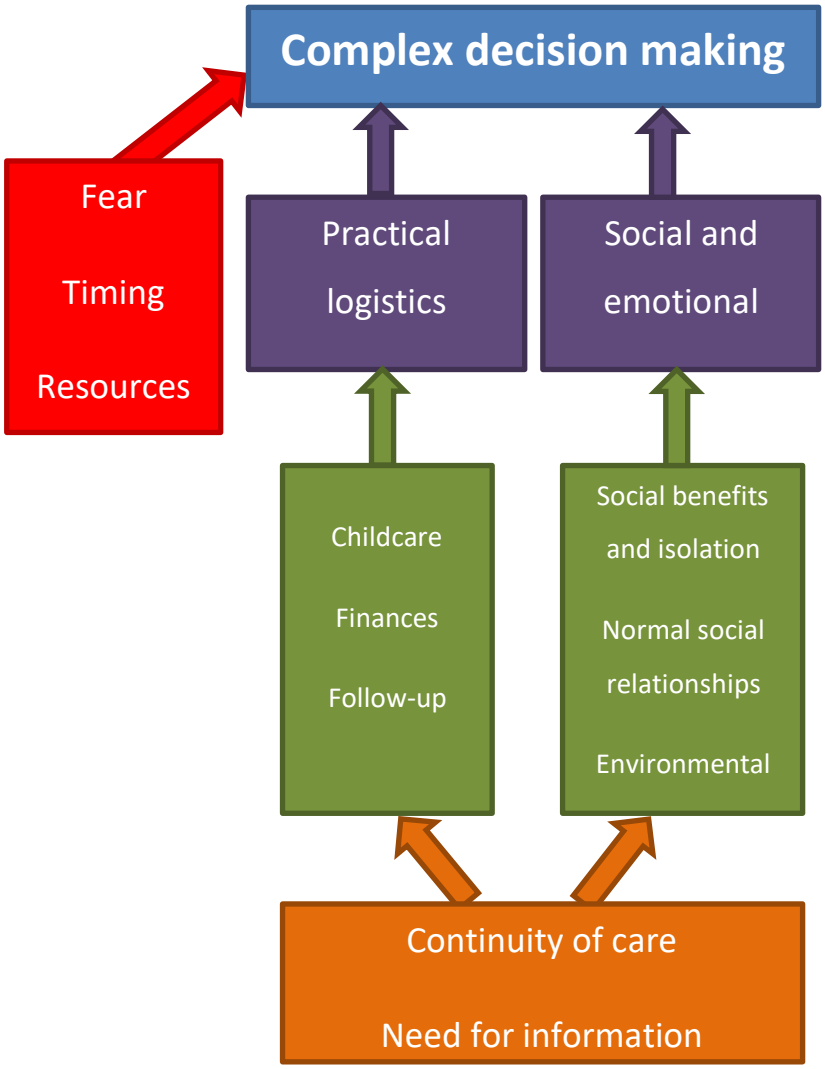

Figure 13 - Overarching model of qualitative synthesis of experiences of early discharge. Blue: overarching theme, Red: influences upon decision making, Purple: major themes (factors considered), Green: subthemes, Orange: potential positive aspects of future strategies

Complexities of decision making and influences on this

Throughout the included literature, it is clear that the process of decision making about early discharge is complex. It became apparent early in the analysis of the data that the factors influencing this decision could not be simply split into barriers and facilitators, as I had initially presumed. Instead, certain aspects could at times help families to accept an early discharge regime and at others prevent this without the factor itself changing. Instead, it appears that combinations of features work in various ways to influence a decision, and perhaps instead of focussing on particular aspects of a regime, services should instead aim to facilitate acceptance through creating a milieu that best supports positive decisions for families.

Participants acknowledged the challenges of conflicting feelings about outpatient care. For them, it appears that there is a delicate balance between what is good about an early discharge option and what is not. There were obvious difficulties in assigning importance to different aspects of the decision making, and, for parents, in balancing what is best for the child physically and emotionally, whilst simultaneously considering the needs of different family members. Parents also discussed the challenge of seeking reassurance about their concerns without feeling they were placing excessive demands on the healthcare service.(157) Furthermore, the dilemma of incongruent patient, family and healthcare worker priorities was also acknowledged. (153)

Various factors impacted on the decisions made by participants. One overarching influence was that of fear, particularly related to potential deterioration in the outpatient environment. This was occasionally explicitly stated but can also be seen in parental requests for more information about what to do in the case of such eventualities. Indeed, the idea of patient safety, including the specific safety issues of a regime, was only discussed within the context of fearful situations. The literature did not discuss the patient safety risks of remaining in hospital.

Another clear influence is that of timing. Diorio et al describe how prior experiences influenced decisions made by parents of children with febrile neutropenia, as did the health status of the child at the time of the episode.(151) This introduces the concept of biographical time, such that the impact of an episode of illness may have different meaning and disruption dependent on the current internal 'biography' of a child or family.(159) Relevant to febrile neutropenia, parents reported feeling more confident in their own abilities to care for their child and to identify any deterioration in their condition as they became 'experts' in this field. Meanwhile, previous events such as an admission to intensive care could influence a decision for early discharge in a negative way. Thus families' ongoing interpretation of the biographical experience of having a child with cancer may be as important as the chronological time, the child's age or the specific stage of treatment. Dealing with the various contingencies of a paediatric cancer diagnosis, therefore, could be an important part of the process of resilience that is discussed further in the discussion section of this synthesis.

A further influence on decision making about early discharge is that of resources - physical, social and psychological. Participants in various studies alluded to the importance of physical resources on their ability to manage successfully within a regime. For parents, having the practical skills to care for their child and the confidence to use these skills facilitated acceptance of an outpatient regimen. Similarly, having the economic resources to deal with the financial demands of a regimen was discussed by many participants. This is expanded further with the theme of practical logistics.

Meanwhile, participants in Sartain et al's study commented on how social resources were needed to support their inpatient regimens, whilst a participant in Hally et al's work had struggled with an outpatient regimen because of a lack of social resources.(154,156) The main social resources mentioned were other family members, including grandparents, who were nearby and willing to help with some of the practical aspects of a regimen such as transportation to and from hospital. However, a close network of friends could also fulfil this resource need. The need for certain social resources seemed closely linked to the family structure, particularly whether there were other children within the household, for whom childcare would be required during an inpatient stay.

Finally psychological resources, although not explicitly mentioned in any of the reports, became apparent as a clear influence when the literature was reviewed as a whole. These resources include optimism, confidence, and a sense of control. Optimism in particular helps to overcome some of the negative feelings associated with treatment regimes, whilst simultaneously allowing easier identification and use of available practical and social resources.(160) Families who responded to a regimen by accepting and adapting to the stressful situation seemed to tolerate any regimen more easily. This was seen in comments such as:

> *"You slot it in - it becomes a way of life."(150)*

Meanwhile a lack of these psychological resources was evidenced in those who felt an increased sense of disruption or anxiety with certain regimens:

> *"…the other parents visited…. one because she had anxiety attacks in hospital." (150)*
> *"[Clinic visits] are very disruptive to family life."(151)*

Practical logistics

When it comes to logistical issues related to outpatient care, the included studies outlined three main challenges for patients and their families. The first surrounds the care of other children within the household. Parents with other children often stated that outpatient treatment was preferable as it avoided the need for additional childcare arrangements.

The second logistical issue is that of the financial costs of a regime. These can be described as including additional costs and lost income, and occur in both the inpatient and the outpatient setting. Families treated as inpatients spoke of the challenges of paying for food and television cards whilst in hospital, whilst outpatient families incurred costs from travelling to and from clinics. Parents in both locations mentioned parking costs at the hospital as a logistical issue.

The final logistical challenge for patients and families is in attendance at follow-up. Parents whose children were treated as outpatients and were required to visit the clinic regularly found this to be a particularly negative aspect of treatment and sometimes preferred to stay as inpatients. Meanwhile, in other reports, where frequent clinic attendance was not required, participants seemed to prefer the outpatient management option.

Social and emotional issues

Social and emotional factors also featured greatly in the experiences of outpatient treatment. It is important to note that although none of the included studies explicitly used ethnographic methods and few gave details on the social, cultural and economic situation of their participants. Nonetheless, the data frequently shows that these are of great influence on the experience of care. Families who were economically less well-off reported more of the practical challenges related to finances. Depending on their social organisation, families had different experiences of the practical challenges of childcare, the social benefits and isolation of various regimes and had different social resources to call upon during the episode of illness. Meanwhile, Tatman et al described the challenges for Bangladeshi families in meeting their need for information when interpreting services were limited.(150)

The literature reveals multiple mentions of the importance of social interaction at all points within treatment. The concepts of both social benefit and social isolation are used by recipients of both inpatient and outpatient care (see Table 16). In particular, the feelings of being isolated and alone are raised in both hospital and home settings. Participants receiving hospital care felt that staff were too busy to be available to them, and that staff did not enquire about deeper feelings regarding early discharge. Meanwhile, parents at home reported that there was a lack of follow-up, where they would have appreciated knowing who to call with a problem, or if staff contacted them at home to enquire about the child. Notably some children and young people also stated that they experienced a feeling of abandonment and social isolation in hospital. However, other children described social benefits from being in hospital and some preferred this to being at home.

Table 16 - Themes of social benefits and isolation/abandonment expressed by various participants receiving both inpatient and outpatient care

	Inpatient care	**Outpatient care/early discharge**
Social benefits	**"… and you can meet loads of friends as well here, like I met Laura last Monday when I came in, I met her and then I've**	"They [parents] perceived HAH [Hospital at Home] as causing less social disruption…"(156)

	known her every time I come in I'm always in the bed next to her." (155) "they [the children] had the opportunity to make friends and play."(158) "Two children made friends"(156)	*"If you're staying with your child you may as well be at home… you've got family around…."*(156) "Just over half of the children interviewed said it was nice to remain at home with the family.." (156)
Isolation/abandonment	**" I don't get to see half of my friends because I was in hospital"** (155) **"I missed going to school and playing with my friends…"**(155) *"…you know when you're in hospital…., you're sort of isolated in a sense….."*(156)	**"like it being in hospital because, it's like dead boring here [at home] and you've got people to play with you [at the hospital]… and I meet people…"** (155)

Key: black – words of report author(s), *blue* – words of parents, **red** – words of children

The fact that isolation is discussed in both locations needs further consideration. Participants may be describing two forms of isolation – 'isolation from their normal social life' and 'isolation from medical support'. This idea could explain the identification of similar feelings within both locations, but is refuted by the description of the first form of isolation within patients who are at home. Therefore, I concluded that isolation is a complex but singular concept. Secondly, it is difficult to assess whether the participants' responses about isolation are a result of objective increases or decreases in social contact, or whether they instead reflect altered perceptions due to a change in need for social input during the increased stress of an illness. However, the responses do appear dependent upon both the individual themselves and the situation within which they find themselves.

The issue of isolation should be considered to be potentially important in the setting of febrile neutropenia as many inpatients are placed in 'source isolation' to prevent the spread of infection to other patients within the hospital. Source isolation restricts the child to a single room with en-suite bathroom facilities. Parents are allowed to leave the room but will usually spend most of their time with their child. This situation may exacerbate the feelings of social isolation as families are much less likely to interact with other inpatients and thus experience less of the social benefits available on a paediatric ward.

Other social and emotional issues discussed within the literature relate to the interruption of normal social relationships for children. These include relationships with siblings, school friends and playmates. In this area, the process of early discharge appears to provide a more favourable environment for the maintenance of these relationships. Furthermore, the importance of familiar surroundings, toys and meals to the emotional wellbeing of children was also strongly emphasized by participants. These environmental factors were mentioned by both teenagers and the parents of younger children.

Despite this being a main theme within the studies involving patients and families, the social and emotional issues of early discharge experienced by staff were discussed in only one paper. It is unclear whether the remaining projects found no social and emotional issues for staff, or whether this aspect of experience was not explored. Freund and Siegel considered the feelings of staff on early discharge of a child from a bone marrow transplantation unit.(152) Here the close and long-term relationship between staff and patients was recognised and the challenges for staff were acknowledged. In particular, staff were seen to worry about the safety of children discharged early and were keen to follow-up with children after discharge. Furthermore, this concern was recognised as potentially causing complications to the process of early discharge. These issues are relevant to febrile neutropenia, where staff also tend to know the children very well due to ongoing contact with the service. Furthermore, staff might also have concerns about safety at home, particularly during the early phases of the introduction of a new outpatient treatment regimen.

Continuity of care and need for information

Linked to the theme of social isolation, participants within the literature described wanting ongoing care after discharge. In particular, they highlighted the importance of ensuring that teams in the community and the hospital communicate and that someone contacts the family following discharge to find out how they are getting on. It seems that families did not want to come into the hospital for this contact but would have preferred for it to happen at home. There was praise of nurses coming out from 'hospital at home' schemes with a clear dislike of coming into clinic on a regular basis. Parents stated that they would prefer contact from professionals that they already knew, particularly those at the hospital who had already been involved in this episode of care.(157)

Almost contiguous with the desire for continued care in the community was the message that families felt a need for more information during the process of early discharge. Comments about information transfer appear through roughly half the reports. Families report feeling that they needed more information about the problems that their child currently had and how they could expect that condition to change over the time following discharge. They would have liked to have

information regarding what to do if something went wrong following discharge (for example a further seizure or fever) and who to contact if they were concerned. One report told of a feeling of inconsistency of information from the healthcare team and how this influenced the parent's perception of early discharge. Indeed, the provision of information (or lack of it) seemed to influence the feeling of emotional wellbeing for parents.

For staff, the need for continuous care with good transfer of information was also felt to be particularly important. Communication between teams was mentioned as a challenge, by both the discharging inpatient team and the receiving outpatient team across a number of the included reports.

It seems particularly interesting that staff would like the opportunity to follow up on the progress of children following discharge and parents report that they would appreciate such a service; however this ongoing continuity does not appear to be present within these studies. It is unclear why from the literature with the review. However, potential barriers to the follow-up of patients include time and resource constraints for healthcare workers and a culture within services of not contacting patients who have been recently discharged – instead families must travel to the clinic. Further consideration needs to be given to the fact that families may resent returning for frequent clinic appointments but would like more contact following discharge. Services should reflect on whether some of these appointments could be replaced with more timely contact via telephone alongside or as an alternative to hospital at home visits.

Contributions to the synthesis

Within the review of the literature, I identified that there was a small amount of material surrounding early discharge in paediatric situations, albeit not febrile neutropenia. This allowed consideration of the social issues experienced by paediatric patients as I had intended to do at the outset of this review (see Figure 11). However, there was minimal data about either adult or paediatric experiences with febrile neutropenia, and this has limited the opportunities for analysis of disease specific themes.

The study by Diorio et al was most closely linked with the area of interest for this synthesis.(151) This did provide some helpful subject-specific information, including the practical challenges of a paediatric haematology and oncology service, particularly frequent clinic follow-up for outpatient management of febrile neutropenia. However, the study was limited to a single centre and to the perspectives of parents, without input from patients or health care professionals who are also key stakeholders with this situation.

Interestingly, the Diorio et al report did not allude to the concept of social isolation or abandonment. There are a number of reasons why this might be the case. This could have been mentioned within the interviews of this study, but not felt to be a clear theme within the authors' scheme and thus not have been reported. If it was not discussed this may be due to the brevity of an episode of febrile neutropenia and thus minimal impact on the family's social environment. Alternatively, the fact that a degree of social change has previously happened within the child's illness may mean that families are more adaptable to current changes in their social support structure. Finally, long-term relationships with staff and other families within a paediatric haematology and oncology service may mean that there is considerable social support both within and outside the hospital environment*: "….the known nursing staff [that] made the child feel very comfortable in hospital."*(151)

However, despite lacking this negative theme, the participants of the Diorio study appeared to be less positive about outpatient care than the other studies, where early discharge options were generally preferred. It is difficult to ascertain exactly why this is the case. The main considerations are whether this is a study specific phenomenon, which is dependent on the centre and participants involved, or whether this is a disease specific issue, where other families at risk of febrile neutropenia might have similar attitudes to these regimens.

The most notably different report within this synthesis is that of Fuji et al. (153) This study, including adult patient participants, described many similar themes to that of the paediatric studies. In particular concerns about abandonment and continuity of care persisted and participants were emphatic about their need for more information when they were discharged early. This study also contributed valuable data about staff experiences, which were not so apparent elsewhere within the literature. Practical issues were not raised by Fuji et al. This may be because the demands of childcare and attendance at follow-up were less for this group compared with the paediatric population, and thus justifies the approach of including both adult febrile neutropenia and childhood chronic conditions to ensure different aspects were considered in this synthesis (Figure 11).

When considering whether the quality of a study influenced the themes it contributed to the synthesis, there were no obvious differences between higher and lower quality studies. Indeed, the lower quality studies contributed similar themes, in similar quantities and with similar depth to the higher quality studies. However, it should be noted that the studies scored similarly on the assessment of their quality, and the aspects missing were comparable across the included works. There was no apparent difference in the studies from the UK compared to North America, or from any particular professional or theoretical interest.

Reflexivity

Consistent with qualitative tradition, I feel it is important to be reflexive about my own influences on this review. Reflexivity with qualitative research is discussed extensively within Phase three of this thesis and forms a key tenet within the qualitative paradigm. It enables consideration of the inherent influences and biases of researchers, methods and societal norms and values on the findings of a study. As such, it can be seen as of benefit to consider these issues in the reporting of a qualitative synthesis, which holds many similar challenges to a piece of primary qualitative work.

As a health care professional with experience in both general paediatrics and paediatric haematology and oncology, I acknowledge that role undoubtedly influences my opinions and interpretations. However, other members of my supervisory team are non-clinician researchers who have provided different perspectives and ensured that other views have been considered. Furthermore, through reflection on my own experiences and those of other supervisors within this population, I consider the model to be credible to those working within this environment, whilst recognising that some areas require further in-depth exploration and validation.

Discussion

This meta-ethnography has found that decisions about early discharge are complex and difficult. Some of the main influences on these decisions are fear, resources and timing. Practical logistics and social and emotional issues are some of the key factors considered in the decision. Participants described a need for increased continuity of care and a desire for more information if they are to consider early discharge. These key themes are represented visually in **Error! R eference source not found.**.

Possible mechanisms/explanations

The concepts of trust and confidence offer an overarching theoretical explanation for my findings. Participants need to trust both their healthcare professionals and themselves when accepting an early discharge programme and require confidence in their own caring skills as well as feeling confident that healthcare professionals are contactable and would give appropriate advice once they are discharged.

The issues of trust and confidence appear to be interdependent with the resources available to families – both facilities are required in order to be able to manage an early discharge regime. Trust and confidence enable families to recognise the resources available to them and to be able to mobilise those resources. Meanwhile, families who might otherwise have the trust and confidence to thrive in an early discharge situation also need resources to be available to them so as to make it possible for them to fully achieve the potential for outpatient care.

This suggests that socially informed resilience is particularly relevant to early discharge strategies. Resilience has been defined in many ways, but the overarching themes are that resilience describes a process (rather than a personality trait) in which individuals, families and communities respond to adversity in an adaptive way that enables them to continue to function adequately.(161) Resilience is a spectrum of time and situation dependent responses - a person may have resilience within their work life but meanwhile not be functioning well in their personal life. Resilience takes into account psychological influences, in this case trust and confidence, alongside the social context in which they have to be realised, such as physical and social resources. Interestingly, resilience is a common response to adversity.(162)

In order to consider resilience, it is important to define adversity, which ranges from prolonged exposure to personal adversity, such as chronic disease, to single catastrophic events, including natural disasters. An episode of febrile neutropenia might be considered as a single acute event which occurs on the background of prolonged adversity experienced by the family of a child with cancer. It is important to consider whether individuals regard an episode of febrile neutropenia as an adverse event and, if they do, what they perceive its severity to be. These perceptions may be vital in defining the need to employ resilient processes and the extent to which resources may need to be accessed. These perceptions of adversity are likely also to be time, situation and context dependent, just as resilience is.

Research describes various predictors of resilience, including biological, psychological and social influences. Gender and age both affect responses to adversity.(162) Ethnicity may also play a role in resilience, however the social and cultural influences are more difficult to control for when assessing this factor.(162) High levels of perceived social support can foster resilience, whilst multiple life stressors may reduce resilience.(162) Positive family relationships, flexibility and adaptability within adverse situations are known attributes of family resilience, as are positive relationships with health-care professionals.(163)

It is also important to consider the impact of financial resources on resilience - any loss of income may result in a less resilient response, independent of the initial or final income.(162) This may be of particular importance in the paediatric haematology and oncology population where the additional costs of caring for a child with cancer average £367 per month.(164) Furthermore, families often experience a loss of income at diagnosis as parents often are unable to work as much as they had prior to diagnosis. Families of children with cancer may therefore be less able to demonstrate resilience during an episode of febrile neutropenia.

Resilience can be supported through encouraging developmental resilience, strengthening family and social relationships, increasing the availability of resources and ensuring that services are

designed to promote resilience.(161,162) In relation to febrile neutropenia, this might include fostering relationships of trust and honesty and encouraging families to identify the resources already available to them, whilst providing additional resources of pre-discharge information, practical home nursing support, accessible advice in the community and achievable follow-up regimes.

Finally, the desire to improve resilience to disadvantage should not take place without also aiming to deal with that disadvantage. This may include improving practical assistance, such as free parking, transport or parental meals in hospital, and considering the structure of an outpatient strategy to reduce the burden on families by reducing clinic visits where possible and ensuring easy access to professional advice. By providing services are more accessible and appropriate for patients, the amount of resilience needed to deal with episodes of febrile neutropenia and the resultant treatment may be reduced.

Strengths and limitations of synthesis

A specific strength of this synthesis is in its structured scientific methodology and transparent approach, which allows readers to make their own judgement as to its credibility. I performed thorough, systematic searching of the literature using predefined inclusion and exclusion criteria. I note that CLUSTER searching added little data to the review beyond reference searching and contacting the authors. The use of a wide breadth of literature to inform this unique clinical problem has enabled me to formulate an initial theoretical construct and will enable the shaping of future qualitative research.

The key limitation of this work is that it has not been possible to clarify some of the issues of concern, because of the restricted data available. In particular, the voices of participants are potentially skewed as key stakeholder perspectives are missing or minimal represented. Furthermore, there is insufficient disease-specific data to allow complete confidence in the conclusions about the experience within paediatric febrile neutropenia without further replication of primary studies

The lack of social information within the included studies also limits the scope of this synthesis. The impact of family structure could play a particularly important role in the experiences of patients and families, for example lone parents may struggle with practical logistics more than nuclear families, whilst families including other children with health problems may feel more confident using care skills in the home, but it is not possible to assess these hypotheses within the current literature base. Meanwhile, the impact of inequalities and cultural diversity is also muted within the accounts but could be further explored if future primary research provides relevant

data. Similar to this, the role of healthcare service design could not be fully explored through this review because of the limited information given by the included studies.

Emerging Research Problems

Overall, this review provides a preliminary theoretical framework for considering early discharge for children and young people with febrile neutropenia. It describes the logistic, socio-economic and psychobehavioural factors involved from various perspectives, providing detail to this essential and yet often poorly understood and underestimated aspect of healthcare.

Following on from this work, further research was clearly required to explore the disease-specific challenges for patients with febrile neutropenia who are being offered early discharge strategies. I use this section of the chapter to explore the issues still to be addressed and thus highlight some of the reasons for the design and execution of the study described in phase three of this thesis. The study aimed to identify whether the negative attitudes found by Diorio et al are also present in other populations and to explore the reasons behind any barriers to acceptance in this group. It also aimed to collect more detailed contextual information from participants, so as to be able to investigate the influence of social, cultural and environmental factors on the perceptions of participants.

It is appropriate to aim to represent the voices of young people and healthcare professionals, particularly hospital-based physicians, involved in early discharge regimens for febrile neutropenia. Further, it is necessary to expand on the experiences of parents as individuals, as the current literature has a risk of 'double silencing'.(63) This is where parents report on their perceptions of their child's experience. This results in silencing of the child's voice as they are not directly asked about their experiences, but also silencing of the parent's voice as their own experiences, independent of their child, are not explored. To avoid double silencing, participants should be encouraged to speak about their own experiences and the perceptions of both children and their parents should be sought. This is the rationale of holding separate focus groups for parents and young people in the following phase of the thesis.

In particular, it has been difficult to fully explore the issue of resilience because of the descriptive, rather than explanatory nature of the literature base. The future work aimed to confirm whether resilience is an important process in the acceptance of early discharge, and if so, the features which make some families more resilient than others in this situation and the influence of family structure on resilience.

Summary

This synthesis has begun to explore some of the issues raised within the systematic review of effectiveness. In particular, I have established the previously identified challenges to the acceptance of studies that offer early discharge or reduced therapy. This meta-ethnography confirms the assumption from the studies included in the quantitative systematic review that practical aspects of a regime can act as potential barriers to participation. However, although the systematic review suggested that there may be a perceived lack of safety of outpatient regimes, this theme was not particularly prominent within the qualitative synthesis.

Overall, the synthesis has found that decisions about early discharge are complex and influenced by fear, resources and timing. Practical logistics and social and emotional issues are key factors considered in the decision. There is a clear need for increased continuity of care and a desire for more information for families considering early discharge approaches. Socially informed resilience provides theoretical explanations for the experiences and perceptions found within this meta-ethnography. The ways in which resilience is fostered and negotiated may mediate the ability and inclination of families to care for their children within their home during episodes of febrile neutropenia. Services should consider how to recognise and encourage action to enhance resilience within the communities they serve.

Many of the future research issues suggested from this meta-ethnography are addressed in the qualitative study that forms phase three of the thesis. This aims to explore the disease-specific issues relating to early discharge in febrile neutropenia along with inclusion of the voices of young people and healthcare professionals, alongside those of parents. It will also investigate whether resilience is confirmed as an important feature in this setting and will evaluate the overarching theory of this meta-ethnography.

Chapter 5: Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals

Introduction

Following on from, and drawing together the results of, the systematic review in Chapter 3 and the qualitative synthesis in Chapter 4, this chapter provides a description of the methods used in the qualitative study. It explores the methodological choices made and the potential impact of these on the study findings. It outlines the aims and objectives for the work and then provides the rationale for the use of the chosen methods. I explain the process of study site identification and the practicalities of patient recruitment. There is then an outline and justification of the focus group discussions, including explanations for each segment of the topic guide. The details of data management and maintenance of confidentiality are given before a discussion of the analytical process along with examples of how the data were brought together to provide the findings chapters of this thesis. I close the chapter with a reflexive account of the challenges relating to the planning and procedure of performing this study and a consideration of the additional ethical and governance issues related to this work.

Consistent with the traditions of presenting qualitative research, I weave the theoretical background and rationale with empirical material which demonstrates the application of this theory to the research.(56) As such, there are times when I refer to the findings of the study within this methodology chapter so as to illustrate the decisions made in the performance of the work.

Background and rationale

Given the limitations of the qualitative synthesis described in Chapter 4, I aimed to conduct a primary research study to obtain further data to build understanding about perceptions of early discharge for paediatric febrile neutropenia so as to inform future policy and practice. I felt it was particularly important to further explore the disease specific features of low risk febrile neutropenia that may have a role in the acceptance of early discharge strategies, given that only one of the previous studies had considered this.(151) I also wanted to explore the contextual features that might influence the experience of individual patients and families undergoing treatment for an episode of febrile neutropenia, such as socioeconomic situation and family structure, and the role of different features within healthcare service designs that then impact on the experiences of key stakeholders. Furthermore, it is important that the voices of children and

young people are listened to when planning services that affect this age group as discussed in Chapter 2. Given that these have so far been under-recorded in this area, I chose to include this group within the study. I discuss the rationale behind this decision and the evidence for including children and young people in research within the *other ethical issues surrounding the research* section of this chapter. As the literature of healthcare professionals' experiences and perceptions is also limited, I aimed to collect data that could provide depth to our understanding of the challenges of providing care for children with low risk febrile neutropenia. This would allow triangulation with patient and parent accounts, such that service design issues could be considered from all three perspectives. This is explored later in this chapter when considering methods used to enhance the credibility of the research performed. The benefits gained from including various groups and centres are further expanded on and discussed later in the chapter. By beginning to understand these issues and the resultant decision making process, this study may then inform the development of future services.

Research Governance and funding

This study was presented to the University of York Health Sciences Research Governance Committee and received positive feedback and approval. It was then submitted to the NHS Research Ethics Committee and was approved (REC reference: 15/YH/0208, see Appendix 5.8 for all REC Approvals). Minor amendments were made to the original protocol to accommodate the recommendations of the Research Ethics Committee that a time limit be set for withdrawal from the study, that there need be no delay in consenting participants once they had expressed a wish to take part and that an assistant moderator be present at each focus group discussion.

Two substantial amendments were made to the original protocol, which are discussed further later in this chapter. The first substantial amendment was made prior to the study opening in any site. The second major amendment was made following the challenges in recruitment to parent and young person focus groups. This amendment was approved by REC on 14th December 2015 and was implemented at the involved sites within 7 days of this amendment.

At each site within the study, local Research and Development approval was obtained prior to the site opening and for each amendment. Site specific collaborators were identified to act as links with myself as Chief Investigator and to take on the role of identifying and approaching eligible participants. They were also responsible for highlighting the study to healthcare professionals within their centre, encouraging the recruitment of this group to the research. They identified a lead research nurse for each project, who carried out much of the site specific collaborators' work and who were my main contact with each site during the conduct of the study.

Aims and objectives

Box 8- Research Questions

1. What factors influence decision making about outpatient therapy in paediatric low-risk febrile neutropenia?
2. What are the barriers and facilitators to acceptance of an outpatient therapy strategy from the point of view of patients, parents and healthcare professionals?
3. What are the similarities and differences in acceptance between young people, their parents and the professionals caring for them?
4. How can service provision best reflect the views of different stakeholders?

This study aimed to explore experiences and perceptions of outpatient management of paediatric low risk febrile neutropenia. It examined decision making about these strategies, specifically aiming to identify the factors involved in decision making and the context in which people make these choices. It sought the perspectives of patients, parents and health care professionals within paediatric haematology and oncology services in the UK. This study investigated the similarities and differences between the various groups, and considered how these might be aligned so as to provide an acceptable service for all. The main aims and objectives of the study were as outlined in Box 8. Balancing the various attitudes and opinions to provide maximal benefits for key stakeholders was identified as a potential challenge early in the research process. The decisions made in combining preferences or in negotiating tensions surrounding key aspects of the service design and the rationale behind these decisions are discussed later in the thesis as part of Chapter 8.

Methodology

To achieve its applied health research aims, this study used a pragmatic approach intending to solve particular problems in the care of children with febrile neutropenia, and to identify barriers and facilitators to acceptance of reduced therapy regimes. The methods used and discussions of findings are theoretically informed so as to provide high quality research with the ability to impact on healthcare policy and practice.

Qualitative methods are an excellent pairing with the quantitative methods used earlier in the thesis as they will provide a deeper understanding of why we have seen the results identified in Chapter 3 in relation to the low rates of consent to reduced therapy regimes. This combination of techniques also allows methodological and theoretical triangulation to identify the problems

surrounding the potential implementation of outpatient care of febrile neutropenia in children and thus provides credibility to the overarching thesis.

Qualitative methods allow consideration of the experiences, perceptions and interpretations of participants in a detailed manner. As such, they help to expand upon, illuminate and contextualise the quantitative findings. They enable participants to talk about the issues relevant and important to them; a distinct benefit over quantitative or survey based approaches in which participants are provided with a selection of options and asked to select the most significant. The iterative process in qualitative methods ensures new and individualised responses can be raised by participants and the interactions between factors can be discussed and explored beyond a simple ranking of importance. Thus, the use of qualitative methods encourages the expression of uncertainty and the complex challenges of dealing with it, which is likely to be particularly important within this setting.

I selected focus group discussions as the method for data collection within this study for six reasons:

First, focus group discussions provide an opportunity to explore normative values and assumptions within groups of participants. This allows an understanding of what the group processes are when coming to an opinion, through identifying the unspoken knowledge about societal norms.(165) Through exploring these, often implicit, aspects of community culture and thinking, it becomes clearer why certain choices might be made in preference to others. For example, by exploring professional discussions of their concerns about early discharge it became more apparent that the normative value is that children within paediatric oncology services are considered different to general paediatric populations even when the risks to them are statistically similar, and that this is rarely articulated in discussions about service design. Thus through the focus group discussion process, participants are encouraged to participate in 'retrospective introspection' in an attempt to identify their own assumptions and to identify the nuances in each of them. In my analysis, I further explore these issues and consider the influence of the social, cultural and environmental context upon them.

Second, and leading on from this, focus groups allow for discussions of uncertainty about the conflicting normative values and assumptions of different groups within society, particularly given that participants often have multiple group identities (such as parent, care-giver, accountant and young woman) and these subtly influence their normative beliefs.(165) Thus a focus group may provide a space for the identification of value conflicts and for a closer inspection of why these occur and how they might be resolved. For example, junior clinicians who have previously had general training but now enter the subspecialty and must acknowledge the differences in

normative values and assumptions of their new colleagues and then negotiate how they will adapt their own views.

Third, the use of focus group discussions was particularly appropriate in this situation as the subject matter is potentially contentious, with multiple possible conflicting viewpoints. Some groups may feel that early discharge is an unsafe or unnecessary change to current practice which places undue stress upon parents to monitor and treat their child at home. Others might argue that the benefits of improved quality of life and reduced service pressures outweigh these concerns. Through in-depth focus group discussions, I aimed to provide a clearer understanding of these various viewpoints to ensure that the nuances of the debate can be taken into account when making changes in care pathways.

Fourth, given the potential differences of opinion over the role of early discharge in low risk febrile neutropenia, focus group discussions also enabled me to examine how social interaction may change opinions about the different service design options. The process through which participants present their own views, but also how they change or modify their views following interaction with others in the discussion, is a particular advantage of using the focus group method.(56) The “sharing and comparing” of experiences and opinions can be seen to be a key strength of focus group work, and may also reflect the ways in which groups interact outside of the research environment through the use of “structured eavesdropping”.(56,166) For example, in this research, reflecting how patients and families might share experiences and discuss service changes whilst sitting in a clinic waiting room or whilst making a meal in the ward kitchen.

Fifth, outpatient treatment of low-risk febrile neutropenia was likely to be a treatment strategy that some participants had not fully considered. By bringing together groups of people, rather than conducting individual interviews, a greater depth of discussion can be achieved as different aspects of the problem were considered by different members.(166) Furthermore, focus groups can make the expression of dissatisfaction with services easier than within the confines of an individual interview, particularly considering that I, the moderator, am a healthcare professional.(167) Thus focus groups provided an environment in which the process of reflecting on the issue and debating the potential barriers and facilitators could be observed and analysed.(168)

Finally, focus groups have been found to be particularly useful for obtaining qualitative data from young people, who may feel intimidated in the one-to-one environment of semi-structured interviews.(169) Given that this group have been traditionally under-researched, both in this field and elsewhere, I was particularly keen to develop a study which was accessible to them and in

which they felt comfortable participating. Thus the decision to use a focus group method was also strongly influenced by the desire to hear the 'voice' of teenage participants.

In summary, these six factors combined meant that focus group discussions were felt to be the most appropriate method for this study, given its aims and objectives. Although interviews were also considered, they would not allow for such thorough exploration of the social context in which decisions about the management of febrile neutropenia are most likely to be made.

Incorporation of the systematic review and qualitative synthesis

The results of the systematic review and qualitative synthesis are used throughout this qualitative study to inform the study design, the focus group topic guides and the analysis of the data, consistent with the overarching mixed methods approach to the thesis. Within this section I describe how the systematic review and qualitative synthesis impacted upon the design, performance, analysis and interpretation of the qualitative study, showing mixing at many levels through the work. The systematic review of effectiveness provides evidence that is appropriate to perform such a qualitative study. Had the systematic review found that early discharge regimens were either unsafe or had particularly high rates of treatment failure, then it would have been inappropriate to discuss reduced therapy regimens any further. It also provided the data about reduced rates of consent to these regimes and therefore stimulated further research into the perceptions of early discharge regimens. The systematic review then provided stimulus information for the focus group topic guides, initially by allowing the description of various service design options, and then using the results of the meta-analysis to outline the particular safety and treatment failure rates for participants to discuss. Thus, the qualitative study did not only address generalised opinions of inpatient versus outpatient care but also specifically discussed whether the known risks of outpatient treatment influenced the decisions of participants, thus providing information which allows the interpretation and application of the systematic review in a way which is consistent with the views of key stakeholders. Furthermore, the qualitative study allows observation and assessment of the way in which the statistical results of the systematic review are viewed by key audiences, thereby informing the findings of the original phase.

The qualitative synthesis reported in Chapter 4 contributed to the design of this study by identifying the current gaps in the primary literature. I was therefore able to focus on participants whose perceptions had not yet been explored and could develop aims to complement the existing literature. Furthermore, the qualitative synthesis delineated themes that could be identified within the discussion and which also made me more aware when participants began to discuss new themes that have not been explored elsewhere. Thus, I could probe further into these aspects of the conversation so that deeper and more insightful data could be obtained. The

synthesis of qualitative studies has also informed the analysis of this research by identifying the issues that are specific to febrile neutropenia, compared with those that are more generally associated with early-discharge regimens.

Study site identification and recruitment

This first stage of this work involved the identification of study sites. The aim of a sampling plan should be to enable the collection of material to inform the research question.(167) This can start with choosing larger "units" within which participants are grouped.(170) For this study, it was appropriate to select multiple study sites within the different Primary Treatment Centres of the UK from which to then sample the individual participants.

I decided to use multiple study locations within the UK to enable investigation of the role of various centre-level factors. Data from a recently published survey were obtained from the authors and used to identify centres with different approaches to risk stratification (and tool used), low risk protocol (particularly in relation to current timing of discharge), shared care services and geographical spread of patients.(40) These features were selected because they were thought likely to influence the experiences of participants. For examples, centres which do not currently use a risk stratification tool will treat all patients as if at high risk of septic complications of their febrile neutropenia and are thus likely to keep low risk patients in hospital for a longer duration than those centres where risk stratification is performed. Early discharge may then feel like a substantial change from their current practice and there may be more concerns about the safety and practicalities of these regimens than for other centres where low risk patients are already treated on reduced therapy regimens compared with higher risk patients. Meanwhile, centres with a large geographical spread might mean participants are less keen on early discharge strategies because of the distance to travel if a child deteriorates in an outpatient setting, or because of the challenges of attending clinic for follow-up on a regular basis. Having a large shared-care network may ameliorate some of these issues, thus resulting in a more positive attitude from participants in these centres. The design of acceptable early discharge services is likely to need to take into account these nuances and thus provide different care dependant on these factors.

Four main centres were purposively selected based on the design of their service. I then approached the appropriate centres through known contacts within the paediatric haematology and oncology community. I had already created good relationships with the centres through professional groups such as the Children's Cancer and Leukaemia Group (CCLG), and the clinicians at these centres had voiced an interest in potentially being involved in this research when the plans had been discussed at national meetings. This personal approach allowed centre staff to ask

questions about the study before agreeing to participate. At two centres I also gave presentations to the healthcare professionals' at their regular meetings to ensure as many people as possible were engaged with the research. The work for the study then involved creating greater links with each centre to ensure that key collaborators were identified, Research and Development approvals were obtained, recruitment processes were established and practical arrangements made for each focus group.

There was one particular challenge during the recruitment of centres. Although three centres were keen to participate when approached, finding a fourth proved challenging. I had originally hoped to include a centre where the current treatment of febrile neutropenia involves a length of stay of greater than 48 hours. I approached both of the centres that responded to the survey stating that this was their practice. Unfortunately, both centres were unable to commit to participation in the study, owing to challenges related to workload, their current personnel resources, and internal political issues. As no other site within the UK fulfilled these criteria, it was not possible to recruit a fourth centre to the study. No other UK centre could be considered a reasonable replacement. The study, therefore, does not include centres with long current admissions.

Three centres were therefore involved in the study. Centre 1 has around 25 inpatient beds at the Primary Treatment Centre and sees 100-150 new cases of childhood cancer per year. There is minimal care of febrile neutropenia in its shared care centres. Centre 2 also sees between 100 and 150 new cases of childhood cancer per year and has around 25 inpatient beds. Centre 2 has some shared care services but the majority of cases of febrile neutropenia are managed in the Primary Treatment Centres. The service is in the process of reviewing its febrile neutropenia policy and there have been open discussions about how to reduce the burden of treatment for young people at low risk of septic complications. The final centre, Centre 3, treats over 160 new children per year in their unit, which has more than 30 beds. They have a strong shared care network involving multiple Paediatric Oncology Shared Care Units (POSCUs) and the majority of episodes of low risk febrile neutropenia are managed outside of the Primary Treatment Centre. This is consistent with three other centres within the UK.

The study opened in July 2015 in one centre and in October 2015 in the other two centres. Focus group discussions generally took place within 2 weeks of recruiting the final participant, dependent upon finding a date that was convenient for all. In all centres, the healthcare professional groups recruited most easily and were performed between 9 and 16 weeks from the study site opening. Focus groups for parents of children under the age of 13 years took place 17 to 29 weeks after study site opening. The groups for young people and parents of children over the age of 13 took place 38 weeks after opening in Centre 1. As discussed in detail later in this

chapter, recruitment young people and parents of children over the age of 13 in centres two and three was difficult, and hence focus groups were not formed.

Analysis of protocols

In order to prepare for the focus group discussions and inform the analysis of the discussions observed, the febrile neutropenia protocol for each centre was obtained. These were reviewed and compared with the NICE guidelines for neutropenic sepsis.(21) As Table 17 demonstrates, the NICE guidance was generally followed, though certain deviations were present and will be highlighted within this section. All centres use the NICE definition of neutropenia and centres 1 and 3 also use the NICE definition of fever, with centre 2 choosing a slightly higher threshold for diagnosis.

Table 17 - Summary of febrile neutropenia protocols from each centre alongside NICE guidance

	NICE CG151	**Centre 1**	**Centre 2**	**Centre 3**
Definition of fever	Higher than 38°C	≥38°C	>38.5°C on one occasion or >38°C on two or more occasions recorded at least 1 hour apart	≥38°C
Definition of neutropenia	≤0.5x10^9/L	≤0.5x10^9/L	<0.5x10^9/L	≤0.5x10^9/L
Risk stratification	Advised Suggests modified Alexander rule	Yes Modified Alexander rule	Yes SPOG 2003 rule (Note: currently not used to discharge patients)	Yes Modified Alexander rule
First line antibiotics	IV Piperacillin with tazobactam unless there are patient-specific or local microbiological indications	IV Piperacillin with tazobactam	IV Piperacillin with tazobactam for standard risk patients, Oral ciprofloxacin and co-amoxiclav for low risk patients (not currently in use).	IV Piperacillin/ tazobactam and IV Gentamicin (except patients with bone tumours)
Timing of discharge for	Consider outpatient care	Step down to oral	According to risk tool, at 8-22 hours but not yet	48 hours with oral co-amoxiclav

low risk patients	for low risk patients	ciprofloxacin and co-amoxiclav at 24 hours then discharge from 48 hours	approved, therefore treated as per standard risk patients and eligible for discharge at 36-48 hours	

Centres 1 and 3 follow protocols which closely match the NICE guideline, with the addition of gentamicin to the standard antibiotic regime in Centre 3 being due to local microbiological indications. Centre 2 appears to be the most different in terms of their management of febrile neutropenia. This is a centre in the process of transitioning between management strategies. Therefore, although the protocol describes the SPOG rule and then risk stratified treatments including oral antibiotics with early discharge for children with low risk febrile neutropenia, there are clear notes within the document advising staff that these changes are not to be implemented and that currently all patients should follow the standard risk protocol, which involves a 48 hour admission for intravenous antibiotics. Therefore, all included centres currently follow a protocol that involves a roughly 48 hour admission with administration of intravenous antibiotics for at least 24 hours in low risk patients.

This exploration of the written protocols gives a contextual grounding to the focus group discussions. It allows consideration of the extent to which these protocols have been translated into the clinical practice described by participants. Areas where participants describe different behaviour to the protocols are explored later in the thesis, and the influence of the centre culture is examined so as to give greater understanding of the issues surrounding a move to outpatient care of paediatric low risk febrile neutropenia.

Identification, recruitment and consent of participants

Four focus group discussions were planned in each of the three study sites (i.e. 12 focus groups, see Table 18). Separate focus groups were offered for each of the following categories of participant:

- Patients (age 13-18 yrs)
- Parents of teenagers (13-18 yrs)
- Parents of younger children (under 13 yrs)
- Healthcare professionals

For the purpose of this study, patients and their parents/caregivers were only invited to participate if the patient was considered to be at risk of low risk febrile neutropenia, or within 6 months following being at risk. This was assessed using the modified Alexander rule (121), as this is the tool advised by the NICE guidelines, and was defined as requiring all of:

1. Current age >1 year
2. Currently receiving myelosuppressive chemotherapy or radiotherapy, or within 6 months following completion of final course
3. NOT any of:
    a. All leukaemia except Acute Lymphoblastic Leukaemia (ALL) on maintenance chemotherapy for at least one month
    b. B Cell Non-Hodgkin's lymphoma
    c. Any high dose chemotherapy regimen requiring stem cell support within the last 90 days
    d. Allogeneic bone marrow transplant recipient within the last year
4. NOT receiving palliative care alone

I chose to exclude both high risk patients and patients receiving palliative care alone, as the perceptions of these groups were likely to be substantially different to those of patients who may potentially have episodes of low risk febrile neutropenia. Given that the main aims of the study relate to understanding perceptions of management and providing key features of an acceptable service design for children with low risk febrile neutropenia, I worked to ensure that the study included participants who were most likely to fall within this group. Although I recognise that it is the episode of febrile neutropenia that is ultimately risk stratified, I aimed to include those patients who might be eligible for an outpatient regimen and thus excluded patients on highly intensive courses of treatment. Patients receiving palliative care alone are generally managed according to patient choice and as such are unlikely to be treated strictly according to such protocols, even if instituted.

Participants in the young people's focus group discussions were between 13 and 18 years old. This age range was selected as this group of patients are generally treated in Teenage and Young Adult Services, compared to paediatric services for those under 13 years old, and hence this is a clinically meaningful age cut-off in the design of services. Each of the Teenage and Young Adult services involved is situated within the same centre, and provided predominantly by the same team, as the paediatric services included. However, teenage patients tend to be managed in slightly different environments (separate wards or beds specifically for teenage patients within the Primary Treatment Centre) and therefore may have a different experience of care.

I recognise that the age range for the teenage group is rather broad and that participants aged 13 and 18 may actually be very different developmentally and socially. This could mean that the focus group discussions for this group of participants would be more difficult to moderate.

However, there were two main reasons for choosing to accept this potential difference. The first is a very pragmatic reason, in that there are very few teenagers diagnosed with a malignancy between the ages of 13 and 18 each year in the UK. When the patients with non-Hodgkin's lymphoma, most haematological malignancies and those who receive high dose therapies are excluded, the number of potential participants are even smaller. Given that this age group are known to often be quite difficult to recruit to research studies, having a broader age range was felt to beneficial in increasing the rates of recruitment. The second reason for accepting a broad age range for the TYA groups was that the main area of interest for the study is the experiences and perceptions of patients with low risk febrile neutropenia. Therefore, as all participants would be able to contribute to a discussion of this area, these groups were actually relatively homogenous, and differences in age, opinions or social structures were only likely to be as relevant to this group as they were to the parental or healthcare professional groups, where similar diversity in age or social positioning was likely to occur. The experiences of recruiting to and moderating of teenage focus groups are discussed later in this chapter.

Participants were invited with a view to obtaining maximal diversity based on age, gender, ethnicity, socioeconomic/educational group, diagnosis, family structure, number of siblings, distance from home to hospital, likely location of treatment of febrile neutropenia (Paediatric Oncology Shared Care Unit/Primary Treatment Centre) and previous febrile neutropenia experience (including both high risk and low risk episodes). (171) The successes in achieving this, the challenges I faced, the reasons for these difficulties and the impact upon the findings are all discussed in the following sections of the chapter.

Parents and caregivers of selected children were also invited to take part in one of the focus groups. Parents and caregivers of children under the age of 13 were eligible to take part in a separate focus group, provided the index patient met the low risk criteria given. Separate focus groups for parents of children aged under 13 and over 13 were performed as it was anticipated that these groups would have different opinions about the services to be provided for their children. Both of a patient's parents were eligible to be involved if they were interested. This occurred twice within the groups. For the young people over the age of 13, it was not a requirement that both patient and parents/caregivers take part in the study. However, in most cases, this did occur as both parties shared similar views about the research. Parent couples and parent-child dyads were not explicitly recruited nor were they excluded, but I took note when this occurred and used this data to inform the findings.

Health care professionals from the teams looking after these children were invited, also in a purposive way, to give maximal diversity around the areas of age, gender, ethnicity, professional background (only doctors and nurses working actively with children and young people with low

risk febrile neutropenia), and level of experience. Table 18 shows the focus groups performed at each centre.

Table 18 - Summary of focus group discussions

	Healthcare Professionals	Parents of patients aged under 13 years	Parents of patients aged over 13 years	Young People aged 13-18 years
Centre 1				
Centre 2				
Centre 3				

Key: Green – focus group performed, Red – focus group desired but precluded by poor recruitment

Participants had to be able to participate in focus group discussions in English. This reflected the practicalities of being an English speaking researcher but was also justified as the majority of people from an ethnic minority have English as their first or second language and thus the study was likely to obtain breadth and depth of concepts without the need for interpretation. There are a number of potential difficulties facing participants who do not have English as a first language, particularly in understanding the frequently rapid flow of focus group discussions, or in understanding the idioms which are often used by those for whom English is the first language. I closely observed participants within the focus group for signs that they did not understand the language used and aimed to provide further explanation when complex issues were raised.

The choice to include only English language speakers does mean that some participants who do not speak English might be excluded. This group of participants may face particular challenges when a child is diagnosed with cancer and may have additional concerns about reduced therapy regimes, which relate to both language and cultural differences. These may differ across cultural groups and would therefore require a particularly large study to explore. The challenges of interpretation, recruitment and analysis are beyond the scope of this study and therefore, readers must take into account that this group have not been approached. The clinical application of the findings therefore may not be appropriate for this group, and particular care should be taken when reduced therapy regimes are being offered to those for whom English is not their first language and thus reporting problems and re-accessing care may be more problematic.

Patients and caregivers were identified and invited by their local team to participate in the study, and were provided with appropriate participant information sheets. In the case of healthcare professionals, participants were invited to take part through announcements at local team meetings and through emails sent by the site specific collaborator (see Appendix 5.2).

There were five different participant information sheets for this study, so as to cover the five main groups who needed to be informed about the work (see Appendix 5.1). These were:

- Young people aged 13-16 years, who were asked to give assent for their own participation
- Parents of young people aged 13-18 years, who were asked to give consent for their children to participate
- Adult patient participants aged 16-18 years, who were asked to give consent for their own participation
- Parent participants (parents of children/young people at risk of low risk febrile neutropenia), who were asked to give consent for their own participation
- Healthcare professionals, who were asked to give consent for their own participation

Prior to the submission of the study for ethical review, draft participant information sheets were reviewed by young people, parents and healthcare professionals. The young people were of varying ages from 11 to 18 years and were being treated within paediatric haematology and oncology services. I specifically asked younger people to review the information sheet than would be eligible to take part, to ensure that they were comprehensible to those with a younger reading age. I checked with all young people that they understood the terminology used, in particular the phrase 'febrile neutropenia' and all were very clear that this was familiar to them and did not need to be changed. Parents of children of all ages were also asked to review the information sheets and stated similar agreement with the young people, that the sheets were understandable, clear and covered all their questions. I approached only patients and parents who would not be eligible to take part in the study to review the participant information sheets so as not to reduce the pool of potential participants for the study. However, all those who reviewed the participant information sheets stated that, based on the information sheet, they would have been keen to take part if they had been eligible. All feedback about changes to the information sheets was taken on board and incorporated into the versions submitted to the ethics committee.

When potential participants had read the patient information sheets, they were asked by the local team if they were interested in taking part in the study, and if so, verbal consent was obtained to share their name, address and telephone number with the study team. After this verbal consent had been given, the study team then contacted the potential participants to obtain consent for the study and to determine their availability for the focus groups. In the case of participants under the age of 16, consent was sought from someone with parental responsibility, but the assent of the participant was also essential for entry into the study.(172)

Participants were made aware that they could withdraw from the study at any point up to two weeks following the focus group discussion and that a decision to withdraw would not impact on clinical care. They were made aware that should they withdraw, all personal data that they had provided up to that point would be removed from the study. Their quotations from the focus groups would not be used in the analysis or any reports and publications. However, the rest of the data from their focus group (which related to other participants' quotations) would continue to be used.

The time limitation in the right to withdraw from the study was advised by the Research Ethics Committee. It reflects the challenges of analysis within qualitative research should a participant withdraw from the study at a point when the key themes and arguments have been identified and the thesis is on the verge of submission. Furthermore, it was felt that participants who had not felt the need to withdraw after this 'cooling-off' period following the focus group, were unlikely to wish to do so at a later point. The participants within the study were comfortable with this aspect of the research process and no participant chose to withdraw from the study following their participation in a focus group.

Patient participants were also asked for permission to inform their GP about their participation in the study. (See Appendix 5.6.) The GPs of parent or healthcare professional participants were not informed.

Immediately prior to the focus group, the patient/caregiver participants were asked to complete a basic data collection form providing:

1. Name, age, gender, ethnicity
2. Address (to obtain distance from hospital)
3. Family structure
4. Data on socio-economic level – to include occupation of parent(s), parents' highest educational level and the family's housing situation
5. GP (to inform about participation in the study)

Young people were encouraged to involve their parent(s)/caregiver(s) in this process to ensure that as much detail as possible was provided.

After the focus group in which written consent had been obtained, the local team were asked to provide the following data for each index patient:

1. Diagnosis (and date of diagnosis) and treatment regimen (including current/most recent course)
2. Dates of previous episodes of febrile neutropenia, whether each episode was low or high risk, location of treatment (POSCU/PTC), treatment received, duration of admission, complications arising.

Healthcare professionals were asked to provide their name, age, gender, ethnicity, profession, grade, time spent at current grade, and time spent at current centre. All basic data collection forms are provided in Appendix 5.4. This information was used to inform trends within the data and to further understanding about the influences on perceptions of early discharge.

Focus Group Participants

The participants in the study are described within this section. As mentioned earlier in this chapter, the study faced substantial challenges related to the recruitment of participants, which will be discussed further in this section and the one that follows. The aim is to consider the representativeness of the sample and how this impacts upon the findings of the study. This process complements the reflexive nature of the study as a whole and is included within this methodology chapter because it explores many of the methodological issues surrounding recruitment and then informs the later chapters on the conceptual findings of the work.

Whilst the healthcare professionals groups recruited well at all centres, parents and young people were less easy to recruit. Potential participants reported various different reasons for declining to take part, including difficulties with childcare during focus groups, distance of travel and a preference not to come to the hospital on days when they did not have treatment. Some of these problems were difficult to solve, but I did realise that there was a need to recognise the time commitment of participants. I therefore applied for further funding and submitted a substantial amendment to the Research Ethics Committee to provide parent and young person participants with a £20 Amazon voucher. Following implementation of this amendment the recruitment rates to the study appeared to increase; the rates of acceptance of the Amazon vouchers were high, whilst travel expenses claims were minimal.

In addition to these changes, various steps were taken to reduce the rates of non-attendance at focus groups. However, the majority of groups experienced at least one non-attender. For one group, the number of non-attenders was sufficient to mean that the discussion could not take place on that occasion and hence was rearranged for another time. The reasons for the majority of the non-attendances were unknown as participants did not contact any member of the research team before or after the group to explain. In situations where the reasons for non-attendance were given, child-care issues predominated for parents and clinical pressures for healthcare professionals. No withdrawals occurred following the performance of any focus group discussion.

The composition of each of the focus groups is outlined in Table 19. In total, 13 healthcare professionals participated in the discussions, of whom six were medical and seven nursing staff

who were evenly distributed through the groups. Participants of various professional grades had been purposively recruited. There was a wide range of experience within the specialty of paediatric haematology and oncology, and within each centre. The majority of healthcare professionals who took part were female (10 female, 3 male). The gender imbalance was more pronounced in the nursing participants, which reflects the workforce structure in this area. All the male healthcare professional participants took part in the focus group conducted at centre 1. The majority of participants self-identified as white British, with a mixture of other ethnicities. The focus group at centre 3 was the most homogenous, containing three white British women.

In the groups for parents of children under the age of 13 years, there were 11 participants, the majority of whom were mothers. They were between 35 and 44 years old, all described themselves as White British and all were in committed relationships. They had between two and seven children of varying ages. In centres 1 and 3, all participants were employed. In centre 2, the majority of participants were not currently employed. Participants had a wide range of educational levels. Their partners' educational and employment levels were similar to their own. Seven participants were owner occupiers, with 4 participants renting their homes. Both parents from one family participated, therefore there were ten affected children represented.

The affected children were between 2 and 10 years old. Six children had ALL, two had brain tumours, and two had other solid tumours. These index children had experienced between two and 10 episodes of febrile neutropenia each. The majority of episodes were high risk. In centres 1 and 2, almost all episodes were managed in the PTC; in centre 3 all were initially managed in a POSCU (Paediatric Oncology Shared Care Unit). Only one child had ever been admitted to a paediatric intensive care unit (PICU). The most common complication was a delay in the administration of the next course of chemotherapy. The duration of admissions for febrile neutropenia was between 2 and 19 days, with the median duration of admission being slightly longer at centre 2 than elsewhere.

In the focus group for parents of children over the age of 13 years, there were 5 participants; 3 mothers and 2 fathers. These participants were understandably older than in the other parent groups, being 41-53 years old. They all described themselves as White British. Three were from nuclear families with 2-3 children, one couple (both parents present) were a blended family with three children. There were a range of educational levels and the majority were employed. Their partners were of similar educational and employment levels. All owned their own house.

The four index children were 13-16 years old. Two children had Hodgkin's disease and two had ALL, one of whom had relapsed disease. Two children had minimal experience of febrile neutropenia (one or fewer low risk episodes, no high risk episodes). The other two children each

had 6-7 previous episodes of febrile neutropenia, the majority of which were high risk episodes. All episodes had been treated at the PTC, although two had presented to the local POSCU and then been transferred in to the PTC. No patient had ever been admitted to intensive care, but two course of chemotherapy had been delayed. The duration of past febrile neutropenia episodes was 2 to 10 days, with the majority being 5-6 days.

Table 19 - Table of focus group composition

Location	Group	Number of participants	M:F ratio	Age	Ethnicity (self-defined)	Composition notes
Centre 1	Young people	3	0:3	15-16 years	3 White British	2 participants with Hodgkin's disease, one with ALL. One participant with no febrile neutropenia episodes, one with one low risk episode, one with 6 high risk episodes. All episodes treated at PTC (two episodes started at POSCU but transferred to PTC). No ICU admissions. One course of chemo delayed following high risk episode. Admissions 2-10 days (most 5-6 days).
Centre 1	Parents of Under 13s	3	0:3	36-43 years	3 White British	All nuclear families with two children. 2 degree level education, one GCSE level. All employed. Partners same educational and employment. Two own house, one rents privately. Affected children aged 4-10 years. Two ALL, one medulloblastoma. Between 2-10 episodes of FN; 0-8 high risk episodes each, 1-2 low risk episodes each. All managed at PTC. No ICU. One removal of line. One delayed course of chemo. Admissions 2 - 19 days (most 48-72 hours)

Table 20 - Table of focus group composition

Centre 1	Parents of Over 13s	5	2:3	41-53 years	All White British	3 nuclear families with 2-3 children. One blended family (both parents present), with three children. One degree level education, one A Level, one ONC, two GCSE level. All employed except one who is semi-retired (to care for child). Partners same educational and employment levels. All own house, four with mortgage. Four have children who participated in young people's group. Affected children 13-16 years old. 2 with Hodgkin's disease, one with ALL, one with relapsed ALL. One patient with no febrile neutropenia episodes, one with one low risk episode, one with 6 high risk episodes, one with 7 high risk episodes and one low risk episode. All episodes treated at PTC (two episodes started at POSCU but transferred to PTC). No ICU admissions. Two courses of chemo delayed following high risk episodes. Admissions 2-10 days (most 5-6 days).
Centre 1	Healthcare Professionals	7	3:4	30-51 years	6 White British, 1 Chinese	3 medical (SHO, registrar and consultant), 4 nursing (bands 5-7). 1-13 years at current grade. 1-24 years at current centre.

Table 21 - Table of focus group composition

Centre 2	Parents of Under 13s	5	1:4	35-44 years	All White British	All nuclear families with 2-7 children. Two participants from same family. Three with degree level education, two with O levels. One employed, four homemakers/carers. Partners – one degree level education, one A levels, one HNC, two with O levels. 2 employed, one self-employed, two homemakers/carers. Three own house (two with mortgage), two rent privately. Affected children 2-9 years old. Diseases relapsed Wilm's tumour, ALL, osteosarcoma, ependymoma. 2-7 episodes of febrile neutropenia; 1-5 high risk episodes each, 0-2 low risk episodes each. All but one managed in PTC. No ICU admissions. One course of chemo delayed. Admissions 2-14 days (median 4 days).
Centre 2	Healthcare Professionals	3	0:3	43-60 years	1 White British, 1 Indian (British), 1 Pakistani	2 medical (registrar, consultant), 1 nursing. 7 months - 20 years at current grade. 7 months - 28 years at current centre.

Table 22 - Table of focus group composition

Centre 3	Parents of Under 13s	3	0:3	36-45 years	All White British	2 nuclear families with two children. One blended family with 7 children. One A level education, 2 O level. All employed. Partners same educational and employment levels. Two own house (with mortgage), one rents from Local Authority. Affected children 4-8 years old. All with ALL. 4-9 episodes of febrile neutropenia; 1-8 high risk episodes each, 0-3 low risk episodes each. All in POSCU (one later transferred to PTC). One admission to PICU after high risk episode. 3 delayed courses of chemo after high risk episodes. Admissions 2-14 days (most 48-72hrs).
Centre 3	Healthcare Professionals	3	0:3	30-55 years	All White British	1 medical, 2 nursing (band 7). 3-12 years at current grade. 5-12 years at current centre.

The participants in the young people's group all had parents who had participated in the relevant focus group discussion. These young people were 15-16 years old, all female and all described themselves as White British. Two had Hodgkin's disease and one had ALL. Two had minimal experience with febrile neutropenia and one had considerable experience with high risk disease. Further details, including family demographics, are discussed in the paragraph relating to their parents.

Discussion of recruitment difficulties and implications for findings

This study aimed to purposively sample participants from a broad range of ages, genders, ethnicities, socio-economic backgrounds, family structures, locations of home and care, and previous febrile neutropenia experiences. Although these aspirations were attained for some factors, including age, gender, location of care and previous febrile neutropenia experiences, the sample was limited in terms of ethnicity, socio-economic background and family structures. Within this section of the chapter and consistent with the reflexive nature of this research project, I reflect upon potential reasons for the recruitment challenges and what these may mean for the findings of the research as a whole.

There are a number of reasons why these difficulties in recruitment may have occurred. First, the staff involved in recruiting to the study at each centre may have made judgements about which participants would be most likely to be interested in such a study, and therefore affected recruitment of certain groups through their choices of people to approach or their presentation of their research to these groups. One research nurse had raised this particular issue with me during one contact discussion, stating she was specifically approaching only participants who lived close to the location of the focus group discussion. At this point, I stressed the importance of having a wide variety of views present and therefore a desire for sample diversity, which she appeared to take on board. However, it is still possible that pre-conceived ideas about potential participants continued to play a part in the recruitment at this and the other centres. These challenges of using 'gatekeepers' to access participants have been described in the literature.(56)

The second possible explanation for the lack of diversity in certain areas may be that particular groups of people chose not to take part in the study. This could be that potential participants are not interested in participating in research of any type, or are choosing not to participate in this study specifically. The parents who choose to participate in focus groups are most likely to be those who are actively involved in their child's treatment, who are more likely to engage with treatment plans when discharged, and who want to contribute to improving future services. They may also be the participants who have strong opinions about the current care of children with febrile neutropenia and may be more likely to be the parents who are dissatisfied with the care

which is currently given, particularly as the information given to participants joining this study clearly states its intentions to consider ways to redesign services. The parents of children under the age of 13 at Centre 2 astutely identified the issues surrounding parent involvement in the following exchange of conversation:

> *"4: yeah but what I'm saying is there's parents that perhaps think well I can't be bothered to go in*
> *5: them parents aren't here are they?*
> *Rest: no*
> *5: that speaks for itself doesn't it so?" (Centre 2, parents of under 13s)*

Population groups who are very busy, or time-poor, are likely to struggle to attend groups, even when they have an interest in the research area. This explains the given reasons for non-attendance, with parents being busy caring for children and attending treatment, whilst professionals have significant clinical commitments. Linked to this, some parent and young people participants commented on the regularity of their attendance at hospital and a desire not to make any further trips in order to participate in the research. Unfortunately, attempting to hold groups which co-ordinated with their clinic visits would have been logistically impossible given that participants have appointments at different times.

For the healthcare professionals group, participants of more junior grades might have felt less inclined to take part in the research, given that they are not used to being asked their opinions about care and how it should be changed. As conveying these kinds of opinions is usually the role of more senior healthcare professionals, social norms may have prevented junior professionals from attending discussions. I made specific attempts to prevent this by asking local contacts to approach junior colleagues and emphasise how important all opinions were in this work. Despite this, the group at Centre 3 consisted solely of senior professionals.

The challenges for participants for whom English is not their first language, have already been discussed earlier in this chapter. This did not seem to be a problem within the groups, given that the majority of participants had English as their first language. Two healthcare professionals did not speak English as their first language, but used it extensively in their working lives and so did not appear to struggle with the content of the focus group discussions. However, other participants may have chosen not to participate because of their concerns about being unable to follow a discussion carried out in English.

In the final point about the possible reasons for the recruitment difficulties, it is important to discuss what may have precluded holding the young people's groups in centres 2 and 3. Along with the issues mentioned above, there were additional challenges obtaining teenage

participants. First, the numbers of teenagers diagnosed with cancer each year are thankfully small, but results in a small pool of potential participants to invite at each centre. Furthermore, teenagers tend to be particularly busy with school, exams and work, especially during maintenance therapies for their cancer. As this makes up a considerable portion of the population at risk of low risk febrile neutropenia, this had a dramatic impact on both willing participants and successful date setting for these groups. In addition, a number of teenagers who were approached to participate in the group stated that they would be prepared to take part in individual interviews about their thoughts and experiences but were reluctant to talk within the group setting. This was somewhat at odds with the rationale for selecting focus groups methods for this study discussed earlier in this chapter.

Next I consider the potential implications of the difficulties in recruitment to the study. The aim of including varied groups of participants was to draw out broad similarities and differences from this diverse sample, instead of noting individual differences between participants. Some aspects of this aim were potentially compromised by the difficulties in the recruitment and these are primarily reflected in two areas.

The first is that the voice of young people within the findings is less prominent than that of the parents and health care professionals. This is in part due to the smaller numbers of participants and the single focus group when compared to the other participant groups. This group were also relatively reserved in their discussions and required more prompting and encouragement to participate than the adult groups. The young people's group was the shortest discussion within the study, lasting 45 minutes. When they did articulate their experiences and perceptions, the young people generally expressed views which were consistent with the parental groups, although often with less nuance and depth to the concepts. This may be due to the small size of this group, with less people to further the discussion, but may also represent different ways of considering the issues. Where the young people's voice coincides with the parental views, I have aimed to highlight this within the presentation of the analysis. Where the young people's experiences are at odds to their parents or the healthcare professionals' perceptions of them, I have provided further discussion. Further work which could be done to investigate and represent the teenage voice in this area is discussed within Chapter 9.

The second area to discuss in relation to the implications of the recruitment problems is the issue of diversity in family structure. It is known that compliance to home maintenance therapy for children with leukaemia is strongly associated with family status, where patients whose parents are not in stable partnerships are less likely to be compliant. (173) This is relevant to the issue of febrile neutropenia as this may also apply to administration of home antibiotics. Furthermore, these parents might have different preferences when it comes to the location of care – either

preferring to stay in hospital where they may feel they have more support, or having more responsibilities at home that cannot be easily shared and therefore be much more keen on early discharge. As this study was unable to recruit from this group, it is difficult to be sure about these issues, although the included participants did discuss these issues. Their views are presented later in Chapter 7.

Focus group discussions

Each group aimed to include between 5 and 8 participants. After participant details had been given to me and they had confirmed their interest in the study, I began to identify potential dates for the focus group discussion. Once I had contacted all participants, the date which suited the most participants and which both I and the assistant moderator could attend was chosen as the date for the discussion. The process of identifying potential dates could take a number of telephone calls to participants and frequently took two to three weeks of chronological time. The date for a discussion was not set until at least 5 participants had agreed to attend on that date. Participants were then contacted to confirm the date and time of the focus group. Other participants who were recruited following date setting were invited to attend at this specific date and time.

I contacted each participant a few days prior to the focus group to remind them of the date, time and location and to attempt to reduce the number of participants who did not attend. At the time of the focus group, if three or more participants attended then the discussion proceeded as planned. At all focus groups, at least one participant failed to attend, despite the efforts made to reduce the likelihood of this occurring. If fewer than three participants attended, the group was cancelled and rearranged for another date. This occurred on one occasion, with all the original participants also attending the second group.

In one healthcare professional group, a participant arrived very late due to unexpected clinical work. Given that the discussion was well established by this point, including the introduction of the systematic review results, I felt that introducing a new member to the discussion at this point would be detrimental to the group. I therefore thanked the new participant for coming but asked that they not take part in the group at this point. They were very understanding of this and the group then continued from where it had been interrupted.

Focus groups were held in private meeting rooms in a convenient location (see also *Rapport building, engagement and participant experience* section of this chapter) and at a convenient time for the participants.(168) Each focus group session lasted between 45 and 86 minutes (median 73 minutes), with 30 minutes or so prior to starting the discussion used to allow participants to

review the information sheet, complete consent and data collection forms, and ask any questions about the study. Thus in total, most participants spent 90 minutes to two hours attending the group.

I facilitated each focus group session. An assistant moderator, HH, who is also a junior doctor and a researcher, attended each group to provide additional practical support and also aimed to record data on ordering of speech and any non-verbal communication. An assistant researcher plays a key role in the performance of focus group studies. They facilitate the smooth running of the group by assisting with practical aspects such as group set-up and attendance to matters arising during a group.(168) In this study, this involved entertaining children who had been brought to two groups as families had struggled with child-care and taking consent from late-comers to two groups. Assistant moderators also help through the recording of key information during the group so as to provide a backup in case of the loss of the digital recording and to help with the ordering of speech when transcribing from the recording.(167,168) Finally, they act as an observer within the group, noting non-verbal behaviour, participant responses and interactions. They can therefore help the primary researcher through de-briefing discussions to record initial responses to focus groups and identify key areas for discussion within the findings.

The researchers performing or assisting in focus groups had an enhanced CRB check and the research complied with all guidance issued as part of the Government sponsored Vetting and Barring Scheme.(174)

Researchers carried photographic identity cards at all times to reassure participants of the academic nature of the study. Policies of the University of York for the physical and emotional protection of researchers were followed throughout the study to ensure that the researcher and assistant were safe during each episode of field work. Mechanisms were in place for any difficult or distressing situations for researchers to be debriefed by Professor Karl Atkin and followed up as appropriate. Thankfully, no such situation occurred.

All focus group discussions began with a reminder of the aims of the study, and with the setting of ground rules. The main ground rules for the study were to respect other participants and their opinions, and to keep confidential the things that were shared in the focus group. I also encouraged participants to talk freely, as the main aim of the study was to find out about their experiences, perceptions and the influences on decision that they make about febrile neutropenia. Finally, I used this time to restate the right to withdraw from the study up to two weeks following the focus group and gave the opportunity for participants to ask any outstanding questions.

Participants in the focus groups for healthcare professionals were reminded that the research team were only interested in their general views and would not be discussing the details of individual cases. It was clearly explained that if identifiable information was given about a patient then, on the first occasion, this part of the discussion would be interrupted and participants reminded of the need to keep patient information confidential. On the second occasion of providing identifiable information, the focus group discussion would be discontinued.

Topic guides were prepared for the focus group discussions so as to provide structure to the 'guided conversations'.(175) The guides were informed by the findings of the syntheses of quantitative and qualitative studies described in Chapters 2 and 4 respectively. (144,176) Discussions with key stakeholders also aided in the development of the topic guides, which were reviewed by qualitative researchers and healthcare professionals from other centres in the UK who were therefore not eligible to be participants. The focus group topic guides are provided in Appendix 5.5.

The introductory questions for groups of young people and parent participants focused on their understanding of febrile neutropenia and experience of treatment for previous episodes of febrile neutropenia. This provided an opportunity for participants to become comfortable speaking in the focus group environment and also allowed the moderator to introduce the idea of risk stratification of episodes and differences in current treatment strategies. It provided the data that allowed consideration of the influence of past experiences on future acceptance of early discharge, and was used as key information within the analysis.

I then introduced the idea of different possible treatment strategies based upon those found within the literature of the systematic review within Chapter 3 (without providing the detailed evidence from the systematic review) and allowed participants time to discuss the various options. This allowed me to establish initial responses to a reduced therapy regime and then later identify the role of data in shaping and changing these responses, if this happened at all.

The treatment failure, admission and safety rates were then brought into the discussion based on the information obtained through the meta-analysis in Chapter 3 and further discussion about preferences was encouraged.(144) I explored how participants responded to the data, both in their understanding and attitudes towards early discharge.

The focus group discussion was then guided to the issue of outpatient treatment and I probed into the different factors involved in decision making about this option. In particular, I asked about the various issues identified by the qualitative synthesis in Chapter 4, being sure to note which issues were raised spontaneously by participants and which required prompting.(176) The

aims of this process were to provide as much clarity and depth to the data as possible and to allow the further consideration of the concepts seen within the Qualitative Synthesis.

The questions following this then focused on the influence of other members of the family and of healthcare professionals on the perceptions of participants. This section of the focus group intended to explore the social and environmental influences on the decisions made about outpatient therapy, and to give more contextual data for the analysis of different preferences. Furthermore, this allowed me to investigate the nature of triadic decision making in this setting and the influence of the power balance within triads when making choices.

Finally, participants were asked about how the specific aspects of an outpatient service could be designed so as to make it most acceptable to them. This allowed the consideration of how different issues could be resolved in the most acceptable way for participants.

Meanwhile, the focus group discussions for health care professionals used a similar thread of discussions, adjusted so as to be more relevant to the health care professionals' situation but still enabling the comparison and linking of accounts across groups (see topic guides in Appendix 5.5). I asked the healthcare professionals more in-depth questions about potential service design as this group were more likely to have experience of the design process and the specific service challenges in the regional and national arenas. This approach allowed comparisons of similar responses between the different participant groups, whilst also creating an environment that allows them to reflect on their professional experiences.

Throughout the discussions, I used prompts and probes including phrases such as *"go on…"* or *"anyone else want to say anything there?".* In one group, I asked: *"can I get you all to expand a little bit more about the frustration thing… that's a word that's come up three times now… why?"* (Centre 1, HCP focus group). This helped to provide more precise and elaborate data about why participants brought up certain points, or the meanings of the phrases they used. This encouraged participants to be more explicit about some of the points made within the group, in an attempt to improve the information received and ensure that the interpretation of vague comments was correct from the participants' point of view. I also used these short interjections to ensure that all participants' voices on a topic were noted, particularly when I felt that they might not agree with the responses given by others. For example, in one group for parents of under 13s, one participant who had previously been very involved in the group stayed quiet during the initial discussion about early discharge approaches when the other participants had been quite vocal about not wanting outpatient care. When I then directed the discussion to this participant, she spoke about how her opinions regarding the location of care had changed, and provided real

insight into her own thoughts and feelings, which were somewhat different to the rest of the group:

> *"Mod: …so, you said you live 20 minutes away, does that mean you might say something different to these guys about what was on offer?*
> *3: probably I think circumstances have sort of changed my mind… last time we were supposed to have the focus group (note: focus group initially planned for a different date and poor attendance so rearranged for this session)I was dead cert on I think I should go home every time cos I only live 20 minutes away but then just being on the ward again last week and then I get a little bit nervous and then I think no I'd definitely prefer to stay so I think it's the circumstances that changed my mind but you know when we had the last one I was convinced my answer was gonna be just send me home every time*
> *Mod: so what … what changed your mind?*
> *3: just remembering really how you feel uncertain when you do come in with a temperature… erm…. And then we often come in late at night so… although its 48 hours, it ends up being longer because the bloods have gone so late at night… erm… and I suppose the night's scary as well isn't it… when you get the temperature in the night… erm… so yeah… I think just the realisation of coming into hospital recently has probably made me slightly change my mind…" (Centre 3, mother of under 13)*

Rapport building, engagement and participant experience

> *"Rapport refers to the sense of respect, trust and positive regard between research and study participants that enhances openness in information sharing."(170)*

Developing rapport and engagement serves two main purposes in focus group discussion studies. The first is to improve the material collected to answer the research questions, as discussed in the above quote from Padgett. The second is to improve the participant experience such that they feel an important part of the research process, that their views are listened to and important, and that being a participant was a worthwhile experience.(167,168) Rapport is developed over time through the initial contacts with the participants through to the focus group itself and then the follow-up to the study.(170)

There were a number of features of the groups in this study that helped to build rapport and create an atmosphere that encouraged participants to talk freely and provided interesting and illuminating data for the study. A main feature in building rapport was the fact that many participants already knew each other. As previously discussed, this was a purposeful design point

for healthcare professional groups. Although not planned, individuals also knew each other in a number of the parent and young people groups. It was not however unexpected as the number of families involved in paediatric haematology and oncology services is relatively small, and the eligibility criteria for the study limited participation to patients being treated at the same time. Participants had therefore met at previous clinic appointments, during admissions to the wards or through local social media groups. Within the study, all interactions between participants who already knew each other seemed to be positive events helping to both initiate small talk before the formal focus group discussion started and to put people at ease during the groups.

Nonetheless, it should be recognised that there may be some disadvantages to convening groups where the participants know each other and move in similar social circles. Participants may feel less able to disclose negative opinions or behaviours which may not be socially acceptable to the group for fear of being judged by their contemporaries, or if anxious about other members of the focus group not maintaining confidentiality. Interestingly, this did not appear to be the case in this study as participants disclosed behaviours such as non-attendance with febrile neutropenia, even when other participants had voiced strong views that this was not something they approved of.

Another feature which may have built rapport was the fact that some participants knew me and the assistant moderator. The influence of this on the data collected is discussed elsewhere, but this may have helped participants to discuss their experiences, in healthcare professional, parent and young people's focus groups. Furthermore, their confidence that we would understand terms such as 'port' or 'Hickman' allowed them to talk freely about subjects without needing to frequently stop to clarify such phrases.

There were other key points of study design that helped to develop rapport. As discussed in the recruitment and ethical issues sections of this chapter, the consent process took place over a series of discussions with participants, which allowed me to engage with them over the weeks prior to focus groups taking place. Another rapport building action was to pick a location which participants could easily locate, knew how to access and felt comfortable talking in. For healthcare professionals, this was a meeting room which they routinely used within their work, and thus could attend easily and felt relaxed in. The locations for parent groups were more varied and included clinic waiting rooms (at a time when the clinic was closed to patients), meeting rooms near the hospital wards and a local library. Each of these were locations that participants could easily find and where transport and parking arrangements were familiar. By reducing the preparation required to attend and through using known spaces, I aimed to reduce participants' anxiety and increase the likelihood of attendance.

Once within the group setting, the task of completing the necessary paperwork provided a short period of time for small talk between participants and a chance for brief introductions. I then started each group with a brief round of introductions of each participant and, where it was a parent group, a chance to speak about their child. This, followed by a question about previous experiences of febrile neutropenia, allowed participants to become comfortable in answering simple discussion-starting questions within the group setting, thus developing rapport within the group that was not solely related to interactions with me.(167) I also included a short question to participants asking what febrile neutropenia is, to ensure that we were all using the same definition when discussing this topic. Other technical language used throughout the group was checked when participants introduced it, as were local issues, such as when names of specific people were used, I would ask about what their roles were. Throughout the group discussion, I aimed to use positive and encouraging language and open prompts to show that I was keen to hear and understand the experiences and perspectives of the participants, using phrases such as *"why do you think that is?"*

The engagement of participants with the research topic was apparent. In each group, either during the discussion or following the point where recording stopped, the participants asked about the likely impact of this study, including how I thought things would change in the future, and the likely timing of the process. All participants were keen to receive the final findings of the study in writing. At the end of the focus groups, participants were very positive about the experiences:

> *"Mod: …and can I double check would you like the results when they are available…*
> *3: yes*
> *1: yes definitely be interested in having the results*
> *Mod: it will take as I said at least six months but then I'll happily send them to z (research nurse) and a (PI) and I'm sure I'll be here presenting*
> *1: thank you that was lovely*
> *2: yeah thank you that was really interesting" (Centre 3, Healthcare professional group, doctor (3) and nurse (1+2)*

In the days and weeks following the discussions a number of participants also contacted me to encourage me in the work, or to discuss further the points which they had found particularly interesting within their group. Their feedback regarding the experience was particularly gratifying as I felt that the rapport I had developed with these participants meant they felt able to engage more deeply with the study itself and the complex issue of management of low risk febrile neutropenia.

Recording and transcribing focus group discussions

An encrypted digital audio recording of each focus group was obtained with the permission of the participants. The recording was then transcribed and anonymised in order to allow for analysis. I transcribed all focus groups myself, within one week of the date of each group. This provided distinct benefits as I could more easily identify the speakers within the flow of the discussion and could remember many of the issues discussed. Furthermore, through reviewing the group again prior to the next discussion, I was able to consider the areas for further exploration in future groups, whilst also identifying areas for improvement in my own moderation skills.

Alongside these benefits, there was also one particular challenge present in transcription that has already been discussed in the literature.(165) As focus groups include many people who may talk over each other, there were a small number of occasions where it was not possible to separate the various voices. Each of these occasions was short lived and generally short phrases within these episodes could be captured for the analysis.

Following the initial transcription period, all transcripts were reviewed repeatedly whilst listening to the recording of the group to ensure the quality of transcription and to further familiarise myself with the data. Analysis notes were taken throughout this process as codes became clear and connections between and within groups began to form.

A research journal was kept throughout the period of research. This included field notes and reflections made during and immediately after each of the focus group discussions. It also recorded the analytical points as they developed and documented the challenges involved in performing the work. For example, one section of the HCP group from Centre 1 was initially coded as 'special', however over time this then was recognised to be within the 'roles' code and was assimilated. The process of this was captured in the research journal as follows:

> *"I've been thinking through the 'special' code for the Centre 1 HCPs + trying to figure out where it fits. Today, suddenly realised it's about role negotiation – how we see ourselves as HCPs and how that then would need to change if we went to outpt care and began being 'normal'. It also links in the parent issues from Centre 2 [HCP group] – at the moment we know our roles and parents' roles but these would have to change + we're not sure we trust parents to take on the roles that we think we are 'special' for doing. After chatting to [supervisor], realised it also links to experiences in other specialties that have already changed quite a lot eg diabetes - ?something more generalizable about how when systems change people need signposting to their new roles and help in reframing who they are and what they do. We need to actively address their concerns*

about their own changing roles – not just purely focus on pts + families." (Research journal, January 2016)

Data from both the transcripts and the research journal were used to inform the research questions.

Data handling and confidentiality

Respect for the privacy of research participants and the confidentiality of their information is a key ethical principle in health services research, and is underpinned by various legal frameworks.(56,167) Practically, maintaining confidentiality involves consideration of issues which participants might consider to be private and then protecting these through restriction of access to this information or through the use of anonymising techniques, so as to ensure that the participant is not identifiable in any oral or written discussions of the research.(56,170)

In this work, the data handling and confidentiality plans applied to three main aspects of the work. Firstly in the conduct of the focus groups themselves, where consideration was given to the maintenance of participant confidentiality and that of the patients of healthcare professionals. Secondly, in the storage and management of the digital audio recordings and transcripts, including transcription and anonymization techniques (of over 9 hours of recording and almost two hundred pages of transcript). Thirdly, in the presentations of the work, both orally and in this written thesis. Each of these three areas will now be explored more explicitly.

The issue of confidentiality was discussed in the Participant Information Sheets and was a specific statement on signed consent and assent forms (see Appendix 5.3). Furthermore, it was emphasised at the beginning of each focus group that as I was keeping all their data confidential, it was also expected that participants respect other participants by keeping confidentiality and not discussing the comments of other participants outside of the focus group discussion.

As discussed earlier in the Focus group discussions section of this chapter, in the discussions with healthcare professionals, there was also a potential for disclosure of patient information for those within the study, as well as patients not recruited to this work. Participant information sheets clearly stated that healthcare professionals should not discuss the details of cases where this might make the patient identifiable. This principle was then repeated at the beginning of the focus group discussions. If such a disclosure occurred, the research team would have interrupted the discussion, explained that this data would not be used for the research and reiterated the requirement that individual cases not be discussed. If the discussion persisted following this initial warning or a further disclosure was made, the researcher would call an end to the focus group

discussion at that point. Thankfully, this situation did not occur and all healthcare professional participants maintained patient confidentiality throughout the groups.

Data were stored according to the laws of the Data Protection Act.(177) Participants' identifiable information was at all times stored separately from the data produced from the focus groups. Digital audio recordings of focus groups were uploaded to a double password protected University computer immediately on return from the study site and accessed only by the research team.

Except for their initial secure transfer, between the study site and the University of York, written material did not leave the University site and was stored in secured filing cabinets, in my office, to which only the research team have access. Only me and the supervisory team had access to written material, such as transcripts, generated by the project. Both transcripts and identifiable information were stored on University of York servers within encrypted, double password protected files. The passwords and associated electronic material were available to only myself and Professor Karl Atkin. The document linking study identification numbers with identifiable information was stored securely as for the transcripts and identifiable information. Audio files were deleted once they were transcribed. All other data will be kept by the University for five years. This process was reviewed and monitored by the University of York, Department of Health Sciences' Data Protection Committee – using guidance available at www.york.ac.uk/records-management/dp/policy/.

At all stages of transcript analysis, data were anonymised using unique study identification numbers to refer to participants, so as to be able to follow consistent lines of discussion. For the purpose of the thesis and future publications, these unique study identification numbers were used to allow for ease of comparison. Care was taken throughout the writing of the thesis to make sure that participants were not identifiable by the demographic information given as this is a small community and some participant backgrounds were unique. Thus, for parents and young people diagnoses were only given as broad groups, for example Acute Lymphoblastic Leukaemia or Hodgkin's disease, rather than to more precise information such as stage of treatment, as this might narrow down potential participants to too small a group. Similarly, for healthcare professionals, the demographics given are relatively broad (consultant or non-consultant grade for doctors, and junior or senior for nurses) so as to prevent the identification of participants within the study.

Within presentations of data to both clinical and academic audiences, care was taken to ensure that both centres and participants were not identifiable, using techniques similar to those used within this thesis. After one presentation in which a number of audience members were study

participants, I later discussed privately with a couple of participants whether they felt that these methods had maintained their confidentiality. Positively, they stated that they could not identify which centre was their own centre, nor could they identify the other two centres within the study. Furthermore, they stated that although they recognised some of the issues discussed, this was more of a familiarity with codes and themes rather than being able to identify the speakers within the quotes. They clearly stated that they were happy with the way in which they had been kept anonymous in the presentation of the work.

Analysis

Qualitative analysis can take a number of forms, with the main focus being upon conveying the participants' experience to the reader through a rigorous process involving the identification of key material and the in-depth interpretation of the findings in relation to the research problem and questions. This study used a constant comparison approach, when analysing the fieldwork material, in which repeated comparing of the different individuals and groups, allowed parallel and contrasting themes to be identified and explored. Various additional methods can be employed to increase the credibility of the resultant account and these will be discussed in the following section.(165–168) The main aim of this section is to transparently describe the analytical process undertaken in this study, including the rationale for the decision made and providing evidence of the analysis process within the appendices.

The overlaying of descriptive and conceptual findings allows a more nuanced consideration of the issues discussed, providing both straight-forward clinical answers to questions about preferences as well as a deeper, more sociological reflection upon the underlying complexities of the decision making process. The explicit process of considering social and contextual information and providing "insightful interpretation", also known as thick description, allows the reader to consider the application of the findings elsewhere and hence provides a degree of transferability to the work.(170,178) This is consistent with the pragmatic aims of the study. An example of where thick description was particularly helpful in the analysis was in the consideration of non-attendance with febrile neutropenia, where detailed consideration of the role, experiences and previously expressed attitudes of different participants provided nuance to the interpretation of the data.

The data obtained from the focus group discussions was analysed iteratively, using traditional methods with pen and paper. I had initially intended to use ATLAS.ti software to perform the analysis but given the risks of losing analytical notes and my own preference for paper-based analysis, I decided not to take this route.

When using the constant comparative approach, the recognition of patterning within the data requires rigorous and structured reading and reviewing of the date. As previously discussed, transcripts and field notes were read repeatedly to identify codes described within them. Each transcript was individually coded using a coloured key, for ease of identification of coded sections. Notes were taken around the transcript and on separate sheets to record key points and possible new codes. An example page of coded transcript is given in Appendix 5.9. At this intra-group stage of the analysis, particular care was taken to follow individual voices through the focus group so as to identify codes which occurred more frequently, or with different quality, dependent upon the characteristics of different individuals. An example of this is seen in the code *negotiation within a spectrum of* control where parents with more experience of the paediatric haematology and oncology service used different means to negotiate compared with those who had been in the service for a shorter period of time.

Codes were specifically identified to give the findings about current experiences and preferences for future care within paediatric low risk febrile neutropenia services. Care was taken to identify the precise features of service design which participants particularly preferred or disliked, for example, the particular location of follow-up, or the frequency of contact between healthcare professionals and families at home. I also focused on the factors likely to play a role in these preferences, including the demographic and social backgrounds of each participant as well as their past experiences with febrile neutropenia. I also considered the role of the current service with which participants were associated so as to establish how this might also influence their preferences in the descriptive aspects of the findings. In the next stage of the analysis, each focus group discussion was analysed for codes and concepts in relation to other groups.This process was carried out comparing focus groups of each type of participant (healthcare professionals, parents of under 13s, parents of over 13s and young people) and then each centre. Codes were then linked through mapping for each group and encircling themes were identified (see Appendix 5.10). It was at this inter-group analytical stage that the voices of each group of participants were considered and the similarities and differences identified. Thus the data obtained specifically through the triangulation of centres and participant groups were explicitly considered and explored.

These maps were then overlaid to provide a network through with the themes were compared (also provided in Appendix 5.10). This network shows the interlinking of the identified themes. This framework of overarching concepts is presented in the thesis as the line of argument. The analysis has been presented transparently so as to allow readers to follow a thread from data through to the final line of argument.

Within this phase, I explicitly looked for similarities and differences between the various locations and aimed to identify the possible reasons for these perspectives. I anticipated that the current methods of management in each location might exert an environmental influence on attitudes and opinions to early discharge. I hypothesised that participants in centres with longer current durations of admission might be more concerned about early discharge strategies than those at centres where discharge at around 48 hours is more common. This aspect of the analysis was somewhat complicated by the problems with centre recruitment which are discussed elsewhere in this chapter. However, although the included centres have similar timings of discharge according to their protocols, it became apparent that practice was sometimes different and therefore consideration of these issues became possible through the course of the data collection.

Additionally, I aimed to identify relationships between the attitudes of different participant groups. As discussed earlier in this chapter, I was particularly interested in how the ideas and opinions of young people are similar or different to those of parents and healthcare professionals. The literature reveals that young people often have different opinions to the adults in their lives and may be willing to take greater risks for given potential benefits.(17–21) I was keen to see how this applies to low risk febrile neutropenia management and have attempted to present the voice of the young people about this aspect of their care, within the limitations I have already discussed. I also anticipated differences between families and the healthcare professionals caring for them.

I then explored whether past experiences and education about febrile neutropenia contribute to differences in attitude towards early discharge. For example, whether healthcare professionals with experience of patients who are critically unwell with febrile neutropenia felt more anxious about potential early discharge. I aimed to investigate the role of the sense of professional responsibility or duty on the attitudes of healthcare professionals.

Continuing my use of the constant comparison, I went on to compare my findings to the qualitative synthesis reported in Chapter 4, looking for points that confirmed or refuted concepts within the existing literature, and aimed to adjust and expand the model provided in the qualitative synthesis as one of the outputs of the qualitative study. I contextualised the findings of the study within the existing theoretical debates in this area described within the earlier chapters of this thesis and, where possible, located it within broader healthcare policy, including considering how these findings might impact on the implementation of current guidance from national bodies.(181,182) I aimed to provide both descriptive details of the service designs suggested by participants so as to depict the various strategies which might be most acceptable,

and also a theoretical exploration of the comments supporting these suggestions so as to allow greater understanding of the complexities involved in changing these services.

Throughout the findings chapters, anonymised quotations have been used, with associated stimuli and numerical identification of speakers, to ensure that the voice of the participants is conveyed throughout the research.

During the analysis and writing up process, I met with my supervisory team regularly to ensure agreement with the progress being made and discuss future directions of the work. I also presented preliminary analyses at both clinical and academic meetings so as to receive feedback on whether codes and themes resonated with those involved. This was a very positive process as audiences became actively involved in discussing the issues, and often raised analytical points that I had already described in my writing but had not shared within the presentations. The fact that these topics were evoked spontaneously reassured me that the analysis had appropriately captured these within my own consideration of the issues. The final framework and line of argument were also presented to both participants and peers for critical review, prior to submission for the award of a PhD.

Methods used to enhance credibility

Credibility describes the way in which the quality of qualitative work can be assessed to be 'believable' and 'trustworthy' to participants and the readers of the work.(183) Within the relativist epistemology, the aim is to evidence a trustworthy and believable constructed truth, located within the context of culture and history, which can be contrasted with the positivist singular truth which is more often associated with quantitative works.(183) In other words, credibility can be used to describe how successful a piece of research is in capturing the lived experience of the research participants.(178) Multiple methods have been advised to improve the credibility of qualitative research.(178,184,185) Many of these have been employed within this study, including transparency of method, triangulation, case studies, quotations critical review of the work during production and using a reflexive process. The issues of triangulation, case studies and quotations are explored further within this section. The other methods listed (transparency, critical review and reflexivity) are evidenced elsewhere in this chapter.

Triangulation describes the use of various data sources, methods and theories to provide multiple viewpoints on a research topic, so as to increase the credibility of a piece of research.(178) This study primarily uses the triangulation of data sources, through multiple key stakeholders and multiple centres to address the issue of early discharge in paediatric low risk febrile neutropenia. Through the comparison of data from different locations or different groups, it becomes possible

to identify key or recurring themes between and within groups, along with features which may influence the different perspectives on these themes.(168)

Having stated the benefits of identifying recurring themes in triangulation, the pure reliance on prevalence as a marker of qualitative importance or 'truth' is somewhat reductionist, as well as dependent on the ontological beliefs of the researcher as to what constitutes 'truth' and where it lies.(165,186) Pragmatically though, triangulation allows the exploration of the occurrence of themes and the identification of frequency without necessarily applying worth or 'truth' within these. Furthermore, by exploring the various perspectives, a deeper understanding of the research area is achieved and richer description allows appreciation of the nuances within the research field.(167) This use of data source triangulation clearly complements the multiple methods nature of the thesis, whereby various methods are applied to provide depth and greater understanding of the area of research, for example in attempting to understand the reasons for low levels of consent to studies of reduced therapy regimens.

To provide further contributions to the credibility of this work, I have also employed a case study within the analytical design so as to ensure focus upon codes which appear infrequently, and upon the perspectives which specifically stand out as inconsistent with other aspects of the data.(186) Focusing on areas of maximum variation within the data aims to capture the diverse range of experiences of febrile neutropenia and is consistent with the qualitative paradigm, which contrasts with the aims of obtaining a representative sample in quantitative work.(56) The selection of case studies which are more extreme than the "normal" experience offers the ability to compare and contrast experiences and to consider the influence of different circumstances and characteristics on participants' responses. Through exploring possible explanations for the different interpretations given by the case study family and the potential tensions arising from them, it was then possible to evaluate the themes previously identified within the findings, make adjustments to them and thus illuminate some of the more nuanced aspects of attitudes to febrile neutropenia care.(167)

Quotations are used in qualitative work for a number of reasons, which I employ within this thesis, as a further means to enhance its credibility. Quotations provide the raw data to back up the findings reported to the reader. This degree of transparency lends credibility in itself and allows the reader to follow the researcher's analytical processes. Quotes can work specifically in two distinct ways. The first is to evidence the typical responses given to a particular prompt or issue. In this situation, the quote chosen provides a representative sample of the findings of the work. In the second use of quotes, they can be used to illustrate the diversity within the participants. This occurs within this work within the discussions about shared care within the professional roles subtheme in Chapter 6. Where appropriate, I have provided quotations which

include participants conversing to highlight these areas where the response are typical or diverse and also to demonstrate the development of the conversations within the groups.(168)

Reflexivity

Reflexivity is the process in which the researcher reflects on how their own experiences, perceptions and beliefs influence the work being performed, along with locating the work within its broader social and political context.(185) The ways in which the researcher affects the process of research, the participants and the subsequent analysis are explicitly explored and transparently presented to the reader to allow them to draw their own conclusions as to the credibility, and quality, of the research as a whole. Furthermore, through giving clear justification about the decisions taken when doing the research, reflexivity aims to provide the reader with the underlying rationale for key judgement points. The presence of reflexivity throughout this thesis is intended to achieve these aims. The discussions surrounding recruitment difficulties as well as rapport building and engagement have already considered a number of topics relevant to reflexivity. I discuss some additional considerations here and will demonstrate further reflexivity within the findings and discussion in Chapters 6-8.

Throughout the planning of this research, I considered the impact of myself as a researcher on the study itself. Specifically, as a paediatric registrar, I may have unintentionally influenced the expressed ideas of the participants. As a doctor, I hold a position of social influence which may be particularly felt by young people and parents who may have felt that there was a 'right' answer to some of the focus group questions. Furthermore, within the healthcare professional focus group discussions, there were numerous potential influences between myself and nursing colleagues, and with more senior medical colleagues. For this reason, each focus group began with a clear discussion that there is no 'right' answer and that, in this situation, I was working in the role of qualitative researcher and not as a junior doctor.

In some ways, however, being a healthcare professional provided an advantage to the focus groups. I was able to follow the more technical aspects of the discussions without needing to interrupt participants to request the definitions of various technical words. This allowed aspects of the conversation to flow more smoothly than they might have done with a lay moderator.

Given the relatively small number of people involved in the specialty of paediatric haematology and oncology, there was a potential that, in some focus group discussions, I might already know some participants in a professional manner either as their colleague or as their or their child's doctor. Thus the importance of emphasising confidentiality was heightened. This was clearly outlined in the Participant Information Sheets and in the introduction to discussions.

Finally I recognised the potential influence of my own experiences of healthcare, as both professional and patient. Within the analysis, I aimed to consider all possible viewpoints, and acknowledge where some viewpoints differ from those I personally hold. I have aimed to present balanced findings that express each viewpoint without the influence of researcher attitudes and particularly focused on this where my own views or reactions to comments are strong. I believe that this reflexivity about my own impact on this research improves the credibility of my findings to the audience. Further reflections on the performance of the research are included in Chapter 8.

Other ethical issues surrounding the research

All researchers involved in this study had received formal training in ethics and clinical governance, e.g. Good Clinical Practice. I completed a formal Level 7 qualification in Qualitative methods and also attended formal training in the performance of Focus Group research. Within my medical career, I have also received training in obtaining consent, advanced communication skills and child protection procedures. I thus brought certain skills and attributes to the performance of the study. My practice was closely supervised by all co-investigators of the study.

Informed consent was sought from all participants. Within my role as a paediatric specialist trainee, I have been trained in gaining consent and have experience of gaining consent from young people and their families on a regular basis. In the case of participants under the age of 16, consent was sought from someone with parental responsibility, but the assent of the participant was also essential for entry into the study. This is consistent with current guidance for medical research involving children.(187) Sample consent and assent forms are included within the Appendix 5.3.

For this study, the process of consent was actually through a series of discussions with participants, with the consent and assent forms providing written confirmation that the process covered each of the necessary points. The first discussions with participants were by the research nurses with the basic information about the study being given verbally and a copy of the information sheet being given to provide further details. Once participants had decided they were interested in the study and gave permission for me to be given their contact information, I telephoned them to go through the study in detail and to ensure that all points on the consent form had been covered. Following confirmation of the dates and times of the focus group, participants were contacted again to ensure that these details were given and to further check they were interested in participating. Many participants were also in contact via email between these set telephone discussions. On attendance at the focus group, I then had a further one-to-one discussion with each participant and formally completed the consent and assent form with them as this was often the first time we had met in person. The signing of this form represented

the various discussions that we had had over the preceding weeks of conversation. This process made me feel particularly confident that participants had given informed consent to the research as they had numerous occasions to receive information and to ask questions, through a variety of formats, with each discussion covering the key points and then further tailored to meet the individual participant's needs. Furthermore, these conversations prior to the focus group discussion allowed me to begin to build a personal rapport with the participants, setting the tone for the focus group to be interactive and therefore informative.

Initially, there was to be no financial incentive to participate in this research. However, after the first substantial amendment advised by the Research Ethics Committee, participants were offered travel expenses, as per INVOLVE guidelines, such that they were not disadvantaged by participating.(188) Only one application for travel expenses was received; all other participants declined this offer.

Following the challenges with recruitment to parent and young people groups, a second substantial amendment was approved to allow the provision of a £20 Amazon voucher to each parent and young person participant, and the placement of promotional posters around the involved departments (see Appendix 5.7). This is also consistent with INVOLVE guidelines and reflects the time commitment involved in participating in this research.(188) Participants who took part in focus group discussions prior to this amendment were contacted and offered the voucher in retrospect. 74% of the 19 participants eligible for the Amazon vouchers claimed for them.

I felt it was particularly important to investigate the experiences and perceptions of young people within paediatric haematology and oncology services. The importance of listening to young people can be found in many places, from the United Nations Convention on the Rights of the Child (Article 12 respect for the views of the child 'Every child has the right to say what they think in all matters affecting them, and to have their views taken seriously') through to the Department of Health Documents 'No decision about me, without me' and 'You're welcome', and is further explored in Chapter 2.(30–33) Thus, this study actively sought their opinions and attitudes. I have considerable experience in communicating with and working alongside young people, as has the assistant moderator, in our clinical roles as paediatric specialty trainees. I have completed formal training in communication with adolescents, along with the full curriculum of the RCPCH Adolescent Health Programme. This provided me with specific skills for running focus groups with young people.

As this was a study involving young people, there was a potential for disclosure of safeguarding issues, although this was felt to be unlikely within a single focus group discussion. Nevertheless,

this potential was mentioned in the relevant patient information sheet and was discussed at the beginning of the focus group discussions for young people. Both I and the assistant moderator have completed formal training in Child Protection and, as paediatric registrars, are familiar with the procedures to be followed in the event of a disclosure. Any concerns raised regarding safeguarding of children and young people were to be reported to the local lead for Safeguarding at the participant's treating centre. Thankfully this was not necessary.

I recognised that discussions about possible variations in treatment for low risk febrile neutropenia might raise concerns from participants about previous episodes of febrile neutropenia. There may have been difficult memories for families who had experience of higher risk episodes, perhaps even with admission to critical care services. Furthermore, participants might also have been stimulated to ask questions about the future treatment of low risk febrile neutropenia in their centre. Opportunities to discuss this further were offered to all participants at the end of the focus group discussions. All medical queries raised by the participants during the research were to be redirected to their clinical care team, but did not occur.

Meanwhile, I considered that healthcare professionals might question their current practice in febrile neutropenia. They were offered information about where they could obtain continuing professional education on the management of paediatric febrile neutropenia. Debriefing was offered to participants immediately after the focus group discussions and a telephone number was also provided in case they wished to discuss any further issues with the research.

In regards to the performance of the study, in two centres, the support from the research team was excellent. There was regular contact between myself and the research nurses to communicate successes and challenges for both parties and enabling consistent progress on recruitment and organisation of the work. However, with the final centre, communication with the research team was more challenging and it was difficult to speak with the key individuals in a timely manner. This site also struggled more with recruitment and the practical aspects of organisation which were the responsibility of the study site, perhaps due to limited research nurse time. To compensate for these issues, I changed my own preferred communication style to one more suited to my link person and took on more of the organisational roles myself, including the preparation of focus group paperwork and the booking of rooms for the discussions to take place. These two actions seemed to mitigate some of the earlier problems, but required considerably more time working on this site's preparation than others.

Funding

All funding for the study was provided by Candlelighters children's cancer charity (Registered Charity No: 1045077). My own salary was paid for by a Clinical Research Fellowship awarded by the charity in 2013. A second funding request was put in to Candlelighters to allow for the provision of travel expenses to participants and to provide the grant to each study site for the research nurse time involved in recruitment. This request was approved, and following the second major amendment was adjusted to allow this money to also be used for the provision of vouchers to parent and young person participants. Each study site received funding to recognise the research nurse time taken in supporting the study, informed by NHS pay scales and anticipating how much research nurse time would be involved. This money was paid as a block sum to the department involved at the completion of the study. All financial records for the study were kept by Candlelighters charity. Candlelighters have had no influence over the design, execution or analysis of the study.

Summary

Through this chapter I have described and explored the methodology adopted in the focus group discussion study. In response to the findings of the qualitative synthesis, the study aimed to explore the experiences and perceptions of patients, parents and healthcare professionals in regards to paediatric, low risk febrile neutropenia. I have described the process of recruitment, including the challenges involved, and have provided information on the participants included within the study. The conduct of the focus groups, including rapport building and use of topic guides that drew upon the results of the systematic review and meta-analyses reported in Chapter 3, have been explored I have described the methods used to record and transcribe focus group discussions, and to handle, anonymise and store the collected material. I have provided a detailed account of the methods used in the analyses and of the approaches taken to increase the credibility of the thesis. This chapter therefore provides a foundation to understanding the study conduct and the way in which the findings presented in Chapters 6 and 7.

Chapter 6: Qualitative Study Findings - The quest for certainty, attaining mutual trust and sharing roles and responsibility

Overview of findings

The next two chapters detail the findings of the qualitative study, combining both thick description and deeper explanatory accounts of the data. The three emergent themes of the *quest for certainty*, *attaining mutual trust and sharing roles and responsibility*, and *the potential for realised discretion* are comprehensively explored within these chapters with supporting material provided throughout. Their interrelated nature is highlighted and I cross-reference the key recurring threads, exploring the themes from the perspectives of the different stakeholders.

As this thesis aims to help inform service re-design I also draw attention to practical issues that emerged during discussions and which may help to improve the experiences of paediatric patients with low risk febrile neutropenia.

When describing the findings of this work, I use the word participants to reflect patients, parents and healthcare professionals. Similarly, when I use 'families', this means both young people and parents. Where the findings are specific to a single group, I will describe the particular group I am referring to.

In the following paragraphs, I provide a summary of the findings which introduces the key themes and provides a guide to the chapters to come. This overview of the major concepts aims to assist the reader in navigating the following, more detailed, account and seeks to demonstrate the main links between the themes so as to prepare the structure for the subsequent work. These findings have been split into two chapters for easier management of the extensive data. Each of the two chapters include two of key themes within the work, Chapter 6 relates to *the quest for certainty* and *attaining mutual trust and sharing roles and responsibilities,* whilst Chapter 7 covers the *potential for realised discretion* and *the impact upon future service design.*

The quest for certainty began with understanding, expressing and negotiating risk*,* where personal experience often held greater value than statistical findings and occasional inconsistencies enabled emotional reactions to risk to be balanced with the evidence. The benefits of following strict protocols in an attempt to control this risk were recognised but their rigidity was resented given the need to consider the individuality of febrile neutropenic episodes. Alongside this theme, the multiplicity of parties involved in paediatric haematology and oncology services led to an acknowledgement that relationships could be complex and challenging. *Attaining mutual trust and sharing roles and responsibility* was seen as vital for participants when considering reduced

therapy strategies for the management of low risk febrile neutropenia. The different roles identified by participants are explored, including different professional groups, shared care units and parental roles in the care of febrile neutropenia. The contrasts in attitudes between participant groups and the different centres are considered. Participants discussed how roles and responsibilities would need to change if reduced therapy regimens were implemented; they considered the challenges this would pose and the vital role that mutual trust would play in successfully achieving outpatient care.

In the following chapter, I explain how the integration of the quest for certainty and mutual trust was achieved after establishing the spectrum of control and negotiating key points so as to reach the *potential for realised discretion*. Participants expressed a need for discretion, or individualised care, in the management of low risk febrile neutropenia so as to be able to take into account personal preferences expressed in the *quest for certainty*. Recognising that the current control over decision making lies with the protocol and the healthcare professionals, families' expressed their frustrations with the limitations placed upon them and discussed how they managed within the current system. I present the material surrounding non-attendance with febrile neutropenia as an example of when parents have control of decision making, judging the risks of the potential courses of action, and considering the different roles involved in their child's care. The factors which might promote non-attendance with febrile neutropenia are explored and I consider the impact that reduced therapy regimes might have upon these dilemmas. The *Impact upon future service design* of these three key themes is explored throughout this chapter and in more detail within its own specific passage. I consider why certain groups might prefer specific options for the timing of discharge and route of administration of antibiotics, along with the follow-up choices that might made. I outline a specific case study in which the family's preference differed from many of the other participants, and detail how this is consistent with the previously described themes and how it has informed and developed the work. Finally within these findings, I report the considerations of the participants about the low rates of consent seen in Chapter 3 so as to understand from the key stakeholders' view what might have prevented families and clinicians from taking part in these reduced therapy studies.

To support the findings and provide evidence of the analytical processes used, a sample of coded transcript and the progression of structural maps which eventually resulted in these findings are provided in Appendices 5.9 and 5.10.

The quest for certainty

The quest for certainty theme encapsulates the challenges of *understanding, expressing and negotiating risk; articulating and interpreting protocols;* and *preferences for care*. The discomfort

of the uncertainty involved in risk assessments is balanced against the certainty implied by current protocols. The perceived benefits and harms of inpatient care that participants have previously experienced inform their appraisals of future treatment strategies. The judgements made about these three main codes and the weight given to each of them varied between groups, and particularly between families and professionals. The tensions that arise from this are highlighted and explored throughout this section.

Understanding, expressing and negotiating risk

Conceptually, the subtheme of *understanding, expressing and negotiating risk* encapsulates a number of subthemes, including problems with risk stratification, emotional responses to risk, understanding statistical risks, illogicality and comparisons with risks in other situations.

In all centres, even those where risk stratification is routinely used, healthcare professional participants struggled to cognitively separate different febrile neutropenia risk groups. Thus in each group, specific examples were used in which the child or young person described by the professional would not have met the criteria for inclusion within a low risk treatment strategy. This was usually identified, either by the participant giving the narrative or by another participant within the group. The misperceptions surrounding risk stratification demonstrated unfamiliarity with the tools used, and challenges in applying them to particular children. It also reveals that participants tend to think about children as having 'febrile neutropenia, rather than low risk or high risk disease. This failure to cognitively differentiate between levels of risk impacts upon both perceived risks and potential future management strategies.

> *"4: I think it's just I've been here for an awful long time and that's what we've done and I know it's the small number of children that you can remember that just … that just do.. collapse within less than 8 hours…*
> *Mod: without giving us patient identifiable data, could you describe one?*
> *4: mm...oh God… erm… ermm… yeah probably the most vivid one was when I was over at [another hospital] … so I couldn't even tell you the name of the patient... erm… but walked onto the ward having had a single fever at home... and within… within minutes we were resuscitating him…*
> *1: but he wouldn't be low risk would he?*
> *4: he wouldn't no but that's the bit that I don't know why but that's the bit that sticks in my mind…" (Centre 1, nurse (4) and doctor (1))*

It is not surprising therefore that the healthcare professional participants had quite emotional responses to the idea of early discharge, which generally evoked anxiety or fear. This was expressed physically in centre 1 when a participant shivered at the mention of outpatient

treatment (discharge at less than 8 hours). After this physical reaction, they went on to clearly express their anxieties about early discharge which related to past experiences of children deteriorating with febrile neutropenia, as described above. On three further occasions during that group, phrases relating to this participant shivering were used to identify emotional responses to aspects of early discharge that made the group feel uncomfortable:

> *"1: it's not like they won't be febrile at home… they'd be going home febrile wouldn't they (murmur of agreement) so then you'd have to work out what…*
> *4: [4] shivered again!!! (laughter)" (Centre 1, doctor (1) and nurse (4))*

Interesting, laughter was also a common feature of the healthcare professional discussions. At times, this appeared to be a collegial – giving the impression of a group of colleagues enjoying a comfortable conversation about shared aspects of the work environment. At other times however, laughter was used as another example of a physical response to anxiety or a form of emotional release, to signify a point at which a participant was uncomfortable within the discussion or with the opinions that had just shared.

In contrast to the health care professionals, parents and young people groups participants were unfamiliar with the concept of formal risk stratification, and were almost universally unaware that this was performed at all. To compensate for this, parents employed their own methods to establish the dangers posed by an episode of febrile neutropenia, encapsulated within the code 'well/not well'. Participants, particularly those with considerable experience of their child having febrile neutropenia, differentiated episodes into those where the child appeared unwell, was not their usual self, and caused the parents to worry, from those in which the child had a fever but their behaviour did not otherwise concern their parents. As such, the idea of being 'well' or 'unwell' formed an instinctive risk stratification 'tool' which enabled the grouping of children into different risk categories. Participants envisaged that the management of these groups would be adapted according to the severity of 'unwellness'.

Parents spoke about how they felt they were generally the best judges of whether their child was well or unwell, and expressed concerns that professionals sometimes neglected to take these assessments into account, resulting in parents repeatedly presenting to the hospital: *"we're their mums so we can tell when our kids are just having a bit of an off moment or when there's something quite serious"* (Centre 3, parents of under 13s) Occasionally however, this confidence waned and parents doubted their ability to detect deterioration: *"I think you know… nurses and doctors can spot things that parents can't although you might think they look alright I think er…"* (Centre 1, parents of under 13s). Professionals also alluded to the instinctive knowledge that parents have of their child, and that sometimes they also had an innate sense of when a child was

not fit for discharge: *"I suppose being a nurse though you'd have the intuition to say don't… [discharge]"* (Centre 1, healthcare professionals).

Interestingly, when formal risk stratification tools were introduced into the parents' focus groups discussions, participants spoke about how clearly knowing whether their child was at low or high risk of significant complications from febrile neutropenia, facilitated their own decision making about preferred care.

> *"2: I think it probably is… I mean I've seen b) with much higher temperatures than that and he's again still been really alert and just respond very quickly to antibiotics and now that I know that you've said that he's in a lower risk group then actually maybe I wouldn't have panicked quite so much and thought you know… and if the option would have been there… I would have probably gone with it but not knowing that information and … and just being told 38 degrees he's got to go in and …. And I just follow protocol… I follow the rules…" (Centre 1, parents of under 13s)*

This clear acceptance by parents of risk stratification as a concept, and their current use of a similar assessment strategy, suggests that increased communication of the level of a child's risk may support shared decision making between families and healthcare professionals. Furthermore, this explicit stating of the level of risk for a child may also quieten some of the emotional responses that healthcare professionals have towards reduced therapy regimens for children with low risk febrile neutropenic episodes.

Related to these risk stratification discussions, parent and young people participants sometimes struggled to differentiate between episodes of febrile neutropenia, and those of febrile non-neutropenia. This issue became particularly apparent in the groups for teenagers and their parents. Here, one of the young people had never had an episode of febrile neutropenia, but had had a number of episodes of fever without neutropenia. Within the discussions, both the young person and their parent discussed these episodes as if they were experiences of febrile neutropenia. This lack of clarity about whether an episode is febrile neutropenia or not, raises similar issues to the healthcare professionals' difficulties in separating high and low risk episodes, in that it leads to inappropriate assessments of the level of risk involved, and as such attitudes to certain management strategies may be modified.

The challenge of deciphering the statistical evidence presented regarding the risks of different strategies was also evident within the healthcare professionals groups. In one group, misunderstandings about systematic review methodology, and confusion over statistical issues, such as power, led to mistrust of the evidence.

"Mod: … 2660 episodes of data, how much more would people need to be more confident in this number (points to treatment failure rate)?

1: I think it would need quite a lot, cos we don't know whether this is just from one centre… several centres

Mod: lots of centres, lots of centres, 37….

1: is that international?

Mod: yes it's international around the world

2: so if it's all round the world?

Mod: we analysed the differences between different countries and the countries don't show differences

2: right, so that's not just the UK

Mod: no

2: so actually you could say it's a small number if it's…

1: there's the whole world...

2: yeah couldn't you? and how many within each study? That would be the other thing

Mod: very variable, between 20 up to the biggest number is a few hundred.

2: so you would be looking at the few hundred as being a more… study that you would want as opposed to 20, wouldn't you?

1: because if the numbers were high, people would be more convinced that this is real, I think if er… you know I'd see, for instance this is just an example, if you had 500,000 episodes and then you saw this, you'd say yeah that's it, this is what we need to go for (murmur of agreement from (2)) but two and a half thousand odd is not going to be convincing." (Centre 2, doctor (1) and nurse (2))

Alongside this poor statistical literacy, in all healthcare professional groups, there were moments within the discussion where comments made seemed disconnected and were not consistent with other beliefs they held. For example, in Centre 2, one participant stated *"but if you look at the 0.1% risk [of PICU admission or death in low risk febrile neutropenia], it's still high, in that group, because your range is between 0.03 to 0.3%, and you've got 0.1%".* Considering a 0.1% risk of PICU admission or death to be high seems unusual: in the field of paediatric haematology and oncology, 3% of children diagnosed with cancer die of infection and around 15% will die of progressive disease.(1,193) Certain aspects of interpreting risk seemed specific to early discharge and may link to the common anecdote that professionals find it more difficult to lose a child to treatment-related effects compared to the death of a child due to progressive disease as professionals feel more directly responsible for the death of a child due to side-effects of therapy, including neutropenic sepsis.

Discussion by professionals about their own decision making revealed and acknowledged tension between making judgements based on research evidence and individual emotional experience. This was concisely summarised by centre 1 participants at two points within their discussion:

> *"4: yeah… it's bad you know the more you say it sounds more like an irrational anxiety…*
> *2: but then that's your experience isn't it so it's the … it's the … it's the experience that you've had over years versus what's in a paper that someone's telling you…" (Centre 1, nurse (4) and doctor (2))*
> *"2: I think the interesting thing there for me [Mod] is that you've presented us with the evidence (laughter from others) which is by far and away saying that this is a safe thing to do…*
> *4: we've chosen to ignore it…*
> *2: but we've chosen to ignore it… so we're practicing non-evidence based anecdotal medicine (ongoing laughter) but it's what we're comfortable with…*
> *Mod: ok… so what factors played the role in making that decision…*
> *2: non evidence based anecdotal…*
> *4: anxiety...*
> *(laughter and indiscernible mutterings)" (Centre 1, doctor (2) and nurse (4))*

The emotional, anecdotal accounts of participants were a greater factor in their opinions regarding early discharge than the empirical evidence, despite their training and knowledge that this was inconsistent with evidence based medicine. Interestingly, in Centre 3, where there is greater shared care and fewer patients with low risk febrile neutropenia are managed in the primary treatment centre, professionals used fewer anecdotal accounts of patient deteriorations and appeared to have a less emotional, and more positive, response to suggestions of early discharge.

One method that healthcare professional participants used in all centres both in an attempt to understand the risk statistics and to express the inconsistency of their discussions was to compare the risks in febrile neutropenia to other clinical situations, both within the context of other haematology and oncology conditions and within other specialties, particularly general paediatrics. When talking within their own specialty, participants highlighted the risks involved in the discharge of patients following VIDE.[4]

> *"1: I mean if you're that worried about infection you could argue that after every course of chemotherapy I don't know on VIDE for example you might have a one in three, one*

[4] VIDE is an acronym for the four drugs used in a specific course of chemotherapy most commonly used for children and young people with a particular bone cancer.

in four chance of coming back in so if you're really… whereas we're saying these ones have got a less…. Lower chance than that so you should… you could argue that well we need to keep you in after every course of VIDE chemotherapy until your count recovers or something cos there's a ….

2: no… that's what I'm trying to say like we don't keep them in…

4: except on this occasion you've probably got a lower chance of them coming back than on your initial discharge from your chemotherapy…" (Centre 1, doctors (1+2) and nurse (4))

Meanwhile, when comparing to other settings, participants discussed how children with fever would be managed in general paediatrics, where they seemed comfortable with the concept of children being managed in a less intensive way.

"3: (mumbles) I think my point, I was about to say was that sometimes you can get children who do have febrile neutropenia but they're very coryzal, and you know they're viral, they've been in general paediatrics and then you would've just sent them home with paracetamol and fluids but because they've got febrile neutropenia, they're febrile, maybe a spike of 38.4 and their neutrophils are 0.5, you still have to treat them with antibiotics, it does…" (Centre 2, doctor)

They discussed how children with febrile neutropenia (as a whole) are different from immunocompetent children, and therefore there are challenges in determining how closely the care of low risk febrile neutropenic children should resemble general paediatric care compared with that of children with high risk febrile neutropenia.

The presence of a central venous catheter ("line") was one of these differences for both parents and healthcare professionals. This was discussed in almost all groups, most frequently pertaining to their increased infection risks. However, healthcare professionals also spoke about how children with central venous line infections are frequently managed on an ambulatory basis, which is readily accepted by the paediatric haematology and oncology community. They drew attention to the illogical contrast between these two groups, and suggested that "line" services could be extended to children receiving outpatient care for febrile neutropenia.

"1: … but the only other issue is when you look at when you've got a line infection you're treating with teicoplanin[5], they're quite happy to come and go, come and go, come and go, and we're quite happy to do that aren't we?

[5] Teicoplanin, often shortened to 'teic', is an antibiotic.

2: the community do them once they go on to daily teic, that's not a problem but then they're not necessarily pyrexial neutropenic all the time.
1: no but we've assessed them, and then we've sent them out" (Centre 2, doctor (1) and nurse (2))

Finally, the professional participants were very clear about the extent of influence that healthcare staff should have over families' perceptions of risk – each group commenting on this in one way or another. In Centre 3, the professionals spoke about the dilemma of how much influence should be exerted over families, clearly commenting on how far this influence should reach. In the following quote, when a group were discussing the issue of non-attendance following fever (which is further explored later in this chapter), a participant outlines their perception of the role of healthcare professionals in communicating risk to families.

"…and then you have to try and put the frighteners on them and you have to gauge that right as to how… because I've had people saying oh I… oh I know … we've got four hours to wait… and I say well sometimes children deteriorate more rapidly than that….erm… but it's really difficult to know quite how… how scary to be with them isn't it?" (Centre 3, doctor)

Throughout the *understanding, expressing and negotiating risk* code, it is clear that participants struggled with the uncertainty of risk. They sought the illusion of certainty, aiming to find security in the absolute, irrespective of the reality of its non-existence. This may be founded in limited understanding or familiarity with statistical concepts, with evidence showing that both laypeople and healthcare professionals frequently struggle with the basic concepts of statistical literacy related to risk.(194) However, the assessment of risk is not a purely technical act but instead a political and social construct. There are many underlying social, emotional and cultural elements to the desire for certainty, which will be explored within the discussions in Chapter 7.

Articulating and interpreting protocols

This subtheme captures the various concepts surrounding fixed protocols that were discussed within the focus groups. These lie between the need to assess risks in the previous section and then determine the preferences of individuals for care which are covered in the following section so as to make a judgement about suitable future care. The benefits of illusory certainty and challenges of having strict and limiting protocols, such as those outlined in Chapter 5, are explored within this section. There are clear links between the frustrations found here and the later discussions about the spectrum of control between key stakeholders and the need for discretion when applying protocols to individual participants.

It is worth noting during this section that all the documents referred to as protocols and discussed earlier in Chapter 5 of this thesis are in fact entitled guidelines. The choice of the words seems relevant here as guidelines suggest a degree of flexibility in their usage, whilst protocols are more formal and rigid. Participants during the focus group discussions used the word protocol almost exclusively and appeared to understand and use these documents as protocols. I have therefore used this terminology in this section.

Healthcare professional participants in all groups spoke about problems with febrile neutropenia protocols, both their current versions and any future protocol suggestions. Participants struggled to remember the details of current protocols, frequently correcting each other on points such as temperature definitions or duration of admission. In particular, participants were very clear about the actions to be taken on the presentation of a child with febrile neutropenia, perhaps as a results of the promotion of "one hour to first dose of antibiotic" concepts, but then struggled to explain the later points of the process, usually requiring prompting to elucidate the timings of discharge and factors involved in deciding about this. Centre 3 referred to their protocol repeatedly, suggesting a culture in which reference to the document is expected; the other centres did not refer to these documents other than to state that shared care colleagues have copies of these.

It is perhaps unsurprising then that parents had a more fluid approach to protocols. Although all four groups mentioned existence of the protocol, there were some areas where they were unclear about its instructions. In the Centre 3 group for parents of under 13s, parents noted recent changes in the definition of fever and of neutropenia. This made parents uneasy as the alterations had not been communicated to them in advance and instead were simply enacted on arrival in hospital with their child's next episodes of febrile neutropenia. Through this parents expressed their wish to be informed of protocol changes, and treated as valid team members in their child's care.

Parents' main concern regarding the protocol related to the issue of delayed discharge in current practice. Throughout the focus group discussions for parents of children under the age of 13, participants were clear that discharge from hospital rarely occurred at the point where it was theoretically possible due to the protocol. Parents distinguished between times when delays were appropriate due to the child's ill health, which they were more than willing to tolerate, and those which they felt were in some way avoidable. Avoidable delays were those due to the timing of the child's admission, side effects of treatment, delays in liaising between centres and setbacks in obtaining blood culture results, which I now expand upon.

Parents clearly voice their frustration about how services, and decision making, were conditional upon the timing of a child's presentation with low risk febrile neutropenia. The staff present in the hospital out of normal working hours may not be as senior or as experienced in oncological management as those who provide routine services, and as such, parents recognised that they may make different judgements about the levels of risk involved or may not feel able to take on the responsibility of discharging a child with febrile neutropenia. Furthermore, certain laboratory services, particularly those relating to blood cultures, are often not available out of hours. This may therefore impact upon the time at which the child would be considered eligible for discharge, as protocols often require a negative blood culture result (at either 36 or 48 hours) before a child can be considered for discharge. If the blood culture process is not commenced until later in the child's hospital stay, sometimes days later, for example if the child is admitted at the start of a long weekend with no laboratory service, this can result in substantial delays in decision-making.

As discussed later in this theme, parents reported various side effects of antibiotic treatment, particularly diarrhoea, which result in increased healthcare needs and therefore delays a child's discharge. Participants viewed these delays as avoidable as they considered that if the protocol were less rigid, then certain doses of antibiotics might be avoided in children with previous adverse effects. Finally, participants in Centre 3, which has a significant amount of shared care, participants reported irritation with delays which occurred when healthcare professionals in the POSCUs needed to contact the PTC for advice and these conversations took prolonged periods of time. This is evident in the following quote from the focus group discussion for parents of children under 13:

> *"3:… you know and we love all the staff at [POSCU], you know we cannot fault them, they are really really nice but the other thing that you have is that they, you ask them a question and they go oh we'll have to ask [PTC], and then we could be waiting 8 hours for the answer and then you might have a question on top of that answer and then you're waiting another 8 hours…*
> *1: and in some cases they don't, they actually wait until they do all their rounds before they phone [PTC]*
> *3: and you know it gets really frustrating…" (Centre 3, Parents of under 13s)*

Astutely, parents in a number of groups identified that the blood culture results were a particularly significant factor in professionals' decision making in regards to discharge and that most protocols demanded a negative blood culture result before a child with low risk febrile neutropenia could be evaluated for discharge home. As such, when blood culture results were delayed at any point, parents became particularly dissatisfied as they had identified that this would then prevent them leaving hospital. This comment from Centre 3 demonstrates this point:

"1: then my frustration comes with the process and blood culturing and that, towards the end of a stay, is what just really really narks me, that we actually spend at least an extra day in because they don't culture the bloods when you get in straight away, so if we were admitted on Monday at noon or after, they don't start culturing the bloods until Tuesday at 9am…" (Centre 3, parent of under 13s)

Thus, blood cultures symbolise the potential for parents to escape from the trap of hospital treatment for febrile neutropenia and delays in obtaining results capture parents' greatest dislike of current services – apparently unnecessarily prolonged hospital stays with a well child.

The healthcare professionals groups also acknowledged that blood cultures were important for current decision making about discharge but this was mostly referred to in passing, when referring to the requirements of the protocol. No healthcare professionals mentioned the challenges for patients and parents of waiting for delayed blood cultures, although one group alluded to their own frustrations with waiting. In Centre 1, the group discussed whether the duration of time waited before declaring a negative culture could or should be shortened:

"2: but I think the other thing is... the main point of evidence that we would usually go on discharge apart from the patient themselves is the blood cultures and we wait for 48 hours so I would probably like to know from the evidence that you're presenting with us how many patients it would have made a difference between sending them home at 24 hours and 48 hours from the blood cultures so do we just arbitrarily keep them in for 48 hours because that's what our standard practice is or can we…. Is there a… can we have some evidence that actually you could even send them home at 24 hours and just review the blood cultures after 24 hours cos the majority of cases aren't going to grow anything after 24 hours… cos it's not just about how the patient is it's also about the investigations that we do….

3: doesn't the 48 hours thing come from how long the machine takes to work cos I know some of the like… when I did neonates they said that there was like… NICE and everything its 36 hours cos normal … you know... machines take 36 but in this hospital or the Trust I think its 48 hours until you get the….

1: I thought it's just historical … you're just waiting for the bugs to produce whatever gas and that sets the alarm off isn't it?

2: yeah I think they survey…. There's a more… more of a continuum of it now…

1: I don't think there's any evidence…

2: …whereas I think there used to be… they used to show in the machine at 48 hours they'd look at it…

6: so let's say you get a blood culture, a child comes in at like midnight and the blood culture gets sent who... does someone deal with that in microbiology straight… when do they …

3: probably at 9 in the morning

6: that's what I mean so that's … so 48 hours isn't 48 hours is it?

2: no but I think the way…

1: … cos it's culturing as soon as you put it in the bottle…

2: …yeah…

6: does it?

2: …yeah... as soon as you put it in the bottle, the way the new culture bottles work as soon as you put it in the bottle it starts culturing so it will be 24 hours…

6: ok…. Right... so it doesn't need to go in a special machine like….

2: no... it used to when we used to have the big glass bottles … I mean it used to have to go onto the machines then the culture start at the time it was put in….

6: …so it would be eight hours…

2: but the new bottles I think they culture straight away…" (Centre 1, healthcare professionals, doctors (1, 2 +3) and nurse (6))

Linked to the issue of delayed blood culture results and the theme of *attaining mutual trust and sharing role and responsibilities* was a separate concern from families about a future early discharge strategy. Many had previous experiences of blood test results being lost or identified late, meaning parents did not trust that professionals would appropriately monitor test results when their child was not in hospital. In a number of groups, they asserted that, if their child was managed in the outpatient environment, then the results of all investigations should be communicated to them via telephone, regardless of any abnormalities.

"1: I had a couple of occasions where I was told that erm… if you need to come back for some more blood tests we'll be in touch with you, if you don't hear from us, you'll know everything's ok, now I don't particularly like that.

[laugher from rest]

4: you want to be told, you want to be rung no matter whether it's good or bad, you to be told…

1: I want to know somebody's checked the results and just told me what it was

5: see I don't even like that for myself this you know, you know when they take your blood results… I want them to tell me either way…I don't just want a phone call telling me oh yeah something's wrong" (Centre 1, parents of over 13s)

Although the direction given by protocols provided reassurance to healthcare professionals, certain features of current protocols could be interpreted as constraining and strict, resulting in frustration for the professionals involved:

> *"1: I think the other thing that makes it frustrating its very protocol driven innit?*
> *(2: (at the same time) yeah)*
> *1: I think people stick rigidly to 48 hours as though it's a magic number and nobody can go home at 43 hours and etcetera…so I think it's very very rigid err which is done for good reasons but I think if you dare to suggest that you veer from that you're scorned upon…" (Centre 1, doctors)*

Throughout the study, both professionals and parents used language to describe the protocol requirements which implied an inability to deviate from them. The sense of the protocol controlling and limiting decisions was communicated throughout the protocol discussions: *"you still have to treat them with antibiotics"* (Centre 2, doctor). This language is echoed in other areas of the transcripts which I examine later in the *spectrum of control* subtheme.

Participants varied in how much flexibility they thought there should be within a protocol. Despite the frustrations of working within protocols, participants described risks of working outside the protocol, in particularly relating to receiving criticism from colleagues, with groups only briefly referring to the safety risks to patients of deviating from a protocol. Notably, they referred to the risks to patients of other professionals departing from the protocol but the risks of criticism refer to their own practice. This difference between their own practice and that of others is further discussed within the *professional roles* section of the chapter.

The issue of flexibility in application of a protocol was particularly apparent when considering the role of appropriate clinical judgements. Participants asserted that the clinical assessment of a child should, at times, lead to appropriate deviation from the protocol. However, the general approach to protocol deviations varied from centre to centre. Centre 1 spoke of the importance of having a strict protocol with minimal deviations due to the multiple professionals involved in the care of children with febrile neutropenia (see role discussion in following paragraph) and were willing to accept a greater degree of frustration because of this. Meanwhile, centre 2 gave considerable weight to clinical reviews, with minimal references to protocols as a guiding feature; *"personally I'm one of those individuals, I like to review and review and review so I think where you have got 14% treatment failure, if you're able to review and review at appropriate times you may be able to also shorten the amount of time somebody has oral antibiotics…" (Centre 2, doctor)* Combining these two approaches, professionals at centre 3 spoke about the integration of protocol and clinical judgement:

"1: like you've got the protocol there but actually if you know your patient… me and the consultant might make a decision on our patient that isn't what the protocol says but we're happy with that clinical decision" (Centre 3, nurse)

Preferences for care

Participants' past experiences help to inform and find balance between the uncertainty of risks and the certainty of protocols and begin to demonstrate the need for discretion and the importance of individualised care for paediatric low risk febrile neutropenia. This subtheme explores how past experiences within current febrile neutropenia services impact upon attitudes to future care and the concept of hospital being a 'safe' place is debated. I examine how participants anticipated other key stakeholders' thoughts and how accurate these expectations were. Although a number of issues discussed here had been identified in the Qualitative Synthesis of Chapter 4, many of these were explored in greater detail during the study and various new codes were iteratively ascertained. The potential explanations for these new codes are deliberated upon within this passage.

Parents spoke in all focus groups about the difficulties they had experienced when their child had previously had febrile neutropenia, particularly the challenges of juggling many different demands besides responding to this episode of illness. As covered in the Qualitative Synthesis, they spoke about both practical and emotional issues. Practically, problems associated with travelling to and from the hospital featured in all focus groups, except the group for parents at Centre 3. Participants spoke of the tiring nature of travelling, particularly at night time or during the rush hour. The distance from the hospital where the febrile neutropenia would be treated played a key role in discussions about whether early discharge regimens would be accepted, with families living close to the treating hospital being more likely to accept outpatient care whilst those further away tended to feel that inpatient care might be preferable. Interestingly, the degree of shared care performed in the centre seemed to impact upon this issue. Participants in the centre where febrile neutropenia is treated in POSCUs, barely mentioned travelling as an issue, presumably because they already live close to their treating centres, whereas in centres where participants would travel to the PTC with febrile neutropenia, distance was a more significant concern, particularly if the journey would take over half an hour.

Another practical issue mentioned in the Qualitative Synthesis was that of finances, related to travel, parking, hospital food and lost income. This issue was quite vividly described by some participants, including the loss of a self-run business, repossession of a car and the receipt of benefits such as free school meals. The magnitude of these financial concerns are unlikely to be purely from febrile neutropenia admissions, but instead reflect the acute-on-chronic nature of

febrile neutropenia, in which families are already under financial strain due to their child's cancer diagnosis and then a further hospital admission adds additional burdens. Nevertheless, one focus group discussed how the unpredictable nature of febrile neutropenia episodes proved more problematic than scheduled attendances for review or chemotherapy as it did not allow them to plan other aspects of their lives, chiefly their work.

The third issue related to prior experiences which parents found to be particularly influential was the psychological impact of admission to hospital upon their child. Participants spoke about how their children would become quiet, anxious or angry when their temperatures were checked at home and they anticipated they might need to travel to hospital. Parents related the ways in which febrile neutropenia episodes would feel inevitable once a child's temperature had begun to rise, and how the interval between recognising a slight increase in temperature and recording a figure over the defined fever threshold was filled with trepidation about the impending excursion.

Furthermore, parents shared how, once admitted, children became distressed by procedures, refused to eat or open their bowels, and would withdraw socially. Children would become upset about the social isolation from their friends and their siblings. Following discharge, psychological effects would continue for some time:

> *"1: we're definitely a more stressed family when he's admitted…definitely… and it takes a long time for the family to get back on track, it's not just he's home and we're all fine, you actually have to completely collapse and rebuild and that takes a couple of days… it's a really bizarre explanation but it's just like you are all on this adrenaline and what've we got to do to get by and where has everybody got to go and then you're all home and you go ahhh and then you start to… just try and get back that routine… it's not easy to get back that routine if there is a routine but… yeah… there is a psychological impact on it definitely…"(centre 3, parents of under 13s)*

Linked to the psychological impact on the affected child, parents spoke extensively about the impact on the child's siblings. This included practical issues such as sleeping at other people's houses (one young person spoke about their younger sibling having *"this little suitcase"* for when she was in hospital), eating in the hospital and the impact of lots of hospital visits. However, parents placed more intense emphasis upon the psychological impact on siblings. They spoke about split families, where one parent was in hospital with the affected child and the other at home with their siblings, with occasional 'handovers' of care. Some families discussed how they felt that the oncology ward was not suitable for siblings as so many children were so unwell. They voiced siblings' needs to see professional counsellors or Community and Adolescent Mental Health Services as a marker of the severity of the impact of a family cancer diagnosis. Finally,

parents expressed guilt over the choices they needed to make when faced with the differing needs of their children:

> *"3: …and then I start feeling guilty and I'm like, my other kids need me as well, obviously his health is one of the most important things but while I'm concentrating on his health, who's concentrating on the others you know and it is. Horrible…*
> *2: oh it is… [sister] slipped in b)'s first year on treatment and she cut her eye here [indicates area between eyebrow and upper eyelid] and she needed to go to A+E and have it glued and b) was… they get so clingy don't they and she was, it was a steroid week and she would scream if I left the room never mind the house and [sister] was crying, she was saying but you take b) to the hospital, don't I matter as much*
> *1: why won't you take me?*
> *2: so I did take [sister] to the hospital and left her (points at b) home screaming and [husband] said she screamed for like three, three and a half hours, cos when they're on steroids they just don't stop do they? And… but she was right, like, you can't not put them first sometimes too…*
> *3: that's it… horrible…" (Centre 3, parents of under 13s)*

Concerns about siblings' needs were seen in all parental groups and expressed by all participants; however, parents with many other children seemed to find this particularly difficult. This appeared to influence their attitudes towards early discharge, with all but one parents of three or more children expressing a strong desire for outpatient care.

Alongside the negative impact of repeated hospital admissions upon the relationships between siblings, and then between parents and their children, participants also spoke about how current services impact upon their relationships as couples. They talked about being frequently separated so as to provide childcare to different children, but also about how the affected child would often want to sleep with one parent even when at home. The parent who took on the role of primary carer during admissions often had a deeper relationship with the child when they returned home as well, and thus the other parent could feel rejected or 'worthless' . The negative impact upon relationships was prevalent in many of the focus group discussions. Although this effect of admission on family relationships had been discussed within the qualitative synthesis (Chapter 4), the intensity of these concerns was not as apparent as demonstrated in this study. This may again relate to the acute-on-chronic nature of the problem, such that frequent, intermittent and unpredictable admissions cause more distressing effects on families.

When the professionals reflected on current febrile neutropenia services, they mostly spoke about the experiences of patients and families, with very few references to their own

perspectives. They mentioned each of the key issues mentioned above but provided less detail to the individual topics and did not identify more nuanced issues about the patient experience.

> *"… so you have problems, like sibling problems, with the parents having to be in hospital all the time with their siblings, you get bad eating habits, you get rule changes, so many things, so many side effects of being in hospital… is my thoughts…" (Centre 3, nurse)*

When it came to their own perceptions of care, healthcare professionals appeared to project their feelings and emotions onto families. It seemed that within the groups, professionals described families feeling anxious or frustrated when perhaps these were their own views and feelings. There is a clear link here with the anxieties described in the *understanding, expressing and negotiating risk* code.

> *"1: I still… I mean… It can be done, but I think the key issue is parents wanting to know what are the failure rates, what are the chances of…*
> *2: I think it's more the doctors disagreeing on what they want" (Centre 2, doctor (1) and nurse (2))*

This situation, where healthcare professionals conveyed the thoughts and feelings of parents instead of their own, resulted in double silencing of both parents and professional voices. In the following quote the parents and family views are not appropriately heard, as they are being spoken by a proxy, and the healthcare professionals do not express their own experience, despite being explicitly asked. Thus the healthcare professionals' voices are also masked.

> *""Mod: … how do you feel as professionals responsible for these children when they're in your care or the thought of them having that at home? So your feeling rather than the parents feeling*
> *6: erm… depends on how… what the... the timespan is of discharge… I think if they were going to do that they'd need… the families would need a lot of … would need support… I don't think we could just say… right after eight hours...erm... we've given you piptazo we've sent you home you're not going to hear from us again…they need support... it shouldn't be up to the families then to ring us it's a problem like many families… like we do say if there's ever a problem any temperatures just ring us… I think there should be a phone call then put in place to them…*
> *4: I've found that the families that we send home that are extremely anxious about going home and don't want to leave us cos they feel safe when you leave them for 48 hours they realise that when you get home they are safe, they can carry on with getting along with what they did and when you actually see them, they're fine and all those*

anxieties that you saw 48 hours before have just completely disappeared, so I think it is … I think the anxieties are based on their experience … so if they go home and have an absolute awful time then next time they're gonna have huge anxieties about going home but when they go home and have an alright time… they'll be fine next time…" (Centre 1, nurses)

In addition to the challenges previously discussed in the qualitative synthesis, and expanded upon through this study, eight further codes were identified. First, the professionals spoke clearly about how these are generally well children who are active, noisy and boisterous on a ward with other, much more significantly unwell children; *"well they get in the way! Up and down the wards on bikes and cars and goodness knows what!!" (Centre 2, nurse)* They therefore reported boredom and frustration over the process of an admission for low risk febrile neutropenia.

"1: well the children are often quite well… they've just got a cough or a cold or something and their parents know they're well. But they're sat there in hospital wasting time when they could be at home... not wasting time but
*4: *laughing**
1: but they … you know that they're well… it's frustrating
4: (at the same time) it's frustrating" (Centre 1, doctor (1) and nurse (4))

Parents expressed these feelings even more strongly. They spoke about feeling guilty for having their well child on the ward and were concerned about disturbing other children who were more unwell. Interestingly, this was not an issue which the young people raised, perhaps as two had minimal experience of febrile neutropenia and the other, who is discussed further in a later section of this chapter, enjoyed being in the hospital environment.

The second new code is that of 'hospital acquired infection'. This was a particular concern to parents, who spoke about the risks of wards or hospitals which were not clean. One exchange in centre 2's group for parents of children under 13 years clearly summed up this issue:

"1: and I've always worried about that, I mean I know it's a very clean ward, the nurses are great, everyone washes their hands everything else but there's floating around in the air…
5: there's people coming in though…
1: there's visitors…
5: and some of them don't look the healthiest do they?

1: there's other children, absolutely…so for me as well, I think, surely at home where I can say, there's just me, her brother and her dad, that's it until she's better, isn't that better isolation than being on a ward with…" (Centre 2, parents of under 13s)

Staff in two of the focus groups in this study also spoke about the risks of nosocomial infection. This feature had been notably absent in the Qualitative Synthesis.

The third new code related to source isolation. Participants, both professionals and parents, commented on this in two distinct ways. The first links with the initial new code, in that well-children who are the source isolated are usually even more bored or frustrated and therefore this can be a very unpleasant period of time for families. The second way in which source isolation was discussed relates to the following code – where source isolation beds are limited, staff can feel that these are unavailable to sicker patients when children with low risk febrile neutropenia are admitted to them. Parents were also acutely aware of this issue, expressing guilt for using resources which might otherwise be isolated to children considered to be more unwell.

Staff expanded on the issue of bed pressure within the fourth new code relating to current experiences. Here they spoke about the intense challenges faced by health services, where the numbers of bed spaces are reduced and the costs of occupying a bed are high. Although mentioned in all groups, this seemed a particular issue in centre 2, perhaps related to the fact that this is a smaller centre that the other two centres and has a minimal shared care network. There, this issue was most often brought up by one particular participant who has a management role within the team and hence may be particularly aware of certain service pressures.

"6: …maybe delay children for chemotherapy…need the beds… that's I imagine frustrating… you can't get other children in…
Mod: so you're describing service pressure as well?
6: probably yeah… cos your beds are full aren't they? They're full of well… potentially well children who could have gone home" (Centre 1, nurse)

The fifth code, discussed only by parents and young people, related to side effects of antibiotics and other treatments. Clear descriptions were given of the diarrhoea caused by antibiotics, which necessitated source isolation, and all its associated challenges, and might also cause the child to need intravenous fluids or total parenteral nutrition[6], thus delaying their discharge from hospital. Parents voiced a clear preference for reduced amounts of antibiotics, particularly those given intravenously, so as to prevent these side effects. In addition, parents spoke about their concerns

[6] Total Parenteral Nutrition (or TPN) is an intravenous solution which aims to provide a patient's nutritional needs when these are not being met via the enteral route. It includes carbohydrates, fats, vitamins and electrolytes tailored to the individual patient's needs.

regarding antibiotic resistance and how this might impact on their child in the future. This added further to their wish for reduced therapy. Perhaps importantly, these issues were not raised in the healthcare professional focus group discussions. This may be due to the differences in risk assessment by professionals and families, such that professionals feel the risks of a poor febrile neutropenia outcome outweigh the harms of side effects or antibiotic resistance.

In the fifth code, healthcare professional participants in Centre 3 discussed the long-term impact of current febrile neutropenic care. They spoke about the psychological effects of being considered an ill child and how recurrent admissions contribute to a family adopting a sick role for their child. The professionals felt this had the potential to impact on a child's future perceptions of their health.

> *"… as a late effects nurse… the risk of repeated hospitalisations and family seeing their child as sick and continuing to do so after the… and never really recovering from that sick child mentality… I don't know if that's a bit strong… I see the late effect of that when you've still got families who haven't been able to stop treating their child as a sick child right up until the child being in their early adulthood… I don't know how you'd ever measure that to balance it against that 0.1% risk…" (Centre 3, nurse)*

Alongside these five codes which capture some of the more difficult aspects of previous experiences, three codes describing the benefits of inpatient care were also found. The most pervasive, which also ran as a subtle undercurrent through many sections of the discussions, was the concept that hospital is a safe place, where professionals looked after and cared for their child's health, though focused mainly on the physical aspects of this. Despite the concerns about hospital acquired infections and about considerable psychological impact, parents clearly stated that hospital was the place they would prefer their child to be if they judged them to be unwell, through their own risk stratification. Parents and young people felt comforted by the presence of healthcare staff with whom they had good relationships and by the ritual of performing regular observations, although a couple of groups did highlight that many observations could be done at home. This feeling of safety and comfort may be accentuated by the benefits of relinquishing a degree of responsibility for their child and control over decision making for this brief period. These issues are discussed later in this chapter. The feeling of safety was also dependent upon the ward and the hospital in which the child was located, and this is again discussed further in the following theme.

The second main positive code is that hospital can be fun. This was primarily brought up in the groups for young people and their parents. One family in particular spoke about enjoying the input of youth support co-ordinators and the various activities that are organised in the hospital.

The social element of hospital admission was certainly appreciated by this family. In one other group, for parents of under 13s, one parent mentioned how their child enjoyed the playroom in the hospital, and sometimes did not want to leave this space. However, this did not seem to play a major role in decision making and this parent was clear that they would still prefer a reduced therapy strategy for episodes of low risk febrile neutropenia.

The final positive code relates to the relational benefits that children and young people gained from the undivided attention of a parent, who, at home, might be distracted by other siblings and by the hubbub of daily life.

> *"4: I think that's why d) liked being in hospital because it was one-to-one she just had me, she didn't have to share me with anybody…*
> *5: yeah*
> *4: you know so I could run round after her and I didn't have to worry about [other two daughters] or you [referring to husband], it was just me or her so I think she quite liked that… errr… you know that I wasn't going to work or doing anything but 100% here for d)" (Centre 1, parents of over 13s)*

The potential reasons for why these new codes were not discussed in the qualitative synthesis data most likely relate to three key factors. The first is that a number of the problems, including the challenges of well children being kept in hospital, are very disease specific features. Therefore, as the qualitative synthesis included only one paper specific to febrile neutropenia, it is perhaps understandable that these points were not discussed.

The second feature that may explain some of the findings is that these are patients and parents who have prolonged contact with healthcare services. They therefore become more perceptive about issues related to admissions and through repeated experiences have identified problems which are recurrent, compared to those which are 'one-off' negative aspects of care. Thus the population involved in these focus groups is likely to be more sensitive to the challenges of frequent hospital admissions. However, they have also developed deeper relationships with healthcare staff members and thus may benefit more from the positive influences of care on a ward which they know. Although this explanatory factor is not specifically disease related, it is associated with having a chronic disease involving regular contact with healthcare services and periodic admissions. As this was not the case with some of the studies included within the systematic review, this may explain why certain codes had not been previously identified.

The final possible explanatory factor is that of the current healthcare climate within the UK, where austerity measures and staffing crises reduce the funding available and mean that the

limitations of inpatient services are more apparent to professionals than in the times and locations of the studies included in the qualitative synthesis.

When participants discussed the preferences of other participant groups, there were often inaccuracies in the perceived desires of others. The most clearly apparent areas of imprecision were between the groups of young people and their parents. Here, parents were relatively certain that their children would prefer outpatient treatment regimens for low risk febrile neutropenia and just one teenager was predicted to be unsure about leaving hospital. However, when the young people themselves were questions, this one teenager was very clear that she would prefer to always remain in hospital, and another teenager voiced that she would probably also elect for a period of admission following a fever. In the end only one young person stated she would select a reduced therapy option. Meanwhile, the young people anticipated that their parents would all rather receive inpatient care, which was at odds to the parents' stated preferences.

It is unclear precisely why these conflicting opinions occurred. It may be that each group felt that they knew what the response of the other member(s) of their dyad or triad would give and thus adjusted their own expressed posture accordingly. This suggestion is supported by the fact that in each group, participants stated that they would take their parent or child's opinions into account when deciding about future treatment options.

> *"1: if my mum agreed with the doctors, then I'd just do what she said, cos they don't like… when I'm saying something its normally cos it's what I'd prefer, when my mum tells me to do something its what's best for me… so… I'd probably whinge about having to staying in hospital but then… I'd just stay anyway.*
> *2: I don't know… I don't think I'd really… I think my mum would just do what's right for me. Yeah" (Centre 3, Young people)*

Attaining mutual trust and sharing roles and responsibility

In this theme, participants spoke of the different roles within febrile neutropenia services and how these would need to change if outpatient or early discharge schemes were implemented, how mutual trust, though already present in some ways, would need to be fostered and strengthened and how responsibility would need to be redistributed between groups. Encapsulated within this theme were the relationships between and within patients and families, the roles of various professional groups, attitudes to shared care networks, external influences on services, the interactions between families and professionals, and the challenges of attaining mutual trust and sharing responsibility. Links with other themes are explored and expanded.

Relationships within and between families

The impact of current febrile neutropenia management strategies on relationships within families has already been discussed in the *Preferences for care section* of the previous theme. Participants also spoke about how relationships between families being treated by paediatric haematology and oncology services, influenced experiences and perceptions. Parent participants spoke about how they learnt about different methods of managing problems through discussing them with other parents, and learning about their attitudes towards different hospitals or trials. Parents in Centre 3 also talked about the support they got from social media networks in living with and understanding their child's condition, particularly as the significant shared care network meant families were less connected geographically. Parents viewed these relationships in a positive, or at least informative, way but stated they gave most weight to professional opinions.

In contrast, the healthcare professionals raised concerns about relationships between families. They felt that providing individualised care could be complicated by parents speaking to each other and being displeased because children were managed in different ways for the same condition, creating more work for professionals in explaining the rationale for different choices. This could potentially complicate the management of children who are perceived to have a single condition, reflecting participants' struggles to separate the various risk groups within febrile neutropenia. Were discussions about risks and shared decision making to occur, then families could be supported to understand and accept the differences in care for febrile neutropenia. Professionals also spoke about how groups of parents could influence the attitudes of a whole centre's population towards certain changes in practice and thus prevent introduction of new policies. This is discussed further in the *interactions between families and professionals* section.

Professional roles

Professional roles were clearly defined for all participants within the focus groups, with very few distinctions between professional, parent and young peoples' voices in this area. Where there are differences, these are highlighted at the appropriate point. The ways in which medical and nursing roles are currently set up for febrile neutropenia were quite explicit:

> *"Mod: tell me about how you treat low risk febrile neutropenia in this hospital*
> *7: Well… they come through the door, they should s'pose get seen within an hour by the doctor ...um... but in that time the nurse does her assessments, accesses the port, takes*

bloods, um.. administers calpol if they've got a 'PGD'[7] or… bleeps the doctor then it goes from there.

3: Usually the junior doctor arrives, prescribes the first dose of IV piptaz[8]...um... does the peripheral cultures if they're necessary and sees the child and assesses for any focus of infection, assess whether it's actually likely to be a line infection or whether it's likely to be another form of infection, whether serious infection or not, and then we usually bleep our more senior doctors for a review if we're not sure." (Centre 1, nurse (7) and doctor (3))

With regards to medical roles, there were very clear distinctions drawn between junior doctors and consultants. Throughout the study, junior doctors were discussed in either a functional way or an unfavourable tone. Junior doctors were considered to be less able to manage children appropriately, needing stricter protocols, and were often felt to be less confident in decision making. These negative comments appeared in all groups, but were most frequent in the healthcare professional group with the most junior doctors present, though these comments did not come from the junior doctors themselves. Similar comments came from the other groups of both parents and professionals.

Comments on nursing roles were more variable. Predominantly, there was clear respect and recognition of the skills that both hospital and community nurses bring to febrile neutropenia services, both in supporting patients and in guiding medical staff. However, there were occasional undertones of negativity towards nursing contributions:

"so you could do reviewing in two ways, you would either have clinical nurse specialists trained, and there are centres that are doing that, where they train them, they're not actually doctors but they're able to do assessments and things, erm… and they go in and they assess and feedback and assess and that works, but only to an extent…." (Centre 2, doctor)

A further set of key healthcare professional roles and relationships related to shared care teams. As discussed in Chapter 5, the involved centres were purposively selected with some of the selection criteria relating to the amount of febrile neutropenia treated in shared care centres. Thus, Centres 1 and 2 had small shared care networks with few episodes of low risk febrile neutropenia being managed outside of the Primary Treatment Centres. However, Centre 3 has a very different structure, where almost all children with low risk febrile neutropenia are managed

[7] A PGD, or Patient Group Direction, allows nursing staff to assess a patient's need and administer prescription-only medicines, without an individual prescription from a doctor, provided that the patient and medication fall under those described within the PGD.

[8] 'piptaz' is a common shortening of the combination antibiotic piperacillin/tazobactam.

by shared care teams and the Primary Treatment Centre simply provide support through the provision of protocols and intermittent contact to provide advice on individual patient care. Given these differences in service design, it is perhaps unsurprising that the attitudes towards shared care and the anticipated roles to be played by colleagues in POSCUs differed.

In Centres 1 and 2 healthcare professional groups, shared care units were only minimally discussed, and generally in a negative fashion. Both groups talked about how changes to services ought to be changed at the PTC prior to being rolled out across the shared care network. They did not discuss the involvement of shared care staff in developing future protocols and they did not clearly outline a role for these staff in any suggested outpatient service.

> *"4: and then I suppose we have to think about are we then happy to make that policy general and include shared care hospitals and are we happy that… the same safety applies to the shared care centres…*
> *2: that would be a major concern for me… (laughter)… having taken phone calls from shared care centres… yeah…*
> *1: it'd be harder for them… I mean… we see I dunno ten a week or so… they see one every month sometimes don't they…*
> *2: I would have thought this kind of thing had to be… done here first…" (Centre 1, nurse (4) and doctors (1+2))*

Centre 3, however, generally spoke very positively of their shared care colleagues, and of the current services set up for children in their area. They did highlight particular challenges to the PTC including frequent requests for advice from POSCUs, which were sometimes felt to be inappropriate as they related to 'general paediatric problems', and the difficulties that arise when the local lead for paediatric oncology in the POSCU is unavailable and the team subsequently need significantly more support.

> *"3: they're sometimes encouraged to talk to the… by the local consultants apparently…*
> *2: again, you only have usually one lead consultant who is knowledgeable and the others…*
> *3: so one of the difficulties happens that I know that the people who hold the phone here have is people in the local hospitals where the child is, asking for us to make what is a clinical decision about when to stop the antibiotics and that's quite difficult, I think…*
> *2: and also asking for just… asking questions that, with their paediatric hat on, they are able to answer…" (Centre 3, doctor (3) and nurse (2))*

When considering the design of future services, Centre 3 spoke about how shared care centres might easily adapt to an outpatient regime, and also shared how these changes would need to be communicated, highlighting some of the complications experienced when changing protocols in the past.

The opinions of young people and parents about shared care generally echoed those of the healthcare professionals at each centre. Within Centres 1 and 2, shared care was spoken about disapprovingly. Parents spoke about how staff at shared care hospitals did not know their child, had less understanding of oncological issues, were unclean and their treatment was less effective than in the Primary Treatment Centres. One participant did highlight that they found it difficult to differentiate between the nursing and medical skills which might be considered as specialist to oncology and more generic skills, as demonstrated in the following quote:

> *"4: cos nobody's there to access her port[9]…*
> *5: nobody accesses ports there...*
> *4: nobody could do it…*
> *5: nobody could do it cos they're all nervous about doing anything over there*
> *4: and they said something like the lady that could do ports was off for three days or it was… it was shocking*
> *5: which we found really odd but obviously when we've asked the nurses here… they said yeah we do ports all the time, said its nothing to us but when they've been other places then they're asked to train people to access ports… so we though oh ok then it starts to make sense a bit… you sort of get in your mind-set a nurse is a nurse and a doctor's a doctor and they'll just get on and do it but obviously with specialisations and things you don't think of these things, you just want your child to be dealt with don't you… so… in the proper way but…" (Centre 1, parents of over 13s)*

Due to their concerns about care in the shared care units, parents in these centres preferred to travel to the PTC for treatment of febrile neutropenia, even though this increased the distance travelled and thus impacted poorly upon their current experience of care as demonstrated in the *Quest for certainty* theme, outlined above.

[9] A Port-a-cath is an implantable central venous access device in which a small box, or 'port', is sited under the skin (usually on the anterior or lateral chest wall) and connected to a catheter within a large vein (usually the subclavian vein). This allows the administration of certain medications such as chemotherapy and easy access to blood samples. 'Accessing' the Port-a-cath involves placing a needle into the 'port' under aseptic conditions, and requires a degree of technical skill and training. Most staff working outside oncology units do not have this skill.

Meanwhile, in Centre 3, parents spoke differently of their care in POSCUs. They shared how they had formed relationships with the staff in the POSCUs and could identify the knowledgeable staff in the centres. Furthermore, parents spoke about how they helped to educate staff about oncology issues and took more responsibility for communicating about their child's disease and in directing care. Generally, this seemed to be interpreted as a positive occurrence as parents took on this role of educators and became valid team members alongside the shared care staff. Participants did complain about delays when POSCU staff needed to liaise with the PTC, but at no point did the parent participants at Centre 3 voice a desire to have their child's febrile neutropenia managed at the PTC itself. Issues of cleanliness or poor skills were not mentioned in Centre 3, other than one issue related to Port-a-cath access in which the deficiency was felt to be related to individuals rather than to the whole shared care team.

Between the discourse about shared care and considerations of professional roles were discussions about the role of community nurses. These staff members were highlighted by all groups as particularly busy, if not overstretched, in the current demands upon them. Their skills both in sampling from central venous lines and, increasingly, in the assessment of children were recognised and highly valued by teams. Indeed, despite their current work pressures, all groups felt that community nurses should constitute key roles within an outpatient service. Their expertise in liaison between patients, families and treatment centres meant that they were recognised as having proficiencies which participants would like to be multiplied either through the employment of further community nurses or the development of these skills in other staff groups.

> *"…Community nurses are by nature usually very experienced nurses and often of higher grades and by educating them and by them having the links with both primary treatment centres and… which they're very used to doing I think that they're very well able to support the family and to act as their advocate and to link in with the primary treatment centres…. And I think that you don't want people who are just going in to do bloods and things, that is a really good time for education and so, maybe strengthening of community services in some way, so that it's not just seen as a 'I've got to do a job for the PTC' more as a 'I am part of the team that is helping to support, advocate and educate this family'." (Centre 3, nurse)*

When discussing other professional roles, external influences upon clinicians were apparent throughout the healthcare professionals' focus groups, though notably absent in the groups for parents and for teenagers. In two groups there were comments about the anticipated opinions of the participants' colleagues, with Centre 2 appearing to be particularly anxious about the fact they may have conveyed perceptions that others would not approve of:

"so in the study will it say (centre name) feedback? Cos they're probably all going to say "well we didn't say that, we don't agree with what you three have said"" (Centre 2, nurse)

This highlights a concern (or perception) that other, more 'powerful' parties might not approve of what the participants have said; and a real worry about conflict and disagreement within the unit, particularly as this centre are currently undergoing significant changes of policy in this area. Interestingly, this centre, and this participant in particular, had already discussed disagreements as a prominent feature in febrile neutropenia discussions:

"…but it is very controversial with the doctors, cos our consultants, there's disagreements isn't there on what we should do? And I know that's probably throughout the UK as well, throughout the universe probably…" (Centre 2, nurse)

The influence of parties outside the participants' departments was also demonstrated, through discussions about managers' opinions and relationships with other professionals. For example, in regards to relationships with microbiologists, some aspects of the discussions were very positive (*"…we have a very good relationship with the microbiologist and virologist here*," Centre 2, doctor), whilst others were less so (*"cos a lot of the time when you ring the lab…they'll usually say oh it won't be positive but they won't say for definite so…."* Centre 1, doctor)

A particular challenge to healthcare professionals involved in these groups related to how these roles and relationships would need to be negotiated if early discharge regimes were instigated. The change in activities of different professional groups, within departments, hospitals and shared care networks, as well as the increased responsibility of patients and families inevitably made healthcare professionals feel quite uncomfortable. This links to their wish to mitigate the risks to their patients wherever possible, as well as to their wish for discretion as to how much a child's treatment they control, as in the earlier discussion of determinism.

One particular professional, a doctor, described the difficulties of changing roles particularly well. This was captured within two key quotes; one, previously discussed in the methodology chapter, relates to the issue of role negotiation and professional identity, the second to whether outcomes are "written in the stars". The first quote explores how paediatric oncology patients are considered "special" and different from children within other paediatric services. This transfers to the professionals' identity in paediatric oncology and haematology, which defines this group as people who care for children who are "special". Changing the manner in which these children are treated so as to be more like "normal" children then also brings the professionals' identity into dispute. Recognising this dilemma illuminates the emotional reactions of participants to early

discharge options, and provides understanding as to why instigating change in this area has proved problematic.

> *"really what you're saying at this point is that in… to a certain respect… if they're a low risk patient you would treat them pretty much the same as you do a general paediatric patient… and it's about moving... that shift of your opinion that our patients are 'special' ([4] laughs) or susceptible whereas actually what you're saying is they're... they're not. And in which case, you're moving away from the oncology kind of let's protect everybody kind of approach to more of a general paediatrics approach of somethings really gotta be wrong in order for us to kind of worry about this child. So I don't know... but I agree with [1] and [4] I think… I don't know whether going from your 48 hours to immediate discharge…" (Centre 1, Doctor)*

The second key quote from this professional also relates to role identity. Here, the data from the systematic review stimulated the participant to consider how current febrile neutropenia strategies do not prevent all deaths in paediatric low risk disease. He calls into question the efficacy of professionals in this area, challenging the traditional roles of clinicians outlined in determinism as people who cure disease. Surprisingly, this realisation does not appear to cause an identity crisis, but instead is laughed at and provides a moment of levity within the group, followed by a period of quiet contemplation before the conversation moves on. This comment seemed to allow participants to recognise that the change in roles to one of lesser involvement might not have a negative effect on their patient, and permitted them to consider a reduced therapy regime with a little less anxiety.

> *"but what you're saying from that data is the ones who died, it didn't really make any difference that we were already treating them... and that's the thing isn't it? Is whether we actually think that what we do makes a difference (laughter) or whether that that stuff that happens is already kind of written in the stars so to speak…." (Centre 1, Doctor)*

Interactions between families and professionals

As well as the roles of professionals, the relationships between families and their healthcare professionals played a vital part in decisions about the management of low risk febrile neutropenia. The ways in which roles and responsibilities were currently assigned were acknowledged and the challenges of negotiating and redefining these relationships were delineated.

Parents expressed themselves as playing three key roles in the care of their children with febrile neutropenia. First, they spoke repeatedly about their responsibility to protect their children from acquiring infection and thus prevent them developing febrile neutropenia. Parents deliberated over difficult decisions including when to send their child to school and how much socialising to allow their child to engage with. They also discussed the influence of siblings on a child's risk of infection and how to prevent the transfer of microbes between siblings and the affected child, including also limiting a sibling's attendance at school during outbreaks of infections. Practically, parents would carry out routines and rituals to prevent infection, including using bleach to clean their houses or by insisting on frequent hand washing of both family members and visitors:

> *"4: I bleached d)'s bedroom yeah… I became obsessed with…*
> *5: that's what we… our two youngest, we got them a little bit obsessed with washing hands and things, we had the err… alcohol as you come in the door*
> *1: yeah well my husband insisted on that but nobody liked it*
> *5: and they… [youngest child] would literally take it when d)'s friends came, take it to the door like you can't come in…*
> *4: [other child]'s gone the other way now, we have to … we have to try stop her washing her hands…*
> *5: we've got to be careful with her…" (Centre 1, parents of over 13s)*

Finally, parents recognised that they engaged in superstitious behaviours such as keeping a packed hospital bag in the boot of their cars in the belief that this would prevent admissions with febrile neutropenia. This may reflect a desire to take control over the situation and to feel as if they have a means to prevent their child's febrile neutropenia. This links with the issues of control discussed later in Chapter 7.

Secondly, parents identified their roles in performing many essential care tasks for their children. These included the management of nasogastric or gastrostomy tube feeding, the care of central venous line dressings and the administration of oral chemotherapeutic agents. Participants spoke about how these were vital to their child's wellbeing and to the successful completion of their child's treatment for cancer. However, parents felt that these tasks were often undervalued by healthcare professionals and seemed arbitrary in the degree of responsibility devolved. In the centre 2 group for parents of children under the age of 13, one participant shared that she felt if she was able to deliver oral chemotherapy to her child at home, then she would be happy to observe him with febrile neutropenia.

> *"2: …they trust me to do that massive job, I think those sorts of things, you know, individually have to be considered…*

5: definitely…

2: so from that point of view I think I'm more than happy to take on that responsibility, I'm taking on so many others with it and…" (Centre 2, parents of under 13s)

Finally, parents viewed their role to be to care for their child's overall health, including the physical, psychological and social factors beyond their febrile neutropenia, as described in the *Preferences for care* subtheme of the *Quest for certainty* theme of the study. This responsibility to draw attention to the broader impact of admissions for febrile neutropenia and to represent the needs of other family members formed a central tenet of the parent role.

In response to these considered roles, participants recognised marked variation in family attitudes to febrile neutropenia episodes which then translated into behaviours, with some being very anxious, others "playing it by the book" and doing as healthcare professionals instruct, and others with a relatively laisse-faire approach to fever in their children. Indeed, parent participants in centre 2 spoke very negatively about another parent who they perceived to have endangered their child through poor adherence to central line infection prevention advice.

Interestingly none of these three parental roles were acknowledged within the healthcare professionals' focus groups. In fact, professionals identified very few roles for parents within the management of low risk febrile neutropenia. They did discuss the issue of non-presentation of a child with a fever (which is discussed later within the *Potential for realised discretion* theme) and thus implied that a key part of the parental role is in conveying the child to hospital immediately upon the detection of fever.

Another role that healthcare professionals assigned to parents was that of disrupting attempts to reduce therapy. Professionals anticipated that families might have a negative opinion of early discharge regimens and that parent groups could undermine service changes in this direction:

"1: one of the things that they used to do in [other centre] *is they'd look at the blood count and monocytes, if they were coming up then you know that within a day or so before they're not gonna be neutropenic and it worked to a point, but again of course its parents, parent group get hold of it and say "oh this is happening, that's happening, not happy with it", you have then got to change your policy because you're not going to get compliance, and that's a key problem for a lot of these things" (Centre 2, doctor)*

Juxtaposing this, the only time parents spoke about what future services they thought professionals might choose, they considered that it was healthcare professionals who were disinclined to allow early discharge and who were likely to delay the introduction of reduced

therapy regimens, Parents were understanding of this level of caution on the behalf of professionals, recognising the degree of responsibility felt by them:

"2: well they've got a lot of responsibility
4: it's on their shoulders isn't it if they discharge you
2: and something happens
Rest: yeah
2: that's a big deal really isn't it? So it's difficult for them…
1: yeah I can imagine it is… it's got to be…" (Centre 2, parents of under 13s)

Within these groups, participants identified a need to change the current balance of roles, with each centre discussing how responsibility would have to be shared between professionals and families. Healthcare professional participants raised concerns that although they would be willing to share responsibility with families, families might be unwilling or untrustworthy at times. Further, professionals were worried that blame for any adverse outcomes would be assigned to them, despite this renegotiation of responsibility (see *the quest for certainty* theme).

"2: … but I think it's also a balance between we're very paternalistic... we wanna look after our patients we don't want them to die which is understandable but also parents and families understanding that if you want to do this kind of thing you actually have to take a bit of responsibility yourself and we're saying that you know yes this is a low risk thing but there are still very occasional cases where it goes wrong so you have to make… I think we need to maybe move more to care agreements with patients than necessarily dictating what happens to them but there has to be a dual responsibility with us saying this is the evidence, this is what we think but if you're willing to accept that risk then... you know… then we can do this management pathway… if that's what people want to do…
6: do you think a lot of our families would take that on board [2]? I know some would… but I know a lot…
2: I don't think they would… no...
6: ...no… no…
2: and I think ultimately at the end of the day if it went wrong it would come back to us as our responsibility but we're kind of... that's the healthcare system that we're working in at the moment…people want choice but equally…
3: …no responsibility with it…." (Centre 1, doctors (2+3) and nurses (6+7)

The parental responses to possible increases in responsibility also varied. One parent in Centre 3 voiced her concerns twice about taking on more of this:

"2: I guess the difficulty is that if they have a rule that says you know, you listen to the parents, if the parents say we want to take them home and then something happens, I guess, is that on the hospital, is that on the parents…erm… I don't know" (centre 3, parents of over 13s)

However, in centre 2, parents drew attention to how the role of parent to any child involves enormous responsibility and stated unambiguously that they felt primarily responsible for each of their children. This was also the group who had described the additional care tasks that they had already taken on for their child with cancer and who therefore felt that administering antibiotics and monitoring febrile neutropenia did not constitute a significant increase in the responsibility that they bore.

Particularly mentioned within this subtheme of shared responsibilities were teenage patients and the challenges that they held for healthcare professionals. Throughout the material provided by healthcare professional groups, teenagers were viewed quite negatively, being felt to be most likely to be non-adherent to specific regimes and being unlikely to present with episodes of febrile neutropenia. In one group, the professionals spoke about how an early discharge regime might increase the likelihood of presenting to hospital following a fever. This links nicely to the discussions of non-attendance later in Chapter 7.

"I think for the teenagers that is slightly easier cos I think they're a lot more in control so if they're not feeling very well they won't tell anybody they're got… they're not feeling well they won't have their temperatures taken and they have a temperature and they'll be at home for an awful lot longer but if there's the option there potentially coming for one dose of IV antibiotics and then orals maybe as an outpatient then that might make them a bit more compliant with telling someone they're not feeling very well and having their temperature taken and getting in quicker
(murmur of agreement from other participants)" (Centre 1, nurse)

Mutual trust

The concept of mutual trust runs through these discussions of roles and responsibility. In order to redistribute their roles and responsibilities, healthcare professionals would need to trust parents and/or other professional colleagues to undertake these additional features, whilst parents would need to trust that professionals continue to fulfil the remaining aspects of care. Through the focus groups, trust was discussed in various ways.

For professionals, the degree of trust between groups appears dependent upon their knowledge of each other. Thus in centres where shared care is regularly practiced and thus professionals at

the PTC are more familiar with staff at the POSCUs there seemed to be increased trust in the POSCUs to be able to care for children with febrile neutropenia appropriately. Conversely, for centres with minimal shared care currently in situ, the trust in shared care to be able to manage this condition was less clear. This aspect of roles and responsibilities has already be discussed in depth earlier in the chapter.

For parent and young people participants, the levels of trust they had in professionals was also dependent upon their familiarity with them. Thus participants who had regular contact with their shared care centres tended to trust the care they received there, whilst those who attended POSCUs infrequently were not so confident in the professionals there (see also the *professional roles* subtheme). Meanwhile, when participants were managed on a different ward within their usual hospital or were cared for by agency (temporary) staff, they also disliked this experience.

When discussing their usual healthcare professionals, parents in certain groups, almost entirely in Centres 1 and 2, spoke about having complete trust: *"…we trust them you know 100% so you just go by what they say so if they say well you're here then you're here you know because you just trust exactly what they say…"* (Centre 1, parents of over 13s). Notwithstanding the statistical issues with this comment, this implies certainty in the trust which parents have in their child's clinicians. Although the conviction of this certainty was undermined at other points in the groups, such as when parents spoke about being unable to trust professionals to follow-up on blood test results and act on them accordingly (as discussed in the *quest for certainty* theme), generally discussions were very positive about the trustworthiness of healthcare professionals.

In contrast, healthcare professionals in these centres spoke rather negatively of the parents of the children they cared for (as discussed in the earlier subtheme about *Interactions between families and professionals*). Professionals struggled to believe that parents would appropriately present children for care, ensure the administration of medications and be able to identify any acute deterioration in their child at home. This may again relate to the issue of healthcare professionals feeling 'special', as allowing parents to manage children with a fever at home becomes akin to general paediatric management. This negotiation of the professional role seems not to be something which the participants were willing to consider.

Meanwhile, in centre 3 where significant shared care occurred, trust was moderated, parents felt more responsible for their child's care and placed less trust in healthcare professionals, often guiding them towards what they felt was more appropriate care. Similarly, professionals in the shared care units trusted families more to be in contact with them when appropriate and to be able to identify when their child became more unwell.

"1: I think they're very good at phoning … well I can only speak for my patients really… but I think they're very good at making contact and even if it's… I mean I suppose I always educate my families that even if they… even if you think your child is unwell… and you know your child best and they haven't got a temperature, you still need to call in and seek advice if you think something's wrong… so it is a bit about education…" (Centre 3, healthcare professionals)

The difference between centres, which appears at least partly dependent upon the degree of shared care, seems to correlate with the amount of control apportioned to parents. The polarity of trust in those centres where febrile neutropenia is managed in PTCs reflects the degree of control and responsibility given to parents of children with cancer. Meanwhile in shared care centres, where parents take on greater responsibility for educating staff, the amount of control they have over their child's care increases and enhanced levels of mutual trust are also seen. It is unclear which is the causative feature of these differences – do centres which relinquish more control to families foster increased mutual trust, or do centres with more mutual trust tend to increase the amount of control that families have?

Summary

This chapter has explore the two themes of *the quest for certainty* and *attaining mutual trust and sharing roles and responsibilities.* I have demonstrated how participants in all groups struggled with understanding, expressing and negotiating risk, the challenges in articulating and interpreting protocols and the various influences on preferences for care. Alongside this, I considered the relationships within and between families, professional roles, interactions between families and professionals and the mutual trust found between different stakeholders involved in the care of children and young people with febrile neutropenia. The next chapter will explore how these two themes come together through a process of negotiation to impact upon desires for future service design.

Chapter 7: Qualitative Study Findings – The potential for realised discretion and the impact upon future service design

Introduction

This chapter continues in the presentation of the findings from the qualitative study. It intends to build upon the two key themes from Chapter 6. In the discussion of the *potential for realised discretion* I consider the differences between professionals and parents in the need for discretion and desire for individualised care. I then discuss the challenges of negotiation within a spectrum of control before going on to explore non-attendance with febrile neutropenia as an example of when the spectrum of control is altered and risks, roles and responsibilities also change. Following on from this, I explore how the three earlier themes impact upon participants' desires for future service design, considering issues such as location of care and follow-up arrangements, before considering a particular case study as an example of how these themes might be applied. Finally, I present the participants' views on the poor consent rates seen in the studies in Chapter 3, with a view to further understanding the potential reasons for these rates of decline.

Potential for realised discretion

Drawing together the previous themes of *the quest for certainty* and *attaining mutual trust and sharing responsibility,* this chapter explores how patients, parents and healthcare professionals make decisions about the selection of a treatment path when children present with febrile neutropenia. This theme specifically focuses on the codes which relate to the need for discretion, a desire for individualised care, utilisation of a spectrum of control and the process of negotiation. Here, I also present the data relating to non-attendance with febrile neutropenia as a worked example of how these issues interconnect.

The need for discretion and individualised care

The codes entitled *need for discretion* and *individualised care* were used by healthcare professionals and families respectively. These concepts are similar in the fact that they express the need to respond to the social setting of patients and their families, including their proximity to emergency care, their comprehension of febrile neutropenia and its treatment, their prior experiences of febrile neutropenia, and their opinions about early discharge for their child; *"it's a bit like one size doesn't fit all does it?"* (Centre 3, nurse). However, the two codes differ in the participants' approaches to achieving these aims.

The *need for discretion,* used by healthcare professionals, encapsulates a desire to have a single over-arching protocol, where the management of children and young people with low risk febrile neutropenia is generally the same, but with small areas of flexibility to adapt to the specific situation. Furthermore, participants desired the ability to move away from the strict rigidity of the treatment protocol should they feel this was necessary without the risk of criticism from their colleagues.

The amount of discretion in adherence to the protocol felt to be appropriate by participants was clearly dependent on a professional's role and experience - those in shared care centres and junior doctors were deemed less appropriate to apply flexibility within the protocol (if at all) compared with consultants at the primary treatment centre:

> *"…you're gonna have people who don't potentially know these patients or the protocols properly… what they're doing… what you want them to do for that period of time when… you know... their consultants aren't actually around to make the decisions as well….so it's safer in that aspect…" (Centre 1, doctor)*

Meanwhile, when parents used the code *individualised care* they were communicating a desire for considerably more flexibility than the healthcare professionals suggest. Parents preferred that care be created to support the needs and choices of the individual child, and their family, without being constrained by a protocol. Instead options would be created with parents able to contribute at key decision points, such as timing of discharge and the nature of follow-up reviews for each individual episode.

> *"5: definitely… and also… I can't stress enough, its gotta be down to the individual parents…*
> *Rest: absolutely, yes*
> *5: you know I don't think can be a full gone conclusion*
> *2: and all those things, like we were saying, how long it's going to take to get here, if it…*
> *5: all the factors*
> *2: all of the factors need to be sort of listed…*
> *5: on a personal basis it's got to be done hasn't it" (Centre 2, parents of under 13s)*

The differences between the *need for discretion* and *individualised care* codes are understandable when the focus of participants is considered. Parents place emphasis on their own child and family, independent of any other, and thus express a desire for the care and service which would best meet that child's need during individual episodes of febrile neutropenia. Professionals meanwhile are compelled to consider the care of all children with febrile neutropenia, and as

such a pre-specified pathway may increase the efficiency of care, reduce the cognitive workload associated with each presentation and allow consideration of resource requirements and distribution across a whole service. Thus professionals meet the conflict of caring for individual patients and population health.

Negotiation within a spectrum of control

These two codes of *need for discretion and individualised care* connect to the *attaining mutual trust and sharing responsibility* theme through the code of *a spectrum of control*. The need for the amount of control given to each party within decision making to be flexible was discussed by all participant groups, with the degree of control desired changing over time and dependent on the situation, as discussed through the *preferences for care* section of Chapter 6, and explored later in this chapter. Some families may not wish to have control over decision making and this will also be discussed further within this section. Professionals also spoke about the degree of control given to the protocol, which links strongly with their discussion of discretion in relation to the protocol, and which I will cover first before moving to shared control between families and professionals.

Professionals within the focus groups expressed a desire to make their own judgements about a child's treatment, yet also a wish to have the responsibility for the situation relieved, for example by decisions being made by the protocol. Relinquishing control to the protocol in certain aspects of treatment allowed professionals to avoid the risks of criticism by colleagues or the dissatisfaction of patients and families, although parent participants did recognise this technique and certainly were frustrated by the rigidity of attitudes towards the protocols. The position of individual healthcare professionals upon this spectrum of control derived from their own personal attitudes, affected by the clinical situation, their past experiences and the centre culture surrounding this matter.

This feature of decision making, where a spectrum of control is desired, has been described within the literature and discussed in Chapter 2 in the *decision making theories* section, where some patients may wish to make all of their own healthcare decisions whilst others choose to relinquish this control to healthcare professionals, with many of these preferences actually being situation and mood dependent. Recognising this within healthcare professional decision making challenges the presumption that healthcare professionals and patients inherently make decisions in different ways. Although there are nuanced differences in decision making, many of the underlying features of clinical decision making may be similar.

Moving away from the influence of the protocol towards the spectrum of control between professionals and families, parents generally noted that there was minimal negotiation about the treatment of febrile neutropenia in current services:

> *"1: would it really be our decision in the end? Wouldn't be the hospital's decision whether we should… whether they're happy for us to go home and I'm sure both of us would say right great fine lets go home... yeah…" (Centre 1, parents of under 13s)*

This was seen across centres, with agreement between parents about their inability to influence the management of their child:

> *"1: I don't see that there's any negotiation with them.*
> *3: no there isn't" (Centre 3, parents of under 13s)*

Similar to the healthcare professional responses to the protocol, parents used passive language in which they and their child are the objects, rather than participants in the decision making process: *"we were sent home on the Sunday morning and we had to come on Tuesday and have his bloods done"* (Centre 1, parents of under 13s) Whilst much of this language was used without comment, seeming to be accepting of the paternalistic nature of the decision making, one parent expressed her anger about the restriction of her influence:

> *"…we go with what we're told to go with, we don't really, we don't have any control of how our children are treated at all... you know I mean at one point I said to them, I wanted them to stop the 6MP[10] and not give it to him because that is one of his worse chemos and I was like, he needs a break from it, but his bloods are fine so he's got to have it so why can you decide when he can stop having it but I'm not allowed to… you know and they ended up having to stop it because the side effects just took over" (Centre 3, parents of under 13s)*

Other parents gave examples of related decisions about their children where they also felt frustrated with their lack of control and the perceived irrationality of the healthcare professionals. These seemed to particularly occur in relation to situations where professionals insisted that the child be completely well before discharge but the parent felt that the behavioural aspects of their health would only improve at home. Thus parents felt they were not being listened to and that they were trapped in the hospital because of these cyclical requirements over which they had no control:

[10] 6MP or mercaptopurine is a chemotherapeutic agent.

"3: Has this happened yet? Oh right then well I can't let you go home then… but it will happen if you let him go home, he'll poo when he's goes home, he won't poo in hospital either, you know he does…" (Centre 3, parents of under 13s)

Elsewhere, parents expressed how they would need to consider the approach they took in attempting to negotiate with professionals, either through showing the evidence they had recorded of side effects or 'presenting their reasons' for wanting to take a different course to that suggested by professionals. Participants also discussed how the balance of the spectrum of control changed and developed over time. Initially, parents stated they had been anxious and unable to participate in decision making at the beginning of their child's treatment for cancer. However, those participants who had had a long relationship with the service began to question the paternalistic system of decision making and instead began to contribute to discussions about appropriate courses of action:

"3: … in the early stages the doctors said we just did it… I suppose now we're more confident to discuss with the doctors rather than just accepting whatever you're told to start with… its more open you know… we've been doing it that long so if we're not quite happy about anything or you know uncertain, is there another way of doing it? Can we go home? Can we do this?" (Centre 1, parents of over 13s)

This may reflect a decrease in trust, or doubt, in healthcare professionals, but is perhaps more likely to represent growth in families' understanding of risk, augmented by past experiences, and an increase of confidence in their own abilities, such that they are better able to discuss with professionals the options for individualised care for their child.

When professionals spoke about the involvement of parents in decision making, some acknowledged this imbalance in the power distribution:

"even though we think we give parents choice, I don't think we do, we set boundaries of keeping them in for 48 hours or five days…" (Centre 1, healthcare professionals)

However, they did express desires to increase care that was sensitive to families' needs and negotiated between the involved parties:

"2: I think if we're saying that we're working with our parents and children, as in child and family centred care, we should take their views on board, and if it's that they want to be in, I think that we should use that as an opportunity to strengthen their understanding and educate them and work towards it… and work towards what they

would think would be acceptable so it may be increasing… getting another home visit in… I don't know…" (Centre 3, healthcare professionals)

When healthcare professional participants were asked about how they negotiate with teenagers, the responses remained paternalistic and very little control was granted to teenagers. One group spoke about professionals giving teenagers set criteria that they must meet to be allowed home, whereas another participant stated that parental opinions were more important than the teenagers when they disagreed with their healthcare professionals, thus reducing situations involving teenagers back to a dyadic relationship between parents and professionals.

"Mod: what would your teenager's parents say?
1: "oh I don't think he'll manage, he won't take it" will be the first thing, and then they say, "well, will you take it", "yeah I will mum I will" so there will be this discourse between parents but eventually I think one has to listen to the parents because although they're teenagers they are under the jurisdiction of paediatrics so you'd have to work with the parent and again it boils down to convincing the parents that oral antibiotics are a good thing." (Centre 2, doctor)

The young people themselves generally stated that they would ask questions about their options, in similar ways to their parents, when trying to negotiate. Others spoke about using their parents as mediators to the discussion, choosing to relinquish this control to them:

"Mod: So, say the doctors were saying something and you didn't quite agree with what they were saying, they were saying go home and you didn't really want to, or they were saying stay in and you didn't really want to, how would you tackle that?
2: probably just tell my mum.
Mod: and expect her to…
2: talk to them about it.
1: when I've been told to like stay and I want to go, I've always like been… I've always asked if there's like, is there not another way…erm… and I get told no so I just do what the doctor says…" (Centre 1, Young people)

Throughout this theme, the challenges of sharing control are appreciated. Currently, the balance of power lies with the protocol and the professionals when deciding about treatment of children with febrile neutropenia, whilst parents and young people have minimal input to the care they receive. If parents were to be increasingly included within decision making, some of this control would be relinquished to them. In conjunction with this right to control comes the responsibility for any negative consequences of the decision taken. Parents may therefore become more aware

of the risks associated with the various options and the uncertainty involved in making choices which have previously been the domain of professionals. The variation in professionals' willingness to surrender this control and parents willingness to accept it has already been discussed.

Non-attendance with febrile neutropenia

One facet of febrile neutropenia which was discussed in all the healthcare professional groups and two of the three groups for parents of under 13s was that of non-attendance when a child had a fever, which goes against current professional advice. Exploring this aspect of decision making seems essential as it allows the understanding of a situation where the process takes a different direction from that planned by service providers.

Professionals' responses to families who do not attend with febrile neutropenia were almost exclusively negative:

> *"2: and as the treatment goes on, they… we have more families where we come across that…. We've….you know we visit weekly for the bloods and they've waited… they had a temperature the day before and they've waited because they know that they're…. you know their words… they would know if their child was ill…*
> *3: and then you have to try and put the frighteners on them" (Centre 3, nurse (2) and doctor (3))*

Meanwhile, parents spoke of these incidents in a more measured way. Some parents said they would always attend with a fever. Others, having considered the predominantly negative experiences of previous care, including the deleterious effects of admission on the social and psychological health of their child, along with their perceived risks from an episode of febrile neutropenia when their child appeared to be well, had previously decided to observe their child at home rather than immediately present them to the healthcare professionals. Indeed, one parent from Centre 2 spoke of the guilt she felt when she did bring her child to hospital in the following quote:

> *"1: whereas I knew… there were times when I knew and there were times when I sat there, when they were putting her on antibiotics, thinking I wish I hadn't come, I really wish I hadn't come… because I'm going to be in here 48 hours, she's not going to eat, she's not going to drink, it's probably going to end up being long…*
> *4: we'll be in here a week*
> *5: it's a week isn't it?*
> *1: yeah" (Centre 2, parents of under 13s)*

These parents were mostly those with prior experience of febrile neutropenia, who reported being dissatisfied with the duration of previous admissions and the impact which this had on their child and family. It is worth mentioning that the occurrence of these discussions reflects the good rapport and safe environment created within the focus groups for parents, where they felt they could discuss this relatively prohibited behaviour.

The differences in assessing the risks of non-attendance and the relative harms of hospital admissions may well explain the challenges in negotiation between professionals and parents, as they come from different viewpoints about these issues. Professionals may have distorted opinions of the relative risks of this non-attendance, as they may be unaware of a number of episodes in which children are not brought to hospital following fever. This incorrect 'denominator' for the risk means that they may then consider it to be a much more dangerous practice than the families who engage in it:

> *"1: I would like a study to be done on how many patients actually don't come in when they've got a temperature and they're neutropenic…*
> *1: and they're ill?*
> *2: no, they're not ill, they just get away with it. That would be quite interesting because I think… well there definitely are people who do that…" (Centre 2, nurse (2) and doctor (1)*

Furthermore, the issue of non-attendance also links to the need of healthcare professionals to feel in control and to have a voice in negotiating about a child's care. As the decision about when a child is presented to hospital is usually taken primarily by the parents, professionals are excluded from this. It is one of the few aspects of febrile neutropenia care where parents can exercise control and influence their child's care, as once admitted to febrile neutropenia services, parents can feel unable to escape from the protocol-driven pathway. If they do decide to attend hospital, parents are choosing to accept the benefits of a hospital admission but also the harms that come with it.

An alternative way to view non-attendance with febrile neutropenia is instead as a self-instigated reduced therapy regime, where families have made an active decision about this choice. Through allowing outpatient treatment to be negotiated following presentation with FN, parents and young people may feel more comfortable with presenting for assessment, as the response is more likely to be graded to the child's illness and there will be shared discussion of the different actions, rather than an immediate inpatient admission without negotiation. This is consistent with the findings presented in the *Interactions between families and professionals* subtheme in Chapter 6. To healthcare professionals the introduction of the option for reduced therapy regimes provides the benefits of more patients attending following a fever, and therefore

increased likelihood of detecting children and young people with high risk febrile neutropenia. Beneficially, it could also allow the assessment of the numbers of patients who did not previously attend following fevers, and professionals might have more exposure to patients with low risk febrile neutropenia who have a favourable outcome, thus bringing their personal risk assessments more in line with that of patients and parents.

Impact upon future service design

Participants within this study had multiple views about possible future service designs for children with low risk febrile neutropenia. Some of the ideas given were consistent across all focus groups; others were more specific to individual groups. However, they can generally be categorised into the codes of the preferred timings of discharge, follow-up requirements, the presence of clear criteria and practical issues of space and personnel, to gain agreement from multiple groups prior to any change in service provision. Through this section I aim to demonstrate how these views are linked to the earlier findings of the study and are influenced by the quest for certainty, mutual trust, roles, responsibilities and the spectrum of control.

Within the healthcare professional groups, each group had different overarching opinions about the timing of early discharge in low risk febrile neutropenia. The group from centre 2 were against early discharge as a potential future treatment strategy and the general attitude within this group is perhaps best summed up as *"…putting the dampener on it, but I'm not so sure I can ever see it happening anyway"* (centre 2, nurse).

Meanwhile, the centre 1 group were willing to consider early discharge as a potential future option, but seemed hesitant about changing in the near future and anxious about the rate of change being too rapid.

> *"1: I am certainly in favour of the very low risk ones bringing it down from 48 hours … but not saying send them home again in an hour if you've got blood results and everything and you… but …*
> *6: somewhere midway…*
> *1: somewhere… 8, 24… talk about sitting on the fence… but…" (Centre 1, doctor (1) and nurse (6))*

In contrast, centre 3 healthcare professionals were keen on the possibility of an early discharge model, tending to focus more on the positive aspects of a reduced therapy regime than the other groups: *"if you turn this on its head though... 86 children out of every hundred didn't have to spend 48 hours in hospital and I think that's good... that's a wonderful achievement!"*

The potential explanations for these differences between the healthcare professionals at the centres are multiple. As with all research, the findings may simply be a result of the particular structure of these specific groups, the individuals within them and the "snapshot" nature of focus groups as a methodology that records a specific place and date in time. However, there are other possible explanations which also appear credible, each of which relate to the specific cultural environment within which the participants operate. The positive attitude towards early discharge regimes of the healthcare professional focus group in centre 3 may relate to the fact that this centre already operates a significant shared care service. Therefore healthcare professionals are more familiar with relinquishing control over the care of patients to others and have established trusting relationships with parents and other professionals. They have experienced the risks and benefits of allowing a child to be cared for outside of the primary treatment centre. Furthermore, these healthcare professionals have already renegotiated their own roles in services for low risk febrile neutropenia to that of providing support to those administering the immediate care and giving advice remotely. Thus it can be seen that the change in practice for this group when redesigning their service to an early discharge regime would be smaller than for those in centres 1 and 2.

> *"2: so I don't think necessarily the PTC would change because a lot of the low risk febrile neutropenics are being managed by shared care… what would need to change is the shared care centres and particularly the community services… yeah… and… where they'd come in for review, how that would happen and who would review them….*
> *1: which mostly is set up anyway, isn't it? Because all our shared care patients have 24 hour access to the shared care centre and a pathway for being reviewed and not going through A+E…*
> *2: and I'm think I'm right in saying, all shared care centres… oncology children that go into a shared care centre have to be reviewed by a registrar or above so actually that's a… that seems fairly safe even if you discharged early… to my mind…" (Centre 3, nurses)*

Parental attitudes to the timing of discharge were also quite diverse. First, participants were keen to stress the importance of the initial review at the hospital following a temperature. They felt comforted by the fact that their child had been reviewed by a doctor and had been thoroughly assessed, reflecting the parental assessment of roles and of their trust in the clinicians caring for their child. The hospital visit also allowed parents to discuss questions that they had and to ensure they understood the best ways to care for their child at home, as a means of defining their roles and responsibilities. Their opinions about what would constitute best care after this point were heterogeneous. One family were keen to stay in hospital and be treated by the current protocol – their experiences are discussed further in the case study later in this section. All other participants

were keen to reduce the duration of admissions for febrile neutropenia by varying degrees. Some parents, especially those at centre 2 but also some participants elsewhere and one of the young people, wished to be discharged immediately following the first review. These families were generally those who had extensive experience of febrile neutropenia, whose children had been treated for cancer for some time. Other parents, and two of the young people, were a little more cautious and preferred to stay in hospital for the first 24 hours or so following a fever. This provided them with the reassurance that the child was not deteriorating and allowed review by a senior clinician prior to discharge. Finally, some parents voiced that the condition of their child, at the time of presentation would greatly influence their judgement about the timing of discharge. Thus, on some occasions, they might wish to go home immediately, whilst on other occasions they might prefer a brief admission. The right to use their parental acumen to make contemporaneous decisions was felt to be a vital part of individualised care. Thus it can be seen that parents had personalised responses to risk that were situation-dependent and that would then inform their choices about individualised care for their child.

Significantly, parents' views were more variable within centres. Where healthcare professionals tended to agree with each other within the groups, parents expressed a range of views. This may relate to the professional hierarchy, in which the views of the most high-ranking participants are assumed by the rest of the group, or may simply reflect that the professionals are pre-existing groups who are exposed to similar professional and cultural influences, and may thus be constrained in the choices that they identify. Furthermore, it also mirrors similar issues to those discussed in the *need for discretion and individualised care* subtheme, in which professionals preferred a single choice with small adaptations for each child, whilst parents wanted a more diverse range of options.

Recognising the individuality of decision making, participants clearly stated that they thought some parents might make more cautious decisions than those recorded in the study, highlighting younger parents, single parents, parents of newly diagnosed children, those without transport and those living further from the hospital as groups who might be more guarded about outpatient regimes. Although it was not possible to capture the views of young and single parents within this research, the other assessments made captured key social influences on decision making that have already been discussed.

> *"4: I mean to be honest, I suppose you've got young mums, single mums maybe that wouldn't want to take them home because obviously*
> *1: their situation might not allow it" (Centre 2, parents of under 13s)*

For parents, another key feature of future services was the route of administration of their child's antibiotics. Whilst healthcare professionals barely mentioned this other than to note the increase in staff members required to administer intravenous antibiotics in the community, the route of antibiotics was a significant matter for parents. Linked with the previously discussed focus on central lines, a major consideration was the presence of absence of a central venous line. Those parents whose child did not have an indwelling line were keen to avoid intravenous antibiotics where possible and universally opted for oral antibiotics. For parents whose child had a line, they showed little preference between routes of administration. However, the issue of who administers intravenous antibiotics came to the fore. Some parents were willing to learn to administer the intravenous medications themselves, and saw this as a further extension of their role in performing care tasks. Others felt that this should not be their responsibility and preferred for community nurses to administer the antibiotics at home, though they appreciated the staff time and costs of this option. This demonstrates again, the preference of families for individualised care which best suits the needs of their child and their family and the need for a negotiation of roles should current services change. These issues had not been appreciated by professional participants.

When thinking about the design of follow-up services following early discharge for febrile neutropenia, healthcare professional groups focused on two main models of care. The first was ambulatory care in which patients return to the hospital for regular review, with physical space and staff located within the hospital. This is consistent with more traditional healthcare service designs, but also has challenges as discussed in Chapter 4 where patients may struggle with the practicalities of attending the hospital frequently. At one point, healthcare professionals at centre 2 discussed an even more traditional approach, where patients would stay at a "home from home" located close to the hospital for the duration of their episode. This desire reflects the risk- and change-averse nature of the group at this centre, along with a distrust of parents to re-present their child in case of deterioration. The second suggested service design was that of community based care, where after discharge, families were visited at home to administer antibiotics and monitor progress. Participants in centre 1 discussed a model which bridged ambulatory and community based approaches through a "virtual ward":

> *"2: …where patients were still on your ward for 48 hours but they weren't actually in and if there was a role for ambulatory antibiotics as in like almost home antibiotics ward for the service where … and they do this in certain adult services… where the antibiotics are administered at home rather than in hospital and at 48 hours when the cultures come back you could then discharge them off your virtual ward…*

7: you know using the community team more which is why that…" (Centre 1, doctor (2) and nurse (7))

Most parents and young people leaned towards a more community based approach, with repeated visits to the hospital generally viewed negatively, although parents were happy to comply with these if necessary. This reflects the experiences of parents and young people in which hospital visits can be socially and psychologically disruptive for a child, as described in the *preferences for care* subtheme. The amount of community input felt to be appropriate varied from participant to participant though, which correlates well with *the need for discretion and individualised care* described earlier in this chapter:

"3: if it was more at home, it would be useful to have some point of contact that you can ring, so that you're gonna speak to somebody who knows what they're talking about
Mod: and would you want that to be just when you needed it, so you just ring when you want to talk about stuff, or would you want the staff to ring regularly?
3: I don't think there's a black and white answer to that one cos some people would need the regular contact and some wouldn't and for us, I think we'd prefer to get on with it, leave us to it, if we're not sure we'll ring up but other people wouldn't like that so…
5: I quite like the idea of a review…
4: well I quite like the idea of the Macmillan nurse popping in… I know that's all distance and... and time…" (Centre 1, Parents of over 13s)

In regards to follow-up, all participant groups touched upon the issues of isolation noted in the qualitative synthesis and considered how this could be reduced. They spoke positively about the input of community services and about telephone calls (both staff making calls to the patient and an advice line for patients to call in to) as methods to support families who were discharged early. The issue of contacting families with blood culture and test results, discussed in the *quest for certainty* theme, was also relevant here as a feature which families felt strongly should be part of their follow-up and would provide them with confidence that they were being supported by the hospital in the care of their child.

All participant groups spoke clearly about how, if patients were to be discharged early, families would need clear criteria for home management which should be consistently communicated, so as to establish their roles and responsibilities. For professionals, these criteria would predominantly relate to when a child needed to return to hospital, for example, with repeated fevers. For parents, meanwhile, the focus was somewhat broader. They did ask for clear criteria for reassessment, but also desired guidance about care of the child at home, including the rules

for social contact (eg school attendance, visits with friends) when receiving treatment for febrile neutropenia. Finally, parents spoke about the burden of medicines administration and how this demanded a lot of their attention. In the focus group for parents of over 13s, participants particularly spoke about the benefits of medication cards or applications to support accurate medication delivery at home. Healthcare professionals in Centre 2 also discussed the potential for at home monitoring of observations and the ability of applications to make these accessible to clinicians in the hospital environment.

The benefits of having clear criteria for treatment at home are that they give the appearance of controlling risks and provide a similar illusion of certainty as that provided by protocols. They are also a formal way of negotiating responsibilities between parents and professionals and provide a gradual transfer of control compared with current care. Thus all stakeholders may feel able to accede to the introduction of early discharge regimens.

A final concern about future services for healthcare professionals that was raised in Centre 3, perhaps due to their large shared care network, was the risk of deskilling professionals when they have reduced exposure to children with febrile neutropenia. The group discussed whether this was a reasonable fear to have and the factors which might mitigate against this. Future services should aim to modify this risk wherever possible rather than using this as a reason to prevent change to reduced therapy regimens.

> *"2: yeah… my only concern would be… and I'm really for it… for as less time in the hospital the better… my only concern would be… for… erm… perhaps two concerns… reduce… for parents feeling isolated in being… not even having shared care centre now… now they're literally on their own in the house… but that could be ameliorated to some degree by the support of community services and then the other thing is you will actually have reduced number of children in your shared care oncology centres and if they're not visible… erm… then that need… people's triggers to get trained in oncology would be less and you would have people who would have even less experience of oncology unless you're shoving out some of your sicker children which seems to be the case anyway… like bone marrows and things which never used to come…*
> *3: I don't think it'll reduce that much you'll still have people…won't you… you'll still have people… that aren't low risk…*
> *2: a lot of the inpatient work at shared care for oncology is low risk febrile neutropenia*
> *1: is your low risk ALLs… 48 hours...*
> *3: but you do get lots of line infections...*
> *1: yeah true*
> *3: and they'll still end up in… so I don't think… I don't think you'll really*

2: no… but the potential's there" (Centre 3, nurses (1+2) and doctor (3)

One factor which professionals felt would influence families' assessment of future service design was the timing of change to a new protocol. Each centre's group spoke about how the families who were treated during a change in febrile neutropenia policy might struggle with the reduction in admission time, but those families who came to the service after the policy change would be unlikely to have as many concerns about an early discharge strategy. Interestingly, no professionals acknowledged that they might also be included within this sentiment, with professionals who are established within the setting being more likely to struggle with a change in practice than those who come into the specialty at a later point.

"Mod: what do you think families would think if you started doing outpatients?
1: I think they'd be worried at first…
2: they wouldn't know anything different at the end…
3: the new ones wouldn't know any different, the ones in the transition would have to have their anxieties allayed wouldn't they and there would be some people who wouldn't wear it and some people who'd cheer…" (Centre 3, nurses (1+2) and doctor (3))

Notably, this issue of change over time was rarely discussed within the young people and parents' groups, though the group for parents of over 13s at Centre 1 did mention it briefly. The neglect of this concept in other discussions may be simply an oversight on the part of participants, or may reflect parents being more willing to change current services or more adaptable to changes which are placed upon them, as discussed in the *articulating and interpreting protocols* subtheme of the *quest for certainty* theme.

Finally, when discussing future services, healthcare professional participants spoke about the practical issues surrounding designing an outpatient or early discharge programme, and their main focuses were on the physical space required to allow this and the personnel needed to provide care, with participants generally feeling that more of both of these resources would be needed. These features were primarily discussed by Centre 1 and 2, with Centre 3 considering these issues as predominantly solved by their current shared care structure. The practical issue of personnel required for future care options is covered within the earlier *professional roles* subtheme of the *attaining mutual trust and sharing responsibility* theme.

Case study: diversity in family perceptions impacts upon future service design preferences

Though many participants had concerns about early discharge strategies and declared a wish for considered change without substantially increasing risks, there was one family who were

distinctive in their attitudes and opinions. The affected child of this family participated in the focus group for young people whilst both her parents attended the focus group for parents of over 13s. This family stated that they would prefer inpatient care for febrile neutropenia, that they enjoyed the time that they spent in hospital and that reduced therapy regimes would not be appealing to them. The possible rationale for these differences is explored within this section of the chapter, focused around the key threads of uncertainty, trust and control. I decided to specifically explore this case so as to better understand this more unusual perspective which represents maximum variation within the sample, considering the ways in which it informs the findings and provides more nuance to the analysis, as discussed earlier in Chapter 5.

This family appeared to have different attitudes to the risks and harms of different locations of treatment for febrile neutropenic episodes. They were particularly risk averse, and this was enforced by struggling to understand some key concepts of the statistics of risk:

> *"5: as soon as you started talking about percentages, erm… all that I think is I don't care if its only 85% chance of coming in, I wanna come in now because there's you know, a 14, 15% chance that something might change and I get a bit… I get a bit erm…. I prefer to then just be in hospital… like before when you were saying it I was thinking, oh yeah, at home, we do this but then when you start saying that you know, there's chances they'd need to come in, I think, just might as well be in…" (Centre 1, parents of over 13s)*

This heightened awareness of risk was balanced with a strong belief that hospital was safe and previously very positive experiences of being in hospital. Thus this family attempted to gain certainty through opting for inpatient care of febrile neutropenia.

Furthermore, this family spoke about how their child struggled to trust them but she, and they, had complete trust in the healthcare professionals caring for her:

> *"… she wouldn't take our word or even though we knew… we had to ring up and she could speak to a doctor or a nurse on the ward because we didn't know anything did we…we were useless. She needed them to be told… [laughs]"*

These polarised levels of trust, as discussed earlier in the chapter, may have been accentuated through high levels of PTC care and relatively low levels of family control in regards to febrile neutropenia. In fact, this family chose to relinquish their control about many decisions by allowing their child's consultant to make decisions about treatment. This case therefore demonstrates an extreme example of the issues already discussed within this findings chapter.

Poor consent rates to studies

For the final section of this chapter, I summarise the data in which participants were asked to consider the reasons why studies of reduced therapy regimens might have poor rates of consent. This section of the focus group discussions was intended to provide supplementary information to explain the poor recruitment to the studies included in the systematic review of Chapter 3. Although many of the findings already discussed relating to early discharge regimes were to be relevant to this decision, the decision making challenges for standard care and for trials were slightly different. Therefore, it is reasonable to examine this situation independently.

There was a spectrum of responses from the participants when asked why they thought the consent rates to the studies had been relatively low. First, the healthcare professionals in Centre 2 did not feel the consent rates for the studies were particularly poor and did not discuss reasons for patients to decline these kinds of study. The other focus group discussions pointed out a number of reasons why people may not be keen to be involved. Many of these mapped closely to the themes which feature strongly in the rest of this study.

Participants spoke about how the risks of taking part in a study of early discharge may be perceived to be too large for patients to be happy with:

> *"if you asked me that question and I thought that it was going to have some sort of effect on d) as in erm… she would be asked to go home because she's part of the study then I would have probably said no because as I said, when you start talking about percentage things if its 2% that something could go wrong and its d), she stays in, you know and I would prefer to do that than take any sort of risk, I want to take out every type of risk. So if I thought you were asking me to go into a study where… erm… this person will stay in and d) will go home because she's part of the study, erm… then I would've said no because again I would've just want you to go to what they already know and they already know and they've done for a long time…" (Centre 1, parents of over 13s)*

Accentuating this, the use of the word trial or study suggested to families that clinicians and researchers were unsure about the risks involved and increased the degree of uncertainty about a treatment: *"…I want the trial to be when there's nothing more you can do… and you know then you'd try anything…"* (Centre 2, parents of under 13s). These attitudes towards trial participation have been well-described in the literature.(180–183) Interestingly though, they contrast with the healthcare professional views within this study, where the idea of additional research was very

acceptable, and often requested by participants. The potential reasons for this professional attitude are discussed in Chapter 9.

Linked to the quest for certainty and consistent with the existing literature, participants also commented that they disliked the idea of randomisation of an episode of febrile neutropenia on arrival at the hospital. They spoke about how they would want to know what treatment to expect before they had arrived and desired a familiarity to the processes involved. The additional factors which correlate with the *quest for certainty* theme are that parents spoke about how the distance to travel to the hospital would influence their decision to take part, whilst healthcare professionals cited other studies of de-escalating therapy and stated that anxiety was the reason for reduced rates of consent.

Alongside the issues of risk, participants also spoke about how relationships influenced choices to participate in studies and healthcare professionals acknowledged their own influence on parents' choices. Parent participants spoke about their role in protecting their child and taking responsibility for decisions to enrol in research. A number of groups discussed how parents might feel guilty if they had enrolled their child in a reduced therapy study and then the child had had a bad experience. The parent might then have felt responsible for that outcome and therefore some families might choose not to enrol their child at the outset. However, participants also spoke about feeling guilt for refusing to participate in research because they appreciated the fact that other families had joined research projects in the past which were now benefitting their child.

Finally, linked to the *potential for realised discretion* theme, one participant spoke about how they had relinquished the control of their decisions to enter another study to their child's consultant as they felt that this was not a choice that they could make and because they trust her judgement (ultimately their child was not enrolled in the study). They proposed this might also be a reason for other families choosing not to take part in studies about the management of low risk febrile neutropenia.

Summary

This and the previous chapter have reported the findings of the focus group study. Chapter 6 explored how *the quest for certainty* influences decisions made by key stakeholders in paediatric febrile neutropenia. The discomfort of the uncertainty involved in risk assessments is balanced against the certainty implied by current protocols. The perceived benefits and harms of inpatient care that participants have previously experienced inform their appraisals of future treatment strategies. In *attaining mutual trust and sharing roles and relationships*, participants described

how interactions between these stakeholders play a key role in shaping perceptions of care. They spoke of the different roles within febrile neutropenia services and how these would need to change if outpatient or early discharge schemes were implemented, how mutual trust, though already present in some ways, would need to be fostered and strengthened and how responsibility would need to be redistributed between groups.

Chapter 7, details how having identified a need for discretion and a desire for individualised care, negotiating the spectrum of control allows achievement of the *potential for realised discretion.* I have discussed how non-attendance with febrile neutropenia is an example of where the prevailing model of professional control is disrupted and families use their own assessments of risk and mutual trust, along with their previous experiences, to make decisions about their child's care.

In the final sections of this chapter I have explored the way the earlier themes might impact on re-designed future services, with a focus on individualising care for children and young people. I have described a case which addresses many of the issues identified within the analysis, particularly relating to attitudes to risk and trust. I have also presented the participants views on the poor consent rates observed in the studies in Chapter 3 and how these relate to the remainder of the findings in the study. The following chapter will discuss these findings further, relating to them to the earlier literature explored in Chapters 3 and 4, considering the possible reasons for their occurrence and providing a reflexive account of the research process.

Chapter 8: Discussion of Qualitative Study Findings

Introduction

This chapter summarises the findings of the qualitative study and considers them in relation to the findings of the qualitative synthesis presented in Chapter 4. I outline possible explanations for the findings and the key threads that tie the themes together. The chapter continues with my reflexive considerations on the conduct of the study and the influences upon its findings. I conclude with a discussion of the strengths and limitations of the study. The implications of the findings upon policy and practice and the considerations for future research are discussed in the final conclusions chapter that follows.

Review of findings

This study involved 32 participants in 8 focus group discussions across three paediatric haematology and oncology centres in the UK and sought to identify factors involved in decision making about outpatient therapy in paediatric low risk febrile neutropenia. It identified three interrelated themes of the *quest for certainty, attaining mutual trust and sharing roles and responsibilities* and *the potential for realised discretion.* It then explored how these themes impact upon participants' preferences for future service design aiming to inform those involved in structuring services of the potential impact of changes in care.

Participants described a *quest for certainty*, in which they attempted to balance the uncertainty involved in understanding, expressing and negotiating risk with the illusion of certainty provided by strict protocols. Risks were assessed using both formal and informal stratification tools, overlaid with the emotional reactions to risk and experiences of risk within other situations. Understanding statistical expressions of risk proved challenging for patients, parents and healthcare professionals. Meanwhile, the benefits of certainty provided by protocols resulted in frustration at the strict constraints they mandated. The perceived benefits and harms of inpatient care that participants had previously experienced informed their appraisals of future treatment strategies and provided them with both more confidence in their risk assessments and a greater desire for flexibility within protocols.

Alongside this quest for certainty, participants' worked to *attain mutual trust and share roles and responsibilities*. They spoke about the relationships between families, professionals' roles and the relationships between families and professionals. The benefits of good relationships and the challenges involved in maintaining these were discussed within the subtheme of mutual trust. Parents and young people generally had high levels of trust in professionals, though this was

dependent upon their familiarity with them, and this trust could be undermined by issues such as failing to follow-up on blood tests. Professionals meanwhile spoke negatively of parents and raised concerns about some families' trustworthiness, though this response was more muted in the centre with increased shared care. Also within this theme, participants were clear about the difficulties in other relationships between groups, such as between the PTC and shared care units and with management. They discussed how these could impact negatively on experiences of febrile neutropenia. Furthermore, they acknowledged that roles and responsibilities would need to change to accommodate reduced therapy regimens; healthcare professionals would need to trust parents to undertake additional aspects of care, whilst parents would need to trust that professionals continue to fulfil the remaining tasks.

These two themes of the *quest for certainty* and *attaining mutual trust and sharing roles and responsibilities* were drawn together through the need for discretion and individualised care. Participant groups used these concepts to speak differently about how care should be structured for children and young people. Professionals wanted a general protocol with the facility for discretional change based on the individual patient. However, families sought a more flexible approach designed around their child and family, without the need for specific protocols. Though both of these concepts suggest a more personalised treatment strategy than currently, they suggest different methods of achieving this goal.

The process of negotiation was outlined and potential difficulties in redistributing responsibilities to families were voiced. The degree of control held by each party in decision making was explored and found to be unbalanced between families and healthcare professionals. The decision making involved in non-attendance with febrile neutropenia was considered as a counter example where control is reversed and families take the lead in managing their child's care. The *potential for realised discretion* along this spectrum, and influenced by the two earlier themes, forms a key feature of this work.

Finally, the means by which the three earlier themes come together to impact upon participants' perceptions of future service designs are reported. The differences between key stakeholder groups have been described and the challenges in providing a service that satisfies everyone are considered. This theme begins to explore many of the more practical aspects of future services and attempts to inform those involved in designing these about the conflicting opinions between groups along with why these might occur.

Relation to the existing literature

In this section I explore the ways in which the findings from the qualitative study mix with the broader subject-specific literature which has been systematically and extensively explored within the qualitative synthesis described in Chapter 4. Locating this research within the existing narrative about early discharge enables identification of the similarities in this field, whilst also highlighting the areas where this thesis contributes new and informative material that extends and adds nuance and depth to the preceding works.

Many of the key similarities and differences between the synthesis and the new data relate to practical logistics and social issues that have been outlined within the *preferences for care* sub-theme in Chapter 6. There are additional features to address here. I also discuss how the study relates to the decision making theories discussed in Chapter 2, reviewing correlations with the psychological and sociological literature.

Many of the key factors from the qualitative synthesis were confirmed and expanded upon within the qualitative study. The complexity of decision making has been described in detail in Chapter 6 and a number of the influences confirmed, as I discuss further in the following paragraphs. The code relating to fear within the qualitative synthesis has become more nuanced in the qualitative study.(151,152,157) Although fear is described, the participants in the study spoke more clearly about anxieties and worry, reflecting a more complex emotional impact upon their perceptions of early discharge. Furthermore, the feature of timing also played a role. Consistent with the studies in the qualitative synthesis, participants clearly described the influence of timing of febrile neutropenia within a child's treatment for cancer, and spoke about how previous experiences of febrile neutropenia had changed their views over time.(151) This study also adds the perspective of healthcare professional experiences, which was largely absent from the synthesis.

The social and emotional impacts of an admission for febrile neutropenia were also identified but have been re-structured and greater weight given to the roles and relationships between families and healthcare professionals. This most likely reflects the long term nature of relationships between children with cancer and their families, and the healthcare professionals who care for them compared to some of the other conditions included in the synthesis. Thus the development of mutual trust within these relationships plays a greater role than in the settings included within the qualitative synthesis.

The established nature of relationships between participants in this study also explains why the continuity of care code from the qualitative synthesis does not occur in the qualitative study. Participants in the study know that their care is generally provided by the same small team of

professionals and as such the concerns about being known to the professionals providing an early discharge service are diminished. Continuity of care within the population of this study seems to have been taken for granted by the participants.

Elsewhere, the study adds to the synthesis in different ways. The subtheme of negotiation and a spectrum of control arose iteratively from the study. Its appearance is probably related to the prolonged nature of the relationships between these families and the professionals, as those with a longer duration of treatment became more aware of their lack of control and had an increasing desire to negotiate a change in care. Furthermore, the parents included in this study already carry a considerable care burden in relation to their child's disease, and thus view themselves as having a greater role in the provision of treatment. As such, it can be seen that they may be more likely to want to be included in decision making than many of the families included within the studies in the qualitative synthesis.

Compared to the Diorio et al study of parental preferences for treatment of paediatric febrile neutropenia included in the qualitative synthesis, the parents included in this study were generally more positive about reduced therapy regimens.(151) This may be due to a number of different factors. First, and perhaps most importantly, the Diorio et al study asked participants to choose between four potential service designs for low risk febrile neutropenia. The outpatient service design was therefore pre-specified with no opportunity for participants to discuss how they would ideally like their child to be treated. In my study, participants were asked to talk about how they would like febrile neutropenia services to be organised. This may have facilitated acceptance of outpatient care, but may also indicate that services need to be co-designed to satisfy patients and families. Indeed, if I had introduced a specific outpatient regime for discussion, I may have found similar responses to those of Diorio et al.

Another factor that may have resulted in the different findings between this study and Diorio et al is in their current treatment regimens. Although Diorio et al do not give precise details of how children in their centre are managed for febrile neutropenia, their paper suggests that this is with inpatient treatment for over 48 hours, as they describe a 48 hour admission as an early discharge regime. For the centres in my study, 48 hours was considered to be a standard admission length rather than an early discharge option, so the participants may already have been used to a shorter stay in hospital. This observation lends support to the hypothesis that participants' current duration of stay for febrile neutropenia may impact upon their perceptions of reduced therapy regimes, with gradual reductions in length of stay perhaps being more acceptable than larger changes.

On a slightly separate note, it is reassuring that Diorio et al also struggled to recruit parents of teenagers. This suggests that the problems that I had with this group are related to intrinsic factors within the lives of families with children of this age and in their experiences of treatment for cancer. Future studies may wish to consider alternative methods to capture the views of this group, perhaps through telephone or online interviews and focus groups.

The issue of resilience discussed within the qualitative synthesis (Chapter 4) was less evident in this study. Although trust and confidence in healthcare professionals was a key theme in the study, participants spoke less about resources than had been identified in the qualitative synthesis. Financial pressures did play a role in the study findings but participants spoke little about their social and psychological resources, and where they did discuss them, they were framed differently to the synthesis. This may relate to the fact that all parent participants were in committed relationships and thus received social support from their partners.

The absence of the resilience theme in the study may also reflect the fact that parents, in particular, were less likely to see early discharge as an adverse event, instead framing it as a potential tool to improve the adverse nature of an admission for febrile neutropenia. Alternatively, families may have already developed significant resilience during the period of their child's diagnosis with cancer, and thus their perception of their need for increased resilience may have altered. This would be consistent with evidence in the study about the perceived risks of febrile neutropenia.

To locate this research within some of the broader literature, findings of this study echo, in some ways, the Health Belief Model described by Rosenstock, Hochbaum and Kegels described in Chapter 2.(74) I have found that the perceptions of risk and the patient's known experiences of admissions for febrile neutropenia have an impact upon their opinions about early discharge. Although families of a child with low risk febrile neutropenia are unlikely to have had cues to action before their child's diagnosis with cancer or from mainstream media outlets, they can be influenced by information from healthcare professionals and other parents within paediatric haematology and oncology services during the course of their child's cancer treatment. Furthermore, my research has outlined the modifying factors of centre culture, past experience and personal preferences for control of decision making, when thinking about reduced therapy regimens. Thus, the Health Belief Model captures some of the key features of the work I describe. However, it can be seen to be incomplete when applied to this study, as it does not capture the relational nature of decision making in chronic conditions, where trust between different stakeholders plays a vital part and where different roles and values must be negotiated before deciding upon an initial course of action. It also does not capture the influence of culture, including the direct pressure of protocols but also the more subtle normative values and

assumptions of society when making healthcare choices. Thus this thesis adds nuance and detail to the Health Belief Model when thinking about the management of low risk febrile neutropenia.

Interpretation of the findings

I will now discuss certain aspects of the study and potential explanations for the findings in detail. In particular, I will consider differences in focus, paternalism and determinism, and shared decision making.

Differences in focus between families and healthcare professionals.

Throughout the study, the differences in focus between families and healthcare professionals became apparent in a number of distinct ways. First, participants had different degrees of focus concerning health. Healthcare professionals had a limited focus on the physical health of a child during an episode of febrile neutropenia and almost entirely focused on the prevention of an intensive care admission or death of a child. Thus their focus for individual children was relatively narrow, though they had a broader focus on the number of families impacted, taking into account their service population and the variety of different patients with whom they come into contact. Parents meanwhile focused on the broader aspects of child health, including the side effects of possible interventions, social and emotional impacts and wider family health. However, parents mostly concentrated on their individual child. Though they did discuss how others might differ in their opinions and desires when considering future services, it was the optimum regimen for their child and family that was put forward most strongly. Thus it can be seen that the priorities and objectives for future care were different between families and healthcare professionals. As discussed within Chapter 6, this is understandable given the responsibilities of these two different groups.

Linked to this difference in focus on health, another distinction came when participants discussed negative consequences of care. Throughout the focus group discussions, participants used 'horror stories' to illustrate the difficult and distressing aspects of being involved with children and young people with febrile neutropenia. 'Horror stories' have been described as a method which participants employ to demonstrate key points within focus group discussions, forming an important part of their narrative reconstruction and assuming symbolic meaning relative to their beliefs and priorities.(168) Horror stories should thus be given significant thought by the researcher.(168) When considering the horror stories told by healthcare professionals within this study, they almost always discussed bad outcomes such as intensive care admission or death as their primary adverse experiences of febrile neutropenia. Meanwhile, parents focused much more upon their experiences of poor care, such as certain encounters at shared care centres, delayed identification of positive culture growth, difficult venous access issues and the failure of

professionals to identify what they perceived to be an unwell child. This again highlights the differences in consideration of health between the two groups, whilst emphasising the fact that many parents have no experience of death or intensive care admissions related to febrile neutropenia. Thus their perceptions of risk of these events were somewhat different to those of professionals who often do have experience of these due to high risk febrile neutropenic episodes. To young people and parents therefore, who experience more of the burdens of inpatient febrile neutropenia care, it is the failures to provide care focused on a holistic definition of health which play a significant role in their experience.

It is important here to note that these differences in focus further inform the interpretation of the findings of the systematic review in Chapter 3. This review used outcomes that can be seen to more closely reflect the focus of healthcare professionals – intensive care, death and healthcare service usage, as opposed to those of the families receiving care. This reflects the common findings in the literature that traditionally studies (which eventually form part of systematic reviews) are designed by professionals to detect these outcomes and fail to take into account the experiences of care that families value more highly, meaning these outcomes are also hidden in secondary research. This qualitative study highlights, particularly in relation to the *quest for certainty*, the way in which stakeholders then weigh the information provided by the systematic review differently, based on their prior experiences and consideration of other benefits and harms. This indicates that study design should involve more public and patient involvement in the outcome setting stage, but also that the interpretation of quantitative research should involve discussions with patients and families so as to gain more insight into the different viewpoints on specific statistical findings.

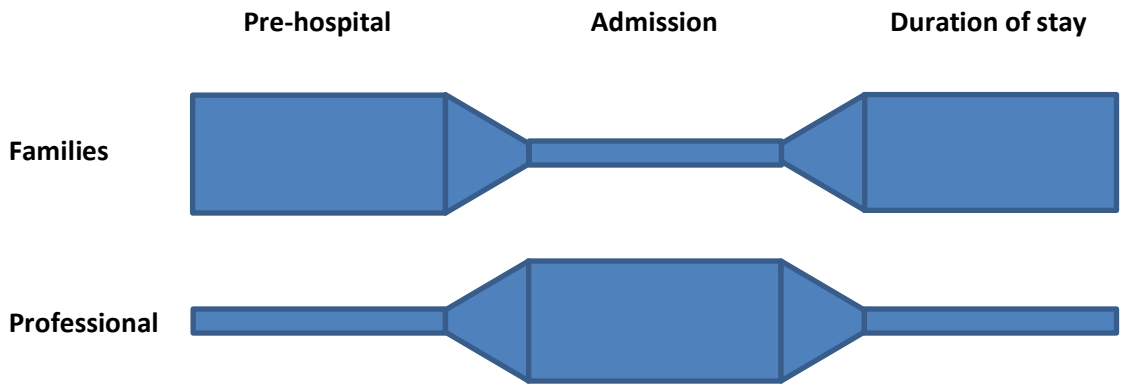

Figure 14 – Schematic comparison of family and healthcare professional narrative focus during an episode of febrile neutropenia, where the height of the bar represents the weight given to each timeframe within the episode

The final divergence in focus that was seen within this study was in the narrative weight given to each phase of a febrile neutropenia admission (Figure 14). Young people and their parents vividly described the period of time leading up to the presentation of a child with fever, including attempts to prevent infections, the emotional stress of anticipating a fever and the practical and logistical implications of attending the hospital. Following arrival at the hospital, they barely mentioned the assessment and admission of their child to their local centre, but then focused on the duration of the hospital admission and the interval between admission and discharge as a key feature of their experiences. In direct contrast to this, healthcare professionals said very little about the pre-hospital stage. Instead their narrative focused on the assessment of a child presenting with febrile neutropenia and the initial management of these patients. In each group, the healthcare professional groups did not review the management of the later phases of the admission until prompted. This waxing and waning of focus within an episode of febrile neutropenia is pictorially represented in Figure 14. Thus it can be seen that healthcare professionals may not consider the timing of discharge, or the changing of this, to be a particularly important issue in the management of febrile neutropenia. This may give further information, combined with that provided earlier in Chapter 6, to explain why this aspect of care has not been modified, despite the increasing evidence of safety and the potential benefits for patients. Through performing this study and then disseminating and promoting its results I hope to stimulate healthcare professionals to think more about this stage of febrile neutropenia care and to highlight the material available to them to facilitate future decision making.

The influence of paternalism and determinism

Historically, paternalism and determinism have shaped healthcare culture and both play key roles in illuminating why the key themes of certainty and control run through findings of this study.(194) In the deterministic worldview which was predominant in early medicine, the role of the physicians was to establish the definitive causes and treatments for disease. The clinician should and would strive to control each aspect of a patient's health so as to have control over their outcomes.(194) This focused viewpoint does not allow for the uncertainty and risk that is inherent in contemporary medicine, where diagnostic tests are recognised to be fallible, risky behaviours do not necessarily result in harm and treatments may have high numbers that need to be treated so as to obtain individual patient benefit. Determinism inspires and promotes the creation of certainty, and thus where this cannot be achieved, the illusion of certainty can be considered a reasonable replacement as it provides a sense of control and reassurance within difficult situations. Understanding statistical risks and making decisions based upon them is not prioritised, instead: *"The goal is certainty, rather than learning how to live with uncertainty"*.(194) In low risk febrile neutropenia, as in all healthcare, there is no certainty. The data shown in

Chapter 3, and discussed within the focus groups, shows that there is low (but not no) risk of serious safety events, regardless of the location of care, with variable rates of treatment failure dependent upon the timing of discharge from hospital. Sharing these risks, acknowledging the uncertainty and engaging in shared decision making based on patient and healthcare professional agreed values, is a difficult but necessary step to improving patient care in this area.

Historically, healthcare professionals, particularly physicians, were considered trustworthy and reliable. They could be depended upon to make the 'right choice' and deliver decisions about patients without significant discussion. Within this paternalistic paradigm and culture, patients were not informed of the risks and benefits of treatment options and would instead be told the 'correct' choice of action. This was seen to be in the best interest of the patient, who was believed unlikely to have access to the specialist knowledge required for medical decision making. Although they did express certain frustrations about specific aspects of care, parents and particularly young people in this study appeared to be relatively accepting of their lack of control over febrile neutropenia decisions. This may link with the implicit amounts of control within their social roles. For example, young people may be used to having less control in negotiations with their parents or their teachers on a day to day basis, which then transfers to their acceptance of reduced control over healthcare decisions. Furthermore, for both them and their parents, the historically paternalistic culture associated with medicine means that they may be culturally influenced to relinquish more control in situations related to healthcare than in other areas of life. This may be even more prominent given their cancer diagnosis, which also conveys many social, emotional and cultural influences upon their responses and behaviours.

Patient choice and shared decision making

Issues relating to patient choice and decision making run throughout this thesis, and particularly through this qualitative study, and so I will discuss this further within this segment of the chapter. As has already been covered, some participants within the study did not want to take on the responsibilities associated with making their own choices about treatment of febrile neutropenia. Indeed one family had made an active choice to devolve decision making to the healthcare professionals. Other families were very keen to have a say in their child's care, and wished to take more control for the decisions made when their children had febrile neutropenia. Although many of the potential personal reasons behind these choices are discussed in Chapter 7 there may also have been social and cultural influences upon this decision. Of note, the families participating in the qualitative study will generally have been exposed to the current healthcare narrative regarding patient choice, though this was not explicitly mentioned within the focus group discussions. Whilst it is not clear that this narrative made differences to individuals' attitudes about who should make decisions about patients' care, it may be that the balance between those

who wish to make decision and those who do not, on a societal level, may have been altered by the cultural and political background related to patient choice. Thus it may be that the proportion of families wishing to play an active role in decision making is increasing over time. Further issues related to patients choosing to let professionals make their healthcare decisions were discussed in Chapter 2, and will also be considered in the following sections about shared decision making in febrile neutropenia care.

Shared decision making has been suggested as an appropriate next step in overcoming paternalism and determinism, recognising differences in focus and beginning to respect the rights of patients to have autonomy over their healthcare decisions.

In contemporary medicine, shared decision making is becoming increasingly valued. With the current political climate prioritising the right for patient choice and involvement in their own healthcare and the 'nothing about me without me' agenda, shared decision making is a prominent feature throughout policy.(199) Indeed, the Department of Health's policy document 'Equity and excellence: Liberating the NHS' outlines a strategy in which one of the first statements is that *"Shared decision-making will become the norm"*(200). Supporting shared decision making has also been included within the duties of a doctor outlined by the General Medical Council:

> *"Work in partnership with patients.*
>
> - *Listen to, and respond to, their concerns and preferences.*
> - *Give patients the information they want or needs in a way they can understand.*
> - *Respect patients' right to reach decisions with you about their treatment and care.*
> - *Support patients in caring for themselves to improve and maintain their health."(59)*

There are numerous definitions of shared decision making in healthcare. However, the essential features of all consider sharing of information about treatment options, their potential risks and benefits, identifying the patient's key values and priorities and then patient and professionals working together in partnership to select the most appropriate option for the individual, based on the best available evidence.(201) As discussed in Chapter 2, in the case of children and young people, this process is complicated by the presence of three parties. Many of the challenges of achieving true patient choice related to children have already been discussed and explored (see Chapter 2).

Despite the political and cultural drives to increase shared decision making, it is often not fully optimised. In many cases, medical paternalism, including retaining power over information and control over treatment pathways, remains the predominant method of decision making.(87,202)

Elsewhere, professionals may feel that they engage in shared decision making, but research has found they often do not engage in discussions about patient values or providing accurate representations of options and risks to patients.(203) As such, patients still frequently report a desire to receive more information and to be more involved in decisions about their care.(204) This is exacerbated in paediatric decisions by the issues discussed in Chapter 2.

It has been suggested that shared decision making is most suited to particular situations in which there is no clear evidence of the most appropriate course of action, and where the patient's values or preferences might play a more important role in resolving this equipoise.(83,87,202,203) In low risk paediatric febrile neutropenia, this could now be considered to be the case for the decision about timing of discharge from hospital. Although previously there has not been sufficient data to support this as a 'preference-sensitive' decision, this thesis provides material suggesting that serious safety events are not obviously affected by the location of care and as such individualised judgements about other treatment failure features and patient preferences become more prominent. Furthermore, this thesis provides clarification on the rates of treatment failure at different discharge time points and may therefore assist in shared decision making by facilitating more accurate discussions of the associated risks of the various options. Specifically, there has been a drive to use shared decision making *"where the balance of risks and benefits varies widely in different medical, social and health care situations".*(203) Given the findings reported in Chapter 6, it might be considered that patients' social circumstances, along with the individual psychological impact of admission, might lead to a different balance of risks and benefits for each family.

Finally, shared decision making is particularly useful for patients who are involved in increased numbers of healthcare decision and who have prolonged contact with services over time. Shared decision making provides a method for empowering and enabling patients, within partnerships with healthcare professionals involving mutual trust and autonomy. In children and young people with cancer, shared decision making could be achieved through continuing discussions about the management of their febrile neutropenia. The priorities identified and skills developed through this situation can then be transferred to other healthcare decisions for these patients.

I therefore argue that shared decision making for children and young people with low risk febrile neutropenia is the most appropriate approach for making decisions about timing of discharge. This would involve sharing risks with patients and their parents, discussing their priorities and values, including past experiences, before negotiating a decision about how to manage this episode of febrile neutropenia. It would facilitate a redistribution of control and appreciation of each other's roles, responsibilities and areas of focus. Furthermore, this process would improve communication in general, allow young people to feel included in the process as much as they are

willing and able to, and might encourage clinicians to use the approach in similar decision making situations. I will discuss further how this might be achieved in Chapter 9.

Before implementation can be planned, there are many challenges that stand in the way of implementing shared decision making which must be considered. These can include professionals not knowing the risks associated with various options, not understanding the statistics shared in the literature, or being unable or unwilling to communicate these. In addition to this, although they may be encouraged to discuss uncertainty with patients, professionals can feel that sharing their lack of certainty may jeopardise their patient's trust, thus undermining the paternalistic nature of medicine.(87,205) In contrast to this, others have proposed that through sharing their lack of certainty, professionals may instead help to create a more balanced power dynamic with patients and thus allow a more equal balance in the decision making.(83)

Following this discussion, patients, having been presented with the risks, may weigh these differently to the professional and autonomously choose the 'wrong' option.(87,194,206) Indeed, a number of studies have found that patients who are enabled through a shared decision making process to make choice about their healthcare, often reduce the amount of intervention that would have been suggested by clinicians. The lack of paternalistic control over such decisions can be disconcerting for clinicians and wrests some of their own sense of certainty from them through the unpredictable nature of patient choice, particularly when they feel that there is a 'correct' way to manage the situation.(87)

For patients and families, concern about making the wrong choice is also prominent, as evidenced in this study. This concern was particularly strong for parents compared with patients, which reflects previous research that making decisions about your children is more stressful than making decisions for yourself.(84) Participants worried about the potential negative effects of particular choices and some were concerned about the increased accountability that would come with a choice for reduced therapy options. This expression of a Damoclean sword, in which the power to make decisions about their child's care also came with the responsibility for any adverse outcomes, was more prominent for some participants than others.

Another challenge to the implementation of shared decision making is that professionals may feel that they can assess which patients wish to participate in shared decision making and which might prefer a more paternalistic approach, therefore some participants might not be offered the opportunity to share decision making and are therefore prevented from accessing its benefits. Although the literature suggests that certain groups are more likely to want to participate in healthcare decision making, as discussed in Chapter 2, it is not possible to predict this with certainty. Certain factors can influence the desire for shared decision making and the most

relevant for this study is that of trust. Kraetschmer et al found that patients who show blind trust in their clinicians (defined as an average Trust-in Physician Scale score of 5.0) are more likely to be passive in their decision making, where as those with moderate to high levels of trust prefer a shared decision making approach.(207) This seems to fit with the findings of my study, particularly in the example of the outlier case, where complete trust resulted in a more passive approach to decision making. Meanwhile, most participants had high levels of trust in the healthcare professionals caring for them along with a desire to shared decision making about discharge in low risk febrile neutropenia. Furthermore, participants with increased knowledge about febrile neutropenia and increased experience of this condition tended to be more keen to be involved in decision making, which is also consistent with Kraetschmer et al's findings.(208)

Linked to the issue of patients' trust in professionals, others have looked at how professionals' trust in patients may impact upon shared decision making. Here, research shows that professionals who trust their patients and believe in their competence to understand and make decisions are more likely to engage in shared decision making.(208) This also seems to hold true in my study, in which Centre 3, who showed a more positive attitude to parents and their competence felt more willing to engage in discussions about early discharge. In Centre 2, where professionals spoke relatively negatively of the families in their care, there was less willingness to consider a change in practice.

Although it is important to identify those patients who wish to be involved in shared decision making, it is also vital to recognise that involving all patients in shared decision making can have positive effects on a number of outcomes, regardless of preferences. Participation in shared decision making has been found to improve patients' quality of life, increase knowledge, and reduce the degree of decisional conflict experienced.(206,209) Though few studies have found strict clinical benefits, this is perhaps not the aim of shared decision making, given that these are usually situations with equipoise.(210) Instead, it might be considered that patient and family centred outcomes are as important as purely clinical ones, linking with the differences in focus between professionals and families.

Another challenge frequently discussed in the literature about shared decision making is the pressure of time.(201,202,205) In the UK, where there is a culture of efficiency and increasing demand on healthcare services, including paediatric haematology and oncology, any increase in the time taken to see a patient can be viewed negatively.(202) Professionals feel they struggle with current workloads and so adding anything which is perceived to increase their time demands may be avoided. In the case of febrile neutropenia, this pressure may be particularly acute as clinicians know that outcomes for children are improved if initial antibiotics are administered within 1 hour of presentation. If professionals feel that all aspects of discussion and decision

making need to be performed at once, then they may attempt to perform the quickest pathway possible, which is perceived to be paternalistic, protocol driven care. These time concerns can be addressed in two ways. First, the literature currently does not provide clear evidence of how much time is involved in facilitating shared decision making.(209) However, for decision aids (which will be discussed further in Chapter 9), a recent systematic review found that their introduction increases the duration of consultations by a median of 2.55 minutes (range 8 minutes shorter to 23 minutes longer).(211) Having this information may help professionals to realise that shared decision making does not seem to greatly increase the time taken to make decisions. Furthermore, time spent in shared decision making discussions may be compensated by time saved on future discussions about care, or through inpatient treatment, should the family choose a reduced therapy option. Secondly, healthcare professionals in paediatric haematology and oncology could be encouraged to reduce some of the felt time pressure by uncoupling the decision to administer the initial dose of antibiotic and the decision about ongoing care of febrile neutropenia. In this way, the first decision would need to be made within 1 hour but the second decision could then take as much time as necessary to meet a shared choice. Methods to facilitate the second decision could be developed and will be discussed in the following chapter.

Within this section, I have explored why shared decision making is now particularly important in discussions about low risk febrile neutropenia. I have discussed some of the challenges to introducing shared decision making to this condition, whilst relating these back to the findings shared in Chapter 6. There are a number of methods proposed to increase shared decision making in healthcare and these will be discussed in the following chapter, along with the other practice and policy implications of this work.

Strengths and limitations

This qualitative study has a number of key features which allow it to add to and develop the previous literature in this area. In particular, it involves new voices in the qualitative discussion of febrile neutropenia management. It provides data on the experiences and perceptions of young people, their parents and healthcare professionals involved in paediatric haematology and oncology services. Furthermore it facilitates a deeper consideration of the disease-specific factors relating to febrile neutropenia which influence stakeholders' experiences and inform their decisions about future care.

The inclusion of multiple centres within the study allows for an understanding of the impact of service design and centre culture upon the perceptions of management options. As such, I have been able to explore features which would not have been apparent had this study simply explored the experiences in a single centre. This was facilitated by working in a country in which

there is considerable range in the provision of care for febrile neutropenia and through the recruitment of Centre 2 during its change in febrile neutropenia protocol. Without doubt, the success of this study was made possible through the existence of a strong network of paediatric oncology and haematology services in the UK and more specifically through the availability of the regular febrile neutropenia audits performed by the Children's Cancer and Leukaemia Group. (40,42)

Another particular asset of this work lies in its reflexive approach. I hope that this provides for a transparent account of the work performed and enables the assessment of the credibility of this thesis. Through clearly explaining the decisions made within the design and execution of the study, I aim to allow the reader to assess the extent to which this relation of the findings captures the participant experience and provides possible underlying explanations for the data.

Linked with this, the limitations of this study have been discussed openly and reflexively through the previous chapters. The majority of the challenges relate to the groups which proved difficult to recruit, including some demographic groups and those who have a limited ability to communicate in English. This reflects broader problems within the research community of engaging with participants from social disadvantaged groups and those from multi-cultural contexts.(165,168) In addition, like many other research projects, this study struggled to engage with the young people in its target population. The implications of these limitations have already been discussed extensively in Chapter 5 and I hope have been limited as far as possible by the active responses made to these challenges. These resulted in improvements in recruitment over time and thus have helped to reduce any shortcomings. Future studies with these populations may wish to integrate other methodologies, including interviews or online focus groups for those who do not wish to participate in face-to-face groups.

A further limitation lies in the inclusion of only English centres. Despite my intentions to include centres elsewhere in the UK, this was limited by the small numbers of PTCs outside England and the purposive selection strategy discussed in Chapter 5. Given the strong networking between all centres across the UK through the Children's Cancer and Leukaemia Group, the treatment strategies and ethos of these centres are unlikely to be vastly different from those included within this study. However, I recognise that health services have been devolved to other UK nations and thus the political management of healthcare is different in Scotland, Wales and Northern Ireland. Furthermore, particularly in Scotland, patients frequently have a long distance to travel for their treatment, exceeding that of most English centres. As this study found that the issue of duration of journey to the hospital did impact upon participants' perceptions of care, those families living in particularly rural areas of Scotland may feel less comfortable with reduced therapy regimens and thus care should be taken when planning services for this population.

Finally, the small size of some of the focus groups may be considered a limitation by some academics as they may lead to relatively restricted discussions and the presence of particular character traits, such as shy participants or dominating participants, may have a more acute effect on the group. However, for others, smaller groups of three to six participants have been purported by others to be beneficial in focus group discussions involving complex subjects, of which febrile neutropenia is certainly one, or in groups of experts, such as the healthcare professionals in this study.(165,166,212)

Reflexivity

The methodological decisions relating to the qualitative study have been explored and evaluated in Chapter 5 of this thesis, whilst the procedural influences on the work were highlighted where necessary in Chapters 6 and 7. This additional section therefore aims to specifically discuss the political and cultural setting of the research and my personal influences upon the work.

Political and cultural reflexivity

Culture is a complex and frequently ill-defined term, which generally refers to the shared values and behaviours of groups of people.(213) A single individual can be part of many cultures, with differing social expectations and practices, which each provide their own freedoms and constraints to thoughts and actions. There are a number of cultural influences upon this work, including the concepts of paternalism and determinism covered in the earlier sections of this chapter. Through considering these influences, I hope to not only locate the work within the broader debates but also provide an account of how these might influence the interpretation of the findings.

Certain features of Western culture may have played a role in the development and interpretation of the study, such as societal attitudes to children, who hold a particular value but are also innately vulnerable and require protection by responsible adults.(214) Furthermore, this study takes place in a societal structure which values individuality and personal autonomy, thus collective decision making is unusual throughout people's lives. This may explain some of the difficulties in coming to a shared decision, where individualisation is desired by families but achieved through a partnership process with professionals.

More narrowly than this generic Western culture, the professional culture within the health service has become relatively risk averse. Where clinicians are concerned about the risk of litigation, the practice of defensive medicine is prevalent.(215,216) This culture may have contributed to the attitudes of healthcare professionals in this study by increasing their sensitivity

to the risk of death or intensive care, increasing their sense of responsibility for these, and heightening their awareness of external scrutiny.

Furthermore and speculating about other potential influences on participants, the discussions of the healthcare professionals in the focus group discussions at times mimicked culturally that of Lipsky's 'street-level bureaucrats' where the volume of cases and limited resources require professionals to adapt their attitudes and behaviours so that they can provide a service within the constraints of a larger system, perhaps explaining the 'need for discretion' in professionals as a contrast to 'individualised care.(217) As a result of this system, professionals are unable to provide the individualised service that they originally aspired to, and may change their stated beliefs so as to reduce the feeling of failure in the provision of the service that they are limited to. Furthermore, 'street-level bureaucrats' often seek more control over the people they work to serve so as to ensure that the system is not over-stretched. (217) This echoes with a number of the codes relating to the healthcare professionals, particularly the discussions about protocol constraints, individualised care and the spectrum of control within febrile neutropenia. Lipsky suggests three main methods for facilitating change in street-level bureaucracies: encouraging the autonomy of patients (clients), improving current practice, and equipping the bureaucrats with the skills to instigate change.(217) Some of these issues resonate with the discussions of shared decision making, practice implications and the education and training of professionals in the following chapter. Future studies may wish to intentionally and explicitly examine the role of healthcare professionals as 'street-level bureaucrats', in paediatric oncology services and elsewhere in child health.

UK healthcare has also seen a rising emphasis on increasing quality of life for patients, with consideration of the negative impacts of treatment upon this. As such, small survival advantages of treatment may not be felt beneficial if accompanied by a significant reduction in the quality of life. This is relevant in the care of low risk febrile neutropenia, where the survival advantages of inpatient admission have not been identified but are unlikely to be large, given the data in Chapter 3.

In addition to these general issues, I have already explored the cultural background to the physician's role in this setting, within the earlier section on *the influence of paternalism and determinism*. The influence of the specific paediatric haematology and oncology culture in which patients and, by proxy, professionals are viewed as different or 'special', along with the influences of centre culture upon perceptions of early discharge, have been discussed within the findings chapter.

Personal influences

Many of my influences on the study have been considered in the methodology (Chapter 6) and in my accounts of the participants' responses to my role as doctor within the *Professional roles* subtheme of the findings. I noted two additional important features during the study. The first related to the negative comments about junior doctors, which are also described in the *Professional roles* subtheme. Here, I debated whether, as a junior doctor myself, I was sensitive to these comments, particularly given the political climate in the UK during the study (where junior doctors' contract renegotiations had failed and doctors at my level of training were involved in industrial action). I therefore took great care to review the transcripts repeatedly to ensure this code had been accurately captured. I was reassured of this when the initial healthcare professional findings were presented to a clinical audience, as this code did appear to resonate with both senior and junior clinicians, who felt the narrative had been accurate to their experience.

The second relates to my own experiences within paediatric haematology and oncology services. The main centre within which I have worked has a relatively positive approach to reduced therapy for febrile neutropenia. Their current protocol involves risk stratification and discharge at 48 hours for low risk children. There is minimal shared care with other centres. Furthermore, this PTC does a relatively large amount of supportive care research and there have been frequent discussions within the team about febrile neutropenia management. On a personal note, I have experience of patients with febrile neutropenia, including my own 'horror stories' in which patients have died suddenly or been seriously unwell due to febrile neutropenia. Similarly, I have known many patients with low risk febrile neutropenia and their families, who have shared with me their frustrations of being in hospital with a 'well' child following a single temperature.

Each of these features therefore could influence my own research as I might consider them to be the 'normal' with other factors being identified as aberrant. I was aware of this potential and took steps to reduce this effect. This took two main forms. First, through being aware of these potential biases, I was able to identify where these might impact and took care to examine areas which might be affected by my own experiences. I used an approach which looked specifically for issues which both agreed with and challenged my own experiences, and for each of these considered the potential reasons for this. Secondly, I had supervisory teams with different clinical and academic backgrounds who were involved within the analysis stage and provided honest critique of these issues where necessary.

Finally, it is important to reflect upon the impact of this study upon me as a researcher. At times, the findings of this study caused me to feel anger or sadness, particularly relating to the impact of

febrile neutropenia admissions on children and their families. Occasionally, this resulted in a feeling of blame towards professionals' for their choices, which could be felt to be due to poor judgement and based on minimal scientific evidence. Acknowledging this feeling, discussing and debriefing this with my supervisors enabled me to make substantial progress with the analysis. I recognise that professionals are making difficult decisions with what they feel to be the patients' best interests at heart in challenging cultural settings and thus have aimed to accurately voice the professionals' experiences and to represent their viewpoint alongside that of parents and young people. Through recounting the personal impact that the management of febrile neutropenia has on healthcare professionals, I hope to communicate the challenges that they encounter in treating this 'simple' problem.

This experience has resulted in a change in my own professional practice, having questioned my own professional identity and role, through the performance and analysis of this research. Overall, I feel I am more aware of the importance of gaining families' perspective, of my own personal influences in febrile neutropenia decisions and the value in sharing more information with families and working together to make choices which everyone is happy with, within the confines of the current centre protocol. Finally, I have an increased desire to discuss the findings of this research with the professional community so as to provide a voice to all parties and to raise awareness of previously hidden issues and to aim to impact policy and practice for the benefit of both families and professionals.

Summary

In this chapter I have summarised the findings of the multi-centre focus group discussion study, relating them to the findings from the other research projects undertaken as part of this thesis, and to the broader literature. I considered the differences in focus between parents and healthcare professionals in relation to health in general, and to the experience of an episode of febrile neutropenia specifically. I have also considered the influence of paternalism and determinism on medial culture and how this impacts upon decision making in low risk febrile neutropenia. Leading on from this, I have presented shared decision making as a way to improve communication surrounding febrile neutropenia, to balance the degree of control and to facilitate negotiation between families and healthcare professionals. I have concluded this discussion chapter with a reflexive section considering the political, cultural and personal influences on the study process and its findings. The following chapter combines these findings with those of the earlier chapters, summarising the thesis as a whole and identifying the implications of the work upon future research, policy and practice.

Chapter 9: Conclusions

Introduction

This final chapter aims to draw together the findings of the three phases of the thesis – the systematic review of reduced therapy regimens for paediatric low risk febrile neutropenia, the qualitative synthesis of experiences of early discharge, and the qualitative study exploring experiences and perceptions of early discharge in paediatric febrile neutropenia. I intend to demonstrate how the overarching aims of the thesis have been met through the sequence of three interlinking projects and to identify the future implications of these results for practice, policy and research. I will expand on the strengths and limitations of the thesis as a whole and will explicitly outline its original contributions to the literature in paediatric febrile neutropenia.

Summary of thesis

Febrile neutropenia is the commonest life-threatening complication of treatment of children with cancer.(1) Many episodes of febrile neutropenia will have no septic complications and these children will remain essentially well during the event. Previous research has identified various risk stratification tools, which help to identify these low risk episodes from those at higher risk of serious complications.(10) Current treatment in the UK for children with low risk febrile neutropenia varies but generally involves at least 48 hours in hospital and the administration of intravenous antibiotics.(40) Recent NICE guidelines advise consideration of outpatient antibiotic therapy for this group, which is at odds with current paediatric practice.(21)

This thesis used a sequential mixed methods approach to undertake three consecutive phases utilising different research methodologies to further investigate important issues surrounding the reduction of therapy for children and young people with low risk febrile neutropenia. In the first phase, I intended to systematically review the evidence for reduced therapy regimens and identify the safety, adequacy and treatment failure rates for these at different timings of reductions in therapy. I then planned to explore attitudes to early discharge regimes, through three different methods. First, through assessing the rates of consent to studies within the systematic review; second, through a qualitative synthesis of the primary studies in areas relating to paediatric febrile neutropenia (Phase 2); and finally through a focus group study involving young people, parents and professionals (Phase 3). I intended to establish the factors influencing decision making about outpatient therapy in febrile neutropenia and to establish the barriers and facilitators to this. I also aimed to compare the views of key personnel in these decisions and to consider how service provision could best reflect the views of these different stakeholders. The

research questions for different phases of the thesis were outlined in Chapter 1, Figure 2 and the findings in response to these are summarised within this chapter, Figure 15.

Phase 1: Systematic review of reduced therapy regimens for children with low-risk febrile neutropenia

The systematic review of effectiveness for reduced therapy regimes is described in Chapter 3. In this review, I identified 37 different studies including 3205 episodes of paediatric low risk febrile neutropenia. Two deaths and two intensive care admissions occurred within these episodes, giving a proportion of severe safety events of 0.1% (95% CI 0.03-0.3%). There was no obvious association between occurrence and route or location of treatment. It was therefore essential to examine the treatment failure rates at different times of discharge. The meta-analysis found that 14% (95% CI 9.7-19%) of episodes managed entirely with outpatient care resulted in treatment failure. Meanwhile, treatment failure occurred in 2.2% (95% CI 1.2-4.1%) of episodes managed with at least 48 hours of inpatient care. Although these data were from observational cohorts and therefore it is not appropriate to statistically compare these groups, the trend would seem clinically plausible. When considering consent rates to the studies included in the systematic review, 19.3% (range 1.3-30.1%) of patients failed to consent to enrolment, whilst 8.3-12% failed to confirm consent after enrolment. This rate of refusal was uncharacteristic in the context of children's cancer, where high recruitment rates are generally seen.(143) Clinicians declined to enrol patients into studies at similar rates. This suggested that there are concerns within the paediatric haematology and oncology community about reduced therapy regimes, and justified the following two phases of the thesis. This review provided a robust and up-to-date summary of the evidence to inform the focus group participants' discussions of risk in Phase 3, meaning that considerations were focused on realistic estimates of the outcomes of possible future service designs.

Phase 2: Experiences of early discharge, with a focus on paediatric febrile neutropenia: a meta-ethnography

The first step in exploring the nature of concerns about the acceptability of reduced therapy regimens was the conduct of the qualitative synthesis described in Chapter 4. This aimed to draw together the evidence relating to early discharge in paediatric febrile neutropenia, including data from studies of adult febrile neutropenia and other paediatric chronic conditions with life threatening consequences. In total, nine papers were included in the meta-ethnography, with varied participants and methods. This work found that early discharge involved complex and difficult decision making, influenced by fear, timing and resources. Participants struggled with practical aspects of reduced therapy regimes, particularly those relating to childcare, finances and

attendance at follow-up. They also experienced social and emotional problems, including isolation, relational and environmental challenges. Finally participants focused on the importance of receiving information and continuity of care, emphasising that increasing these would help to circumvent some of the difficulties they faced in accepting early discharge regimes. I proposed resilience as a theory that could draw together these interrelated themes and which was applicable to the evidence found in this review.

However, the synthesis had specific challenges, mostly related to the literature available, with only one study that explored paediatric febrile neutropenia and minimal material on the experiences of young people and healthcare professionals. As these are key players in decision making about paediatric febrile neutropenia, I designed the third phase of the thesis to explicitly take these issues into account.

Phase 3: A multi-centre focus group study of experiences and perceptions of early discharge in paediatric low-risk febrile neutropenia involving patients, parents and healthcare professionals

The final phase of the thesis involved a multi-centre focus group study including young people, parents and healthcare professionals in discussions about potential treatment options for paediatric low risk febrile neutropenia. The systematic review and qualitative synthesis impacted upon the design, performance, analysis and interpretation of the qualitative study, showing mixing at many levels through the work. The study included 8 focus group discussions in three different centres, which were purposively selected from a large national survey for their differences in their service structure and febrile neutropenia management. In the findings (Chapters 6 and 7), I depict the three main interrelating themes, cross-referencing the recurrent threads and emphasising areas of agreement and contrast between the various groups. The nuanced nature of the decision making involved is explored in detail and practical issues that may help to improve the experiences of children and their families during an episode of febrile neutropenia are highlighted.

The study found that *the quest for certainty* influences decisions made by key stakeholders in paediatric febrile neutropenia. The discomfort of the uncertainty involved in risk assessments is balanced against the certainty implied by current protocols. The perceived benefits and harms of inpatient care that participants have previously experienced inform their appraisals of future treatment strategies. In *attaining mutual trust and sharing roles and relationships*, participants described how interactions between these stakeholders play a key role in shaping perceptions of care. They spoke of the different roles within febrile neutropenia services and how these would need to change if outpatient or early discharge schemes were implemented, how mutual trust,

though already present in some ways, would need to be fostered and strengthened and how responsibility would need to be redistributed between groups.

Having identified a need for discretion and a desire for individualised care, negotiation within a spectrum of control allows achievement of *the potential for realised discretion*. Non-attendance with febrile neutropenia is an example of when the spectrum of control is different and families use their own assessments of risk and mutual trust, along with their previous experiences, to make decisions about their child's care. The earlier themes impact on desired future services in a number of ways, most of which aim to individualise care for children and young people. Their influence on preferred future services was demonstrated using one family as a case study.

The findings highlighted the differences in focus between families and healthcare professionals, in relation to children's health in general and to the experience of an episode of febrile neutropenia in particular. Furthermore, they enabled a deeper understanding of the qualitative literature explored in Chapter 4 – providing highlights of features which are disease specific, exploring how patients and professionals negotiate in these situations, and detailing the specific aspects of reduced therapy regimes which stakeholders desire. This phase also demonstrated how the statistics identified in phase 1 are interpreted and used by key stakeholders in different ways to assess risk, and how families in particular can view the harms of therapeutic options as different from those outcomes identified and used in the systematic review, as discussed in further detail within the section on *Differences in focus between families and healthcare professionals* in Chapter 3. This combining and translating between the different phases of the research gives a depth and richness to the thesis as a whole and provides a more nuanced consideration of the research problem.

Overall, the findings suggest that introducing shared decision making could improve current paediatric low-risk febrile neutropenia services, which fits with the current NHS narrative of increasing patient choice. This process would be supported and facilitated by the good relationships that are already present within the paediatric haematology and oncology community.

In summary, this thesis has defined the safety risks in low risk febrile neutropenia and the relative benefits of varied durations of hospital admission. The advantages of prolonged admissions are smaller than anticipated, particularly for serious safety events. The work has highlighted the previously underestimated harms of admission for febrile neutropenia and the paternalistic nature of decision making about febrile neutropenia care, along with the frustrations and challenges for all parties involved in caring for these children. This research justifies a

reassessment of the appropriateness of current treatment strategies for these children and their families and exploration of the potential to introduce shared decision making.

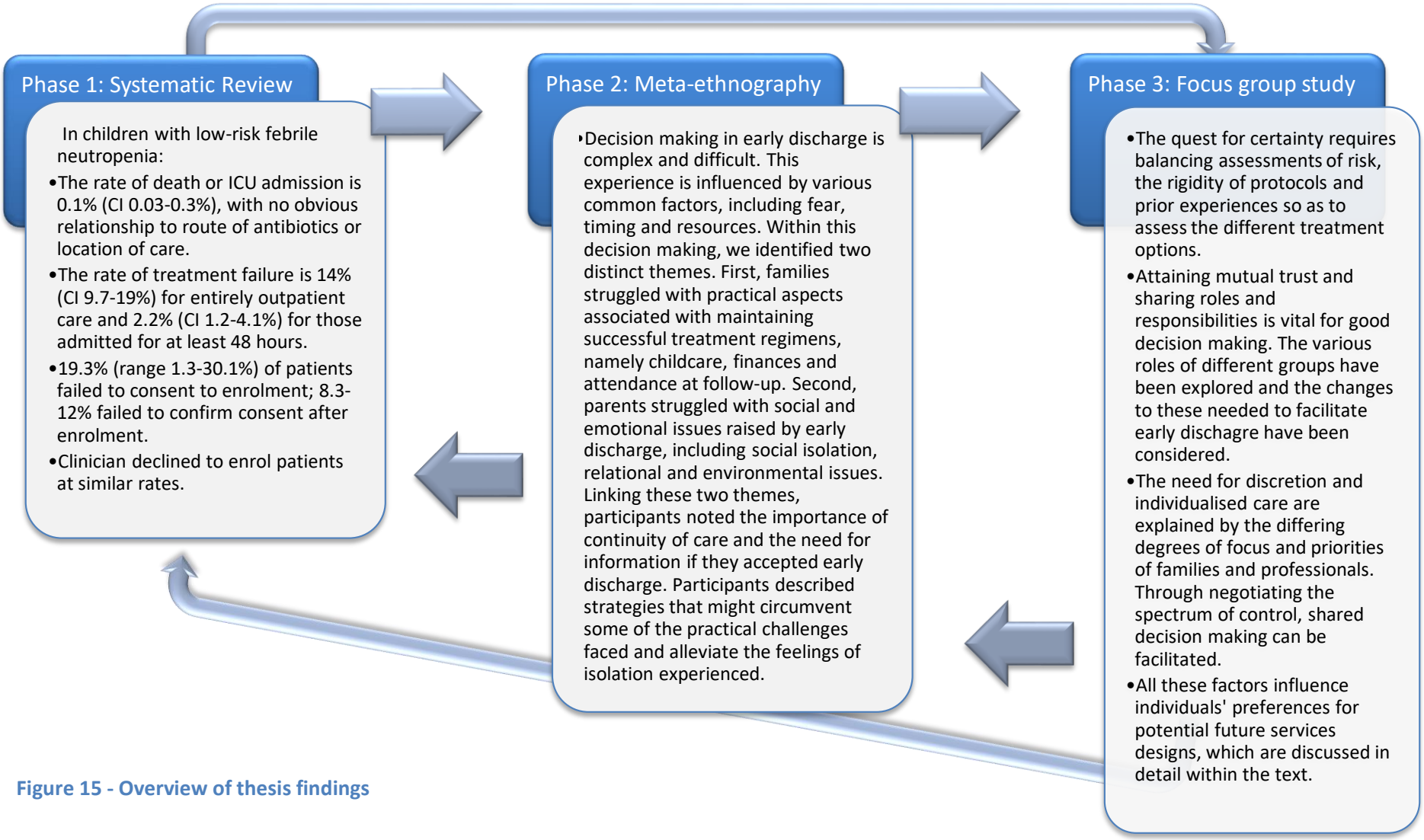

Figure 15 - Overview of thesis findings

Reflections on the use of mixed methods in the thesis

I have described many of the specific reflections on each phase of the thesis within the relevant chapters. This section therefore aims to review the impact of certain decisions related to the design of the thesis as a whole. I will also reflect upon the original contributions of this thesis to the wider literature.

The use of multiple methods within the thesis has allowed me to explore the complexity surrounding reduced therapy for febrile neutropenia. Instead of simply focusing on the strict clinical outcomes, I have also been able to ascertain a number of surrounding issues, including the concomitant social and psychological repercussions of each strategy, which provide richness and depth to the evidence. Through the inclusion of qualitative methods, the different perspectives upon the research problem are considered, and each key stakeholder is given a voice. This breadth of deliberation on the issues provides a unique and significant contribution to the pre-existing literature, and will allow for enhanced consultations regarding future service design in this area, which is complemented by the pragmatic nature of the research.

However, as noted in Chapter 1, challenges can arise in mixed methods research when the underlying epistemological and ontological beliefs of quantitative and qualitative paradigms appear to conflict.(53) I hope to have managed these challenges within the thesis by adhering to a pragmatic approach, in which the best methods have been selected at each stage. This has been the focus of many discussions between myself and my supervisor team, and the thesis hopes to present work that is scientifically robust whilst still being accessible to those from either research paradigm, and most specifically to healthcare professionals work within this field.

The three interwoven phases of the thesis contribute to the current debates in the area in a number of ways, and have built upon and informed each other in a manner consistent with the mixed methods paradigm. The systematic review demonstrated that reductions in therapy in paediatric low risk febrile neutropenia are associated with increased readmission rates, but do not increase the risk of serious adverse events. The risk of treatment failure seemed to be higher when reduced intensity therapies were used immediately after assessment, with lower rates observed when these were introduced after 48 hours. This exploration of the quantitative literature is more extensive than in previous works and has specifically considered the influence of timing on the outcomes of interest. It provides healthcare professionals and service commissioners with more precise and robust data to inform the design of future services. This review also explored the issue of failure to consent to reduced therapy trials, which has not previously been investigated in a systematic fashion.

The findings of the systematic review informed the qualitative synthesis which provides a unique exploration of the literature in order to understand the issues surrounding early discharge. This work highlighted the areas which had not yet been researched in relation to early discharge. In particular, the voices of children and young people, and healthcare professionals have been relatively under-researched and there is minimal disease specific data relating to febrile neutropenia.

The qualitative synthesis therefore stimulated a focused qualitative study that aimed to address these key limitations in the current literature and thus the study is able to make a number of contributions to the existing debates. The work has highlighted the previously underestimated harms of admission for febrile neutropenia and the paternalistic nature of decision making, along with the frustrations and challenges for all parties involved in caring for these children. It has aimed to provide both practical and conceptual information to the research problems outlined at the beginning of the thesis. It has advanced the understanding of attitudes to early discharge in febrile neutropenia and has underlined the importance of considering these alongside the quantitative data when considering the design of services for children and young people in the future.

Relating the findings from the qualitative study back to the syntheses, the challenges of consenting to the studies included in the systematic review have been highlighted by this later phase of the work. More than this, the focus groups have highlighted the contrast between families and healthcare professionals in terms of their focus in relation to febrile neutropenia care and the way in which this impacts upon the systematic review findings have been discussed within Chapter 8. The interpretation of the statistics included in the systematic review by the participants of the qualitative study has shown the variation in opinions between individuals and stakeholder groups. Meanwhile, the study has also expanded upon and provided deeper insight into the qualitative synthesis, identifying both disease-specific aspects of reducing therapy in paediatric low risk febrile neutropenia, but also more generic insight into the experiences and perceptions of key stakeholders involved in caring for families of children with chronic diseases. This is also explored in more detail within Chapter 8.

Implications on research, policy and practice

Throughout this doctorate I have used a pragmatic approach, stimulated by and grounded in my own clinical practice to consider the particular issue of reduced therapies in the management of paediatric low risk febrile neutropenia in the future. I have demonstrated that although multiple methods and perspectives can add complexity, high quality clinical research can and should be combined with policy and practice considerations in order to advance the field of paediatric

haematology and oncology. Consistent with these underlying values of the thesis and with its aim to provide clinically informative and practically useful outcomes, this section will provide a practical account of the direct implications on research, practice and policy that result from this thesis so as to inform the next phases for development in the care of children and young people with low risk febrile neutropenia.

I intend to outline the main areas for future work in terms of immediate, medium and long-term actions that may result in improved service design (see Box 9). This timeframe correlates relatively well with the extent of change or the volume of work required before they can be implemented. Some of the changes are comparatively straightforward and thus can be undertaken quickly and with minimal resources, whilst other improvements in practice are more significant and may take more time. Additionally, whilst a number of changes can be taken immediately on account of the current evidence, other factors may require further research before they can be implemented.

Within this section, I will also consider how to accomplish these developments, specifically noting the research methods which may be employed in the future. The options I have chosen to discuss are not exclusive and consideration should be given as to the strengths and weaknesses of different combinations of strategies for progress in this area. Many of the immediate and medium term options will impact upon the long-term change and, if successful, will help to inform other decisions. I have drawn attention to the relationships between different options where these exist and have attempted to outline the potential benefits of different strategies.

Box 9 – Policy and practice implications

Immediate

- Dissemination of thesis findings
- Education of healthcare professionals
- Discussion of risk
- Communication of all test results to parents
- Implementation of current guidelines

Medium term

- Blood culture research
- Development of decision aids for febrile neutropenia
- Further febrile neutropenia research, including introduction of reduced therapy regimens
- Ongoing development of shared care networks

Long term

- Culture changes regarding shared decision making, roles and responsibility

Immediate implications

The most important work to be done in the immediate period following the submission of this thesis is in the dissemination of its results. The systematic review has already been published, the qualitative synthesis submitted for publication, and many of the other key findings have been presented at local, national and international meetings.(144) This distribution of the work is vital to informing and educating healthcare professionals about the various issues surrounding the management of paediatric low risk febrile neutropenia, including the importance of differentiating between low and high risk episodes when talking and writing about febrile neutropenia. I hope to stimulate clinicians to think about both how they view low risk febrile neutropenia and the way they communicate about it to families. Furthermore, I plan to increase awareness of patients' and families' current experiences of hospital admissions for febrile neutropenia, particularly the difficulties they face and the accompanying adverse effects on the child's physical, emotional and social health. I intend to highlight the current challenges in regards to protocols, control and negotiation and to explore with professionals the reasons that these occur. Many of the immediate actions from the thesis follow on from these points and are dependent upon this communication strategy. I believe that educating and empowering healthcare professionals to think and act

differently when treating a child with febrile neutropenia is as important as any enforced practice change.

There are two main areas for education and immediate discussion. The first of these relates to the challenges of understanding risk. I discussed in Chapter 6 how statistical literacy among patients, parents and professionals was generally poor and that this is consistent with others' findings within the literature.(194) As a result of this, specific time and effort is needed to communicate the risks of early discharge in low risk febrile neutropenia to professionals and then to facilitate them in communicating risk to patients. This will involve providing informative materials using natural frequencies as well as direct encouragement to participate in risk discussions. Practically, this might mean something as simple as including a question within febrile neutropenia treatment booklets which, after the completion of a risk stratification tool, asks "Have you discussed this risk level with the patient and their family?" and then requires the clinician to indicate a "Yes/No" response. This practice may have two benefits. The first is that the discussion informs, involves and empowers the family experiencing this febrile neutropenic episode. The second is that this encourages healthcare professionals to acknowledge the differences between patients with high risk and low risk episodes, thus engaging them in consideration of the variations in risk in this condition.

The second main area for changing practice is in the disclosure of test results to parents. In the qualitative study, parents stated that the failure of professionals to inform them of their child's test results, particularly blood cultures, was a negative aspect of their care. Through informing clinicians of the desire for this simple change and encouraging centres to establish pathways for this to occur, it may be possible to change behaviours and enhance the patient experience. In the longer term, centres may choose to use pre-existing tools such as PatientView[11] to enable patients to access their own results in the community, thus allowing families to review their tests online and saving staff time in communicating simple results.(218)

Alongside educational and dissemination plans, another immediate implication of this thesis is to encourage the application of current guidelines regarding paediatric febrile neutropenia. Poor compliance to NICE CG151 is evidenced within recent surveys and audits and may result in longer admissions for patients and confusing communications to families.(40,42) The qualitative study within this thesis also suggests that centres are not fully compliant with this guideline and that parents feel the delays in discharge that result from this have a detrimental effect on their child and

[11] PatientView is an online tool which enables patients to view their personal health record, including information about their diagnoses, as well as up-to-date lists of their medications and real-time test results. It was first developed for patients with renal disease but is now available for a wide variety of conditions.

family. Obtaining a more comparable service throughout the UK may improve current febrile neutropenia outcomes, simply by conveying the benefits of previous research to those patients who are not currently exposed to such practices. Specifically, the introduction of risk stratification throughout all centres and a more evidence based approach to empirical antibiotic choice may reduce the healthcare burden for families without reducing the safety or efficacy of treatment strategies. Furthermore, consistency in local guidelines and practice may allow for clearer instruction to families moving between centres, greater understanding between professionals when discussing patient care, and a basic groundwork from which to build further changes and to develop further research.

Medium term implications

The majority of medium term implications of this work that I will discuss relate to potential further research. These, not surprisingly, include methods for introducing reduced therapy treatment regimens to the UK, alongside other suggestions for research into decision aids for patients and research about blood cultures (as one of the key influences of decision making in low risk febrile neutropenia). The final medium term implication I will discuss is that of the ongoing development of shared care networks.

The first medium term area for progression from this thesis involves the implementation of strategies which offer reduced durations of hospitalisation for children with low risk febrile neutropenia in the UK. This thesis provides evidence supporting these options as both safe and efficacious in the management of such children. Some of the barriers and facilitators for stakeholders have been explored and as such it may be possible to design a service which is most acceptable to patients, families and healthcare professionals. Having said this, there are significant challenges facing the implementation of such changes. These include the need for networked implementation, which although clearly present within paediatric oncology for the delivery of treatment for malignancies is less well developed for the implementation of supportive care initiatives. Furthermore, the anxieties of both staff and families will need to be addressed, most likely with phased introduction of changes and clear practical guidance, both in relation to patient eligibility and management of a patient on an outpatient low risk febrile neutropenia pathway.

The introduction of some of these changes in practice may best be served using a quality improvement (QI) initiative. QI methods allow a structured approach to implementation, along with frequent reassessment of the progress made and the issues that arise. This rapid, focused methodology allows responsiveness to patient and staff experience, as well as to local factors QI may be particularly applicable to the problem of the management of low risk febrile neutropenia

given that this research has found that it is a complex issue where early discharge is safe but has varying rates of treatment failures, and where experiences and preferences vary by centre, between families and professionals and between individuals. As such an implementation model which involves regular review and reconsideration of best quality care may enable changes to be made to best suit the specific situation of a service. If these efforts were co-ordinated and findings were shared throughout centres, as well as prospectively documented and assessed, the benefits to all centres in the UK may be maximised within a relatively short time frame.

However, this approach brings some challenges. First, the precise details of a strategy would need to be defined at least initially so as to provide a framework on which to work. This thesis can suggest basic structures of the various service options, but cannot give evidence for features beyond this. A centre would therefore have to agree on the most appropriate way forward. Secondly, QI projects require a strict methodology and careful planning and documentation so as to obtain the most helpful information and to allow the sharing of findings with other organisations.(219,220) This is likely to require significant personnel, time and resources to achieve in a meaningful manner, along with a clear institutional commitment to publication of results if they were to benefit patients in other locations. For many centres, there may not be the experience with these new methods to enable to the institution of such a large national project.

The alternative to QI methodologies may be to perform further formal research to provide more detailed and comprehensive data. This option was requested by two of the three healthcare professional focus groups in the qualitative study and may therefore be the approach which is more familiar to by the paediatric haematology and oncology team. Before discussing potential future research methods, it is important to consider whether the request for further research reflects two additional issues for healthcare professionals. The first is that 'needs further research' is often a taught response to the question of 'What next?' for healthcare professionals. Within teaching about research for professional groups, this is a standard response to the discussion of original research and hence our participants may have been primed to reply in this way. Secondly, the request for further research may represent a delaying tactic for professionals. The knowledge that the design, funding and set-up for such a trial may take years, if achieved at all, means that professionals may choose consciously or unconsciously to ask for further research so as to postpone the implementation of a change. This is particularly likely if the change is one which professionals are anxious or unsure about, and thus a delay in implementation performs a role in relieving that anxiety and allows further time to consider the option and potentially to act to prevent its implementation at a later point. Acknowledging this anxiety and negotiating ways to alleviate it is likely to be more

productive both practically and emotionally than simply taking at face value the request for further research.

However, performing additional research may bring unique benefits, beyond that of further data in this field. The introduction of research trials into supportive care may help to alleviate concerns by providing professionals with a framework of practice with which they are familiar and which is held in high esteem within the paediatric oncology community, as discussed in Chapter 7. Additionally, the performance of a trial may result in better adherence to proposed changes than that seen with a change in guidelines, as trials may limit, or at least require explanation, for deviation from the given protocol. Finally, the culture of trial performance in paediatric oncology has resulted in a quietly competitive attitude to recruitment, in which centres are able to review their own success in recruiting to certain studies, with the benefit of better trial recruitment and increased research data which provides more powerful evidence for the interventions being investigated. Utilising this culture may allow future febrile neutropenia research in the UK to be outstanding within this field.

Should the performance of further research be felt appropriate, one option, which may be particularly successful is a multi-arm, multi-stage (MAMS) trial. This methodology allows the investigation of multiple experimental arms at one time against a single control arm and then the adaptation and progression of research questions and interventions as the initial data is gathered and analysed.(221) This provides a more rapid answer to multiple questions than running multiple individual RCTS, thus the MAMS approach forms an efficient approach to research areas like paediatric febrile neutropenia where there are a variety of different treatment options which should be considered. However, the MAMS approach requires considerable planning in regards to which interventions to trial first, the appropriate stopping rules for each research arm, complex statistical analyses required to assess multiple interventions at once and often substantial financial costs, all of which must be considered before embarking on such a project.

Fortunately, MAMS trials are not a new concept in the field of paediatric oncology and many centres will be familiar with running trials such as the SIOPEN High Risk Neuroblastoma Study (Clinicaltrials.gov Identifier NCT01704716) and the BEACON-Neuroblastoma Trial (Clinicaltrials.gov Identifier NCT02308527). However, large scale supportive care trials are less well established within the UK and as such any further research may experience significant challenges in both set-up and recruitment. The MAMS approach allows researchers to introduce interventions that are more likely to be acceptable as initial stages. In paediatric febrile neutropenia, these might be the interventions advised by NICE guidelines or investigations of biomarkers for infection, whilst also allowing centres to set up the infrastructure for febrile neutropenia data collection and creating a positive culture

around supportive care research. Over time, as professionals become more comfortable with this then more complex randomisations could be introduced and it may be at this point that the challenging four way randomisation of both location of treatment and route of antibiotic administration could be achieved.

Key clinical outcome measures in febrile neutropenia have been defined for some time and should be used.(222) Other issues which might also be addressed within the programme of research are the assessment of risk stratification tools, the timings of assessments (including follow-up), economic analyses of the interventions implemented and ongoing work into the experiences of the key stakeholders involved in paediatric haematology and oncology services.

The number of participants required to provide conclusive data about each individual treatment option is likely to be large, when compared to the small paediatric haematology and oncology population. Furthermore, a large clinical study of such a design would require significant funding, particularly in the initial period of set-up and liaison with study centres. However, this seems consistent with the National Institute for Health Research aims of providing well-designed research of tangible benefit to patients and families, with the potential to improve healthcare systems and be good stewards of healthcare costs.(223) An overarching study into the diagnosis, management and prognostic features of febrile neutropenia in children, whilst simultaneously increasing shared decision making, could arguably be seen to meet these aims and as such be eligible for many funding streams, along with the support of the Clinical Research Network Portfolio.

Along with these larger studies of management of low risk febrile neutropenia, there are two other important areas for research in the medium term. The first group of research questions relates to the issue of blood cultures. As discussed in Chapter 6, parents within the focus group study spoke about blood cultures as being a key feature that they had identified in professionals' decision making about early discharge and that delays in obtaining blood culture results caused significant frustrations for families. There are a number of possible solutions to be considered here. It may be important for certain centres to consider their current blood culture processes as these may be improved through faster arrival and processing at the laboratory to initiate sample testing, or through more timely reporting of blood culture results. Elsewhere, service providers may wish to consider the economic impacts of earlier discharge throughout the hospital compared to employing additional microbiology staff overnight or at weekends. From a research point of view, one key question is whether the current time limit of 48 hours for a blood culture to be declared negative remains accurate. This test cut-off was defined at a time when blood culture techniques were less advanced than contemporary processes and as technology has developed, we may find that a

shorter time frame provides sufficient confidence in a negative blood culture. Given that blood culture results are such an important feature of febrile neutropenia decision making, shortening the time needed to obtain results may also allow for shorter admissions with febrile neutropenia.

The second area for additional research lies in methods to aid decision making. Decision aids can facilitate shared decision making through providing a framework for discussions, including informing patients of accurate representations of risk, identifying treatment options and assisting in making a choice. They are intended to support in the process of shared decision making rather than replacing consultations between patients and professionals.(224) There has been broad and wide-ranging exploration of the use of decision aids in medicine, particularly for decisions about health screening and management of chronic conditions such as hypertension and hypercholesterolaemia.(119,205–210) A recent Cochrane review found high quality evidence that decision aids can increase knowledge and reduce decisional conflict.(225) Furthermore, they can encourage increased shared decision making and understanding of risk. It should be noted however, that the use of decision aids does not necessarily result in patients making the desired choice of healthcare professionals.(206–208) This has been discussed most extensively in relation to screening programmes, where decision aids can decrease the number of patients choosing to participate in screening, after being informed of the relative risks and benefits. For low risk febrile neutropenia, the results of introducing decision aids may be unclear. Some patients may choose to remain as inpatients receiving treatment similar to that currently provided, others may choose outpatient care. Ultimately however, it may be argued that the aim is not to increase the uptake of a particular option, but instead to facilitate discussions about difficult choices in which allowing the patient to select the choice most appropriate for their individual situation and their personal values is the key aim.

As discussed in Chapter 2, decision making in paediatric populations can be even more complicated due to the triadic nature of the consultations. Decision aids and other support for shared decision making in children may need to be adapted to account for this and for the different developmental ages of the children and young people involved. According to a recent Cochrane review, there has been no research into decision aids for children with cancer.(228) Furthermore, in contemporary society *"real-world clinical decision making is also mediated by technology and teamwork"*(76). Therefore the decision aids may also take an electronic form, particularly given that children and young people are frequently very competent in using these forms of communication. Finally, discussions about febrile neutropenia decisions would need to be ongoing during episodes, as families may decide that after 24 hours a different treatment strategy is more appropriate, and between episodes, as they are influenced by prior experiences and by increasing knowledge about

their child's cancer and febrile neutropenia itself. Decision aids will need to take this into account and be usable throughout a febrile neutropenia episode and should help to inform future decisions about febrile neutropenia care for that child or young person.

Informed by all these issues, it may be that future research aims to develop a decision aid in the form of an app for children with low risk febrile neutropenia in which the healthcare professional, patient and family work together through the process of risk stratification. The risks of different treatment options would then be provided from the systematic review in Chapter 3 of this thesis, using natural frequencies for ease of understanding and tailored to different age groups. The app could then help guide discussions which identify values, priorities and parental skills, before helping the team come to a decision. Once a decision has been made, the team can then design a treatment plan (including follow up and stopping rules) and define their roles and responsibilities. Once at home, families could use the app to record symptoms, provide reminders for antibiotic administration and communicate with healthcare professionals in the hospital. Finally, such a programme could collect data on the process of decision making and the treatment of febrile neutropenia along with the outcomes achieved.

This kind of decision aid and associated technological support may form part of future trials for febrile neutropenia and be assessed alongside the treatment strategies, as discussed earlier in this section. Given that decision aids can influence the choices made by patients and their families, it is important that they are well-designed to provide accurate information, without bias, using appropriate evidence to inform the individual patient and support their personal decisions.(224) The International Patient Decision Aids Standards (IPDAS) Collaboration have created a checklist of criteria assess the quality of patient decision aids.(224) These criteria may also be used as points to assist researchers in the development of high-quality future decision aids. Ultimately, the aim should be tools that inform both patients and clinicians, are easily accessible and that will be suitable for use within the time-pressured everyday practice of the NHS.(230)

In the final suggested change for the medium term, centres may wish to dedicate time and effort to the ongoing development of shared care networks, so as to resolve some of the issues with shared care that were discussed in the qualitative study, including that POSCU staff did not know the patients, had poor understanding of oncological issues, provided less effective treatment and did not have specialty specific skills such as Port-a-cath access (see Chapter 6). Centres with minimal shared care input may find that the knowledge and skills of shared care professionals would benefit from increased investment and could then be kept at safe levels through the attendance of more children at the POSCUs instead of travelling directly to the PTC. Families would benefit from reduced travel

time, easier visiting from friends and family members, and developing relationships with these staff, therefore increasing mutual trust and confidence. As was seen in the qualitative study, those families who attend shared care centres with febrile neutropenia are more likely to take on an increased role in their child's care and to feel in control of their child's condition (see Chapter 7). Thus there are many potential benefits from increased shared care. However, I acknowledge the many concerns from centres where POSCU management of febrile neutropenia is unusual. This kind of change is likely to require increased time, resources and support in the early stages. Any efforts to increase shared care involvement should recognise that the initial period of change may be the most challenging time for families and for professionals at both POSCUs and the PTC.

Long term implications

Long term, the findings of this thesis suggest that cultural changes are required to improve the care of children and young people with low risk febrile neutropenia. A move away from the traditional paternalism and determinism of medicine towards increased shared decision making would allow closer adherence to the values of contemporary healthcare. In order to achieve this, there is a need to consider how to establish a culture in which shared decision making is valued, professionals have the skills to support it and these are put into practice in everyday healthcare.(230) This change requires acknowledgement of the uncertainty involved in all areas of medicine, open communication of the thoughts and values of patients and healthcare professionals, the redistribution of responsibility and the provision of various options for care, which can be adapted to suit the individual. To achieve such an aim will require diverse and multi-level interventions within the complexity of current services and as such, this is likely to take a considerable period to instigate and then achieve.(231,232) However, I feel this should be the long term action that springs from the research presented in this thesis.

A key feature in effecting culture change is that of engaging leaders and key influential figures within organisations at both local and national levels, so as to encourage the development of shared decision making practice and to champion the role of patients in making choices about healthcare on individual and collective levels.(230) These leaders should come from multi-disciplinary backgrounds and should also include patients and families in the discussions about service development in order to promote the values of service users in the organisation and to facilitate engagement.(230,231) These leaders should aim to inspire the community to understand why change is necessary and how it can be achieved. Through engaging many different members of staff in this endeavour to change the behaviours and underlying values of the community, leaders play a key role in developing cultural change. Furthermore, by encouraging colleagues to acknowledge the unspoken norms and

values that promote ongoing paternalism and determinism, including a failure to recognise parental roles or the belief that all non-attendance with febrile neutropenia is bad, leaders can stimulate their colleagues to question these assumptions and consider a change in practice.(233)

There are a number of practical actions which could also facilitate cultural change in the paediatric haematology and oncology community. Centres will need to consider the specific challenges related to their service and how these might be addressed, just as the study participants did in their discussions of future service design. This may require changes in physical space, staffing and resources available to professionals. Equipping professionals with the communication skills to facilitate shared decision making will require provision of appropriate training resources and a prominence of this topic within undergraduate and postgraduate professional training, along with recognition of the importance and value of these skills within the professions.(86,206)Many of the actions set out in the previous two sections discussing immediate and medium term implications of this research, if achieved, will help the paediatric haematology and oncology community to move forward in these practical aspects to support cultural change and will mean that positive steps have already been taken to increase shared decision making with families.

Summary

Febrile neutropenia is a common complication of childhood cancer and its treatment. Over the last 70 years there has been considerable progress in its management such that the majority of children will have no significant complications of its occurrence, but there are still improvements to be made. This thesis has examined whether the current treatment for febrile neutropenia could be reduced in those children for whom the risk of complications is low, with anticipated benefits for children, their families and the healthcare service. I used a sequential mixed methods approach to undertake three consecutive phases utilising different research methodologies to further investigate important issues surrounding the reduction of therapy for children and young people with low risk febrile neutropenia. I performed two in-depth systematic reviews of the literature which provide detailed data on the safety and treatment failure rates when treatment is reduced at different time points, as well as an interpretive account of the experiences of early discharge, which I have related to paediatric febrile neutropenia. Drawing on both of these pieces of research I performed a multi-centre study determining the experiences and perceptions of key stakeholders in febrile neutropenia care in the UK.

These three interwoven phases of the thesis have demonstrated the challenges involved in developing these services. The significance of shared decision making in improving the experience of

all involved through sharing risks, developing mutual trust and negotiating control to achieve individualised treatment cannot be underestimated. This thesis has outlined aspirations for the future care of these children and young people and charted various actions to achieve these goals. Despite the complexity of options and opinions in this area, I believe that this thesis presents the paediatric haematology and oncology community with an imperative to act to deliver services that better suit the needs and desires of the population we serve.

Appendices

Appendix A

This Appendix includes all appendices related to chapter 3 of the thesis.

Appendix 3.1: Database search strategies

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present> was searched on 02/04/2014, using the OVID SP interface.

1408 records were retrieved

Key:

/=index term (MeSH heading)

*=truncation

?= embedded truncation

ti=title field

ab=abstract

tw= textword

.ti,ab=terms were searched for in either title or abstract

adj = terms adjacent to each other (same order)

adj1 = terms within one word of each other (any order)

adj2 = terms within two words of each other (any order)

1 Agranulocytosis/ or neutropenia/ or leukopenia/ (26903)

2 exp Fever/ or exp "Fever of Unknown Origin"/ or exp Body Temperature/ (103535)

3 (1 and 2) or febrile neutropenia/ (2868)

4 (febrile adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (5241)

5 ((fever or temperature or temp) adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (2727)

6 3 or 4 or 5 (8261)

7 (antibiotic* or antimicrob* or anti-biotic* or anti-microb*).tw. (293708)

8 exp anti-bacterial agents/ (522999)

9 exp beta-lactamases/ or exp beta-lactams/ (114490)

10 exp penicillins/ or penicillin*.tw. (89738)

11 tazobactam*.tw. (2549)

12 ureidopenicillin*.tw. (203)

13 exp ticarcillin/ or ticarcillin*.tw. (2002)

14 exp piperacillin/ or piperacillin*.tw. (5122)

15 exp quinolones/ or quinolone*.tw. (38463)

16 exp ciprofloxacin/ or ciprofloxacin*.tw. (20215)

17 exp ceftazidime/ or ceftazidime*.tw. (7133)

18 meropenem*.tw. (3297)

19 exp imipenem/ or imipenem*.tw. (8147)

20 exp aztreonam/ or astreonam*.tw. (1269)

21 exp aminoglycosides/ (126292)

22 aminoglycoside*.tw. (14842)

23 exp amikacin/ or amikacin*.tw. (7485)

24 exp gentamicins/ or gentam?cin*.tw. (27182)

25 exp tobramycin/ or tobram?cin*.tw. (6382)

26 exp kanamycin/ or kanam?cin*.tw. (17391)

27 exp netilmicin/ or netilm?cin*.tw. (1885)

28 (beta-lactam* or beta?lactam*).tw. (30330)

29 or/7-28 (762602)

30 exp "length of stay"/ or exp patient admission/ or exp patient discharge/ or exp patient readmission/ or exp inpatients/ or exp outpatients/ (109775)

31 (discharge* or (length* adj2 stay*) or (duration* adj2 stay*) or admission* or readmission* or inpatient* or outpatient*).tw. (428579)

32 30 or 31 (475681)

33 29 or 32 (1211026)

34 adolescent/ or exp child/ or exp infant/ or exp young adult/ (2972677)

35 (newborn* or new-born* or baby* or babies or neonat* or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or young person* or young people or young adult* or child* or schoolchild* or schoolage* or school* or preschool*).tw. (1838751)

36 34 or 35 (3514897)

37 6 and 33 and 36 (1408)

Cochrane Database of Systematic Reviews Issue 4 of 12, April 2014 was searched on 03/04/2014, using the Cochrane Library interface.

367 records were retrieved from The Cochrane Library, of which 5 were from CDSR.

Key:

*=truncation

ti=title field

ab=abstract

.ti,ab.=terms were searched for in either title or abstract

near/1 = terms within one word of each other (any order)

near/2 = terms within two words of each other (any order)

next = terms are next to each other

ID Search Hits

#1 MeSH descriptor: [Agranulocytosis] this term only 309

#2 MeSH descriptor: [Neutropenia] this term only 1449

#3 MeSH descriptor: [Leukopenia] this term only 514

#4 {or #1-#3} 2101

#5 MeSH descriptor: [Fever] this term only 1646

#6 MeSH descriptor: [Fever of Unknown Origin] this term only 72

#7 MeSH descriptor: [Body Temperature] explode all trees 3323

#8 {or #5-#7} 4863

#9 #4 and #8 522

#10 MeSH descriptor: [Febrile Neutropenia] this term only 0

#11 #9 or #10 522

#12 ("febrile" near/5 (neutropen* or granulocytop* or agranulocyto* or leukocytop*ni*)):ti,ab 1176

#13 (("fever" or "temperature" or "temp") near/5 (neutropen* or granulocytop* or agranulocyto* or leukocytop*ni*)):ti,ab 460

#14 {or #11-#13} 1574

#15 (antibiotic* or antimicrob* or anti-biotic* or anti-microb*):ti,ab 15148

#16 MeSH descriptor: [Anti-Bacterial Agents] explode all trees 9158

#17 MeSH descriptor: [beta-Lactamases] explode all trees 131

#18 MeSH descriptor: [beta-Lactams] explode all trees 7776

#19 MeSH descriptor: [Penicillins] explode all trees 4621

#20 penicillin*:ti,ab 1799

#21 tazobactam*:ti,ab 229

#22 ureidopenicillin*:ti,ab 10

#23 MeSH descriptor: [Ticarcillin] explode all trees 147

#24 ticarcillin*:ti,ab 215

#25 MeSH descriptor: [Piperacillin] explode all trees 336

#26 piperacillin*:ti,ab 520

#27 MeSH descriptor: [Quinolones] explode all trees 3106

#28 quinolone*:ti,ab 402

#29 MeSH descriptor: [Ciprofloxacin] explode all trees 960

#30 ciprofloxacin*:ti,ab 1488

#31 MeSH descriptor: [Ceftazidime] explode all trees 404

#32 ceftazidime*:ti,ab 692

#33 meropenem*:ti,ab 197

#34 MeSH descriptor: [Imipenem] explode all trees 262

#35 imipenem*:ti,ab 410

#36 MeSH descriptor: [Aztreonam] explode all trees 142

#37 aztreonam*:ti,ab 221

#38 MeSH descriptor: [Aminoglycosides] explode all trees 6668

#39 aminoglycoside*:ti,ab 567

#40 MeSH descriptor: [Amikacin] explode all trees 312

#41 amikacin*:ti,ab 548

#42 MeSH descriptor: [Gentamicins] explode all trees 1056

#43 gentam*cin*:ti,ab 1374

#44 MeSH descriptor: [Tobramycin] explode all trees 484

#45 tobram*cin*:ti,ab 875

#46 MeSH descriptor: [Kanamycin] explode all trees 849

#47 kanam*cin*:ti,ab 75

#48 MeSH descriptor: [Netilmicin] explode all trees 149

#49 netilm*cin*:ti,ab 243

#50 beta-lactam* or beta*lactam*:ti,ab 1021

#51 {or #15-#50} 31219

#52 MeSH descriptor: [Length of Stay] explode all trees 6581

#53 MeSH descriptor: [Patient Admission] explode all trees 564

#54 MeSH descriptor: [Patient Discharge] explode all trees 1064

#55 MeSH descriptor: [Patient Readmission] explode all trees 787

#56 MeSH descriptor: [Inpatients] explode all trees 657

#57 MeSH descriptor: [Outpatients] explode all trees 831

#58 (discharge* or (length* near/2 stay*) or (duration* near/2 stay*) or admission* or readmission* or inpatient* or outpatient*):ti,ab 39686

#59 {or #52-#58} 44114

#60 #51 or #59 72787

#61 MeSH descriptor: [Adolescent] explode all trees 76133

#62 MeSH descriptor: [Child] explode all trees 78

#63 MeSH descriptor: [Infant] explode all trees 13097

#64 MeSH descriptor: [Young Adult] explode all trees 113

#65 (newborn* or new-born* or baby* or "babies" or neonat* or infan* or "kid" or "kids" or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or ("young" next person*) or "young people" or ("young" next adult*) or child* or schoolchild* or schoolage* or school* or preschool*):ti,ab 91703

#66 {or #61-#65} 151768

#67 #14 and #60 and #66 367

CENTRAL (Issue 3 of 12 March 2014), Database of Abstracts of Reviews of Effects, DARE (Issue 1 of 4 January 2014) and Health Technology Database, HTA (Issue 1 of 4, January 2014) were searched on 03/04/2014, using the Cochrane Library interface.

520 records were retrieved from The Cochrane Library, of which 415 were from CENTRAL, 20 were from DARE, 1 was from HTA and the remainder were from CDSR (and therefore discarded).

Key:

/=index term (MeSH heading)

*=truncation

?= embedded truncation

ti=title field

ab=abstract

tw= textword

.ti,ab=terms were searched for in either title or abstract

#1 MeSH descriptor: [Agranulocytosis] this term only 309

#2 MeSH descriptor: [Neutropenia] this term only 1449

#3 MeSH descriptor: [Leukopenia] this term only 514

#4 {or #1-#3} 2101

#5 MeSH descriptor: [Fever] this term only 1646

#6 MeSH descriptor: [Fever of Unknown Origin] this term only 72

#7 MeSH descriptor: [Body Temperature] explode all trees 3323

#8 {or #5-#7} 4863

#9 #4 and #8 522

#10 MeSH descriptor: [Febrile Neutropenia] this term only 0

#11 #9 or #10 522

#12 ("febrile" near/5 (neutropen* or granulocytop* or agranulocyto* or leukocytop*ni*)) 1566

#13 (("fever" or "temperature" or "temp") near/5 (neutropen* or granulocytop* or agranulocyto* or leukocytop*ni*)) 643

#14 {or #11-#13} 2000

#15 (antibiotic* or antimicrob* or anti-biotic* or anti-microb*) 22059

#16 MeSH descriptor: [Anti-Bacterial Agents] explode all trees 9158

#17 MeSH descriptor: [beta-Lactamases] explode all trees 131

#18 MeSH descriptor: [beta-Lactams] explode all trees 7776

#19 MeSH descriptor: [Penicillins] explode all trees 4621

#20 penicillin* 3272

#21 tazobactam* 297

#22 ureidopenicillin* 13

#23 MeSH descriptor: [Ticarcillin] explode all trees 147

#24 ticarcillin* 279

#25 MeSH descriptor: [Piperacillin] explode all trees 336

#26 piperacillin* 660

#27 MeSH descriptor: [Quinolones] explode all trees 3106

#28 quinolone* 1191

#29 MeSH descriptor: [Ciprofloxacin] explode all trees 960

#30 ciprofloxacin* 1866

#31 MeSH descriptor: [Ceftazidime] explode all trees 404

#32 ceftazidime* 849

#33 meropenem* 263

#34 MeSH descriptor: [Imipenem] explode all trees 262

#35 imipenem* 527

#36 MeSH descriptor: [Aztreonam] explode all trees 142

#37 aztreonam* 291

#38 MeSH descriptor: [Aminoglycosides] explode all trees 6668

#39 aminoglycoside* 836

#40 MeSH descriptor: [Amikacin] explode all trees 312

#41 amikacin* 680

#42 MeSH descriptor: [Gentamicins] explode all trees 1056

#43 gentam*cin* 1844

#44 MeSH descriptor: [Tobramycin] explode all trees 484

#45 tobram*cin* 1059

#46 MeSH descriptor: [Kanamycin] explode all trees 849

#47 kanam*cin* 194

#48 MeSH descriptor: [Netilmicin] explode all trees 149

#49 netilm*cin* 302

#50 beta-lactam* or beta*lactam* 1022

#51 {or #15-#50} 35898

#52 MeSH descriptor: [Length of Stay] explode all trees 6581

#53 MeSH descriptor: [Patient Admission] explode all trees 564

#54 MeSH descriptor: [Patient Discharge] explode all trees 1064

#55 MeSH descriptor: [Patient Readmission] explode all trees 787

#56 MeSH descriptor: [Inpatients] explode all trees 657

#57 MeSH descriptor: [Outpatients] explode all trees 831

#58 (discharge* or (length* near/2 stay*) or (duration* near/2 stay*) or admission* or readmission* or inpatient* or outpatient*) 54270

#59 {or #52-#58} 54270

#60 #51 or #59 85611

#61 MeSH descriptor: [Adolescent] explode all trees 76133

#62 MeSH descriptor: [Child] explode all trees 78

#63 MeSH descriptor: [Infant] explode all trees 13097

#64 MeSH descriptor: [Young Adult] explode all trees 113

#65 (newborn* or new-born* or baby* or "babies" or neonat* or infan* or "kid" or "kids" or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or ("young" next person*) or "young people" or ("young" next adult*) or child* or schoolchild* or schoolage* or school* or preschool*) 228756

#66 {or #61-#65} 228756

#67 #14 and #60 and #66 520

EMBASE <1974 to 2014 April 02> was searched on 03/04/2014, using the OVID SP interface.

1327 records were retrieved

Key:

Key:

/ = indexing term (EMTREE heading)

* = focussed EMTREE heading

exp = exploded EMTREE heading

* = truncation

? = embedded truncation

.ti,ab. = terms in either title or abstract fields

.tw.= textword

adj = terms adjacent to each other (same order)

adj1 = terms within one word of each other (any order)

adj2 = terms within two words of each other (any order)

1 *Agranulocytosis/ or *neutropenia/ or *leukopenia/ (19402)

2 *Fever/ or *pyrexia idiopathica/ or exp *Body Temperature/ (36896)

3 (1 and 2) or *febrile neutropenia/ (3340)

4 (febrile adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (8453)

5 ((fever or temperature or temp) adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (3832)

6 3 or 4 or 5 (12398)

7 (antibiotic* or antimicrob* or anti-biotic* or anti-microb*).tw. (373110)

8 exp *antiinfective agent/ (1071546)

9 *beta lactamase/ or *beta lactam/ (9024)

10 exp *penicillin derivative/ or penicillin*.tw. (126214)

11 tazobactam*.tw. (4083)

12 ureidopenicillin*.tw. (242)

13 *ticarcillin/ or ticarcillin*.tw. (4356)

14 *piperacillin/ or piperacillin*.tw. (9280)

15 *quinolone/ or quinolone*.tw. (13985)

16 *ciprofloxacin/ or ciprofloxacin*.tw. (27190)

17 *ceftazidime/ or ceftazidime*.tw. (11063)

18 meropenem*.tw. (5362)

19 *imipenem/ or imipenem*.tw. (11955)

20 *aztreonam/ or astreonam*.tw. (2260)

21 *aminoglycoside/ (3461)

22 aminoglycoside*.tw. (17847)

23 *amikacin/ or amikacin*.tw. (14248)

24 *gentamicin/ or gentam?cin*.tw. (45689)

25 *tobramycin/ or tobram?cin*.tw. (13380)

26 *kanamycin/ or kanam?cin*.tw. (16149)

27 *netilmicin/ or netilm?cin*.tw. (3859)

28 (beta-lactam* or beta?lactam*).tw. (37408)

29 or/7-28 (1288501)

30 *"length of stay"/ or *hospital admission/ or *hospital discharge/ or *hospital readmission/ or exp *hospital patient/ or *outpatient/ (44885)

31 (discharge* or (length* adj2 stay*) or (duration* adj2 stay*) or admission* or readmission* or inpatient* or outpatient*).tw. (595967)

32 30 or 31 (609598)

33 29 or 32 (1857828)

34 adolescent/ or exp child/ or exp infant/ or young adult/ (2668461)

35 (newborn* or new-born* or baby* or babies or neonat* or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or young person* or young people or young adult* or child* or schoolchild* or schoolage* or school* or preschool*).tw. (2226295)

36 34 or 35 (3421519)

37 6 and 33 and 36 (1327)

LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde) - http://lilacs.bvsalud.org/en/ was searched on 11/04/2014

Key:

tw=. Text word

$= truncation

mh= index term

To make the most of the interface, a number of different strategies were run, and duplicates removed from the final results. Overall, 450 different records were retrieved.

Search 1:

(tw:((febrile AND (neutropen$ or granulocytop$ or agranulocyto$ or leukocytop$)))) OR (tw:((fever AND (neutropen$ or granulocytop$ or agranulocyto$ or leukocytop$)))) OR (tw:((temperature AND (neutropen$ or granulocytop$ or agranulocyto$ or leukocytop$)))) OR (tw:((temp AND (neutropen$ or granulocytop$ or agranulocyto$ or leukocytop$))))

Retrieved 225 records

Search 2:

((mh:(Agranulocytosis)) OR (mh:(neutropenia)) OR (mh:(leukopenia)) AND (mh:(Fever)) OR (mh:("Fever of Unknown Origin")) OR (mh:(Body Temperature)))

Retrieved 94 records

Search 3:

((C15.378.553.546) OR (C15.378.553.546.184) OR (C15.378.553.546.184.564) OR (Leucopenia) OR (Agranulocitosis) OR (Agranulocitose)) AND ((C23.888.119.344) OR (C23.888.119.344.345) OR (Fiebre) OR (Febre) OR (Fiebre de Origen Desconocido) OR (Febre de Causa Desconhecida))

Retrieved 246 records

Search 4:

(C15.378.553.546.184.564.750) OR (Neutropenia Febril)

Retrieved 135 records

Appendix 3.2: Data extraction form

General Information

Person performing data extraction: Choose an item.

Date of data extraction: Click here to enter a date.

Study title: Click here to enter text.

Study Author, Year: Click here to enter text.

Language: Choose an item.

Country of origin: Click here to enter text.

Source of funding: Choose an item.

Study Information

Aim of study: Click here to enter text.

Study design: Choose an item.

Appropriate risk of bias tool completed: ☐

Inclusion criteria: Click here to enter text.

Exclusion criteria: Click here to enter text.

Definition of fever used: Click here to enter text.

Definition of neutropenia used: Click here to enter text.

Risk stratification tool/definition of low-risk: Click here to enter text.

Timing of risk stratification: Click here to enter text.

Details of randomisation/selection of cohorts: Click here to enter text.

Participants

Number of participants: Click here to enter text.

Number in each group: Click here to enter text.

Number withdrawn: Click here to enter text.

Number included in analysis: Click here to enter text.

Age – provide details for each group: Click here to enter text.

Gender – provide details for each group: Click here to enter text.

Ethnicity (if given): Click here to enter text.

Socio-economic status (if given): Click here to enter text.

Disease(s): Click here to enter text.

Are recruitment/refusal to consent numbers given? If so, please record details including, if given, number, distribution, reasons for declining:

Click here to enter text.

Intervention

Describe the intervention(s) (eg. how long inpatient, if outpatient how often reviewed and where, antibiotics used, route, time of change):

Click here to enter text.

Give details of control/routine care:

Click here to enter text.

Outcomes:

Definition of treatment failure used: Click here to enter text.

Primary outcome(s):

Click here to enter text.

Secondary outcome(s):

Click here to enter text.

Results:

All data should be in unit numbers, not percentages or proportions

Dichotomous outcomes

Outcome	**Group 1**		**Group 2**		**Group 3**		**Notes**
	Observed (n)	**Total (N)**	**Observed (n)**	**Total (N)**	**Observed (n)**	**Total (N)**	
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.

Continuous outcomes

Outcome	Timing of outcome assessment	Group 1			Group 2			Group 3			Notes
		Mean/ mean difference	**SD**	**N**	**Mean/ mean difference**	**SD**	**N**	**Mean/ mean difference**	**SD**	**N**	
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.

Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.

Other information/Comments

Click here to enter text.

Appendix 3.3: Reasons for study exclusion

Study	Reason for exclusion
Acuna, 1987(234)	Not intervention of interest
Ahmed, 2007(235)	Mixed risk groups
Ammann, 2004(236)	Correspondence
Ammann, 2005(237)	Review article
Anak, 1989(238)	Not intervention of interest
Anoop, 2007(239)	Correspondence
Aquino, 1997a(240)	Retrospective
Aquino, 1997b(241)	Retrospective
Arceci, 2000(242)	Editorial
Barnes, 1988(243)	Adult study
Barsanti, 1988(244)	Review article
Bellesso, 2013(245)	Review article
Buchanan, 1992(246)	Correspondence
Chamberlain, 2005(247)	Audit
Cohen, 1995(248)	Not intervention of interest
Cornely, 1997(249)	Mixed population
De Pauw, 1997(250)	Adult study
Dominic, 2007(251)	Adult study
Escalante, 2004(252)	Adult study
Fink, 1989(253)	Retrospective

Fleischhack, 1997(254)	Not intervention of interest
Freifeld, 1999(255)	Mixed population
Gala Peralta, 2006(256)	Article describing interview
Gaya, 1979(257)	Adult study
Girmenia, 2007(258)	Adult study
Hodgson-Viden, 2005(259)	Retrospective
Holdsworth, 1995(260)	Not low risk patients
Innes, 2003(261)	Adult study
Jaksic, 2006(262)	Adult study
Jin, 2010(263)	Adult study
Kaplan, 1991(264)	Retrospective
Karthaus, 1998(265)	Mixed population
Karthaus, 2000(266)	Adult study
Katz, 1993(267)	Review article
Kern, 1999(268)	Mixed population
Kern, 2013(269)	Adult study
Klastersky, 1977(270)	Adult study
Lee, 2010(271)	Retrospective
Lehrnbecher, 2002(272)	Retrospective
Lopez Hernandez, 2010(273)	Mixed population
Martino, 1992(274)	Mixed population
Maschmeyer, 1994(275)	Adult study

Mullen, 1990 (276)	Retrospective
Mullen, 1998 (277)	Conference abstract of full article already included
Mullen, 1999 (48)	Economic outcomes of study already included
Mullen, 2001 (16)	Review article
Nenova, 2003 (278)	Adult study
Nijhuis, 2005 (30)	Mixed population
O'Connell, 1998 (279)	Retrospective
Oppenheim, 2000 (280)	Review article
Paganini, 2007 (281)	Review article
Patrick, 1999 (282)	Review article
Pennington, 1977 (283)	Adult study
Petrilli, 1989 (284)	Not intervention of interest
Pizzo, 1979 (285)	<80% paediatric patients
Pizzo, 1982 (286)	<80% paediatric patients
Preis, 1997 (287)	Correspondence
Rodriguez, 1973 (288)	Adult study
Rubenstein, 1993 (289)	Adult study
Rubin, 1989 (290)	Correspondence
Sahu, 1997 (291)	Mixed risk groups
Saini, 2007(292)	Review article
Santolaya, 1997 (293)	Not studying outcome of interest
Santolaya, 2001(294)	Review article

Santos-Machado, 1999 (295)	Retrospective
Shemesh, 1998 (47)	Retrospective
Talcott, 1994 (296)	Adult study
Talcott, 2011 (297)	Adult study
Tomiak, 1994 (298)	Adult study
Tordecilla, 1994 (299)	Not intervention of interest
Villanueva, 2013 (300)	Retrospective
Wacker, 1997 (301)	Not intervention of interest
Willoughby, 1994 (302)	Review article
Wiwanitkit, 2010 (303)	Correspondence
Zubizarreta, 2002 (304)	Correspondence

Appendix 3.4: Risk of bias tables

Randomised Controlled Trials

	Random Sequence Generation (selection bias)	Allocation Concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Brack et al, 2012 (17)	-	-	+	+	-	-
Cagol et al, 2009 (107)	-	-	+	+	?	?
Gupta et al, 2009 (108)	-	?	+	+	-	-
Klaassen et al 2000 (109)	-	?	-	-	-	-
Mullen et al, 1999 (110)	-	-	+	+	-	-
Orme et al, 2014 (111)	-	?	+	+	-	-
Paganini et al, 2003 (112)	-	-	+	+	-	-
Paganini et al, 2001 (113)	-	-	+	+	-	-
Paganini et al, 2000 (114)	-	-	+	+	-	-
Petrilli et al, 2000 (115)	?	?	+	+	-	-
Santolaya et al, 2004 (116)	?	?	+	+	-	-
Shenep et al, 2001 (117)	-	?	+	+	-	-
Varan et al, 2005 (118)	?	?	+	+	-	-

Key: - low risk of bias, ? unclear risk of bias, + high risk of bias

Prospective Observational cohorts

	Population of interest	Loss to follow-up	Prognostic factor	Outcome of interest	Potential confounders	Statistical analysis
Abbas et al, 2003 (119)	-	-	-	-	-	-
Aquino et al, 2000 (120)	-	-	-	-	-	-
Bash et al, 1994 (18)	-	-	-	-	-	-
Dommett et al, 2009 (121)	-	-	-	-	-	?
Doyle et al, 1996 (122)	-	-	-	-	-	-
Fernandez et al, 2012 (123)	-	-	-	-	-	-
Kaplinsky et al, 1994 (124)	-	?	-	-	-	-
Karthaus et al, 2000 (125)	-	-	-	-	-	-
Lau et al, 1994 (126)	-	-	-	-	?	-
Malik, 1997(127)	-	-	-	-	-	-
Miedema et al, 2012 (128)	-	?	-	?	-	-
Mustafa et al, 1996 (305)	-	-	-	-	-	-
Paganini et al, 2001 (129)	-	?	-	-	-	-
Paganini, 2003 (131)	-	-	-	-	-	-
Paganini, 2000 (130)	-	-	-	-	-	-
Park et al, 2003 (132)	?	-	-	-	-	-
Petrilli et al, 2007 (133)	-	-	-	?	-	-
Phillips et al, 2006 (134)	?	-	-	-	-	-

Preis et al, 1993 (135)	?	-	-	?	-	-
Quezada et al, 2007 (136)	-	-	?	?	?	-
Sari et al, 2007 (137)	-	-	-	?	-	-
Shrestha et al, 2009 (138)	-	?	-	-	-	-
Tordecilla et al, 1998 (139)	-	?	?	?	-	-
Wiernikowski et al, 1991 (140)	?	-	-	-	-	-

Key: - low risk of bias, ? unclear risk of bias, + high risk of bias

Appendix B

This Appendix includes all appendices related to chapter 4 of the thesis.

Appendix 4.1: Database search strategy

British Nursing Index (BNI) (ProQuest – http://search.proquest.com/)

1994 to current

Searched on 18/07/2014

Retrieved 315 hits (after automatic de-duplication by BNI)

Search Strategy (Febrile neutropenia OR early discharge):=

Key:

ti(terms) = searches terms in title field

ab(terms) = searches terms in abstract field

NEAR/1 = terms within one word of each other (any order)

NEAR/2 = terms within two words of each other (any order)

* = truncation – unlimited characters

?? = two wild characters

SU.EXACT = single indexing term

SU.EXACT.EXPLODE = exploded indexing term

(ti(early NEAR/2 discharge*) OR ab(early NEAR/2 discharge*) OR (SU.EXACT("Patients : Discharge") AND SU.EXACT("Patients : Admission"))) OR ((ti(febrile NEAR/5 (neutropen* OR granulocytop* OR agranulocyto* OR leukocytop??ni* OR leukocytop?ni*)) OR ab(febrile NEAR/5 (neutropen* OR granulocytop* OR agranulocyto* OR leukocytop??ni* OR leukocytop?ni*))) OR (ti((fever OR temperature OR temp) NEAR/5 (neutropen* OR granulocytop* OR agranulocyto* OR leukocytop??ni*)) OR ab((fever OR temperature OR temp) NEAR/5 (neutropen* OR granulocytop* OR agranulocyto* OR leukocytop??ni*))) OR (SU.EXACT("Fever") AND SU.EXACT.EXPLODE("Blood and Blood Disorders")))

CINAHL - Cumulative Index to Nursing & Allied Health Literature (EBSCO – http://www.ebscohost.com/)

1981 - current

Searched on 12/06/2014

Retrieved 517 hits

CINAHL (EBSCO)

Key

MH = indexing term (CINAHL heading)

+ =exploded CINAHL heading

* = truncation

? = embedded truncation

“ “ = phrase search

ZT = publication type

n1 = terms within one word of each other (any order)

n2 = terms within two words of each other (any order)

Search Strategy – ((febrile neutropenia AND early discharge) OR (children AND early discharge)):

S25 S23 OR S24 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

517 hits

S24 S3 AND S22 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

508 hits

S23 S3 AND S17 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

21 hits

S22 S18 OR S19 OR S20 OR S21 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

745,047 hits

S21 TI (newborn* or new-born* or baby* or babies or neonat* or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or “young person*” or “young people” or “young adult*” or child* or schoolchild* or schoolage* or school* or preschool*) OR AB (newborn* or new-born* or baby* or babies or neonat* or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or “young person*” or “young people” or “young adult*” or child* or schoolchild* or schoolage* or school* or preschool*) Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

453,137 hits

S20 (MH "Young Adult") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

89,795 hits

S19 (MH "Adolescence+") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

302,618 hits

S18 (MH "Child+") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

404,639 hits

S17 S11 OR S16 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

1,187 hits

S16 S12 OR S13 OR S14 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

1,041 hits

S15 TI (temp N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) OR AB (temp N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

0 hits

S14 TI (temperature N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) OR AB (temperature N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

2 hits

S13 TI (fever N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) OR AB (fever N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

288 hits

S12 TI (febrile N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) OR AB (febrile N5 (neutropen* or granulocytop* or agranulocyto* or leukocytopeni*)) Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

824 hits

S11 S7 AND S10 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

480 hits

S10 S8 OR S9 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

12,808 hits

S9 (MH "Body Temperature+") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

6,820 hits

S8 (MH "Fever+") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

6,543 hits

S7 S4 OR S5 OR S6 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

2,901 hits

S6 (MH "Agranulocytosis") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

229 hits

S5 (MH "Neutropenia") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

2,448 hits

S4 (MH "Leukopenia") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

319 hits

S3 S1 OR S2 Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

1,472 hits

S2 TI early n2 discharge* OR AB early n2 discharge* Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

1,064 hits

S1 (MH "Early Patient Discharge") Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

730 hits

EMBASE:

Febrile neutropenia and length of stay

EMBASE <1974 to 2014 May 20> was searched on 21/05/2015, using the OVID SP interface.

1326 records were retrieved

Early discharge and children

EMBASE <1974 to 2014 July 22> was searched on 23/07/2015, using the OVID SP interface.

778 records were retrieved

Key:

/ = indexing term (EMTREE heading)

* = focussed EMTREE heading

exp = exploded EMTREE heading

* = truncation

? = embedded truncation

.ti,ab. = terms in either title or abstract fields

.tw.= textword

adj = terms adjacent to each other (same order)

adj1 = terms within one word of each other (any order)

adj2 = terms within two words of each other (any order)

Strategy - Febrile neutropenia and length of stay:

1 *Agranulocytosis/ or *neutropenia/ or *leukopenia/ (19460)

2 *Fever/ or *pyrexia idiopathica/ or exp *Body Temperature/ (37027)

3 (1 and 2) or *febrile neutropenia/ (3365)

4 (febrile adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (8603)

5 ((fever or temperature or temp) adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (3879)

6 3 or 4 or 5 (12590)

7 *"length of stay"/ or *hospital admission/ or *hospital discharge/ or *hospital readmission/ or exp *hospital patient/ or *outpatient/ (45807)

8 (discharge* or (length* adj2 stay*) or (duration* adj2 stay*) or admission* or readmission* or inpatient* or outpatient*).tw. (606089)

9 7 or 8 (619909)

10 6 and 9 (1326)

Strategy - Early discharge and children:

1 (early adj2 discharge*).ti,ab. (3877)

2 *"length of stay"/ and *hospital discharge/ (302)

3 or/1-2 (4096)

4 (baby* or babies or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or young person* or young people or young adult* or child* or schoolchild* or schoolage* or school* or preschool*).tw. (2080868)

5 *adolescent/ or exp *child/ or *infant/ or *young adult/ (201877)

6 or/4-5 (2144190)

7 3 and 6 (778)

Medline:

Febrile neutropenia and length of stay:

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present> was searched on 21/05/2014, using the OVID SP interface.

882 records were retrieved

Early discharge and children:

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present> was searched on 01/07/2014, using the OVID SP interface.

1850 records were retrieved

Key:

/=index term (MeSH heading)

*=truncation

?= embedded truncation

ti=title field

ab=abstract

tw= textword

.ti,ab=terms were searched for in either title or abstract

adj = terms adjacent to each other (same order)

adj1 = terms within one word of each other (any order)

adj2 = terms within two words of each other (any order)

Strategy - Febrile neutropenia and length of stay:

1 Agranulocytosis/ or neutropenia/ or leukopenia/ (26987)

2 exp Fever/ or exp "Fever of Unknown Origin"/ or exp Body Temperature/ (103894)

3 (1 and 2) or febrile neutropenia/ (2887)

4 (febrile adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (5283)

5 ((fever or temperature or temp) adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (2742)

6 3 or 4 or 5 (8323)

7 exp "length of stay"/ or exp patient admission/ or exp patient discharge/ or exp patient readmission/ or exp inpatients/ or exp outpatients/ (110907)

8 (discharge* or (length* adj2 stay*) or (duration* adj2 stay*) or admission* or readmission* or inpatient* or outpatient*).tw. (433243)

9 7 or 8 (480710)

10 6 and 9 (882)

Strategy - Early discharge and children:

1 (early adj2 discharge*).ti,ab. (2808)

2 "length of stay"/ and patient discharge/ (3610)

3 patient discharge/ and Time Factors/ (2067)

4 or/1-3 (7230)

5 adolescent/ or exp child/ or infant/ or exp young adult/ (2748218)

6 (baby* or babies or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or young person* or young people or young adult* or child* or schoolchild* or schoolage* or school* or preschool*).tw. (1703554)

7 5 or 6 (3323001)

8 4 and 7 (2008)

9 8 (2008)

10 limit 9 to english language (1850)

11 10 (1850)

12 limit 11 to yr="1950 -Current" (1850)

PsycINFO (Ovid Online – http://www.ovid.com/) 1806 to July Week 1 2014 was searched on 04/07/2014

Retrieved 501 hits

Key:

/ = indexing term

$ = truncation

? = embedded truncation

md = methodology field

.ti,ab. = terms in either title or abstract fields

adj = terms adjacent to each other (same order)

adj1 = terms within one word of each other (any order)

adj2 = terms within two words of each other (any order)

Search Strategy – (Early discharge AND child) OR febrile neutropenia:

1 (early adj2 discharge*).ti,ab. (237)

2 Hospital Discharge/ (1547)

3 1 or 2 (1734)

4 (baby* or babies or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or junevil* or youth* or puber* or prepuber* or pubescen*or prepubescen* or pediatric* or paediatric* or young person* or young people or young adult* or child* or schoolchild* or schoolage* or school* or preschool*).tw. (922624)

5 3 and 4 (225)

6 limit 3 to (100 childhood <birth to age 12 yrs> or 140 infancy <2 to 23 mo> or 160 preschool age <age 2 to 5 yrs> or 180 school age <age 6 to 12 yrs> or 200 adolescence <age 13 to 17 yrs> or 320 young adulthood <age 18 to 29 yrs>) (409)

7 5 or 6 (473)

8 (febrile adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (13)

9 ((fever or temperature or temp) adj5 (neutropen* or granulocytop* or agranulocyto* or leukocytop??ni*)).ti,ab. (9)

10 "febrile neutropenia".id. (6)

11 exp "Blood and Lymphatic Disorders"/ (3658)

12 hyperthermia/ (813)

13 11 and 12 (21)

14 8 or 9 or 10 or 13 (39)

15 7 or 14 (512)

16 limit 15 to english language (501)

Appendix 4.2: Reasons for study exclusion

Study	**Reason for exclusion**
Beguin et al, 2002 (306)	Not primary research
Belanger, 2001(307)	Not patient group of interest
Burke, 1999 (308)	Review article
Carpenter, 1998 (309)	Neonatal
Charles and Prystowsky, 1995 (310)	Neonatal
Finkelstein, 1980 (311)	Not patient group of interest
Flowers and Karten, 2013 (312)	Commentary
Forsander, 1995 (313)	Quantitative
Freifeld and Sepkowitz, 2011 (314)	Commentary
Gatford, 2004 (315)	Not early discharge
Graumlich et al, 2008 (316)	Quantitative
Gunnell et al, 2000 (317)	Not patient group of interest
Jester and Hicks, 2003a (318)	Not patient group of interest
Jester and Hicks, 2003b (319)	Not patient group of interest
Jones, 2007 (320)	Not patient group of interest
Karthaus et al, 2000 (125)	Quantitative
Kibbler and Prentice, 1997 (321)	Review article
King, 1996 (322)	Review article
Krupski and Domm, 2014 (323)	Commentary
Lingaratnam et al, 2010 (324)	Quantitative
Luker et al, 2003 (325)	Not patient group of interest

Margolan et al, 2004(326)	Not early discharge
Menahem et al, 1997 (327)	Not early discharge
Mendler et al, 1996 (328)	Neonatal
Meropol et al, 1994 (329)	Quantitative
Mikkelsen et al, 2008 (330)	Not early discharge
Moxley, 1977 (331)	Not patient group of interest
Mullen, 1998 (277)	Quantitative
Mullen, 2001 (16)	Review article
Orme et al, 2010 (332)	Quantitative
Ouvrier et al, 2006 (333)	Correspondence
Patrick and Shenep, 1999 (282)	Review article
Paulson, 1987 (334)	Review article
Pinto et al, 2010 (335)	Qualitative synthesis
Richards et al, 1998 (336)	Quantitative
Rolston et al, 1996 (337)	Review article
Rubenstein and Rolston, 1995 (338)	Review article
Silva and High, 1998 (339)	Review article
Slavin and Thursky, 2013 (340)	Review article
Svahn et al, 2004 (341)	Quantitative
Tice, 1998 (342)	Review article
Turley and Higgins, 1996 (343)	Quantitative
Uzark et al, 1994 (344)	Quantitative
Uzun and Anaissie, 1999 (345)	Review article

Youngblut et al, 1994 (346)	Quantitative

Appendix 4.3: Results of CLUSTER searches

Step 1 - Pearl citation	Step 2 - Check reference list of pearl citation for citations by authors	Step 3 - Recheck 'database of search results' EndNote library – search using authors from pearl	Step 4 - Search for author publication lists (number of authors searched)	Step 5 - Citation searches on Web of Science and Google Scholar for pearl citation	Step 6 - Searches on project name/identifier	Step 7 - Make contact with lead author	Number of studies included in synthesis
Sartain et al(156)	0	0	25 (2)	15, 30	26	0	1
Freund and Siegel(152)	0	0	118 (2)	30, 49	n/a	0	0
Diorio et al(151)	1	40	200 (2)	4	n/a	0	0

Study	Diorio et al, 2011(151)
Does the report clearly state the philosophical and theoretical premises on which the study is based?	No
Does the report clearly state the methodological approach adopted on which the study is based?	Yes
Is there congruence between the two?	?
Is the study methodology appropriate for addressing the research question?	Yes
Are the data collection methods appropriate to the methodology?	Yes
Are the data analysed and represented in ways that are congruent with the stated methodological position?	Yes
Are the results interpreted in ways that are appropriate to the methodology?	Yes
Are the researchers' beliefs and values, and their potential influence on the study declared?	No
Is the potential for the researcher to influence the study and for the potential of the research process itself to influence the researcher and her/his interpretations acknowledged and addressed?	No
Are participants, and their voices, adequately represented?	Yes
Has the study been ethically approved by an appropriate body?	Yes
Do the conclusions drawn in the research report appear to flow from the analysis, or interpretation, of the data?	Yes

Freund and Siegel, 1986(152)	No	?	?	Yes	?	Yes	Yes	No	No	?	No	?
Fuji et al, 2013(153)	No	?	?	?	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Hally et al, 1977(154)	No	No	?	?	?	?	?	No	No	?	?	Yes
Sartain et al, 2000(155)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Sartain et al, 2001(156)	No	No	?	?	Yes	Yes	Yes	No	No	Yes	?	Yes
Smith and Daughtrey, 2000(157)	No	?	?	?	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Tatman et al, 1992(150)	No	No	?	?	?	?	?	No	No	Yes	?	Yes
While, 1992(158)	?	No	?	Yes	?	?	Yes	No	?	Yes	?	Yes

? = Unclear

Appendix C

This Appendix includes all appendices related to chapter 5 of the thesis.

Appendix 5.1: Participant Information Sheets

Young Person Participant Information Sheet

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Young Person Participant Information Sheet

Date: 30/11/15

Version: 3

Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals

We would like to invite you to take part in the above named research study. Before you decide whether or not you would like to take part, we would like to tell you more about the study and about what being part of it would involve. If you would like to ask any questions about the study, we have provided details of who to contact at the end of this leaflet.

What is the purpose of this study?

Neutrophils are the commonest form of white blood cells and play an important role in the immune system. Treatment for cancer can result in low neutrophils, also known as neutropenia. This results in an increased risk of infection. When someone with neutropenia develops a temperature, this is called febrile neutropenia. Sometimes febrile neutropenia is very serious, but most of the time it does not cause any serious medical problems. We are working to look at the possibility of reducing the length of time that children and young people spend in hospital when we predict that they will not have serious problems from their febrile neutropenia.

For this particular study, we are interested in hearing about what young people, their parents and their doctors and nurses, think about them spending less time in hospital. This information may then help to inform how we design services for children and young people who develop febrile neutropenia in the future.

Who is doing the study?

This study is being conducted as part of a PhD project by Dr Jessica Morgan from the University of York. Her work will be supervised by Professor Karl Atkin (also at University of York). There are further supervisory and advisory researchers involved in the work, as part of the university training procedures. All the researchers who contact you have been checked out by the Criminal

Records Bureau to ensure they are appropriately qualified to undertake research. This research has been funded by Candlelighters Childhood Cancer Charity (Registered Charity No: 1045077).

Why have I been asked to participate?

You have been asked to take part because we are interested in talking to young people, age 13 to 18 years old, who have had treatment for cancer at some point within the last six months and who, if they developed febrile neutropenia, might be considered at low risk of serious complications. You are the people who are able to tell us about how you would prefer to be treated if this were to happen to you. We are also interested to talk to your parents and your doctors and nurses, because we know that that decisions about treatment are often made by taking into consideration all of these people's opinions. We are going to ask these questions at groups at different hospitals around the UK as we think that people in different places, where the services are designed differently, might have different opinions about this problem. You will probably have been invited to take part because someone who looks after you felt that you were able to talk about what you think about this issue.

Do I have to take part?

No, this study is entirely voluntary. You can chose not to take part and this will not affect your treatment at all. If you decide to take part, you will be given this information sheet to keep and you will be asked to sign an assent form. Because of legal requirements, someone who has parental responsibility for you will also be asked to consent on your behalf. It is important that you both agree that you should take part in the study. After you have signed the consent and assent forms, you are still free to withdraw from the study at any time up to two weeks following the focus group discussion. If you withdraw from the study your quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used. You do not need to give a reason for withdrawing.

What will be involved if I take part in this study?

We would ask you to take part in a group discussion with between four and seven other young people, and led by a researcher. We would talk about your experiences of being treated for febrile neutropenia in the past - don't worry if you have never had febrile neutropenia – we are specifically asking some people with no experience to the groups. We will then ask you about what you think about shorter hospital stays for febrile neutropenia. The discussion would take about 90 minutes and would be audio-recorded. We would choose people to try to reflect a range

of possible opinions. The discussion will take place in or close to the hospital and the time will be selected to be convenient for as many participants as possible.

What are the advantages of taking part?

At the end of the work, when we have been able to look at all the discussions which will take place, we will provide you with a summary of our findings and the recommendations we make about improving future services.

What are the disadvantages of taking part?

Sometimes talking about your experiences can bring up some difficult memories. You may also start to think more about febrile neutropenia happening again in the future. People involved in your care will be available to talk to you about any questions you have about your own treatment after this study.

Will I be paid to take part in this study?

You will be offered a £20 Amazon voucher, provided by Candlelighters Children's Cancer Charity, to recognise the time commitment involved in this study. If you chose to accept this, it will be sent to you following the focus group via email or post, depending on which you prefer.

Candlelighters Children's Cancer Charity have also given us funding to provide you with your travel expenses. This will be 45 pence per mile if you drive to the group discussion, or the price of a standard rate ticket for public transport. This will be sent to you following the focus group.

Will the information obtained in the study be confidential?

All information you give to us will be confidential. We will not tell anyone (including your family or the professionals who look after you) about what you share with us. The only exception to this is if you tell us things which we believe place you or other people at serious risk. If this happens, we are required to tell other people about it so as to protect you (or other people) from harm.

The audio-recordings from the discussions will be listened to and everything that is said will be written down. This creates a document called a transcript. All information that is written or recorded will be kept in locked offices at the University of York. Only the research team will be able to see them. All the information you provide will have a code allocated to it and this will be stored separately from your personal details. No names will be used in the transcripts, our notes or any writing we do about this work. At the end of the study, the audio recordings will be erased. The data will be stored for five years, so that if the research needs to be checked or further

analysis needs to be done then this is available. At all times, all data will be treated in accordance with the current Data Protection Act.

What will happen to the results of the study?

The results of this study will be used in a number of ways. We will write a summary of the work for you to read and to know what was found from the research. Other members of the public will also be able to read this summary. The work will also be written as a full academic report for the PhD thesis of Dr Jessica Morgan. As well as this, it will also be submitted for publication in scientific journals. You can call members of the research team at any time to discuss the progress of the research.

Who has reviewed this study?

The plans for this study have been reviewed by the University of York Research Governance Committee, as well as an NHS Research Ethics Committee. The progress of the research will be monitored throughout by the University of York.

Who do I contact in the event of a complaint?

Please raise any difficulties or questions with Dr Jessica Morgan (01904) 321082 (8am to 5pm weekdays) email jem539@york.ac.uk or Professor Karl Atkin (01904) 321355 email karl.atkin@york.ac.uk. If the research team are unable to give you a satisfactory answer, please contact Professor Lesley Stewart, (01904) 321093, email lesley.stewart@york.ac.uk.

If you agree to take part, would like more information or have any questions or concerns about the study please contact Dr Jessica Morgan, Chief Investigator, Centre for Reviews and Dissemination, University of York, Tel 01904 321082, Email jem539@york.ac.uk

Thank you for taking the time to read this information sheet.

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Parent's Information Sheet

Date: 30/11/15

Version: 3

Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals

We would like to invite you to consent for your child to take part in the above named research study. Before you decide whether or not you would like them to take part, we would like to tell you more about the study and about what your child being part of it would involve. If you would like to ask any questions about the study, we have provided details of who to contact at the end of this leaflet.

What is the purpose of this study?

Neutrophils are the commonest form of white blood cells and play an important role in the immune system. Treatment for cancer can result in low neutrophils, also known as neutropenia. This results in an increased risk of infection. When someone with neutropenia develops a temperature, this is called febrile neutropenia. Sometimes febrile neutropenia is very serious, but most of the time it does not cause any serious medical problems. We are working to look at the possibility of reducing the length of time that children and young people spend in hospital when we predict that they will not have serious problems from their febrile neutropenia. For this particular study, we are interested in hearing about what young people, their parents and their doctors and nurses, think about them spending less time in hospital. This information may then help to inform how we design services for children and young people who develop febrile neutropenia in the future.

Who is doing the study?

This study is being conducted as part of a PhD project by Dr Jessica Morgan from the University of York. Her work will be supervised by Professor Karl Atkin (also at University of York). There are further supervisory and advisory researchers involved in the work, as part of the university training procedures. All the researchers who contact you have been checked out by the Criminal

Records Bureau to ensure they are appropriately qualified to undertake research. This research has been funded by Candlelighters Childhood Cancer Charity (Registered Charity No: 1045077).

Why has your child been asked to participate?

Your child has been asked to take part because we are interested in talking to young people, age 13 to 18 years old, who have had treatment for cancer at some point within the last six months and who, if they developed febrile neutropenia, might be considered at low risk of serious complications. These young people are the ones who are able to tell us about how they would prefer to be treated if this were to happen to them. We are also interested to talk to their parents and their doctors and nurses, because we know that that decisions about treatment are often made by taking into consideration all of these people's opinions. (You may also have been asked to take part in this study yourself, in which care, you will receive another information sheet about your own participation.) We are going to ask these questions at groups at different hospitals around the UK as we think that people in different places, where the services are designed differently, might have different opinions about this problem. Your child will probably have been invited to take part because someone who looks after them felt that they were able to talk about what they think about this issue.

Does my child have to take part?

No, this study is entirely voluntary. You can chose for your child not to take part and this will not affect their treatment at all. If you decide to let them take part, you will be given this information sheet to keep and you will be asked to sign a consent form. We will also ask your child to sign a form stating that they would like to take part. It is important that you both agree whether your child should take part in the study. After you have signed the consent and assent forms, you are still free to withdraw your child from the study at any time up to two weeks following the focus group discussion. If you withdraw your child from the study their quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used. You do not need to give a reason for withdrawing.

What will be involved if my child takes part in this study?

We would ask your child to take part in a group discussion with between four and seven other young people, and led by a researcher. We would talk about their experiences of being treated for febrile neutropenia in the past - don't worry if they have never had febrile neutropenia – we are specifically asking some people with no experience to the groups. We will then ask your child about what they think about shorter hospital stays for febrile neutropenia. The discussion would

take about 90 minutes and would be audio-recorded. We would choose people to try to reflect a range of possible opinions. The discussion will take place in or close to the hospital and the time will be selected to be convenient for as many participants as possible.

What are the advantages of taking part?

At the end of the work, when we have been able to look at all the discussions which will take place, we will provide you and your child with a summary of our findings and the recommendations we make about improving future services.

What are the disadvantages of taking part?

Sometimes talking about their experiences can bring up some difficult memories for your child. They may also start to think more about febrile neutropenia happening again in the future. People involved in your child's care will be available to talk to you and your child about any questions you have about their treatment after this study.

Will I be paid if my child takes part in this study?

You will be offered a £20 Amazon voucher, provided by Candlelighters Children's Cancer Charity, to recognise the time commitment involved in this study. If you chose to accept this, it will be sent to you following the focus group via email or post, depending on which you prefer.

Candlelighters Children's Cancer Charity have also given us funding to provide you with your travel expenses. This will be 45 pence per mile if you drive to the group discussion, or the price of a standard rate ticket for public transport. This will be sent to you following the focus group.

Will the information obtained in the study be confidential?

All information you and your child give to us will be confidential. We will not tell anyone (including yourself, your family or the professionals who look after your child) about what they chose to share with us in the discussion. The only exception to this is if your child tells us things which we believe place them or other people at serious risk. If this happens, we are required to tell the relevant authorities so as to protect them (or other people) from harm.

The audio-recordings from the discussions will be listened to and everything that is said will be written down. This creates a document called a transcript. All information that is written or recorded will be kept in locked offices at the University of York. Only the research team will be able to see them. All the information you and your child provide will have a code allocated to it and this will be stored separately from your child's personal details. No names will be used in the

transcripts, our notes or any writing we do about this work. At the end of the study, the audio recordings will be erased. The data will be stored for five years, so that if the research needs to be checked or further analysis needs to be done then this is available. At all times, all data will be treated in accordance with the current Data Protection Act.

What will happen to the results of the study?

The results of this study will be used in a number of ways. We will write a summary of the work for you and your child to read and to know what was found from the research. Other members of the public will also be able to read this summary. The work will also be written as a full academic report for the PhD thesis of Dr Jessica Morgan. As well as this, it will also be submitted for publication in scientific journals. You can call members of the research team at any time to discuss the progress of the research.

Who has reviewed this study?

The plans for this study have been reviewed by the University of York Research Governance Committee, as well as an NHS Research Ethics Committee. The progress of the research will be monitored throughout by the University of York.

Who do I contact in the event of a complaint?

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If you agree to take part, would like more information or have any questions or concerns about the study please contact Dr Jessica Morgan, Chief Investigator, Centre for Reviews and Dissemination, University of York, Tel 01904 321082, Email jem539@york.ac.uk

Thank you for taking the time to read this information sheet.

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Adult Patient Participant Information Sheet

Date: 30.11.15

Version: 3

Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals

We would like to invite you to take part in the above named research study. Before you decide whether or not you would like to take part, we would like to tell you more about the study and about what being part of it would involve. If you would like to ask any questions about the study, we have provided details of who to contact at the end of this leaflet.

What is the purpose of this study?

Neutrophils are the commonest form of white blood cells and play an important role in the immune system. Treatment for cancer can result in low neutrophils, also known as neutropenia. This results in an increased risk of infection. When someone with neutropenia develops a temperature, this is called febrile neutropenia. Sometimes febrile neutropenia is very serious, but most of the time it does not cause any serious medical problems. We are working to look at the possibility of reducing the length of time that children and young people spend in hospital when we predict that they will not have serious problems from their febrile neutropenia.

For this particular study, we are interested in hearing about what young people, their parents and their doctors and nurses, think about them spending less time in hospital. This information may then help to inform how we design services for children and young people who develop febrile neutropenia in the future.

Who is doing the study?

This study is being conducted as part of a PhD project by Dr Jessica Morgan from the University of York. Her work will be supervised by Professor Karl Atkin (also at University of York). There are further supervisory and advisory researchers involved in the work, as part of the university training procedures. All the researchers who contact you have been checked out by the Criminal Records Bureau to ensure they are appropriately qualified to undertake research. This research has been funded by Candlelighters Childhood Cancer Charity (Registered Charity No: 1045077).

Why have I been asked to participate?

You have been asked to take part because we are interested in talking to young people, age 13 to 18 years old, who have had treatment for cancer at some point within the last six months and who, if they developed febrile neutropenia, might be considered at low risk of serious complications. You are the people who are able to tell us about how you would prefer to be treated if this were to happen to you. We are also interested to talk to your parents and your doctors and nurses, because we know that that decisions about treatment are often made by taking into consideration all of these people's opinions. We are going to ask these questions at groups at different hospitals around the UK as we think that people in different places, where the services are designed differently, might have different opinions about this problem. You will probably have been invited to take part because someone who looks after you felt that you were able to talk about what you think about this issue.

Do I have to take part?

No, this study is entirely voluntary. You can chose not to take part and this will not affect your treatment at all. If you decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form. After you have signed the consent form, you are still free to withdraw from the study at any time up to two weeks following the focus group discussion. If you withdraw from the study your quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used. You do not need to give a reason for withdrawing.

What will be involved if I take part in this study?

We would ask you to take part in a group discussion with between four and seven other young people, and led by a researcher. We would talk about your experiences of being treated for febrile neutropenia in the past - don't worry if you have never had febrile neutropenia – we are specifically asking some people with no experience to the groups. We will then ask you about what you think about shorter hospital stays for febrile neutropenia. The discussion would take about 90 minutes and would be audio-recorded. We would choose people to try to reflect a range of possible opinions. The discussion will take place in or close to the hospital and the time will be selected to be convenient for as many participants as possible.

What are the advantages of taking part?

At the end of the work, when we have been able to look at all the discussions which will take place, we will provide you with a summary of our findings and the recommendations we make about improving future services.

What are the disadvantages of taking part?

Sometimes talking about your experiences can bring up some difficult memories. You may also start to think more about febrile neutropenia happening again in the future. People involved in your care will be available to talk to you about any questions you have about your own treatment after this study.

Will I be paid to take part in this study?

You will be offered a £20 Amazon voucher, provided by Candlelighters Children's Cancer Charity, to recognise the time commitment involved in this study. If you chose to accept this, it will be sent to you following the focus group via email or post, depending on which you prefer.

Candlelighters Children's Cancer Charity have also given us funding to provide you with your travel expenses. This will be 45 pence per mile if you drive to the group discussion, or the price of a standard rate ticket for public transport. This will be paid to you in cash on the day and we will need you to sign a receipt. This will be sent to you following the focus group.

Will the information obtained in the study be confidential?

All information you give to us will be confidential. We will not tell anyone (including your family or the professionals who look after you) about what you share with us. The only exception to this is if you tell us things which we believe place you or other people at serious risk. If this happens, we are required to tell other people about it so as to protect you (or other people) from harm.

The audio-recordings from the discussions will be listened to and everything that is said will be written down. This creates a document called a transcript. All information that is written or recorded will be kept in locked offices at the University of York. Only the research team will be able to see them. All the information you provide will have a code allocated to it and this will be stored separately from your personal details. No names will be used in the transcripts, our notes or any writing we do about this work. At the end of the study, the audio recordings will be erased. The data will be stored for five years, so that if the research needs to be checked or further analysis needs to be done then this is available. At all times, all data will be treated in accordance with the current Data Protection Act.

What will happen to the results of the study?

The results of this study will be used in a number of ways. We will write a summary of the work for you to read and to know what was found from the research. Other members of the public will also be able to read this summary. The work will also be written as a full academic report for the PhD thesis of Dr Jessica Morgan. As well as this, it will also be submitted for publication in scientific journals. You can call members of the research team at any time to discuss the progress of the research.

Who has reviewed this study?

The plans for this study have been reviewed by the University of York Research Governance Committee, as well as an NHS Research Ethics Committee. The progress of the research will be monitored throughout by the University of York.

Who do I contact in the event of a complaint?

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If you agree to take part, would like more information or have any questions or concerns about the study please contact Dr Jessica Morgan, Chief Investigator, Centre for Reviews and Dissemination, University of York, Tel 01904 321082, Email jem539@york.ac.uk

Thank you for taking the time to read this information sheet.

- **Early discharge in paediatric febrile neutropenia:**
- **experiences and perceptions of young people, parents and healthcare professionals**

Adult Participant Information Sheet

Date: 30/11/15

Version: 3

- **Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals**
-

We would like to invite you to take part in the above named research study. Before you decide whether or not you would like to take part, we would like to tell you more about the study and about what being part of it would involve. If you would like to ask any questions about the study, we have provided details of who to contact at the end of this leaflet.

What is the purpose of this study?

Neutrophils are the commonest form of white blood cells and play an important role in the immune system. Treatment for cancer can result in low neutrophils, also known as neutropenia. This results in an increased risk of infection. When someone with neutropenia develops a temperature, this is called febrile neutropenia. Sometimes febrile neutropenia is very serious, but most of the time it does not cause any serious medical problems. We are working to look at the possibility of reducing the length of time that children and young people spend in hospital when we predict that they will not have serious problems from their febrile neutropenia. For this particular study, we are interested in hearing about what young people, their parents and their doctors and nurses, think about them spending less time in hospital. This information may then help to inform how we design services for children and young people who develop febrile neutropenia in the future.

Who is doing the study?

This study is being conducted as part of a PhD project by Dr Jessica Morgan from the University of York. Her work will be supervised by Professor Karl Atkin (also at University of York). There are further supervisory and advisory researchers involved in the work, as part of the university training procedures. All the researchers who contact you have been checked out by the Criminal

Records Bureau to ensure they are appropriately qualified to undertake research. This research has been funded by Candlelighters Childhood Cancer Charity (Registered Charity No: 1045077).

Why have I been asked to participate?

You have been asked to take part because you are the parent of a child or young person who has had treatment for cancer at some point within the last six months and who, if they developed febrile neutropenia, might be considered at low risk of serious complications. You are the people who are able to tell us about how you would prefer your child to be treated if this were to happen to them. We are also interested to talk to some young people and to doctors and nurses about this issue, because we know that that decisions about treatment are often made by taking into consideration all of these people's opinions. We are going to ask our questions to groups at different hospitals around the UK as we think that people in different places, where the services are designed differently, might have different opinions about this problem. You will probably have been invited to take part because someone who looks after your child felt that you were able to talk about what you think about this issue.

Do I have to take part?

No, this study is entirely voluntary. You can chose not to take part and this will not affect your child's treatment at all. If you decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form. After you have signed the consent form, you are still free to withdraw from the study at any time up to two weeks following the focus group discussion. If you withdraw from the study your quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used. You do not need to give a reason for withdrawing.

What will be involved if I take part in this study?

We would ask you to take part in a group discussion with between four and seven other people, and led by a researcher. We would talk about your experiences of your child being treated for febrile neutropenia in the past - don't worry if your child has never had febrile neutropenia – we are specifically asking some people with no experience to the groups. We will then ask you about what you think about shorter hospital stays for febrile neutropenia. The discussion would take about 90 minutes and would be audio-recorded. We would choose people to try to reflect a range of possible opinions. The discussion will take place in or close to the hospital and the time will be selected to be convenient for as many participants as possible.

What are the advantages of taking part?

At the end of the work, when we have been able to look at all the discussions which will take place, we will provide you with a summary of our findings and the recommendations we make about improving future services.

What are the disadvantages of taking part?

Sometimes talking about your experiences can bring up some difficult memories. You may also start to think more about febrile neutropenia happening again in the future. People involved in your child's care will be available to talk to you about any questions you have about your child's treatment after this study.

Will I be paid to take part in this study?

You will be offered a £20 Amazon voucher, provided by Candlelighters Children's Cancer Charity, to recognise the time commitment involved in this study. If you chose to accept this, it will be sent to you following the focus group via email or post, depending on which you prefer.

Candlelighters Children's Cancer Charity have also given us funding to provide you with your travel expenses. This will be 45 pence per mile if you drive to the group discussion, or the price of a standard rate ticket for public transport. This will be sent to you following the focus group.

Will the information obtained in the study be confidential?

All information you give to us will be confidential. We will not tell anyone (including your family or the professionals who look after your child) about what you share with us. The only exception to this is if you tell us things which we believe place you, your child or other people at serious risk. If this happens, we are required to tell the relevant authorities so as to protect you (or your child or other people) from harm.

The audio-recordings from the discussions will be listened to and everything that is said will be written down. This creates a document called a transcript. All information that is written or recorded will be kept in locked offices at the University of York. Only the research team will be able to see them. All the information you provide will have a code allocated to it and this will be stored separately from your personal details. No names will be used in the transcripts, our notes or any writing we do about this work. At the end of the study, the audio recordings will be erased. The data will be stored for five years, so that if the research needs to be checked or further analysis needs to be done then this is available. At all times, all data will be treated in accordance with the current Data Protection Act.

What will happen to the results of the study?

The results of this study will be used in a number of ways. We will write a summary of the work for you to read and to know what was found from the research. Other members of the public will also be able to read this summary. The work will also be written as a full academic report for the PhD thesis of Dr Jessica Morgan. As well as this, it will also be submitted for publication in scientific journals. You can call members of the research team at any time to discuss the progress of the research.

Who has reviewed this study?

The plans for this study have been reviewed by the University of York Research Governance Committee, as well as an NHS Research Ethics Committee. The progress of the research will be monitored throughout by the University of York.

Who do I contact in the event of a complaint?

Please raise any difficulties or questions with Dr Jessica Morgan (01904) 321082 (8am to 5pm weekdays) email jem539@york.ac.uk or Professor Karl Atkin (01904) 321355 email karl.atkin@york.ac.uk. If the research team are unable to give you a satisfactory answer, please contact Professor Lesley Stewart, (01904) 321093, email lesley.stewart@york.ac.uk.

If you agree to take part, would like more information or have any questions or concerns about the study please contact Dr Jessica Morgan, Chief Investigator, Centre for Reviews and Dissemination, University of York, Tel 01904 321082, Email jem539@york.ac.uk

Thank you for taking the time to read this information sheet.

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Healthcare Professional Participant Information Sheet

Date: 27.5.15

Version: 2

Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals

We would like to invite you to take part in the above named research study. Before you decide whether or not you would like to take part, we would like to tell you more about the study and about what being part of it would involve. If you would like to ask any questions about the study, we have provided details of who to contact at the end of this leaflet.

What is the purpose of this study?

We are researchers who are interested in the management of paediatric low risk febrile neutropenia. We are working to look at the possibility of reducing the length of time that children and young people spend in hospital with low risk febrile neutropenia. For this particular study, we are interested in hearing about what young people, their parents and their doctors and nurses, think about strategies involving outpatient therapy or early discharge from hospital. This information may then help to inform how services are designed for children and young people who develop febrile neutropenia in the future.

Who is doing the study?

This study is being conducted as part of a PhD project by Dr Jessica Morgan from the University of York. Her work will be supervised by Professor Karl Atkin (also at University of York). There are further supervisory and advisory researchers involved in the work, as part of the university training procedures. This research has been funded by Candlelighters Childhood Cancer Charity (Registered Charity No: 1045077).

Why have I been asked to participate?

You have been asked to take part because you are a healthcare professional involved in the care of children and young people with low risk febrile neutropenia. You are the people who are able

to tell us about how you feel patients and families should be treated. We are also interested to talk to patients who may develop low risk febrile neutropenia and their families, because we recognise that decisions about treatment are often made by taking into consideration all of these people's opinions. This will be a multicentre study within the UK as we anticipate that where populations and services designs are different there might be different opinions about this issue.

Do I have to take part?

No, this study is entirely voluntary. If you decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form. After you have signed the consent form, you are still free to withdraw from the study at any time up to two weeks following the focus group discussion. If you withdraw from the study your quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used. You do not need to give a reason for withdrawing.

What will be involved if I take part in this study?

We would ask you to take part in a group discussion with between four and seven healthcare professionals, and led by a researcher. We would talk about your experiences of treating febrile neutropenia and then about what you think about shorter hospital stays for febrile neutropenia. The discussion would take about 90 minutes and would be audio-recorded. We would choose people to try to reflect a range of possible opinions. The discussion will take place in or close to the hospital and the time will be selected to be convenient for as many participants as possible. You will not be required to travel away from your centre in order to take part.

What are the advantages of taking part?

At the end of the work, we will provide you with a summary of our findings and the recommendations we make about improving future services.

What are the disadvantages of taking part?

You might question your own practice, but you will be offered information about where you can obtain continuing professional education on the management of paediatric febrile neutropenia.

Will I be paid to take part in this study?

No, but we don't want you to be disadvantaged by taking part. Candlelighters Children's Cancer Charity have given us funding to provide you with your travel expenses. This will be 45 pence per

mile if you drive to the group discussion, or the price of a standard rate ticket for public transport. This will be paid to you in cash on the day and we will need you to sign a receipt.

Will the information obtained in the study be confidential?

All information you give to us will be confidential. It is important to note that the research team are only interested in your general views and that you should not discuss the details of individual cases where this may make the patient identifiable. We will not tell anyone about what you share with us. The only exception to this is if you disclose information which we believe place you or other people at serious risk. If this happens, we are required to tell the relevant authorities so as to protect you (or other people) from harm.

The audio-recordings from the discussions will be listened to and everything that is said will be written down. This creates a document called a transcript. All information that is written or recorded will be kept in locked offices at the University of York. Only the research team will be able to see them. All the information you provide will have a code allocated to it and this will be stored separately from your personal details. No names will be used in the transcripts, our notes or any writing we do about this work. At the end of the study, the audio recordings will be erased. The data will be stored for five years, so that if the research needs to be checked or further analysis needs to be done then this is available. At all times, all data will be treated in accordance with the current Data Protection Act.

What will happen to the results of the study?

The results of this study will be used in a number of ways. We will write a summary of the work for you to read and to know what was found from the research. Other participants and members of the public will also be able to read this summary. The work will also be written as a full academic report for the PhD thesis of Dr Jessica Morgan. As well as this, it will also be submitted for publication in scientific journals. We will look to present the results of the research at each study site. You can call members of the research team at any time to discuss the progress of the research.

Who has reviewed this study?

The plans for this study have been reviewed by the University of York Research Governance Committee, as well as an NHS Research Ethics Committee. The progress of the research will be monitored throughout by the University of York.

Who do I contact in the event of a complaint?

Please raise any difficulties or questions with Dr Jessica Morgan (01904) 321082 (8am to 5pm weekdays) email jem539@york.ac.uk or Professor Karl Atkin (01904) 321355 email karl.atkin@york.ac.uk. If the research team are unable to give you a satisfactory answer, please contact Professor Lesley Stewart, (01904) 321093, email lesley.stewart@york.ac.uk.

If you agree to take part, would like more information or have any questions or concerns about the study please contact Dr Jessica Morgan, Chief Investigator, Centre for Reviews and Dissemination, University of York, Tel 01904 321082, Email jem539@york.ac.uk

Thank you for taking the time to read this information sheet.

Appendix 5.2: Invitation email to Healthcare Professionals

Dear colleague,

I am writing to inform you about a new research study opening at our centre, *Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals.* This study is being conducted with the University of York and will involve various focus group discussions about outpatient therapy and early discharge strategies for the management of paediatric low risk febrile neutropenia. I would like to offer you the chance to take part in the healthcare professionals' focus group for our centre. The study team are keen to hear from doctors and nurses who have experience of caring for these parents. You could be acting in a junior or senior role and could be new to the service or have been here for a long time– as many different opinions as possible are wanted. I have attached the Healthcare Professionals' Participant Information Sheet. If you would like more details or would like to take part in the study, please contact the Chief Investigator, Dr Jessica Morgan (01904) 321082.

Best wishes

Site specific coordinator

Appendix 5.3: Participant Consent and Assent forms

Young Person Participant Assent Form

Young Person Participant

Assent Form

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Date: 27/5/15

Version: 2

Chief Investigator: Dr Jessica Morgan

Focus Group Moderator: Dr Jessica Morgan

	Please confirm agreement to the statements by putting your initials in the boxes below
I have read and understood the participant information sheet: _____ (Version) for the above study.	
I have had the opportunity to ask questions and discuss this study	
I have received satisfactory answers to all of my questions	
I have received enough information about the study	
I understand my participation in the study is voluntary and that I am free to withdraw from the study at any time up to two weeks following the focus group discussion	

without having to give a reason for withdrawing and without affecting my medical care or legal rights. I understand that if I withdraw from the study my quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used.	
I understand that the focus group that I am part of will be audio-recorded.	
I agree to respect the rights of other participants in the focus group and to maintain confidentiality of matters discussed within the focus group.	
I understand that sections of my medical notes and data collected during the study may be looked at by researchers, where it is relevant to this research. I give permission for these individuals to have access to my records.	
I agree to my GP being informed of my participation in the study.	
I understand that any information I provide, including personal details, will be kept confidential, stored securely and only accessed by those carrying out the study.	
I understand that any information I give may be included in published documents but all information will be anonymised.	
I agree to take part in this study	
Participant Signature …… Date	

Name of Participant
Researcher Signature ……. Date
Name of Researcher

Parent Consent Form

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Date: 27/5/15

Version: 2

Chief Investigator: Dr Jessica Morgan

Focus Group Moderator: Dr Jessica Morgan

	Please confirm agreement to the statements by putting your initials in the boxes below
I have read and understood the participant information sheet: _____ (Version) for the above study.	
I have had the opportunity to ask questions and discuss this study	
I have received satisfactory answers to all of my questions	
I have received enough information about the study	
I understand my child's participation in the study is voluntary and that I am free to withdraw them from the study at any time up to two weeks following the focus group discussion without having to give a reason for withdrawing and without affecting their medical care or our legal rights. I understand that if I withdraw my child from the study their quotations from the focus group will not be used in the analysis or any reports and	

publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used.	
I understand that the focus group that my child is part of will be audio-recorded.	
I will encourage my child to respect the rights of other participants in the focus group and to maintain confidentiality of matters discussed within the focus group.	
I understand that sections of my child's medical notes and data collected during the study may be looked at by researchers, where it is relevant to this research. I give permission for these individuals to have access to my child's records.	
I agree to my child's GP being informed of their participation in the study.	
I understand that any information I or my child provide, including personal details, will be kept confidential, stored securely and only accessed by those carrying out the study.	
I understand that any information I or my child give may be included in published documents but all information will be anonymised.	
I agree to my child taking part in this study	
Parent Signature …… Date	

Name of Parent
Name of Child
Researcher Signature …….. Date
Name of Researcher

Adult Patient Participant

Consent Form

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Date: 27/5/15

Version: 2

Chief Investigator: Dr Jessica Morgan

Focus Group Moderator: Dr Jessica Morgan

	Please confirm agreement to the statements by putting your initials in the boxes below
I have read and understood the participant information sheet: _____ (Version) for the above study.	
I have had the opportunity to ask questions and discuss this study	
I have received satisfactory answers to all of my questions	
I have received enough information about the study	

I understand my participation in the study is voluntary and that I am free to withdraw from the study at any time up to two weeks following the focus group discussion without having to give a reason for withdrawing and without affecting my medical care or legal rights. I understand that if I withdraw from the study my quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used.	
I understand that the focus group that I am part of will be audio-recorded.	
I agree to respect the rights of other participants in the focus group and to maintain confidentiality of matters discussed within the focus group.	
I understand that sections of my medical notes and data collected during the study may be looked at by researchers, where it is relevant to this research. I give permission for these individuals to have access to my records.	
I agree to my GP being informed of my participation in the study.	
I understand that any information I provide, including personal details, will be kept confidential, stored securely and only accessed by those carrying out the study.	
I understand that any information I give may be included in published documents but all information will be anonymised.	
I agree to take part in this study	

Participant Signature …… Date
Name of Participant
Researcher Signature ……. Date
Name of Researcher

Parent Participant

Consent Form

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Date: 27/5/15

Version: 2

Chief Investigator: Dr Jessica Morgan

Focus Group Moderator: Dr Jessica Morgan

	Please confirm agreement to the statements by putting your initials in the boxes below
I have read and understood the participant information sheet: _____ (Version) for the above study.	
I have had the opportunity to ask questions and discuss this study	
I have received satisfactory answers to all of my questions	
I have received enough information about the study	

I understand my participation in the study is voluntary and that I am free to withdraw from the study at any time up to two weeks following the focus group discussion without having to give a reason for withdrawing and without affecting my medical care or legal rights. I understand that if I withdraw from the study my quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used.	
I understand that the focus group that I am part of will be audio-recorded.	
I agree to respect the rights of other participants in the focus group and to maintain confidentiality of matters discussed within the focus group.	
I understand that sections of my child's medical notes and data collected during the study may be looked at by researchers, where it is relevant to this research. I give permission for these individuals to have access to my child's records.	
I understand that any information I provide, including personal details, will be kept confidential, stored securely and only accessed by those carrying out the study.	
I understand that any information I give may be included in published documents but all information will be anonymised.	
I agree to take part in this study	
Participant Signature …… Date	

Name of Participant
Researcher Signature …….. Date
Name of Researcher

Health Care Professional Participant

Consent Form

Early discharge in paediatric febrile neutropenia:

experiences and perceptions of young people, parents and healthcare professionals

Date: 27/5/15

Version: 2

Chief Investigator: Dr Jessica Morgan

Focus Group Moderator: Dr Jessica Morgan

	Please confirm agreement to the statements by putting your initials in the boxes below
I have read and understood the participant information sheet: _____ (Version) for the above study.	
I have had the opportunity to ask questions and discuss this study	
I have received satisfactory answers to all of my questions	
I have received enough information about the study	

I understand my participation in the study is voluntary and that I am free to withdraw from the study at any time up to two weeks following the focus group discussion without having to give a reason for withdrawing and without affecting my legal rights. I understand that if I withdraw from the study my quotations from the focus group will not be used in the analysis or any reports and publications. However, the rest of the information from the focus group (which relates to other participants' quotations) will continue to be used.	
I understand that the focus group that I am part of will be audio-recorded.	
I agree to respect the rights of other participants in the focus group and to maintain confidentiality of matters discussed within the focus group.	
I understand that any information I provide, including personal details, will be kept confidential, stored securely and only accessed by those carrying out the study.	
I understand that any information I give may be included in published documents but all information will be anonymised.	
I agree to take part in this study	
Participant Signature …… Date	
Name of Participant	
Researcher Signature …….. Date	

Name of Researcher

Appendix 5.4: Participant Basic Data Collection forms

Young Person Basic Data Collection Form

Young person basic data collection form

Participant to complete

Name:	
Age (years):	
Gender:	Male ☐ Female ☐
Ethnicity:	White British ☐ White Irish ☐ White, other European ☐ Any other White Background ☐ Indian ☐ Pakistani ☐ Bangladeshi ☐ Any other Asian Background ☐ Black Caribbean ☐ Black African ☐

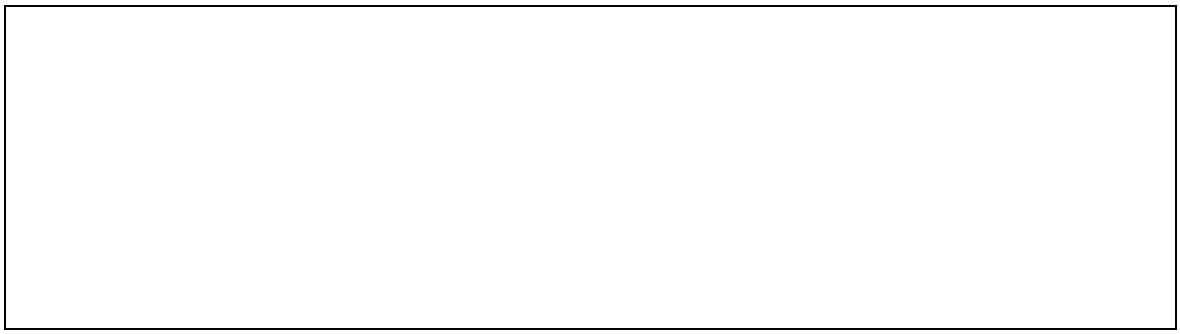
	Any other Black background ☐ Chinese ☐ Mixed White and Black Caribbean ☐ Mixed White and Black African ☐ Mixed White and Asian ☐ Any other mixed background ☐ Other (please state) ☐
Address:	
Who I live with most often (please tell us your relationship to them and their age, if under 18 years) *You do not have to give their names if you do not want to.* eg, mum, stepfather, sister (16), half-brother (10), grandmother (mum's mum)	
Other important people in my immediate family who I don't live with all the time eg. dad, sister (12)	

Mother's highest level of educational qualification	Degree or higher degree ☐ A levels or Highers ☐ HNC/HND ☐ ONC/BTEX ☐ O level or GCSE equivalent (Grade A-C) ☐ O level or GCSE equivalent (Grade D-G) ☐ No formal qualifications ☐ Still studying ☐ Other (give details) ☐
Father's highest level of educational qualification	Degree or higher degree ☐ A levels or Highers ☐ HNC/HND ☐ ONC/BTEX ☐ O level or GCSE equivalent (Grade A-C) ☐ O level or GCSE equivalent (Grade D-G) ☐

	No formal qualifications ☐ Still studying ☐ Other (give details) ☐
Mother's occupation	
Father's occupation	
Which best describes your family's living arrangements	Own house (outright) ☐ Own house (mortgage) ☐ Rent from Local Authority/Housing Association ☐ Rent privately ☐ Other (eg. living with family and friends) ☐
Your GP (if you agree to us informing them that you are taking part in this study)	
Is anyone else in your family taking part in this study? If so, please give their name and their relationship to you.	

Local team to complete:

Study site	
Diagnosis	
Date of initial diagnosis	
Treatment regimen	
Current/most recent course of treatment	
Previous episodes of febrile neutropenia *(please give for each – dates, high or low risk episode, location of treatment (PTC/POSCU), treatment received, duration of admission, complications arising (eg PICU admission, removal of central line, delay in further treatment, etc)*	



Parent participant basic data collection form

Participant to complete

Name:	
Age (years):	
Gender:	Male ☐ Female ☐
Ethnicity:	White British ☐ White Irish ☐ White, other European ☐ Any other White Background ☐ Indian ☐ Pakistani ☐ Bangladeshi ☐ Any other Asian Background ☐ Black Caribbean ☐ Black African ☐ Any other Black background ☐

	Chinese ☐ Mixed White and Black Caribbean ☐ Mixed White and Black African ☐ Mixed White and Asian ☐ Any other mixed background ☐ Other (please state) ☐
Address:	
You have been asked to participate in this study because one of your children is at risk of low risk febrile neutropenia. Please could you tell us how old this child is(in years)	
Who I live with most often (please tell us your relationship to them and their age, if under 18 years) *You do not have to give their names if you do not want to.* eg, Husband/wife, daughter (12), step son (9), mother	

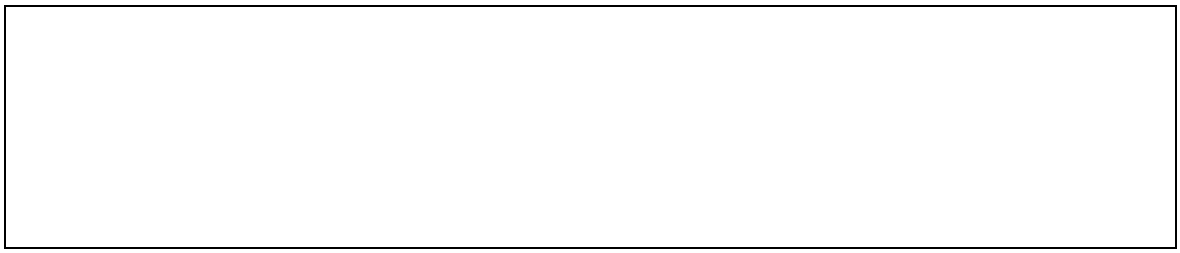
Other important people in my immediate family who I don't live with all the time eg. son (17)	
What is your highest level of educational qualification	Degree or higher degree ☐ A levels or Highers ☐ HNC/HND ☐ ONC/BTEX ☐ O level or GCSE equivalent (Grade A-C) ☐ O level or GCSE equivalent (Grade D-G) ☐ No formal qualifications ☐ Still studying ☐ Other (give details) ☐
What is your child's other parent's highest level of educational qualification	Degree or higher degree ☐ A levels or Highers ☐ HNC/HND ☐ ONC/BTEX ☐

	O level or GCSE equivalent (Grade A-C) ☐ O level or GCSE equivalent (Grade D-G) ☐ No formal qualifications ☐ Still studying ☐ Other (give details) ☐
Your occupation	
Your child's other parent's occupation	
Which best describes your family's living arrangements	Own house (outright) ☐ Own house (mortgage) ☐ Rent from Local Authority/Housing Association ☐ Rent privately ☐ Other (eg. living with family and friends) ☐
Is anyone else in your family taking part in this study? If so, please give their name and their relationship to you.	

Local team to complete the following information about your child:

Study site	

Diagnosis	
Date of initial diagnosis	
Treatment regimen	
Current/most recent course of treatment	
Previous episodes of febrile neutropenia *(please give for each – dates, high or low risk episode, location of treatment (PTC/POSCU), treatment received, duration of admission, complications arising (eg PICU admission, removal of central line, delay in further treatment, etc)*	



Healthcare professional basic data collection form

Participant to complete

Study site	
Name:	
Age (years):	
Gender:	Male ☐ Female ☐
Ethnicity:	White British ☐ White Irish ☐ White, other European ☐ Any other White Background ☐ Indian ☐ Pakistani ☐ Bangladeshi ☐ Any other Asian Background ☐ Black Caribbean ☐ Black African ☐

	Any other Black background ☐ Chinese ☐ Mixed White and Black Caribbean ☐ Mixed White and Black African ☐ Mixed White and Asian ☐ Any other mixed background ☐ Other (please state) ☐
Your profession	Doctor - General Paediatrics ☐ - Oncology ☐ - Haematology ☐ - Infectious Diseases /Microbiology ☐ Nurse
Your Grade (eg. consultant, staff nurse)	
Time spent at current grade (years)	
Time spent at current centre (years) Note: this may include time spent at a different grade	

Appendix 5.5: Topic Guides

Focus group topic guides

Summary Topic Guide for Focus Group Discussions with young people and parent participants

All focus groups will begin with a reminder of the aims of the study, verbal confirmation of consent, the restating of the right to withdraw from the study up to two weeks following the focus group discussion and the opportunity for participants to ask any outstanding questions.

Introductory questions

1. What do you understand about febrile neutropenia?
    - Do you know anything about how to decide if someone has low risk or high risk febrile neutropenia?
2. Have you ever had an episode of febrile neutropenia? Can you tell me about it/them?
    - What is the treatment like in your hospital?
    - What were the best things about the episode of treatment? What were the worst? Why?

Explanation of current research and different possible treatment strategies.

3. What do you think about these different options? If they were all offered at your hospital, which would you pick and why?

It would be good to talk more about outpatient treatment of febrile neutropenia.

4. Tell me more about what you think of this option. Would you want it for you/your child?
5. Can you tell me a bit about how you decided if you would or wouldn't? What factors played a part in your decision making? How important was each factor?
    - If not mentioned, ask about: practical issues (eg transport, distance from hospital, finances, care of other children), emotional/social issues (eg. wanting to be together as a family, fear of going home, feeling of not being able to cope at home), trust in health care professionals
6. How would what your family/child feel influence your decision? What do you think they would say about outpatient care? If disagreements occurred, how should these be negotiated?
7. How would what your doctor/nurse feel influence your decision? What do you think they would say about outpatient care? If disagreements occurred, how should these be negotiated?

Introduce evidence about failure to consent rates.

8. Why do you think this might be?
9. Do you want to say more about the questions we just discussed in the light of this research?

Service design

10. How do you think an outpatient febrile neutropenia service could be designed to make you most happy with it?

- If not mentioned discuss: when go home, route of antibiotics, how followed up (home/clinic), what symptoms would be tolerated at home (eg repeated fever)

Any other issues/questions/comments?

All medical queries raised by the participants during the focus group discussions will be redirected to their clinical care team. Debriefing will be offered to participants immediately after the focus group discussions and a telephone number (Dr Jessica Morgan, Tel 01904 321082) will also be provided in case they wish to discuss any further issues with the research.

Summary Topic Guide for Focus Group Discussions with health care professionals

All focus groups will begin with a reminder of the aims of the study, verbal confirmation of consent, the restating of the right to withdraw from the study up to two weeks following the focus group discussion and the opportunity for participants to ask any outstanding questions. Participants in the focus groups for healthcare professionals will be reminded that the research team are only interested in their general views and will not be discussing the details of individual cases.

Introductory questions

1. What is your role in looking after children with low risk febrile neutropenia?
2. Tell me about the treatment of low risk febrile neutropenia in your hospital?
3. What sort of issues develop when caring for patients with low risk febrile neutropenia?

Explanation of current research and different possible treatment strategies.

4. What do you think about these different options? Which one(s) do you think it is appropriate to offer to your patients?

It would be good to talk more about outpatient treatment of febrile neutropenia.

5. Tell me more about what you think of this option. Would you want it for your patients?
6. Can you tell me a bit about how you decided if you would or wouldn't? What factors played a part in your decision making? How important was each factor?
    - If not mentioned, ask about: practical issues (eg transport, distance from hospital, finances, care of other children), emotional/social issues (eg. wanting to be together as a family, fear of going home, feeling of not being able to cope at home), trust in health care professionals
7. How would what the family/child feel influence your decision? What do you think they would say about outpatient care? If disagreements occurred, how should these be negotiated?

Introduce evidence about failure to consent rates.

8. Why do you think this might be?
9. Do you want to say more about the questions we just discussed in the light of this research?

Service design

10. How do you think an outpatient febrile neutropenia service could be designed to make you most happy with it?
    - If not mentioned discuss: when go home, route of antibiotics, how followed up (home/clinic), what symptoms would be tolerated at home (eg repeated fever)
11. How does the design of the healthcare service as a whole influence how services could be delivered?
12. Who makes decisions about these kinds of changes? What do you think they would think/say?

Any other issues/questions/comments?

Debriefing will be offered to participants immediately after the focus group discussions and a telephone number (Dr Jessica Morgan, Tel 01904 321082) will also be provided in case they wish to discuss any further issues with the research.

Appendix 5.6: Information Letter for General Practitioners

Dear Doctor,

This letter is to inform you that your patient, _____ (name, DOB, address) has agreed to take part in a research study, *Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals.* This study is being conducted by the University of York along with your local paediatric haematology and oncology service at _____ (centre). Your patient will be taking part in a single focus group discussion around outpatient therapy and early discharge strategies for the management of paediatric low risk febrile neutropenia. Your patient has been invited as they are: a young person at risk of low risk febrile neutropenia/the parent of a child or young adult with low risk febrile neutropenia.

If you have any questions about this research, or would like to know more about the study, please contact Dr Jessica Morgan, (01904) 321082, jem539@york.ac.uk.

Yours sincerely,

Dr Jessica Morgan
Clinical Research Fellow
Centre for Reviews and Dissemination
University of York
York
YO10 5DD

Appendix 5.7: Promotional Poster

Study site logo here

Participants wanted! Can you help?

Get a £20 Amazon voucher

We have a research study open in this centre to find out what you think about how to treat temperatures in children and young people with cancer.

You might be able to take part if you are a:

PATIENT

Aged 13 – 18 years old

Have had chemotherapy or radiotherapy in the last six months

Have a solid tumour (not NHL) OR have ALL on maintenance therapy

OR

PARENT

Your child is 1-18 years old

Your child has had chemotherapy or radiotherapy in the last six months

Your child has a solid tumour (not NHL) OR has ALL on maintenance therapy

What does the study involve?

Coming to a focus group discussion for about 90 mins and talking with people about your experiences and what you think we can do to make this better. You'll get a £20 Amazon voucher for taking part, as well as travel expenses and refreshments.

If you want to take part or have some questions about this research, please contact the research nurses …. or the lead researcher, Jess Morgan, 01904 321082, jem539@york.ac.uk

Appendix 5.8: Research Ethics Committee Approvals

(taken from PDF letters)

NRES Committee Yorkshire & The Humber - Leeds West
Room 001, Jarrow Business Centre
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Telephone: 0191 4283548

18 May 2015

Dr Jessica Morgan
Centre for Reviews and Dissemination
University of York
York
YO10 5DD

Dear Dr Morgan

Study title:	**Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals**
REC reference:	
IRAS project ID:	**15/YH/0208**

The Research Ethics Committee reviewed the above application at the meeting held on 08 May 2015. Thank you for attending to discuss the application.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager Miss Christie Ord, nrescommittee.yorkandhumber-leedswest@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Summary of discussion at the meeting

Other ethical issues were raised and resolved in preliminary discussion before your attendance at the meeting.

Ethical issues raised by the Committee in private discussion, together with responses given by the researcher when invited into the meeting

Social or scientific value; scientific design and conduct of the study

The Committee congratulated the applicant on her use of patient and public involvement and thanked her for submitting a good application.

The REC queried whether the patient and public involvement group included younger children.

You confirmed that the youngest child was 11 and a half and stated that it was beneficial to have their views even though the age range was higher than this. You added that a 15 and a 17 year old had also reviewed the documentation and that all feedback had been incorporated.

The Committee noted that you intended to moderate the focus groups solely and queried whether it would be feasible to share these responsibilities with another individual to allow for better management of the groups.

You explained that you had to consider this when designing your project and stated that you would consider getting support if someone was willing to help.

The Committee advised that a medical student or psychology student would be grateful for the research experience and that this would be a good place to canvas for help. The REC stated that additional support may be particularly useful if a problem arose within a focus group as it would enable the group to run with limited disruptions.

You confirmed that you would consider this advice.

Recruitment arrangements and access to health information, and fair participant selection

The Committee noted that the applicant would allow one week for individuals to consider consenting and stated that this may be problematic as the children may forget or be difficult to re-contact. Members advised that if children expressed an interest, the applicant could suggest and agree a time and day to telephone the children to give them further information.

You thanked the Committee for this advice and confirmed that you would do this.

The Committee queried whether travel expenses would be reimbursed.

You confirmed that there was no allowance for this within her grant currently but that you would be applying for a further grant to allow for this.

The Committee accepted this response and noted that this should be submitted to the REC as a substantial amendment.

Members queried whether the applicant was confident that younger children would remain in the study and not lose interest.

You accepted that this may be a concern but explained that you had structured the interviews to allow movement between topics and to keep attention. You explained that you had received independent advice on the suitability of the study information for the target population.

Suitability of supporting information

The Committee queried whether the topic guide had been piloted.

You confirmed that it had not as the target population was quite small and you did not want ruin your project by ultimately piloting the topic guide on the individuals that you may recruit. You confirmed that your PPI group had seen the topic guide.

Informed consent process and the adequacy and completeness of participant information

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		
GP/consultant information sheets or letters [Information letter for General Practitioners]		
Interview schedules or topic guides for participants [Focus group topic guides]		
Letter from funder [Funding Letter]	1	24 March 2015
Letter from sponsor	1	30 January 2015
Letters of invitation to participant [Invitation email to Healthcare Practitioners]		
Other [K. Atkin CV]	1	19 February 2015
Other [R. Phillips CV]	1	18 February 2015
Other [Responses to Research Governance Committee Decision Letter]		
Other [Young Person basic data collection form]	1	30 March 2015
Other [Parent participant basic data collection form]	1	30 March 2015
Other [Healthcare professional basic data collection form]	1	30 March 2015
Participant consent form [Young Person Participant Assent Form]	1	18 February 2015
Participant consent form [Parent Consent Form]	1	18 February 2015
Participant consent form [Adult Patient Participant Consent Form]	1	18 February 2015
Participant consent form [Parent Participant Consent Form]	1	18 February 2015
Participant consent form [Healthcare Professional Participant Consent Form]		
Participant information sheet (PIS) [Young Person Participant Information Sheet]		
Participant information sheet (PIS) [Parent's Information Sheet]	1	28 October 2014
Participant information sheet (PIS) [Adult Patient Participant Information Sheet]		
Participant information sheet (PIS) [Adult Participant Information Sheet]		
Participant information sheet (PIS) [Healthcare Professional Participant Information Sheet]		
REC Application Form [REC_Form_13042015]		13 April 2015
Referee's report or other scientific critique report [University of York Research Governance Committee Decision Letter]		
Research protocol or project proposal [Protocol]	1	30 March 2015
Summary CV for Chief Investigator (CI) [Jessica Morgan CV]	1	30 March 2015

The REC advised that the applicant should protect her data by setting a time limit for withdrawal of date and suggested that she make clear to participants that they would have up to 2 weeks after the focus group to withdraw their data.

You confirmed that you would do this.

Independent review

The Committee commended the applicant on the independent reviews obtained.

You left the meeting.

Approved documents

The documents reviewed and approved at the meeting were:

Summary CV for supervisor (student research)

Membership of the Committee

The members of the Ethics Committee who were pr
attached sheet.

After ethical review

Reporting requirements

The attached document "After ethical review – guid
guidance on reporting requirements for studies with

Notifying substantial amendments
Adding new sites and investigators
Notification of serious breaches of the protocol Progress and safety reports
Notifying the end of the study

The HRA website also provides guidance on these
changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually strivin
applicants and sponsors. You are invited to give yo
and the application procedure. If you wish to make
form available on the HRA website: http://www.hra.
assurance/

HRA Training

We are pleased to welcome researchers and R&D
http://www.hra.nhs.uk/hra-training/

15/YH/0208	**Please quote this number on a**

With the Committee's best wishes for the success o

Yours sincerely

pp

Dr Sheila E. Fisher
Chair

E-mail: nrescommittee.yorkandhumber-leedswest@

Enclosures: *List of names and professio*
meeting and those who sub

Document	*Version*	*Date*
	Minor Amendment	

Research protocol or project proposal

Statement of compliance

The Committee is constituted in accordance with the Gove
Research Ethics Committees and complies fully with the S
Research Ethics Committees in the UK.

15/YH/0208: Please quote this number

Yours sincerely

Kirstie Penman
REC Assistant

Email: nrescommittee.yorkandhumber-leedswest@nhs.net

Copy to: *Mr Mohammed Khan, Leeds Teach*

Sue Final, University of York

NRES Committee Yorkshire & The Humber - Leeds West
Room 001, Jarrow Business Centre
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Tel: 0191 428 3444

22 June 2015

Dr Jessica Morgan
Centre for Reviews and Dissemination
University of York
York
YO10 5DD

Dear Dr Morgan

Study title:	**Early discharge in paediatric febrile neutropenia: experiences and perceptions of young people, parents and healthcare professionals**
REC reference:	**15/YH/0208**
Amendment number:	**Substantial Amendment 1**
Amendment date:	**08 June 2015**
IRAS project ID:	**142973**

The above amendment was reviewed by the Sub-Committee in correspondence.

Summary of amendment

This amendment was submitted following the advice given from the Committee to offer travel expenses to participants. This would be paid at a rate of 45p per mile if the participant was to drive to the research site or the cost of a standard ticket for public transport as advised by INVOLVE guidelines. This would be paid in cash by the Chief Investigator as the participant arrived for the focus group discussion. All payments would be recorded on the receipt and would be kept on file for the duration of the study.

The study team had also obtained funding for the research nurse time spent on the project. This will be paid as a block sum of £550 to the department involved at completion of the study.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Notice of Substantial Amendment (non-CTIMP)	1	08 June 2015
Other [Focus Group Topic Guides]	2	27 May 2015
Participant consent form [Adult Patient Participant Consent Form]	1	18 February 2015
Participant consent form [Health Care Professional Participant Consent Form]		
Participant consent form [Parent Consent Form]	2	27 May 2015
Participant consent form [Parent Participant Consent Form]	2	27 May 2015
Participant consent form [Young Person Participant Assent Form]	2	27 May 2015
Participant information sheet (PIS) [Adult Participant Information Sheet]		
Participant information sheet (PIS) [Adult Patient Participant Information Sheet]		
Participant information sheet (PIS) [Healthcare Professional Participant Information Sheet]		
Participant information sheet (PIS) [Parent's Information Sheet]	2	27 May 2015
Participant information sheet (PIS) [Young Person Participant Information Sheet]		
Research protocol or project proposal	2	27 May 2015

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

Please quote this number on all correspondence

Yours sincerely

pp

Mr Anthony Warnock-Smith
Alternate Vice-Chair

E-mail: nrescommittee.yorkandhumber-leedswest@nhs.net

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Promotional Poster]		
Notice of Substantial Amendment (non-CTIMP)	SA2	30 November 2015
Participant information sheet (PIS) [Adult Participant Information Sheet]		
Participant information sheet (PIS) [Adult Patient Participant Information Sheet]		

Participant information sheet (PIS) [Parents Information Sheet]	3	30 November 2015
Participant information sheet (PIS) [Young Person Participant Information Sheet]		
Research protocol or project proposal		30 November 2015

30 November 20153

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

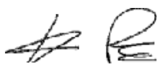
We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

15/YH/0208

Please quote this number on all correspondence

Yours sincerely

pp



Dr Sheila E. Fisher
Chair

E-mail: nrescommittee.yorkandhumber-leedswest@nhs.net

Enclosures:

List of names and professions of members who took part in the review

Copy to:

Mr Mohammed Khan, Leeds Teaching Hospitals NHS Trust

Ms Sue Final, University of York

Appendix 5.9: Samples of Coded Transcripts

The following two pages provide a sample of transcript from the focus group discussions for parents of under 13s at Centre 2 and then the healthcare professionals at Centre 1.

(taken from PDFs)

Centre 2 U13

2: there isn't any flexibility, no, and its quite frustrating with a well child being on a ward with lots of quite poorly children, its...

5: they could pick up something else...

4: and for us, we'd know that it was rhinovirus, we were put in isolation, we're taking up that room when another child who could have chicken pox or whatever had come in and we felt that we could deal with her at home... which would have been a lot easier...

5: frees up the isolation room as well... doesn't it?

4: I mean cos she had it all the way through as well, for the two years she was kind of here... we were always in isolation as well

5: she wasn't poorly with it.. when she had rhinovirus she was never poorly with it, it was just a temperature, that was it so she wasn't unwell in herself...

4: just the one temperature and then it would go down and that would be it...but we couldn't be on the ward...

2: so would the antibiotics take that temperature down then?

5: no temperature would come down maybe with the paracetamol, after they'd took her bloods, they'd give her some paracetamol, calpol, it would come down like a normal child would that wasn't neutropenic and then...but that was it...

2: would she be on antibiotics though?

5: they'd give her some

4: they start them as soon as you come in with a temperature... and then do the swabs, the nose and the throat and all that and then you wait don't you

5: yeah she'd always go on the antibiotics for the five days but most of the time, apart from probably 5 occasions, through the 16 months when we were here she didn't... that was all it was... that's all it amounted to... and in them cases, we could've gone home... they know...

4: when she came in with a line infection, you could tell just by the way she was that it was more serious than just a temperature and a cold, she was sleepy, she was lethargic, she wouldn't eat, and we knew didn't we, and they did the same thing, they start her on the antibiotics, and luckily it had been the right one that they'd started her on, but we knew that it wasn't just a cold so you kind of get to know your kids and how they react to a certain temperature, if it was just a cold, she'd have a temperature but she'd carry one wouldn't she?

5: she would

4: and she'd still play and do all the usual things, when she was really poorly, she just wouldn't do anything... and then you knew, this is not just a cold and that's when you need to be here and...

(1:13:40)

4: I...I think what sits with me comfortably is we got to our current position over quite a long time by developing some knowledge... um.. some evidence that what we're doing is safe and erm... it sounds from what [1] said... for me its ... you know taking a step... saying we're now ... you know we've got to 48 hours and we don't have any evidence that that's less safe ... its probably time to move it back a bit and get some evidence that that's still safe... rather than just...

3: like a 36 hour..

4: yeah... just an hour...

3: then 24 hour...

(laughter)

2: really what you're saying at this point is that in... to a certain respect... if they're a low risk patient you would treat them pretty much the same as you do a general paediatric patient... and its about moving... that shift of your opinion that our patients are 'special' ([4]laughs) or susceptible whereas actually what you're saying is they're... they're not. And in which case, you're moving away from the oncology kind of let's protect everybody kind of approach to more of a general paediatrics approach of somethings really gotta be wrong in order for us to kind of worry about this child. So I don't know... but I agree with [1] and [4] I think... I don't know whether going from your 48 hours to immediate discharge...

7:...47....47 hours...

3:....47 and a half....

(laughter)

2: how far off your retirement are you [4]?

4: and then I suppose we have to think about are we then happy to make that policy general and include shared care hospitals and are we happy that... the same safety applies to the shared care centres...

2: that would be a major concern for me... (laughter)... having taken phone calls from shared care centres... yeah...

1: it'd be harder for them... I mean... we see I dunno ten a week or so... they see one every month sometimes don't they...

2: I would have thought this kind of thing had to be... done here first...

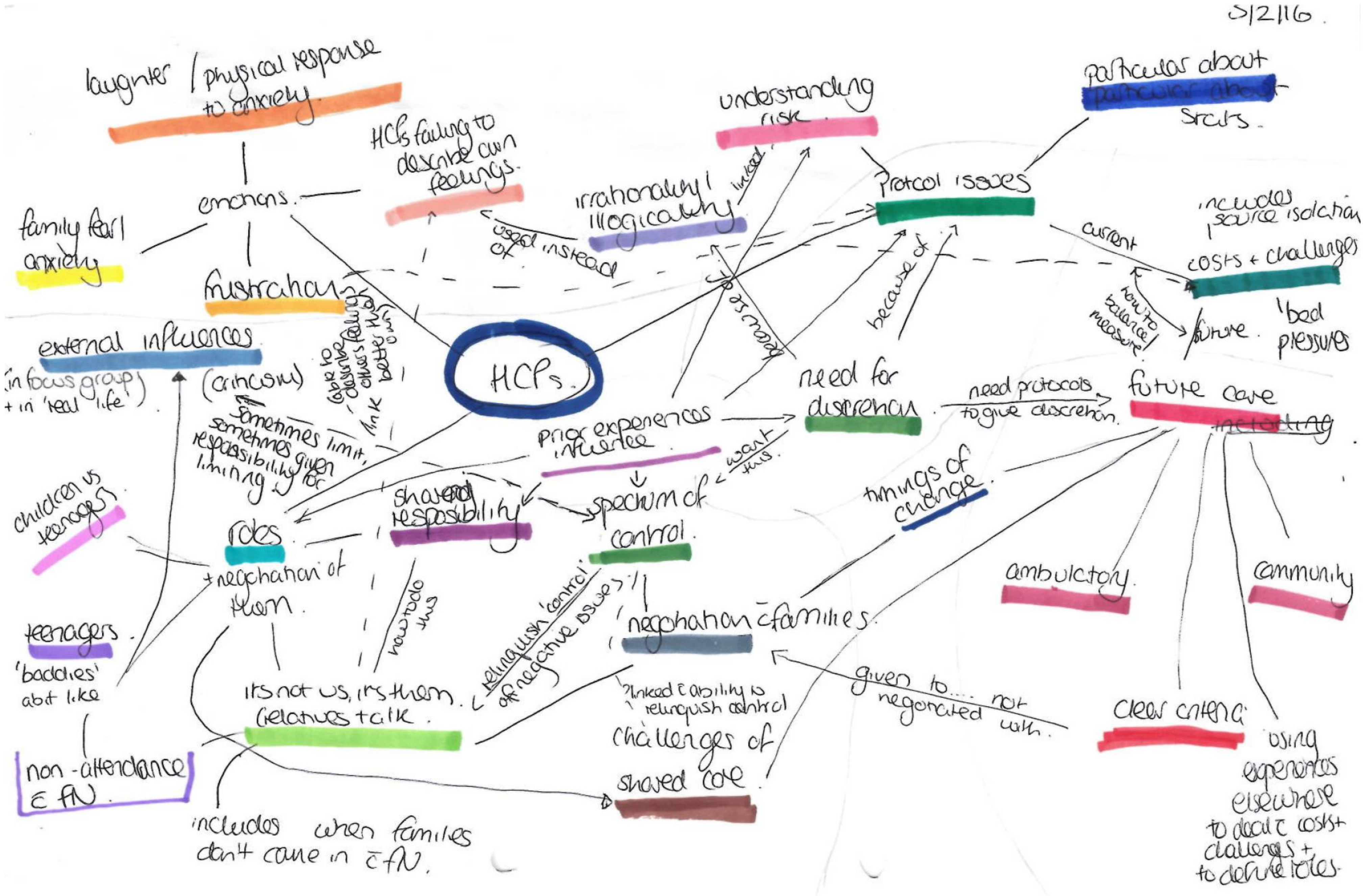
4: yeah but the low risk are the backbone of what we want shared care to do...

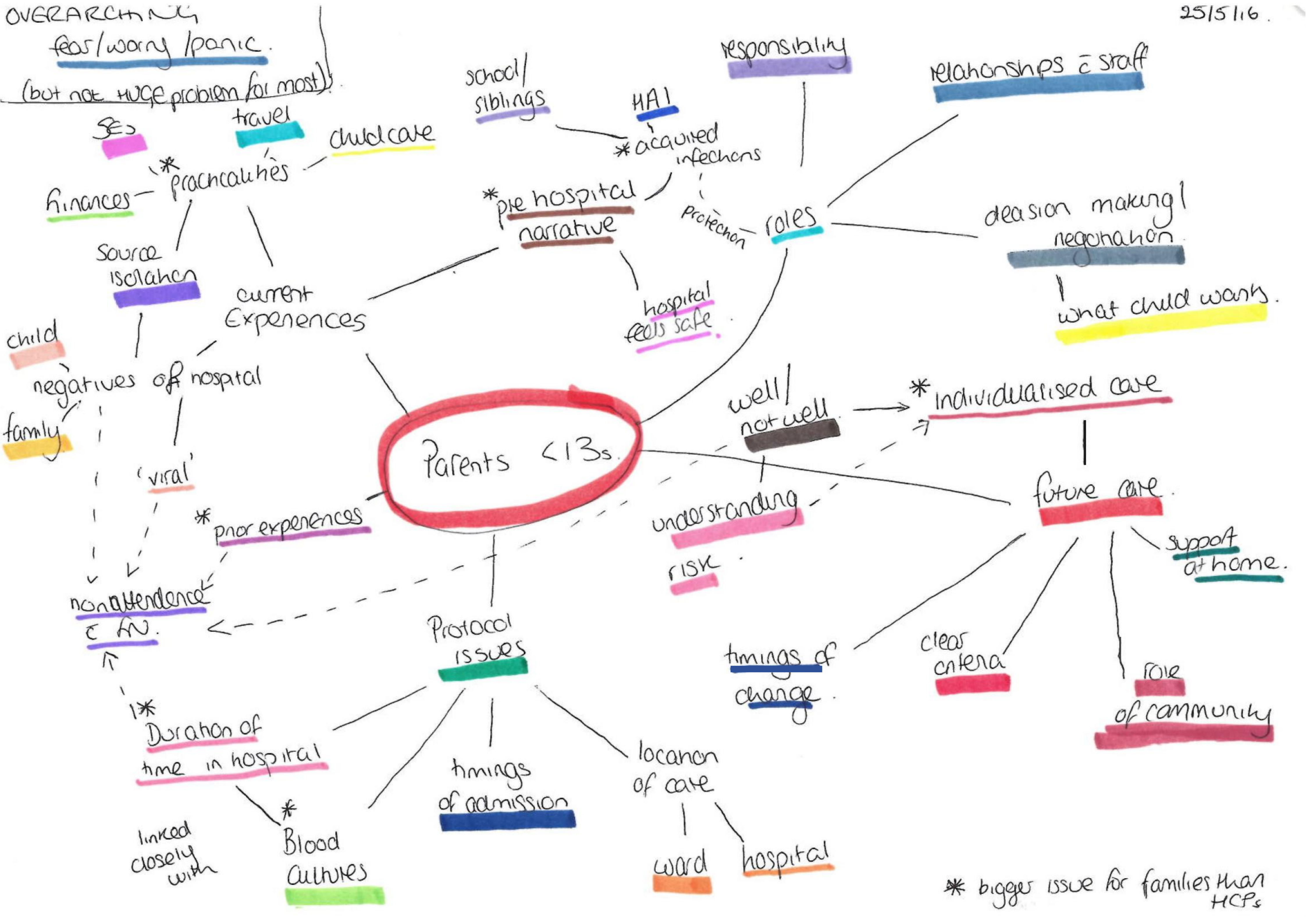
2: but you'd have to start off here see that it worked here over a year... two years... work out that you're happy with it... and maybe mention it to shared care...

(laugher)

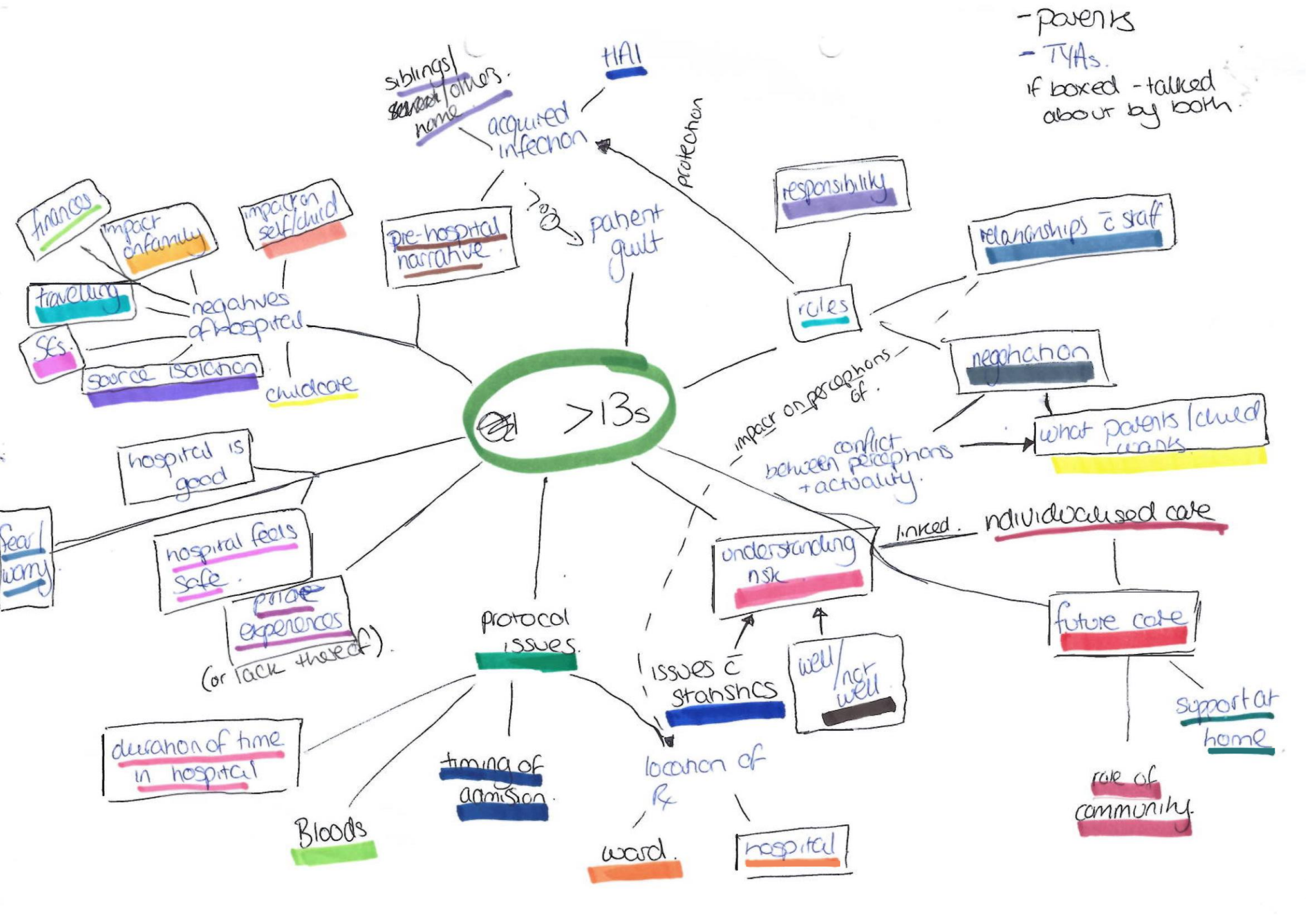
Appendix 5.10: Mapping of themes

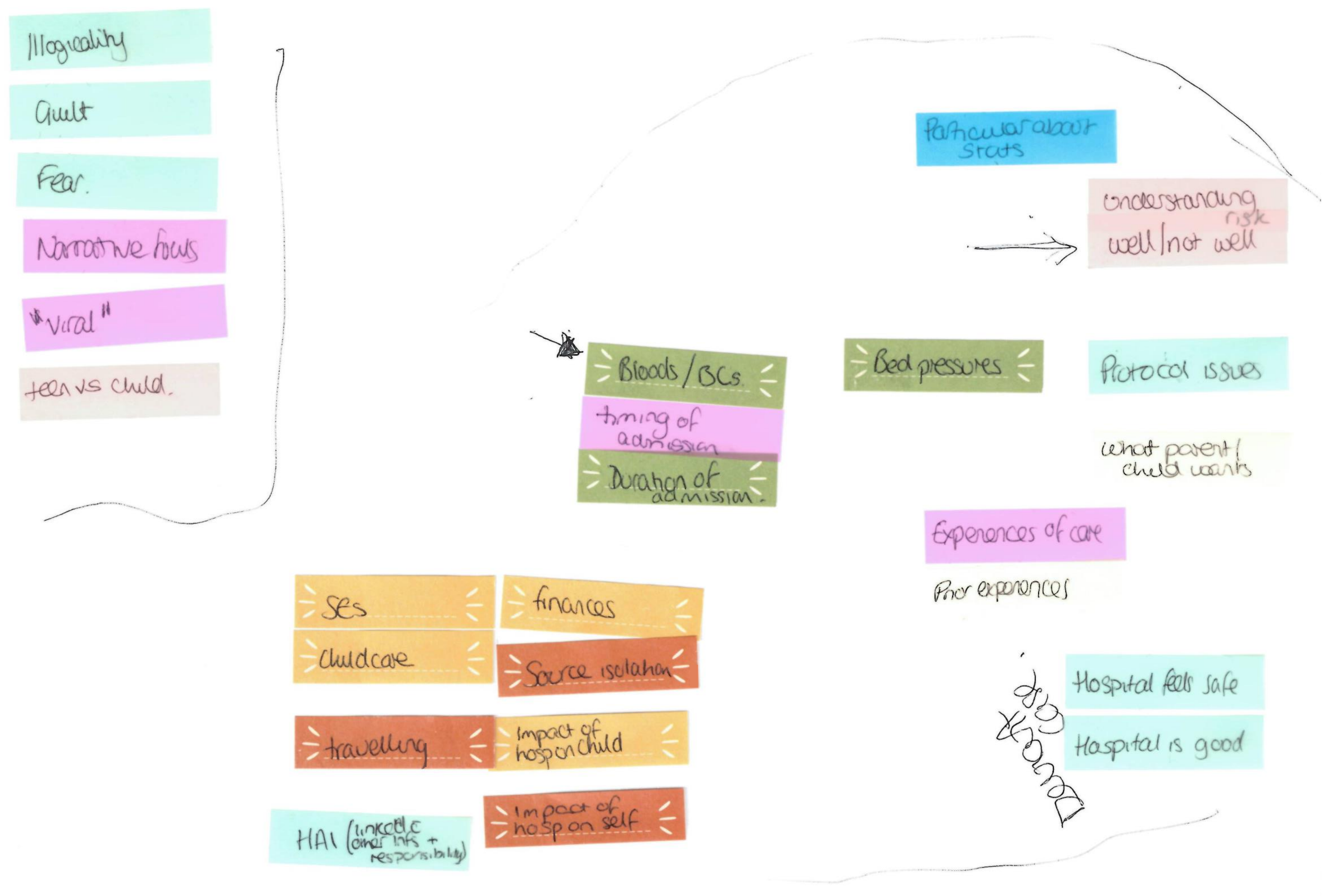
The following pages show the conceptual maps of the work for the groups of participants and then for the overarching findings (taken from PDFs). They demonstrate the development of the connections and cross-referencing and evidence how the analysis changed over time.


5/2/16.
laughter / physical response to anxiety
HCPs failing to describe own feelings.
understanding risk
particular about
particular about
Staff.
emotions.
family fear/ anxiety
frustration
irrationality / illogicality
instead
used instead of
Protocol issues
includes source isolation
current
costs + challenges
'bed pressures'
future.
how to balance measure
because of
because of
external influences
in focus groups + in 'real life'
(criticism)
able to describe others feelings better than own
think
HCPs.
need for discretion.
need protocols to give discretion.
future care including
prior experiences influence
sometimes limit, sometimes given responsibility for limiting.
want this.
spectrum of control.
shared responsibility
timings of change.
children vs teenagers
roles + negotiation of them.
ambulatory.
community
teenagers.
'baddies' a bit like
how to do this
relinquish 'control' of negative issues
negotiation c families.
its not us, its them. Relatives talk.
linked c ability to relinquish control
given to... not negotiated with.
clear criteria
challenges of shared care.
using experiences elsewhere to deal c costs + challenges + to define roles.
non-attendance c FN.
includes when families don't come in c FN.



OVERARCHING
fear/worry/panic.
(but not HUGE problem for most).
25/5/16.
Parents <13s.
*practicalities
SES
travel
childcare
finances
source isolation
current Experiences
child
negatives of hospital
family
'viral'
*prior experiences
non attendence c FN.
school/siblings
HAI
*acquired infections
*pre hospital narrative
hospital feels safe.
protection
roles
responsibility
relationships c staff
decision making/negotiation.
what child wants.
well/not well
*individualised care
understanding
risk.
future care.
support at home.
timings of change.
clear criteria
role of community
Protocol issues
1* Duration of time in hospital
*Blood cultures
linked closely with
timings of admission
location of care
ward
hospital
* bigger issue for families than HCPs


- parents
- TYAs.
if boxed - talked about by both.
siblings/ others.
none
HAI
acquired infection
protection
responsibility
pre-hospital narrative
patient guilt
finances
impact on family
impact on self/child
travelling
negatives of hospital
SEs.
source isolation
childcare
relationships c staff
roles
negotiation
impact on perceptions of.
conflict between perceptions + actuality.
what parents/child wants
>13s
hospital is good
fear/ worry
hospital feels safe.
prior experiences
(or lack thereof)
protocol issues.
understanding risk
linked.
individualised care
future care
support at home
role of community.
issues c stashes
well/ not well
location of Rx
ward.
hospital
duration of time in hospital
timing of admission.
Bloods


Illogicality
Guilt
Fear.
Narrative focus
"Viral"
teen vs child.
Bloods / BCs.
timing of admission
Duration of admission.
Bed pressures
Particular about stats
Understanding risk
well / not well
Protocol issues
what parent / child wants
Experiences of care
Prior experiences
Hospital feels safe
Hospital is good
SES
finances
childcare
Source isolation
travelling
impact of hosp on child
HAI (link to other infs + responsibility)
impact of hosp on self


Individualised care
understanding + recognising
expressing + risk
? uncertainty link
Potential for
realised / created
discretion
(can have or not have)
Need for discretion
Spectrum of control
Negotiation
Non-attendance
Responsibility
Shared responsibility
Future care
Clear criteria
role of community
Support at home
Relationships
Staff - external influences
Shared care
Location of treatment (hospital)
its not us - its them
Staff - family
Location of treatment (ward)
in family
(link to prior experiences)
Roles
role of community
shared care
Family "its not us its them"
"Baddies" / teens
'others'
shared care
MUST + shared responsibility
parents responsible for preventing infection.

References

1. Basu SK, Fernandez ID, Fisher SG, Asselin BL, Lyman GH. Length of Stay and Mortality Associated With Febrile Neutropenia Among Children With Cancer. J Clin Oncol. 2005 Nov 1;23(31):7958–66.

2. Hsieh MM, Everhart JE, Byrd-Holt DD, Tisdale JF, Rodgers GP. Prevalence of Neutropenia in the U.S. Population: Age, Sex, Smoking Status, and Ethnic Differences. Ann Intern Med. 2007 Apr 3;146(7):486–92.

3. Hoffbrand AV, Moss PAH, Pettit JE. Essential Haematology. 5th Edition. Oxford, UK: Blackwell Publishing Ltd; 2006.

4. Gibson F, Soames L, editors. Cancer in Children and Young People. Chichester, England: John Wiley & Sons, Ltd; 2008.

5. Castagnola E, Fontana V, Caviglia I, Caruso S, Faraci M, Fioredda F, et al. A Prospective Study on the Epidemiology of Febrile Episodes during Chemotherapy-Induced Neutropenia in Children with Cancer or after Hemopoietic Stem Cell Transplantation. Clin Infect Dis. 2007 Nov 15;45(10):1296–304.

6. Ammann RA, Teuffel O, Agyeman P, Amport N, Leibundgut K. The influence of different fever definitions on the rate of fever in neutropenia diagnosed in children with cancer. PloS One. 2015;10(2):e0117528.

7. Hargrave DR, Hann IM, Richards SM, Hill FG, Lilleyman JS, Kinsey S, et al. Progressive reduction in treatment-related deaths in Medical Research Council childhood lymphoblastic leukaemia trials from 1980 to 1997 (UKALL VIII, X and XI). Br J Haematol. 2001 Feb 1;112(2):293–9.

8. Phillips B, Wade R, Stewart LA, Sutton AJ. Systematic review and meta-analysis of the discriminatory performance of risk prediction rules in febrile neutropaenic episodes in children and young people. Eur J Cancer. 2010 Nov;46(16):2950–64.

9. Chisholm JC, Dommett R. The evolution towards ambulatory and day-case management of febrile neutropenia. Br J Haematol. 2006;135(1):3–16.

10. Phillips RS, Lehrnbecher T, Alexander S, Sung L. Updated systematic review and meta-analysis of the performance of risk prediction rules in children and young people with febrile neutropenia. PloS One. 2012;7(5):e38300.

11. Bodey GP. The treatment of febrile neutropenia: from the Dark Ages to the present. Support Care Cancer. 1997 Sep 1;5(5):351–7.

12. Hersh EM, Bodey GP, Nies BA, Freireich E. Causes of death in acute leukemia: A ten-year study of 414 patients from 1954-1963. JAMA. 1965 Jul 12;193(2):105–9.

13. Bodey GP, Buckley M, Sathe YS, Freireich EJ. Quantitative Relationships Between Circulating Leukocytes and Infection in Patients with Acute Leukemia. Ann Intern Med. 1966 Feb 1;64(2):328–40.

14. Curtin JA, Marshall BD Jr. Use of antibiotics in cancer and leukemia. J Chronic Dis. 1962 Jul;15:713–8.

15. Wolff LJ. Supportive care for children with cancer. Guidelines of the Childrens Cancer Study Group. Use of prophylactic antibiotics. Am J Pediatr Hematol Oncol. 1984;6(3):267–76.

16. Mullen CA. Which children with fever and neutropenia can be safely treated as outpatients? Br J Haematol. 2001;112(4):832–837.

17. Brack E, Bodmer N, Simon A, Leibundgut K, Kühne T, Niggli FK, et al. First-day step-down to oral outpatient treatment versus continued standard treatment in children with cancer and low-risk fever in neutropenia. A randomized controlled trial within the multicenter SPOG 2003 FN study. Pediatr Blood Cancer. 2012;59(3):423–430.

18. Bash RO, Katz JA, Cash JV, Buchanan GR. Safety and cost effectiveness of early hospital discharge of lower risk children with cancer admitted for fever and neutropenia. Cancer. 1994;74(1):189–96.

19. Talcott JA, Finberg R, Mayer RJ, Goldman L. The medical course of cancer patients with fever and neutropenia: Clinical identification of a low-risk subgroup at presentation. Arch Intern Med. 1988 Dec 1;148(12):2561–8.

20. Klastersky J, Paesmans M, Rubenstein EB, Boyer M, Elting L, Feld R, et al. The Multinational Association for Supportive Care in Cancer Risk Index: A Multinational Scoring System for Identifying Low-Risk Febrile Neutropenic Cancer Patients. J Clin Oncol. 2000 Aug 16;18(16):3038–51.

21. NICE. CG151 Neutropenic sepsis: NICE guideline [Internet]. NICE. [cited 2013 Sep 11]. Available from: http://www.nice.org.uk/

22. Sung L, Phillips R, Lehrnbecher T. Time for paediatric febrile neutropenia guidelines - children are not little adults. Eur J Cancer Oxf Engl 1990. 2011 Apr;47(6):811–3.

23. Hann I, Viscoli C, Paesmans M, Gaya H, Glauser M. A comparison of outcome from febrile neutropenic episodes in children compared with adults: results from four EORTC studies. International Antimicrobial Therapy Cooperative Group (IATCG) of the European Organization for Research and Treatment of Cancer (EORTC). Br J Haematol. 1997 Dec;99(3):580–8.

24. Klaassen RJ, Goodman TR, Pham B, Doyle JJ. “Low-risk” prediction rule for pediatric oncology patients presenting with fever and neutropenia. J Clin Oncol Off J Am Soc Clin Oncol. 2000 Mar;18(5):1012–9.

25. Ammann RA, Bodmer N, Hirt A, Niggli FK, Nadal D, Simon A, et al. Predicting Adverse Events in Children With Fever and Chemotherapy-Induced Neutropenia: The Prospective Multicenter SPOG 2003 FN Study. J Clin Oncol. 2010 Apr 20;28(12):2008–14.

26. Santolaya ME, Alvarez AM, Avilés CL, Becker A, Cofré J, Enríquez N, et al. Prospective Evaluation of a Model of Prediction of Invasive Bacterial Infection Risk among Children with Cancer, Fever, and Neutropenia. Clin Infect Dis. 2002 Sep 15;35(6):678–83.

27. Alexander SW, Wade KC, Hibberd PL, Parsons SK. Evaluation of risk prediction criteria for episodes of febrile neutropenia in children with cancer. J Pediatr Hematol Oncol. 2002 Jan;24(1):38–42.

28. Phillips RS, Sutton AJ, Riley RD, Chisholm JC, Picton SV, Stewart LA. Predicting infectious complications in neutropenic children and young people with cancer (IPD protocol). Syst Rev. 2012 Feb 9;1:8.

29. Phillips RS, Sung L, Amman RA, Riley RD, Castagnola E, Haeusler GM, et al. Predicting microbiologically defined infection in febrile neutropenic episodes in children: global individual participant data multivariable meta-analysis. Br J Cancer. 2016 Mar 15;114(6):623–30.

30. Oude Nijhuis C, Kamps WA, Daenen SMG, Gietema JA, van der Graaf WTA, Groen HJM, et al. Feasibility of withholding antibiotics in selected febrile neutropenic cancer patients. J Clin Oncol Off J Am Soc Clin Oncol. 2005 Oct 20;23(30):7437–44.

31. Spiers G, Gridley K, Cusworth L, Mukherjee S, Parker G, Heaton J, et al. Understanding care closer to home for ill children and young people. Nurs Child Young People. 2012 Jun 7;24(5):29–34.

32. Department of Health. National service framework: children, young people and maternity services - Children and Young People who are Ill [Internet]. [cited 2013 Nov 11]. Available from: https://www.gov.uk/government/publications/national-service-framework-children-young-people-and-maternity-services

33. Health D of. Healthy lives, brighter futures - The strategy for children and young people's health [Internet]. 2009 [cited 2013 Nov 11]. Available from: http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/publicationsandstatistics/publications/publicationspolicyandguidance/DH_094400

34. Teuffel O, Cheng S, Ethier MC, Diorio C, Martino J, Mayo C, et al. Health-related quality of life anticipated with different management strategies for febrile neutropenia in adult cancer patients. Support Care Cancer Off J Multinatl Assoc Support Care Cancer. 2012 Nov;20(11):2755–64.

35. Sung L, Feldman BM, Schwamborn G, Paczesny D, Cochrane A, Greenberg ML, et al. Inpatient versus outpatient management of low-risk pediatric febrile neutropenia: measuring parents' and healthcare professionals' preferences. J Clin Oncol Off J Am Soc Clin Oncol. 2004 Oct 1;22(19):3922–9.

36. Sung L, Aplenc R, Alonzo TA, Gerbing RB, Lehrnbecher T, Gamis AS. Effectiveness of supportive care measures to reduce infections in pediatric AML: a report from the Children's Oncology Group. Blood. 2013 May 2;121(18):3573–7.

37. Mustafa MM, Aquino VM, Pappo A, Tkaczewski I, Buchanan GR. A pilot study of outpatient management of febrile neutropenic children with cancer at low risk of bacteremia. J Pediatr. 1996 Jun;128(6):847–9.

38. Teuffel O, Amir E, Alibhai SMH, Beyene J, Sung L. Cost-effectiveness of outpatient management for febrile neutropenia in children with cancer. Pediatrics. 2011 Feb;127(2):e279-286.

39. Teuffel O, Sung L. Advances in management of low-risk febrile neutropenia: Curr Opin Pediatr. 2012 Feb;24(1):40–5.

40. Bate J, Gibson F, Selwood K, Skinner R, Phillips B, Chisholm JC. A reaudit of current febrile neutropenia practice in UK paediatric oncology centres prior to implementation of NICE guidance. Arch Dis Child. 2013 Apr 1;98(4):315–6.

41. Phillips B, Selwood K, Lane SM, Skinner R, Gibson F, Chisholm JC, et al. Variation in policies for the management of febrile neutropenia in United Kingdom Children's Cancer Study Group centres. Arch Dis Child. 2007 Jun;92(6):495–8.

42. Johnson E, Phillips RS, Chisholm J, Bate J, Herd F, on behalf of the CCLG Supportive Care Group. CCLG National Febrile Neutropenia Audit Report 2015 [Internet]. CCLG Supportive Care Group; 2015. Available from: http://www.cclg.org.uk/member-area/febrile-neutropenia-audit-2015

43. Children's Cancer and Leukaemia Group (CCLG). Specialist Hospitals (Principal Treatment Centres) [Internet]. CCLG. Available from: http://www.cclg.org.uk/In-hospital/Specialist-hospitals

44. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines?: A framework for improvement. JAMA. 1999 Oct 20;282(15):1458–65.

45. Freifeld A, Sankaranarayanan J, Ullrich F, Sun J. Clinical practice patterns of managing low-risk adult febrile neutropenia during cancer chemotherapy in the USA. Support Care Cancer. 2008 Feb;16(2):181–91.

46. Cheng S, Teuffel O, Ethier MC, Diorio C, Martino J, Mayo C, et al. Health-related quality of life anticipated with different management strategies for paediatric febrile neutropaenia. Br J Cancer. 2011 Aug 23;105(5):606–11.

47. Shemesh E, Yaniv I, Drucker M, Hadad S, Goshen Y, Stein J, et al. Home intravenous antibiotic treatment for febrile episodes in immune-compromised pediatric patients. Med Pediatr Oncol. 1998;30(2):95–100.

48. Mullen CA, Petropoulos D, Roberts WM, Rytting M, Zipf T, Chan KW, et al. Economic and resource utilization analysis of outpatient management of fever and neutropenia in low-risk pediatric patients with cancer. J Pediatr Hematol Oncol. 1999;21(3):212–8.

49. Sung L, Alibhai SM, Ethier M-C, Teuffel O, Cheng S, Fisman D, et al. Discrete choice experiment produced estimates of acceptable risks of therapeutic options in cancer patients with febrile neutropenia. J Clin Epidemiol. 2012 Jun;65(6):627–34.

50. Cox K, Mcgarry J. Why patients don't take part in cancer clinical trials: an overview of the literature. Eur J Cancer Care (Engl). 2003;12(2):114–122.

51. Saks M, Allsop J, editors. Researching health: qualitative, quantitative and mixed methods. 2nd Edition. Los Angeles, Calif ; London: SAGE Publications, Ltd; 2013.

52. Curry L, Nunez-Smith M. Mixed Methods in Health Sciences Research: A Practical Primer. California: Sage Publications, Inc; 2015. (SAGE Mixed Methods Research Series).

53. Tashakkori A, Teddlie C, editors. Handbook of Mixed Methods in Social & Behavioural Research. California: Sage Publications, Inc; 2003.

54. Walker D-M, editor. An introduction to health services research. London, England: SAGE Publications, Ltd; 2014.

55. Morgan DL. Paradigms Lost and Pragmatism Regained Methodological Implications of Combining Qualitative and Quantitative Methods. J Mix Methods Res. 2007 Jan 1;1(1):48–76.

56. Barbour R. Introducing Qualitative Research: A Student's Guide. 2nd ed. London: SAGE Publications, Ltd; 2014.

57. Flemming K, Graham H, Heirs M, Fox D, Sowden A. Smoking in pregnancy: a systematic review of qualitative research of women who commence pregnancy as smokers. J Adv Nurs. 2013 May;69(5):1023–36.

58. Henderson S, Petersen A, editors. Consuming Health: The commodification of health care. London, England: Routledge; 2002.

59. General Medical Council. Duties of a doctor. In: Good Medical Practice [Internet]. 2013 [cited 2014 Mar 3]. Available from: http://www.gmc-uk.org/guidance/good_medical_practice/communication_partnership_teamwork.asp

60. UNCRC. United Nations Convention on the Rights of the Child. 1989 [cited 2014 Mar 3]; Available from: http://www.unicef.org/crc/index_30177.html

61. Royal College of Paediatrics and Child Health. Rights of the child [Internet]. 2014 [cited 2015 Jun 9]. Available from: http://www.rcpch.ac.uk/what-we-do/children-and-young-peoples-participation/rights-child/rights-child

62. Coad JE, Shaw KL. Is children's choice in health care rhetoric or reality? A scoping review. J Adv Nurs. 2008 Nov;64(4):318–27.

63. Dixon-Woods M, Young B, Heney D. Childhood cancer and users' views: a critical perspective. Eur J Cancer Care (Engl). 2002;11(3):173–7.

64. Coad J, Flay J, Aspinall M, Bilverstone B, Coxhead E, Hones B. Evaluating the impact of involving young people in developing children's services in an acute hospital trust. J Clin Nurs. 2008;17(23):3115–3122.

65. Tates K, Meeuwesen L. Doctor–parent–child communication. A (re)view of the literature. Soc Sci Med. 2001 Mar;52(6):839–51.

66. Moules T. "They wouldn"t know how it feels . . .': characteristics of quality care from young people's perspectives: a participatory research project. J Child Health Care. 2009 Dec 1;13(4):322–32.

67. Chapman GB, Sonnenberg FA. Decision making in healthcare: Theory, Psychology and Applications. Cambridge University Press; 2000.

68. Brown JE, Mann L. The relationship between family structure and process variables and adolescent decision making. J Adolesc. 1990 Mar;13(1):25–37.

69. Barach P, Berwick DM. Patient Safety and the Reliability of Health Care Systems. Ann Intern Med. 2003 Jun 17;138(12):997–8.

70. Zwaanswijk M, Tates K, van Dulmen S, Hoogerbrugge PM, Kamps WA, Bensing JM. Young patients', parents', and survivors' communication preferences in paediatric oncology: Results of online focus groups. BMC Pediatr. 2007 Nov 9;7:35.

71. Zwaanswijk M, Tates K, van Dulmen S, Hoogerbrugge PM, Kamps WA, Beishuizen A, et al. Communicating with child patients in pediatric oncology consultations: a vignette study on child patients', parents', and survivors' communication preferences. Psychooncology. 2011;20(3):269–277.

72. Twigg J, Atkin K. Carers perceived: policy and practice in informal care. Buckingham: Open University Press; 1994.

73. October TW, Fisher KR, Feudtner C, Hinds PS. The parent perspective: "being a good parent" when making critical decisions in the PICU. Pediatr Crit Care Med J Soc Crit Care Med World Fed Pediatr Intensive Crit Care Soc. 2014 May;15(4):291–8.

74. Janz NK, Becker MH. The Health Belief Model: A Decade Later. Health Educ Behav. 1984 Mar 1;11(1):1–47.

75. Caviola L, Mannino A, Savulescu J, Faulmüller N. Cognitive biases can affect moral intuitions about cognitive enhancement. Front Syst Neurosci [Internet]. 2014 Oct 15 [cited 2015 Aug 6];8. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4197737/

76. Blumenthal-Barby JS, Krieger H. Cognitive Biases and Heuristics in Medical Decision Making A Critical Review Using a Systematic Search Strategy. Med Decis Making. 2015 May 1;35(4):539–57.

77. Bilton T, Bonnett K, Jones P, Lawson T, Stanworth M, Webster A. Introductory Sociology. 4th Edition. Basingstoke, Hampshire: Palgrave Macmillan; 2002.

78. Bauman Z. Thinking Sociologically. Oxford, UK: Basil Blackwell, Ltd; 1990.

79. Clark JA, Potter DA, McKinlay JB. Bringing social structure back into clinical decision making. Soc Sci Med 1982. 1991;32(8):853–66.

80. Hinds PS, Oakes LL, Hicks J, Powell B, Srivastava DK, Spunt SL, et al. "Trying to be a good parent" as defined by interviews with parents who made phase I, terminal care, and resuscitation decisions for their children. J Clin Oncol Off J Am Soc Clin Oncol. 2009 Dec 10;27(35):5979–85.

81. Beauchamp TL, Childress JF. Principles of Biomedical Ethics. Oxford University Press; 2009. 417 p.

82. General Medical Council. Consent guidance: Partnership [Internet]. [cited 2015 Sep 8]. Available from: http://www.gmc-uk.org/guidance/ethical_guidance/consent_guidance_partnership.asp

83. Berger Z. Navigating the Unknown: Shared Decision-Making in the Face of Uncertainty. J Gen Intern Med. 2015 May;30(5):675–8.

84. Pyke-Grimm KA, Stewart JL, Kelly KP, Degner LF. Parents of Children With Cancer: Factors Influencing Their Treatment Decision Making Roles. J Pediatr Nurs. 2006 Oct;21(5):350–61.

85. Wirtz V, Cribb A, Barber N. Patient-doctor decision-making about treatment within the consultation--a critical analysis of models. Soc Sci Med 1982. 2006 Jan;62(1):116–24.

86. Say RE, Thomson R. The importance of patient preferences in treatment decisions—challenges for doctors. BMJ. 2003 Sep 4;327(7414):542–5.

87. Pollard S, Bansback N, Bryan S. Physician attitudes toward shared decision making: A systematic review. Patient Educ Couns. 2015 Sep;98(9):1046–57.

88. General Medical Council. 0-18 years: guidance for all doctors [Internet]. General Medical Council; 2007 [cited 2014 Jan 13]. Available from: http://www.gmc-uk.org/guidance/ethical_guidance/children_guidance_contents.asp

89. Rocca CH, Kimport K, Roberts SCM, Gould H, Neuhaus J, Foster DG. Decision Rightness and Emotional Responses to Abortion in the United States: A Longitudinal Study. PLoS ONE [Internet]. 2015 Jul 8 [cited 2015 Sep 8];10(7). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4496083/

90. Sung L, Regier DA. Decision making in pediatric oncology: Evaluation and incorporation of patient and parent preferences. Pediatr Blood Cancer. 2013;60(4):558–563.

91. General Medical Council. Good practice in research and Consent to research [Internet]. 2010 [cited 2015 Jul 17]. Available from: http://www.gmc-uk.org/guidance/ethical_guidance/5993.asp

92. ICH harmonized tripartite guideline: Guideline for Good Clinical Practice. J Postgrad Med. 2001 Jan 1;47(1):45.

93. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects [Internet]. 2013 [cited 2015 Aug 13]. Available from: http://www.wma.net/en/30publications/10policies/b3/index.html

94. The Nuremberg Code (1947). BMJ. 1996 Dec 7;313(7070):1448.

95. Shaw M. Competence and consent to treatment in children and adolescents. Adv Psychiatr Treat. 2001 Mar 1;7(2):150–9.

96. Roth LH, Meisel A, Lidz CW. Tests of competency to consent to treatment. Am J Psychiatry. 1977 Mar;134(3):279–84.

97. Tulstrup M, Larsen HB, Castor A, Rossel P, Grell K, Heyman M, et al. Parents' and Adolescents' Preferences for Intensified or Reduced Treatment in Randomized Lymphoblastic Leukemia Trials. Pediatr Blood Cancer. 2016 May 1;63(5):865–71.

98. Manji A, Beyene J, Dupuis LL, Phillips R, Lehrnbecher T, Sung L. Outpatient and oral antibiotic management of low-risk febrile neutropenia are effective in children - A systematic review of prospective trials. Support Care Cancer. 2012;20(6):1135–45.

99. Vidal L, Ben Dor I, Paul M, Eliakim-Raz N, Pokroy E, Soares-Weiser K, et al. Oral versus intravenous antibiotic treatment for febrile neutropenia in cancer patients. Cochrane Database Syst Rev. 2013;10:CD003992.

100. Centre for Reviews and Dissemination. Systematic Reviews: CRD's guidance for undertaking reviews in health care. CRD, University of York; 2009. 281 p.

101. Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. Version 5.1.0. The Cochrane Collaboration; 2011. Available from: www.cochrane-handbook.org

102. Morgan JE, Stewart L, Phillips RS. Protocol for a systematic review of reductions in therapy for children with low-risk febrile neutropenia. Syst Rev. 2014 Oct 21;3(1):119.

103. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009 Jul 21;6(7):e1000097.

104. Feld R, Paesmans M, Freifeld AG, Klastersky J, Pizzo PA, Rolston KVI, et al. Methodology for Clinical Trials Involving Patients with Cancer Who Have Febrile Neutropenia: Updated Guidelines of the Immunocompromised Host Society/Multinational Association for

Supportive Care in Cancer, with Emphasis on Outpatient Studies. Clin Infect Dis. 2002 Dec 15;35(12):1463–8.

105. National Institute for Health and Clinical Excellence. Appendix I: Methodology checklist: prognostic studies. From The guidelines manual [Internet]. London: National Institute for Health and Clinical Excellence; 2012 [cited 2014 Feb 14]. Available from: www.nice.org.uk/article/pmg6b/chapter/Appendix-I-Methodology-checklist-prognostic-studies

106. R Core Team. R: A language and environment for statistical computing. [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2013. Available from: http://www.R-project.org

107. Cagol AR, Castro Junior CG, Martins MC, Machado AL, Ribeiro RC, Gregianin LJ, et al. Oral vs. intravenous empirical antimicrobial therapy in febrile neutropenic patients receiving childhood cancer chemotherapy. J Pediatr (Rio J). 2009;85(6):531–5.

108. Gupta A, Swaroop C, Agarwala S, Pandey RM, Bakhshi S. Randomized controlled trial comparing oral amoxicillin-clavulanate and ofloxacin with intravenous ceftriaxone and amikacin as outpatient therapy in pediatric low-risk febrile neutropenia. J Pediatr Hematol Oncol. 2009;31(9):635–41.

109. Klaassen RJ, Allen U, Doyle JJ. Randomized placebo-controlled trial of oral antibiotics in pediatric oncology patients at low-risk with fever and neutropenia. J Pediatr Hematol Oncol. 2000;22(5):405–11.

110. Mullen CA, Petropoulos D, Roberts WM, Rytting M, Zipf T, Chan KW, et al. Outpatient treatment of fever and neutropenia for low risk pediatric cancer patients. Cancer. 1999;86(1):126–34.

111. Orme L, Babl F, Barnes C, Barnett P, Donath S, Ashley D. Outpatient Versus Inpatient IV antibiotic Management for Pediatric Oncology Patients with Low Risk Febrile Neutropenia: A Randomised Trial. Pediatr Blood Cancer. 2014;61:1427–33.

112. Paganini H, Gomez S, Ruvinsky S, Zubizarreta P, Latella A, Fraquelli L, et al. Outpatient, sequential, parenteral-oral antibiotic therapy for lower risk febrile neutropenia in children with malignant disease: a single-center, randomized, controlled trial in Argentina. Cancer. 2003;97(7):1775–80.

113. Paganini H, Rodriguez-Brieshcke T, Zubizarreta P, Latella A, Firpo V, Casimir L, et al. Oral ciprofloxacin in the management of children with cancer with lower risk febrile neutropenia. Cancer. 2001;91(8):1563–7.

114. Paganini HR, Sarkis CM, De Martino MG, Zubizarreta PA, Casimir L, Fernandez C, et al. Oral administration of cefixime to lower risk febrile neutropenic children with cancer. Cancer. 2000;88(12):2848–52.

115. Petrilli AS, Dantas LS, Campos MC, Tanaka C, Ginani VC, Seber A. Oral ciprofloxacin vs. intravenous ceftriaxone administered in an outpatient setting for fever and neutropenia in low-risk pediatric oncology patients: randomized prospective trial. Med Pediatr Oncol. 2000;34(2):87–91.

116. Santolaya ME, Alvarez AM, Aviles CL, Becker A, Cofre J, Cumsille MA, et al. Early hospital discharge followed by outpatient management versus continued hospitalization of children

with cancer, fever, and neutropenia at low risk for invasive bacterial infection. J Clin Oncol. 2004;22(18):3784–9.

117. Shenep JL, Flynn PM, Baker DK, Hetherington SV, Hudson MM, Hughes WT, et al. Oral cefixime is similar to continued intravenous antibiotics in the empirical treatment of febrile neutropenic children with cancer. Clin Infect Dis. 2001;32(1):36–43.

118. Varan A, Koksal Y, Akyuz C, Ceyhan M, Kanra G, Buyukpamukcu M. The Outpatient Management of Febrile Neutropenia in Selected Children with Cancer; A Preliminary Report. Pediatr Blood Cancer. 2005;45(4):512.

119. Abbas AAH, Felimban SK, Cittana BA, Yousef AA, Fayea NY, Khattab TM, et al. Once daily ceftriaxone and amikacin for outpatient treatment of neutropenic fever in children with acute lymphoblastic leukaemia. Haema. 2003;6(4):501–6.

120. Aquino VM, Herrera L, Sandler ES, Buchanan GR. Feasibility of oral ciprofloxacin for the outpatient management of febrile neutropenia in selected children with cancer. Cancer. 2000;88(7):1710–4.

121. Dommett R, Geary J, Freeman S, Hartley J, Sharland M, Davidson A, et al. Successful introduction and audit of a step-down oral antibiotic strategy for low risk paediatric febrile neutropaenia in a UK, multicentre, shared care setting. Eur J Cancer. 2009;45(16):2843–9.

122. Doyle JJ, King SM, Comay SA, Freedman MH. Oral Antibiotic Therapy for “low Risk” Febrile Neutropenic Episodes (fne). Pediatr Res. 1996 Apr;39(S4):154–154.

123. Fernandez CM, Saavedra-Lozano J, Huerta J, Garrido C, Belendez C, Cela E, et al. Risk-based therapy for febrile patients with neutropenia: A role for early hospital discharge. Pediatr Blood Cancer. 2012;59 (6):1113–4.

124. Kaplinsky C, Drucker M, Goshen J, Tamary H, Cohen IJ, Zaizov R. Ambulatory treatment with ceftriaxone in febrile neutropenic children. Isr J Med Sci. 1994;30(8):649–51.

125. Karthaus M, Egerer G, Jurgens H. Outpatient treatment of cancer patients with fever and neutropenia. Antibiot Chemother. 2000;50:47–58.

126. Lau RC, Doyle JJ, Freedman MH, King SM, Richardson SE. Early discharge of pediatric febrile neutropenic cancer patients by substitution of oral for intravenous antibiotics. Pediatr Hematol Oncol. 1994;11(4):417–21.

127. Malik IA. Out-patient management of febrile neutropenia in indigent paediatric patients. Ann Acad Med Singapore. 1997;26(6):742–6.

128. Miedema K, Tissing W, Van Vliet M, De Vries W, Kamps W, Abbink F, et al. Risk-adapted approach for fever and neutropenia in pediatric cancer patients. Support Care Cancer. 2012;20:S155.

129. Paganini HR, Rodriguez Brieshcke T, Zubizarreta P, Latella A, Firpo V, Fernandez C, et al. [Criteria of low risk of mortality in children with neutropenia and fever during cancer chemotherapy]. Medicina (Mex). 2001;61(1):63–6.

130. Paganini H. Tratamiento secuencial parenteral-oral con antibióticos en niños con patología onco-hematológica con bajo riesgo de bacteriemia Sequential antibiotic parenteral-oral therapy in onco-hematologic patients with low-risk for bacteriemia. Arch Argent Pediatr. 2000 10PY - 2000;98(5):291–5.

131. Paganini H. Tratamiento ambulatorio secuencia parenteral-oral de niños con neutropenia y fiebre de riesgo de mortalidad Sequential oral-parenteral outpatient treatment on low-risk children with fever and neutropenia. Arch Argent Pediatr. 2003 02PY - 2003;101(1):31–6.

132. Park JR, Coughlin J, Hawkins D, Friedman DL, Burns JL, Pendergrass T. Ciprofloxacin and amoxicillin as continuation treatment of febrile neutropenia in pediatric cancer patients. Med Pediatr Oncol. 2003;40(2):93–8.

133. Petrilli AS, Carlesse FA, Pereira CAP. Oral gatifloxacin in the outpatient treatment of children with cancer fever and neutropenia. Pediatr Blood Cancer. 2007;49(5):682–6.

134. Phillips R, Phelan L, Picton S. An audit of the use of oral antibiotics and early discharge in the treatment of low risk febrile neutropenia in children. Arch Dis Child. 2006 Apr 1;91 Suppl 1:A80–2.

135. Preis S, Jurgens H, Friedland C, Oudekotte-David AA, Thomas L, Gobel U. Ceftriaxone alone or in Combination with Teicoplanin in the Management of Febrile Episodes in Neutropenic Children and Adolescents with Cancer on an Outpatient Base. Klin Padiatr. 1993;205(4):295–9.

136. Quezada G, Sunderland T, Chan KW, Rolston K, Mullen CA. Medical and non-medical barriers to outpatient treatment of fever and neutropenia in children with cancer. Pediatr Blood Cancer. 2007;48(3):273–7.

137. Sari N, Aki A, Ocal R, Karaman N, Ilhan I. Oral Ciprofloxacin and Amoxicillin/Clavulanate Treatment in Pediatric Cancer Patients with Low-Risk Febrile Neutropenia. In Pediatric Blood and Cancer; 2007. p. 481.

138. Shrestha PN, Sah KP, Rana R. Emperical oral antibiotic therapy for children with low risk febrile neutropenia during cancer chemotherapy. J Nepal Paediatr Soc. 2009;29(1):22–5.

139. Tordecilla C J, Campbell Bull M, Joannon S P, Rizzardini L C, Soto A V. Criterios de alta precoz en niños con cáncer y neutropenia febril Criteria of early discharge in children with cancer and febrile neutropenia. Rev Chil Pediatr. 1998 12PY - 1998;69(6):247–51.

140. Wiernikowski JT, Rothney M, Dawson S, Andrew M. Evaluation of a home intravenous antibiotic program in pediatric oncology. Am J Pediatr Hematol Oncol. 1991;13(2):144–7.

141. Bash RO, Katz JA, Cash JV, Buchanan GR. Safety and cost effectiveness of early hospital discharge of lower risk children with cancer admitted for fever and neutropenia. Cancer. 1994;74(1):189–96.

142. Brack E, Bodmer N, Simon A, Leibundgut K, Kuhne T, Niggli FK, et al. First-day step-down to oral outpatient treatment versus continued standard treatment in children with cancer and low-risk fever in neutropenia. A randomized controlled trial within the multicenter SPOG 2003 FN study. Pediatr Blood Cancer. 2012;59(3):423–30.

143. Ablett S, Pinkerton CR. Recruiting children into cancer trials–role of the United Kingdom Children's Cancer Study Group (UKCCSG). Br J Cancer. 2003;88(11):1661–5.

144. Morgan JE, Cleminson J, Atkin K, Stewart LA, Phillips RS. Systematic review of reduced therapy regimens for children with low risk febrile neutropenia. Support Care Cancer Off J Multinatl Assoc Support Care Cancer. 2016 Jan 13;

145. Pope C, Mays N, Popay J. Synthesizing Qualitative and Quantitative Health Evidence. Maidenhead, England: Open University Press; 2007.

146. Noblit GW, Hare RD. Meta-ethnography: Synthesizing Qualitative Studies. Sage Publications, Inc; 1988. 88 p. (Qualitative Research Methods Series 11).

147. Hannes K, Lockwood, editors. Synthesizing Qualitative Research: Choosing the right approach. Chichester, England: John Wiley & Sons, Ltd; 2012.

148. Tong A, Flemming K, McInnes E, Oliver S, Craig J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Med Res Methodol. 2012 Nov 27;12:181.

149. The Joanna Briggs Institute. Joanna Briggs Institute Reviewers' Manual: 2014 edition [Internet]. Australia: The Joanna Briggs Institute; 2014. Available from: http://joannabriggs.org/assets/docs/sumari/reviewersmanual-2014.pdf

150. Tatman MA, Woodroffe C, Kelly PJ, Harris RJ. Paediatric home care in Tower Hamlets: a working partnership with parents. Qual Health Care. 1992;1(2):98–103.

151. Diorio C, Martino J, Boydell KM, Ethier MC, Mayo C, Wing R, et al. Parental perspectives on inpatient versus outpatient management of pediatric febrile neutropenia. J Pediatr Oncol Nurs. 2011;28(6):355–62.

152. Freund BL, Siegel K. Problems in transition following bone marrow transplantation: Psychosocial aspects. Am J Orthopsychiatry. 1986 Apr;56(2):244–52.

153. Fuji KT, Abbott AA, Norris JF. Exploring Care Transitions From Patient, Caregiver, and Health-Care Provider Perspectives. Clin Nurs Res. 2013;22(3):258–74.

154. Hally MR, Holohan A, Jackson RH, Reedy BL, Walker JH. Paediatric home nursing scheme in Gateshead. Br Med J. 1977 Mar 19;1(6063):762–4.

155. Sartain SA, Clarke CL, Heyman R. Hearing the voices of children with chronic illness. J Adv Nurs. 2000 Oct;32(4):913–21.

156. Sartain SA, Maxwell MJ, Todd PJ, Haycox AR, Bundred PE. Users' views on hospital and home care for acute illness in childhood. Health Soc Care Community. 2001;9(2):108–17.

157. Smith L, Daughtrey H. Weaving the seamless web of care: an analysis of parents' perceptions of their needs following discharge of their child from hospital. J Adv Nurs. 2000 Apr;31(4):812–20.

158. While AE. Consumer views of health care: a comparison of hospital and home care. Child Care Health Dev. 1992 Mar 1;18(2):107–16.

159. Dixon-Woods M, Young B, Heney D. Rethinking Experiences of Childhood Cancer: A Multidisciplinary Approach to Chronic Childhood Illness. Maidenhead, England: Open University Press; 2005.

160. Taylor SE, Kemeny ME, Reed GM, Bower JE, Gruenewald TL. Psychological resources, positive illusions, and health. Am Psychol. 2000 Jan;55(1):99–109.

161. Southwick SM, Bonanno GA, Masten AS, Panter-Brick C, Yehuda R. Resilience definitions, theory, and challenges: interdisciplinary perspectives. Eur J Psychotraumatology [Internet]. 2014 Oct 1 [cited 2015 Mar 2];5. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4185134/

162. Bonanno GA, Galea S, Bucciarelli A, Vlahov D. What predicts psychological resilience after disaster? The role of demographics, resources, and life stress. J Consult Clin Psychol. 2007 Oct;75(5):671–82.

163. Lee I, Lee E-O, Kim HS, Park YS, Song M, Park YH. Concept development of family resilience: a study of Korean families with a chronically ill child. J Clin Nurs. 2004 Jul 1;13(5):636–45.

164. Financial Support [Internet]. CLIC Sargent. [cited 2015 Mar 20]. Available from: www.clicsargent.org.uk/content/financial-support-1

165. Bloor M, Frankland J, Thomas M, Robson K. Focus groups in Social Research. 2001.

166. Morgan DL. Focus Groups as Qualitative Research. 2nd ed. London: Sage Publications, Inc; 1997. (Qualitative Research Methods Series 16).

167. Green J, Thorogood N. Qualitative Methods for Health Research. 2nd ed. SAGE Publications, Ltd; 2009.

168. Barbour R. Doing Focus Groups. London: SAGE Publications, Ltd; 2007.

169. Krueger RA, Casey MA. Focus Groups: A Practical Guide for Applied Research. 4th edition. United States of America: Sage Publications, Inc; 2009.

170. Padgett DK. Qualitative Methods in Social Work Research. 2nd ed. California: Sage Publications, Inc; 2008. (SAGE Sourcebookes for the Human Services).

171. Smith SK, Dixon A, Trevena L, Nutbeam D, McCaffery KJ. Exploring patient involvement in healthcare decision making across different education and functional health literacy groups. Soc Sci Med 1982. 2009 Dec;69(12):1805–12.

172. Hein IM, Troost PW, Lindeboom R, et al. ACcuracy of the macarthur competence assessment tool for clinical research (maccat-cr) for measuring children's competence to consent to clinical research. JAMA Pediatr. 2014 Dec 1;168(12):1147–53.

173. Phillips B, Richards M, Boys R, Hodgkin M, Kinsey S. A home-based maintenance therapy program for acute lymphoblastic leukemia-practical and safe? J Pediatr Hematol Oncol. 2011 Aug;33(6):433–6.

174. About - Disclosure and Barring Service - GOV.UK [Internet]. [cited 2015 Jun 3]. Available from: https://www.gov.uk/government/organisations/disclosure-and-barring-service/about

175. Given LM. The Sage encyclopedia of qualitative research methods [electronic resource]. Los Angeles, Calif ; London: SAGE; 2008. 1 p.

176. Morgan J, Cleminson J, Atkin K. Qualitative synthesis of experiences of early discharge, with a focus on paediatric febrile neutropenia. Submiss.

177. Great Britain. Data Protection Act. London: Stationery Office; 1998.

178. Lincoln YS, Guba EG. Naturalistic inquiry. Sage Publications; 1985.

179. Cheng S, Teuffel O, Ethier MC, Diorio C, Martino J, Mayo C, et al. Health-related quality of life anticipated with different management strategies for paediatric febrile neutropaenia. Br J Cancer. 2011;105(5):606–11.

180. Sung L, Alibhai SM, Ethier MC, Teuffel O, Cheng S, Fisman D, et al. Discrete choice experiment produced estimates of acceptable risks of therapeutic options in cancer patients with febrile neutropenia. J Clin Epidemiol. 2012;65(6):627–34.

181. NICE. CG151 Neutropenic sepsis: full guideline [Internet]. NICE. [cited 2013 Sep 25]. Available from: http://www.nice.org.uk/

182. Department of Health. Improving Outcomes: A Strategy for Cancer [Internet]. 2011. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213785/dh_123394.pdf

183. Corbin J, Strauss A. Basics of Qualitative Research. 3rd ed. SAGE Publications, Ltd; 2008.

184. Glaser B, Strauss A. Discovery of Grounded Theory. Aldine Publishing Company; 1967.

185. Krefting L. Rigor in Qualitative Research: The Assessment of Trustworthiness. Am J Occup Ther. 1991 Mar 1;45(3):214–22.

186. Silverman D. Doing Qualitative Research. 3rd ed. London: SAGE Publications, Ltd; 2010.

187. Medical Research Council. MRC Ethics Guide: Medical research involving children [Internet]. Medical Research Council; 2004. Available from: http://www.mrc.ac.uk/documents/pdf/medical-research-involving-children/

188. Mental Health Research Network and INVOLVE. Budgeting for Involvement: Practical advice for budgeting for actively involving the public in research studies [Internet]. Mental Heatlh Research Network, London and INVOLVE, Eastleigh; 2013 [cited 2015 Jul 2]. Available from: http://www.invo.org.uk/wp-content/uploads/2014/11/10002-INVOLVE-Budgeting-Tool-Publication-WEB.pdf

189. United Nations. Convention on the Rights of the Child [Internet]. 1989. Available from: http://www.ohchr.org/en/professionalinterest/pages/crc.aspx

190. Coulter A, Collins A. Making shared decision-making a reality: No decision about me, without me [Internet]. London, England: The King's Fund; 2011 [cited 2014 Nov 26]. Available from: http://www.kingsfund.org.uk/publications/making-shared-decision-making-reality

191. Great Britain. Dept. of Health. Liberating the NHS [electronic resource] : no decision about me, without me ; Government response. London: Department of Health; 2012. 39 p.

192. Department of Health. You're Welcome - Quality criteria for young people friendly health services [Internet]. 2011. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216350/dh_127632.pdf

193. National Cancer Intelligence Network. National Registry of Childhood Tumours Progress Report. Oxford, UK: NRCT; 2012.

194. Gigerenzer G, Gaissmaier W, Kurz-Mileke E, Schwartz LM, Woloshin S. Helping Doctors and Patients Make Sense of Health Statistics. Psychol Sci Public Interest. 2008;8(2):53–96.

195. Brown RF, Cadet DL, Houlihan RH, Thomson MD, Pratt EC, Sullivan A, et al. Perceptions of Participation in a Phase I, II, or III Clinical Trial Among African American Patients With Cancer: What Do Refusers Say? J Oncol Pract. 2013 Nov 1;9(6):287–93.

196. Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S, Gibbons MC, et al. Barriers to recruiting underrepresented populations to cancer clinical trials: A systematic review. Cancer. 2008 Jan 15;112(2):228–42.

197. Ross S, Grant A, Counsell C, Gillespie W, Russell I, Prescott R. Barriers to Participation in Randomised Controlled Trials: A Systematic Review. J Clin Epidemiol. 1999 Dec;52(12):1143–56.

198. Mills EJ, Seely D, Rachlis B, Griffith L, Wu P, Wilson K, et al. Barriers to participation in clinical trials of cancer: a meta-analysis and systematic review of patient-reported factors. Lancet Oncol. 2006 Feb;7(2):141–8.

199. Delbanco T, Berwick DM, Boufford JI, Edgman-Levitan S, Ollenschläger G, Plamping D, et al. Healthcare in a land called PeoplePower: nothing about me without me. Health Expect Int J Public Particip Health Care Health Policy. 2001 Sep;4(3):144–50.

200. Department of Health. Equity and excellence: Liberating the NHS [Internet]. The Stationery Office; 2010 [cited 2016 Jul 15]. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213823/dh_117794.pdf

201. Légaré F, Stacey D, Turcotte S, Cossi M-J, Kryworuchko J, Graham ID, et al. Interventions for improving the adoption of shared decision making by healthcare professionals. Cochrane Database Syst Rev. 2014;(9):CD006732.

202. Elwyn G. Idealistic, impractical, impossible? Shared decision making in the real world. Br J Gen Pract. 2006 Jun 1;56(527):403–4.

203. Ferrer RL, Gill JM. Shared Decision Making, Contextualized. Ann Fam Med. 2013 Jul;11(4):303–5.

204. Smith J. Decisions, decisions . . . BMJ. 2010 Nov 3;341:c6236.

205. Gulbrandsen P. What's in shared decision-making for the physician? Patient Educ Couns. 2014 Nov;97(2):145–6.

206. Thornton H. Shared decision-making: Personal, professional and political. Int J Surg. 2011;9(3):195–7.

207. Kraetschmer N, Sharpe N, Urowitz S, Deber RB. How does trust affect patient preferences for participation in decision-making? Health Expect. 2004 Dec 1;7(4):317–26.

208. Entwistle V. Trust and shared decision-making: an emerging research agenda. Health Expect. 2004 Dec 1;7(4):271–3.

209. Légaré F, Ratté S, Gravel K, Graham ID. Barriers and facilitators to implementing shared decision-making in clinical practice: update of a systematic review of health professionals' perceptions. Patient Educ Couns. 2008 Dec;73(3):526–35.

210. Graham ID, O'Connor AM. Research in shared decision making is growing deeper roots and more branches. Patient Educ Couns. 2006 Nov;63(3):259–61.

211. Stacey D, Bennett CL, Barry MJ, Col NF, Eden KB, Holmes-Rovner M, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2011;(10):CD001431.

212. Barbour RS, Kitzinger J, editors. Developing Focus Group Research: Politics, Theory and Practice. London: SAGE Publications, Ltd; 1999.

213. Charles C, Gafni A, Whelan T, O'Brien MA. Cultural influences on the physician-patient encounter: The case of shared treatment decision-making. Patient Educ Couns. 2006 Nov;63(3):262–7.

214. Clarke A. The Sociology of Healthcare. 2nd ed. Harlow, England: Pearson Education Limited; 2010.

215. Hoffman JR, Kanzaria HK. Intolerance of error and culture of blame drive medical excess. BMJ. 2014 Oct 14;349:g5702.

216. Catino M, Celotti S. The problem of defensive medicine: two Italian surveys. Stud Health Technol Inform. 2009;148:206–21.

217. Lipsky M. Street-level Bureaucracy: Dilemmas of the Individual in Public Services. New York, NY: The Russell Sage Foundation; 1980.

218. About PatientView – what it can do and how [Internet]. [cited 2016 Jun 29]. Available from: http://rixg.org/patientview2/

219. Mittman BS. Creating the Evidence Base for Quality Improvement Collaboratives. Ann Intern Med. 2004 Jun 1;140(11):897–901.

220. Shojania KG, Grimshaw JM. Evidence-Based Quality Improvement: The State Of The Science. Health Aff (Millwood). 2005 Jan 1;24(1):138–50.

221. Sydes MR, Parmar MK, James ND, Clarke NW, Dearnaley DP, Mason MD, et al. Issues in applying multi-arm multi-stage methodology to a clinical trial in prostate cancer: the MRC STAMPEDE trial. Trials. 2009;10:39.

222. Haeusler GM, Phillips RS, Lehrnbecher T, Thursky KA, Sung L, Ammann RA. Core outcomes and definitions for pediatric fever and neutropenia research: A consensus statement from an international panel. Pediatr Blood Cancer. 2015 Mar 1;62(3):483–9.

223. National Institute for Health Research (NIHR). Brief overview of the National Institue for Health Research [Internet]. Available from: http://www.nihr.ac.uk/documents/about-NIHR/NIHR-Publications/2015-11-13%20NIHR%20Overview%20Document.pdf

224. Elwyn G, O'Connor A, Stacey D, Volk R, Edwards A, Coulter A, et al. Developing a quality criteria framework for patient decision aids: online international Delphi consensus process. BMJ. 2006 Aug 24;333(7565):417.

225. Stacey D, Légaré F, Col NF, Bennett CL, Barry MJ, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2014;(1):CD001431.

226. Smith J. Decisions, decisions . . . BMJ. 2010 Nov 3;341:c6236.

227. Brownlee S, Wennberg JE, Barry MJ, Fisher ES, Goodman DC, Bynum JP. Improving Patient Decision-Making in Health Care: A 2011 Dartmouth Atlas Report Highlighting Minnesota [Internet]. The Dartmouth Atlas Project; 2011 [cited 2016 Jun 23]. Available from: http://www.dartmouthatlas.org/downloads/reports/Decision_making_report_022411.pdf

228. Coyne I, O'Mathúna DP, Gibson F, Shields L, Sheaf G. Interventions for promoting participation in shared decision-making for children with cancer. Cochrane Database Syst Rev. 2013;(6):CD008970.

229. Thomson RG, Eccles MP, Steen IN, Greenaway J, Stobbart L, Murtagh MJ, et al. A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: randomised controlled trial. Qual Saf Health Care. 2007 Jun 1;16(3):216–23.

230. Elwyn G, Laitner S, Coulter A, Walker E, Watson P, Thomson R. Implementing shared decision making in the NHS. BMJ. 2010 Oct 14;341:c5146.

231. Muls A, Dougherty L, Doyle N, Shaw C, Soanes L, Stevens A-M. Influencing organisational culture: a leadership challenge. Br J Nurs. 2015 Jun 25;24(12):633–8.

232. Davies HTO, Mannion R. Will prescriptions for cultural change improve the NHS? BMJ. 2013 Mar 1;346:f1305.

233. Upton T, Brooks B. Managing Change in the NHS. London: Kogan Page Ltd; 1995.

234. Acuña Leiva G, Lira Vergara P. Manejo del paciente febril neutropénico Management of the febrile neutropenic patient. Bol Esc Med. 1987 12PY - 1987;17(4):42–7.

235. Ahmed N, El-Mahallawy HA, Ahmed IA, Nassif S, El-Beshlawy A, El-Haddad A. Early hospital discharge versus continued hospitalization in febrile pediatric cancer patients with prolonged neutropenia: A randomized, prospective study. Pediatr Blood Cancer. 2007;49(6):786–92.

236. Ammann RA. Outpatient, sequential, parenteral-oral antibiotic therapy for lower risk febrile neutropenia in children with malignant disease: a single-center, randomized, controlled trial in Argentina. Cancer. 2004;100(7):1547; author reply 1547-8.

237. Ammann RA, Simon A, De Bont ESJM. Low risk episodes of fever and neutropenia in pediatric oncology: Is outpatient oral antibiotic therapy the new gold standard of care? Pediatr Blood Cancer. 2005;45(3):244–7.

238. Anak S, Devecioglou O, Agaoglu L, Zulfikar B, Ayan I, Atilgan N, et al. A study of various antibiotic combinations for the empiric treatment of neutropenic febrile children. Bone Marrow Transplant. 1989;4(SUPPL. 3):104.

239. Anoop P, Anjay MA. Febrile neutropenia: transition towards a risk-directed approach. Arch Dis Child. 2007;92(5):467–8.

240. Aquino VM, Buchanan GR, Tkaczewski I, Mustafa MM. Safety of early hospital discharge of selected febrile children and adolescents with cancer with prolonged neutropenia. Med Pediatr Oncol. 1997;28(3):191–5.

241. Aquino VM, Tkaczewski I, Buchanan GR. Early discharge of low-risk febrile neutropenic children and adolescents with cancer. Clin Infect Dis. 1997;25(1):74–8.

242. Arceci RJ. Fever and neutropenia: changing patterns of medical practice. J Pediatr Hematol Oncol. 2000;22(5):397.

243. Barnes RA, Rogers TR. Response rates to a staged antibiotic regimen in febrile neutropenic patients. J Antimicrob Chemother. 1988;22(5):759–63.

244. Barsanti AC, Tartas N. Manejo del huésped inmunocomprometido neutropénico y febril Treatment of the immunocompromised neutropenic and febrile patient. Med B Aires. 1988 00PY - 1988;48(6):679–94.

245. Bellesso M. Febrile neutropenia studies in Brazil: treatment and cost management based on analyses of cases. Rev Bras Hematol Hemoter. 2013 00PY - 2013;35(1):3–4.

246. Buchanan GR. Management of the febrile patient with cancer and neutropenia. J Pediatr. 1992;120(4 Pt 1):669–70.

247. Chamberlain JD, Smibert E, Skeen J, Alvaro F. Prospective audit of treatment of paediatric febrile neutropenia in Australasia. J Paediatr Child Health. 2005;41(11):598–603.

248. Cohen KJ, Leamer K, Odom L, Greffe B, Stork L. Cessation of antibiotics regardless of ANC is safe in children with febrile neutropenia. A preliminary prospective trial. J Pediatr Hematol Oncol. 1995;17(4):325–30.

249. Cornely OA, Karthaus M, Wolf HH, Kampfe D, Jurgens H, Wilhelm M. New approaches in the treatment of febrile episodes in neutropenic cancer patients - Empirical stationary and ambulatory therapy of febrile neutropenia with ceftriaxone. [German] Neue Ansatze zur Behandlung febriler Episoden neutropenischer Krebspatienten - Empirische stationare und ambulante Therapie febriler Neutropenien mit Ceftriaxon. Antiinfective Drugs Chemother. 1997;15(2–3):116–9.

250. De Pauw BE, Raemaekers JM, Schattenberg T, Donnelly JP. Empirical and subsequent use of antibacterial agents in the febrile neutropenic patient. J Intern Med Suppl. 1997;740:69–77.

251. Dominic JF, Kumar L, Kochupillai V, Raina V, Sharma A, Bakhshi S, et al. A randomized, prospective open labelled study of oral amoxicillin-clavulanate and levofloxacin with intravenous ceftriaxone and amikacin in chemotherapy induced low risk febrile neutropenia. Indian J Med Paediatr Oncol. 2007;28(2):7–14.

252. Escalante CP, Weiser MA, Manzullo E, Benjamin R, Rivera E, Lam T, et al. Outcomes of treatment pathways in outpatient treatment of low risk febrile neutropenic cancer patients. Support Care Cancer. 2004;12(9):657–62.

253. Fink FM, Frischhut-Schiffer EM, Ausserer B, Allerberger F, Guggenbichler JP. Empirical antimicrobial treatment of septicemia and fever of unidentified origin in neutropenic pediatric patients following cytotoxic chemotherapy. [German] Empirische Antimikrobielle Therapie Von Sepsis- Und Fieberepisoden Bei Kindern Und Jugenlichen Mit Neutropenie Infolge Zytotoxischer Chemotherapie. Padiatr Padol. 1989;24(1):33–42.

254. Fleischhack G, Bode U, Kokert S, Bauch R, Mertens R, Kuhl J, et al. Therapy of infections in pediatric oncology. [German] Therapie von Infektionen in der padiatrischen Onkologie. Onkologe. 1997;3(SUPPL. 1):S44–8.

255. Freifeld A, Marchigiani D, Walsh T, Chanock S, Lewis L, Hiemenz J, et al. A double-blind comparison of empirical oral and intravenous antibiotic therapy for low-risk febrile patients with neutropenia during cancer chemotherapy. N Engl J Med. 1999;341(5):305–11.

256. Gala Peralta S. Febrile syndrome and neutropenia in oncological pediatric patients. Risk factors and ambulatory antibiotic treatment. [Spanish] Neutropenia y sindrome febril en

pacientes pediatricos oncologicos. Factores de riesgo y tratamiento antibiotico ambulatorio. Salud(i)Ciencia. 2006;14(4):214–6.

257. Gaya H. Empirical therapy in febrile granulocytopenic patients. Eur J Cancer Oxf. 1979;15 Suppl:51–8.

258. Girmenia C, Russo E, Carmosino I, Breccia M, Dragoni F, Latagliata R, et al. Early hospital discharge with oral antimicrobial therapy in patients with hematologic malignancies and low-risk febrile neutropenia. Ann Hematol. 2007;86(4):263–70.

259. Hodgson-Viden H, Grundy PE, Robinson JL. Early discontinuation of intravenous antimicrobial therapy in pediatric oncology patients with febrile neutropenia. BMC Pediatr. 2005;5(1):10.

260. Holdsworth MT, Duncan MH. Health care outcomes case study: Febrile neutropenia. Am J Health Syst Pharm. 1995;52(19 Suppl 4):S15-8.

261. Innes HE, Smith DB, O'Reilly SM, Clark PI, Kelly V, Marshall E. Oral antibiotics with early hospital discharge compared with in-patient intravenous antibiotics for low-risk febrile neutropenia in patients with cancer: a prospective randomised controlled single centre study. Br J Cancer. 2003;89(1):43–9.

262. Jaksic B, Martinelli G, Perez-Oteyza J, Hartman CS, Leonard LB, Tack KJ. Efficacy and safety of linezolid compared with vancomycin in a randomized, double-blind study of febrile neutropenic patients with cancer. Clin Infect Dis. 2006;42(5):597–607.

263. Jin J, Lee YM, Ding Y, Koh LP, Lim SE, Lim R, et al. Prospective audit of febrile neutropenia management at a tertiary university hospital in Singapore. Ann Acad Med Singapore. 2010;39(6):453–9.

264. Kaplan AH, Weber DJ, Davis L, Israel F, Wells RJ. Short courses of antibiotics in selected febrile neutropenic patients. Am J Med Sci. 1991;302(6):353–4.

265. Karthaus M, Egerer G, Kullmann KH, Ritter J, Jurgens H. Ceftriaxone in the outpatient treatment of cancer patients with fever and neutropenia. Eur J Clin Microbiol Infect Dis. 1998;17(7):501–4.

266. Karthaus M, Sudhoff T, Egerer G, Fenchel K, Kampfe D, Ritter J, et al. Interventional once-daily administration of ceftriaxone in leukemia and lymphoma patients with febrile neutropenia. Antibiot Chemother. 2000;50:26–36.

267. Katz JA, Mustafa MM. Management of fever in granulocytopenic children with cancer. Pediatr Infect Dis J. 1993;12(4):330–7.

268. Kern WV, Cometta A, De Bock R, Langenaeken J, Paesmans M, Gaya H. Oral versus intravenous empirical antimicrobial therapy for fever in patients with granulocytopenia who are receiving cancer chemotherapy. International Antimicrobial Therapy Cooperative Group of the European Organization for Research and Treatment of Cancer. N Engl J Med. 1999;341(5):312–8.

269. Kern WV, Marchetti O, Drgona L, Akan H, Aoun M, Akova M, et al. Oral antibiotics for fever in low-risk neutropenic patients with cancer: a double-blind, randomized, multicenter trial comparing single daily moxifloxacin with twice daily ciprofloxacin plus amoxicillin/clavulanic acid combination therapy--EORTC infectious diseases group trial XV. J Clin Oncol. 2013;31(9):1149–56.

270. Klastersky J, Debusscher L, Weerts-Ruhl D, Prevost JM. Carbenicillin, cefazolin, and amikacin as an empiric therapy for febrile granulocytopenic cancer patients. Cancer Treat Rep. 1977;61(8):1433–9.

271. Lee JA, Kang CI, Joung MK, Moon SY, Chung DR, Ko KS, et al. Efficacy of cefepime therapy for Enterobacter bacteraemia, with special emphasis on febrile neutropenic patients. Scand J Infect Dis. 2010;42(6–7):557–9.

272. Lehrnbecher T, Stanescu A, Kuhl J. Short courses of intravenous empirical antibiotic treatment in selected febrile neutropenic children with cancer. Infection. 2002;30(1):17–21.

273. Lopez Hernandez MA, Herrera Alvarez W, Sibaja Nieto L, Alvarez Vera JL. Low-risk febrile neutropenia in patients with lymphoblastic acute leukemia. Amikacin-ceftriaxone or oral fluoroquinolones. [Spanish] Neutropenia febril de bajo riesgo en pacientes con leucemia aguda linfoblastica. Amikacina-ceftriaxona o fluoroquinolonas orales. Med Interna Mex. 2010;26(3):219–25.

274. Martino P, Girmenia C, Raccah R, Micozzi A, Cimino G, Sgadari C, et al. Single daily dose ceftriaxone plus amikacin treatment of febrile episodes in neutropenic patients attending day hospital for hematologic malignancies. Oncology. 1992;49(1):49–52.

275. Maschmeyer G, Link H, Hiddemann W, Meyer P, Helmerking M, Eisenmann E, et al. [Empirical antimicrobial therapy in neutropenic patients. Results of a multicenter study by the Infections in Hematology Study Group of the Paul Ehrlich Society]. Med Klin. 1994;89(3):114–23.

276. Mullen CA, Buchanan GR. Early hospital discharge of children with cancer treated for fever and neutropenia: identification and management of the low-risk patient. J Clin Oncol. 1990;8(12):1998–2004.

277. Mullen C. Outpatient management of fever and neutropenia in children with cancer. Int J Pediatr Hematol. 1998;5(1):63.

278. Nenova IS, Goranov SE, Mateva NG, Ananoshtev NH. Treatment with fluorated quinolones of febrile neutropenia in patients with hematologic malignancies. Folia Medica Plovdiv. 2003;45(1):13–9.

279. O'Connell B, Marcus R, Broadbent V, Williams MV, Ludlam H. Can a single antibiotic policy for the empirical treatment of febrile neutropenic patients be used for all categories of haematology/oncology patient in the same institution? J Antimicrob Chemother. 1998;42(5):677–8.

280. Oppenheim BA, Anderson H. Management of febrile neutropenia in low risk cancer patients. Thorax. 2000;55 Suppl 1:S63-9.

281. Paganini H. Enfoque clínico y tratamiento de los niños con neutropenia y fiebre Clinical approach and treatment of children with neutropenia and fever. Arch Argent Pediatr. 2007 06PY - 2007;105(3):225–35.

282. Patrick CC, Shenep JL. Outpatient management of the febrile neutropenic child with cancer. Adv Pediatr Infect Dis. 1999;14:29–47.

283. Pennington JE. Fever, neutropenia and malignancy: a clinical syndrome in evolution. Cancer. 1977;39(3):1345–9.

284. Petrilli AS, Bianchi A, Melaragno R, De Camargo B, Kusano E, Da Silva Mendonca J, et al. Evaluation of two antibiotic schemes used in episodes of fever and granulocytopenia in children with cancer. [Spanish] Evaluacion De Dos Esquemas Antimicrobianos En Episodios De Fiebre Y Granulocitopenia En Ninos Con Cancer. Bol Med Hosp Infant Mex. 1989;46(12):761–6.

285. Pizzo PA, Robichaud KJ, Gill FA, Witebsky FG, Levine AS, Deisseroth AB, et al. Duration of empiric antibiotic therapy in granulocytopenic patients with cancer. Am J Med. 1979;67(2):194–200.

286. Pizzo PA, Robichaud KJ, Gill FA, Witebsky FG. Empiric antibiotic and antifungal therapy for cancer patients with prolonged fever and granulocytopenia. Am J Med. 1982;72(1):101–11.

287. Preis S, Gobel U, Jurgens H. Outpatient treatment with ceftriaxone alone or in combination with teicoplanin in febrile neutropenic children and adolescents with cancer. J Pediatr. 1997;130(3):500–1.

288. Rodriguez V, Burgess M, Bodey GP. Management of fever of unknown origin in patients with neoplasms and neutropenia. Cancer. 1973;32(4):1007–12.

289. Rubenstein EB, Rolston K, Benjamin RS, Loewy J, Escalante C, Manzullo E, et al. Outpatient treatment of febrile episodes in low-risk neutropenic patients with cancer. Cancer. 1993;71(11):3640–6.

290. Rubin M, Pizzo PA, Shenep JL, Hughes WT. Antibiotics for the treatment of febrile children with neutropenia and cancer. N Engl J Med. 1989;320(14):939.

291. Sahu S, Bapna A, Pai SK, Nair CN, Kurkure PA, Advani SH. Outpatient antimicrobial protocol for febrile neutropenia: a nonrandomized prospective trial using ceftriaxone, amikacin, and oral adjuvant agents. Pediatr Hematol Oncol. 1997;14(3):205–11.

292. Saini S, Rosoff PM. Are we finally ready for outpatient management of febrile neutropenia? Pediatr Blood Cancer. 2007;49(6):765–6.

293. Santolaya ME, Villarroel M, Avendano LF, Cofre J. Discontinuation of antimicrobial therapy for febrile, neutropenic children with cancer: a prospective study. Clin Infect Dis. 1997;25(1):92–7.

294. Santolaya ME. Febrile neutropenia in the child with cancer. Current concepts about risk assessment and selective management. [Spanish] Neutropenia febril en el nino con cancer. Conceptos actuales sobre criterios de riesgo y manejo selectivo. Rev Med Chil. 2001;129(12):1449–54.

295. Santos-Machado TM, De Aquino MZ, Almeida MTA, Bakhit S, Cristofani LM, Maluf PT, et al. Short-term intravenous antibiotic therapy and early discharge of febrile neutropenic patients. Int J Pediatr Hematol. 1999;6(1):33–8.

296. Talcott JA, Whalen A, Clark J, Rieker PP, Finberg R. Home antibiotic therapy for low-risk cancer patients with fever and neutropenia: a pilot study of 30 patients based on a validated prediction rule. J Clin Oncol. 1994;12(1):107–14.

297. Talcott JA, Yeap BY, Clark JA, Siegel RD, Loggers ET, Lu C, et al. Safety of early discharge for low-risk patients with febrile neutropenia: a multicenter randomized controlled trial. J Clin Oncol. 2011;29(30):3977–83.

298. Tomiak AT, Yau JC, Huan SD, Cripps MC, Goel R, Perrault DJ, et al. Duration of intravenous antibiotics for patients with neutropenic fever. Ann Oncol. 1994;5(5):441–5.

299. Tordecilla C J, Campbell B M, Joannon S P, Rodríguez R N. Alta precoz de niños con cáncer y neutropenia febril Early discharge of children with cancer and febrile neutropenia. Rev Chil Pediatr. 1994 10PY - 1994;65(5):260–3.

300. Villanueva M, August K. Low incidence of readmission and subsequent infections following discharge of febrile neutropenic patients despite persistent neutropenia. Pediatr Blood Cancer. 2013;60:S44.

301. Wacker P, Halperin DS, Wyss M, Humbert J. Early hospital discharge of children with fever and neutropenia: a prospective study. J Pediatr Hematol Oncol. 1997;19(3):208–11.

302. Willoughby ML. Early discharge in febrile neutropenia. Pediatr Hematol Oncol. 1994;11(6):571–3.

303. Wiwanitkit V. Article: Oral vs. intravenous empirical antimicrobial therapy in febrile neutropenic patients receiving childhood cancer chemotherapy. J Pediatr (Rio J). 2010;86(3):254; author reply 254.

304. Zubizarreta P, Paganini H. Assessment and treatment of low-risk febrile neutropenic (LRFN) pediatric patients with cancer. Med Pediatr Oncol. 2002;38(4):292.

305. Mustafa MM, Aquino VM, Pappo A, Tkaczewski I, Buchanan GR. A pilot study of outpatient management of febrile neutropenic children with cancer at low risk of bacteremia. J Pediatr. 1996;128(6):847–9.

306. Beguin Y, Benoit Y, Crokaert F, Selleslag D, Vandercam B. Outpatient and home parenteral antibiotic therapy (OHPAT) in low-risk febrile neutropenia: Consensus statement of a Belgian panel. Acta Clin Belg. 2002 Nov;57(6):309–16.

307. Bélanger G. Coordinating from hospital to home - special challenges for the pediatric patient requiring IV antibiotics. Canadian Intravenous Nurses Association 26th Annual Conference, November 14-16, 2001. CINA Off J Can Intraven Nurses Assoc. 2001;17:14–14.

308. Burke BL. Moving children with cancer from hospital to home. Can Nurse. 1999;95(2):25–8.

309. Carpenter JA. Shortening the short stay. AWHONN Lifelines. 1998;2(1):28–34.

310. Charles S, Prystowsky B. Early discharge, in the end: maternal abuse, child neglect, and physician harassment. Pediatrics. 1995 Oct;96(4 Pt 1):746–7.

311. Finkelstein NE. Family-centered group care. Child Welfare. 1980 Jan;59(1):33–41.

312. Flowers CR, Karten C. Communicating safe outpatient management of fever and neutropenia. J Oncol Pract Soc Clin Oncol. 2013 Jul;9(4):207–10.

313. Forsander G. Family attitudes to different management regimens in diabetes mellitus. Pract Diabetes Int. 1995;12(2):80–5.

314. Freifeld AG, Sepkowitz KA. No place like home? Outpatient management of patients with febrile neutropenia and low risk. J Clin Oncol. 2011 Oct 20;29(30):3952–4.

315. Gatford A. Time to go home: Putting together a package of care. Child Care Health Dev. 2004 May;30(3):243–6.

316. Graumlich JF, Novotny NL, Aldag JC. Brief scale measuring patient preparedness for hospital discharge to home: Psychometric properties. J Hosp Med. 2008 Nov;3(6):446–54.

317. Gunnell D, Coast J, Richards S. How great a burden does early discharge to hospital at home impose on carers? A randomized controlled trial. Age Ageing. 2000;29(2):137–42.

318. Jester R, Hicks C. Using cost-effectiveness analysis to compare Hospital at Home and in-patient interventions, part 1. J Clin Nurs. 2003;12(1):13–9.

319. Jester R, Hicks C. Using cost-effectiveness analysis to compare Hospital at Home and in-patient interventions, part 2. J Clin Nurs. 2003;12(1):20–7.

320. Jones SG. Negotiating time: The significance of timing in ending inpatient work. J Child Psychother. 2007 Dec;33(3):325–44.

321. Kibbler CC, Prentice HG. Which febrile neutropenic patients are suitable for outpatient management? Curr Opin Infect Dis. 1997;10(4):251–4.

322. King M. Paediatric home outreach. Vis 11749784. 1996;2(2):8–9.

323. Krupski C, Domm J. Is it time to consider early discharge for pediatric patients after hematopoietic stem cell transplant? Pediatr Transplant. 2014 Jun;18(4):325–6.

324. Lingaratnam S, Kirsa S, Slavin M, Worth L, Thursky K. Organisational readiness assessment across Western and Central Melbourne Integrated Cancer Services (WCMICS) hospitals in preparation for implementation of an ambulatory care program for management of low risk patients with febrile neutropenia. Asia Pac J Clin Oncol. 2010 Nov;6:196.

325. Luker K, Wilson K, Pateman B, Beaver K. The role of district nursing: Perspectives of cancer patients and their carers before and after hospital discharge. Eur J Cancer Care (Engl). 2003 Dec;12(4):308–16.

326. Margolan H, Fraser J, Lenton S. Parental experience of services when their child requires long-term ventilation. Implications for commissioning and providing services. Child Care Health Dev. 2004;30(3):257–64.

327. Menahem S, Roth D, Haramati S. Psychiatric collaboration in a paediatric department. Aust N Z J Psychiatry. 1997;31(2):214–8.

328. Mendler VM, Scallen DJ, Kovtun LA, Balesky J, Lewis C. The conception, birth, and infancy of an early discharge program. MCN Am J Matern Child Nurs. 1996;21(5):241–6.

329. Meropol NJ, Fox KR, Vaughn DJ, Zeiber N. A pilot study of early hospital discharge in adult patients with fever and neutropenia. Eur J Cancer. 1994;30A(10):1595–6.

330. Mikkelsen TH, Sondergaard J, Jensen AB, Olesen F. Cancer rehabilitation: Psychosocial rehabilitation needs after discharge from hospital? A qualitative interview study. Scand J Prim Health Care. 2008;26(4):216–21.

331. Moxley VM. The pre- and post-hospital experiences of rural Midwest adolescent mental patients. Diss Abstr Int. 1977 Dec;38(6–B):2613.

332. Orme L, Babl F, Barnes C, Barnett P, Donath S, Ashley D. Quality of life: A randomized trial of outpatient versus inpatient iv antibiotics for paediatric oncology patients with low risk febrile neutropaenia. Pediatr Blood Cancer. 2010;55 (5):823–4.

333. Ouvrier MJ, Thery JC, Blot E. Outpatient oral antibiotics for febrile neutropenic cancer patients. J Clin Oncol. 2006 Dec 10;24(35):5614; author reply 5614-5.

334. Paulson PR. Nursing considerations for discharging children home on low-flow oxygen. Issues Compr Pediatr Nurs. 1987 Jul;10(4):209–14.

335. Pinto JP, Ribeiro CA, Pettengill MAM. The recovery process of children after discharge from hospital: an integrative review. Acta Paul Enferm. 2010;23(6):837–42.

336. Richards S, Coast J, Gunnell D. Randomised controlled trial comparing effectiveness and acceptability of an early discharge, hospital at home scheme with acute hospital care. BMJ Clin Res Ed. 1998;316(7147):1796–801.

337. Rolston KVI, Rubenstein EB, Freifeld A. Early empiric antibiotic therapy for febrile neutropenia patients at low risk. Infect Dis Clin North Am. 1996;10(2):223–37.

338. Rubenstein EB, Rolston KV. Outpatient treatment of febrile neutropenic patients with cancer. Eur J Cancer. 1995;31A(1):2–4.

339. Silva IC, High KP. Outpatient treatment for febrile neutropenic patients. Infect Dis Clin Pract. 1998 Sep;7(7):307–11.

340. Slavin MA, Thursky KA. Outpatient therapy for fever and neutropenia is safe but implementation is the key. J Clin Oncol. 2013 Mar 20;31(9):1128–9.

341. Svahn BM, Bjurman B, Myrback KE, Aschan J, Ringden O. Is it safe to treat allogeneic stem cell transplanted recipients at home during the pancytopenic phase? A pilot trial. Presse Med. 2004;33(7):474–8.

342. Tice AD. Outpatient parenteral antibiotic therapy for fever and neutropenia. Infect Dis Clin North Am. 1998 Dec;12(4):963–77, viii.

343. Turley KM, Higgins SS. When parents participate in critical pathway management following pediatric cardiovascular surgery. MCN Am J Matern Child Nurs. 1996 Sep;21(5):229–34.

344. Uzark K, LeRoy S, Callow L, Cameron J, Rosenthal A. The pediatric nurse practitioner as case manager in the delivery of services to children with heart disease. J Pediatr Health Care. 1994 Mar;8(2):74–8.

345. Uzun O, Anaissie EJ. Outpatient therapy for febrile neutropenia: who, when, and how? J Antimicrob Chemother. 1999 Mar;43(3):317–20.

346. Youngblut JM, Brennan PF, Swegart LA. Families with medically fragile children: an exploratory study. Pediatr Nurs. 1994;20(5):463–8.