AN INVESTIGATION INTO THE EXPERIENCES, AND ASSOCIATED ISSUES, CONCERNING CHILDREN AND YOUNG PEOPLE PRESCRIBED REGULAR MEDICATION

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Thesis summary

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There is little information concerning the treatment-related experiences when children or young people are prescribed long-term medication. To identify treatment-related problems following the initiation of a new medication, a telephone survey of parents or children/young people was undertaken. Participants were asked about information requirements, medication-related concerns, administration, adverse effects, adherence and their experiences of arranging medication supply.

The role of community pharmacists in supporting children taking medication was explored through a postal survey. Pharmacists were asked about their experiences of undertaking medication review in this group and the types of medication-related support this cohort sought from them. These included: advice about adherence, requests for information and the type of problems reported to them including administration and supply issues.

The treatment-related experiences of children, young people and their parents/carers when a child takes regular medication were identified through interviews with patients and their parents/carers. Participants were asked to describe their experiences of: the impact of medication on their daily lives, the formulation, adverse effects, negotiating the healthcare system around supply of medication and the social burden of medication.

The first three studies identified that some parents made changes to their child's medication without informing a healthcare professional. Therefore, a postal survey of parents/carers of children prescribed long-term medication was undertaken. Parents/carers were asked about delaying/with-holding/not initiating treatment, making changes to the administration, altering the dose and adjustments to the regimen to make it compatible with daily life.

This research has identified that parents/carers and patients experience many challenges when a child is prescribed long-term medication. Greater engagement is required to ensure that the treatment choice and regimen are achievable for patients and their parents/carers. Further research is required to identify effective interventions to support this cohort, one of which could be a paediatric medication review.

Key words

Paediatrics; Medication Therapy Management; Drug Therapy; Self-Management

Dedication

I wish to thank my wife, Fiona, and my children, Harry and George, for being patient and supportive throughout my studies.

I also wish to thank my supervisor, Dr David Terry, and co-supervisor Regius Professor Keith Wilson, for their support, advice and very helpful comments on my individual study write-ups, publications and final thesis.

Contents

Abbreviations

ADHA	Attention Deficit Hyperactivity Disorder
BCH	Birmingham Children's Hospital
ePACT	Electronic Prescribing Analysis and Costing
GP	General Practitioner
HBM	Health Belief Model
ICS	Integrated Care Systems
MUR	Medicines Use Review
NHS	National Health Service
NHSBSA	National Health Service Business Services Authority
NICE	National Institute for Health and Care Excellence
NMS	New Medicines Service
NPPG	Neonatal and Paediatric Pharmacists Group
PedsQL	Paediatric Quality of Life
PI	Principal Investigator
PIL	Participant Information Leaflet
RCPCH	Royal College of Paediatrics and Child Health
RPS	Royal Pharmaceutical Society
SPSS	Statistical Package for the Social Sciences
STP	Sustainability and Transformations Partnership
TPB	Theory of Planned Behaviour

Tables and Figures

1.0 Introduction and background

Globally, the total amount of medication consumed will increase by about 3% by 2021 with medication spend approaching $1.5 trillion.[1] The most comprehensive snapshot of spending on National Health Service (NHS) medication shows that the cost, based on list prices, rose from £13 billion in 2010/11 to £17.4 billion in 2016/17.[2] The cost of medication waste in the NHS has been estimated to be £300 million per annum.[3] Therefore, initiatives that have been described to reduce waste[3] will be of increasing importance.

Medications play a crucial role in maintaining health, preventing illness, managing chronic conditions and curing disease.[4] Indeed, the prescription of a medication is the most common therapeutic intervention in healthcare.[5] However, medication use is considered to be sub-optimal and the Royal Pharmaceutical Society (RPS) has developed a patient focussed multidisciplinary 'medicines optimisation' guide.[4] The goal is to help patients improve their outcomes, take their medication correctly, avoid taking unnecessary medication, reduce wastage of medication and improve medication safety.[4] Making medicines optimisation part of routine practice requires healthcare professionals to routinely discuss with each other, patients and their carers how to get the best outcomes from medication throughout the patient's care.[4] The National Institute for Health and Care Excellence (NICE) has published guidance on 'medicines optimisation' including a range of recommendations.[5] One of these, 'medication review', is designed as a 'structured critical examination of a person's medicines with the objective of reaching an agreement with the person about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste'.[5] It is not known if medication review is effective at reducing sub-optimal use of medication in children.[5]

A number of factors may affect how parents, children and young people administer/take medication. These include their beliefs about medication, factors affecting adherence and the burden that taking medication places on everyday life. It is currently unclear how medication review may support this parent/patient cohort. In particular, whether parents and their children have different experiences when a child takes medication compared with an adult and hence requiring a medication review with a different scope to those currently available.

1.1 Health behaviour

There are a number of variables that are related to the performance of health behaviours that can be summarised in to six distinct factors[6]:

1. Accessibility of healthcare services
2. Attitudes to health (beliefs about quality and benefits of treatment)
3. Perceptions of disease threat
4. Knowledge about disease
5. Social network characteristics
6. Demographic factors

With the exception of demographics these represent cognitive factors that are central to a number of models of the determinants of health behaviours. There are a number of commonly used social cognition models that determine and predict behaviour.[6] These include the Health Belief Model (HBM) and the Theory of Planned Behaviour (TPB). The HBM uses two aspects of an individual's representations of health behaviour in response to the threat of illness and evaluation of behaviours to counteract that threat to predict behaviour. In particular, the likelihood of experiencing a health problem, the severity of the consequences of that problem, and the perceived benefits of a preventative behaviour, in combination with costs, has been shown to shape health-related behaviour.[6] The TPB proposes that determinants of behaviour are the intention to engage in that behaviour and perceptions of control over that behaviour. The intention to engage in a behaviour are a function of one's evaluation of personally engaging in that behaviour, one's perception of whether significant others think one should or should not perform the behaviour and the perceptions of one's control over performance of the behaviour.[6] In general individuals are more likely to engage in positively valued behaviours that are believed to be achievable.[6] Social cognitive factors can predict health behaviour and are observed in studies determining adherence to medication.

Adherence to medication has been shown to be correlated with patients' beliefs of concerns and necessity of treatment.[7] In a study of 324 adult patients across four illness groups (asthma, renal, cardiac and oncology) the relationship between beliefs about medication and reported adherence were investigated.[7] Where patients' rated the necessity of their medication higher than their concerns their reported adherence was greater. The converse was found for those patients rating their concerns higher than their perception of necessity

for treatment. The study also found that some illnesses and associated treatments showed different adherence rates than others.

Medication adherence may also be influenced by patients' beliefs about medication in general. Horne *et al* compared 524 adult patients' commonly held general medication beliefs with their beliefs about their own treatment.[8] They demonstrated that patients' general beliefs about the necessity of their medication, concerns about treatment and perceived over use of medication reflected what patients believed about their own treatment. For example, there was a positive correlation between those patients who perceived that medication was overused in general and their perceived need for their own medication. Patients should be asked about their prior beliefs and understanding about medication before new treatments are prescribed and when current medication is reviewed.[9]

Goodfellow *et al* undertook a multi-method study in 100 children with cystic fibrosis and their parents.[10] They assessed adherence to enzyme supplements, vitamins and chest physiotherapy. Parental beliefs about the necessity of treatment were shown to be predictive of their child's adherence to enzyme supplements and chest physiotherapy. Children whose parents had reported high necessity beliefs regarding their child's use of enzyme supplements or chest physiotherapy were significantly more likely to be classed as high adherers to these treatments. Significant differences were also found between parent and child beliefs about the necessity of treatment.

In a cross-sectional survey of 597 parents of children with asthma, 14% reported being fully adherent with their child's asthma preventer asthma medication.[11] Parents showing a greater degree of necessity, compared with concern, for their child's medication had higher adherence scores. Greater use of alternative therapies was associated with higher concern scores. Non-ethnic minority parents were more likely to consider that their child's medication was necessary and were less likely to be concerned about treatment compared with ethnic minority parents.

A further study of 43 caregivers of children aged 2 to 5 years demonstrated that increased caregiver negative health beliefs, but not parental stress, were associated with poorer inhaled corticosteroid adherence.[12] These included beliefs about their ability to administer their child's medication, effectiveness of treatment as well as misconceptions, for example believing that their child will still have asthma symptoms even on medication.

A number of factors affecting adolescent patients' adherence to antiepileptic medication were identified through semi-structured interviews with 94 patients and/or parents.[13] Factors affecting adherence included age of the patient's mother, size of immediate family, number of medications, stability of parents' marriage, family support, seizure frequency and relationship with healthcare providers. Good adherence was associated with positive health beliefs about the necessity of treatment whereas concerns were associated with poorer adherence. Although another study of caregivers of 112 aged 2 to 14 years did not show a statistically significant correlation between beliefs about treatment necessity or concerns with medication adherence.[14]

In a follow-up study of 33 children diagnosed with attention deficit hyperactivity disorder (ADHD), and their parents, at 3 monthly intervals a number of recommendations to support adherence were identified based upon child and parental attitudes towards psychostimulant medication.[15] It was proposed that clinicians wishing to improve adherence could do so by increasing parental perceived benefits of the medication as soon as possible after initiation of treatment.

Within the field of paediatrics, it is not only the patient that may influence medication taking. A more complex partnership exists with caregiver-medical team, child-medical team and caregiver-child relationships.[16] Some parallels may be drawn from when a companion attends a consultation with an adult patient creating a triadic encounter.[17] In the context of chronic pain a systematic review identified both positive, by improving patient outcome, and negative encounters, through limiting the exchange of information.[17] In paediatrics these triadic relationships and encounters will change over time as a child develops through age and hence are more dynamic.[16] In addition to parental anxiety, child misconceptions about medications can also impact on whether they receive/take their prescribed treatment.[18] Whilst this programme of research focusses on paediatrics parallels may be drawn with carers of adult patients for example carers of elderly patients with dementia.

1.2 Adherence to prescribed medication

There are 2 overlapping categories of non-adherence to medication – unintentional and intentional.[9] Unintentional non-adherence occurs when a patient wishes to follow the agreed treatment regimen but is prevented from doing so by barriers beyond their control.[9] Examples include poor recall or difficulties understanding the instructions, problems using the treatment, inability to pay or forgetfulness.[9] Intentional non-adherence refers to when a patient decides not to follow the treatment recommendations.[9] This decision is influenced by

a person's beliefs and preferences that impact on their motivation to start and continue with treatment.[9]

People prescribed self-administered medication typically take about half their doses and efforts to assist patients with adherence might improve the benefits of prescribed medication.[19] Barber *et al*, in a study of 258 adult patients newly started on chronic medication, found that they quickly became non-adherent.[20] After 10 days 30% of patients were non-adherent and 25% of those remaining on their medication at 4 weeks were non-adherent.[20] The proportion of intended vs non-intended adherence was similar at 10 days (45% vs 55%) and 4 weeks (44% vs 56%).[20] A number of medication-related problems and information needs were identified including side effects, concerns about taking a new medication, difficulty in swallowing the medication and remembering the regimen.

A recent systematic review of treatment non-adherence in paediatric long-term conditions identified 6 main themes from 19 qualitative papers.[21] These were: beliefs about long-term conditions and treatments, difficulty of the treatment regimen, child resistance, relationships within families, preserving normal life and input from healthcare professionals. The most commonly reported theme was carers' beliefs which impacted on their decisions relating to adherence. Carer beliefs included concerns and fears about the condition being treated, perceived effectiveness of treatment and risk of side effects. The review also identified that caregivers were adapting medication regimes to 'normal life', the challenges of dealing with child resistance to taking medication and the balance between a child's independence to manage their own condition and caregivers wishing to ensure treatment adherence. Family relationships were shown to be strained through a child's repetitive resistance to treatment, handing over responsibility for medication to older children and the child having a different view of the treatment/condition than the caregiver. The reported input from healthcare professionals was generally positive with caregivers seeking support where they experienced problems with medication. However, caregivers' views were not always in agreement with those of the healthcare professional.

A further systematic review of barriers to medication adherence among chronically ill adolescents identified the following key themes: relationship with peers, parents and health professionals, the strive for normality, treatment perceptions and worries, forgetfulness, medication complexity and financial costs.[22] Conflicts between adolescents and parents was a major reason for non-adherence and focussed around parent's difficulty in delegating treatment responsibility and lack of parental support.

A study of 132 children, aged 2 to 6 years, prescribed an inhaled corticosteroid using a Smartinhaler™ measured adherence to treatment electronically and explored parental experiences of non-adherence during follow-up clinics.[23] Adherence to prescribed medication ranged from 1% to 99%. Median adherence reduced over time from 68.5% at three months to 50.4% at 12 months. Frequently cited reasons by parents for non-adherence were: forgetfulness, child refused and being too busy. Other reasons included their own 'therapeutic trial' off medication to determine if it was still required, parental separation with the other caregiver not administering medication and missing evening doses when the child falls asleep prior to the medication being administered.

Disease-specific family-reported barriers to medication adherence in 74 adolescents aged 13 to 17 years with inflammatory bowel disease were identified using a semi-structured interview and the Medical Adherence Measure.[24] The most commonly reported barriers to medication adherence included forgetting (87.8%), being away from home (47.3%), refusal (17.6%), lack of supply (16.2%), feeling unwell (16.2%) and a belief that the medication was not necessary (14.9%). Neither demographic or disease severity scores were related to the number of reported barriers to adherence. Better adherence was reported by adolescents and families where there were fewer reported barriers.

Failure to keep clinic appointments was identified as a factor associated with treatment non-adherence in 147 children diagnosed with epilepsy.[25] Parents cited wrongly registered appointments, forgetfulness and being too busy to attend as reasons for missing appointments. Reduced adherence to medication was also associated with the use of alternative medicine, a perception that their child was not susceptible, dissatisfaction with the provided health service and side effects from treatment.

A systematic review of medication adherence in paediatric and adult patients with ADHD identified the reasons behind patient and parent/carers' decisions to discontinue treatment.[26] The top 3 reasons were adverse effects, ineffective/suboptimal response and parent/carer decision. Other reasons included dosing inconvenience, patient attitude, social stigma and patient-physician communication.

In semi-structured interviews with parents of 24 children with ADHD a number of reasons for non-adherence were recorded.[27] These included side effects, lack of effectiveness, long waiting times/procedural delays in hospital, fear of addiction to medication, problems accessing medication, the perceived careless attitude of healthcare professionals and high cost of medication. In some cases, other family members opposed the use of the medication.

Cormier undertook a series of interviews, using a grounded theory approach, with 13 mothers and 3 fathers of 16 children diagnosed with ADHD.[28] Parents were found to move through several stages with regard to initiating and maintaining adherence to medication in their child. These were: resisting the initiation of medication, challenges in finding the right kind of help, making the decision to try medication, enjoying the benefits that medication brought to their child, managing the problems created by medication such as adverse effects and finally accepting that their child's ADHD required treatment with medication.

Simons and Blount have developed scales for measuring parent and patient/adolescent medication barrier scales through qualitative interviews with 78 patients and their parents.[29] These scales can support the identification of the most problematic areas that are interfering with adherence. Sixteen items were identified in the parental barriers scale and included 'my child feels that it gets in the way of his/her activities', 'my child has too many pills to take' and 'I am not always there to remind my child to take his/her medication'.

1.3 The burden associated with taking chronic medication

The burden that taking medication places on the lives of patients and their families will also contribute to their ability to gain the most out of their prescribed treatment. A recent systematic review examined the burden that taking medication places on adult patients' day-to-day lives.[30] A number of themes were identified. Patients experienced burden around the routine of taking medicines including administration, monitoring and travelling with medicines. Some patients were reliant on family members and others adjusted the medicine taking schedule to maintain their daily lives. The characteristics of the medication itself including size, number of medicines taken each day, packaging and changes in brand also added to the burden of taking medicines. Adverse effects provided an additional anxiety requiring coping strategies and the need to balance the adverse effect against the benefits of treatment. Patients also described their experiences of negotiating the healthcare system – travel/waiting time, the provision of information and the failure of the healthcare system to identify the patient as a partner in their own healthcare. Taking medicines was also shown to impact socially with an effect on social life, ability to visit friends, take holidays and the fear of social stigma.

Sav *et al* undertook semi-structured interviews with 97 people with chronic illness and their carers to identify the burden that treating a chronic illness has on their lives.[31] Participants described the burden associated with using medicines. These included adverse effects,

polypharmacy, the inconvenience of organising their medicines (supply and administration), the stigma associated with taking medicine and the confusion relating to brand changes.

A focus group study of 9 adolescents, and 14 parents of children, with asthma explored their experiences of living with asthma.[32] A number of medication related themes emerged in this study including the stigma that children/young people may feel about having a chronic illness and thus using their inhaled medicine out of sight of their peers. Issues with using medicines in schools was raised, with staff knowledge and remembering to administer the medicine being problematic. Some adolescents described the input their friends had in reminding them to take their medicine. Anxiety existed among parents about their level of knowledge and inhaler technique.

A survey of 34 patients with cystic fibrosis identified the impact on social life, not having enough time and a perception that the medicine is not required reduced treatment adherence.[33] Non-compliant patients tended to be adolescents and possibly had competing challenges and problems at that stage of their lives, including the desire to hide their illness. Similarly changes in attitude towards medicine with age is observed in young people with attention deficit hyperactivity disorder. Some adolescents may willingly use medication as they can perceive the benefits whereas others are more concerned about feeling ostracised socially and fear that there is a stigma associated with the use of medication.[34]

The quality of life of 36 adolescents with inflammatory bowel disease taking 6-mercaptopurine/azathioprine and 6-aminosalicylic acid was assessed using the PedsQL (Paediatric Quality of Life) 4.0 measure.[35] Disease severity was similar across the sample and rated as mild to moderate or better. The study found that those patients taking a more complex medication regimen (number of different medications and doses per day) may be related to a poorer quality of life. A contributing factor for those taking a more complex regimen could be the need to use a medication in front of peers hence impacting on the social aspect of their quality of life.

Interviews with 3 sets of parents of children on continuous insulin infusions found that they had to accept a new way of life.[36] They described giving up a social life, the need to plan activities such as swimming in advance and the reliance on others such as grandparents.

A survey of patients aged 14 to 25 years (n = 146) with cystic fibrosis and their parents (n = 269) to explore the barriers to treatment adherence found a positive correlation between treatment burden and adherence.[37] Common reasons cited were: difficulty finding time to

take medicines, forgetting, preference to be with friends rather than take medicines, too tired to take medicine and not willing to take medicines in public. A high level of polypharmacy was considered to be problematic. Health professionals need to not only consider the optimal medicines required for treatment but also have insight in to living with the disease. Adolescents facing adherence barriers had more quarrels with their parents and subsequently these families were less likely to support one another increasing non-adherence.

Medication taken post organ transplant impact upon the lives of patients and their families.[38] [39] Interviews of 42 paediatric liver transplant patients and their parents identified the inconvenience and frustration of taking medicines every day.[38] The adverse effects associated with treatment impacted on the patients' sense of comfort and view of self, leading to problematic behaviours such as excessive dieting. A mixed-methods study of 10 parents of liver/kidney transplant patients found that the lack of flexibility around the immunosuppressant medicines, and the lack of trust in others to administer them, were barriers to adhering to the regimen.[39]

A systematic review of self-reported barriers to medicine adherence in chronically ill adolescents found a number of barriers relating to the impact of a medication on a patient's daily life.[22] Living with a chronic condition encompasses many behaviours that the patient has to add to daily routines including taking medication.[22] The effect of medicines on patients' lives, and hence adherence, included the desire to achieve normality, for example: not carrying medicines with them, the restrictions that taking medicines placed on their lives leading to patient-led changes to the regimen, interruptions to sleep and the hassle of visiting the school nurse for a medicine.

Many children with chronic conditions, such as asthma and diabetes, will be required to take medication at school.[40] A survey and semi-structured interviews of 157 parents/children with diabetes, attention deficit hyperactivity disorder or asthma were undertaken to find out their experiences of medication use in schools.[40] Children experienced embarrassment or anger and being teased about taking medicines in front of other students. Medicine taking also impacted on the development of friendships. In another study, a series of face-to-face interviews with 69 young people, and their parents, determined how they managed asthma or diabetes at school.[41] They found that: patients were not always able to have their medication with them, the area of administration may not be private, patients had to rely on their friends for assistance with medicine taking, teachers had inadequate understanding of their condition, and that patients had to use their medication during sporting activities in front

of their peers. A number of ways to accommodate medicine taking at school were developed by patients and their parents.

A study of young people with juvenile arthritis analysed blog entries, survey results and case notes to investigate the relationship between identity and medication use.[42] An analysis of the blogs that 21 young people and 6 parents posted found that young people received help from their mothers with many aspects of medication use including obtaining further supplies, setting routines and administering medication. In 1 case a young person had a different opinion from their parents regarding changing their medication. The survey results showed that 4 out of 10 young people had insufficient information on their medication and 7 out of 10 reported that they had problems with their medication including adverse effects, used up their supplies or kept forgetting to take their medication. The case note review identified the issues that young people had when transitioning to adult care including the need for further support to order and collect prescriptions.

The challenges associated with prescribing for children at the interfaces of care have been described.[43] In particular, the difficulties obtaining unlicensed medicines from community pharmacies, the transfer of medication related information and the decision about who retains prescribing responsibility.[43] These issues will undoubtedly contribute to the experiences of some patients and/or their caregivers when starting a new medication.

Treatment burden can lead to poor adherence, wasted resources and poor outcomes.[44] The decision to prescribe minimally disruptive medicine that seeks to tailor treatment regimens to the realities of the daily lives of patients could greatly improve the care and quality of life of patients.[44]

1.4 Medication review

In the England two funded medication review services are available through community pharmacy to support patients taking medicines. The New Medicines Service (NMS) and the Medication Use Review (MUR).

The NMS was set up in 2011 to help improve medicines adherence.[45] The service specifically targets medicines for asthma/chronic obstructive pulmonary disease, type II diabetes, antiplatelet/anticoagulant therapy and hypertension.[46] Whilst the NMS may be provided to a child, the child must be competent to consent to the service.[47] In addition the service is not accessible to carers.[47] A recent evaluation of the effectiveness of the NMS

concluded that it can improve adherence by 10% and increase the number of medicines problems identified and resolved compared with a control group.[48]

The MUR service is designed to help patients manage their medicines more effectively.[49] The scheme particularly attempts to improve patients understanding of their medicines, identify any problems that they may be having and reduce waste.[49] The national target groups are: patients taking high risk medicines, patients discharged from hospital with changes to their medication and patients with respiratory or cardiovascular disease.[50] A child may access this service if they are competent and hence can consent.[49] An MUR cannot be conducted with the parent or carer of a child.[49]

The National Service Framework for Children includes recommendations for supporting children taking medicines.[51] This includes the need for children and parents to receive clear and understandable information about medicines, the provision of greater support for children taking medicines at home and equitable access to medicines.[51]

The objectives and rationale of medication review could be expected to apply to chronic diseases in children.[52] Issues such as polypharmacy, wastage, repeat prescriptions and medication problems are likely to be similar.[52] The benefits of medication review seen in adults may also occur in children and medication review may possibly have a role in the management of medication in children.[52]

Recent guidance from the NICE recommends further research concerning medication review in children.[5] The outcomes should include suboptimal prescribing, medication-related patient safety incidents, patient reported outcomes, quality of life, clinical outcomes, medication-related problems and health and social care resource use.[5]

1.5 Programme of research

This portfolio of evidence builds upon the work previously published in adults, broadens that which has been undertaken in children and supports the Government strategy for paediatrics. The broad theme is medication optimisation in paediatric patients with the research undertaken through four linked projects.

The experiences of children/young people and their parents/carers when a child starts a new medication were not known. Therefore, it was also unknown whether any potential adverse

experiences would fall within the purview of a formal medication review for example the NMS. Hence project one was developed.

As a child/young person or their carer may not be able to access the NMS or MUR services in community pharmacy, they may not receive the same level of support as an adult when taking long-term medication. It was not known if community pharmacists were undertaking formal medication review in this cohort or if children/young people presented to community pharmacists with medication-related issues that might fall within the criteria of current medication review services. Hence, the second project was developed to explore these questions.

Study one investigated the experiences of children and their parents/carers during the first few weeks after starting a new medication. Due to the limited data in the published literature and the experiences of medication burden in adults, project three was developed to explore the burden that taking long-term medication places on children and their families. This would further identify areas where additional support was required for patients and their parents allowing for the optimal choice and use of medication to fit around their daily lives.

A common theme which was identified in each of the first three studies was that parents made changes to their child's medication regimen without informing the prescriber. Thus, the final study focussed on intended non-adherence to prescribed medication by parents/carers. This provided an opportunity to further identify where medication use can be optimised in this patient cohort.

The titles of the studies presented in this thesis are as follows:

1. A Telephone Survey to Determine the Experiences of Children and their Parents/Carers, Following the Initiation of a New Medication

2. Children/Young People Taking Long-Term Medicines: A Survey of Community Pharmacists' Experiences in England

3. A Qualitative Study to Explore Treatment-Related Experiences When Children and Young People take Regular Prescribed Medication

4. A Postal Survey of Parent/Carers to Investigate Intended Non-Adherence to their Child's Medication Regimen

2.0 Methods

Health service research methods are commonly distinguished as being either qualitative or quantitative.[53] Both approaches, in addition to a combination of these methods, were considered when developing the methods for this programme of research.

2.1 Qualitative research

Qualitative research methods explore processes and patterns in peoples' thoughts and behaviour.[53] They are a useful way of identifying meanings that people attach to events and to establish their priorities and concerns. With qualitative methods it is possible to investigate self-perception from the subject's perspective rather than to study perceptions from the point of view of the researcher's own beliefs or to attempt to apply models developed by others.

The most commonly employed qualitative approach used in health services and pharmacy practice research is the qualitative interview using either an unstructured or semi-structured design.[53] Other methods include focus groups and observational studies. A major advantage of the interview is its adaptability.[54] A skilful interviewer can follow up ideas, probe responses and investigate motives and feelings, which the questionnaire cannot do. Another advantage of using interviews is that of improved response rate.[55] A postal questionnaire may easily produce a response rate below 40%. Other advantages of the interview include the ability to offer standardised explanations to certain problems that arise, prevent any misunderstandings and maintain control over the order or sequence in which the questions are answered.[55]

However, interviews, their associated transcriptions and analysis are time consuming and due to the highly subjective technique there is always the danger of bias.[54] Qualitative research enables hypothesis generation and theory building but is not designed to test the extent to which the identified characteristics apply to a large population.[53] A quantitative study is required to enable generalisations to be made to a wider population.[53]

2.2 Quantitative research

Quantitative research deals with quantities and relationships between attributes; it involves the collection and analysis of highly structured data.[56] Social survey methods are the most commonly used approach by pharmacy practice researchers.[53] Surveys are usually carried

out to describe populations, to study associations between variables and to establish trends.[56]

A common method of data collection is the postal survey. Oppenheim has described the main advantages and disadvantages of postal surveys.[55] The advantages include: a relatively low cost of data collection, low cost of processing, avoidance of interviewer bias and the ability to reach respondents who reside at widely dispersed addresses. The disadvantages include low response rates and consequent biases, no opportunities to correct misunderstandings or to probe, offer explanation or help and no control over the order in which questions are answered or incomplete questionnaires. It is also important that the survey design has undergone appropriate validity testing to ensure integrity of the data collected. The validity of a research instrument refers to the extent to which it actually measures what it is designed to measure.[53] Validity includes face validity (to uncover obvious problems with the questions), criterion validity (correlation with other measures of the same variable), construct validity (that instrument is measuring the underlying concept it purports to measure) content validity (the extent to which the instrument covers the relevant issues).[53 56]

2.3 Triangulation

Research methods may also be combined within a study. The combining of different processes is known as triangulation.[53] In health services research, triangulation is employed to provide different perspectives of phenomena, to obtain data on a range of issues in relation to a research question and to assess and demonstrate the validity of research findings.

2.4 Current programme of research

Qualitative, quantitative or a combination of research methods were considered for each project.

Project One included two interviews. The first, a face-to-face structured interview, was designed to determine what medication-related information study participants' could recall from their out-patient appointment. This was delivered by the out-patient pharmacist enabling further interpretation of the questions as required. A structured interview method was utilised as it required an accurate account of participants' recollection about specific aspects of their medication, for example, were they informed about the dose regimen, side effects and how

long to take the medication for? Participants then received telephone follow-up six weeks later by the study principal investigator to determine what experiences they had had of their new medication. A semi-structured interview was undertaken with each participant. A more qualitative approach was undertaken for this part of the study as it was intended to explore participants' personal experiences of starting a new medication. This approach allowed the researcher to probe further in to the responses given including the rationale behind any decisions made by the participants relating to their new medication. A purely quantitative approach would not have afforded this opportunity.

Project Two employed a postal self-completed questionnaire. This project required the views of a large number of community pharmacists to determine current practice relating to undertaking medication review in children or their parents/carers. In addition, a further aim of the study was to identify the types of medication-related issues that present to community pharmacists from this cohort. A purely qualitative technique would have investigated a smaller number of participants thus reducing the ability to determine of the extent of current practice. It would have provided a greater depth of information from a smaller number of participants. However, the ability to generalise the results was considered important to reflect current practice hence a quantitative approach was used.

The third study was designed to explore the burden that taking medication places on patients and their families. An in-depth view and the opportunity to further explore participants experiences was required to determine how peoples' lives were affected with having a child taking long-term multiple prescribed medication. A quantitative study would not enable this in-depth view from the participant perspective. Hence a qualitative technique was undertaken with semi-structured interviews of parents and children.

Project Four was developed following findings from the first three studies which identified that parents were making changes to their child's medication without informing a healthcare professional. These studies did not identify the extent to which this finding was happening thus study four was developed. A quantitative approach, using a self-completed postal questionnaire, was selected as a qualitative technique would not cover a sufficient number of participants to provide an idea of frequency of occurrence.

Across studies 1, 3 and 4 participants were all patients or parents of patients currently under the care of Birmingham Children's Hospital. The trust has a transition age of between 16 and 18 years. All patients were eligible for inclusion in the studies in accordance with the study inclusion criteria.

3.0 Study 1 - A telephone survey to determine the experiences of children and their parents/carers, following the initiation of a new medication

3.1 Aim

The aim of this study was to determine the medication-related issues that were experienced during the first few weeks of treatment by patients, and their parents/carers, when a child/young person has been prescribed a new medication.

3.2 Research ethics committee approval

The Yorkshire and the Humber –Sheffield National Research Ethics Service committee reviewed and approved this study 23rd September 2014 (REC reference 14/YH/1086, IRAS project ID 148123).

3.3 Method

3.3.1 Setting

The study was undertaken at Birmingham Children's Hospital, part of the Birmingham Women's and Children's NHS Trust, which is a specialist UK paediatric hospital hosting 34 specialties, with 361 in-patient beds and over 174,000 out-patient visits per year.

3.3.2 Participant recruitment

Potential participants were identified through presentation of a prescription to the outpatient pharmacy which met the study inclusion criteria. The outpatient pharmacy processes on average 284 prescriptions each day. Potential participants were provided with age-related participant information leaflets (Appendices I to IV) to read prior to consent being taken. Consent and recruitment were undertaken by one of four pharmacists based in the hospital's outpatient pharmacy while the participant waited for their prescription. Recruiting pharmacists had completed their Good Clinical Practice training and were trained by the study principal investigator on the study requirements and consent taking. Written consent was taken from the patient's parent/carer if the child was below 16 years or the patient, if 16 years or older. An assent form was used for patients aged 12 to 15 years and was signed by the patient

alongside the parent/carer consent form. To minimise impact on service delivery a convenience sample of participants were recruited during the period February to July 2015. This study was exploratory and a recruitment number of 100 participants was considered to a provide sufficient range of specialties and participants to identify important findings. There were no known published studies to guide recruitment numbers.

3.3.3 Inclusion criteria

Potential participants were eligible for inclusion in to the study if they met the following criteria:

- The patient (if 16 years or older) or their caregiver (if the patient was under 16 years old) were able to understand written and spoken English as confirmed by the pharmacist taking consent through participants' understanding of the study.

- The patient was prescribed a new medication to be taken for 6 weeks or longer. Six weeks was considered to have provided the patient, and their parent/carer, sufficient experience of taking a new medication prior to follow-up.

- The participant had access to a telephone for follow-up after 6 weeks.

3.3.4 Exclusion criteria

Potential participants were excluded from study recruitment according to the following criteria:

- The participant was unable to understand written or spoken English.

- The participant was educationally/intellectually disabled.

- The patient was receiving treatment for a possible life limiting condition.

3.3.5 Data collection

Following consent, the current knowledge that participants had of their new medication was identified through a structured interview administered by the out-patient pharmacists. The

out-patient pharmacists were trained in the study and had undertaken good clinical practice training. This would identify what participants could recall from their out-patient clinic consultation. They were asked whether they knew the name(s) of their new medication(s), indication(s), dose(s) to be taken, how to take or administer the medication(s), the duration of treatment and any side effects to be aware of. Participants were also asked if other current medications were being taken or if they had recently taken long-term (for >6 weeks) medications. This was to assess participant familiarity with medication. Pharmacist led counselling and supplementary information (e.g. the provision of a patient information leaflet) followed the provision of their new medication(s) as per standard practice. The following demographic and background information was collected from the patient's prescription: medical/surgical clinic attended, patient's age, patient's gender, medication prescribed and indication. Participants were also asked for contact details, including appropriate times to call for the telephone interview part of the study. The initial information and advance warning of a telephone interview with flexibility to call back at a more convenient time have been shown to increase response in telephone interviews.[55 56]

Six weeks following the dispensing of their new medication participants received telephone follow-up by the study principal investigator. Telephone follow-up was undertaken to identify any challenges that they might be having with their new medication and to determine adherence to the prescribed instructions. A semi-structured interview was used as the research instrument. Face validity of the interview questions and piloting was assessed with a parent of a child taking multiple long-term medication. All study documents were also reviewed by Birmingham Children's Hospital Patient Information Department. Following confirmation of consent the interview was completed by telephone with direct support from the principal investigator. Participants were asked about the following themes:

- Whether they had researched further information themselves about their new medication, their reason for doing so and what resources were used.
- Any concerns or questions that they had about the new medication.
- Any potential problems regarding administration.
- Whether the patient had experienced any possible adverse effects.
- If they had experienced any problems arranging further supplies of their medication.

- Whether they had intentionally or unintentionally omitted any doses of their new medication and why.

- Anything else that the participant wished to inform the researcher about their experiences of starting a new medication.

The answers to the questions were transcribed in real time on to a data collection proforma by the principal investigator during the telephone interview.

3.3.6 Data management

All data collected was used for the sole purpose of this study and for no other purpose. The data was stored in a secure department (Pharmacy Department) at Birmingham Children's Hospital during the study. Anonymised data, completed questionnaires, telephone interview notes and study site file contents were archived at the School of Life and Health Sciences, Aston University.

Electronic records of interview responses were stored on a secure server on a Birmingham Children's Hospital PC only accessible by the researcher. Paper copies of the questionnaire were stored in a locked cupboard in a secure office in the Pharmacy department at Birmingham Children's Hospital.

All data was anonymised at the earliest opportunity and pseudonyms were used in place of participant names to maintain anonymity. No confidential/identifiable data was stored following completion of the study in accordance with information governance. Only anonymised questionnaire data was retained during the study.

If any information was provided in the questionnaire that raised any concerns from a child protection or safeguarding perspective the Principal Investigator (PI) was to seek advice from the Child Protection and Safeguarding Team at Birmingham Children's Hospital. This was also to be recorded as an 'adverse event' within the study.

The data was analysed by the PI and his academic supervisors. Analysis took place on hospital premises with anonymised data being analysed at the researcher's private residence and Aston University. Transfer of anonymised data was via a BCH (Birmingham Children's Hospital) encrypted memory stick.

3.3.7 Data analysis

The quantitative elements of the study were analysed using descriptive statistics. The Statistical Package for Social Sciences (SPSS) version 22 was used to assist this analysis. The results of the semi-structured telephone interviews were analysed using thematic analysis. The responses were listed, grouped by similar/related theme and analysed using NVivo version 10.

3.4 Results

3.4.1 Demographic/background information

One hundred participants were recruited in to the study. Fifty-one patients were female and 49 male with a mean age of 8 years (range 0.33 years - 17 years). Patients were clinically managed by 1 of 15 specialities (Table 1).

Table 1 Specialities Responsible for Patient Care

Speciality	N
General Paediatrics	23
Ear, Nose and Throat	14
Neurology	13
Dermatology	10
Urology	9
Respiratory	7
Rheumatology	5
Emergency Department	3
Gastroenterology	3
Hepatology	3
Nephrology	3
Ophthalmology	3
Cardiology	2
Inherited Metabolic Diseases	1
Plastics	1

In total 145 medications were prescribed which patients had not previously received (Table 2).

Table 2 Medications Prescribed for Study Participants

Therapeutic Use	**Number of Medicines (%)**	**Medicine (n)**
Eczema	27 (18.6%)	Topical corticosteroid (13)
		Emollient (7)
		Dressings (3)
		Hydroxyzine (2)
		Potassium Permanganate (1)
		Topical tacrolimus (1)
Asthma	17(11.7%)	Beclomethasone (6)
		Montelukast (4)
		Fluticasone (2)
		Fluticasone/Salmeterol (2)
		Salbutamol (2)
		Ipratropium (1)
Allergy	14(9.7%)	Fluticasone (8)
		Cetirizine (2)
		Adrenaline (1)
		Chlorphenamine (1)
		Desloratadine (1)
		Nutramigen (1)
Urinary Frequency/Enuresis	14 (9.7%)	Desmopressin (6)
		Oxybutinin (6)
		Tolterodine (2)
Migraine/Headache	11(7.6%)	Pizotifen (6)
		Propranolol (2)
		Sumatriptan (2)
		Migraleve (1)
Gastro-0esophageal Reflux	9 (6.2%)	Ranitidine (7)
		Lansoprazole (1)
		Omeprazole (1)

Therapeutic Use	**Number of Medicines (%)**	**Medicine (n)**
Epilepsy	8 (5.5%)	Levetiracetam (2)
		Acetazolamide (1)
		Carbamazepine (1)
		Lamotrigine (1)
		Sodium valproate (1)
		Stiripentol (1)
		Topiramate (1)
Infection	8(5.5%)	Trimethoprim (3)
		Amoxicillin (1)
		Azithromycin (1)
		Co-trimoxazole (1)
		Erythromycin (1)
		Itraconazole (1)
Constipation	6 (4.1%)	Macrocols (5)
		Senna (1)
Vitamins	6 (4.1%)	Colecalciferol (2)
		Folic Acid (2)
		Alfacalcidol (1)
		Ergocalciferol (1)
Rheumatic diseases	5 (3.4%)	Nifedipine (2)
		Piroxicam (2)
		Hydroxychloroquine (1)
Immunosuppression	4 (2.8%)	Azathioprine (2)
		Ciclosporin (1)
		Methotrexate (1)
Cardiovascular	3 (2.1%)	Atorvastatin (1)
		Enalapril (1)
		Losartan (1)

Therapeutic Use	Number of Medicines (%)	Medicine (n)
Ophthalmic	3 (2.1%)	Prednisolone (2)
		Fluorometholone (1)
Cholestasis	2 (1.4%)	Ursodeoxycholic acid (2)
Emesis	2 (1.4%)	Ondansetron (2)
Other	6 (4.1%)	Amitriptyline (1)
		Cholestyramine (1)
		Dexamethasone/framycetin/gramicidin (1)
		Levomepromazine (1)
		Melatonin (1)
		Propranolol (1)

Eighty-six participants (85 parents and one 15 year old young person) received telephone follow-up 6 weeks following the dispensing of their medication. Fourteen participants were not contactable. The mean age of those patients not contactable was 6.15 years (range 1.3 years to 13 years), compared with 8.34 years (range 0.33 years to 16 years) of those contactable for telephone interview.

Overall, 49/100 patients were currently taking other long-term medications and 2/100 had been on long-term medications in the previous 6 months. Forty-nine participants had no recent experience (in the last 6 months) of taking/administering medication for the patient listed on the prescription. Of the 86 participants contacted for telephone follow-up, 38 (44.2%) were currently on other long-term medications and 2 (2.3%) had been on other long-term medications in the last 6 months. Forty-six (53.5%) participants had no recent experience of being on long-term medications. Of the 14 participants who were not contactable for telephone follow-up, 11 (78.6%) were currently on other long-term medications and 3 (21.4%) had no recent experience of being on long-term medications.

All specialities represented in the 14 respondents who were not contactable for telephone follow-up (General Paediatrics (4), Dermatology (4), Ear, Nose and Throat (2), Respiratory (2), Nephrology (1) and Neurology (1)) were represented in those responding to telephone follow-up (General Paediatrics (19), Ear, Nose and Throat (12), Neurology (12), Dermatology (6), Respiratory (5) and Nephrology (2)).

3.4.2 Participants initial knowledge of their new medication(s)

Following their out-patient clinic appointment, participants were able to recall the names of 96 (66%) medications and were aware of the therapeutic indication for 142 (97.9%) medications. The dose regimen was accurately described by the participants for 120 (82.8%) medications with the duration of treatment known for 132 (91%). Participants mentioned that they had been advised about side effects for 44 (30.3%) medications. Specific counselling points identified from the current edition of the British National Formulary for Children[57], were either omitted or not recalled by participants, following their consultation with the prescriber, for the following systemic treatments: cetirizine (1), chlorphenamine (1), desmopressin (2), hydroxyzine (2), itraconazole (1), piroxicam (2), methotrexate (1), stiripentol (1) and topiramate (1).

3.4.3 Participants' experiences of their medication six weeks following first prescription

Intended Non-Compliance (medication not started)

Telephone follow-up revealed that 6/86 (7%) participants had not initiated the new medication. Two caregivers were concerned about side effects (macrogol and topical corticosteroid), 2 patients had not needed to take their medication (chlorphenamine, pizotifen and sumatriptan), 1 patient refused to be administered a macrogol suspension and 1 patient was concerned about how nifedipine would interact with her other medicines.

"I read the leaflet that it came with. I read that then decided to try naturally. I haven't started her on it yet. They said that she wasn't drinking enough. I pushed the fluids and she's been better than she was. She goes every other day now. I didn't want to try them personally if she's just not drinking enough. I read the information leaflet that came with it. It can cause diarrhoea and I didn't want to send her the other way. She's had diarrhoea at school before and it's not very nice. Especially now she's getting older. I'm seeing the consultant next month and I'll discuss it with her then." Parent of Patient 18 (macrogol)

"We did look online. We took on board what the pharmacist said, looked on line and got frightened off by it." Parent of Patient 34 (betamethasone valerate 0.1% / clioquinol 3% ointment)

"I haven't been taking it because I couldn't find out if it was compatible with my other medicines. I'm doing my exams at the moment so I didn't think it would be very smart to take them now." Patient 46 (nifedipine)

Undertaking Further Research

In the first 6 weeks following initiation of their medication, 26 (30.2%) participants had researched further information on their medication. Twenty-two participants researched the internet, one asked other parents of children taking the same medicine, one asked a friend, one, a doctor, looked in the British National Formulary and one participant asked a relative who was a pharmacist.

The reasons participants undertook further research into their medications was categorised into 5 themes –general interest was cited by 5 participants, further information about possible side effects was identified by 13 participants, researching a specific query relating to their medication was undertaken by 3 participants, 4 participants sought further reassurance about the appropriateness of treatment and 3 wanted to confirm that there were no interactions with concomitant medication.

"I'm giving something new. I want to know what side effects there are. [Patient 6] is on lots of medicines, she's having seizures and I want to see how it interacts with the others. As [Patient 6] has had lots of seizures I don't want to make these worse." Parent of Patient 6 (levomepromazine)

"*I think because of what had been said in the initial consultation about side effects. Some of them were not very nice. We decided to go ahead but in view of what was said I wanted to look them up myself.*" Parent of Patient 15 (ciclosporin)

"*Basically, is that the right drug? Is it common to use it at this stage?*" Parent of Patient 75 (azathioprine)

Concerns and Further Questions

Twenty-four (30%) participants who had taken/administered their medication had reported that they had experienced concerns about their medicine over the first 6 weeks of treatment. Concerns related to side effects were most common (10, 41.7%) followed by efficacy (6, 25%), administration (4, 16.7%) and other concerns (4, 25%). Other concerns were the

perceived stigma of taking an antidepressant, the impact of a friend questioning the choice of therapy, perceived possible supply problems through the General Practitioner (GP) prescribing route and the advice provided by a pharmacist.

"She has recently been having seizures. She was given Keppra starting slowly. She's now on 6 mL and Epilim has been added. She has seven a day, six a day then a seizure break. I keep phoning, they increase the dose. How do they know when it will work? They keep increasing the dose, adding in new ones, when will they work? Two weeks?" Parent of Patient 6 (levomepromazine)

"There was one thing. My friend works in a hospital, I'm not sure what she does, but when she saw what [Patient 11] was on she said that they'd been told to stop using them. I don't know why that is?" Parent of Patient 11 (piroxicam)

"The granules. Is there any other way of giving these? She has a bottle at night and then she's full so it's very difficult giving the montelukast in yogurt as she's full up and drifts off." Parent of Patient 17 (montelukast)

"No, only thing is, absolutely fine when he first started taking it but now it's not working so well. The doctor did say that he might need to increase the dose. He's sort of left it up to us about that through the GP. But then when I got the letter it said about a follow up appointment so he contradicted himself a bit there. Not sure what's going on." Parent of Patient 51 (desmopressin)

"No certainty or idea about how long she is to take this for. They said 3 months then a break but I don't know how long the break is or when to start. My next appointment is in a year's time." Parent of Patient 96 (desmopressin)

Seven (29.2%) had sought further advice from the hospital team.

"We had an issue in that she started taking for two weeks and it was fine. Her symptoms improved, eyes, skin and asthma were good. Then three weeks ago she became unwell. I looked at the ciclosporin side effects. After she was unwell for a week, I contacted Birmingham, [the consultant] said that yes it sounds like side effects. She suggested halving the dose over the next few days and rung again. [Patient 15] was no better then stopped 2 weeks ago. She hasn't got any better yet and will be off it for a month." Parent of Patient 15 (ciclosporin)

"Yes, phoned [consultant's] secretary but no reply. Should he have his blood pressure checked again after the dose increase? Should the dose be 3mg/kg? Back to GP but won't do anything about it as not in BNFc. I've also weighed him and he's now 9.7kg so I need to titrate the dose against this but the GP said no and to contact the consultant." Parent of Patient 66 (propranolol)

"Contacted [the consultant]. He wanted to check with the Liver Team about the medicines. Because the letter mentioned this, the GP would not prescribe them. He's now gone two weeks without his medicine. Spoke to the [consultant's] secretary three days ago and she said they would send a prescription out to the house then write to the GP but no prescription has come. It started well and now we've gone back a few steps." Parent of Patient 7 (cholestyramine and alfcalcidol)

Administration Issues

Issues regarding the administration of patients' medication were experienced by 21 (26.3%) participants. The most common experience (11, 52.4%) was a dislike of the taste or smell of the medicine. The timing of administration was a problem for 3 (3.8%) participants. Two (9.5%) patients experienced difficulties in taking their medication possibly as a result of autism and learning difficulties. Other (5, 23.8%) experiences included the manipulation of a tablet to obtain a part dose, problems extracting a tablet from a blister pack, fear of an inhaled spacer device, the absence of a bottle adapter when dispensed to the patient and problems swallowing a tablet.

"She has a PEG so it is easy. I crush the tablets and mix with water. Originally told to put in 5mL water then take. I'm now just putting half in. When I mix it, have I mixed it well enough then get rid of some. Now cut tablet in half, then mix in 5mL water then remove one mL. I worry that I haven't got the right amount." Parent of Patient 6 (levomepromazine)

"When I got a prescription from the local pharmacy on receipt they were blue. She has learning difficulties and she didn't like the blue ones. She missed two doses…" Parent of Patient 22 (oxybutynin)

"I think because he's autistic it took quite a while before he started using it. I had to try it out quite a bit before he got used to it. The Bottle looks a bit scary for someone who hasn't had it before. The bottle is slightly bulky, so difficult trying to push up. Use to doing it now." Parent of Patient 63 (fluticasone nasal spray)

"It was difficult to find a suitable time as needed to be taken on an empty stomach an hour before food. She took it at school as there's no afternoon break. In the morning she has breakfast, then there's lunchtime. When she comes home she has an evening meal and then she's tired and it's time for bed." Parent of Patient 23 (lansoprazole)

"He's got a new spacer now as he couldn't cope with the big one. It scared him. He's got a smaller one with bears on it now which is fine. He got the smaller one from the GP." Parent of P33 (beclomethasone inhaler)

Adverse Effects

Whilst cause and effect were not established, adverse effects were reported by 29 (36.3%) participants.

"Upper abdominal pain under her rib cage for three weeks, periodic headache, exhausted, very, very tired, her menstrual cycle has gone haywire. She's been off school for three weeks. I'm desperate to find out the cause to alleviate her symptoms. My head tells me it's the side effects from the drug or are they something else? It's quite a worrying little period with her not getting better." Parent of Patient 15 (ciclosporin)

"I was told one of the side effects was increased appetite. But her appetite is much greater now. I didn't realise just how much it would increase." Parent of Patient 30 (pizotifen)

"When she first started taking them she developed diarrhoea. I only give them every couple of days now. It's supposed to be every day but alternate days now. The doctor said that I may need to give a lower dose." Parent of Patient 85 (macrogol)

A summary of the adverse effects experienced by patients are listed in Table 3.

Table 3 Reported Adverse Effects

Therapeutic Use	Medicine	Number of Participants Reporting Effect	Reported Adverse Effect(s)
Eczema	Topical corticosteroid	1	Staining of clothing.
	Hydroxyzine	1	Drowsiness
Allergy	Fluticasone	2	Nose bleed, sore throat
Urinary Frequency/Enuresis	Oxybutinin	2	Drowsiness, dry mouth.
	Tolterodine	2	Drowsiness, dry mouth, constipation, abdominal pain.
Migraine/Headache	Pizotifen	3	Behavioural changes, constipation, increased appetite.
	Propranolol	1	Fatigue
Gastro-Oesophageal Reflux	Ranitidine	1	Vomiting
Epilepsy	Levetiracetam	2	Behavioural changes
	Acetazolamide	1	Behavioural changes
	Lamotrigine	1	Suicidal ideation
Constipation	Marogol	1	Diarrhoea
Rheumatic diseases	Nifedipine	1	Nausea, dizziness.
	Hydroxychloroquine	1	Abdominal pain.
Immunosuppression	Azathioprine	2	Blacking out/fainting, hair loss.
	Ciclosporin	1	Abdominal pain, headache, fatigued, menstrual cycle changes.
	Methotrexate	1	Abdominal pain.

Therapeutic Use	Medicine	Number of Participants Reporting Effect	Reported Adverse Effect(s)
Other	Amitriptyline	1	Drowsiness
	Atorvastatin	1	Jaundice
	Enalapril	1	Dry cough
	Itraconazole	1	Abdominal pain.
	Propranolol	1	Coldness of the extremities

Further Supply Issues

Within the first 6 weeks of treatment 12 (15%) participants experienced difficulties obtaining further supplies of their medicine. Forty-eight (60%) still had sufficient supplies from the hospital and 21 (26.3%) had obtained further supplies from their GP. The problems experienced by patients included delays in the posting out of clinic letters to the GP (4), insufficient information on the letter for a repeat prescription (3), the misreading of a letter by the GP (1), insufficient quantities prescribed by the GP (2), the cancellation of a follow-up out-patient appointment where a repeat prescription was going to be provided (1) and confusion due to a therapy substitution by the hospital pharmacy which then did not match the medication information included in the clinic letter (1).

"Yes, there was some confusion between the doctors. The hospital hadn't written to the GP, the letter hadn't been sent so I had to phone the consultant who organised the letter. Missed a week of the antibiotic." Parent of Patient 26 (co-trimoxazole)

"Ran out of tablets. The doctor said to take the course and we'll see you back. Out-patient on 8th June cancelled by the hospital and arranged for much later in August. Had to phone up and get it brought forward. The doctor said to take it for six weeks. We only had a four-week supply. It's hard to have any contact with doctors at the hospital. It's easy to talk to the GP." Parent of Patient 45 (amitriptyline)

"The doctor only prescribed thirty days and we're not seeing the neurologist until next Friday. We were due to run out two days after coming back from holiday. I phoned the receptionist at A&E who said that the GP needed to fax them. So, I phoned the GP receptionist and they

said that they don't usually do this. The GP said that he hadn't got a letter. The hospital had sent no information. When we came back from holiday the hospital had sent a letter about the MRI but nothing about the medicines. I went to the GP with the box and he kindly prescribed." Parent of Patient 8 (pizotifen)

"When I took the medicine from the hospital, I had the 2mg strength tablets. But when I went to the [community] pharmacy they gave me capsules. They are 4mg. I mentioned that I usually have tablets to the pharmacist and he checked with the GP. The letter from the hospital said 4mg capsules. I was worried because it is twice the amount that he was having." Parent of Patient 32 (tolterodine)

"I knocked a bottle over. The letter didn't state the dose so I had to go back to the hospital." Parent of Patient 79 (ranitidine)

Adherence to the Prescribed Regimen

Thirty-two (40%) participants admitted to occasionally forgetting to administer/take a dose of medication.

"Only because I'd forgotten. We were advised to take it with or after food. If I'd forgotten I didn't know if I could then give it and so I would miss the dose and give his next one." Parent of Patient 61 (ursodeoxycholic acid)

"I don't find it difficult to stick to the plan because I know we have to stick to it because it's for his eyes. A bit inconvenienced…it blows his weekend out. We give it on a Saturday morning so we can do something on a Friday night if we want to. I sometimes forget the folic acid as he has three days off when he's on the methotrexate." Parent of Patient 20 (methotrexate)

Four (12.5%) participants advised that they had purchased medication compliance aids to support adherence.

"She's using a pill case. Wanted to be an adult, didn't like us asking her each morning if she'd had it." Parent of Patient 59 (lamotrigine)

"Pill boxes are super. Add medicines to a pill box to help him remember. He's very mature regarding his epilepsy." Parent of Patient 2 (levetiracetam)

Eighteen (22.5%) participants omitted doses for reasons other than forgetting. These were due to adverse effects (5), concurrent acute illness (3), difficulty in the timing of administration (3), the desire to look up more information prior to starting the medicines (2), incorrect use of the medicine (2), child not wanting to take their medicine (1), a mum not wanting their child to have the medication as, although not used for this indication, they were an antidepressant (1) and ran out of supplies (1).

"He was poorly once and was taking Calpol, Nurofen and antibiotics. So, I stopped giving it then as I thought it was a bit much." Parent of Patient 100 (ranitidine)

"Only the first night because of reading the side effects. My husband did look on the internet. Therefore, not given. Then we read the information the doctor gave us and realised it was more related to children and my husband was much happier so we gave it to them." Parent of Patient 56 and Patient 57 (desmopressin)

"She very active and swims a lot. She swims until 9 o'clock. She needed a drink, it was a bit late so we missed a dose." Parent of Patient 96 (desmopressin)

"Hand on heart, I didn't really follow up on the fact that she had only 4 weeks supply as didn't really want her to take it." Parent of Patient 45 (amitriptyline)

Three (3.8%) participants reduced/stopped the medication because the patient was feeling worse when they took it. Six (7.5%) participants sometimes stopped their child's medication because they felt that their symptoms were under control.

"I use my discretion. If it's a cold wet day I don't give it. If it is a hot day and the pollen count is high, I give it." Parent of Patient 89 (fluticasone nasal spray)

"She has a headache she takes them. When better she doesn't bother with it. When I ask her if she's taken them, she says yes but I know she hasn't so I gave her the tablets to take." Parent of Patient 40 (propranolol)

Two (2.5%) participants increased the amount of medication their child was taking as they felt that it was needed.

"Sometimes when itching a lot, I give an extra application. Only very occasionally if very itchy" Parent of Patient 41 (hydrocortisone 1%/miconazole 2% cream)

Sub-Group Analysis

The associated between age category and medication related issues is shown in Table 4. The Chi Square test showed a significant difference between the age groups and ‘any questions/concerns’ Approximately half of participants in the 7 to 12 years and 13 years and older age groups experienced concerns or had questions over the first 6 weeks of therapy compared with 7 (22.6%) of those in the 6 years and younger age group. A statistically significant difference was also shown for any adverse effects experienced. Most (13, 61.9%) adverse effects were experienced by the 13 years and older age group compared with 12 (42.9%) for 7 to 12 years and 4 (12.9%) for the 6 years and younger category.

The influence of prior experience of taking/administering medicines by/to the patient on the issues that may occur during therapy are presented in Table 5. The Chi Square test showed there to be no statistically significant difference between the two groups for each medication related issue.

Table 4 The Relationship Between Age and Medication Related Issues Occurring During Therapy

Age Category	**Number of Patients**	**Concerns or questions**	**Administration issues**	**Adverse effects**	**Unintended non-compliance**	**Intended non-compliance**
6 years and under	31	7 (22.6%)	9 (29%)	4 (12.9%)	12 (38.7%)	7 (22.6%)
7 – 12 years	28	14 (50%)	9 (32.1%)	12 (42.9%)	12 (42.9%)	4 (14.3%)
13 years and older	21	11 (52.4%)	5 (23.8%)	13 (61.9%)	8 (38.1%)	6 (28.6%)
Chi-square test for independence		$\chi^2 = 6.43$ $p = 0.04$ Cramers V = 0.28	$\chi^2 = 0.41$ $P = 0.82$ Cramers V = 0.071	$\chi^2 = 13.82$ $P = 0.001$ Cramers V = 0.42	$\chi^2 = 0.15$ $P = 0.93$ Cramers V = 0.043	$\chi^2 = 1.52$ $P = 0.47$ Cramers V = 0.14

Table 5 The Relationship Between Prior Experience and Medication Related Issues Occurring During Therapy

Experience	**Number of Patients**	**Concerns or questions**	**Administration issues**	**Adverse effects**	**Unintended non-compliance**	**Intended non-compliance**
No prior experience medicine use in patient	42	18 (42.9%)	11 (26.2%)	13 (31.0%)	15 (35.7%)	8 (19.0%)
Prior experience of medicine use in patient	38	14 (36.8%)	12 (31.6%)	16 (42.1%)	17 (44.7%)	9 (23.7%)
Chi-square test for independence (with Yates Continuity Correction)		$\chi^2 = 0.102$ *p* = 0.749 *phi* = -0.061	$\chi^2 = 0.081$ *P* = 0.776 *phi* = 0.059	$\chi^2 = 0.645$ *P* = 0.442 *phi* = 0.116	$\chi^2 = 0.258$ *P* = 0.611 *phi* = 0.083	$\chi^2 = 0.031$ *P* = 0.860 *phi* = 0.051

The effect of a participant having concerns or questions within the first 6 weeks of using their new medicine(s) on intended non-adherence is summarised in Table 6. Although there was a higher proportion of non-adherence in the concerns/questions group, no significant difference was demonstrated using the Chi Square test for independence.

Table 6 The Influence of Participant's Concerns or Questions on Intended Non-Compliance

Experience	Number of Patients	Intended non-compliance
No concerns or questions about the medicine(s)	48	8 (16.7%)
Concerns or questions expressed by participant about their medicine(s)	32	9 (28.1%)
Chi-square test for independence (with Yates Continuity Correction)		$\chi^2 = 0.90$ *P* = 0.34 *phi* = 0.14

The effect that the number of newly prescribed medicines has on medication related issues occurring during therapy is listed in Table 7. There was no statistically significant different between those prescribed single or multiple medications. However, the results for 'concerns or questions' approaches clinical significance ($p = 0.065$).

Table 7 The Relationship Between the Number of New Medicines Prescribed and Medication Related Issues Occurring During Therapy

Number of Medicines Prescribed	**Number of Patients**	**Concerns or questions**	**Administration issues**	**Adverse effects**	**Unintended non-compliance**	**Intended non-compliance***
Prescribed one new medicine	60	28 (46.7%)	16 (26.7%)	24 (40%)	24 (40%)	14 (23.3%)
Prescribed more than one new medicine	20	4 (20%)	7 (35%)	5 (25%)	8 (40%)	3 (15%)
Chi-square test for independence (with Yates Continuity Correction) *Fishers exact test		$\chi^2 = 3.40$ $p = 0.065$ *phi* = -0.236	$\chi^2 = 0.183$ $P = 0.669$ *phi* = 0.080	$\chi^2 = 0.883$ $P = 0.347$ *phi* = -0.135	$\chi^2 = 0$ $P = 1$ *phi* = 0	Fisher's exact test: $P = 0.517$

3.5 Discussion

General paediatrics was the medical speciality with the largest number of patients in this study and these made up 23% of all patients. This is very similar to that observed for paediatric out-patient attendances in England for 2013/2014 where Paediatrics was the most common speciality making up 23.8% of all attendences.[58] Ear, Nose and Throat (ENT), Neurology and Dermatology were frequent specialities in this study. ENT and Dermatology were both in the top 10 specialities for out-patient attendences in England in 2013/14 but Paediatric Neurology was less common at 19th position. All specialities from this study were represented in the top 33% of all 2013/2014 paediatric outpatient attendances. This current study was undertaken in a tertiary centre and only recruited patients prescribed a medication from a convenience sample of patients. The national data will reflect all attendances across England irrespective of type of healthcare centre or whether a medication has been prescribed. Whilst it is to be expected that the frequencies of specialities were likely to be different the current study does seem to broadly represent the national picture.

On telephone follow-up this study achieved a response rate of 86%. A response greater than 75% is considered to be good.[56] The age range of responders was greater than that seen with non-responders group and all specialities from the non-responders group were represented in the group who received telephone follow-up. Thus, the risk of bias was low.

Following an out-patient consultation, where a new medication was prescribed, children and their caregivers were usually able to recall the indication, dose regimen and duration of treatment. However, few were able to recall, or were told about, possible adverse effects. This included some important medication specific effects that require vigilance during treatment. Patients, along with their families and carers, should be involved in the decision to prescribe a medication.[9] This includes a discussion about the benefits of the medicine on the patient's condition and possible adverse effects.[9] Treatment side effects have been shown to be a factor in non-adherence in paediatric long-term medical conditions.[21] Practitioners should explain to patients, and their family members or carers where appropriate, how to identify and report medication-related patient safety incidents.[5] However, this study suggests that medical staff may not be discussing the adverse effects of medication with patients or their caregivers. The reason for this is not known. On telephone follow-up 29 (36.3%) participants felt that the patient had experienced a side effect with their medication thus reinforcing the importance of discussing these potential effects at the point of initiating a new medication.

More partnership working between clinicians and patients is fundamentally important and, in particular, that shared decision-making about treatment choice is needed for reasons of both effectiveness and ethics.[59] But an assumption that an agreement has been reached may fail to recognise the multiplicity of factors that influence medicines-taking behaviour and the reality of what actually happens when a person leaves the pharmacy or consulting room.[60] In paediatrics the partnership is more complex with caregiver-medical team, child-medical team and caregiver-child relationships.[16] A study of older adult patients prescribed a new chronic medicine found that once a patient has experienced their medication, they gain some knowledge of what it does to them and new questions arise.[20] This is further supported by patients not contacting an acute hospital telephone helpline to discuss their treatment regimen until six to seven weeks post-discharge.[60] Whilst these data relate to adults this current study has shown that children and their caregivers have similar experiences after the first few weeks of therapy. This is illustrated by 26 (30.2%) participants researching further information about their new medicines and 24 (30%) having concerns or further questions arising over the first few weeks of therapy. The reasons for further research were wide ranging with the most common being for more general information (13, 50%) and questions/concerns related to adverse effects (10, 41.7%). Whilst this may be due to insufficient information provided during the out-patient consultation or the assumption that an agreement to treat had been reached, it could also be that patients/caregivers did not disclose and discuss their concerns. Poor communication may lead patients to obtain information about medication outside of a consultation with a healthcare professional.[61] Horne *et al* found a significant association between concerns about a medication and adherence in adult long-term conditions.[62] If concordance is to be achieved it is necessary for both patients and practitioners to disclose and discuss their concerns and views rather than adopting an asymmetrical paternalistic interaction.[61] The interaction between prescriber and patient/caregiver was outside of the scope of this current study. Further research in to the shared decision-making process in the paediatric out-patient clinic when a new long-term medication is prescribed is required to further support medication adherence and the patient safety agenda.

The information gap created when patients have experienced their new medication, developed new questions and how the patients then resolve these questions may lead to inappropriate non-adherence.[20] Eighteen (22.5%) participants intentionally omitted doses of their medication. These omissions included examples where this was due to an erroneous decision made by participants to resolve their own medication related issue. For example, one caregiver temporarily stopped administering ranitidine therapy because their child was initiated on treatment for an intercurrent upper respiratory tract infection. Any information

provided with a medication describes a population response to that medicine and is not specific to that patient.[20] Participants in this study may have benefited from access to a health professional during the first few weeks of treatment to answer any questions arising from their own unique situation.

Patients have a right to decide not to take their medication and may have different views about risks, benefits and side effects.[9] In this current study, of the 6 participants who had not started their medication, 2 caregivers had considered the side effect profile and decided against treatment. In 2 other cases, caregivers had delayed treatment to enable them sufficient time to evaluate the risks and benefits of treatment. Thus, it appears that some caregivers are further reviewing the therapy decision outside of the healthcare setting.
A recent systematic review of treatment non-adherence in paediatric patients identified a number of findings that may contribute to explaining treatment adherence.[21] These included beliefs about the condition or treatment, the treatment regimen, child resistance, relationships within families, preserving normal life and the input from health professionals.[21] Each of these themes were identified in this current study. Whilst the review focussed on long-term conditions it did not identify when during treatment these themes occurred. This current study identified that these themes can occur within the first few weeks after starting a new medication.

Overall, participant reported adherence in this current study was comparable with that published in the paediatric literature.[63 64] Unintentional non-adherence was observed in 32 (40%) participants. Four (12.5%) participants had purchased medication compliance aids. With the limited evidence base currently indicating a lack of patient benefit outcomes with the use of medication compliance aids the RPS recommend the use of original packs dispensing supported by appropriate pharmaceutical care as the preferred intervention.[65]

Unsurprisingly, 21 (26.3%) participants had difficulties administering the medication to their child. Unlike in adults where, oral solid dosage forms such as tablets or capsules will be acceptable to the majority of patients, potential paediatric patients may include neonates, toddlers, young children and adolescents, and as such, will have widely varying needs.[66] A change in formulation is currently excluded from triggering an NMS consultation.[67] Any future paediatric medication review should include changes in formulation as a trigger for review.

The difficulties that patients and caregivers may experience attempting to obtain a prescription in the community pharmacy setting have been described.[43] In this current study the most common issue to affect further ongoing medication supplies was one of

communication between the care settings. There is a substantial body of evidence that shows when patients move between care providers the risk of miscommunication and unintended changes to medication remain a significant problem.[68] This current study shows that this remains a potential issue in paediatrics with 12 (15%) participants experiencing problems arranging a repeat supply. The 2 most common problems were a delay in the GP receiving the clinic letter (4, 33%) and the clinic letter containing insufficient information for a repeat supply to be made (3, 25%).

No particular group of patients was identified as having a greater risk of medication related issues occurring during the first few weeks of treatment. There was no statistically significant effect of prior experience of medication taking or the number of newly prescribed medications on the issues that may occur during therapy. With the exception of new concerns/questions and adverse effects there was no significant difference between the different age categories for issues associated with administration or compliance. In this study the group of patients aged seven years and upwards tended to have more concerns or questions and experience more possible adverse effects. Although some caregivers and patients in the younger age group also experienced these effects. A study of adverse drug reactions causing admission to a paediatric hospital previously identified increasing age as a risk factor for experiencing an adverse drug effect.[69]

Few data are available to inform best practice for young people with existing adherence problems.[70] A recent review of interventions to improve the safe and effective use of medicines by consumers identified a scarcity of evidence in children and young people, carers and those with multiple co-existent conditions. Interventions considered promising but requiring further investigation included involving pharmacists in medicines management, such as medication reviews (with positive effects on adherence and use, medication problems and clinical outcomes) and pharmaceutical care services (consultation between pharmacist and patient to resolve medicines problems, develop a care plan and provide follow-up, with positive effects on adherence and knowledge).[71]

The benefits of a medication review through the NMS have been described.[48] The NMS applies a structured approach to identifying and attempting to resolve the same medication related issues that were identified in this current study.[67] It is however limited to specific conditions, formulation changes would not normally be included and it is not available to children or their caregivers.[45 67] The results of this current study suggest that paediatric patients and their caregivers may benefit from some support initiative after the first few weeks of treatment with one option being an NMS type intervention irrespective of medical

condition, previous experience or type of medication prescribed. In addition to medication review a number of other initiatives may further support patients realising the benefits of their medication. These include fostering better partnerships with patients, the use of telephone helplines for information on medication, developing specific internet support internet websites and improvements to how different healthcare professionals collaborate together.[60] Further work is required to determine the most optimal intervention(s).

3.7 Strengths and limitations

The strength of this study is the detailed insight in to the treatment-related experiences of parents/carers and patients during the first 6 weeks after a child is prescribed a new medication. This study has demonstrated that paediatric patients and their parents/carers experience a range of issues during the first few weeks after starting a new medication. These include adherence, information needs, adverse effects and obtaining medication supplies.

The limitations of this study included sample size which was relatively small. A quantitative study may demonstrate the extent to which people experience these issues. Participants may also have provided answers that they perceived to be acceptable. However, consistency of the interview process was maintained with one interviewer (the study principal investigator) undertaking all the interviews. Undertaking the research at a single tertiary care centre may not be representative of primary care or non-specialist hospital prescribing thus limiting generalisability of the results. The restriction to English language speakers may limit extrapolation of the results to non-English speakers who may have their own unique range of experiences not captured within this current study. The study recruited participants over a period of February to July which may introduce seasonal bias in to the results.

3.8 Further research

Further research is required to determine the type of intervention and how it could be integrated in to practice to help optimise paediatric medication use when a child or young person starts a new medication.

3.9 Conclusion

Paediatric patients and their caregivers experience a range of issues during the first six weeks after starting a new medication. Further research to identify effective intervention(s) at this stage, for example medication review, may provide useful support to both the patient and their parent/carer.

4.0 Study 2 - Children/young people taking long-term medication: a survey of community pharmacists' experiences in England

4.1 Aim

The aims of the study were to determine:

- Whether community pharmacists were undertaking medication review with children/young people or their parents/carers.
- The reason(s) why pharmacists may not be undertaking a medication review in this cohort.
- The type of medication-related experiences being presented to community pharmacists when a child/young person is taking regular medication.
- The type of medication-related issues that are presented to community pharmacists when a child/young person is taking regular medication.

4.2 Research ethics committee approval

The Aston University School of Life and Health Sciences Ethics Committee reviewed and approved this study 14th October 2015 (study ID number 823).

4.3 Method

4.3.1 Setting

Community pharmacists based in England.

4.3.2 Participant recruitment

The NHS Business Services Authority (NHSBSA) ePACT (electronic Prescribing Analysis and Cost) system was accessed to identity community pharmacy addresses who had dispensed prescriptions from Birmingham Children's Hospital during the period November and December 2015. This enabled the targeting of community pharmacies that were known to have dispensed a recent prescription for a child. Where a large chain pharmacy was identified, permission was sought from their superintendent pharmacist by post to send a

questionnaire to their employee community pharmacists. Small chain and independent pharmacies were not approached in advance of the questionnaire being posted.

4.3.3 Inclusion criteria

All community pharmacists who had dispensed a prescription for a child of Birmingham Children's Hospital identified from the NHSBSA ePACT system were included in the study.

4.3.4 Exclusion criteria

There were no exclusion criteria for those community pharmacists who met the inclusion criteria.

4.3.5 Data collection

The research tool in this study was a self-completion postal questionnaire. A number of tactics may be utilised in order to maximise response rates to postal questionnaires.[53-56] These include advance warning, explanation of selection, sponsorship, professional looking envelope addressed to the individual recipient, publicity, incentives, confidentiality, anonymity, appearance, questionnaire length, topic/degree of interest, the use of a cover letter, pre-paid return envelope, repeat mailing and avoidance of holiday periods for data collection. A participant information sheet (Appendix VII), a consent form (Appendix VIII) and a pre-piloted self-completed 13 question questionnaire containing both open and closed questions (Appendix IX) along with a pre-paid return envelope were posted to all community pharmacists identified from the ePACT system. A unique identifier was added to the back of the consent form to allow targeting of non-responders for a repeat mailing. A return date of 3 weeks was included in the consent form and questionnaire. The questionnaire was first posted during January 2016 outside of known school holiday periods. The participant information sheet, consent form and questionnaire were branded with the Aston University logo. Confidentiality was assured in the participant information sheet.

Participants were asked about their practice as a community pharmacist over the preceding twelve months to children/young people aged under 16 years, or their parents/carers, taking long-term medication. For the purpose of this study long-term medication was defined as taking, or expecting to be taking, one or more medications for a period of 6 weeks or longer. The questions were developed based on aspects covered by the NMS and MUR, previous published experiences[20 21 43 72] and the authors' knowledge of managing medication use in

paediatric patients. Face validity along with questionnaire piloting was undertaken with 2 community pharmacists. Participants were asked about the following:

- Whether they had conducted a medication review (NMS, MUR or any other medication review) in a child aged sixteen years or younger or with the child's parent or carer.
- Reasons for not undertaking a medication review (NMS, MUR or any other medication review) in this group of patients/parents or carers including: challenges and practicalities around taking consent, lack funding for medication review in this group, lack of individual accreditation for under taking an NMS or MUR consultation and a lack of confidence in undertaking a medication review in a child or with their parent/carer.

- Whether a child, young person or their parent/carer have personally reported to them any examples of non-compliance to the prescribed regimen without informing the prescriber including: stopping the medication, reducing the dose, increasing the dose and forgetting to take/administer.

- Whether a child, young person or their parent/carer has personally asked them for medication-related information about the following: indication, dose, administration and adverse effects.

- Whether a child, young person or their parent/carer has personally reported to them the following issues associated with their medication: adverse effects, challenges with administration, their GP was unwilling to take over prescribing responsibility for a specialist recommended treatment and challenges with arranging ongoing supplies through community pharmacy, hospital pharmacy or homecare provider.

Participants were able to provide details of any other experiences that they had which were not listed in the questionnaire through the inclusion of open questions. Background information were also collected. Participants were asked about the type of pharmacy worked in (supermarket, health centre, healthy living, high street pharmacy in a large town or small town/suburb pharmacy) and their main type of pharmacy employment (large national chain, medium sized chain, small chain or independent pharmacy). Participants were also asked for their year of registration, number of hours worked per week, how frequently they

encountered children taking long-term medication in their practise and, on average, how many prescription forms they oversaw each month.

Non-responders were telephoned one week after the original return date by the study PI. The PI asked if the original questionnaire was received and, if so, had the questionnaire been posted back. If not, the pharmacist was asked if they would like the opportunity to complete the questionnaire by telephone (on receipt of the first phone call or at a more convenient time for the participant), receive an emailed copy or a further posted version. For questionnaires undertaken by telephone the PI explained the information in the participant information sheet to the pharmacist and took verbal consent (Appendix X). Postal questionnaires were posted to the named pharmacist identified in the telephone follow-up or to an alternative pharmacist as identified during telephone follow-up.

For questionnaires completed by phone the study PI transcribed the answers verbatim onto the questionnaire by hand.

4.3.6 Data management

All data was stored in a secure department (Pharmacy Department) at Birmingham Children's Hospital NHS Foundation Trust. Electronic records were stored on a secure server on a Birmingham Children's Hospital PC only accessible by the researchers. All data was anonymised at the earliest opportunity and pseudonyms were used in place of pharmacist names.

The data was analysed by the research student and his academic supervisors. The data was analysed on hospital premises with anonymised data analysed at the researcher’s private residence.

No confidential data was stored following completion of the study.

4.3.7 Data analysis

The answers listed on the questionnaire were coded for ease of analysis. The results were analysed using descriptive statistics (counts/frequency). The SPSS version 22 was used to analyse the quantitative data. The qualitative responses were grouped by similar/related theme and analysed using thematic analysis. NVivo version 10 was used to analyse the qualitative responses.

4.4 Results

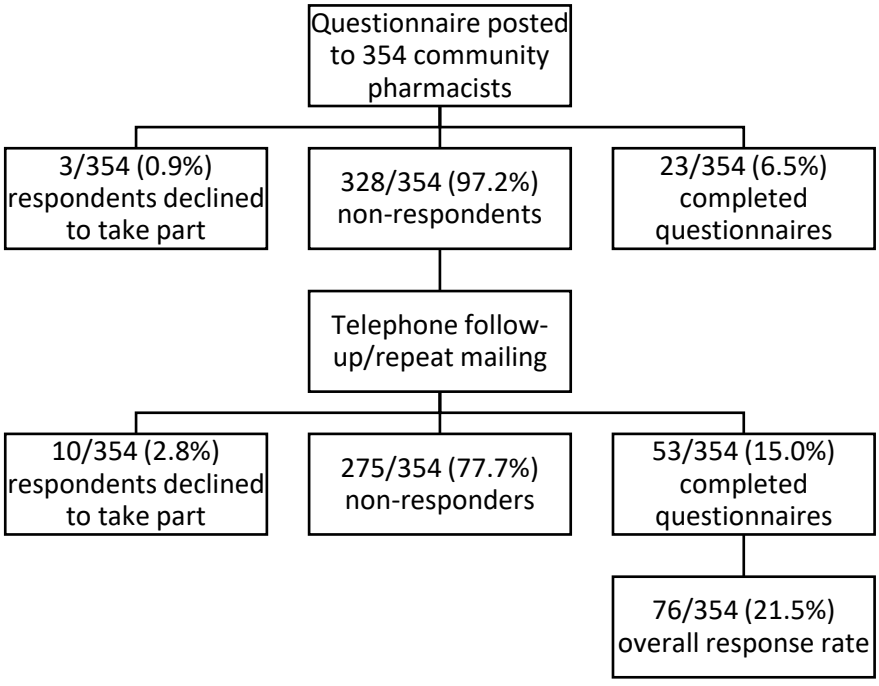
4.4.1 Recruitment

Evaluation of the NHSBSA ePACT data for November and December 2015 identified 354 separate community pharmacies that had dispensed a prescription from Birmingham Children's Hospital.

The response rate (Figure 1) from the first mailing was 26/354 (7.3%). Three (11.5%) of these 26 pharmacists returned the consent form indicating that they did not wish to take part in the study. One pharmacist declined to take part due to time constraints, a second pharmacist felt that they did not see enough paediatric prescriptions to complete the questionnaire and one pharmacist did not give a reason for declining to take part. This provided 23/354 (6.5%) completed questionnaires.

The response rate following telephone follow-up and a re-mailing of non-responders elicited an overall response rate of 76/354 (21.5%). On telephone follow-up 13/328 (4%) pharmacists declined to take part in the study because they were too busy, 1/328 (0.3%) was not interested and 1/328 (0.3%) pharmacy was run on different locums on a daily basis and advised that they were unable to take part.

Figure 1 Response to the Postal Questionnaire



4.4.2 Demographic/background information

The year of registration of participants ranged from 1970-2015 and are summarised in Table 8. Participants worked between 14 hours and 70 hours per week (median 41 hours) in community pharmacy.

Table 8 Year of Registration in the UK

Year of Registration	N (%)
1970-1975	2 (2.6%)
1976-1980	4 (5.3%)
1981-1985	7 (9.2%)
1986-1990	4 (5.3%)
1991-1995	5 (6.6%)
1996-2000	7 (9.2%)
2001-2005	6 (7.9%)
2006-2010	17 (22.4%)
>2011	24 (31.6%)

The main type of community pharmacy employment is listed in Table 9 with the type of pharmacy mostly worked in listed in Table 10.

Table 9 Main Type of Community Pharmacy Employment

Main Type of Community Pharmacy Employment	N (%)
Large National Chain	39 (51.3%)
Small size (≤50 stores)	19 (25%)
Small independent	14 (18.4%)
Medium size (>50 stores)	2 (2.6%)
A combination of a 1,2 and 3 above	1 (1.3%)
A combination of 2 and 3 above	1 (1.3%)

Table 10 Type of Pharmacy Mostly Worked In

Type of Pharmacy Mostly Worked In	N (%)
High street pharmacy in a large town/city	26 (34.2%)
Pharmacy in a small town/suburb	21 (27.6%)
Health centre based pharmacy	15 (19.7%)
Supermarket pharmacy	3 (3.9%)
Healthy living pharmacy	2 (2.6%)
A combination of 1 and 2 above	2 (2.6%)
A combination of 2 and 3 above	2 (2.6%)
A combination of 1, 2 and 3 above	1 (1.3%)
A combination of 1, 4 and 5 above	1 (1.3%)
A combination of 2 and 5 above	1 (1.3%)
A combination of 2, 3 and 5 above	1 (1.3%)
A combination of 3 and 4 above	1 (1.3%)

It was not possible to determine the type of pharmacy with the same level of detail as listed in Table 9 for non-responders. The study principal investigator therefore reviewed the pharmacy address names and determined whether they were a large multiple pharmacy (including supermarket pharmacy) or a non-large multiple pharmacy (Table 11). This enabled a comparison between non-responders and responders.

Table 11 Type of Pharmacy and Response Rate

Type of Pharmacy	Responders	Non-Responders	Total
Large Multiple	45 (59.0%)	114 (41.0%)	155 (43.8%)
Non-Large Multiple	31 (41.0%)	164 (59.0%)	199 (56.0%)

There was a greater proportion of large multiples in the responders group compared with the non-responder's group. However, the Chi-square test for independence (with Yates Continuity correction) indicated no statistically significant difference ($\chi^2 = 3.552$, $p = 0.059$, *phi* = 0.107) between the two groups.

The average number of prescription items overseen each month ranged from 950 – 13,000 with a median of 4000. Five (6.67%) participants did not answer this question.

The frequency with which participants encountered children on long term medicines is listed in Table 12.

Table 12 Frequency of Encountering Children Taking Long-Term Medicines

Frequency	N (%)
Never	0
Once a year	3 (3.9%)
Every 3 months	6 (7.9%)
Once a month	11 (14.5%)
Once a week	12 (15.8%)
More than once a week	44 (57.9%)

4.4.3 Medication review

Participants were asked if they had undertaken a medication review with a child/young person or their parent/carer. A total of 18 (23.7%) participants reported that they had undertaken an MUR either with a child/young person aged 16 or under or with their parent/carer in the previous 12 months. Twenty-two (28.9%) participants advised that they had undertaken an NMS consultation with a child/young person aged 16 or under or with their parent/carer in the previous twelve months. Sixteen (21.1%) reported that they had undertaken some other form of medication review with a child/young person aged 16 or under or with their parent/carer in the previous 12 months. More than one response could be provided to this question, for example, a pharmacist could list that they undertook both an MUR and NMS consultation with a child/young person or their parent/carer.

Table 13 lists the reasons identified by those participants who had indicated that they had not undertaken at least one of MUR, NMS or another type of medication review. Participants had the opportunity to provide reasons why each type of review may not be undertaken and were not restricted to the type of review they indicated that they have not undertaken themselves. The data are expressed against the total number of participants who answered that particular question.

Table 13 Participant Cited Reasons for Not Having Undertaken at Least one of an MUR or NMS Consultation with a Child/Young Person or their Parent/Carer

Reason	N (%)
Difficult /impractical to consent to a **MUR**	42/66 (63.6%)
Not funded to undertake **MUR** with a parent or carer	22/64 (34.4%)
Not accredited to undertake an **MUR**	3/65 (4.6%)
Difficult / impractical to consent to the **NMS**	42/63 (66.7%)
Not funded to undertake **NMS** with a parent or carer	19/62 (30.6%)
Not accredited to undertaken an **NMS** review	2/63 (3.2%)
Not confident in reviewing a child's medicines	7/59 (11.9%)

Respondents were invited to list any other reasons for not undertaking a medication review. Eighteen (23.7%) participants provided additional information. The ability of a child to engage with a medication review was mentioned as a barrier by 6/18 (33.3%) respondents. One (5.6%) respondent acknowledged this but had undertaken an MUR with older children:

"*Have to judge if they can understand your counselling and are capable of putting this in to action. Have carried out MUR on patients fourteen, fifteen, sixteen years old but not younger."* Participant 124

One (5.6%) participant felt that parents already had adequate knowledge of the medication that their child was taking:

"*Parents have received adequate knowledge and training from the hospital or GP and already are aware, or claim to be aware, about the medicine their child is taking.*" Participant 185

Another four (22.2%) respondents identified that the child is not always present when carers collect the prescription from the pharmacy. One (5.6%) respondent believed that this did not allow for a full picture of the patient:

"*Can't always achieve an honest picture of patient's condition and improvement even through representative.* Participant 344

Three (16.7%) participants did not believe that they had enough time, 1 (5.6%) questioned the competency of pharmacists to undertake the task and 1 (5.6%) did not have a counselling room.

Two (11.1%) participants identified having set targets as a barrier to undertake medication review in children/young people because the consultation would not count towards such a target.

"*Usually parents control dosing and a review with a parent/carer does not count towards targets and unless any concerns not usually reviewed.*" Participant 222

One (5.5%) respondent cited litigation as a reason for not undertaking medication review in this group of patients or parents/carers. They did not provide any additional context to their answer.

4.4.4 Adherence to prescribed medication

Participants were asked what experiences had been personally reported to them by a child/young person or their parent/carer relating to adherence. The issues presented to community pharmacists in this study relating to adherence to the prescribed regimen are listed in Table 14.

Table 14 Reported Issues Relating to Adherence

Adherence Issue	N (%)
The patient/carer had decided to stop taking/administering the medicine without informing the prescriber.	24 (31.6%)
The patient/carer had decided to reduce the dose taken/administered without informing the prescriber.	19 (25%)
The patient/carer had decided to increase the dose taken/administered without informing the prescriber.	9 (11.8%)
The Patient/carer had forgotten to take/administer a dose.	36 (47.4%)

Fourteen (18.4%) participants provided additional reasons that they had come across in their practice. These were the impact of side effects (6, 42.9%), lack of efficacy (4, 28.6%), taste (3, 21.4%), a concern about a dose being too high (1, 7.1%) and the impact of being a working parent (1, 7.1%)

One participant (7.1%) considered the use of medication at school to impact on adherence:

"*Not convenient to take medicines to school. Misconceptions about steroid inhalers affecting dose.*" Participant 258

4.4.5 Information requirements

Participants were asked what information had been personally sought from them by children/young people or their parents/carers regarding long-term medication. The type of information requested is presented in Table 15.

Table 15 Information Requested from Participants

Information Need	n (%)
Indication for the medicine.	59 (77.6%)
Information on the dose regimen.	63 (82.9%)
Information on how to take/administer the medicine.	64 (84.2%)
Information on the adverse effects of the medicine.	58 (76.6%)

Twenty-one (27.6%) participants provided additional information requested by patients or their parents/cares. These were the duration of treatment (3, 14.3%), interactions between medications (2, 9.5%), changes in brand/manufacturer/packaging (1, 4.8%), safety of the medication (1, 4.8%), if the medication was the most appropriate for the condition being treated (1, 4.8%) and using a medication at school (1, 4.8%).

"*Information request regarding the timing of doses (i.e. was it necessary to take a supply to school), whether to take it with or after food, could the taste be improved, potential side effects to look for and tell school about.*" Participant 83

One (4.8%) participant believed that information about side effects was not generally provided by the prescriber:

"*Patients (young patients) and their carers are usually more concerned with side effects of medication as opposed to the indication and administration as they have this explained more thoroughly by the doctor.*" Participant 162

4.4.6 Reported experiences with medication use

Participants were asked what experiences had been personally reported to them by children/young people whilst taking long-term medication or by their parents/carers. The issues experienced by children/young people, or their carers, when using their medication are listed in Table 16.

Table 16 Issues Experienced During Medication Use

Reported Issue	n (%)
The patient/carer was experiencing administration difficulties.	51 (67.1%)
The patient/carer was experiencing difficulties obtaining supplies of the medicine from a community pharmacy.	47 (61.8%)
The patient had experienced adverse effects.	39 (51.3%)
The patient's General Practitioner was unwilling to prescribe a hospital recommended medicine.	27 (35.5%)
The patient/carer was experiencing difficulties obtaining supplies of the medicine from a hospital pharmacy.	10 (13.2%)
The patient/carer was experiencing difficulties obtaining supplies of the medicine from a homecare provider.	7 (9.2%)

In addition, 2 participants had experienced problems with the use of 'specials' (unlicensed medications manufactured to meet the needs of an individual patient):

"*GP/Commissioning bodies reluctant on cost basis to prescribe specials –often referred back to the hospital pharmacy.*" Participant 179

"*Issues with GP wanting to prescribe cheaper tablet version of medication, asking patients/parent to crush tablets rather than prescribe the more expensive liquid versions.*" Participant 306

One participant cited a lack of efficacy as an issue experienced by their patients.

4.4.7 Additional experiences not included in the questionnaire

Participants were asked about any personal experiences not covered in the questionnaire. Sixteen (21.1%) participants provided further insight from their own experiences.

Four (25%) participants highlighted themes around special/unlicensed prescribing and the need for additional information on medication:

"*Licensing issues surrounding medicines for children and can mean difficult dosage regimens of licensed medicines due to lack of alternatives.*" Participant 222

"*More information from manufacturers regarding flavour of liquid medicines and whether can be mixed with anything to improve flavour such as fruit juice or mixed with food.*" Participant 83

Better communication was cited by 3 (18.8%) participants:

"*Greater co-ordination between hospital pharmacy and on discharge viz supplies of specials/costs to pharmacy and notes regarding any supply issues.*" Participant 179

"*Patients/parents should be advised by the prescriber on the expected effects of prescribed medicines and the time scale in which to be able to see the effects. Also, pharmacists could regularly stress the dosages and any common adverse effects as a routine. Very often the medicines are packed in bags and handed over which may not always be the best way.*" Participant 16

Remuneration/cost was identified by 3 (18.8%) participants reflecting the current restrictions on applying formal medication review in children.

"*NMS/MUR would be useful for children/young people. This should be remunerated in the same way as other MUR/NMS services.*" Participant 150

Two (12.5%) respondents felt that parents required greater confidence in the prescribed medication.

"*Convincing the parent/carer that the medicine will help the child.*" Participant 260

"*Scales using illustrations could be used to hold conversations with children re their medicines + medication. Visual aids help children express their feelings + concerns to help hold honest conversations.*" Participant 344

Two (12.5%) respondents reinforced the issues around the flavouring of medicines and 1 (6.3%) respondent had experienced their GPs dosing medicines incorrectly due to them not weighing the child. One (6.3%) suggested that specialised pharmacies may help:

"*Specialised pharmacies for certain conditions for children, where care can be more tailored to the individual.*" Participant 263

4.4.8 Additional support

Thirteen (17.1%) respondents suggested additional support that would help them better care for children taking long-term medications. Three (23.1%) listed further support for undertaking a medication review in a child/young person.

"*Best practice guidelines on MUR and NMS for children of variable ages, maturity and abilities.*" Participant 344

Three (23.1%) identified access to medical notes and 2 (15.4%) suggested greater support for formulation issues.

"*Where to obtain the most cost effective special. Exchange of notes regarding product specifics. How not to fall foul of the commissioning body with a warning letter of the cost of a special."* Participant 179

Two (15.4%) identified that further support was needed for patients/carers and 2/13 (15.4%) participants particularly supported the concept of undertaking medication review in this age group.

"*If an annual review with a child and a pharmacist (+guardian) was essential this would really help especially young children with diabetes who's parents overstock as they worry the child may run out."* Participant 185

One (7.7%) suggested that a critical review of paediatric prescribing in the community be undertaken.

"*Critical assessment of prescribing in the community for this age group would be interesting which may prompt a further clinical input by the community pharmacist.*" Participant 16

4.5 Discussion

This study obtained a response rate of 21.5% (76/354). The concern associated with a low response rate is the possibility of introducing bias.[55] Response rates in published survey research among community pharmacists does range from as low as 20%.[53] Little information was known about the non-responders other than the type of pharmacy that the questionnaire was posted to. There was no statistically significant difference in the proportion of large multiples in the non-responders group compared with the responder's group. On telephone follow-up of non-responders following the first mailing 15/328 (4.6%) declined to take part in the study. The most common reason for declining to take part in the study was due to a lack of time (13/328, 4%) rather than any objections to the content of the questionnaire.

The questionnaire was initially posted to 155 (43.8%) large multiples and 199 (56.2%) smaller community pharmacy chains/independents. This is similar to the national profile of community pharmacy employment in which 40% of community pharmacists are employed by a large multiple.[73]

4.7% of all prescription items dispensed in community pharmacies in 2014 were for the young population under the age of nineteen years.[74] Since 2004 there has been an increase of 0.5 million prescriptions for this age group.[74] Most respondents (56, 73.7%) in this current study encountered children or young people taking long-term medicines at least once a week with 67 (88.2%) at least once a month. Given the national trend it is likely that community pharmacists will encounter an increasing number of prescriptions for children/young people in the future.

The current guidance around undertaking NMS and MUR consultations does not preclude the inclusion of children/young people if they are competent to consent but does exclude parents/carers.[47 49] A review of the literature did not identify any published research relating to medication review in children.[75] However, this current study found that around a fifth of participants were undertaking medication reviews in this cohort.

Very few participants felt that they were not confident enough to review a child's medication. The finding that the main reason for not undertaking a medication review related to perceived difficulty in gaining consent is worthy of investigation. Further support for pharmacists around the consent taking process could be provided by the professional bodies such as the RPS. The requirement for these services to be targeted at patients taking specific medications, not all of which will apply to children/young people, may further restrict access to the service.

Whilst most participants had not completed a medication review with a child, they had experienced a number of paediatric related medication issues in their practice that could fall within the remit of a structured medication review. These included adherence, information needs, adverse effects, formulation issues and obtaining further supplies. There was a similarity here with Study 1 of this programme of research. This identified that parents and patients searched for further information commonly on adverse effects, to answer medication specific questions and for further reassurance re the choice of therapy. Study 1 highlighted that information needs occur early following the initiation of a new treatment. This study has demonstrated that community pharmacists are utilised as a resource for medication taking through their direct contact with children or their parents/carers. The Pharmaceutical Service Negotiating Committee (PSNC) could help to enable change to formally allow parents/carers to access the current medication review services for support with their child's medication.

A study of adult patients prescribed a new chronic medication found that once a patient has experienced their medication, they gain some knowledge of what it does to them and new questions arise.[20] The information gap created when patients have experienced their new medications, developed new questions and how the patients then resolve these questions may lead to inappropriate non-adherence. In this current study, participants had experienced patients, or their parents/carers, directly reporting to them that they had either themselves, or through a decision made by a parent/carer, stopped treatment or changed the dose without first having sought advice from the prescriber. Overall, these intended changes to adherence were reported more frequently than forgetting a dose. Research is required to further explore intended non-compliance in this group. This also supports the findings of Study 1 where intended non-compliance was also reported, for example not initiating or delaying starting treatment.

Participants indicated the types of information that they had personally been asked for from paediatric patients and/or their parents/carers. More than three quarters of respondents indicated that they had been personally asked about each of the indication, dose, administration and adverse effects of a medication being taken by a child. A number of

issues were also reported to them, during treatment, relating to a child's medication(s), in particular: administration difficulties, difficulties obtaining further supplies, adverse effects and the patient's GP being unwilling to prescribe a hospital recommended medication. Whilst some of these issues may be more common to paediatrics, such as the difficulties obtaining further supplies of a medicine[43] or administration difficulties[66] most will fall under the current purview of the NMS and MUR services.[47 49] Current information resources on using medication in children aimed at patients and parents/carers are available from www.medicinesforchildren.org.uk. This is a partnership between the Royal College of Paediatrics and Child Health (RCPCH), Neonatal and Paediatric Pharmacists Group (NPPG) and Wellchild.[76] However, it is not known how this resource is utilised by community pharmacists and greater promotion to this group by the NPPG and RPS may be beneficial.

Whilst this current study has demonstrated that community pharmacists are a resource used by paediatric patients and their carers, it did not differentiate between the ages of children or if it was the child or the carer who interacted with the pharmacist. A recent study found that pharmacists were not identified as a source of information and advice by adolescents with juvenile arthritis but were viewed more as providing a technical dispensing service.[77] Interestingly only one respondent in Study 1 mentioned utilising a pharmacist for advice with most research undertaken by participants using the internet.

Medication review is an established part of community pharmacist activity in England[78] and is becoming more common across Europe[79] based on evidence of reductions in polypharmacy and increased appropriateness of prescribing.[78] The NMS has been shown to increase adherence to prescribed medicines by approximately 10% compared with normal practice.[80] A review of interventions to improve the safe and effective use of medicines by consumers identified a scarcity of evidence in children and young people, carers and those with multiple co-existent conditions.[71] Interventions considered promising but requiring further investigation included involving pharmacists in medicines management, such as undertaking medicines reviews.[71] An extension of current medication review services to children and their parents/carers would provide an interaction with the community pharmacist to discuss medication. Indeed, this contact may be the first point at which a healthcare professional has the opportunity to intervene in the optimisation of medication use in this group of patients/carers. The findings of this present study support increasing the access of current medication review services to children, young people and their parents/carers. Further research concerning medication review in children, including minimising medicines related problems, is required.[5]

4.6 Strengths and limitations

This study has demonstrated that community pharmacists are presented with medication-related issues through their direct contact with children, or their parents/carers. The presenting issues have been shown to be those that could fall within the remit of a medication review – either an MUR or NMS type consultation.

The limitations of this study include a small sample size which may limit the validity of the data, how representative the results are of the group investigated and introduce bias. The response rate was within the range observed within published research with community pharmacists which had a lower response of 20%.[53] This current study's response rate was 21.5%. Response rate could have been improved with more than a single reminder and an on-line survey option. Consideration should also be given to an alternative method of data collection for example telephone surveys or the use of a multi-site study. In addition, the targeted mailing of community pharmacists identified from a tertiary hospital ePACT data rather than all community pharmacists may limit the generalisability of the results.

4.7 Further research

Further work is required to determine how community pharmacists could be further utilised in supporting children/young people, and their carers, with their medication. Continuing research has three main themes: to evaluate the potential benefits of medication review in the paediatric group, to explore how the daily lives of paediatric patients and their parents/carers are impacted by medication use and to explore the decision-making process that leads to intended non-compliance.

4.8 Conclusion

Around a quarter of community pharmacists are undertaking a structured medication review with children/young people or their carers. Community pharmacists are utilised as a resource regarding long-term prescribed medication use by children or their parents/carers. These interactions with community pharmacists could fall within the purview of a medication review and hence there is potential benefit to extend this service to this group.

5.0 Study 3 - A qualitative study to explore the treatment-related experiences when children and young people take regular prescribed medication

5.1 Aim

To identify the treatment-related experiences when children and young people are prescribed regular medication as follows:

- To identify the effect of the routine of taking medication on daily life.
- To determine how the formulation or characteristics of the medication impact on use and daily life.
- To identify patients and parent/carer experiences of managing adverse effects from medication.
- To identify the challenges of accessing the healthcare system to obtain and manage a child/young person's medication.
- The social challenges that being on regular medication places on the lives of children/young people and their families.

5.2 Research ethics committee approval

The West of Scotland National Research Ethics Committee reviewed and approved this study 16th March 2017 (REC reference 17/WS/0038, IRAS project ID 213615).

5.3 Method

5.3.1 Setting

This study was undertaken at Birmingham Children's Hospital NHS Foundation Trust - a specialist UK paediatric hospital which hosts 34 specialties, with 361 in-patient beds and has over 174,000 out-patient visits per year.

5.3.2 Participant recruitment

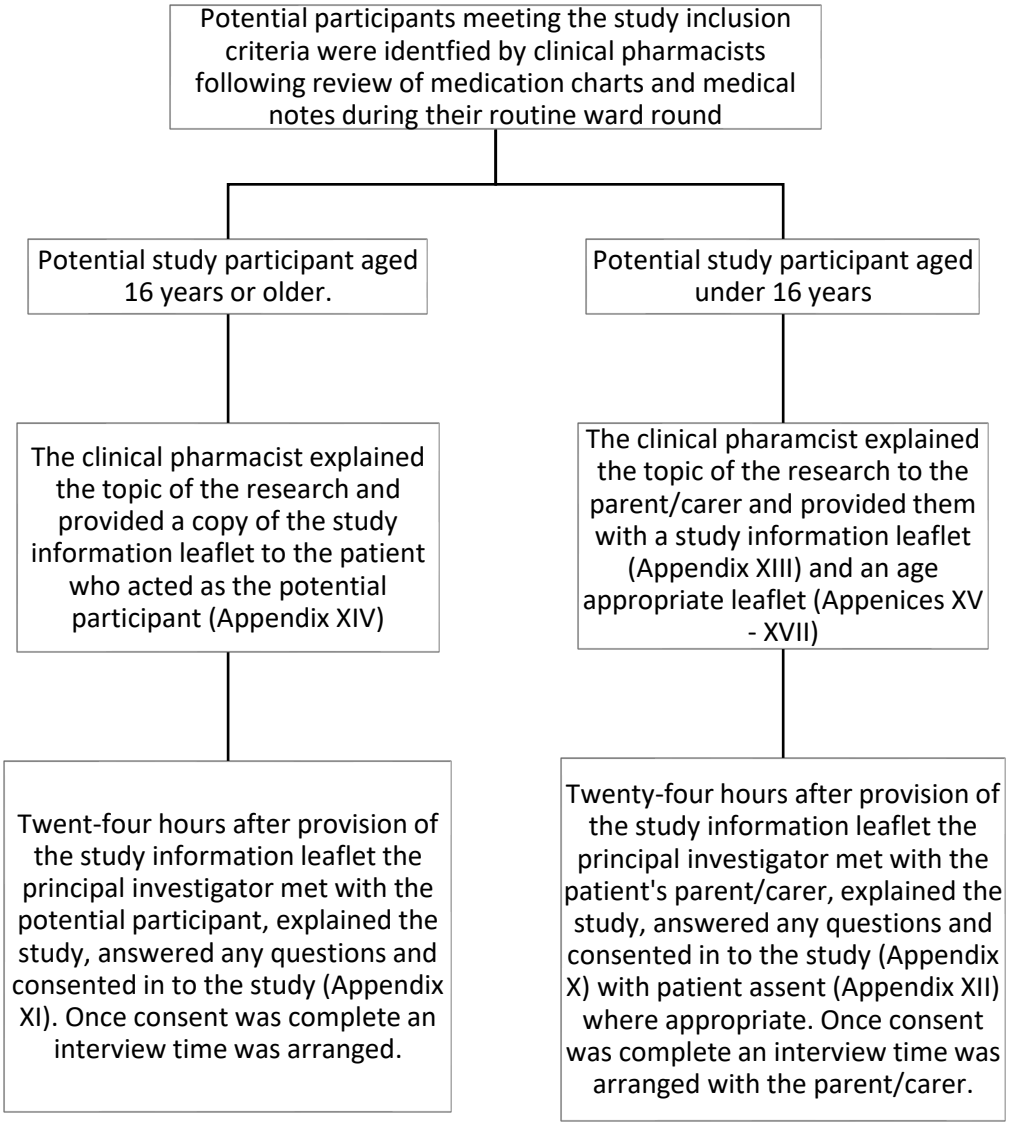
Purposive sampling of potential participants, during June to August 2017, by clinical pharmacists undertaking their daily ward round as part of the direct clinical care team. In-patients meeting the study inclusion criteria were identified from hospital medication charts and medical notes accessed by the clinical pharmacist as part of their usual duties. The study participant was the patient if aged 16 years or older, or the parents/carer if the patient was aged under 16 years. When the clinical pharmacist identified a patient meeting the study inclusion criteria, they provided a copy of the participant information leaflet (PIL) and study questions to the patient if 16 years of age or older and the parent/carer if the patient was under 16 years. The clinical pharmacist introduced the study PI to the potential participant and patient 24 hours after the provision of the PIL. The PI asked potential participants if they would like to take part in the study, answered any questions that they may have had and consented/recruited them in to the study if they agreed to take part.

Written consent was taken from the patient's parent/carer (Appendix X) who acted as the study participant if the child was under 16 years old or the patient (Appendix XI), as study participant, if they were 16 years of age or older. The consent form also included the option for participants to request a copy of the final report. Children aged under 16 years were encouraged to take part in the study interview and assent was taken from patients aged under 16 years, where they were able to sign/understand the study (Appendix XII). This was signed alongside the parent/carer consent form. Age appropriate PILs were provided directly to the parent/carer of patients aged under 16 years for them to go through with the patient to ensure patient engagement at all ages (Appendices XV – XVII). Participants were provided with the PIL and a copy of the interview questions 24 hours before the interview. The interview questions were provided in advance to allow participants time to consider their possible answers. Participants were interviewed during their in-patient stay.

Potential participants of all patient ages up to 18 years were eligible for inclusion in the study if they had been taking 2 or more prescribed medications concurrently for 6 weeks or longer outside of the hospital setting. A total of 24 participants were recruited in to the study -8 from each of the age groups: 0 to 5 years, 6 to 10 years and 11 to 18 years. This age grouping was adopted to identify the burden prior to patients attending school, during early school years and in adolescent/young people, i.e. across the full childhood age range. The sample size was chosen as the authors considered it would provide a sufficient breadth of experiences. For qualitative research, 8 participants are generally considered sufficient.[81] Participants must have been able to understand both written and spoken English. There

were no limitations on the inclusion criteria based on the formulation of medication, regimen prescribed or underlying medical condition. Participants understanding of English was assessed by the study PI, at the point of offer of entry into the study, who was able to determine their understanding of the study. The study was not offered to non-English speakers due to the short time opportunity between recruitment and the time required to arrange an interpreter. Potential participants who were intellectually/educationally disabled were not included in the study. A summary of the recruitment process is listed in Figure 2.

Figure 2 – Recruitment Process



5.3.3 Inclusion criteria

Parents/carers of children/young people aged up to 16 years and patients aged over 16 years were eligible for inclusion in the study if the child/young person had been taking 2 or more prescribed medicines concurrently for 6 weeks or longer outside of the hospital setting.

5.3.4 Exclusion criteria

Potential participants were excluded from study recruitment according to the following criteria:

- The participant was unable to understand written or spoken English.
- The participant was educationally/intellectually disabled.

5.3.5 Data collection

A qualitative method using face-to-face interviews was used as the research tool with a series of open questions undertaken by the study PI. The study PI was not involved in the care of the study patients. The patient information leaflet, consent form and questions were piloted on a parent of a child with multiple co-morbidities and taking long-term multiple medicines. The patient information leaflets for children and young people were also reviewed by the Young Persons Steering Group of the West Midlands National Institute for Health Research Clinical Research Network and the Patient Information Department at Birmingham Children's Hospital NHS Foundation Trust.

The interviews were recorded using a digital voice recorder and transcribed verbatim.

Following signed consent, the PI arranged to conduct the interview in a private room. The participant may have chosen to have other people, for example another family member, sit in on the interview if they wish. Where the study participant was the parent or carer of a child, the child was encouraged to contribute to the interview.

Demographic and background information was recorded from the patient/carer. This included the patient's age, the name and number of specialities involved in the care of the patient and usual long-term medication. The medication chart was used to confirm any missing details

regarding medication use subject to the patient's or guardian's consent. This data was recorded on a participant specific proforma along with the question set (Appendix XVIII).

Study participants were asked to describe the impact of the medication routine on their everyday lives, the impact of the characteristics of the medications being taken, their experiences of adverse effects, their experiences of the healthcare system around the prescribing and supply of medication and the social burden that medication taking has had on their lives. The detailed questions listed under each theme are listed in Appendix XVIII and were developed following a review of the literature, the findings from Study 1 and Study 2 in this programme of research and refined through piloting. A recent systematic on medication-relation burden and patients' lived experience with medicine[30] provided a framework for the subjects covered in this study. Using a semi-structured interview questionnaire can yield highly accurate data reducing the risk of bias.[56] Study participants were advised that they can decline to answer any of the questions.

If the study PI identified that medication had not been taken in accordance with the prescribed regimen he provided advice/education in his capacity as a registered pharmacist. If patient care may have been affected, with patient/guardian consent, the PI was to discuss further with the responsible medical team. Where necessary, dependent upon the individual situation as determined by the PI acting within their capacity as a registered pharmacist, the medical team was to be contacted without prior consent of the patient, parent or guardian.

Following completion of the interview participants were asked if they have any questions and reminded that they can withdraw their consent at any time.

5.3.6 Data management

All data collected was used for the sole purpose of this study and for no other purpose. The data was stored in a secure department (Pharmacy Department) at Birmingham Children's Hospital during the study. Anonymised data, consent/assent forms and study site file contents were archived at the School of Life and Health Sciences, Aston University. Electronic records of interview transcriptions were stored on a secure server on a Birmingham Children's Hospital PC only accessible by the researcher. Paper copies of the demographic data collated from the participant/medication charts/medical notes were stored in a locked cupboard in a secure office in the Pharmacy Department at Birmingham Children's Hospital. All data was anonymised at the earliest opportunity and pseudonyms were used in place of participant names to maintain anonymity.

The data was analysed by the PI and his academic supervisor and anonymised data analysed at the researcher's private residence or Aston University.

Audio files were saved with a unique number to identify the file but nothing that could identify the study participant/patient. The initial file was saved on a secure server at the hospital. Audio files were only be transcribed by the study PI. Following transcription, the audio file was deleted.

No confidential/identifiable data was stored following completion of the study in accordance with information governance. Only anonymised interview transcriptions were retained during the study.

5.3.7 Data analysis

The transcripts from the interviews were entered into and analysed using NVivo version 11. Thematic analysis was undertaken by the PI using the six phases described by Braun and Clarke.[82] The themes identified were independently reviewed by the PI's academic supervisor and academic co-supervisor.

5.4 Results

5.4.1 Demographic/background information

Twenty-four participants were recruited in to the study. Eight in each patient age group 0 to 5 years, 6 to 10 years and 11 years and over. The distribution of patient ages is listed in Table 17.

Table 17: Age Distribution of Patients

Age in Years	Number of Patients
0.25	1
1	1
2	2
3	3
5	1
6	1
7	3
8	1
9	4
11	3
14	3
15	1
16	1

The study participant was the parent in 23 cases. In 1 case a 16-year-old patient was recruited as the study participant. Assent was taken from 5 patients who contributed to the interviews with their parents. Two were aged 11 years, two 14 years and one 15 years. The medication taken by each participant is listed in Appendix XIX. A summary of the medication taken by all patients is listed in Table 18. In total 166 medications were prescribed for patients at home in the study. The number of medications prescribed for each patient ranged from 3 to 15. The mean number of medications taken by each patient was 7 with a mode of 5.

Table 18 Medication Taken by Patients

Medication	Number prescribed
Vitamin and mineral supplementation	18
Antiepileptic	17
Treatment of gastro-oesophageal reflux disease	12
Inhaled bronchodilator	11
Treatment of constipation	11
Prophylactic antibiotics	9
Analgesia	8
Inhaled corticosteroid	6
Oral corticosteroid	6
Antiemetic	5
Nebulised sodium chloride	5
Oral antihistamine	4
Emollient	4
Pancreatin	4
Insulin	3
Nasal corticosteroid	3
Nebulised antibiotic	3
Nebulised DNase	3
Oral bronchodilator	2
Leukotriene antagonist	2
Other medications	30

Sixteen patients were under the care of 1 medical team, 4 were under the care of 3 medical teams, 2 were under the care of 2 medical teams, 1 was under the care of 4 medical teams and 1 patient was under the care of 9 medical teams.

Participants described many experiences of how taking medication impacted on their lives. These have been summarised into common themes. Participants identified additional experiences that were not part of the original interview framework. These included: the rigidity that parents demonstrated around dose times, managing dose changes in school, the internet as an information resource and for liaising with other parents and the influence of medication labelling.

5.4.2 Experiences that were related to the routine of taking medication

Seven participants advised that they had not made any changes to their everyday living to take in to account medication taking/administration. Whilst other participants explained the challenges that they experienced due to the times that medication was administered including: extending the duration of their day, arranging doses around meal times and/or other medication and maintaining a precise time gap between doses. The challenges associated with dose timings, how parents manage these and how they interpret the prescribed dose regimen are illustrated by the following 5 parents' examples.

"For me I think the difficulty is with the weekend because he wants to stay in bed a bit late for the weekend just like us. That disrupts the timings a bit because say he wakes up around 10 o'clock and then ordinarily weekdays he would have had his prednisolone 2 hours earlier so now he needs to take that and then because he needs to have his breakfast, he can't have the ciprofloxacin so fitting in the weekend we loose hours and it becomes a bit more crowded." Father of Patient 3 prescribed oral azathioprine, omeprazole, calcium/vitamin D, ciprofloxacin and prednisolone.

"…timings, like I said the two antiepileptic ones, do they become less effective at the end of 12 hours? I'm struggling with when to give the one that makes her drowsy and so I kind of want to give it her at 10 hours but I'm worried that that means there's 2 hours that she's more likely to fit." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"At the moment we're giving the Senna at 5am…because no one's telling us whether we can give it at the same time as other drugs so we've tried to separate out the drugs." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"Having to get up earlier so that he can fit all the doses that he needs in a day. We don't have to be as strict as like they are at the hospital because they have drug rounds every six hours. Where at home we can close them in a bit more but then one of his medicines you can't have anything for four hours afterwards so that's where it gets a bit…" Mother of Patient 19 prescribed oral colestyramine, senna, inhaled ipratropium and inhaled beclomethasone.

"It's a big routine we just go around. We have to keep the gaps in-between equal, night-time especially because she has to have one [medication] at midnight, one at 2am then she's due one at 6am. So obviously it's a bit tough. I have to stay up late until 2 o'clock and then I sleep after that when I've given her medicine then my Mrs wakes up at 6 o'clock to give her medicines at 8 o'clock as well. So, it is affecting us." Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.

"We have to make sure that she eats at the same time as her medication. Seven, eight o'clock at night is quite late to be eating, again, we've got to keep that space between them. One of the side effects is tiredness. So, if we give it too early in the day it will be a waste of a day because she'll be asleep at 4 o'clock in the afternoon, 5 o'clock and it's just pointless so we give it to her seven to eight." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

5.4.3 Remembering to administer/take medication

Many participants cited remembering to give their child's medication as their biggest challenge. In particular, when a new medication, such as an antibiotic, was added in to the usual regimen and where parents have more than one child to look after. Establishing a routine so that medication taking became part of usual daily activities was considered important to aid adherence.

"Once I've got my routine. I do a routine of which medicine to do. I can't say it's difficult. I suppose if she's given a new medicine like if she needs antibiotics or things that have to stay in the fridge, they're the ones that I'm 'oh! Have I given that?' because they're not in my normal routine." Mother of Patient 23 prescribed oral clobazam, chloral hydrate, topiramate, gabapentin, senna, brivaracetam, potassium chloride, levomepromazine, omeprazole and Movicol®.

Participants described a range of strategies to help them remember to take their medication. These included: using an alarm on a mobile phone or Fitbit device, parental verbal reminders, placing the medication where it acts as a visible prompt, medication compliance aids such as Dosette boxes and the use of reminder charts. As participants became used to their regime the use of aide mémoirs became less over time.

"My Fitbit. It tells me when I need to take my tablets. Before that I would forget when I need to take the tablets on time and then it would be really late when I take them. At one o'clock

my Fitbit will tell me 'I've got to take a tablet now'. I have to make sure I turn it off otherwise it will buzz again." Patient 1 oral Movicol®, cetirizine, theophylline, hydrocortisone (intramuscular if required). Inhaled salbutamol and Seretide®. Intranasal fluticasone.

"What I usually do actually especially with antibiotics because he's been on quite a lot of courses of antibiotics like the fluclox for the infected eczema and everything I just put an alarm on my iPhone the exact time we usually do it. So I'll know it will be 5 o'clock in the eveninig and 11 o'clock and it will be the same 24 hour clock wise so I just kind of leave little memos for myself because most of the time I have to wake up a 5 in the morning to give him that dose and then but then the only way I can do that is to have an alarm on so..." Mother of Patient 12 prescribed topical Cetraben® cream, Eumovate® ointment, Betnovate® RD ointment, coconut oil 25% w/w in emulsifying ointment, Dermol® 500 lotion, Dermol® 600 bath emollient and oral cetirizine.

"I tend to forget around a certain time. I tend to put my medicine next to me in my room. If I do start to forget then that's what I usually tend to do. Either set an alarm [on phone] or put it next to me." Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.

The use of a reminder chart also acted as a record of administration in some cases to help participants remember that a dose had been given.

"I made a treatment chart because before we came in to hospital he was on weaning doses of different medicines and they were weaned on different days. I could literally go down and check off what he was having and when the doses were changing." Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

"I have had to write it down. I've had to put a list, like a checklist, on my fridge to make sure that I know I gave it him as well. I didn't before and I used to feel like I was forgetting so I wrote it down so I know I gave it him or I can look at it and say 'oh, I haven't given that!'. Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

5.4.4 Taking medication at school

A number of participants described their experiences of having a child who needed to receive medication whilst at school. Some parents avoided the need for medication to be

administered at school due to perceived difficulties. These included educating teachers, transporting medication, arranging additional medication for keeping at school and school staff being unable to administer an updated dose of medication following a dose change where the medication label had not been updated in advance of a new supply. Examples of parents' personal experiences with medication and school are described below.

"The only pain is at school you can't carry injections around for obvious reasons so to have a kit with everything there and then we have a...to start with that was a pain in that I understand the doctors didn't want to give us another kit but we tried to say well look we have to remember so many things and you're saying that there should always be one on the person actually [Patient 1] is at school we need to keep one at school. The school want to keep a kit there and then we need one at home then he's got one in his bag but ideally, we should have one in our house. It was the same with blue inhalers. Obviously you don't want to over-order and you don't want to stockpile medicines. I think they're more understanding especially with an 11-year-old boy to have one or two things get lost or put down. He needs one on his person, one in the office at school, he needs one in his bag we need to make sure we have one or two blue inhalers at home." Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone (intramuscular if required) and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

"I try to avoid giving him medicines at school times because it becomes a lot more complicated when teachers have to do it. It's just obviously explaining it to the teachers, making sure that he's had it and bringing the same bottle home every night, remembering to bring it back and take it back again in the morning. It just gets a bit hectic." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

"It's just because it's not labelled correctly if she's gone to an out-patient appointment and her doses have changed. She'll have an old packet that hasn't been labelled properly, then I'm saying to [the school] but the doses have changed now. The school say well we can't give it because the dose that we've got and everything that we've got is incorrect. So, then I'm waiting a week for the prescription to come or potentially wait for two weeks for a letter from the hospital to get to the GP and then the GP to write out a new dose of medication. Quite often I'll have to keep her off school because they can't give her the new dose of medication." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

"There's a school nurse. If I go and say the dose has changed, even with paracetamol and ibuprofen, they have to do a care-plan for it and I've got to sign it. That is probably the most difficult because they will only administer what's on the bottle." Mother of Patient 23 prescribed oral clobazam, chloral hydrate, topiramate, gabapentin, senna, brivaracetam, potassium chloride, levomepromazine, omeprazole and Movicol®.

"The school like to keep the medicines in the school. So, I have to ask for two bottles of gabapentin and two bottles of clobazam and potassium as well and it's a bit awkward with the doctor, why do you need two? It's just too much hassle to be honest so that was the issue." Mother of Patient 23 prescribed oral clobazam, chloral hydrate, topiramate, gabapentin, senna, brivaracetam, potassium chloride, levomepromazine, omeprazole and Movicol®.

"It's more trying to get it around meals and if he's at school. The school won't do four [times daily medication] but they will do three [times daily medication]. Obviously, it depends on what times he's getting up and going to bed. The middle dose has got to be at specific times and there's meals and everything so I'll have to go in to the school then to give it." Parent of Patient 8 prescribed oral mercaptopurine, methotrexate, dexamethasone, ondansetron, metoclopramide, lactulose, morphine, chlorphenamine and co-trimoxazole. Inhaled salbutamol.

"When it's four times a day it's really awkward because I'm trying to give her one before she goes to school, school can only give it if you've got some form of written consent so that's quite awkward." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

One parent did describe a very positive experience about their child taking medication at school.

"His enzymes at school are managed by the dinner ladies. He takes a book with what he's got in his lunch box and how many enzymes for each piece of food. When he's eaten he'll go to them 'I've had this, this and this' and they'll tick off what he's eaten and what he's got left and they'll give him the appropriate enzymes." Mother of Patient 5 prescribed oral itraconazole, vitamin A & D, sodium chloride, ursodeoxycholic acid, montelukast, pancreatin, doxycycline and azithromycin. Inhaled salbumatol, Seretide® and tobramycin. Nebulised Dornase alfa and sodium chloride. Injected insulin.

In two cases patients described their personal experiences of taking their medication at school. Whilst both children were taken out of class one considered this to be more intrusive on their lesson than the other.

"I'm used to it now. It does become a bit of a pain at school...in the middle of a lesson, starting to need an inhaler. It does become a pain because then they'll either stop the lesson or they'll send me down to go down to the sick bay or to our secretary who looks after us. So yeah it does become a bit of a pain with the inhaler." Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

"If I get pain and I, if I'm at school, I might have to come out of lessons to take my medication but it doesn't tend to affect me." Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.

One father of a child with inflammatory bowel disease explained their rationale for not informing his son's school friends about his diagnosis:

"We don't tell them because you know what happens. At the end of the day we don't want other people to know. Especially school friends. Some of them aren't the right ones to know. If it was diabetes or something like that you would tell your closest friends so they would know what to do." Father of Patient 4 prescribed oral azathioprine, mesalazine, hyoscine butylbromide and omeprazole.

5.4.5 The use of family members to support children/young people taking medication

Participants described a range of scenarios where other family members were involved with administering medication in addition to the interviewee. Other family members were mostly partners, sometimes grandparents and occasionally other siblings. Participants listed specific medication-related activities that other family members helped with.

One parent described that she had established a second checking process with her husband to reduce the risk of error.

"My husband and I always check them together to make it easier. In the past my mum did because she was a nurse and she taught me to double check which is brilliant because there have been times when I've been tired or it's been late and we always do it as a little

group…rather than trying to do it when we're tired." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

Other people being able to support with medication administration enabled parents to be away for a period of time including for employment.

"It's like me and grandma that make them in a way so that I don't have to be there all the time. Obviously if I can't be there grandma has to." Mother of Patient 16 prescribed oral phenobarbitone, levetiracetam, carbamazepine, ranitidine, glycopyrronium and sodium feredetate.

My dad. He used to work in a children's hospital, he used to be a paediatric nurse. My dad, he's the only who will and that's just her hydrocortisone because he's sort of, when I'm at work he looks after her so that's why he has to give it to her so yeah he will administer." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

Enabling other relatives to able to administer a child's medication also allowed for overnight stays for example with grandparents.

"She's got a really responsible twelve-year-old brother who has been known to give her medication. There's been times when I've obviously not been able to but with that timescale it's quite difficult. He's really good but her dad does it a lot as well. Sometimes when she stays at nanny's, nanny gives her meds but that's why we've got her twelve-year-old brother to do it because my mum gets quite nervous about doing it because it's such big thing." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Some parents were not comfortable allowing other family members to administer medication to their child due to the complexity of the regimen and the desire to retain medication administration themselves due to the risk of it being administered incorrectly. In addition, some participants described other family members being fearful around administering their child's medication due to the risk of making a mistake.

"They do help in terms of the emollient. I don't tend to explain the steroid part to them because it's just too complicated. It's easier if I do it myself so I don't really leave that to anyone else apart from me and my husband. But the emollient they can just put it on him all day, that's fine." Mother of Patient 12 prescribed topical Cetraben® cream, Eumovate® ointment, Betnovate® RD ointment, coconut oil 25% w/w in emulsifying ointment, Dermol® 500 lotion, Dermol® 600 bath emollient and oral cetirizine.

"I'm a bit OCD. So far as I'm concerned, I'm the best. So, what I try and do is I try like if it was a weekend and my mum wanted to have him, I'd make sure that I'd got his medicines done and then she'd have him so I know he's got a period of time to be so that I didn't have to worry her. Even though she said she'd do stuff I think she's a bit nervous of it so I try and do it so no one else has to worry about doing it." Mother of Patient 19

5.4.6 Making the medication taking schedule fit around daily life

The most common response to this theme was around adjusting the timing of the medication to fit around daily activities or adjusting daily activities, in particular meal times, to take into account medication administration. In addition, establishing a routine was again identified as key to integrating medication taking in to daily life. The greater the complexity of the medication regimen the higher the impact on daily life as described below.

"Well, it's kind of spread through the day, some that he takes at different times so at any time there is something that he's taking more or less three times a day. So, he is on azathioprine, prednisolone now, [mebeverine], omeprazole, ciprofloxacin for the last four weeks, [calcium carbonate]. So because we kind of give some of them in the morning when is on the prednisolone, we give him the prednisolone and the omeprazole in the mornings and then the ciprofloxacin because it's two hours either way of milk so we say ok, breakfast, you can't take it at this time so we have to give a special time and so on so he takes it at school at his break and at night before going to bed. The azathioprine itself when he was taking it we noted that most times in the evenings he will say he has headache, so we though it could be related so we changed the time of it from when he takes it in the morning. So how about taking it before going to bed, so that's what he does with the azathioprine now and we're fine with it. Then the [mebeverine], they say 20 minutes before meals, that now is spread through the day as well. He takes usually the first at school before lunch and sometimes at home and in the evening." Father of Patient 3 prescribed oral azathioprine, omeprazole, calcium/vitamin D, ciprofloxacin and prednisolone.

Working part-time was identified as a particular benefit when having a child on regular medication:

"I think working part-time helps hugely because I'm there and I know exactly what he's had, when he's had it and I organise my time very well, I think. I have to be organised otherwise nothing's going to get done." Mother of Patient 12 prescribed topical Cetraben® cream, Eumovate® ointment, Betnovate® RD ointment, coconut oil 25% w/w in emulsifying ointment, Dermol® 500 lotion, Dermol® 600 bath emollient and oral cetirizine.

One parent admitted to administering a double dose of her child's antibiotic for the first two days back at school following a school holiday. The parent believed that this reduced the risk of their child acquiring an infection:

"The only time when we actually adjust [the dose] is when we're on like half-term. I tend to double up for a couple of days before she goes to school because I just feel that she gets poorly as soon as she goes back to school. I think she's just bombarded with viruses and in general so we tend to take a couple of days of extra before going to school and she seems to be fine then." Mother of Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.

Another parent missed the final daily dose of nebulised aztreonam to reduce the daily burden of taking medication.

"She misses the [aztreonam] on the third dose. It was three times a day. It was too much. Mum of Patient 6

5.4.7 Seeking health professional advice on the schedule of taking medication

The majority of participants had not sought any advice about their schedule of taking/administering medication. Other participants sought advice on clarifying the dose regimen and changing the times that medication was given to better fit in with daily life. A common theme was attempts to replicate the administration regimen used when the patient was an in-patient. This was found to be challenging and parents adjusted the dose times away from the hospital medication round administration times to better fit in with daily life. The impact of this was described by two participants.

"Because it seems to be here when you look at a drug chart he's having two medicines at

half 6, two meds at 12, three meds at 4 and then thinking if we were at home he's going to have set times so it would be nice if like when we come in can we have his certain meds at certain times so that when we do go home at least he's in the same routine instead of being woken up a half past six when he wouldn't wake up at half six." Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.

"The first time he went on them it was like six and six and he was in hospital for three weeks so they were doing them. When at home we were finding that hard because six o'clock it's a difficult time and morning obviously again I would have to be up early to take the medicines so they said to me you can adjust the time hourly over a few days to what time is best for you so I got to nine o'clock." Mother of Patient 16 prescribed oral phenobarbitone, levetiracetam, carbamazepine, ranitidine, glycopyrronium and sodium feredetate.

In addition, two other participants had changed the regimen themselves informing the prescriber at their next appointment. This was to improve efficacy and tolerability:

"A family friend suggested her daughter had asthma and it was probably more general asthma I guess as it gets worse at night and her daughter moved her cetirizine from the morning to the evening. So that was a friend's advice I guess rather than a professional but I just slowly moved it up." Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

"The only one we had to alter was your intraconazole wasn't it and your antibiotics because she used to take the antibiotic first thing in the morning and the intraconazole as soon as she came home from school because she found the doxicycline was making her feel a bit queasy and very, very, tired if she took it in the morning and because the urso you need to have it on an empty stomach she could come in and have a snack straight away so that wasn't working and we kind of just swapped over when she has those. So now she'll have the itraconazole in the morning before her breakfast and the doxycycline at night and she's been a lot better she's not been queasy. We just mentioned them in clinic when we saw them. We said that worked better for her when she's at home." Mother of Patient 5 prescribed oral itraconazole, vitamin A & D, sodium chloride, ursodeoxycholic acid, montelukast, pancreatin, doxycycline and azithromycin. Inhaled salbumatol, Seretide® and tobramycin. Nebulised Dornase alfa and sodium chloride. Injected insulin.

5.4.8 Researching further information about the medication

The most frequently cited resource for looking up further information was the internet. A combination of NHS websites, searches using Google and other websites recommended by healthcare staff were most commonly used. Those participants who were themselves healthcare professionals used standard reference sources. A pharmacist used the summary of product characteristics for their child's medication, a pharmacy technician and a nurse used the British National Formulary. Some participants also used other healthcare professionals such as their local pharmacist as a source of additional information. In one case a parent found out that their child had been prescribed a medication that they were intolerant of which led them to stop treatment:

"I 'Googled' them. I did 'Google' them. And, two weeks ago the consultant added a third medication in to her...clobazam. And I gave her one dose and 'Googled' it. I don't know why I 'Googled' it. Usually we've started the ball rolling and then I 'Google' it to find out, you know, well, this is happening, is it meant to happen kind of thing? And it popped up that it's a benzodiazepine and PT24 has an intolerance to benzodiazepines so I did freak out a bit by that and I stopped using that now. Google is my friend with medications." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Participants were looking up further information for themselves for a variety of reasons. These were out of general interest, to provide assurance around the choice of therapy or to seek alternative treatment options, understand how to use their medication, know what side effects their medication might cause and due to a lack of information provided with their medication.

"Initially I did yes, just on the web. Especially the [glycopyronnium]. The secretions were the main problem. I was looking up how to deal with secretions. There were obviously some other techniques, let's say tracheostomy, radiotherapy or something like that in extreme cases. But I did have a look and thought well these things are not for her actually, they're for like the very extreme stage and I looked what else there was in terms of medication and I looked around and I did find a few of them, I don't remember all of them but the Botox injection or the glycopyrronium." Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.

Two participants described their parental responsibility for the treatment that their child was prescribed and how this impacted their decision making.

“Yes. Not because I don't believe or don't trust it's just that at the end of the day we are responsible for [Patient 1] and like I said, not because people don't know what they're doing but you know you can be offered medicine especially theophylline which people don't, I know it's not regular medicine that a lot of people have so nurses have asked about it and so yes I have researched them but I, I don't understand half of it, but I've got an understanding to maybe ask the right questions and just check because we are responsible for him and we've not had anyone who’s on regular medicines in *the family, paracetamol is as far as it goes which is very rarely.”* Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

“If I need any extra information. With nitrofurantoin, he was prescribed that and I was like ‘oh, I’m sure that causes liver problems’, you know it triggered my mind somewhere. So, I had to know. I couldn’t just get my head round to give it to him I had to ring one of my friends up and say look what shall I do? what is this? And they explained it to me and they’ve done some research for me and then they’ve gone it’s ok, it’s fine and I’m ‘it’s ok, you can give it to him now’”. Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

One mother described the lack of information provided by their community pharmacy led her to research information online.

“We found that some chemists don’t put the leaflets in as well. We had a few chemists where they haven’t put the medication back in the boxes when they’ve labelled them so we’ve just had bottles come home. We’ve had no leaflets or nothing so luckily I Googled them so I know what to look out for.” Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Other participants avoided using the internet to search for medication-related information. This was due to the fear of finding out something that would cause them additional concerns:

“When you have a long-term [medication] child you try not to get too medical. It’s hard to explain but you don’t want to know about everything because, like her diagnosis, you learn that the internet is quite damaging and conflicting and it can say anything anywhere and it doesn’t mean it’s true. So, it would be better to have just one source.” Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

The duration that their child had being taking their medication influenced what additional information was sought. Parents of patients who had been taking medication for a while advised that they had looked up further details early on when their medication was first prescribed but not recently:

"Yeah initially I did when he was first on it just to see, obviously piece of mind to see what side effects they cause or what other forms they come in like what's the other options especially with the sirolimus because obviously there's certain things you can mix it with erm so I did kind of have a look." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

Participants described differing experiences of using on-line support groups/forums. These were accessed to meet other people in a similar position and as a source of advice. Whilst helpful for some they created more uncertainty and anxiety for others reading through other patient's experiences of medication, if other children with the same condition were taking different medication than their child and where practice between hospitals differed. Three parents' personal experiences of using internet support are described below.

"I've joined a parenting group and I thought it would be nice to talk to other parents in the same position and they were saying things like if you give too much Creon then it will do this, if you, you need to provide this sort of thing and it, you know they were sort of doing this and then I ignored it in the end and I thought, you know, it's probably best not to listen to you. Listen to the professionals. Yes. I think they were trying, thinking they was helping but they wasn't." Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

"Different heart mum's groups. They'll say they were on captopril but now they're on something and I'm like well, what's that then is it like captopril so I'm thinking why is your daughter now taken off captopril and put on to this one and I'm thinking can't [Patient 15] be taken off captopril and put on to this one because the side effects and stuff. So, like a lot of the meds he's on, obviously with his liver and kidney's and everything and then a mum will say well we've been switched to this one because there's less." Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.

"I'm on a forum for her condition, great at first. Great Ormond Street were saying with the hydrocortisone that their patients they have erm they go in for a cortisol profile. Just because [Patient 21's] under this hospital and they do serve this area I've asked them, I asked the

consultant did they do it for her and they said no because that's not their policy. Obviously in that terms thankfully [Patient 21's] ok the majority of the time but that is...you do sort of think well what is best. That's just what they do at Great Ormond Street Hospital they do that it's just that some of the parents would say well this child's in for twenty-four-hour profiling and you sort of query it." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

One parent utilised a Facebook page for epilepsy and found that the reassurance provided by the group reduced the need for her to contact her child's medical team for advice:

"I actually joined a parents' for epilepsy Facebook. Sometimes you just think the doctor only has so much time with you and they have so much information that they can give you. And it can be quite lonely out there when you don't know what you're doing and Google is a good place but Google can scare the hell out of you because a lot of things on there that can make you panic. So reading about her hair falling out and the other mums and dads are saying it's fine, give it a few weeks and it will grow back it's not forever, she's not going to end up completely bald. It can be reassuring and I think as well it stops me from being on the phone to the consultants secretary going 'oh my God, oh my God she's got no hair' so I've found it quite a good page to be honest." Mother of Patient 24 prescribed prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Some participants did not wish to find out any further information themselves through concern that they might influence their decision to initiate the prescribed medication for their child. In other cases, participants were assured that the prescribing healthcare professional will have made an informed decision and thus did not consider that they needed to research any further information for themselves.

5.4.9 Experiences with the characteristics of the medication -palatability, dose, formulation and packaging

The palatability/administration of the medication

Child resistance either through disliking the taste, difficulties with administration or refusing a dose were cited as a challenge by a number of participants. The ease of administering tablets compared with liquid formulations was again mentioned. Although any pre-administration preparation, for example dissolving in water, was identified as time consuming. Parents described their children disliking using devices such as spacer devices

for inhalers and nebulisers. Tablet size also posed a problem for swallowing and some participants experienced their chid feeling nauseous while taking some oral medication including methotrexate. The willingness of a child to take their medication also relied upon the colour of the tablet with a brown colour being perceived as less palatable. Other participants did not experience any challenges around medication administration.

Patient 1 described his experience of soluble prednisolone tablets which resulted in him requested a non-soluble version due to the taste:

"Oh my gosh! I can't stand them [prednisolone soluble tablets]! They made me feel like I was about to be sick. Because you've got to put, I was on a big dose, I think it was 6 or so and I had to put them all in a cup of water and then urgh! Then we did ask for some that you could just swallow [prednisolone solid tablets]." Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

The mother of Patient 1 mentioned that she often received a variety of different brands of hydrocortisone which was problematic if she was provided with an unscored tablet making part-dosing more difficult:

"There's a thing with the hydrocortisone. Sometimes we've been given big tablets. But then you can get the smaller tablets, a different make, and they're great because they've already got the quarters cut in." Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

Patient 2 described the ease and speed of using a solid dose form:

"It takes a lot more time to deal with liquids because you have to keep drawing them up and if you're in a rush, if I'm late for school, I can just grab a tablet and quickly take it. But when it comes to liquid, I had to stay over a bit longer and draw it up and then take it. It's a bit more convenient with it being tablets." Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.

Parents personal experiences with their children declining their medication included:

"When they don't want it it's hard to make them take something they don't want especially like, the one thing that is 7 tablets [of methotrexate], he used to have a liquid and he was retching it up nearly every time." Mother of Patient 8 prescribed oral mercaptopurine, methotrexate, dexamethasone, ondansetron, metoclopramide, lactulose, morphine, chlorphenamine and co-trimoxazole. Inhaled salbutamol.

"Sometimes he doesn't like his medicines. There's one, the ranitidine, that I think's got a bit of a sharp taste that he doesn't really like but I think apart from that no, it's if he's in a good mood we're alright." Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

"He doesn't like sitting for a while and having his nebuliser, he doesn't like it. So, I think out of everything that is probably the most difficult. He knows how to use his inhaler himself so that's sort of easier as before he wouldn't have it with the mask over his face." Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

"Looking at his new medication. You look at the tablet form of the warfarin. We've asked him because he's very particular because of the way he is with, what's the word, visual, so he'll see something brown in the tube and he'll be like 'I'm not touching that!'. So, we've sort of asked can we have the liquid form." Father of Patient 15 prescribed oral captopril and inhaled salbutamol.

"He has off days when he doesn't like the taste of certain medicines. He's on sirolimus, which you may know is very vile tasting, not a very nice smelling medicine and sometimes we struggle. He's had it for two years and he still struggles with it. We try to get over the whole texture of it because it's quite thick and oily. Just battling with that and making sure he keeps it down so we literally give one and quickly give the other on top so the taste of it goes away quickly. Sirolimus has to be one of the hardest medicines to give him, it has to be." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

Another parent described the difficulties that she experienced applying topical preparations:

"It's horrible having to apply ointment, absolutely horrible. It sticks to you, it sticks to their clothes and you can't spread it as easily as the cream. I've got the cream actually so I might just switch over to it. I'll put it on large areas, obviously it's his whole body, so trying to apply

the ointment I feel as though I apply more ointment than I do with the cream. It's just the stickiness I can't get rid of it off my hands." Mother of Patient 12 prescribed topical Cetraben® cream, Eumovate® ointment, Betnovate® RD ointment, coconut oil 25% w/w in emulsifying ointment, Dermol® 500 lotion, Dermol® 600 bath emollient and oral cetirizine.

Resolutions to the challenges experienced with palatability and medication administration

A variety of methods were described by participants to aid their child's medication taking where they encountered resistance due to taste or other reasons. The benefit of having a feeding tube (gastrostomy or nasogastric tube) for administering medication was cited as essential on some cases:

"If she doesn't have a [nasogastric tube] then it's really difficult, she won't have her medicines. That's the main thing she needs her [nasogastric tube] for. She won't have the medicines otherwise." Mother of Patient 13 prescribed oral omeprazole, penicillin V, aciclovir, atorvastatin, sevelamer, alfacalcidol and ondansetron. Injectable darbepoietin and ergocalciferol.

Other parents used distraction techniques, persistence and encouragement.

"I think with the Patient 14 situation it depends up…may be give him 5, 10 minutes, try again or try and maybe put the tele on, distract him a little bit, get him a book, or you sing a song you know just something to try and occupy him." Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

"At home we do three small syringes of the Tegretol and two small syringes of Epilim. So, she counts and she knows after three it's done. It's become a bit of a game, a routine that we have to get her in to and when we add in an antibiotic it's just like 'oh no! What are we going to do with this?'. We find a lot of distraction works so it's just like when she's engrossed in a T.V. programme or her iPad. It's like 'Patient 24, open your mouth' and in it goes. We kind of do it that way." Parent of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

"Bribery sometimes, blackmail, taking things away from them, stopping them doing things just as you would any badly-behaved child I suppose." Parent of Patient 5 prescribed oral

itraconazole, vitamin A & D, sodium chloride, ursodeoxycholic acid, montelukast, pancreatin, doxycycline and azithromycin. Inhaled salbumatol, Seretide® and tobramycin. Nebulised Dornase alfa and sodium chloride. Injected insulin.

Parents also tasted the medication so that they could empathise with their child's experience. Whilst others masked the taste or requested a change in formulation.

"We try and be a bit understanding. We try and think he has to have them so the medicine or milk, whatever he's coming home with we'll always try and have a little bit just to get an idea of what he's sort of tasting. We were quite shocked that he'd done so well with the captopril weren't we? Because that wasn't a good taste." Father of Patient 15 prescribed oral captopril and inhaled salbutamol.

"Being an anti-rejection, you can't not keep it down, you have to keep it down so we literally give one and quickly give the other one on top so the taste of it goes away quickly." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

"With aciclovir I went to the doctors to get him the liquid. Then he decided he'd prefer the tablets. Just trying to make it fun with the tablets like the way he calls it magic [when swallowing a tablet], it was 'wow, that was magic! Well done'. That seems to keep him happy, he wants to show everyone his magic. He even tells his friends about his magic as well." Mother of Patient 8 prescribed oral mercaptopurine, methotrexate, dexamethasone, ondansetron, metoclopramide, lactulose, morphine, chlorphenamine and co-trimoxazole. Inhaled salbutamol.

Managing the number of doses taken each day

Whilst some participants did not experience any challenges associated with the number doses administered each day there were many other participants who described the difficulties that they encountered. The frequency of administration was identified as an issue. A four-times-daily dose regimen was found to be the most problematic to adhere to due to the time available with daily activities such as school. Restrictions on when a medication can be given in relation to food and other medication was also highlighted as being difficult to manage. Over time, familiarity with the medication regimen did make it more manageable.

The impact of medication on play and after-school activities were described by 2 participants.

“It was difficult to try and fit all of his medicines in a day and especially being at a young age as well. They don’t want to sit around and have their medicines. If they’re in the middle of playing they don’t want to automatically go and have the medicines.” Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

“If I only take it once a day it’s easier for me to take it and then just forget about it you know what I mean. Whereas when I get home from school I have to be like ‘oh I have to get home to take it’ if you know what I mean. I can’t like do anything [after school].” Patient 4 prescribed oral azathioprine, mesalazine, hyoscine butylbromide and omeprazole.

Experiences with the medication packaging

Most participants did not experience any difficulties with the packaging of their medication. Where participants had experienced problems, these were due to a range of issues. Participants described the challenges associated with travelling with their medication, especially with large bottles. Participants also expressed concern about medication waste which was a consequence of having large bottles dispensed for them disproportional to the dose being taken.

Two participants described the hazards of transporting glass bottles.

“Like I say, sometimes we’ve had it where they haven't come in boxes and trying to transport four or six glass bottles home in a carrier bag, we did get them once sent home in a paper bag in just bottles. I was thinking are you off your head that's going to last me two minutes before I get to the car so I kind of make a mark now of pharmacies that do that and I don't go back to them.” Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

“I mean sometimes the glass bottles are a problem because when we go out and you've got to take them out with you. The glass bottles can be a bit of a problem with weight. I mean we've just been on holiday and obviously trying to carry glass bottles and then the whole thing about they come like sodium bicarb I had 100mL size bottles and I had like 30 or 40 bottles and I'm trying to carry them and a cool bag. That's only the odd occasion though because we were going on holiday. Otherwise I mean the sirolimus comes in glass bottles if it can it would be better in a plastic bottle because if you're going out you can just put it in your bag and not worry about it banging in to something else and breaking that's the main

thing otherwise it's fine." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

One participant also mentioned the benefit of a small compact formulation for carrying around in her purse:

"There is a certain make. They're more difficult to take and the packaging is much bigger so you don't want that really. You want something that's compact if you've got quite a few things. Also, in my purse the smaller tablets, the smaller packaging is great. It's got perforations in so you can break off a couple of tablets. So, for me in my purse I always know that I've got a couple of spare tablets if we're out somewhere." Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

A further three participants described how they wasted medication through no fault of their own.

"The phenytoin, when that came we always had massive bottles of that and as I say I just chucked loads of it away." Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

"The fact that you can't get the anti-sickness in a smaller bottle. They give you a big bottle, sometimes he won't need it that often. So, by the time it's out of date a month later there's nearly a full bottle…it's wasting for them." Mother of Patient 8 prescribed oral mercaptopurine, methotrexate, dexamethasone, ondansetron, metoclopramide, lactulose, morphine, chlorphenamine and co-trimoxazole. Inhaled salbutamol.

"Yes, it's become like a job. Which is fine, we're happy to do it. But I what's on my mind is actually we have actually wasted a lot of stuff because of how we obtain it. For example, he was on phenytoin for a time, only on a very small dose and it was a weaning dose but then I'd put in an order for that and I actually wrote on it that we only needed a small amount but they sent us like three massive bottles so two and three quarters of that just got thrown away." Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

Accessing the medication was found to be difficult for some, for example opening an ampoule or a 'click-lock' lid, was problematic.

“The pump on the Cetraben's annoying because it says 'twist and press' for the pump then when you need multiple applications and you've got a wiggly baby there and you're like 'oh quickly' and then it automatically switches back to the lock when you pump it up so that's annoying. It's rather, I'd rather it just stayed in one place like the old Diprobase that was good maybe it's for infection control actually because it locks off doesn't it. It's really annoying, I struggle with it every day and even at night because when he's scratching at night and he cries literally all night the only thing I can do to is put cream on him because it's so scratchy I don't know what else to do erm but getting that pump when you're half asleep and then it locks and then try to do it and all of a sudden you press too hard and it goes all over the bed.” Mother of Patient 12 prescribed topical Cetraben® cream, Eumovate® ointment, Betnovate® RD ointment, coconut oil 25% w/w in emulsifying ointment, Dermol® 500 lotion, Dermol® 600 bath emollient and oral cetirizine.

“Yes! Even mum can't open some of the child proof caps sometimes. We've had one at the minute, I think it's the vitamin A&D because it's one of these sealed units you've got a tag to pull off all the way round and I've had one that's actually broke on me and now I can't get in to this bottle of vitamins at all. I've obviously go to take that back to the pharmacy and say look what do I do here because I've got to get in to these and I can't it's come off completely.” Mother of Patient 5 prescribed oral itraconazole, vitamin A & D, sodium chloride, ursodeoxycholic acid, montelukast, pancreatin, doxycycline and azithromycin. Inhaled salbumatol, Seretide® and tobramycin. Nebulised Dornase alfa and sodium chloride. Injected insulin.

Some participants expressed the concern that they had felt with the labelling attached to their medication for example the addition of a ‘cytotoxic’ sticker caused one participant to decide against taking their medication. In another example, an ‘unlicensed medication’ sticker was attached to a bottle of phenobarbital.

“When we got it from the pharmacy, we looked at the box and it had a label on it that it was a cytotoxic and agent and we didn't know about it and we were like we don't really know what to do. I changed my mind in the end.” Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.

“I think the other thing was his phenobarbital coming with a great big label on saying ‘unlicensed medicine’ and certainly my mum one day saw it and she was like ‘oh my gosh! what are they doing?’ I tried to explain. Whilst obviously I’ve got a bit of understanding of that but actually if we were completely naïve, I think that would actually have been quite

frightening. Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

Anxiety was also caused due to the differing packaging that different brands of the same medication came in:

"The ones that are given from here [hospital] are always different from the ones that the doctor [GP] gives me. Like packaging and even the colour of the medicine in some cases which can cause a little bit of 'which one's that?' sort of thing." Mother of Patient 23 prescribed oral clobazam, chloral hydrate, topiramate, gabapentin, senna, brivaracetam, potassium chloride, levomepromazine, omeprazole and Movicol®.

Parents also identified difficulties around the storage of medication. These included the space available, maintaining a suitable storage temperature and securing the medication away from other siblings:

"I have, you'll see I've got drugs cupboards and I keep it there so it's where to put it at home away from the other children. Our result to build our own cupboards at height. You know, some of my friends have bought metal cabinets and things. So it's where to keep it can be a problem." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"Definitely the worry of the other children in the family getting hold of them. Particularly now that she's on [buccal midazolam] because it has to be at hand but it's a dangerous, dangerous drug and we have a three-year-old. That worries me." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

5.4.10 Experiences associated with changes to the brand and/or manufacturer of the medication

Few participants described any challenges if the brand or manufacturer of their medication changed. Some described intolerance to different brands. Those on medication that requires them to maintain the same brand where aware of this need although in one case the community pharmacy was not consistent with the brand of sodium valproate and carbamazepine supplied:

“We have to try and keep to the same brand but we've found a lot of community pharmacists try and do it, give us a different brand. Even, to the point now the actual GP puts it on the prescription, Epilim only and Tegretol only. Also, as well, Epilim liquid and syrup they get interchanged. Luckily, they don't have a major issue with her and she can...it's just the syrup isn't good for her teeth, it's quite sugary and quite think to dispense to her. However, we do find one week we'll get liquid and another we'll get syrup but obviously it's what they can get in. So yeah, that's another problem.” Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Others described an uncertainty about whether they were receiving the correct medication when the manufacturer had changed, difficulty using the correct name of their medication when making requests for further supplies:

“There was one change with his Creon packaging and I was a bit wary, I didn’t know what it was because it had got foreign writing on and I was a bit...but when I asked they said they'd changed their manufacturer but it's literally the same stuff but it’s a different packaging so it was ok.” Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

“I'm worried that it's not the same. It sounds stupid but it was the hydrocortisone bottle and it came out pink. And she normally has clear. On the label it was another labelling issue as well. But combined with the fact that it was pink and it was labelled up as hydrochloric acid or something which it clearly wasn't but it was that combined with that I was like no I can’t accept that. I took it home, looked at it and I had to go back to the pharmacy, I'm not sure that that's what that is so you're going to have to have that back and get me another one” Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

“If I order to my GP the receptionist will tell me, I will tell the receptionist I want this one, it hasn't changed but it's actually the actual chemical name and then the label name that is a bit sometimes confusing. I would say ok I want Septrin she will say do you want the cotrimoxazole. I don't remember the exact name on the bottle but...it's cotrimoxazole that one. Names haven't changed in the label. The names stay the same but the GP reception will say which one do you want we need the chemical name. They don't go by the label name they go by the chemical name.” Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.

One child's parents described receiving different formulations of captopril which had both different storage requirements and different strengths without being informed by their community pharmacy leading to a risk of incorrect dosing:

"Captopril is a funny one because again, I don't think it bothers us that they change it but when they don't tell us they're going to change it and we pick it up and think well hang on we had 'fridge' last month so why now have we got 'cupboard'? And you're used to the boxes, you're used to what they're supposed to look like when they come and used to reading the labels about how you've got to take of that so when it comes and it's a different box and a different packaging it like well, what is this one? We don't even know what it is half the time" Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.

"And like I say, the strength-wise if we happen to have to pick a bottle up and it's a different, like I said earlier, it's not a problem again but it's very confusing going from 5mL to 1mL even though it's the same medication." Father of Patient 15 prescribed oral captopril and inhaled salbutamol.

5.4.11 The ability to administer/take the medication exactly as directed by the prescriber

Most participants felt that they were able to administer/take their medication as prescribed. Those that didn't mentioned an inability to administer their medication due to the size of a capsule, patient illness, patient refusal to take, or the timing of doses not being compatible with daily life. The other cited reason was being unable to accurately measure the dose due to a part dose from a liquid being required and the accuracy of the graduations on oral syringes.

"I do have to give one tablet which is crushed in water and then so much is given to her. I think that's the hardest one. Because you know, you crush it in 10mL of water then draw back only 1.2mL and you're not sure whether there's too little or too much of the actual powder in the syringe." Mother of Patient 23 prescribed oral clobazam, chloral hydrate, topiramate, gabapentin, senna, brivaracetam, potassium chloride, levomepromazine, omeprazole and Movicol®.

One parent was estimating the dose onto a spoon for administration.

"Now I've weaned him off the syringe and he's now taking by a spoon which is quite good. Some of the doses are 5mL. If it's 4.5mL I know it's just a tiny bit less than a spoonful." Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

5.4.12 The value of written information provided with medication

Most participants found the information provided with their medication useful. They tended to use the information leaflets provided with their medication to look up information about side effects, especially if their child was feeling unwell, or for general information when a new medication had been prescribed.

"I do when he starts something new. I do actually look at it all, flip through the whole thing but after that I don't. You don't want to keep looking at it." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

"Only when we were supposed to start the hydroxycarbamide. We did have some information but you felt that you wanted more didn't you?" Mother of Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.

Participants did not find the information provided with medication of benefit if their child had been taking the medication for a while as they were familiar with it. Others were satisfied that the prescriber had made the right decision to use the medication and did not feel it necessary to read any further information. Some participants did not wish to read any further information due to the risk of worrying about how the medication will affect their child.

"…I always think to myself the doctors should know what they're doing so if they're happy for him to have it then I should be." Mother of Patient 19 prescribed oral colestyramine, senna, inhaled ipratropium and inhaled beclomethasone.

"No, I think the more you know sometimes the worse it can be. So, the less you know the better it is sometimes. Your mind starts going, is that happening to him, is this happening to him [about side effects]." Father of Patient 4 prescribed oral azathioprine, mesalazine, hyoscine butylbromide and omeprazole.

When asked what additional information they would like participants mentioned further information about side effects and interactions between medication.

"Maybe the main side effects. The most dangerous things that might be worth looking out for and any other drugs that might be dangerous to go with it." Mum of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

In addition to information provided with their medication some participants also described their experiences of receiving information, particularly about dose changes, in clinic. Participants described being verbally provided with information about dose change regimens by the prescriber but not being able to write it down quickly enough or being provided with a hand-written note from the prescriber that was difficult to read/understand.

"I mean, I've often sat there and written it down whereas I said at one point, I did just say to the consultant 'can you jot that down for me?' because on the medications it just says 'as per hospital instructions'. Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

"We usually get a letter sent home or a scribble on a piece of paper when we've come to clinic. That's how we had to learn how to increase the dose, I think it went from 2.5 to 3 to 3.5 to 4 to 4.5 to 6 to 7 over a certain period. It was just a little scribble on a piece of paper from the consultant at first. That can be quite because sometimes the piece of paper and sometimes you get that scribble off him and the actual letter with it in so you can read it good comes about three weeks later which where you have gone three weeks down the line I hope to God that when it finally comes through I've read this squiggle correctly and remembered what he said in clinic." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

5.4.13 Experiences with healthcare associated burden -managing medication supplies

Difficulties obtaining prescriptions or supplies of medication.

Those participants who received all their medication through the hospital described the ease of the immediacy of receiving a prescription in an out-patient clinic consultation and subsequent collection of their medication from the hospital pharmacy. Participants compared this with the challenges that they experienced when they attempted to arrange a prescription in primary care:

"At the moment we're getting them from [the hospital]. As the doctor prescribes them, we just get it from the pharmacy here. If we're at home and we get it from the GP is takes three days to get it done. Three working days, so we have to see ahead if she's about to finish the medicines or like a week before that." Mother of Patient 13 prescribed oral omeprazole, penicillin V, aciclovir, atorvastatin, sevelamer, alfacalcidol and ondansetron. Injectable darbepoietin and ergocalciferol.

"It's a lot easier getting medication [from the hospital]. I'd be quite happy, I mean I don't live that far, fifteen to twenty minutes' drive, but I'd quite happily get the prescriptions from [the hospital] in the week because there's no issues. There's no drama about it whereas in the community there's been quite a few issues. Even to the point that a few weeks ago they'd said that I'd picked up a prescription when I hadn't." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

Participants receiving medication through their GP highlighted community pharmacy prescription collection services and on-line prescription ordering as being useful to facilitate the request for a medication.

"Our pharmacist has got like a repeat prescription service. We go in to the pharmacy, put in the repeats and they'll send them to the GP and they will get it back from the GP and they'll dispense it. They're also very good if the GP misses prescriptions…because they'll loan us some until the scripts actually arrive in the chemist and if it's not there they'll chase the GPs." Mother of Patient 5 prescribed oral itraconazole, vitamin A & D, sodium chloride, ursodeoxycholic acid, montelukast, pancreatin, doxycycline and azithromycin. Inhaled salbumatol, Seretide® and tobramycin. Nebulised Dornase alfa and sodium chloride. Injected insulin.

"I do all mine over the internet. I order them myself, they're sent through to the doctor, the doctor sends them to the chemist and they deliver them to me. So, I have no problems whatsoever." Mother of Patient 17 prescribed inhaled Seretide® and salbutamol. Intranasal fluticasone. Oral theophylline.

However, a number of participants described some difficulties obtaining prescriptions and medication in primary care. These included their GP declining to prescribe the medications, the logistical difficulties through delays in the repeat prescription process and delayed communication between the hospital and the GP regarding changes to medication.

"Initially yes, it was a very big problem. Trying to get the GP to prescribe something that's not listed in his bog standard BNF thing and Drug Tariff was a big issue. I think pricing was a problem as well. The cost of medicines and then adult doses because he's a renal patient, the dosing and stuff, it was a very, very big issue. He refused to prescribe anything so now I literally don't go to the GP anymore because it's just straight here and I get everything through [the hospital]. Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

"There's certain meds the GP just won't prescribe because they're like well hang on they shouldn't be on that med anyway. That's the way that they see it. Even the digoxin, when we brought the forms to the GP after he got discharged he was looking at it and like 'really! Is he on that! Are you sure!?' They associate it with adults." Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.

"The GP will give us 5mg/5mL captopril but they said we don't like giving captopril to children anyway so then when we asked to have the stronger one so he wouldn't have to have so many bottles – 'no, sorry, because we don't feel comfortable in giving you the normal captopril so there's no way we're giving you the stronger captopril'. So, if we have issues with the pharmacy getting his normal bottles, I then have to ring up the hospital and say right we've got no supply so we need some captopril and they'll give me the high dose bottle. So, then we have to thing hang on a minute, when we draw up the meds it's not 5mL!" Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.

Participants described delays in obtaining some of their medication through community pharmacy. This being due to their medication being a 'special' and hence not routinely available or were too high cost for a pharmacy to keep in stock:

"It took us a couple of months of different pharmacies until we found one where they actually said we'll put it on regularly for you. We can't get a pharmacy to even order captopril for us and that's why we end up going so far from the surgery to that particular pharmacy because they're the only ones that said yeah, we'll do it. It's too expensive, that's been an excuse, it's too expensive." Father of Patient 15 prescribed oral captopril and inhaled salbutamol.
"I have had issues before where I'd ordered a bottle of hydrocortisone but [Patient 21] has been in hospital so she hasn't needed that hydrocortisone and the pharmacy has actually phoned me up and said if you're going to keep on doing this, because she's in and out of hospital, then we won't [dispense] her the hydrocortisone because it's costing us lot of money which obviously I understand but I think it's quite unfair for them to be putting that on the

parents head. Especially when she's in and out of hospital anyway as it is. It comes out of their pocket and I understand that but I don't think it's right it's not right." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

"We can't get [phenobarbital] for two weeks and I was a bit fretful and I was like can someone just write us a prescription and I'll go and find another pharmacy and get it but...we got over it we found some. They found some in Shropshire somewhere." Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

Participants described the advanced planning that they had to undertake to arrange repeat supplies of medication to ensure that they did not run out.

"I have to go in to the GP practice to fill in a form to obtain his repeat prescriptions or anything so it's a bit clunky. I know in other areas perhaps we could order it on-line even and that sort of thing. I think some of our challenges are where we live. I think it's been really challenging so far because his medicines have been changing so rapidly and the doses and the weans have been changing but equally, I think the most challenging thing has been with, because we've had such frequent hospital admissions by the time our information has reached our GP the dosages of drugs have changed so trying to obtain prescriptions has been a real challenge." Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

"Well now it used to be you rung up say three days before you needed the prescription. You rang up the pharmacy. The pharmacy would then sort it out with the GP, sent electronically from the GP to the pharmacy and on like the fourth day you'd get a phone call to say it's all ready, packed, bagged ready to go. Now, you're not allowed to go to the pharmacy, you've got to go direct to the GP who then takes 48 hours minimum to do your prescription. You've then got to go to your GP to prescription pick the prescription up to go to the pharmacy so it takes about 5 days now to get it all sorted. And the GPs don't allow you to ring them up on the phone to do repeat prescriptions, you've got to go in or email them and they never look at their emails half the time." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

The farther of Patient 20 did not expect to experience any difficulties obtaining medication from the GP and felt he should have been informed of this possibility prior to discharge from hospital:

"The GP didn't want to prescribe except a couple as most of them are unlicensed I just can't prescribe them so we had to come back to the consultant. That was a bit surprising to me why the hospital did not tell us or why they did not give us enough stock. She missed actually a couple of doses of one of the medicines as well because it took a while to get it sorted. Had we known we would have come straight to the hospital rather than going and keep asking the GP." Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.

Additional challenges were experienced if a bottle of medication was dropped and damaged requiring a further supply which was difficult to obtain.

"I dropped a bottle once. It was a drug you couldn't get. I ended up having to plead, kind of go all round the hospitals and in the end they had one in intensive care at the Children's so I was allowed to go in the middle of the night and get this drug. So, I've had a problem that way so that's why I always have extra in the house." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"It's mainly when there's changes or if there's a problem like when I dropped the bottle of hydrocortisone. If they [community pharmacy] can't get hold of the hydrocortisone oral solution, someone at the children's hospital has given me hydrocortisone tablets previously so I've told my GPs this and the GPs have apparently red labelling that the hydrocortisone tablets can't be dissolved in water so then they won't give it to me for whatever reason, even though the children's hospital has said they can, the GPs just won't have it and won't prescribe them so rather than coming here for the oral solution I could get the tablets from them but they just will not prescribe them so sometimes I've had to ring and get someone to fax a prescription over to my pharmacy, the pharmacy are happy to dispense it but the GP just won't write the prescription for it." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

Participants emphasised the challenges with getting hold of oral syringes in primary care.

"I've got syringes that come now from the community nurses but for many years I didn't. And I've have to sterilise them, I still do by habit. We've got a steriliser we used to have to re-use the non-re-usable syringes and even now we do because you don't get enough in the community. So I would say sometimes no because you've got stoppers that have shrunk or

the words dissappear on the side [of the syringe] because you're putting it in the steriliser." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"Like we get the captopril and initially one bottle was lasting five well the life-span of the bottle which was over three and a bit weeks but we'd only get one syringe with it and our pharmacy would only give one syringe and when he was on the refrigerated one it wouldn't come in a box and you wouldn't get a syringe then you'd be asking for them. It's a nightmare. He was on 5mLs, no he was on 4mLs of captopril, we asked if we could have a couple of syringes to help us through the month because we always get a few when we come to the hospital we always are given a few but obviously they don't last long and the pharmacy says we'll put some in for you, this was obviously out in the community, we got home, opened the bag and he'd put two 1mL syringes in and he's on 4mL of captopril and we was like, doesn't really help. But then you're giving him four lots of medicine for one medication which then frustrates him because why am I having it four times." Father of Patient 15 prescribed oral captopril and inhaled salbutamol.

"I haven't got a prescription for them whatsoever I haven't got any. I have to use her [enteral] syringes for her gastrostomy I haven't had a prescription for [enteral] syringes for seven years for her. I've literally had to come up to the hospital and all my [enteral] syringes are dirty I've got none left can I can some please I've had to throw them. When you wash them continually, when you use single use [enteral] syringes and you re-wash them and re-was them until I'm like literally ok can I see the lines still and because I've got none left. I've got no [enteral] syringes whatsoever." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

The time spent dealing with the healthcare system in order to obtain medication

Participants responses focussed around two themes - the frequency with which they had to arrange ordering medication and the time it took to organise a prescription and supply. Participants described having to frequently arrange supplies of medication because the duration of each supply was not synchronised across all of the patient's medication. This often required ordering at least one of their medications on a weekly basis. The complexity of the supply route through organising a prescription request at the GP surgery, the writing of the prescription and then dispensing at the community pharmacy were cited as requiring considerable investment of time. Those participants who received their medication via the

hospital out-patient pharmacy following a regular clinic appointment did not describe any impact of this route other than the time to wait for the prescription to be dispensed.

"So much time waiting. It's become worse because I used to have a number of my doctors that I could phone up 24 hours a day and leave a note saying I'm phoning up on behalf of [Patient 9] can I reorder this this this and this. And I could do it at my leisure, of an evening when the kids have gone to bed and forget about it. Now, I'm not allowed to phone my doctor because she's not house bound. I have to phone the Boots Pharmacy. Who then phone the doctor and then it gets delivered to them and then delivered to me. That sounds ok but the Boots only go to my doctor twice a week so if I phone them on a Wednesday, I will have missed it going to the doctor until the Friday and then the Friday it won't get delivered until the Tuesday so I'm having to think two weeks ahead of time of what I might run out which isn't great. So that's difficult and then often when she's put on a new drug it's this backwards and forwards because no-ones got a record of it. It's really awkward." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"I mean, not last month, about three months ago before we went on holiday when we did have the problem with the captopril and mum had gone to the pharmacy, no, she'd gone to the surgery and she was speaking to the pharmacy on the phone talking to receptionist (at GP) the pharmacy was saying there's no prescription, the receptionist was saying there was but then the receptionist said no the doctor hasn't signed it. So, there's this whole rigmarole the pharmacist does an emergency delivery because it was already about a week behind at this point and this went on, so you said about how much time this takes this alone took three days. It's not just a half hour or five-minute call of your life it's like trips from one end of Birmingham to the other, from the surgery to the pharmacy and back to the surgery. I mean the one day she had to go from Woeley Castle to Northfield back to Weoley Castle to pick the prescription up because they said actually it's still here. I couldn't say an exact timescale but I would like to sort of say on average it's sort of at least 12 hours a month sorting, just getting the prescription sorted. Minimum of 12 hours a month." Father of Patient 15 prescribed oral captopril and inhaled salbutamol.

"All week. Five days a week. His drugs don't finish together. One will finish one day and they won't prescribe them because they're controlled and this and that so she [mother of Patient 16] has to chase them all the time." Grandmother of Patient 16 prescribed oral phenobarbitone, levetiracetam, carbamazepine, ranitidine, glycopyrronium and sodium feredetate.

"So, it's the phenobarbital in particular isn't it and we were sort of told that we could order it and obtain it within 48 hours. But subsequently actually we need 10 days so I mean we've never run out but there was once in particular it was really challenging and we had a hospital appointment so we thought great we might be able to go to the hospital pharmacy and then the hospital didn't have any did they?" Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

"Quite a bit actually because some bottles are bigger than others so it's not like I can go in with all of them and say I need all of these every month. I can't do that because some last longer than others so I'm constantly toing and froing from the doctors getting prescriptions. I'd love just to have the exact, you know, for a month and them I can go in and go I need all of them with days in advance you know. It is difficult." Mother of Patient 23 prescribed oral clobazam, chloral hydrate, topiramate, gabapentin, senna, brivaracetam, potassium chloride, levomepromazine, omeprazole and Movicol®.

Difficulties with the supplies of medicines were managed in a number of ways depending on the cause. These included maintaining a written plan to aid coordination and confirming who had prescribing responsibility.

"The GP asked a couple of times for discharge letters but he did then confirm that he can't give them and we had to get back to the consultant here. The consultant then after two to three attempts because they wanted to know which medicines they could give and those that the GP can give. So, they said this and this we can give and the rest you can take from the GP. Still, I have to go to two places." Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.

5.4.14 Receiving inadequate or conflicting information about medication

Few participants felt that they had received inadequate or conflicting information about their medication. Those that did felt that they were not told enough about access to medication outside of the hospital, how to use their medication, side effects or the type of medication that was prescribed. Examples include:

"I think it would be really nice to have somebody, you know when you have a child who is on a lot more drugs that there was a written rule because no-one does it you might have a good doctor you might not. It would be good to have a pharmacist in maybe the hospital where they have lots of consultants that would regularly just check that those drugs are up to date,

the best for that child because I'm having issues with her bowels and I really don't know which one to give, I've had conflicting advice. Senna I wouldn't touch for years because they can get reliant on it, the Movicol doesn't really suit her. The original drug she would have had which would help with the bowels it had problem with the heart so they had to take it off so I think it would be really nice if there was someone that would take the time even if the parent went in to them to go through the list of what they're on to make sure, to talk through when's a good time to give it, when isn't because it's guess work at the other end." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"Previously yes I'd say we've had inadequate information as discussed because we haven't really been told about side effects and actually dare I say the obtaining of it because I mean even I took for granted you would just be able to get it quite easily and in the first week that we went home it became very quickly apparent that actually it was going to be a bit of a challenge. I must admit I was quite shocked because being in clinic and then at the end of the week we mentioned to the [clinical nurse specialists] and they were quite flippant about it you know 'oh yes you know it's really hard to get hold of' or 'you'll get used to this' and I must admit part of me was like it would have been helpful to have been told." Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

"Yeah, at the GP so he didn't tell me to apply the steroid first I had to ask that and the emollient and I didn't know, well I suspected, not to use any soaps or bubbles or bath products but nobody specifically told me that. I was doing it before with the boys because obviously the big one was having the whole 'shabang' of bubbles and stuff and then the little one would want to so I just let them play but then it kind of got worse." Mother of Patient 12 prescribed topical Cetraben® cream, Eumovate® ointment, Betnovate® RD ointment, coconut oil 25% w/w in emulsifying ointment, Dermol® 500 lotion, Dermol® 600 bath emollient and oral cetirizine.

"Well, we have some people telling us it's really bad for him to be on [steroids] and when he's older he's going to suffer with his bones but then I'm told he has to go on them because they help him. When we went to the out-of-hours at [the local hospital] it was one of the doctors there. So, we listen to him and then we're told we needs [the corticosteroids by the respiratory team] so I'm like what do I do?" Mother of Patient 17 prescribed inhaled Seretide® and salbutamol. Intranasal fluticasone. Oral theophylline.

"I wasn't told about it being a cytotoxic. I didn't like the idea of it but I wasn't told that in the

beginning and I think if I was told I wouldn't have agreed to it." Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.

"The clobazam. We'd been told that some children don't have the reactions but we've been told that she can't have benzodiazepines. So, to be given a benzodiazepine and not under any controlled situation, Patient 24 doesn't have an allergic reaction, Patient 24 goes in to respiratory arrest. There's been a few benzodiazepines that she's tried and she's gone in to respiratory arrest. I did freak out because I thought oh my God she's at home and she's had this medication and I rang NHS Direct, they freaked out and called an ambulance because you it doesn't calm me down when they're like the paramedics are on their way. Luckily the dose got mixed up from the doctor to the pharmacy so she got given a lower dose than she was meant to." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

5.4.15 How participants were informed about changes to the dose of their medication

A common theme emerged around the timeliness that information gets to the patient's GP from the hospital prescriber. Participants described being advised of a dose change in clinic and initiating the dose change for the next due dose. However, participants encountered difficulty if the letter to the GP containing the updated dose information had not arrived in time for a repeat supply of medication. The difficulties described included running out of medication earlier, the GP being unable to update the dose instructions without clear communication from the prescriber, patients' schools being unable to administer a new dose without it being specified on the pharmacy label attached to the medication and healthcare professional uncertainty when participants advised that they were administering a different dose to the last entry documented in the patient's medical notes. Examples of parents experiences of their knowledge of dose changes not being accepted by healthcare professionals include the following:

"That can be a real pain because for instance the Buccolam because it was just a word of mouth thing, because she'd had a fit the 5 didn't work so I need to give 7.5. It was done over the phone it was done over the phone after I'd left the hospital because they couldn't get hold of the consultant, so I didn't have it on a discharge letter, so there was no proof, it was just me telling someone and when I phoned the prescriptions people at the doctors she said she can't give it you without an email or something from the hospital so then it was left for me to phone the hospital to say look they can't give it can you do an email well we're busy at the moment we'll try and get to do it later. And it's all work for me really." Mother of Patient 9

prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"It eventually goes to the GP. I had to basically do another prescription so I wrote on the repeat form that we get that he' got to have 5mL three times a day. So, then I got a call a week later from the doctor [GP] saying 'what do you mean he's got to have 5mL because he's only on 4?'. I said his cardiologist has changed it to 5mL so then they had to wait until they got confirmation and then we can get it factored in." Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.

"It's quite a while afterwards though you'll get a clinic letter that's obviously been dictated and things. Sometimes you'll get them sometimes you won't get them. And the issue that I have as well is because [Patient 21] is very much swings and roundabouts with her medication and with her bloods. With the desmopressin specifically because that changes most regularly if I've had an over-the-phone consultation, obviously with the consultant or the reg or whoever else sometimes the notes won't be updated. Obviously, it will be in the notes somewhere but they won't be updated so when I'm speaking to a consultant, when she came in today say by A&E they think oh is she still taking such and such and I'm like no, I've had a phone consultation and they're like ok. Then there's a query about am I actually giving the right times and the right amount and who was the one that gave the information so it's quite stressful in that sense because I feel like sort of not accused but I'm doing the wrong thing then." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

5.4.16 The impact of being cared for by more than one medical team on the co-ordination of appointments, prescribing of medication and ordering supplies

Most respondents did not experience any challenges being under more than one medical team. Having a single supply route was identified as key for ease of access to medication. Co-ordination through one prescriber of the main clinical team, collecting medication at hospital appointments and where all medication supplies come through the GP were identified as being the most effective supply routes for parents.

"She's not having anything from respiratory. Renal, we just get it when she has an appointment and she goes for dialysis so whenever we go there and she needs any medicines we just get it. For haematology, if she needs anything I can phone the consultants secretary and she gets it prescribed for her. So, we don't have any problems" Mother of

Patient 13 prescribed oral omeprazole, penicillin V, aciclovir, atorvastatin, sevelamer, alfacalcidol and ondansetron. Injectable darbepoietin and ergocalciferol.

"To be honest, we usually get them at his appointment. Make sure he's got enough to last so we'll be here at the appointment anyway. There'll be travel time but we would have done that anyway. But only because we've organised it that way." Mother of Patient 8 prescribed oral mercaptopurine, methotrexate, dexamethasone, ondansetron, metoclopramide, lactulose, morphine, chlorphenamine and co-trimoxazole. Inhaled salbutamol.

One participant raised a concern about a lack of co-ordination from a clinical perspective. She was concerned that each team looking after her child prescribed very independently of each other. Hence, they were not aware of the consequences of medication choice for treatment prescribed by the other team.

"I knew a different person who was under a different consultant who literally coordinated everything. My drugs are never looked at from each side, you know, if she's given something in the heart department the respiratory don't check its counteracting with their [medication]. There's been one episode quite a while ago when the heart people where happy for her to be below 80% [O_2 saturation]. But the respiratory team were very cross because that can cause lots and lots of lung...you know the pneumonias and so they organised oxygen and then it's like who organised the oxygen and then there's a lot of toing and no coordination." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

5.4.17 Experiences of the social burden experienced when a child/young person is taking regular long-term medication

How medication taking impacts on their family life including social life for example holidays or visiting family/friends

Some participants did not consider that their medication had impacted on their family life. They had been administering medication for many years and were used to it or were on fewer medications and formulations (e.g. tablets) that make travelling with medication straight-forward. The most commonly cited challenges were around travel including day-to-day and holidays. Participants described being restricted when out as they were required to return home by a certain time to administer medication along with a greater risk of forgetting to give a dose. Administering medication when out was considered awkward in the presence of other people.

"We're in a café and we're drawing up meds and everyone's looking at you thinking what are they doing! Especially when you're out and about that's the worst." Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.

The transport of medication was described as a particular problem for day-to-day travel, being out for a period of time such as a day trip and holidaying. Participants used a range of strategies to get around this although carrying refrigerated medication and large bottles remained a challenge. Some participants had purchased oral syringes with caps which they used to carry individual doses. This also reduced the risk of accidentally breaking a bottle of medication. One participant with a patient on refrigerated medication risked the period of time that the medication was transported at room temperature if used the same day.

"If we're going out for a few hours then obviously we will take the exact dose that [Patient 20] is due in a syringe. I don't know the effect, or what effect, it might have for the medicine that we keep refrigerated and we keep it for a few hours outside. I'm not sure about that though." Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.

Other participants used medication compliance aids such as Dosette boxes for holidays and others described using ice blocks to keep medication cool. Additional medication supplies were ordered by some participants in case of difficulties accessing medication.

"When you go on holiday you've got bottles and bottles and bottles of liquid whereas now when we go on holiday I can just put them in to a Dosette box for each day that we're away. It's a lot easier for me then and it's a lot less for me to pack." Mother of Patient 5 prescribed oral itraconazole, vitamin A & D, sodium chloride, ursodeoxycholic acid, montelukast, pancreatin, doxycycline and azithromycin. Inhaled salbumatol, Seretide® and tobramycin. Nebulised Dornase alfa and sodium chloride. Injected insulin.

The complexities that parents experienced when arranging a holiday for a child on regular prescribed medication are described below.

"We went on holiday. We had to have excess baggage. We had to take notes and letters from the GP to say that this is a medicine. I had to offer to drink one of them. I had to go up to the doctors a week before we flew so we had enough to take, we had to photocopy prescriptions for the airport and for any particular persons who might want them and we had to research what they might be called in another country in case we ran out of them while we were away." Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.

"Holidays is a hard one. I mean we had to plan and plan and plan. There's loads of stuff to take. We had to take ice packs and when we got there we had a cold bag with ice packs in it and obviously the ice packs were melting and we had to stop in between and get ice from different shops. Before we even got to the house we had to stop at three different stops to get ice to cool his medicines down which was really hard and then obviously the journey was longer because we could have gone straight. It was so hot the ice was melting. We had to put carrier bags on the ice in the cooler bag just to keep his medicine cool and then when I go there the labels had come off! It does affect us, I think we just suck it, take it in and carry on really. Not much other choice we've got." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

"It does make it difficult. I mean, when we went on holiday and I literally had like a big bag of medicines that I had to take with me. Obviously, I have to take extra in case, you know, any went missing or I broke one you know that sort of thing. So, it can be difficult but I think it's something you have to do isn't it?" Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.

"With days out, I can just put like his inhalers in. With holidays I have to make sure I have

rescue packs and stuff like that in case he's poorly. Got to make sure I've got enough because if I've already had my months' worth or if I've ordered I need to make sure that I've got more." Mother of Patient 17 prescribed inhaled Seretide® and salbutamol. Intranasal fluticasone. Oral theophylline.

"Holidays, yeah we're trying to go to Disneyland Paris, so we know we have to get an 'ok' off the doctor that documents her medication, and a prescription list of what she's got so we can go abroad. We've been abroad before and had to take a prescription list. You have to calculate as well how long you're going to be away for and how many bottles you need to take and what syringes you need. Military precision sometimes." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Other participants had decided to avoid holidays due to medication. This was due to the perceived difficulty in travelling with medication.

"We don't go on holiday. We were going to go on holiday in September and I contacted the hotel we would have been staying in because obviously because morphine's a controlled drug, chemo's cytotoxic, I thought I'd better speak to them first and they were fine about it being there and everything. I thought about it and it's just a lot of hassle to take all his medicines and of course we're further away from the hospital if anything goes wrong. I worry a lot so I cancelled the holiday in the end." Mother of Patient 8 prescribed oral mercaptopurine, methotrexate, dexamethasone, ondansetron, metoclopramide, lactulose, morphine, chlorphenamine and co-trimoxazole. Inhaled salbutamol.

"I haven't been on holiday yet I haven't been abroad because of that. I don't know how it works. I want, we're going to France and we're going on her first family holiday and we're only going on the Eurotunnel for four days to France because I've rang airports and because she has to have emergency injections with her constantly and I'm not happy to take her on an aeroplane even if it's stored away. I want that next to her so I probably wouldn't be able to give it at that time. And a lot of the airlines that I've spoken to won't have that so I don't know if that's just my personal experience but yeah it has stopped us from going on holiday." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

Experiences of travelling with medication

Some participants described their experiences of travelling with medication and attending events. These included the need to trust others to help with their child's medication and transporting medication, for example a refrigerated product.

"If he's going out we have a rucksack so he can take it all to a friend's house or to a film. He has to take his rucksack. It's got his injection kit for his hydrocortisone. Hopefully he'll never need to use it but obviously he has to carry it around. So, you do slightly alter what he does or he's got to be with someone who whose happy to be responsible for taking an injection kit with them." Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone (intramuscular if required) and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

"When you're in a hurry or you've got to get somewhere if you're out at a party or something that's the main time when you kind of if you're out and about that's really hard. If you're enjoying yourself doing something remembering the fact that you've actually got to stop and give him medicine before you do anything else. That kind of thing does get hard." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

"Because of the injection being refrigerated we have to obviously carry ice packs around with us. Because she's gastrostomy fed and she takes her medicines from the gastrostomy I always make sure I've got something to flush with. I constantly take a bag. I've always got a bag that's packed for her that I constantly carry around with me." Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.

Interest in medication by family and/or friends.

Most participants had experienced friends and family asking about their medication. This was out of general interest, to express concern or to offer help and support.

"It's when people see you take it and they're like 'are you ok?' and they think that there's something really wrong with you and ask if you're taking it everyday regularly." Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone (intramuscular if required) and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

“I think certainly my dad's said a few times 'is it dangerous?' I think it just got to the situation where he was just pretty much every day or every couple of days another medication was just being added in and I know my dad made a few comments about well you know do they know what they're doing but equally kind of at what point are they going to start stopping things and it just, I think it has been a worry hasn't it to our families because he is he has been on quite a lot of medication. Seeing this little tiny baby having all this medication squirted. You know it's quite alarming I think for them.” Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

“A lot of my friends ask him because they know what he's on. But other than that. What tablets he takes, how he takes them because he's always poorly so they try and show an interest in him you know what I mean” Mother of Patient 17 prescribed inhaled Seretide® and salbutamol. Intranasal fluticasone. Oral theophylline.

“They do sometimes in the sense that because of his antirejection he's immunosuppressed and so they do kind of ask 'oh what does that mean what can he do'. They're cautious, 'can he have this? can he eat this? is it ok with his medicines?' Interactions they always ask about making sure you know because not everyone else is like this so they always ask.” Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

5.4.18 Experiences of adverse effects from medication

Types of adverse effects experienced

Half of respondents had experienced adverse effects ranging from mild e.g. diarrhoea from antibiotic therapy to thrombocytopenia with tacrolimus.

“He had Montelukast in the past and that was nightmares and night sweats. The first time you went on theophylline to start with you had side effects and the hydrocortisone. I think it was the whole lot together, very sweaty, pale, stomach aches, stomach cramps. Things you can really see are there and it took quite a while for it to all settle down.” Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone (intramuscular if required) and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

“Drowsiness has been his main one I think. It's difficult with [Patient 11] because equally his

condition can cause some of what can be perceived as side effects but I think that sometimes we very much noticed irritability when he was first started on his steroids he had absolute rage for a good 48 hours. He got a really, really upset tummy didn't he. Decreased tone. His swallowing got really difficult not long after he started on the vigabatrin then it's as he's been weaned from that it's improved significantly." Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).

"With the antibiotic initially, she would have loose motions yes. The erythromycin timing is four times a day and I would say we change, I'm not exaggerating, a minimum ten nappies a day we change." Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.

"He had a side effect initially after transplant with the tacrolimus. Hence, he's been moved on to sirolimus. His blood platelets started to break down, his body started to break down his platelets." Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.

Whether adverse effects experienced by patients were known about in advance

Most were aware having being told about the effect directly by the healthcare team, through knowing other people on the same medication or through looking up the information for themselves on the internet or through on-line disease forums.

"We knew because his dad has asthma and we've got a friend whose daughter's quite asthmatic." Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone (intramuscular if required) and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

Management of adverse effects

Most participants sought advice from the hospital providing their care. This was usually a call to the nursing team within their specialty. Mild side effects were managed by the participants.

"Yes, we phoned up the [cystic fibrosis nurses] and said these tablets aren't agreeing with her. She has not had any upset stomachs until she started taking these and because they were making her queasy and stuff." Mother of Patient 5 prescribed oral itraconazole, vitamin A & D, sodium chloride, ursodeoxycholic acid, montelukast, pancreatin, doxycycline and

azithromycin. Inhaled salbumatol, Seretide® and tobramycin. Nebulised Dornase alfa and sodium chloride. Injected insulin.

"At night, if he has asthma at home at night and he's had ten puffs [of salbutamol] we then end up sitting up, we lie there trying to do something on-line, some school work or watch TV or just something normal." Mother of Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone (intramuscular if required) and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

"If you've woken up in the middle of the night and you've had ten inhalers it's difficult to get back to sleep." Patient 1 prescribed oral prednisolone, chlorphenamine, cetirizine, theophylline, hydrocortisone and Movicol®. Intranasal fluticasone. Inhaled salbutamol, ipratropium and Seretide®.

5.5 Discussion

This study has identified many challenges that children, young people and their parents experience when a child or young person is taking regular prescribed medication. Similar experiences to those in the published literature were described including adherence, regimen inflexibility, impact on social activities, travelling with medication, administration at school and arranging repeat supplies. In addition, this study has identified how parents interpret dosing instructions, challenges around implementing dose changes in school and concern about medication waste.

5.5.1 Experiences related to the routine of taking medication

The timing of doses and the extent that participants changed their routine to accommodate when medication was administered was notable. In particular, participants described starting their day earlier, finishing later and administering medication during the night-time to maintain a precise gap between doses. The difficulty of the treatment regimen has been shown to be a barrier to medication adherence in paediatrics.[21] This improves once a routine is established and may require the additional support through practical strategies.[21] Participants in this current study explained how administering/taking medication became easier once a routine had been established. This was noted in participants who had been administering medication for a number of years compared to those more recently started. Further counselling/advice to parents/paediatric patients may help identify those medications that can be given during waking hours or where there may be greater flexibility over the time of

administration. There are opportunities to do this during the prescribing consultation, dispensing and through medication review.

The most challenging aspect about having a child on medication was cited as remembering to administer/take. The consequences of poor adherence are well established.[19 21] Medication compliance aids were self-purchased by many participants in this current study. Whilst the Royal Pharmaceutical Society of Great Britain has recommended that original pack dispensing with appropriate pharmaceutical care should be the preferred option,[65] participants described how they found these to be beneficial when remembering to administer/take their medication. An additional benefit of medication compliance aids was the convenience of transporting medication when travelling. Mobile phone alarms, a Fitbit alarm and wall charts were additional reminders of medication administration. Further research is required to identify effective interventions to improve medication adherence, including those utilised by parents/patients in this study.[19] However, this current study has identified some parent/patient personal preferences for strategies to aid remembering when a dose of medication is due which is counter to that of national guidance. This highlights the importance individualising patient care especially when considering medication use at home which may be influenced by the differing daily routine of each family as well as the medication regimen.

A number of experiences and challenges were identified if medication was required to be taken at school. These were patients feeling anxious about taking medication in view of their peers, access to medication, supply of medication for use in school, participants' experience of medication errors in school, restriction on the number of doses that may be administered in school and the management of dose changes in school. School staff were found to be unable to administer the current dose of a medication if the dispensing label reflected the previous dose. This was due to a recent dose change following a clinic appointment where the medication had not yet been dispensed with the new dose. Patients with asthma and diabetes have described their experiences of taking medication at school.[41] These also included not having access to a private area to take medication and access to medication. A survey of adolescents with cystic fibrosis also identified patients not wanting to take their medication in public.[37] A study of the experiences of patients with diabetes, asthma, attention deficit hyperactivity disorder expressed embarrassment, anger and being teased when taking medication in front of other students.[40] A recent survey of medication use in schools in a region of England identified similar themes to those identified in this current study.[83] Despite there being national guidance on medication use in schools[84] there remains difficulties around a series of common themes. Further work is required to support patients taking

medication in school through better training and information for school staff and improved communication around dose changes to ensure timely updates in dose can occur in school. Guidance and support could be provided by the Royal Pharmaceutical Society of Great Britain or the Royal College of Paediatrics and Child Health. The use of technology to provide more timely information on changes to medication may be enhanced through the electronic transfer of hospital clinic letters to GPs. This is to be mandated in the UK NHS from 1st October 2018 and may reduce the time for a relabelled medication.[85] The use of community pharmacists to further support patients through direct electronic referral from hospital has been shown to be beneficial.[86] This could be adapted to include support to patients and their schools. In addition, mobile medication reconciliation apps may improve the accuracy of transfer of medication information.[87] Such technology may help with the transfer of that information to schools. Of course, schools must maintain appropriate governance measures to ensure that they are administering medication in accordance with the prescriber's wishes irrespective of the method chosen to update them with any changes to their students' medication. Further research is required to optimise patients' use of medication in the school/educational institution setting including better collaboration between schools and healthcare professionals.

Participants varied in their use of family members to help with medication administration. Parents described the complexity of their child's medication regimen being an inhibitory factor in seeking the involvement of other family members. Participants also described the need to be vigilant through their experience of managing different strengths and formulations of the same medication being dispensed on consecutive occasions. One mother had arranged a second checking protocol with her husband to reduce the risk of medication error. Whilst the investigation of medication errors was outside of the scope of this current study the challenges that parents and patients mentioned could provide potential contributory factors towards medication error. These include:

- The number of medications administered
- Arranging the correct time of administration when competing with activities of daily life
- The challenges around obtaining medication in a timely manner
- Unexpected formulation changes from the community pharmacy

- The need to manipulate a tablet formulation to obtain the required dose

- The volume of available information (including differing opinions of healthcare professionals)

- The influence of on-line support/self-help groups and the information available through the internet)

- The way that instructions are communicated about the medication administration regimen from healthcare professional to parent, for example on a hand-written note or verbally with no written information

A systematic review of carers' medication administration errors in the domiciliary setting identified that there is little information about medication administration errors in the patient's home.[88] Thirty-three of 36 articles in the review included parents and 18 of these studied only parents. The review identified a number of errors including: dosage (most common), omitted medication, wrong medication, wrong time of administration, wrong route of administration, giving expired medication and not stopping treatment. Preventative activities identified by carers in the review included planning a routine schedule and using medication compliance aids. Participants in this current study described the benefits of establishing a routine and using medication compliance aids, although this was more to reduce the challenge of medication administration rather than error prevention. The systematic review identified three interventional strategies to prevent carer's administration errors. These were demonstrations with marked oral syringes provided to a sample of parents, a series of weekly lessons on child health and home safety including medicines safety and finally the use of a transitional care nurse to coach people to manage complex medication regimens at home including a home visit to observe medication use. Support for parents of children taking complex medications regimens appears sub-optimal from the findings of this current study with the potential for error. Further research is required to determine interventions to further support this group of parents, children and young people. Such interventions may include the role of the hospital and community medical, nursing and/or pharmacy teams including how these groups communicate with each other and parents/patients. In additional, guidance specific for complex medication regimens could be developed by the partnership programme Medicines for Children. There may also be a role for the Royal Pharmaceutical Society in developing supporting material for pharmacists, parents and patients.

Whilst there were a number of difficulties described with the daily schedule of medication administration, few participants had asked a healthcare professional for help with their medication regimen. Those that did asked about adjusting the timing of administration to fit in with their daily lives. Two respondents admitted to adjusting the regime themselves and advising the medical team of this change at their next clinic appointment. Self-adjustment of prescribed medication was also identified in two previous studies[89 90] and requires further investigation to determine the extent of this observation and the support required to ensure medication use at home is both optimum and safe.

Most participants described looking up further information about their medication. The most common resource being the internet. This is unsurprising and in accordance with published studies.[91 92] The reasons for researching further information were similar to those published including finding out further information about treatment.[91 92] Consultation with healthcare professionals are often constrained by time limiting the opportunity to provide sufficient information.[92] A consequence of this is the desire to seek further information which was explained by participants in this current study. Participants highlighted that they looked up more information about their medication during the initial period of treatment but once established the need for further information was less. Other participants were reluctant to use the internet through a fear of what they may find out. In particular from commercial search engines. In addition, poor interpretation of written information about medicines, especially online information which may not be subject to quality control, could lead to poor compliance.[93] A quality assessment tool may help support children and parents to assess the trustworthiness of online information.[94] There is an opportunity at both the point of prescribing and dispensing medication to 'sign-post' parents, carers and patients to quality assured internet sites. Consistency of any information provided is important as in this current study participants cited examples of differing information provided by healthcare professionals.

Some participants accessed on-line parent support groups/forums. Support groups tended to be accessed to engage with people in a similar position to themselves and as a source of advice. This is similar to other parents of children with long-term conditions as well as young people with long-term conditions.[95-97] Varying experiences were reported with some correspondents finding these groups helpful and informative when they had questions about their medication. Other participants were concerned or uncertain where patients with a similar condition were on different medication to their own child and disliked the 'expert parent' approach taken by some members of the on-line group. These experiences mirror those of other parents of children with chronic conditions.[97] Further research has been

suggested around the input that healthcare professions may have in to on-line health forums/help groups and also the quality of information learned though these forums.[97] This current study supports the need for further research. There is a possible role for community pharmacy to support with the provision of information about how parents and patients may safety utilise on-line health groups. Supporting information could be provided by organisations such as 'Medicines for Children' which already provides supporting information on medication for parents/carers, children and young people.

5.5.2 Experiences with the characteristics of the medication

Unsurprisingly there were a number of issues identified with the palatability of medication, devices used to administer medication such as spacer devices and inhalers. The ease of using solid tablets over liquid formulations was highlighted as beneficial from both an administration and transportation perspective. The use of a feeding tube for medication administration was perceived as highly beneficial for parents to make administering multiple medication easier compared with the oral route. Regulatory changes and the increased focus of formulation scientists on age appropriate medication requires greater collaboration between regulators industry and academia to increase the pace of development.[98] The absence of child friendly formulations was identified as problematic in this current study. In order to further optimise the use of currently available formulations, in particular solid dose forms, training in swallowing medication could be provided by healthcare professionals. Training has proved successful in enabling young children to swallow solid dose forms.[99]

When asked about the challenges associated with the frequency of medication administration participants advised that they often tried to prevent this from interfering with activities of daily living. Taking a medication three times a day was perceived as much better than taking it four times a day. The additional dose required administration at school with associated challenges previously discussed. The medication regimen is a known factor of compliance in paediatrics.[2] Medication regimens which impact on daily activities have been shown to also impact on treatment adherence.[22 29 37] Patients overwhelmed by the burden of their treatment should be identified so that individualised treatment options can be developed to alleviate such burden.[31] There remains the opportunity for pharmacists through medication review to contribute to reducing medication burden in paediatrics.

When participants were asked about the packaging that their medication came in a number described how they wasted much of their medication due to the size of the supply bottle compared with the dose that they used or the number of bottles provided being in excess of

their need. It has been estimated that £300 million of NHS prescribed medication is wasted each year.[3] Globally, the total amount of medication consumed will increase by about 3% through 2021 with spend approaching $1.5 trillion.[1] Waste may be caused by non-compliance, intentional non-adherence, unintentional non-adherence, non-preventable waste and preventable waste.[3] The waste described in this current study is a combination of intentional non-adherence and preventable waste caused by a greater supply prescribed than is needed by the patient. Interventions to rationalise the volume of medications provided on a prescription remain important and many multi-disciplinary partnerships have been described that have successfully reduced waste.[3] This study further supports that medication waste affects paediatric as well as adult care and that parents are concerned about medication waste. The opportunity for pharmacists to work with both prescribers and parents to reduce waste through medication review in paediatric patients should not be overlooked. In addition, a smaller volume or quantity of supply may help with some of the challenges that parents face with transporting medication.

When asked about the written information provided with medication, most participants found these helpful on initiation of a new medication. The most commonly cited additional information required was about side effects. A number of parents described too much information about the medication regimen being provided verbally in clinic. When this happened, respondents cited asking for a written summary from the clinician in clinic but then being provided with a poorly legible hand-written note. Omitting information later found out by patients/parents can also be an issue. One patient decided against taking hydroxycarbamide for after finding out it was a cytotoxic agent after the clinic appointment. Another parent advised that they do not receive information with their medication from the community pharmacist. The quality of instructions provided about medication are known to influence adherence.[19] Healthcare practitioner behaviour in the clinic environment may also influence adherence through how much a patient is engaged with the conversation about medication.[61] This current study has identified that there is insufficient documentation of complex medication regimens provided in a format that parents and patients can take away with them and refer back to from a clinic appointment. This may influence adherence and providing a clear written or electronic record for parents/patients may help support medication taking. In addition, engaging parents/patients in further conversation about medication may address some of the fears or misunderstandings that occur following the healthcare professional/patient consultation.[61] Care needs to be taken to prevent healthcare professionals impeding patient involvement. Patients and parents require clear documentation of medication regimens.

5.5.3 Experiences associated with healthcare associated burden

Communication about dose changes identified challenges around information being provided to primary care in a timely manner to allow repeat supplies. In particular, problems occur when verbal messages are provided to parents/patients by healthcare professionals about changes to therapy. The lack of evidence of such a change prevents these being accepted by the patient's general practitioner or hospital staff on re-admission thus potentially preventing the patient from receiving the most current dose. It is known that the risk of miscommunication and unintended changes to medication is a significant problem.[68] This current study has identified a particular issue with communication by telephone. Recommendation for the content of records for when patients transfer between care settings have been made.[68] The challenge remains to ensure how a complete transfer of information may occur following an unplanned telephone conversation with the clinician. Participants in this current study felt that other professionals were unable to accept an update from the parent but rather prescribe against the latest entry in the medical notes which is not current. The provision of information from these consultations should ideally be in line with good practice and require a communication of any changes to treatment to primary care and an update of the medical notes in secondary/tertiary care. The realisation of the potential benefits of electronic patient's records could provide an opportunity to more easily record a consultation with a patient without having to obtain their physical medical notes. If these were available across care settings then the recording and transfer of up-to-date information could be much better optimised than it is currently. However, a recent review of the personal health record in the UK revealed that the records are very setting specific and that a single record across the healthcare interfaces remains aspirational.[100] There also remains a drive to enable patient access to their electronic health records.[101] This may further support access to current information about medication and hence further enable the continuation of recent changes. As previously mentioned, medication reconciliation apps may also be of benfit.[87]

Participants described the ease of obtaining medication through the hospital pharmacy. They also described the benefits of on-line ordering of medication at the GP surgery and community pharmacy delivery services. However, challenges were described around obtaining prescriptions and supplies of medication in primary care including: GPs declining to prescribe paediatric medication, availability of medication in the community pharmacy, navigating the repeat prescription service, managing when each medication will finish to ensure a continued supply and the difficulty in obtaining an urgent further supply if a bottle is broken accidentally. Many of these issues are well known and have been previously described.[43] However, this current study has identified that they remain problematic for

parents and patients. Parents and patients may not be informed of these potential problems with supply arrangements. This lack of knowledge may provide additional anxiety and parents/patients should be informed about the process of obtaining further medication supplies. Contact between hospital and the patients GP to agree the supply route should take place prior to discharge for patients initiated on long-term medication. Significant burden is placed on the lives of families with children taking regular medication simply to obtain further supplies for multiple reasons. Participants described the time taken to arrange a supply of medication. As a consequence of medication running out at different times participants explained that they needed to arrange supplies on a weekly basis. The time required to arrange the supply varied. For example, if a new medication was added by the hospital then this would take a lot longer to arrange a further supply from the GP. In addition to better communication between hospital and community based health services, better integration of pharmacists and GP working can optimise medication supply including synchronising patients' repeat medications through aligning course length, repeat cycle and simplifying the repeat process.[102] Timely and complete transfer of information is recommended as a standard for good medicines optimisation.[5] In addition it is important to involve a pharmacist in developing care pathways involving medicication.[5] The additional NHS funded clinical pharmacist resource within GP practices is to be expanded and provides an opportunity for streamlining practice prescription processes, medicines optimisation and the management of long-term conditions.[103] These pharmacists will be well placed to support the transition from hospital care to the GP and make the process more seamless for paediatric patients and their parents and/or carers.

The availability of oral syringes through community pharmacy was identified as a problem with many parents describing the challenge in obtaining supplies. This warrants further investigation as UK community pharmacists are reimbursed for providing either a 1mL, 5mL or 10mL oral syringe with oral liquid medication.[104]

5.5.4 Experiences of the social burden of medication

The most commonly cited issues around the social burden of having a child on long-term medication, or being a child taking long-term medication, were around travelling with medication and taking medication outside of the home. A recent systemic review of medication related burden and patients' lived experience with medication found that a lack of public understanding about medication had a detrimental effect on patients' beliefs about medication and self-confidence affecting their activities of social life.[30] Parents in this current study also cited feeling awkward about administering medication outside of their home and

some did not inform friends about their child's medication although family members tended to be aware. Some family members expressed concern about the number of medications being taken. On the whole, with some exceptions, family members tended not to be called upon to help with medication. Some parents felt that the regimen was simply too complex to entrust to anyone other than themselves. However, the benefit of support has been identified as a positive experience.[30] This current study has identified that greater support and advice is required for parents/patients travelling with medication and taking medication on holiday. Parents were making decisions around the stability of medication out of the fridge and outside of the usual packaging (e.g. in a capped oral syringe and medication compliance aid) without seeking healthcare professional advice. Pharmacists are ideally placed to provide this additional support and parents/carers should be directed to this resource. Indeed, current NHS websites providing advice to those travelling with medication do suggest that travellers seek advice from a pharmacist.[105] Travelling with medication should be a standard question when discussing medication with parents and children.

5.5.5 Experience of adverse effects of medication

Approximately half of respondents had experienced some side effects from their medication often resulting in a call to the hospital for advice on management. Participants tended to be aware of these potential effects either having been told directly or through research undertaken by themselves. Community pharmacist are utilised as a resource for information about side effects for children's medication.[89] There remains the need to support parents and children with adverse effects to their medication. Treatment side effects have been shown to be a factor in non-adherence in paediatric long-term medical conditions.[21] Parents and patients should be informed about potential adverse effects, how they should be managed and who to contact for further advice. In addition, there remains an opportunity to understand how patients and parents would like to be informed about their medication.

5.6 Strengths and limitations

The strength of this study is the detailed insight into how medication taking in children impacts on daily life from the perspective of the parent and/or the patient. The results from the study can be incorporated in prescribing and dispensing consultations to further optimise medication use. These findings may also be incorporated in a formal paediatric medication review with individual patients/parents.

Study limitations include the possibility of participants providing answers that they perceived to be acceptable. Consistency of the interview process was maintained with 1 researcher undertaking all interviews. The interviews took place whilst the patient was an in-patient which may have influenced how participants prioritised their experiences. Undertaking the research at a single UK institution may limit the generalisability of the results. However, whilst healthcare systems differ between countries, many of the experiences investigated are likely to be similar. The restriction to English language speakers prevents extrapolation to non-English speakers receiving healthcare in the UK who may have their own unique range of experiences not captured within this current study.

5.7 Further research

Further study using quantitative methodology of a greater number of patients is required to determine the significance of the findings in this current study. In addition, further research is required to determine the most effective interventions to support children, young people and their patents/carers when a child paediatric patient takes regular prescribed medication.

5.8 Conclusion

Parents and patients experience many challenges with their medication. This study has identified the following opportunities for healthcare professionals to contribute towards the optimal use of medication in paediatric patients:

- Engagement with patients and parents regarding medication choice/regimen to ensure treatment is achievable within their daily lives.

- Better collaboration with schools regarding patients' medication especially when changes are made to treatment.

- Provision of clear instructions regarding changes that patients/parents are expected to make to current treatment.

- Sign-posting to quality assured internet sites about medication.

- Provide support to children to swallow solid dose forms.

- Ensure medication quantity is optimised to reduce waste.

- Early collaboration between hospital and primary care health providers to agree medication supply.

Minimally disruptive medication that seeks to tailor treatment to the realities of the daily lives of patients could greatly improve quality of life.[44] This current study has identified how medication taking affects daily life when children and young people take regular medication.

6.0 Study 4 - A postal survey of parent/carers to investigate intended non-adherence to their child's medication regimen

6.1 Aim

1. To identify what intended non-adherence is reported by parents/carers of children and young people taking long-term multiple medication.

2. To identify the rationale behind parent/carer decision making relating to their child's medication.

6.2 Research ethics committee approval

The East of England -Cambridge East Research Ethics Committee reviewed and approved this study 7th February 2018 (REC reference 18/EE/0011, IRAS project ID 234261).

6.3 Method

6.3.1 Setting

The study was undertaken at Birmingham Children's Hospital - a specialist UK paediatric hospital.

6.3.2 Participant recruitment

All parents/carers of patients taking 2 or more medications were identified through the BCH pharmacy homecare patient database. This was done by a data analyst who was employed as part of the BCH pharmacy homecare team, and had access to this database in the course of their usual work duties. The term 'homecare' refers to the process whereby patients have their medication prescribed by their hospital doctor, or other hospital-based healthcare professional, dispensed by a pharmacy and delivered to the patient's home. Homecare is used at BCH for patients on long-term medication and is managed by the BCH Pharmacy Department.

6.3.3 Inclusion criteria

Parents or carers of patients receiving two or more medications through the BCH pharmacy homecare scheme. There were no exclusions based upon the formulation or therapeutic indication of the medication and the age of the patient.

The study was not offered to non-English speakers as it was not possible to develop translated questionnaires in a variety of languages in advance of posting. The language spoken was not known from the pharmacy homecare patient database.

The study was also not offered to patients having their medication administered by a homecare nurse for example parenteral nutrition. This is because the study has been developed to explore parent/carer experiences of their child's medication use and therefore requires them to be responsible for administering their child's medication.

6.3.4 Exclusion criteria

There were no exclusion criteria for those participants who met the inclusion criteria.

6.3.5 Data collection

The research tool in this study was a postal questionnaire. A number of tactics may be utilised in order to maximise response rates to postal questionnaires.[53-56] These include advance warning, explanation of selection, sponsorship, professional looking envelope addressed to the individual recipient, publicity, incentives, confidentiality, anonymity, appearance, questionnaire length, topic/degree of interest, the use of a cover letter, pre-paid return envelope, repeat mailing and avoidance of holiday periods for data collection. A cover letter (Appendix XX), participant information sheet (Appendix XXI), pre-piloted questionnaire (Appendix XXII) and a pre-paid addressed return envelope was posted to 180 parents or carers of children receiving medication through the pharmacy homecare scheme during June 2018 avoiding periods of known school holidays. The envelopes were individually addressed to each recipient. Face validity and piloting of the questionnaire was assessed with a parent of a child who was taking long-term multiple medications. All study documents were also reviewed by Birmingham Children's Hospitals Patient Information Department. Each participant was assigned a unique sequential number to enable non-responders to be identified. This unique number was added to the back of the questionnaire. A second questionnaire, along with a repeat mailing cover letter (Appendix XXIII), participant

information leaflet and pre-paid return envelope were posted to non-responders two weeks following the return-by date. Data collection was arranged by the PI who has access to the pharmacy homecare database in the course of his usual work duties as an employee of BCH. The participant information sheets and questionnaires were formatted and branded in line with Birmingham Children's Hospital standard design. Confidentiality was assured within the participant information sheet and on the questionnaire.

Consent for the study was implied if the questionnaire was completed and returned. A statement explaining this was included on the first page of the questionnaire provided with the invitation to join the study.

A 10-item questionnaire was developed through themes identified in a literature review. Participants were asked about their decision making around their child's medication as per the following themes:

- Deciding to delay the initiation of a new medication.
- Deciding not to initiate a new medication.
- Making changes to the way that medication was administered.
- With-holding usual regular medication for a period of time.
- Administering a higher dose of medication than prescribed.
- Administering a lower dose of medication than prescribed.
- Making changes to medication to fit administration around daily life.
- Making changes to medication to aid administration.

Demographic/background information concerning patient age and medication being taken was also requested.

6.3.6 Data management

All data collected was used for the sole purpose of this study and for no other purpose. The data was stored in a secure department (Pharmacy Department) at Birmingham Children's Hospital during the study. Anonymised data, completed questionnaires and study site file contents were archived at the School of Life and Health Sciences, Aston University.

Data from the paper-based questionnaire were entered in to SPSS and stored on a secure server on a password protected Birmingham Children's Hospital PC only accessible by the researcher. Paper copies of the questionnaire will be stored in a locked cupboard in a secure office in the Pharmacy department at Birmingham Children's Hospital.

All data was anonymised at the earliest opportunity and pseudonyms were used in place of participant names to maintain anonymity. No confidential/identifiable data was stored following completion of the study in accordance with information governance requirements. Only anonymised questionnaire data was retained during the study.

If any information was provided in the questionnaire that raised any concerns from a child protection or safeguarding perspective the PI was to seek advice from the Child Protection and Safeguarding Team at Birmingham Children's Hospital. This was also to be recorded as an 'adverse event' within the study.

The data was analysed by the PI and his academic supervisors. Analysis took place on hospital premises with anonymised data being analysed at the researcher's private residence and Aston University. Transfer of anonymised data was via a BCH encrypted memory stick.

6.3.7 Data analysis

The answers listed on the questionnaire were coded for ease of analysis. The results were analysed and descriptive statistics (counts/frequency) developed. The SPSS version 23 was used to analyse the quantitative data and NVivo version 11 for the qualitative responses to each question using thematic analysis.

6.4 Results

6.4.1 Recruitment

The study response rate after the first mailing was 13/180 (7.2%). Following the second mailing the overall response rate was 34/180 (18.9%). Two (5.9%) respondents returned non-completed questionnaires leaving 32/189 (17.8%) respondents for final analysis.

6.4.2 Demographic/background information

The mean age of the children of respondents was 8.4 years with a range of 0.83 years to 17 years. The total number of prescribed medications was 158 with a median of 4 medications (range 1 – 15 medications). Patients had been taking these for a mean of 4.1 years. The therapeutic indications of prescribed medication are summarised in Table 19. It was not possible to identify 2 single medications from 2 respondents' descriptions.

Table 19 A summary of Prescribed Medication Taken by Respondents' Children

Therapeutic Category	Number of Prescribed Medications (%)
Electrolyte supplementation	22 (13.9%)
Antiepileptic	20 (12.7%)
Immunosuppressant	16 (10.1%)
Anti-oesophageal reflux	12 (7.6%)
Antibacterial	9 (5.7%)
Laxative	9 (5.7%)
Analgesia	5 (3.2%)
Systemic corticosteroid	5 (3.2%)
Diuretic	5 (3.2%)
Insomnia	4 (2.5%)
ACE Inhibitor	3 (1.9%)
Anticoagulant	3 (1.9%)
Beta Blocker	3 (1.9%)
Anti-diarrhoeal	2 (1.3%)
Antifibrinolytic	2 (1.3%)
Antifungal	2 (1.3%)
Antihistamine	2 (1.3%)
Antiplatelet	2 (1.3%)
Bile Acid Analogue	2 (1.3%)
DMARD	2 (1.3%)
Iron supplement	2 (1.3%)
Thyroxine	2 (1.3%)
Unknown	2 (1.3%)
Other	22 (13.9%)

6.4.3 Intended changes to prescribed medication

In total, 16/32 (50%) respondents had intentionally made changes to their child's medication without seeking the advice of a healthcare professional. The most common change (9/32, 28.1%) was adjusting the medication regimen to fit in to daily life followed by delaying the initiation of a new medication (7/32, 20.6%). No respondents indicated that they had not started a newly prescribed medication for their child. The changes made by respondents to their child's medication are summarised below.

6.4.4 Delaying the initiation of a new medication

Respondents were asked if they had ever made the decision to delay beginning a new medication for their child. Seven (21.9%) respondents advised that they had delayed administering a new medication to their child. This was to first find out more information about how to use it (n = 2), to find out more information about side effects (n = 4), to ensure that it was the correct medication to use (n = 2), to first check that it did not affect other concurrently taken medication (n = 2) and to check with the patient's usual medical team first (n = 2). Two parents also cited their child's current health status:

"I sometimes delay starting or increasing my child's medicine because my child sometimes feels better before starting the prescribed medicine." Respondent 101

"I wasn't sure that he needed it as he was progressing ok with other meds, albeit slowly." Respondent 8

6.4.5 Not Initiating a new medication

Respondents were asked if they had ever decided not to begin a new medication at all that was newly prescribed for their child. No respondents indicated that they had ever decided not to initiate new prescribed medication.

6.4.6 Changing the way that medication was administered

Respondents were asked if they had ever decided not to follow the instructions about how their child's medication should be administered without first seeking advice from their doctor, nurse or pharmacist.

Six (18.8%) respondents indicated that they had not followed the instructions regarding administration of their child's medication. This was due to concerns about side effects (n = 3), uncertainty about affecting other concomitant medication (n = 1), prescribed administration time was inconvenient (n = 2) and their child declining to take the medication (n = 1). The decision to deviate from the prescribed/dispensing instructions are illustrated by the two examples below.

"I have ignored instructions to give a medicine an hour before food because it was impractical/impossible - I checked with the liver team who said as long as I do the same every time it was fine." Respondent 41

"Sometimes I wean the medicine based on my child's need, necessity or requirements which only I can monitor on a 24/7 basis. Sometimes my opinion will differ to a doctor/consultant's recommendations and I administer accordingly e.g. meds like diuretics + supplements that correspond to them." Respondent 55

6.4.7 With-holding usual medication

Respondents were asked if they had ever decided to with-hold any of their child's usual medication for a period of time without first seeking advice from a doctor, nurse or pharmacist.

One respondent omitted to answer this question. Four (12.5%) respondents advised that they have withheld their child's medication. The reasons cited were to 'clear her system' allowing a period of time without medication, concern about the effect of intercurrent illness, titration of a dose against effect and experiencing adverse effects. The parental experiences are described below.

"Yes, sometimes I feel my child needs to clear her system and I sometimes stop the meds for some period. Again, these are some prescribed medicines with no effect what-so-ever. I stopped [administering] it without seeking the consent of the doctor." Respondent 101

"When [my child] got Chicken Pox I delayed his morning aspirin until I had spoken to the ward but was administered as soon as I'd spoken to them and knew it was ok to give." Respondent 115

"She was opening her bowels enough, so she didn't require the laxatives every day. Instead I gave her once a week." Respondent 133

"He was reacting badly to it - vomiting and stomach cramps. He was also convulsing after taking another medicine. Not enough faith in the doctor's competence to get the regime correct." Respondent 8

6.4.8 Administering a higher dose of medication

Respondents were asked if they had ever decided to give a higher dose of their child's medication without first seeking advice from a doctor, nurse of pharmacist.

Four (12.5%) respondents communicated that they had given a higher than prescribed dose of their child's medication. This was mainly because they thought it wasn't working well enough (n = 3). One respondent increased their child's dose of tranexamic acid if they were haemorrhaging on their way in to the hospital emergency department.

"Sometimes the dose might be too small, after two days of application and no sign, I sometimes increase the dose slightly." Respondent 101

"Meds such as blood clotting oral syrups like tranexamic acid I give him a higher dose than normal if he has a big bleed out. I give it to tide him over until I can get him to A&E/hospital but I also let the consultants know that I have done this (so as to prevent too much blood loss until he gets urgent medical attention." Respondent 55

6.4.9 Administering a lower dose of medication

Respondents were asked if they had ever decided to give a lower dose of their child's medication without first seeking advice from a doctor, nurse or pharmacist.

Four (12.5%) out of 32 respondents had given a lower dose of their child's medication compared to the prescribed dose. This was due to side effects (n = 3), the perception that their child was feeling well enough not to need as much of their medication (n = 3) and because they felt that their child was feeling worse when taking the medication (n = 2).

6.4.10 Changing medication to enable it to fit in with daily life

Respondents were asked if they had changed the way that their child takes their medication to fit in with their day-to-day lives.

Nine (26.5%) of the 32 respondents had changed the way that their child took their medication to fit in with their daily lives. The reasons were due to patient preference around the formulation (n = 2), to fit around nursery/school times (n = 2) and to fit the dosing

schedule in to daily life (n = 2). Three respondents did not provide further detail on the changes that they made. Five parents provided their personal experiences:

"Unfortunately, my daughter kept being sick and would refuse her medication orally. So, we have had her fitted with a gastrostomy so we can ensure that she receives the correct dose orally." Respondent 117

"Instead of morning doses of medication, I gave her the laxatives after nursery so she didn't have an accident at nursery." Respondent 133

"Giving it with breakfast and after tea rather than "an hour before food" because I had to prioritise…more important to give it 8 hours apart. It has to fit with our daily routine as she'll need to take it for life. Used to take many more when she was little + I was a lot more strict about following guidelines, the younger she was. I'm more relaxed now!" Respondent 41

"Change the times like - give her medicines before and after school. Not giving much after lunch. Instead give her when she comes back home so don't have to send medicines to school." Respondent 54

"Some meds are given four times a day but I may give three times a day to the non-urgent/essential ones" Respondent 55

6.4.11 Changes to medication administration

Respondents were asked if they had changed the way that their child is administered their medication because they were having difficulties taking them, without first seeking advice from their doctor, nurse or pharmacist.

One respondent omitted to answer this question. Three (8.8%) of the 31 respondents who answered this question advised that they had changed the way that their child is administered their medication due to difficulties experienced around administration. All 3 respondents had masked the taste of their child's medication by mixing with a flavoured drink and two additionally masked the taste by mixing with food.

"[My child] was first NG tube fed but when coming off to switch to oral feeds and meds he struggled to take his 10mL dose of propranolol. So, I mixed it with 10mL of his milk in a bottle

and just made sure he drank all 20mL. He was later switched to a higher strength so half the dose which he took orally." Respondent 115

"On occasions in the early years the meds made my daughter feel quite sick and she started to refuse them so had to try and hide them. This didn't work and ended up taking the meds through other methods." Respondent 15

Two (6.2%) respondents were not able to manipulate the way the medication was administered due to underlying medical diagnoses as described below:

"She has most of her medicines through NG tube as she is too young to take pills. She has to have one of the meds precisely at 6 hourly intervals." Respondent 150

"Child has oesophageal stricture so cannot swallow tablets. Have requested pharmacists to give either dispersible forms or syrups." Respondent 55

6.5 Discussion

Patients in this study were prescribed a range of medication, covering a breadth of therapeutic areas, including regular electrolyte supplementation, antiepileptics, immunosuppressants and medication for oesophageal reflux disease. The age range spanned the very young (0.83 years) to young adults (17 years) with a mean of 8.4 years. This suggests that the data is broadly representative of this patient group who are under the care of a range of specialities.

Overall, half of respondents (18/32) had made some changes to their child's regular medication without consultation with a healthcare professional. The burden that medication taking places on the lives of children and their parents was investigated in a Study 3. This study highlighted the timing of doses, the impact of school around medication taking and travelling with medication as being particularly problematic. This current study has identified that parents are making changes to their child's medication regimen to fit around daily life. Indeed, 9 (26.5%) respondents cited changing the medication regimen to fit around daily life including 6 (17.6%) respondents who did not follow their prescribed medication instructions. Examples of respondents' changes to medication included adjusting a four-times-a-day regime to three-times-a-day, not following administration instructions around timing with food due to practicalities and arranging medication around school/nursery. These changes may be detrimental to maximising the expected outcomes of prescribed medication. There remains a need to ensure that the decision to prescribe medication is undertaken in partnership with patients to reduce the risk of sub-optimal benefit from medication.[5] Adherence to medication in long-term paediatric conditions is particularly complex requiring parents to balance the daily needs of their child taking medication with every day family life.[9] Opportunities to discuss barriers to adherence and simplification of medication regimens to reduce the impact on daily life are important for parents.[21] This current study has supported this concept through confirming the presence and types of intended non-compliance with children's medication by parents. A recent qualitative study of the views of general practitioners on barriers and facilitators to medication adherence suggests that there are some overlap with adherence with older patients prescribed chronic medication.[106] These include: independent pausing, stopping or controlling the medication and administration/dosage challenges. There remain opportunities at the point of prescribing, dispensing/supply and through structured medication review to help parents and patients with children's medication. This current study has also identified themes that should be included in such consultations or reviews.

No respondents indicated that they had not started a newly prescribed medication. This may indicate that parents considered treatment was necessary. Indeed, amongst other reasons, health behaviour is dependent upon the severity of the health problem and perceived benefits of a preventative behaviour.[6] Greater adherence has been demonstrated where patients rate the necessity of their medication as high.[8]

Seven (20.6%) respondents, however, advised that they had delayed initiating a newly prescribed medication. Reasons cited included to find out more information -for example about how to use the medication, side effects and treatment rationale. Barber *et al* found that adult patients demonstrating intended non-adherence in the first ten days to four weeks after the initiation of a new medication also cited information needs about their medication.[20] The utilisation of a NMS type approach could provide additional support to parents and paediatric patients newly started a long-term medication. In adults the NMS has been demonstrated to increase adherence and subsequent health gain at reduced overall cost.[107] However, current guidance on the NMS advises that it cannot be provided to carers and whilst it may be provided to a child, the child must be able to consent to take part.[47] The issues identified in this current study fall within the purview of the current NMS standard questions.[108] However, whilst this study has identified that a NMS consultation with a parent may provide an opportunity to support the initiation of a new medication in a child it may not be accessible to them. Further research will also be required to evaluate such an intervention in this patient group.

Respondents indicated that they adjusted the medication regimen themselves through changing the way that medication was administered (6, 17.6%), administering a lower (4, 11.8%) or higher dose (4, 11.8%) than that prescribed and with-holding medication (4, 11.8%). Some changes may be appropriate such as titrating a dose of Movicol® against symptoms of constipation whereas another respondent may have been inappropriately temporarily with-holding medication to give their child a ‘washout’ period. Indeed, NICE supports the self-management of constipation in children by parents but recommends the provision of written information.[109] A number of strategies may support adherence including self-management programmes, simplified dosing regimens, pharmacist led medication reviews and education when combined with other supportive initiatives such as self-management skills training.[71] There is also a need for partnership working between clinicians and patients promoting shared decision making around medication use.[59] Compatibility with patients, or parents, preferences is required to ensure that treatment decisions are not misguided.[71] NICE recommends that a structured medication review should be undertaken in adults, children and young people taking multiple medications.[5] This may provide support to

ensure that parents understand their medication and that its use is optimised. However, the currently funded MUR service through U.K. community pharmacists is not accessible to children who are unable to consent, and it is not available to parents.[49]
Changes to administration was reported by three respondents which is unsurprising. They indicated masking the taste of their child's medication with food or drink. There remains a need for the implementation of pharmaceutical technologies that enable the manufacture of licensed age-appropriate formulations.[98]

6.6 Strengths and limitations

The strengths of this study include the exploration of intended non-compliance to medication with paediatric patients and their parents/carers. The study has demonstrated that approximately half of parents who responded to the questionnaire are making decisions about medication, and changing their child's medication, without the knowledge or support of a healthcare professional. The study has also provided an insight in to what those changes are and the rationale behind them which healthcare practitioners may consider within their consultations with parents.

The limitations of this study include the low response rate of 18.9% which may limit the validity of the data, how representative the results are of this patient group and introduce bias. This response rate was low compared to the range observed for pharmacy clients where questionnaires were handed out in the pharmacy which ranged between 21% to 88%.[53] The reason for the low response rate to this study is not known. The nature of the study may have inhibited some parents from responding if they did not wish to reveal any changes that they were making to their child's medication. Also, parents have many demands on their time, especially if looking after a child with a chronic medical condition, as demonstrated by this study. As the survey was undertaken in a tertiary centre, participants may have been invited to take part in research by other healthcare teams leading to research apathy. In addition, some recipients of the questionnaire may not have had sufficient understanding of written English. This could introduce bias as in a study of parents of children with asthma, non-minority parents were more likely to consider that their child's treatment is necessary and be less concerned about treatment compared with minority parents.[11] Alternative methods of data collection should be considered for further research in to this topic including telephone surveys and on-line self-completion questionnaires. Should a postal survey be considered again, more than a single repeat mailing should be utilised along with increasing the number of participants by using a multi-site approach. Telephone follow-up may also provide an alternative method to improve response rate. Subject to

ethical approval, an investigation of non-responders would be valuable to determine if they have different experiences of managing their child's medication compared with responders. This may also help inform future study design which should also include an option for those not wishing to take part in the research to communicate their reason to the researcher. The study was undertaken at a single institution which may further limit the generalisability of the results. In addition, the mean duration medication use was 4 years which may introduce recall bias with parents not remembering some of the changes that they had previously made.

6.7 Further research

Further research should focus on confirmation of the results of this study through a larger piece of research undertaken at multiple sites. The scope of such a study could also include the view of a multidisciplinary group of experts to determine the clinical significance of intended non-adherence through a Delphi method. In addition, research to determine the successful therapeutic interventions to support the initial choice of medication tailored to the individual and ongoing support to ensure medication use is optimised is required. An additional area of research are those parents who have a poor understanding of English to identify their individual needs around their child's medication.

6.8 Conclusion

Fifty per cent of respondents in this study had made changes to their child's medication. The changes made ranged from self-management type decisions to being unable to comply with the medication regimen due to individual factors such as practical issues around dose frequency. All respondents had started their new medication but where initiation was delayed this was due to a perceived information gap. Parents/carers of children taking regular medication may benefit from greater engagement in therapeutic decisions to ensure that their use of prescribed medication is made more predictable and possibly more optimal. Parents/carers may also benefit from support whilst their child is taking regular medication to ensure that the benefits are maintained.

7.0 Programme of research discussion

This programme of research has explored medication use, and related issues, in paediatric patients. It has investigated the medication-related knowledge of patients, parents or carers following a hospital out-patient consultation where a new medication was prescribed. The research then identified what experiences were had by users of that medication, including parents/carers, during the first six weeks following treatment initiation. The experiences that community pharmacists have in reviewing medication in children/young people were then investigated along with how they are utilised by patients and parents/carers regarding children's medication. Following this, the treatment-related experiences when a child takes long-term medication were identified from the child and parent perspective. A common theme identified through the first three research studies was intended non-adherence to the prescribed treatment. Parents/carers were, along with some patients, making decisions about their medication which were not in accordance with the prescribed instructions. Therefore, the final study investigated intended changes to children's prescribed medication by their parents/carers.

This programme of research found that patients and parents had further information needs following the prescribing of a new medication. The desire for additional information about medication was found to be apparent early after treatment initiation. Patients and parents undertook their own research in to their prescribed medication for a variety of reasons including: for more general information and to answer specific questions or concerns. This may be due to insufficient information provided during their consultations with healthcare professionals or it could be that patients or parents/carers did not disclose and discuss their concerns. In addition, parents gave examples of verbal information being used to convey changes to current medication in an out-patient appointment. The lack of written instructions around changes to complex medication regimens left patients and parents without any instructions to refer to once at home. Further research in to the shared decision-making process in the paediatric out-patient clinic when medication is prescribed is required to further support medication taking in this group. Patients and parents require clearly documented instructions on complex medication regimens, especially if changes are verbally made in clinic, to support compliance. The current development of a medicines management app for parents which will include the ability to add information about medication will be a useful addition to support children, young people and parents.[110] Indeed, the NHS long-term plan aims to make digitally enhanced care mainstream across the NHS.[111] Further research in to how parents, carers and patients utilise additional information about medication could

identify both the benefits and any potential disadvantages about how this information is understood and utilised.

This research programme confirmed the findings of other studies[91 92] that found that patients and parents utilise the internet for medication-related information. In addition, some parents joined on-line support groups to interact with parents of children taking medication for similar conditions with varying experiences of benefit. Patients and their parents should be sign-posted to quality assured websites to ensure that information accessed is suitable and consistent. This could be provided through the Medicines for Children group which already provides information to this cohort of people or professional collages such as the RCPCH or professional groups such as NPPG and RPS. This findings from this programme of research could be used to guide the content of the nhs.uk patient website to meet the needs of this group.

Community pharmacists in this research programme reported that children or their parents/carers had asked them about the indication, dose, administration and adverse effects of a medication. They had also experienced patients, or their parents/carers, directly reporting to them that they had either themselves, or through a decision made by a parent/carer, stopped treatment, or changed the dose without first having sought advice from the prescriber. This presentation to the community pharmacist may provide an opportunity to discuss the medication and undertake a formal medication review. This current study has demonstrated that community pharmacists are a resource used by paediatric patients and their carers. This role should be formalised within NHS care pathways and patients/parents referred to community pharmacy where additional support may be required. Indeed, the NHS long-term plan[111] to expand community multidisciplinary teams with new primary care networks provides the opportunity for community pharmacy to be a recognised provider of support for paediatric medication. The learning needs of community pharmacists should be identified and they should be supported in order to further develop their role in supporting paediatric medication optimisation.

Following the prescribing of a new medication patients may not initiate treatment or may omit doses. The reasons identified for not starting a new medication included the side effect profile and the desire to evaluate the risks and benefits of treatment prior to initiation. This may be a consequence of unilateral decision making by prescribers and not enough attention to shared decision making with patients and their parents. The range of reasons for missing doses included erroneous decisions made by participants to resolve their own medication related issues. This current research programme has established that non-adherence

appears early on during the first few weeks following the initiation of a new treatment. This time period may therefore be critical for supporting medication taking and effecting the clinical benefits of prescribed medication. Interventions to support medication taking should be initiated early on following the initiation of treatment to optimise medication use. The type of intervention(s), e.g. telephone helpline, sign-posting to appropriate resources such as the 'Medicines for Children' website and use of existing opportunities such as the NMS and MUR, should be investigated further to identify clinical and cost-effectiveness. In addition, identifying approaches to deliver a clear and reliable agreement between prescriber and patient/parent regarding what they will actually do with their medication will provide a good initial foundation. Understanding patients' reasons for non-adherence are included in the General Medical Council guidelines on prescribing and medicines management.[112] Conversations about adherence, along with shared decision making, should be entered in to with children and their patients/carers at each consultation with a healthcare professional.

Patients and parents find remembering to take/administer prescribed medication to be the most challenging aspect of treatment. Parents were found to self-purchase medication compliance aids, utilise mobile phone and Fitbit® devices to set up reminder alerts. Whilst there is little evidence base for compliance aids this programme of research has shown that parents may find them useful and demonstrates the importance of individualising support for medication adherence. In addition to improved treatment outcomes better adherence reduces medication waste and associated cost.

This research programme has identified that some parents make changes to their child's medication without seeking advice from the prescriber. Changes are often being made in order to fit the medication regimen around daily life. Parents identified that they experience particular challenges around the timing of doses, the impact that school has on taking medication as prescribed and travelling with medication. Examples of how parents altered their child's prescribed medication include adjusting a four-times-a-day regime to three-times-a-day, not following the advice regarding timing medication around food and arranging the dose times around school or nursery rather than the original prescribed frequency. These changes may be detrimental to the optimal use of their child's medication. This research has also confirmed other changes that parents make to their child's medication including increasing or decreasing the dose, delaying treatment, temporarily suspending treatment and adjusting the timing of administration. Their remains a need to prescribe medication in partnership with patients and parents in order to ensure that the regimen prescribed is achievable for parents and their children to adhere to. In addition, once a treatment regimen

has been initiated further support should be provided through prescriber, nursing and pharmacy roles.

This programme of research has identified that parents place great importance on ensuring an accurate time gap between medication doses which is not always necessary. This has led to parents waking in the night-time, starting their waking day earlier and finishing it later in order to maintain a precise time gap between doses. A discussion with patients and parents/carers about how to implement the dose regime may be useful at the point of prescribing and dispensing. Current counselling about medication might not be delivered in a way that meets the needs of patients and parents. Counselling should go beyond a simple confirmation of the dose and frequency of administration to ensure that patients and parents understand what is practically required.

Across all 4 studies of this research programme it was found that the requirement to take medication at school remains problematic for patients and their parents/carers. The concerns experienced included taking medication in front of peers, access to medication, arranging additional supplies for school, restrictions on the frequency that medication can be administered at school and the risk of medication errors. Particular concerns were raised around effecting changes to the medication regimen in school. The national statutory guidance on medication in schools recommends the development of individual healthcare plans in conjunction with the patient, parent and healthcare professionals.[84] The care plans include the provision for written permission for the child to self-administer or for trained school staff to administer medication. Further advice is provided regarding written instructions for medication which includes the dispensed container and instructions from the parent. In addition, children, where competent, should be allowed to carry their medication and self-administer with appropriate supervision. However, the results of this programme of research suggest that implementation of this guidance might be inconsistent across education providers. This is negatively impacting on patient care and causing greater medication-related burden for patients and families. In one case a parent kept their child off school following a change in dose as the school could not change their administration on the parent's advice alone. This could only take place once the dispensing label had changed. The standard dispensing label on a package does not work with complex medication regimens subject to constant review and change. This requires an alternative agreed approach. Long-term absences due to health problems affect children's educational attainment, their ability to integrate with their peers and general and emotional wellbeing.[84] In 2017 23% of young people aged 11 – 15 years reported that they had a long-term illness or disability.[113] Recent documents to support local authorities and providers in commissioning

and delivering children's public health services acknowledges that parents of children with health needs are often concerned that their child's health will deteriorate when they attend school.[114] Strong partnership working is required to ensure seamless support is provided to children and young people.[114] However, the implementation of current guidance remains insufficient due to the inconsistencies observed around medication taking practices in schools. The need to take medication in school should be seamless for the patient and any updates to treatment should be acted upon without delay. It is suggested that school nursing teams should work collaboratively with other health professionals including general practitioners and community paediatricians.[114] This should be progressed at a pace to ensure better medicines optimisation in the school setting. Further research is required to enhance medication experiences in school including how schools, health professionals and parents collaborate especially when changes to medication are necessary.

The experiences of parents' not having their knowledge acted upon when they communicate updated information about their child's medication is not unique to the school setting. Further examples were provided when health professionals were unable, or required confirmation first, to act upon parental knowledge. Whilst it is important to establish good governance around information with the risk of it being incorrect there remains the need to prescribe the current medication regimen. Indeed, the World Health Organisation (WHO) global patient safety challenge to reduce medication harm recommends that patients, families and their carers are empowered to manage their medication including identifying errors.[115] Medicines-reconciliation is an established part of safe care when patients transition between care settings.[5] However, it wasn't available at the point of prescribing in the cases cited within this programme of research -on admission to Accident and Emergency, the GP surgery and at school. The electronic health record, accessible to patients and parents, has the opportunity to provide current information about medication that could be utilised by all health providers. Parents could also access it to confirm medication changes to schools if needed to reduce delays in actioning dose changes. Whilst the electronic record has been demonstrated to be effective in practice[116] the UK roll out has been beset by challenges.[117] The NHS Long Term Plan has set out the milestones for digital technology.[111] This includes patients with long-term conditions having access to their health record and associated care plan. It is essential that this development includes children, young people and, where appropriate, their parents or carers. This will help empower patients and parents to ensure that their child's medication is accurate when changing care settings and communicating changes to school.

Whilst not the focus of this programme of research, the results have identified a number of examples experienced by patients/parents that could contribute to medication error. These include:

- The challenges around the number of medications a patient is prescribed
- The availability of different formulations
- Fitting medication taking around daily life
- The influence of on-line support groups
- The volume of accessible information available to patients/parents
- How changes to medication are communicated by prescribers
- The transition from hospital to home
- Parental decision making.

The WHO third global patient safety challenge is to reduce harm from medication.[115] This report acknowledges that young children, along with the elderly and those with renal or hepatic disease, are more susceptible to adverse outcomes of medication error. The NHS Improvement Medicines Safety Programme in response to the WHO report has produced phase 1 and potential phase 2 metrics.[118] These, however, are more focussed towards adult care. A number of reasons contribute to medication error in paediatrics including prescribing, administration, communication with patients and sources of information.[119] Observations of medication administration at home in two studies have identified administration errors by parents/carers.[120 121] This current programme of research has identified additional experiences in paediatrics that may uniquely contribute to medication error at home in addition to administration errors. Further research is required to determine the contribution that these experiences may have in relation to medication error and suitable interventions for this group to ensure safe and optimal medication use. A parallel piece of work, alongside that of the adult stream, could be undertaken by NHS Improvement to ensure that children/young people are not harmed by medication especially when taken at home. This could be supported by NPPG, RCPCH and RPS.

Unsurprisingly this research programme found that parents experienced challenges around administering medication. Parents, and patients, find solid dose forms easier to manage once tolerated by their child. This includes the ease of travelling with and transporting medication. There are also very significant potential cost savings with switching to solid dose formulations. Previous research has identified that approximately 80% of prescribed liquid formulations could be substituted with a solid dose form in children over 2 years.[122] The

associated savings in one UK paediatric hospital were estimated to be between £5k and £8k per week.[122] Due to the benefit to patient care and significant cost savings, the NHS should invest in readily available support to help children switch to solid dose forms. This could be through the utilisation of hospital and community pharmacists and pharmacy technicians and/or other healthcare professionals such as nurses and nurse associates.

Parental concern about medication waste was identified in this study with examples of the volume of supply being far greater than what was required. This demonstrates that medication waste affects paediatric as well as adult care. There is an opportunity for pharmacists and prescribers to work together to reduce waste. The place of GP practice-based pharmacists and pharmacist led medication review provide opportunities to review medication supply. Further consideration should be given to more formally extending the current NHS funded medication review services to paediatric patients and their parents or carers. This could be progressed alongside a review of formulation to maximise cost savings and improve patient and parent experience of medication and managing supplies.

Whilst already described in the literature[43] this research programme has confirmed that negotiating the healthcare system to obtain medication remains problematic placing a significant burden on patients and their parents. The challenges faced include establishing prescribing responsibility between the patients GP and hospital doctor, availability of medication in community pharmacy, navigating the repeat prescription service, synchronising the supplies of medication and urgent availability of medication. The current system of medication supply for children seems to be inadequate and inappropriately places the responsibility for managing the issues with the parent. The arrangement for further supplies of medication should be agreed early on following the initiation of a new medication between the hospital-based prescriber and patients GP. Closer working between pharmacists and GPs to synchronise repeat supplies of medication may help reduce the frequency with which additional supplies are ordered. However, a wider review of medication supply should be undertaken at a national level to ensure a better system for users. This should include the provision of suitable support for primary care, secondary and tertiary care to appropriately manage paediatric medication. There may also be benefits for carers of adults by optimising the supply of medication. A recent systematic review of medicines management issues in dementia identified that carers faced some similar challenges around maintaining a supply of medication.[123] These included: monitoring the need for further supplies, delays in the issuing of a prescription and the risk of error.[123]

In this programme of research patients and parents experienced significant challenges when travelling with medication, including administering medication outside of the home. Parents were making decisions around the stability of medication outside of the usual packaging and recommended storage requirement e.g. refrigeration. This research has identified that further support is required for parents and children travelling with medication. Pharmacists are ideally placed to provide this support. Patients and parents could also be sign-posted to NHS websites which provide advice on travelling with medication. The routine counselling of patients and parents/carers should be expanded to include other practical aspects of managing medication such as how best to transport treatment.

Most community pharmacists included in this current research had not completed a medication review with a child, or their parent/carer, yet were shown to be a source of information for parents and children. The current guidance around undertaking NMS and MUR consultations does not preclude the inclusion of children/young people if they are competent to consent but does exclude parents/carers. Yet this programme of research has identified paediatric medication-related issues that could benefit from formal structured medication review. These include agreeing a regimen that is achievable, adherence, information needs, adverse effects, formulation issues, obtaining further supplies and reducing waste. This presentation to the community pharmacist, the most accessible healthcare professional, may provide an opportunity to discuss medication and undertake a medication review. Indeed, this contact may be the first point at which a healthcare professional has the opportunity to intervene in the optimisation of medication use for these patients and carers. The findings of this current research support increasing the access of current medication review services to children, young people or their parents/carers in line with current NICE guidance.[5] In addition, this programme of research has identified the paediatric medication-related themes that should be included in a review aimed at supporting children and their parents. Further research should be undertaken regarding the potential outcomes from paediatric medication review to enable current medication review services to be renegotiated and designed to include children and their parents or carers.

Across the four studies that make up this programme of research a number of medication-related challenges, and how children and their parents react to these challenges, have been identified. This research has identified a key underlying theme -the requirement to ensure that the prescribed medication regimen is achievable for patients and their parents. In the absence of a concordance consultation, ongoing support and consideration of the impact of patients' daily lives on treatment options there remains a risk that medication taking in many children will be sub-optimal. Discussing the values and preferences of treatment with patients

will help clinicians to understand how individual patients prioritise outcomes and treatment burden.[124] Indeed, including information on treatment burden in guidelines would increase their applicability to patients.[124] This programme of research has identified that it will be valuable for paediatric treatment guidelines to incorporate treatment burden and include the need to discuss the impact of treatment on daily life and vice versa with patients and parents. These results contribute to informing the impact that medication burden may have in treatment success in children and young people.

Finally, there have been many examples where healthcare pathways regarding medication have been disjointed leaving the parent to negotiate the healthcare system, and options outside of the formal healthcare system, to resolve problems themselves. Many of the recommendations of this programme of research could be incorporated within NHS Sustainability and Transformation Partnerships (STP) and Integrated Care Systems (ICS) which aim to provide more joined up care. The programme research findings that would particularly benefit from a coordinated approach include seamless access to medication, pharmacist-led structured paediatric medication review and supporting medication taking at school. STP and ICS should consider including optimising medication use in children in future work-plans.

8.0 Programme of research conclusions

Parents and patients experience many challenges with their medication. These challenges occur early on during the first six weeks after starting a new treatment. In addition, long-term medication places a significant burden on the daily lives of children and their parents. Due to the challenges of fitting medication in with daily life parents and children may alter the prescribed medication regimen without consulting a healthcare professional. Community pharmacists have been shown to be utilised as a resource for parents and children about paediatric medication and around a fifth undertake medication review in this group. This study has identified the following opportunities for healthcare professionals to help paediatric patients realise the full benefits of their medication:

- Ensure that patients and their parents/carers are informed about the side effects of their medication and how they should be reported and managed on treatment initiation.

- Ensure that patients and their parents/carers have had the opportunity to discuss the risks and benefits of treatment at the point of prescribing to aid adherence.

- Engagement with patients and parents regarding medication choice/regimen to ensure treatment is achievable within their daily lives.

- Provision of clear instructions regarding changes that patients/parents are expected to make to treatment.

- Provision of support for medication taking during the first few weeks after the initiation of a new medication. This support should include providing the opportunity to answer further questions around treatment choice and issues that may affect adherence, advice regarding administration, medication supply and adverse effects.

- Support for community pharmacists to undertake, where appropriate, structured medication review with children and their parents/carers to optimise their role as a source of advice for paediatric medication taking.

- When undertaking medication review with a child or their parent/carer to include: intended and unintended non-adherence, the compatibility of the prescribed regimen

with daily life, suitability of formulation, ease of obtaining further supplies, and the identification of waste-reduction opportunities through optimising medication quantity.

- Better collaboration with schools regarding patients' medication especially when changes are made to treatment.

- Sign-posting patients and parents/carers to quality assured internet sites about medication.

- Provide support to teach children how to swallow solid dose forms.

- Early collaboration between hospital and primary care health providers to agree medication supply.

Implementation of medical treatment regimens demands a lot of time and effort and can result in substantial burden for patients with chronic conditions.[124] Minimally disruptive medication that seeks to tailor treatment to the realities of the daily lives of patients could greatly improve quality of life.[44] This current study has identified the medication related experiences of children and their parents when children and young people take regular medication.

Further research is required to determine the types of interventions, the settings where these interventions should be provided and the role of each healthcare professional to better optimise medication taking in this cohort. This programme of research has identified the factors that should inform the content of such interventions.

9.0 Summary of publications

9.1 Study 1 publications

9.1.1 Published paper

Aston J, Wilson KA, Sinclair A, Terry D. A telephone survey to determine the experiences of children, and their parents/carers, following the initiation of a new medicine. *Eur J Hosp Pharm* doi:10.1136/ejhpharm-2016-000925 (Appendix XXIV)

9.1.2 Study 1 conference poster presentations

Aston J, Patel N, Samuels J, Aujla T, Malesi G, Huynh C, Wilson KA, Terry DRP Patient/Carers' Recollection of Medicines Related Information from an Out-Patient Clinic Appointment. *Arch Dis Child* 2016 Sep; 101(9):e2. doi: 10.1136/archdischild-2016-311535.53 (Appendix XXV)

Aston J, Wilson KA, Terry DRP. Starting a New Medicine Study-The Experiences of Children and their Caregivers when Starting a New Medicine. *Arch Dis Child* 2016; **101**:e2. doi:10.1136/archdischild-2016-311535.58 (Appendix XXVI)

Aston J, Huynh C, Sinclair A, Wilson K, Terry D. Medication Review of Children on Long-Term Medications: A Review of the Literature. *Arch Dis Child* 2016 Sep; 101(9):e2. doi: 10.1136/archdischild-2016-311535.47 (Appendix XXVII)

9.2 Study 2 publications

9.2.1 Published paper

Aston J, Wilson KA, Terry DR. Children/young people taking long-term medication: a survey of community pharmacists' experiences in England. *Int J Pharm Pract* 2017 doi: 10.1111/ijpp.12371 [published Online First: 2017/04/04] (Appendix XXVIII)

9.2.2 Conference oral presentation

Aston J, Wilson KA, Terry DRP. Children/young people taking long-term medicines -a survey of the experiences of community pharmacists. Paper presented at the Neonatal & Paediatric Pharmacists Group 22nd Annual Professional Conference and Exhibition; 2016 4th – 6th November; Birmingham, UK. (Appendix XXIX)

9.3 Study 3 publications

9.3.1 Published paper

Aston J, Wilson KA, Terry DRP. The treatment-related experience of parents, children and young people with regular prescribed medication. *Int J Clin Pharm* doi.org/10.1007/s11096-018-0756-z

9.4 Study 4 Publications

9.4.1 Conference poster presentation

Aston J, Wilson KA, Terry DRP. Parent/carer Intended Non-Adherence to their Child's Medication Regimen. Poster presented at: the 24h Annual professional conference of the Neonatal and Paediatric Pharmacists Group; 2018 9 – 11 November; Bristol, UK (Appendix XXXI)

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Appendix I Study 1 participant information leaflet for parents/carers and patients aged >16 years

Starting a New Medicine Study

You are being invited to take part in a research study. Before you decide if you would like to take part it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and ask any questions that you have.

What is the purpose of the study?

We would like to learn more about some of the experiences of parents/carers, children and young people during the first few weeks after starting a new medicine.
Some studies in adults have been done to find out what issues they had when they began taking a new medicine. There is very little information about what issues are experienced when children and young people begin taking a new medicine which is why we want to carry out this research study. The results will help us to provide more support for children, young people and their families when a new medicine is started.

Why have I been chosen?

You have been chosen because you have handed in a prescription for a medicine that is to be taken for 6 weeks or longer.

What will happen if I take part?

The study will involve you being asked some questions by the pharmacist giving you the medicine today so that we can find out what you currently know about the new medicine. Then, after about 6 weeks a Pharmacist will telephone you to ask you some questions about how you are getting on with the medicine. The telephone call should only last about 20 minutes and will include questions on:

- What information you needed about the new medicine
- How easy it is to take/give the new medicine
- Any possible side effects that you feel might be due to the medicine

- Obtaining further supplies of the medicine
- Have you been able to give/take the medicine as told to by the doctor

The information provided will be written down so that we can remember what has been said. This will help us when we look at all of the information provided by everyone else in the study.

Do I have to take part?

You do not have to take part in this study and you can change your mind at any time. If you decide not to take part, this will not in any way affect the standard of care you receive here at Birmingham Children's' Hospital.

Will my taking part in this study be kept confidential?

All the information provided by you in this study will be kept confidential. Paper and electronic copies of the information will be stored at Birmingham Children's Hospital and destroyed when the study has finished.
The results from the pharmacist's questions and telephone interview will be added to the results from other parents/carers and children to identify common themes.

What will happen to the results of the research study?

The results may also be published in a medical journal in order to share our findings with other health professionals. Any published results/information will not identify the participants. If you would like a summary of the results from the study please add your contact details to the relevant section of the consent form.

Who is organising and funding the research?

The research is being organised by:
Mr Jeff Aston, Lead Operational Pharmacist, Birmingham Children's Hospital
Dr David Terry, Director, Academic Practice Unit, Birmingham Children's Hospital and Aston University
The research is being funded by:
The Pharmacy Department, Birmingham Children's Hospital NHS Foundation Trust

Who has reviewed the study?

The study has been reviewed by Aston University's Ethics Committee and the NHS Research Ethics Committee.

Who do I contact if I need further Information?

If you have any questions or need any more information please speak to the "Medicines Chest" pharmacist or [redacted]

Who do I contact if I wish to make a complaint about the way in which the study is conducted?

If you have any concerns about the way in which the study has been conducted please contact the secretary of Aston University's ethics committee on [redacted] telephone 0121 204 4869.

Thank you for taking the time to read this information sheet. If you would like to take part please inform the pharmacist when you collect your medicine.

Appendix II Study 1 participant information leaflet for young people (12 to 15 years)

Starting a New Medicine Study

Information for young people

We would like to ask for you and your parent's/carer's help with a study we are doing about the experiences that children and young people have in the first few weeks after starting a new medicine.

Why is the study being done?

We would like to learn more about some of the experiences of parents/carers, children and young people during the first few weeks after starting a new medicine.
Some studies have already been done in adult patients to find out what problems they had when they began taking a new medicine. At the moment we know very little information about the experiences of children and young people when they begin taking a new medicine which is why we want to carry out this study. The information that you tell us will help us to provide more support for children, young people and their families when a new medicine is started.

Why have we been chosen?

You have been chosen because you are about to start taking a new medicine.

What will happen if I take part?

If you decide to take part, your mum, dad or carer will be asked some questions by the pharmacist giving you the medicine today so that we can find out what they already know about your new medicine. Then, after about 6 weeks a pharmacist will telephone your mum, dad or carer to ask you some questions about how you are getting on with your medicine. We might ask questions like:

- What you/they would like to know about your medicine?
- Are you finding it easy to take your medicine?

- Is the medicine having any effects that you are unhappy about?

The answer to these questions will be written down so that we remember what has been said. This will help us when we add the information to what other people in the study have told us.

Do I have to take part?

You and your parent/carer do not have to take part and you can change your mind at any time. If you decide not to take part, this will not in any way affect the care that you receive here at Birmingham Children's' Hospital.

Will other people know that I am taking part in this study?

No, all the information that you give us will be kept confidential.

What will happen to the information that you get?

The information you give us will be added to the information we are given from other children and young people. We might let other people know about what we find out but we won't tell anyone your name. This information can be used to help other children and young people.

Who do I ask if I have any questions?

If you have any questions that you would like to ask us please talk to the "Medicines Chest" pharmacist who gave you this information sheet.

Appendix III Study 1 participant information leaflet for children (aged 6 – 11 years)

Starting a New Medicine Study

Information for children

We would like to ask for your help with a study we are doing. We would like to find out how you are getting on with your new medicine after you have been taking it for a little while.

Why is the study being done?

We would like to learn more about how you are getting on with your new medicine after you have been taking it for a little while.

We already know how adults find taking new medicines from other studies but not children. The information that you tell us will help us to think of new ways to help you with your new medicine.

Why have I been chosen?

You have been chosen because you are about to start taking a new medicine.

What will happen if I take part?

Your mum, dad or carer will be asked some questions by the pharmacist giving you the medicine today so that we can find out what they already know about it. Then, after a few weeks a pharmacist will telephone your mum, dad or carer to ask about how you are getting on with your new medicine. They will write down what has been said to help them remember later on.

Do I have to take part?

You do not have to take part and you can change your mind at any time.

Will other people know that I am taking part in this study?

No. No-one else will know that you are helping with this study.

What will happen to the information that you get?

We will add what your mum, dad or carer tell us to what other people have told us. We might let other people know about what we find out but we won't tell anyone your name. This information can be used to help other children and young people.

Who do I ask if I have any questions?

If you have any questions that you would like to ask us please talk to the pharmacist who gave you this leaflet.

Appendix IV Study 1 participant information leaflet for parents/carers to use with young children (aged <6 years)

Starting a New Medicine Study

Information for parents/carers to go through with young children

- The pharmacist would like to learn about what it is like for you to take a new medicine.

- They would like to ask your mum, dad or the person who looks after you some questions about your new medicine.

- They will ask some questions now and telephone after a few weeks to find out how you are getting on.

- This will help us to know how we can help you more to take your new medicine.

Thank you!

Appendix V Study 1 consent form

Starting a New Medicine Study
Volunteer Consent Form

Project Title: Starting a New Medicine Study

Name of Chief Researcher: Jeff Aston

		Initial Box
1	I confirm that I have read and understood the information sheet for the above study.	
2	I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
3	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without this affecting the care I/my child receives from Birmingham Children's Hospital.	

Name of volunteer	Date	Signature
Name of person taking consent (if different from researcher)	Date	Signature
Name Researcher	Date	Signature

If you would like a copy of the final report from the study please write your contact details (email or postal address) below:

Appendix VI Study 1 assent form

Starting a New Medicine Study

Volunteer Consent Form –*Child and Young Person*

Project Title: Starting a New Medicine Study

Name of Chief Researcher: Jeff Aston

		Please write your initials in each box if you agree with each sentence.
1	I understand what this study is about.	
2	I have asked any questions that I had.	
3	I know that I can change my mind at any time.	

_____	_____	_____
Write your name here	Date	Write your signature here
_____	_____	_____
Name of person taking consent (if different from researcher)	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

Appendix VII Study 2 participant information leaflet

A study of Medication Related Issues Encountered by Community Pharmacists in Children/Young People Prescribed Long-Term Medicines

You are being invited to take part in a research study. Before you decide if you would like to take part it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully.

What is the purpose of the study?

The National Service Framework for Children includes recommendations for supporting children taking medicines. It is known that when adults start new medicines, they may quickly become non-adherent and identify a number of medicine related problems and information needs. These include side effects, concerns about taking a new medicine, difficulty in swallowing the medicine and remembering the regimen. Improved adherence to a medication regimen has been shown to improve disease outcomes. As a community pharmacist you may offer medication review through the Medicines Use Review and New Medicines Services. However, these services may not be accessible to children/young people or their carers and thus they may not receive the same level of support when taking a long-term medicine as an adult does. This research is required to determine the issues that children/young people and their parents/carers have when taking a long-term medicine in the community pharmacy setting.

Why have I been chosen?

You have been chosen because you are a community pharmacist.

What will happen if I take part?

The study will involve you completing the enclosed questionnaire. This will take about 10 minutes.

Do I have to take part?

You do not have to take part in this study and you can change your mind at any time.

Will my taking part in this study be kept confidential?

All the information provided by you in this study will be kept confidential. Paper and electronic copies of the information will be stored at Birmingham Children's Hospital and destroyed when the study has finished.

What will happen to the results of the research study?

The results may also be published in a medical journal in order to share our findings with other health professionals. You will not be identified in any report/publication.

Who is organising and funding the research?

The research is being organised by:

Mr Jeff Aston, Associate Chief Pharmacist, Birmingham Children's Hospital
Dr David Terry, Director, Academic Practice Unit, Birmingham Children's Hospital and Aston University
Professor keith Wilson, Aston University
The research is being funded by:
The Pharmacy Department, Birmingham Children's Hospital NHS Foundation Trust

Who has reviewed the study?

The study has been approved by Aston University's Ethics Committee.

Who do I contact if I need further Information?

If you have any questions or need any more information please speak contact [redacted]

Who do I contact if I wish to make a complaint about the way in which the study is conducted?

If you have any concerns about the way in which the study has been conducted, in the first instance please contact the researcher above. However, if they are unable to resolve them issue you can contact the Secretary of the University Research Ethics Committee [redacted]

Thank you for taking the time to read this information sheet. If you would like to take part please complete the enclosed questionnaire and return in the enclosed pre-paid envelope by*****.**

Appendix VII Study 2 consent form

A Study of Medication Related Issues Encountered by Community Pharmacists in Children/Young People Prescribed Long-Term Medicines

CONSENT FORM

Dear Pharmacist,

If you have read the information sheet and would like to participate in this study please sign below and return to be in the enclosed envelope with the questionnaire by *********

	Initial Box
I confirm that I have read and understood the information sheet for this study.	
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason.	

Name_____ Signature_____ Date_____

You are under no obligation to participate in this study or give a reason for not participating. Any reasons for not participating would be very useful and can be entered in the box below and then returned to me in the enclosed envelope.

The number written on the rear of the consent form will enable me to identify your community pharmacy address so that I know not to contact you again on receipt of your response.
Thank you in anticipation of your help.

Jeff Aston
PharmD Student -Aston University
Associate Chief Pharmacist -Birmingham Children's Hospital NHS Foundation Trust

Appendix VIII Study 2 Questionnaire

A study of Medication Related Issues Encountered by Community Pharmacists in Children/Young People Prescribed Long-Term Medicines

Dear Pharmacist,

Thank you for agreeing to take part in this study.

This questionnaire relates only to your practice as a community pharmacist over the past 12 months.

A 'child/young person' is defined as anyone aged under 16 years.

A 'long term medicine' is defined as being taken for 6 weeks or more.

To answer the questions please circle the appropriate option or insert your answer in the space provided. Please use the 'other' options to add a response not covered by the question or to expand on an answer.

Thank you for your help.

[redacted]

PharmD Student

Aston University/

Associate Chief Pharmacist

Birmingham Children's Hospital NHS Foundation Trust

A study of Medication Related Issues Encountered by Community Pharmacists in Children/Young People Prescribed Long-Term Medicines

Medication Review			
Q1	**In the past 12 months have you:**	**Circle either YES or NO for each question.**	
1.1	Conducted a **Medication Use Review (MUR)** for a child/young person (age <16 years) either with the patient or their parent/carer?	**YES**	**NO**
1.2	Conducted a **New Medicines Service (NMS)** consultation for a child/young person (age <16 years) either with the patient or their parent/carer?	**YES**	**NO**
1.3	Offered any other medication review for a child/young person (<16 years) either to the patient or their parent/carer?	**YES**	**NO**
YOU ANSWERED 'NO' TO ANY OF THE STATEMENTS IN Q1 PLEASE GO TO Q2 OTHERWISE PROCEED TO Q3			

Medication Review			
Q2	**If you have answered 'no' to any of the statements in Q1 is this because:**	**Please circle either YES or NO for each statement.**	
2.1	It is difficult/impractical to consent a child in order to undertake an **MUR**.	**YES**	**NO**
2.2	I am not funded under the current arrangements to undertake an **MUR** on a patient's parent or carer.	**YES**	**NO**
2.3	I am not accredited to undertake **MUR** consultations.	**YES**	**NO**
2.4	It is difficult/impractical to consent a child in order to undertake an **NMS** consultation.	**YES**	**NO**
2.5	I am not funded under the current arrangements to undertake an **NMS** consultation on a patient's parent or carer.	**YES**	**NO**
2.6	I am not accredited to undertake **NMS** consultations.	**YES**	**NO**
2.7	I am not confident in undertaking a review of a child's medicine(s)	**YES**	**NO**
2.8	Please list below any other reasons that may prevent you from undertaking medication reviews in children taking long term medicines:		

Adherence			
Q3	**Has a patient or parent/carer reported any of the following issues relating to the adherence of a child/young person prescribed a long-term medicine?**	**Please circle either YES or NO for each statement.**	
3.1	The patient/carer had decided to stop taking/administering the prescribed medicine without informing the prescriber.	**YES**	**NO**
3.2	The patient/carer had decided to **reduce** the dose taken or administered without informing the prescriber.	**YES**	**NO**
3.3	The patient/carer had decided to **increase** the dose taken or administered without informing the prescriber.	**YES**	**NO**
3.4	The patient/carer has forgotten to take/administer a dose.	**YES**	**NO**
3.5	Please list below any reasons provided for deviating from the prescribed regimen or stopping therapy:		

Information Needs			
Q4	**Has a patient or parent/carer asked you personally for any of the following information relating to a children/young people prescribed a long-term medicine?**	**Please circle either YES or NO for each statement.**	
4.1	INDICATION The patient/carer asked for more information on what the medicine was for (indication).	**YES**	**NO**
4.2	DOSE The patient/carer had asked for more information on the dose regimen.	**YES**	**NO**
4.3	ADMINISTRATION The patient/carer had asked for more information on how to take or administer the medicine(s).	**YES**	**NO**
4.4	SIDE EFFECTS The patient/care had asked for more information on side effects from the medicine(s).	**YES**	**NO**
4.5	Please list below any other information requested by patients/carers or use the space to expand on the above:		

Reported Issues			
Q5	**Has a patient or parent/carer reported to you personally any of the following medication related issues to you relating to a child/young person prescribed a long-term medicine:**	**Please circle either YES or NO for each statement.**	
5.1	The patient was experiencing side effects from their medicine(s)	**YES**	**NO**
5.2	The patient/carer was experiencing difficulties administering the prescribed medicine.	**YES**	**NO**
5.3	The patient's GP was unwilling to prescribe a hospital recommended medicine.	**YES**	**NO**
5.4	The patient/carer was having difficulties obtaining supplies of a medicine from **community pharmacy**.	**YES**	**NO**
5.5	The patient/carer was having difficulties obtaining supplies of a medicine from their **hospital pharmacy**.	**YES**	**NO**
5.6	The patient/carer was having difficulties obtaining supplies of a medicine from their **medicines homecare provider**.	**YES**	**NO**
5.7	Please list below any other issues experienced by patients or their carers:		

Some information about you…

Q6	In which year did you register as a pharmacist in the U.K.?	

Q7	On average, how many hours per week do you work in community pharmacy?	

Q8	Estimate how often you encounter children taking long term medicines in your practise as a community pharmacist?	Tick the most appropriate option for you
8.1	Never	
8.2	Once a year	
8.3	Every 3 months	
8.4	Once a month	
8.5	Once a week	
8.6	More than once a week	

Q9	On average, how many prescription forms do you oversee each month in your practise as a community pharmacist?	

Q10	What type of pharmacy do you mostly work in?	Tick all that apply
10.1	Supermarket pharmacy	
10.2	Health entre based pharmacy	
10.3	Healthy living pharmacy	
10.4	High street pharmacy in a large town/city	
10.5	Pharmacy in a small town/suburb	

Q11	What is your main type of community pharmacy employment?	Tick all that apply
11.1	A large national chain	
11.2	A medium sized (>50 stores) chain	
11.3	A small (≤50 stores) chain	
11.4	A single independent	

Q12	Based on your experience, are there any other points about medicines for children that might be relevant to this study?

Q13	What, if any, additional support would help you better care for children taking long-term medicines?

If you are interested in being involved with further research around supporting children taking their medicines please provide an email address below:

Email_____

Please tick if you would like to receive a summary of the results ☐

THANK YOU FOR COMPLETING THIS SURVEY. PLEASE RETURN IN THE PRE-PAID ENVELOPE PROVIDED

Appendix IX Study 2 telephone consent form for non-responders

A study of Medication Related Issues Encountered by Community Pharmacists in Children/Young People Prescribed Long-Term Medicines

TELEPHONE CONSENT FORM

Pharmacist Name_____ Date_____

	Principal Investigator to Initial Box
The above named person has confirmed that they have understood the information provided as described from the participant information sheet for this study.	
The above named person has confirmed that they understand that their participation is voluntary and that they are free to withdraw at any time without giving any reason.	

Consent taken by:

[redacted] Signed_____ Date_____

Study principal investigator

Participants to be advised that they are under no obligation to participate in this study or to give a reason for not participating. Any reasons for not participating would be very useful for me to record:

Appendix X Study 3 parent/guardian consent form

Parent/Guardian Consent Form

Project Title: A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Research Venue: Birmingham Children's Hospital

IRAS Study Number: 213615

Participant Identification Number:

Name of Researcher: Jeff Aston

Name of Project Supervisor**:** David Terry

		Please initial in each box below.
1	I confirm that I have read and understood the participant information sheet for the above study. I have had the opportunity to consider the information, ask questions and they have been answered satisfactorily.	
2	I understand that the interview may take place with my child present and that they can also take part if they would like to.	
3	I understand that mine and my child's participation is voluntary and that I am free to withdraw at any time, without giving a reason and without mine or my child's care or legal rights being affected.	
4	I understand that relevant sections of any of my child's medical notes and data collected during the study may be looked at by responsible individuals from Aston University, Birmingham Children's Hospital or from the regulatory authorities where it is relevant to my taking part in the research. I give permission for these individuals to have access to my child's records.	

5	I consent to the secure and confidential storage, of personal information for the purposes of this study. I understand that any information that could identify me or my child will be kept strictly confidential and that no personal information will be included in the study report or other publication.	
6	I agree to the interview being digitally audio recorded.	
7	I understand that quotes from this interview may be used in a report that will be shared with others but the researchers will not include mine or my child's name.	

Name of Child: …….

_____	_____	_____
Name of Parent/Guardian	**Signature**	**Date**

_____	_____	_____
Name of Researcher	**Date**	**Signature**

If you would like a summary of the results from this study please provide either an email or postal address below:

1 copy for participant, 1 copy for researcher, 1 copy for patient records

Appendix XI Study 3 patient consent form

Patient Consent Form

Project Title: A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Research Venue: Birmingham Children's Hospital

IRAS Study [redacted]

Participant Identification Number:

Name of Researcher: [redacted]

Name of Project Supervisor**:** [redacted]

		Please initial in each box below.
1	I confirm that I have read and understood the participant information sheet for the above study. I have had the opportunity to consider the information, ask questions and they have been answered satisfactorily.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without my care or legal rights being affected.	
3	I understand that relevant sections of my medical notes and data collected during the study may be looked at by responsible individuals from Aston University, Birmingham Children's Hospital or from the regulatory authorities, where it is relevant to my taking part in the research. I give permission for these individuals to have access to my records.	
4.	I consent to the secure and confidential storage of personal information for the purposes of this study. I understand that any information that could identify me will be kept strictly confidential and that no personal information will be included in the study report or other publication.	
5.	I agree to my interview being digitally audio recorded.	

6.	I understand that quotes from this interview may be used in a report that will be shared with others but the researchers will not include my name.	

_____	_____	_____
Name	**Signature**	**Date**
_____	_____	_____
Name of Researcher	**Date**	**Signature**

If you would like a summary of the results from this study please provide either an email or postal address below:

1 copy for participant, 1 copy for researcher, 1 copy for patient records

Appendix XII Study 3 Assent form

Volunteer Assent Form –*Child and Young Person*

Project: A study to explore how the day to day lives of patients and their families are affected when children and young people take regular medicines

Research Venue: Birmingham Children's Hospital

IRAS Study [redacted]

Participant Identification Number:

Name of Researcher: [redacted]

Name of Project Supervisor: [redacted]

Child to circle all they agree with

Have you read (or had read to you) information about this project?

Yes/No

Has somebody else explained this project to you?

Yes/No

Do you understand what this project is about?

Yes/No

Have you asked the questions you want?

Yes/No

Have you had your questions answered in a way you understand?

Yes/No

Do you understand it's ok to stop taking part at any time?

Yes/No

Are you happy to begin this study?

Yes/No

If any answers are "no" and you don't want to take part, do not sign your name.

If you do want to take part in this study, please sign your name and write today's date.

Your name……

Date…….

Your Mum, Dad or the person who looks after you needs to sign here to show that they are happy for you to take part in the research

_____	_____	_____
Parent/guardian name	Date	Parent/guardian signature

The researcher who explained this project to you needs to sign here too:

_____	_____	_____
Name of Researcher	Date	Signature

1 copy for participant, 1 copy for researcher, 1 copy for patient records

Appendix XIII Study 3 participant information leaflet for parents/carers

A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Information for Parents/Carers

Invitation

Hello, my name is Jeff Aston and I am one of the pharmacists at Birmingham Children's Hospital. I am carrying out a research project as part of my Doctor of Pharmacy degree and would like to invite you to take part.

Before you decide if you want to join in, it is important to understand what the project is about and what it will mean if you take part. So please read this leaflet carefully. Also talk to your family, friends, doctor, nurse or a member of the research team whose details are at the end of this information sheet if you would like to.

What is the purpose of the study?

I would like to learn more about the experiences of parents/carers, children and young people when taking medicines. In particular, how taking medicines impacts on their day-to-day lives. There is very little information about the impact that medicines taking has on the lives of children, young people and their families which is why I want to carry out this study. The results will help guide our decisions around the choice of medicine and how it is taken to provide a more patient and family friendly experience. This will also allow patients to get the most out of their medicines.

Why have I been invited?

Parents/carers of children under 16 years of age and taking two or more regular medicines on a long-term basis are being invited to take part in this study.

What will happen if I take part?

It is important that you have a good understanding of the study and that your child also knows why I am conducting the study. That is why you have also been given an age appropriate information sheet to go through with your child. Before I can start the study, after I have gone through this information sheet and you and your child wish to take part in the study, I will take consent from you and what is called 'assent' from your child if they are

above seven years of age. If you agree to take part in this study, I will ask you some questions about your experiences of looking after a child taking regular medicines and how this has impacted on your daily life. You will have been provided with a copy of the questions with this information leaflet. If your child is over seven years old I will encourage them to take part if they would like to. The interview will take place in your child's room if they are in a single room or in a private room at the hospital. The interview should take approximately 45 minutes. The interview will be audio recorded using a dictaphone so that I can listen to what we talked about and type it up. I may need to look at your child's medical records and use your child's hospital medication chart to help identify what medicines your child usually takes at home.

Do I have to take part?

No, and you do not need to give a reason. It is your and your child's choice whether you, or your child, would like to take part in the study interview. You are free to change your mind at any time. If you do not want to take part just tell me (Jeff). If you, or your child, decide not to take part, this will not in any way affect the care that your child receives here at Birmingham Children's' Hospital.

Will my taking part in this study be kept confidential?

All the information provided by you (and your child) in this study will be kept confidential. Paper and electronic copies of the information will be stored at Birmingham Children's Hospital and destroyed when the study has finished.
Any quotes (taken from the interview) or results that we include in the study report will be anonymised. Anonymised means that you and your child's name will be replaced by a number so that neither you nor your child can be linked to anything included in the report.

How will this research be of benefit to me?

There are unlikely to be any immediate benefits to you or your child. The results of the study could help us when we decide which medicines we chose for patients and if any extra help is needed for our patients taking medicines at home.

What will happen to the results of the research study?

The results may also be published in a medical journal in order to share our findings with other health professionals. Any published results/information will not identify the participants. Please indicate in the box on the consent form if you would like a summary of the results.

Who is organising and funding the research?

The research is being organised by:
Mr Jeff Aston, Deputy Chief Pharmacist, Birmingham Children's Hospital
Dr David Terry, Director, Pharmacy Academic Practice Unit, Birmingham Children's Hospital and Aston University

Who has reviewed the study?

The study has been reviewed/approved by the West of Scotland Research Ethics Committee 3.

Who do I ask if I have any questions?

If you have any questions that you would like to ask us please talk to [redacted] when he visits you next, by phone: [redacted]

What happens when the research project finishes?

The research will be talked about and written down but no one will know that you took part.

Who can I ask for general information about taking part in research?

You can contact the NHS Patient Advisory Liaison Service (PALS) at Birmingham Children's Hospital if you would like advice on taking part in research email pals@bch.nhs.uk or telephone 0121 333 8403.

Who can I contact if I have any concerns?

If you have any concerns about the way in which the study is being carried out you should first contact me Jeff Aston or my supervisor. All our contact details can be found at the end of this information sheet. If we are unable to help you, you can contact Mr John Walter, Director of Governance, Aston University:

Email: [redacted] or telephone 0121 204 4869.

Contact for further information

Researcher: [redacted]
Telephone: 0121 333 9821, [redacted]

Project Supervisor: Dr David Terry
Telephone: 0121 204 3941, email: [redacted]

Thank you for taking the time to read this information sheet. I will come and see you in the next 1 – 2 days to see if you would like to take part and, if so, agree a time to interview you.

Appendix XIV Study 3 participant information leaflet for patients aged ≥16 years

A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Information leaflet for patient aged over 16 years

Invitation

Hello, my name is Jeff Aston and I am one of the pharmacists at Birmingham Children's Hospital. I am carrying out a research project as part of my Doctor of Pharmacy degree and would like to invite you to take part. Before you decide if you want to join in, it is important to understand what the project is about and what it will mean if you take part. So please read this leaflet carefully. Also talk to your family, friends, doctor, nurse or a member of the research team whose details are at the end of this information sheet if you would like to.

What is the purpose of the study?

We would like to learn more about experiences of parents/carers, children and young people when taking medicines. In particular, how taking medicines impacts on their day-to-day lives. There is very little information about the impact that medicines taking has on the lives of children, young people and their families which is why we want to carry out this study.
The results will help guide our decisions around the choice of medicine and how it is taken to provide a more patient and family friendly experience. This will also allow patients to get the most out of their medicines.

Why have I been invited?

You have been chosen because you are taking two or more regular medicines on a long-term basis.

What will happen if I take part?

If you agree to take part in this study, I will ask you some questions about your experiences of using medicines and how they have impacted on your daily life. You will have been given a copy of the questions with this information leaflet. The interview will take place in your room

if you are in a single room or in a private room at the hospital. You may have someone with you at the meeting if you would like. The interview should take approximately 45 minutes. If you agree, the interview will be audio recorded using a dictaphone so that I can listen to what we talked about and type it up. I may need to look at your medical records and use your hospital medication chart to help identify what medicines your child usually takes.

Do I have to take part?

No, and you do not need to give a reason. It is your choice whether you want to take part and you can change your mind at any time. If you do not want to take part just tell me (Jeff). If you decide not to take part, this will not in any way affect the care that you receive here at Birmingham Children's' Hospital.

Will my taking part in this study be kept confidential?

All the information provided by you in this study will be kept confidential. Paper and electronic copies of the information will be stored at Birmingham Children's Hospital and destroyed when the study has finished. Any quotes (taken from the interview) or results that we include in the study report will be anonymised. Anonymised means that your name will be replaced by a number so that you cannot be linked to anything included in the report.

How will this research be of benefit to me?

There are unlikely to be any immediate benefits to you. The results of the study could help us when we decide which medicines we chose for patients and if any extra help is needed for our patients taking medicines at home.

What will happen to the results of the research study?

The results may also be published in a medical journal in order to share our findings with other health professionals. Any published results/information will not identify the participants. Please indicate in the box on the consent form if you would like a summary of the results.

Who is organising and funding the research?

The research is being organised by:
Mr Jeff Aston, Deputy Chief Pharmacist, Birmingham Children's Hospital

Dr David Terry, Director, Pharmacy Academic Practice Unit, Birmingham Children's Hospital and Aston University

Who has reviewed the study?

The study has been reviewed/approved by the West of Scotland Research Ethics Committee 3.

Who do I ask if I have any questions?

If you have any questions that you would like to ask us please talk to [redacted], when he visits you next, by phone: 0121 333 9821 or email: [redacted]

What happens when the research project finishes?

The research will be talked about and written down but no one will know that you took part.

Who can I ask for general information about taking part in research?

You can contact the NHS Patient Advisory Liaison Service (PALS) at Birmingham Children's Hospital if you would like advice on taking part in research email: pals@bch.nhs.uk or telephone: 0121 333 8403.

Who can I contact if I have any concerns?

If you have any concerns about the way in which the study is being carried out you should first contact me Jeff Aston or my supervisor. All of our contact details can be found at the end of this information sheet. If we are unable to help you, you can contact Mr John Walter, Director of Governance, Aston University:
Email: [redacted] telephone 0121 204 4869.

Contact for further information

Researcher: [redacted]
[redacted]

Project Supervisor: [redacted]

Telephone: 0121 204 3941 email: [redacted]

Thank you for taking the time to read this information sheet. I will come and see you in the next 1 – 2 days to see if you would like to take part and, if so, agree a time to interview you.

Appendix XV Study 3 participant information leaflet for young people aged 12 – 15 years

A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Information Leaflet for Young People Aged 12 – 15 Years

Invitation

Hello, my name is Jeff Aston and I am one of the pharmacists at Birmingham Children's Hospital. I am carrying out a research project as part of my Doctor of Pharmacy degree and would like to invite you and your parents or carers to take part. Before you decide if you want to join in, it is important to understand what the project is about and what it will mean if you take part. So please read this leaflet carefully. Also talk to your family, friends, doctor, nurse or a member of the research team whose details are at the end of this information sheet if you would like to.

What is research?

Research is all about finding out something new that will help us and other young people in the future. For example, we hope that the results from this study will help us better support patients, like yourself, and their families when our patients take medicines whilst at home.

Why is the study being done?

We would like to learn more about the experiences of parents/carers, children and young people when they regularly take medicines. We don't know how taking medicines affects your day to day life. When we find this out it will help us when deciding what medicines may suit you best so that they don't affect your daily life too much and what extra help we can provide to help you to take your medicines.

Why have I been invited?

You have been chosen because you usually take two or more medicines every day.

What will happen if I take part?

If you and your parents or carers decide to take part, I will meet with your mum, dad or carer and yourself if you would like to join us. I will ask your parents/carers some questions about how you are all getting on with your medicines and how they might affect what you do each day. You can help with the answers to these questions if you would like to. Your parents/carers will have been given a copy of the questions with their information leaflet. The interview will take place in your room if you are in a single room or in a private room at the hospital. The meeting should take approximately 45 minutes. If your parents/carers agree, our conversations will be audio recorded using a dictaphone so that after the meeting I can listen to what we talked about and type it up. I may need to look at your medical records and use your hospital medication chart to help identify what medicines you usually take.

Do I have to take part?

No, and there is no need to give need to give a reason. It is you and your parents'/carers' choice whether to take part and you can change your minds at any time. If you or your parents/carers do not want to take part, just tell me (Jeff). If you or your parents/carers do not wish to take part, this will not in any way affect the care that you receive here at Birmingham Children's' Hospital.

What if I want to stop taking part?

If you or your parents/carers want to stop taking part, they can just let me know and I will stop our meeting immediately.

Will anyone else know I'm doing this?

All your information will be kept private. This means that if we include any information or anything that has been said in our report, no one will be able to link it back to you.

Will joining in help me?

What we find out may not help you straight away. In the future, the results may help us when we decide which medicines we chose for patients and if any extra help is needed for our patients taking medicines at home.

Will other people know that I am taking part in this study?

No, all the information that you and your parent/carer give us will be kept confidential. If we include anything that has been said in our report, no one will know who has said it.

What will happen to the information that you get?

The information you and your parent/carer give us will be added to the information we are given about the experiences of other children and young people. We might let other people know about what we find out but we won't tell anyone your name or any information about you. This information can be used to help other children and young people.

Who do I ask if I have any questions?

If you have any questions that you would like to ask us please talk to the person who gave you this leaflet or Jeff Aston, when he visits you next, by phone: 0121 333 9821 or email: jeff.aston@nhs.net.

What happens when the research project finishes?

The research will be talked about and written down but no one will know that you took part.

Who can I ask for general information about taking part in research?

You or your parent/carer can contact the NHS Patient Advisory Liaison Service (PALS) at Birmingham Children's Hospital if you would like advice on taking part in research email: pals@bch.nhs.uk or telephone: 0121 333 8403.

Who can I contact if I have any concerns?

If you have any concerns about the way in which the study is being carried out you should first contact me, Jeff Aston, or my supervisor. All of our contact details can be found at the end of this information sheet. If we are unable to help you, you can contact Mr John Walter, Director of Governance, Aston University:
Email: j.g.walter@aston.ac.uk or telephone 0121 204 4869.

Contact for further information

Researcher: [redacted]

Telephone: 0121 333 9821 email: [redacted]

Project Supervisor: [redacted]

Telephone: 0121 204 3941 email: [redacted]

Thank you for taking the time to read this information sheet. I will come and see your parent/carer in the next 1 – 2 days to see if they would like to take part and, if so, agree a time to interview them.

Appendix XVI Study 3 participant information leaflet for children aged 7-11 years

A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Information for children 7 – 11 years

Invitation

Hi, my name is Jeff and I am carrying out a research project. I would like to invite you, your mum, dad or carer to take part in my project. Before you decide if you want to join in, it is important to understand what the project is about and what it will mean if you take part. So please read this leaflet carefully with your mum, dad or carer. Also talk to your family, friends, doctor, nurse or a member of the research team whose details are at the end of this information sheet if you would like to.

What is research?

Research is all about finding out something new that will help us and other children in the future.

Why is the study being done?

I would like to learn more about how you are getting on with your medicines every day. The information that you give me will help us to think of new ways to help children, and their families, with their medicines.

Why have I been invited?

You have been chosen because you take medicines each day at home.

What will happen if I take part?

I will ask you and your mum, dad or carer some questions about how you are finding taking your medicines. They will have been given a copy of the questions with their information leaflet. You can also help with answering the questions if you would like to.

I can ask you and your mum, dad or carer the questions. If you are in your own room I can ask them there or in another private room at the hospital. The meeting should take about 45 minutes. If they agree, the interview will be recorded so that I can listen to what we talked about and type it up. I may need to look at your medical records and use your hospital medication chart to help identify what medicines you usually take.

Do I have to take part?

No, and there is no need give a reason. It is you, your mum, dad or carers choice whether to take part and they can change their mind at any time. If you or your mum, dad or carer decide that you do not want to take part you can just tell me (Jeff). If they decide not to take part, this will not in any way affect the care that you receive here at Birmingham Children's Hospital.

What if I want to stop taking part?

If you or your mum, dad or carer want to stop taking part, just let me know and I will stop our meeting.

Will anyone else know I'm doing this?

All your information will be kept private. This means that if we include any information or anything that you or your mum, dad or carer have said in our report, no one will be able to link it back to you.

Will joining in help me?

What we find out may not help you straight away. In the future, the results may help us when we decide which medicines we chose for patients and if any extra help is needed for our patients taking medicines at home.

What will happen to the information that you get?

We will add what you, your mum, dad or the person who looks after you tell us to what other people have told us. We might let other people know about what we find out but we won't tell anyone your name. This information can be used to help other children and young people.

Who do I ask if I have any questions?

If you have any questions that you would like to ask us, please talk to [redacted], when he visits you next, by phone: 0121 333 9821 or email: [redacted]

What happens when the research project finishes?

The research will be talked about and written down but no one will know that you took part.

Where can I find more information about taking part in research?

Your mum, dad or carer can contact the NHS Patient Advisory Liaison Service (PALS) at Birmingham Children's Hospital if you would like advice on taking part in research email: pals@bch.nhs.uk or telephone 0121 333 8403.

Who can I contact if I have any concerns?

If you or your mum, dad or carer have any concerns about the way in which the study is being carried out they should first contact me, Jeff Aston, or my supervisor. All of our contact details can be found at the end of this information sheet. If we are unable to help you, you can contact [redacted] Director of Governance, Aston University:
Email: [redacted] or telephone 0121 204 4869

Contact for further information

Researcher: [redacted]
Telephone: 0121 333 9821 email: [redacted]

Project Supervisor: [redacted]
Telephone: 0121 204 3941 email: [redacted]

Thank you for taking the time to read this information sheet. I will come and see your mum, dad or carer in the next 1 – 2 days to see if they would like to take part and, if so, agree a time to speak to them.

Appendix XVII Study 3 participant information leaflet for young people aged ≤6 years

A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Information for parents/carers to read with young children

This is a pharmacist.

A pharmacist is someone who works at a hospital and provides you with your medicines.

The pharmacist at the Birmingham Children's hospital would like our help.

They want to find out what it is like for you and us when you have to take medicines and how he can help you to take your medicines.

If you want to help the Pharmacist, you and I can sit down with the Pharmacist. The Pharmacist will talk to me and ask me some questions.

Appendix XVIII Study 3 data collection proforma/interview question prompts

A Study to Explore How the Day to Day lives of Patients and their Families are Affected when Children and Young People take Regular Medicines

Demographic Information					
Patient Initials		Age		Specialities involved in care	

Medicines Reconciliation						
Name	Dose	Frequency	Formulation	Prescribing team	Supply Route*	L/U/O**

**AH = Attend hospital HH = Hospital arranged homecare GP = GP Other (specified)

*L = licensed U = unlicensed O = off-label use (added by study PI)

Medicines Routine
Tell me about your/your child's daily regime of taking medicines? What do you do and when?
What changes have you had to make to your everyday living to take in to account administering/taking medicines?
What aspects of you/your child taking medicines every day do you find the most challenging?
What have you had to do to solve any of the challenges of the routine of taking medicines?
Have you used family members to help with any of your/your child's medicines?
Have you asked a healthcare professional for help with the medicine taking schedule?
How have you managed to make the medicines taking schedule (when you/your child take the medicines) fit around your daily life? Have you adjusted the schedule yourself?

Have you looked up further information about the medicine yourself? Where did you look? Why did you seek further details/what did you want to find out?
Do you use any aids to help with remembering to take medicines e.g. pill box or a record of when administered/taken?
Do you feel that you are able to take/administer the medicine exactly as you have been told to? If not please explain why and how you take it differently.

Medication Characteristics
Have you experiences any problems with taking/administering any of the medicines? What about if there have been any changes to the dose?
Is the number of doses (such as the number of tablets/capsules) difficult to manage? How have you managed to get around this?
Have you found any difficulties with the medicines you take/administer to your child due to the size of tablet, taste of liquid, or any preparation that you have to do to get the right dose. How have you managed to get around this?
Does the packaging that the medicine comes in cause you any difficulties? How have you managed to get around this?
Have you experienced any problems if the brand/manufacturer of your/your child's medicine has changed?
What written instructions were you provided with about your medicines? Were they useful? Why? Would you have liked any additional information? If so what?

If the dose changes, when/how do you usually get told about this? Do you receive any written information? What happens regarding arranging a new supply of medicine?

Adverse Effects
Have you/your child experienced any side effects from any of the medicines?
How did this affect you/your child?
Did you know what to do?
Was it something that you knew could happen or was it a surprise?
Had anyone spoken to you about possible side effects?

Healthcare Associated Medication Related Burden
Have you encountered any difficulties in obtaining prescriptions or supplies of medicines for you/your child? What has been the biggest difficulty for you?
On average, how much time do you spend dealing with the healthcare system –for example travelling time to appointments, waiting time, telephone calls, collecting medication, waiting for medication deliveries. Can you give an example?
If you/your child are under more than one healthcare team has this caused any problems regarding coordinating appointments, the prescribing of medicines and obtaining a supply of the medicine? Please explain.
Have you ever received inadequate or conflicting information about your medicines? What did you do?
Is the way the information is provided to you about medicines suitable? For example face to face with the prescriber, from the pharmacist or nurse. If receiving medicines through home delivery how have you been provided with information about your medicines?

Medication Associated Social Burden
How has the need to take medicines impacted on your family life? Any disruption?
Have any of your family or friends mentioned anything about your medicines? Advice for example.
How has medicines taking impacted on you and/or your child's social life –holidays, visiting family or friends
Do you receive any regular support from family or friends to help with medicines taking for you/your child?

Are there any other challenges around medicines that I haven't mentioned that you'd like to raise?

Appendix XIX Study 3 medication taken by study patients

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
1 (11 years)	Movicol Paediatric	Half a sachet	Once a day	Sachet	L	General practitioner and community pharmacy	Respiratory
	Salbutamol	200 mcg	When required	Inhaler	L		
	Hydrocortisone	7.5mg, 5mg, 2.5mg	7.5mg in the morning, 5mg at midday and 2.5mg in the evening	Tablet	L		
	Cetirizine	5mg	Once a day	Tablet	L		
	Theophylline	250mg	Twice a day	Modified release Capsule	L		
	Fluticasone	50microg	Alternate days	Nasal spray	L		
	Seretide	250 mcg	Twice a day	Inhaler	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
2 (15 years)	Penicillin V	250mg	Twice a day	Tablet	O	General Practitioner and community pharmacy	Haematology
	Folic Acid	5mg	Once a day	Tablet	L		
	Paracetamol	500mg – 1g	Four times a day when required	Tablet	L		
	Ibuprofen	200 – 400mg	Three times a day when required	Tablet	L		
	Morphine sulphate	5mg	Four times a day when required	Solution	L	Hospital medical team and hospital pharmacy	

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
3 (11 years)	Azathioprine	75mg	Once a day	Tablet	L	Hospital medical team and hospital pharmacy	Gastroenterology
	Omeprazole	20mg	Once a day	Capsule	L		
	Calcium carbonate and colecalciferol	1.25g/400iu	Once a day	Tablet	O		
	Ciprofloxacin	200mg	Twice a day	Tablet	L		
	Prednisolone	Decreasing regimen	One a day	Tablet	L		
4 (14 years)	Mesalazine	1g	Three times a day	Tablet	L	Hospital medical team and hospital pharmacy	Gastroenterology
	Azathioprine	75mg	Once a day	Tablet	L		
	Hyoscine butylbromide	20mg	Three times a day	Tablet	L		
	Omeprazole	20mg	Once a day	Capsule	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
5 (14 years)	Itraconazole	200mg	Once a day	Capsule	O	General Practitioner and community pharmacy	Cystic Fibrosis
	Vitamin A and D	2	Once a day	Tablet	L		
	DNase	2.5	Once a day	Nebule	L		
	Sodium chloride	600mg	Twice a day	Modified release tablet	L		
	Ursodeoxycholic acid	300mg	Twice a day	Tablet	L		
	Salbutamol	400mcg	Twice a day	Inhaler	O		
	Seretide	250mcg	Twice a day	Inhaler	O		
	Insulin Lantus	10iu	Once a day	Injection	L		
	Montelukast	10mg	Once a day	Tablet	O		
	Sodium chloride 6%	Neb	Twice a day	Nebule	L		
	Pancreatin	10,000iu	When required	Capsule	L		
	Doxycycline	100mg	Twice a day	Tablet	O		
	Azithromycin	500mg	Once a day	Tablet	O		
	Tobi	28mg	Alt months	Inhalation powder	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
6 (14 years)	Sodium chloride 7%	4mL	Twice a day	Nebule	L (medical device)	General Practitioner and community pharmacy	Cystic fibrosis
	Ibuprofen	400mg	Three times a day	Tablet	L		
	Paracetamol	500mg	Four times a day	Tablet	L		
	Azithromycin	250mg	Alternate days	Tablet	O		
	Aztreonam	75mg	Three times a day	Nebule	L		
	Aspirin	75mg	Once a day	Tablet	O		
	Levemir	10iu	Once a day	Injection	L		
	Vitamin A&D	2	OD	Tablet	CHECK		
	Fluticasone	500mcg	BD	Inhaler	L		
	Salbutamol	400mcg	BD	Inhaler	L		
	Sodium chloride 3%	4mL	BD	Nebule	CHECK		
	DNase	2.5mg	OD	Inhaler	L		
	Fluticasone	27.5mcg	Twice a day	Nasal spray	L		
	Sodium chloride	600mg	Twice a day	MR tablet	L		
	Pancreatin	10,000iu	When required	Capsule	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
7 (16 years)	Acetylcysteine	2 sachets	Twice a day	Sachet	L	General Practitioner and community pharmacy	Cystic Fibrosis
	Vitamin A&D	4 caps	Once a day	Capsule	CHECK		
	Vitamin E	75iu	Once a day	Tablet	L		
	DNase	2.5mg	Once a day	Nebule	L		
	Sodium chloride 3%	4mL	Twice a day	Nebule	CHECK		
	Omeprazole	20mg	Twice a day	Capsule	L		
	Salbutamol	4 puffs	Twice a day	Inhaler	L		
	Prednisolone	5mg	Alternate days	Tablet	L		
	Cholecalciferol	1800iu	Once a day	Solution	U		
	Levemir	MDU	MDU	Injection	L		
	Sodium chloride	600mg	Twice a day	Modified release tablet	L		
	Movicol	4 sachets	Twice a day	Sachet	L		
	Pancreatin	10,000iu	PRN	Capsule	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
8 (6 years)	6-mercaptopurine	75mg	As per regimen	Suspension	L	Hospital medical team and hospital pharmacy	Oncology
	Methotrexate	17.5mg	Once a week	Tablets	L		
	Dexamethasone	7.5mg	As per regimen	Tablets	L		
	Ondansetron	4mg	When required	Solution	L		
	Metoclopramide	3mg	When required	Solution	L		
	Lactulose	10mL	Twice a day	Solution	O		
	Morphine sulphate	2.6mg – 4mg	When required	Solution	L		
	Chlorphenamine	2mg	When required	Solution	L		
	Co-trimoxazole	360mg	Twice a day on Saturdays and Sundays	Suspension	L		
	Salbutamol	200mcg	When required	Inhaler	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
9 (11 years)	Carbamazepine	180mg	Twice a day	Suspension	L	General Practitioner and community pharmacy	Community Paediatrician, Respiratory, Neurology, Ear, Nose and Throat, Cardiology, Ophthalmology, General Surgery, Dermatology, Plastics
	Levetiracetam	600mg	Twice a day	Solution	L		
	Omeprazole	10mg	Twice a day	Capsule (contents dissolved in sodium bicarbonate)	O		
	Midazolam	7.5mg	When required	Buccal solution	L		
	Oxygen	0.5-2L/min	-	-	N/A		
	Senna	10mL	Once a day	Syrup	L		
	Microlax®	One	When required	Rectal solution	L		
	Phosphate	One	When required	Enema	L		
	Movicol®Paediatric	One	When required	Powder for oral solution	L		
	Ibuprofen	100mg – 200mg	When required	Suspension	L		
	Hydrocortisone	One application	When required	Cream	L		
	Fusidic acid	One application	When required	Cream	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
10 (3 years)	Metoclopramide	3mg	Three times a day	Solution	L	Hospital medical team and hospital pharmacy	Oncology
	Ondansetron	4mg	Three times a day	Solution	L		
	Morphine sulphate	2.8mg	When required	Solution	L		
	Beclomethasone	200 mcg	Twice a day	Inhaler	L		
	Salbutamol	200 mcg	When required	Inhaler	L		
	Co-trimoxazole	240mg	Twice a day on Saturdays and Sundays	Suspension	O		
11 (3 months)	Phenytoin	7.8mg	Twice a day	Suspension	L	General Practitioner and community pharmacy	Neurology and General Paediatrics
	Vigabatrin	400mg	Twice a day	Powder sachets	L		
	Ranitidine	3.5mg	Three times a day	Solution	O		
	Levetiracetam 500mg/5mL	20mg	Twice a day	Solution	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
12 (1 year)	Cetraben®	Apply	Three times a day	Cream	L	Initial supply from hospital. Awaiting transfer to GP once hospital supplies used up.	Dermatology.
	Clobetasone butyrate	Apply	Step up and down	0.05% Ointment	L		
	Betamethasone valerate	Apply	Step up and down	0.1% Ointment	L		
	Emulsifying ointment with coconut oil	Apply	At night	Ointment	U		
	Dermol 500	Apply	Bath/shower Once a day	Emollient	L		
	Dermol 600	Apply	Bath/shower Once a day	Emollient	L		
	Cetirizine	2.5mg	Twice a day	Solution	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
13 (9 years)	Omeprazole	20mg	Once a day	Suspension	U	Hospital medical team and hospital pharmacy	Haematology, Nephrology, Respiratory.
	Penicillin V	250mg	Twice a day	Suspension	O		
	Aciclovir	300mg	Twice a day	Suspension	O		
	Atorvastatin	5mg	At night	Tablet	O		
	Sevelamer	1.6g	In overnight feed	Oral powder sachet	L		
	Ondansetron	4mg	Three times a day prn	Solution	L		
	Darbepoietin	30microg	Once weekly	Injection	L		
	Ergocalciferol	50, 000iu	Once weekly	Capsule	CHECK		
	1 alfacalcidol	1.5mcg	Three times a week	Solution	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
14 (3 years)	Vitamin E	50mg	Once a day	Solution	L	General practitioner and community pharmacy	Cystic Fibrosis
	Ranitidine	30mg	Twice a day	Solution	L		
	Sodium chloride 7%	4mL	Twice a day	Nebule	L		
	Pancreatin	1 scoop per 2g of fat.	When required	Granules	L		
	Salbutamol	2 – 4 puffs	When required	Inhaler	L		
	Colomycin	1MU	Twice a day	Nebule	O		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
15 (9 years)	Captopril	5mg	Three times a day	Solution	L	General practitioner and community pharmacy	Cardiology, Gastroenterology, General Paediatrics
	Salbutamol	2 puffs	When required	Inhaler	L		
	Omeprazole	10mg	Once a day	Tablet	L		
16 (2 years)	Phenobarbitone	25mg	Twice a day	Tablets	U	General practitioner and community pharmacy	Neurology, Gastroenterology, Respiratory, Ophthalmology
	Levetiracetam	150mg	Twice a day	Tablets	L		
	Carbamazepine	90mg	Twice a day	Tablets	L		
	Ranitidine	45mg	Twice a day	Solution	O		
	Glycopyronium	0.3mg	Twice a day	Tablets	O		
	Sytron	1mL	Once a day	Solution	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
17 (8 years)	Seretide '125'	2 puffs	Twice a day	Inhaler	L	General practitioner and community pharmacy	Respiratory
	Montelukast	5mg	At night	Tablets	L		
	Avamys	1 spray	Twice a day	Nasal Spray	L		
	Slophyllin	125mg	Twice a day	Tablets	L		
	Salbultamol	2 puffs	When required	Inhaler	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
18 (7 years)	Sirolimus	2.2mg	Once a day	Solution	O	Hospital medical team and homecare supply	Nephrology
	Mycophenolate	250mg	Twice a day	Solution	L		
	Sodium bicarbonate	15mmol	Three times a day	Suspension	U		
	D-Mannose	¼ teaspoon	Twice a day	Powder	U		
	Sodium feredetate	5mL	Three times a day	Solution	L		
19 (5 years)	Beclomethasone	100mcg	Twice a day	Inhaler	L	General practitioner and community pharmacy	Gastroenterology, Nephrology, Craniofacial
	Colestyramine	1g	Twice a day	Sachet	O		
	Ipratropium	20mcg	Three times a day.	Inhaler	L		
	Senna	5mL	Once a day	Solution	L		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
20 (2 years)	Omeprazole	10mg	Once a day	Suspension	U	Hospital medical team and hospital pharmacy	Respiratory
	Erythromycin	25mg	Four times a day	Suspension	O	General practitioner and community pharmacy	
	Dexamethasone	0.6mg	Alternate days	Solution	L	Hospital medical team and hospital pharmacy	
	Glycopyronium	0.5mg	Three times a day	Tab	O	Hospital medical team and hospital pharmacy	
	Co-trimoxazole	240mg	Once a day	Solution	O	General practitioner and community pharmacy	

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
21 (9 years)	Desmopressin	14mcg	In the morning	Oral lyophilisate	O	General practitioner and community pharmacy	Endocrinology, Oncology
		24mcg	At night				
	Levothyroxine	75mcg	In the morning	Tablets	L	General practitioner and community pharmacy	
	Growth Hormone (Genotropin)	0.6mg	Alternate days	Injection	L	Hospital medical team and hospital pharmacy	
		0.8mg	Alternate days				
	Hydrocortisone	3.5mg	In the morning	Solution	U	Hospital medical team and hospital pharmacy	
		3mg	In the afternoon				
		2mg	At night				
	Hydrocortisone	100mg	Immediately when required	Injection	L	Hospital medical team and hospital pharmacy	

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
22 (9 years)	Ranitidine	45mg	BD	Solution	L	General practitioner and community pharmacy	Inherited Metabolic Diseases
	L-carnitine	900mg	TDS	Solution	L		
	Metronidazole	80mg	OD	Suspension	O		

Patient (age)	Medication	Dose	Frequency	Formulation	Licensed (L), unlicensed (U), Off-label (O)	Supply Route	Medical teams involved in care
23 (7 years)	Clobazam	5mg	Three times a day	Suspension	L	General practitioner and community pharmacy	IMD, Neurology, Urology
	Chloral hydrate	480mg	At night, when required	Solution	U		
	Topiramate	10mg	Twice a day	Sprinkle capsule	L		
	Gabapentin	50mg	Three times a day	Suspension	L		
	Senna	3.75mg	At night	Syrup	L		
	Brivaracetam	30mg	Twice a day	Solution	O		
	Potassium chloride	10mmol	Three times a day	Solution	L		
	Levomepromazine	3.125mg	Twice a day	Tablets	O		
	Omeprazole	10mg	Once a day	Suspension	U		
	Movicol Paediatric	1 sachet	Three times a day	Sachets	L		
24 (7 years)	Sodium valproate	300mg	Twice a day	Solution	L	General practitioner and community pharmacy	Neurology
	Carbamazepine	300mg	Twice a day	Suspension	L		
	Salbutamol	200mcg	When required	Inhaler	L		

Appendix XX Study 4 cover letter

Dear Parent/Carer

A STUDY TO FIND OUT THE ABOUT THE CHANGES THAT PARENTS OR CARERS MAKE TO THEIR CHILD'S MEDICINES

My name is [redacted] and I am the Deputy Chief Pharmacist at Birmingham Children's Hospital. Your child is taking regular prescribed medicines on a long-term basis and we ensure you receive deliveries of their medicines arranged through the hospital pharmacy department.

I am writing to obtain your consent to take part in a study I am conducting as part of a PharmD degree course at Aston University. The purpose of the study is to learn more about the changes, if any, that parents/carers make to their child's prescribed regular medicines. Very little information has been published about this and the results will help us better support parents/carers when they have a child taking regular medicines.

Information about your child will be collected using the attached questionnaire and used in line with the Data Protection Act 1998.

I also attach an Information Leaflet which I hope will help you to answer any further questions you might have about the study. If you consent to taking part in this study please complete the attached questionnaire and return it to me in the enclosed pre-paid envelope.

Thank you for your assistance.

Yours sincerely

[redacted]

[redacted]

Deputy Chief Pharmacist

Birmingham Women's and Children's NHS Foundation Trust

PharmD Student

Aston University

Appendix XXI Study 4 Participant information leaflet

INFORMATION LEAFLET

A STUDY TO FIND OUT THE ABOUT THE CHANGES THAT PARENTS OR CARERS MAKE TO THEIR CHILD'S MEDICINES

Before you decide if you would like to take part in this study it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully. If there is anything that is not clear or if you would like more information please do ask. Please feel free to discuss this information with others and thank you for reading.

WHO IS DOING THE RESEARCH?

This study is being conducted by Jeff Aston, who is the Deputy Chief Pharmacist at Birmingham Children's Hospital and undertaking a PharmD degree at Aston University.

WHAT IS THE PURPOSE OF THE STUDY?

We would like to learn more about the changes, if any, that parents/carers make to their child's prescribed regular medicines. Very little information has been published about this. The results will help us better support parents/carers when they have a child taking regular medicines. This might be through the information that we provide about medicines or how we review patients taking long-term medicines over time.

WHY HAVE I BEEN INVITED?

We have chosen a random sample of 200 parents who have a child taking prescribed medicines on a long-term basis. The random sample was chosen from those parents who receive deliveries of their child's medicines arranged through the hospital pharmacy department.

WHAT WILL HAPPEN IF I TAKE PART?

If you agree to take part in this study please complete the enclosed questionnaire. It will take about 10 to 15 minutes to complete. The questions ask you about your experiences of giving

prescribed medicines to your child. Please return the completed questionnaire in the pre-paid envelope provided within the next two weeks.

REMINDER LETTER

After two weeks, if we have not heard from you, we will send reminder letter along with a second questionnaire and another information sheet. This reminder is a final opportunity for you take part in the study. We will not contact you again after this second reminder.

DO I HAVE TO TAKE PART?

No. Your participation is entirely voluntary. If you decide to take part in the study you will be free to withdraw at any time and for any reason. Once withdrawn you can also choose to have your data removed if you notify the researcher by emailing [redacted]. It will not be possible to withdraw your data once the final report has been written as all information will have been made anonymous. If you decide not to take part, this will not affect the standard of care your child receives from Birmingham Children's' Hospital in any way.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

All the information provided by you in this study will be kept confidential. The only time that we will inform other relevant professionals is if we identify any potential safeguarding issues. These will, in accordance with Trust policy, be referred to the safeguarding team for advice. All questionnaires will be filed and stored securely at Birmingham Children's Hospital and will only be accessed by [redacted] Principal Investigator) and [redacted] Chief Investigator). All information from the questionnaire will be transferred into an electronic database. Your name will be removed from all electronic data and replaced by a number, this is called anonymisation. Electronic copies of the data will be stored on a password protected network computer at Birmingham Children's Hospital and on an encrypted USB at Aston University. At the end of the project, the anonymised data and study related documentation will be securely archived in accordance with Aston University's policies and procedures. The study data and documents will be stored securely for six years and after this period all study data and documents will be destroyed.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

The results may be published in a medical journal in order to share our findings with other health professionals. No parents/patients will be identified in our published reports. Please indicate in the box on the front page of the questionnaire if you would like a summary of the results.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

The research is being organised by:
[redacted], Deputy Chief Pharmacist, Birmingham Children's Hospital
[redacted], Director, Pharmacy Academic Practice Unit, Birmingham Children's Hospital and Aston University
The research is being funded by:
The Pharmacy Department, Birmingham Women's and Children's NHS Foundation Trust

WHO HAS REVIEWED THE STUDY?

To ensure the participant's safety, rights, wellbeing and dignity are protected, ethical approval was obtained from NHS Research Ethics Committee, Health Research Authority and Research and Development team of the hospital site.

WHERE CAN I FIND INDEPENDENT INFORMATION ABOUT TAKING PART IN RESEARCH?

You can contact the NHS Patient Advisory Liaison Service (PALS) at Birmingham Women's and Children's NHS Foundation Trust if you would like advice on taking part in research. Email: bwc.pals@nhs.net Telephone: 0121 333 8403.

WHO DO I CONTACT IF I NEED FURTHER INFORMATION?

If you have any questions or need any more information please speak to [redacted], Deputy Chief Pharmacist and lead for the study on 0121 333 9821 or email: [redacted]

WHO DO I CONTACT IF I WISH TO MAKE A COMPLAINT ABOUT THE WAY IN WHICH THE STUDY IS CONDUCTED?

If you have any concerns about the way in which the study has been conducted you should in the first instance [redacted] on 0121 204 3941 or by email: [redacted]. If he is unable to address your concerns or you wish to make a complaint about how the study has been conducted you should contact [redacted], Director of Governance, University, Aston Triangle, Birmingham, B4 7ET; Tel 0121 204 4801; [redacted]

FOR FURTHER INFORMATION PLEASE CONTACT:

Chief investigator	Name [redacted] Address Pharmacy Department, Aston University, Birmingham, B4 7ET. E: d.terry@aston.ac.uk T: 0121 204 3941
Principal Investigator (researcher)	Name [redacted] Address Pharmacy Department, Birmingham Children's Hospital, Steelhouse Lane, Birmingham, B4 6NH E: jeff.aston@nhs.net T:0121 333 9780

Thank you for taking the time to read this information sheet.

Appendix XXII Study 4 questionnaire

A Study to find out the About the Changes that Parents or Carers Make to their Child's Medicines

Name of Researcher: [redacted]n Deputy Chief Pharmacist, Birmingham Women's and Children's NHS Foundation Trust

Name of Project Supervisor: [redacted], Academic Supervisor, Aston University

By completing this questionnaire, *you are confirming your consent to participate in this research.*

All your answers will be kept confidential.

To answer the questions please tick the appropriate box and/or insert your answer in the space provided.

If you would like a summary of the results from this study please provide a name and contact address or email address in the box below:

Questions about when your child first started a new medicine:

Q1	Have you ever made the decision to delay starting a medicine after it was prescribed for your child for the first time? *For example, you waited a day or two before starting the new medicine.*	YES	NO (please go to Q2)
1.1	Was this because you wanted to first find out more information about how to use it?	YES	NO
1.2	Was this because you wanted to first find out more information about its side effects?	YES	NO
1.3	Was this because you wanted to make sure it was the correct medicine to use?	YES	NO
1.4	Was this because you wanted to find out if it might affect any other medicines that your child might take?	YES	NO
1.5	Was this because the medicine was started by another team and you wanted to check with your usual doctor first?	YES	NO
Please list below any other reasons that you may have had for delaying starting a new medicine prescribed for your child:			

Q2	Have you ever decided not to give a medicine <u>at all</u> that was newly prescribed for your child?	YES	NO (please go to Q3)
Please list below the reason(s) that made you decide not to start a new medicine prescribed for your child:			

Questions about your child's usual medicines:

Q3	Have you ever decided not to follow the instructions of how you should administer a medicine? Do not consider occasions when you forgot to give the medicine. *For example, the medicine is prescribed in the morning but you gave it at night.*	YES	NO (please go to Q4)
3.1	Was this because you were concerned about side effects?	YES	NO
3.2	Was this because your child was prescribed another new medicine and you were concerned about how they might affect each other?	YES	NO
3.3	Was this because the time the medicine was due was inconvenient on that day?	YES	NO
3.4	Was this because your child occasionally does not wish to take their medicine?	YES	NO
Please list below any other reasons that you may have to miss giving your child one of their medicines:			

Q4	Have you decided to withhold any of your child's prescribed medicines for a period of time without asking your doctor, nurse or pharmacist? *For example, stopping the medicine for a week or so.*	YES	NO (please go to Q5)
Please list below any reasons that you may have had to intentionally withhold any of your child's medicines:			

Q5	Other than by accident, have you given your child a higher dose of their prescribed medicine without first asking your doctor, nurse or pharmacist? *For example, the prescribed dose is 2mL but you have decided to give 4mL.*	YES	NO (please go to Q6)
5.1	Was this because you thought the medicine wasn't working well enough?	YES	NO
Please list below any other reasons that you may have had for increasing any of your child's medicines:			

Q6	Other than by accident, have you given your child a lower dose of their prescribed medicines without first asking your doctor, nurse or pharmacist? *For example, the prescribed dose is 5mL but you have decided to give 2mL.*	YES	NO (please go to Q7)
6.1	Was this because they were feeling worse when they were taking their medicine?	YES	NO
6.2	Was this because you thought that they may be experiencing side effects from their medicine?	YES	NO
6.3	Was this because you thought that they were feeling well enough not to need as much of their medicine?	YES	NO
Please list below any other reasons that you may have had for reducing any of your child's medicines:			

Q7	Have you had to change the way that your child takes their prescribed medicines to fit in with your day-to-day lives?	YES	NO (please go to Q8)
Please list below any changes that you have made to your child's medicines to fit in with your day to day lives:			

Q8	Have you had to change the method/way that your child takes their medicines because they were having difficulties taking them without first asking your doctor, nurse or pharmacist?	YES	NO (please go to Q9)
8.1	Did you try to hide the taste of the medicine by mixing with food?	YES	NO
8.2	Did you try to hide the taste of the medicine by mixing with a flavoured drink?	YES	NO
Please list any other changes that you have had to make to help your child take their medicine below:			

Some questions about how old your child is and their usual medicines:

Q9. How old is your child?	

Q10. Please list the medicines that your child usually takes in the box below:		
Name of the Medicine	**Type of Medicine (e.g. liquid, tablet, capsule, inhaler, patch, injection, cream or ointment).**	**How long your child has been on this for?**

Thank you for completing this questionnaire. Please return it to me in the enclosed pre-paid envelope within the next 2 weeks.

Appendix XXIII Study 4 repeat mailing cover letter

A STUDY TO FIND OUT THE ABOUT THE CHANGES THAT PARENTS OR CARERS MAKE TO THEIR CHILD'S MEDICINES

Dear Parent/Carer,

We recently wrote to you to invite you to take part in a study that we are undertaking. As we haven't heard back from you, we would like to invite you to take part again.

We would like to learn more about the changes, if any, that parents/carers make to their child's prescribed medicines. Very little information has been published on this topic and this is an opportunity for you to help us by sharing your experiences. All information that you provide will be kept confidential and we will not share your details with anyone else.

I attach another copy of the information sheet explaining the study, a copy of the questionnaire for you to complete and a pre-paid return envelope for you to return the questionnaire to me within the next two weeks.

If you have any questions please do not hesitate to contact me by phone on 0121 333 9780 or email jeff.aston.nhs.net.

Thank you for your time. This is the last time that I will approach you about this study.

[redacted]

[redacted]

Deputy Chief Pharmacist

Birmingham Women's and Children's NHS Foundation Trust

PharmD Student

Aston University

Appendix XXIV Study 1 published paper

A telephone survey to determine the experiences of children and their parents/carers, following the initiation of a new medicine

[redacted]

ABSTRACT

Objective

To determine what issues are experienced during the first few weeks of therapy by patients, and their parents/carers, when a child/young person has been prescribed a new medicine.

Method

One hundred patients aged ≤18 years of age prescribed a new medicine for ≥6 weeks were recruited from a single UK National Health Service specialist paediatric hospital outpatient pharmacy. Six weeks after the first dispensing of their new medicine the patient or their parent/carer received telephone follow-up by a researcher and verbally completed a questionnaire containing both open and closed questions. Patient or parent/carer experiences were identified and analysed using thematic analysis and descriptive statistics.

Results

Eighty-six participants were available for telephone follow-up. Six (7%) had not started their medicine. Paediatric patients and their parents/carers experienced a range of issues during the first few weeks after starting a new medicine. These included additional concerns/questions (24/80, 30%), administration issues (21/80, 26.3%), adverse effects (29/80, 36.3%) and obtaining repeat supplies (12/80, 15%). 32/80 (40%) participants occasionally forgot to take/administer their medicine and 18/80 (22.5%) omitted doses for reasons other than forgetting.

Conclusions

Paediatric patients and their parents/carers experience a range of issues during the first few weeks after starting a new medicine. Further research is required to determine the type of interventions that may further support medicines use in this group of patients.

INTRODUCTION

People prescribed self-administered medicines typically take about half their doses.[1] Efforts to assist patients with adherence might improve the benefits of prescribed medicines.

Medicines taking in children may be influenced by parents/carers beliefs about the condition, treatment regimen, child resistance, relationships within families, desire to preserve normal life and input from health professionals.[2]

A recent study of the experiences of medicine-related issues encountered by parents/carers of paediatric liver transplant patients found they reported problems obtaining their medicine, administering the medicines and side effects (including insufficient knowledge of side effect management).[3]

A review of the medical notes of 11–18 years old patients with juvenile arthritis found that despite the increasing complexity of drug regimens major gaps existed in the documentation of knowledge and skills relevant to the self-management of such regimens by patients.[4]

Barber et al, in a study of adult patients started on chronic medicines, found they quickly became non-adherent and identified a number of medicine-related problems and information needs.[5] These included side effects, concerns about taking a new medicine, swallowing difficulties and remembering the regimen. In response to these issues the National Health Service funded New Medicines Service (NMS) was established in England in 2011.[6] This is a medication review delivered through community pharmacists to support people with long-term conditions newly prescribed a medicine. The NMS improves adherence by 10% and increases the number of medicines problems identified and resolved.[7] Improved medication adherence has been shown to improve disease outcomes in children with cystic fibrosis,[8] asthma[9] and renal disease.[10] However, the NMS may not be available to children and cannot be undertaken with a parent/carer.[6]

The rationale of medication review could apply to children with chronic diseases.[11] Issues such as polypharmacy, wastage and medicine-related problems are likely to be similar to those in adults. However, a literature review, using AMED, British Nursing Index, CINAHL, EMBASE, HMIC, MEDLINE, PsycINFO and Health Business Elite, did not identify any studies of medication review specific to children. Recently, the UK National Institute for Health and Care Excellence recommended further research concerning medication review in children, including minimising medicine-related problems.[12] Other initiatives that may optimise medicines use include better partnerships with patients, telephone helplines, internet support websites and improving collaboration between healthcare professionals.[13]

The present study focused on the experiences of patients and their parents/carers during the first few weeks after a paediatric patient began taking a new medicine.

Aim

To determine what medicine-related issues are experienced during the first few weeks of therapy by patients, and their parents/carers, when a child/young person has been prescribed a new medicine.

METHODS

Setting

The study was undertaken at a specialist UK paediatric hospital (34 specialties, 361 beds, >174 000 outpatient visits per year).[14]

Participant recruitment

Potential participants were identified through presentation of a prescription to the outpatient pharmacy which met the study inclusion criteria. Consent and recruitment were undertaken by pharmacists based in the hospital's outpatient pharmacy while the participant waited for their prescription. Written consent was taken from the patient's parent/carer if the child was below 16 years or the patient if 16 years or older. An assent form was used for patients aged 12–15 years and was signed by the patient alongside the parent/carer consent form. Age-related participant information leaflets were provided. To minimise impact on service delivery a convenience sample of participants were recruited during the period February to July 2015. This study was exploratory and the authors considered a recruitment number of 100

participants would provide sufficient range of specialties and participants to identify important findings. There were no known published studies to guide recruitment numbers.

Inclusion criteria

Participant inclusion criteria were: ages 0–18 years; prescribed a new medicine to be taken for 6 weeks or longer; access to a telephone for follow-up; not receiving medication for a life-limiting condition; could understand written and spoken English. The authors considered a period of 6 weeks to have provided the patient, and their parent/carer, sufficient experience of taking the new medicine prior to follow-up.

Data collection

Demographic information was recorded from the patient's prescription: medical/surgical clinic attended, age/gender of the patient, medicine prescribed and therapeutic indication.

A questionnaire containing both open and closed questions was used as the research instrument. This was completed by telephone with direct support from the lead study researcher. Cognisant testing of the questionnaire was assessed with a parent of a child taking long-term medicines and piloted with five participants. Six weeks following the dispensing of their new medicine participants received telephone follow-up by the study lead researcher. Participants were asked: whether they had researched further information about the new medicine themselves and why, any concerns/questions occurring over the previous 6 weeks, if they had experienced any problems taking/administering the medicine, whether they had experienced adverse effects from their new medicine, any problems arranging repeat supplies and whether they had intentionally or unintentionally omitted any doses and why.

Responses were transcribed in real time by the researcher during the interview.

Data analysis

Responses were analysed using thematic analysis. The responses were listed, grouped by similar/related theme and coded. Collated responses were analysed using NVivo V.10. Quantitative results were analysed using descriptive statistics using The Statistical Package for Social Sciences (SPSS) V.22.

RESULTS

Demographic information

One hundred participants were recruited to the study. Fifty-one patients were female and 49 male with a mean age of 8 years (range 0.33–17 years). Patients were managed by one of 15 specialties (Table 1).

Table 1 Specialities

Speciality	N
General Paediatrics	23
Ear, Nose and Throat	14
Neurology	13
Dermatology	10
Urology	9
Respiratory	7
Rheumatology	5
Emergency Department	3
Gastroenterology	3
Hepatology	3
Nephrology	3
Ophthalmology	3
Cardiology	2
Inherited Metabolic Diseases	1
Plastics	1

In total 145 medicines were prescribed which patients had not previously received (Table 2).

Table 2 Medicines Prescribed for Study Participants

Therapeutic Use	Number of Medicines (%)	Medicine (n)
Eczema	27 (18.6%)	Topical corticosteroid (13)
		Emollient (7)
		Dressings (3)
		Hydroxyzine (2)
		Potassium Permanganate (1)
		Topical tacrolimus (1)
Asthma	17(11.7%)	Beclometasone (6)
		Montelukast (4)
		Fluticasone (2)
		Fluticasone/Salmeterol (2)
		Salbutamol (2)
		Ipratropium (1)
Allergy	14(9.7%)	Fluticasone (8)
		Cetirizine (2)
		Adrenaline (1)
		Chlorphenamine (1)
		Desloratadine (1)
		Nutramigen (1)
Urinary Frequency/Enuresis	14 (9.7%)	Desmopressin (6)
		Oxybutynin (6)
		Tolterodine (2)
Migraine/Headache	11(7.6%)	Pizotifen (6)
		Propranolol (2)
		Sumatriptan (2)
		Migraleve (1)
Gastro-0esophageal Reflux	9 (6.2%)	Ranitidine (7)
		Lansoprazole (1)
		Omeprazole (1)
Epilepsy	8 (5.5%)	Levetiracetam(2)
		Acetazolamide (1)
		Carbamazepine (1)
		Lamotrigine (1)
		Sodium valproate (1)
		Stiripentol (1)
		Topiramate (1)

Therapeutic Use	Number of Medicines (%)	Medicine (N)
Infection	8(5.5%)	Trimethoprim (3)
		Amoxicillin (1)
		Azithromycin (1)
		Co-trimoxazole (1)
		Erythromycin (1)
		Itraconazole (1)
Constipation	6 (4.1%)	Macrogols (5)
		Senna (1)
Vitamins	6 (4.1%)	Colecalciferol (2)
		Folic Acid (2)
		Alfacalcidol (1)
		Ergocalciferol (1)
Rheumatic diseases	5 (3.4%)	Nifedipine (2)
		Piroxicam (2)
		Hydroxychloroquine (1)
Immunosuppression	4 (2.8%)	Azathioprine (2)
		Ciclosporin (1)
		Methotrexate (1)
Cardiovascular	3 (2.1%)	Atorvastatin (1)
		Enalapril (1)
		Losartan (1)
Ophthalmic	3(2.1%)	Prednisolone (2)
		Fluorometholone (1)
Cholestasis	2 (1.4%)	Ursodeoxycholic acid (2)
Emesis	2 (1.4%)	Ondansetron (2)
Other	6 (4.1%)	Amitriptyline (1)
		Colestyramine (1)
		Dexamethasone/framycetin/gramicidin (1)
		Levomepromazine (1)
		Melatonin (1)
		Propranolol (1)

Eighty-six participants received telephone follow-up. Follow-up was undertaken with 83 (96.5%) parents/carers and three (3.5%) young people (two aged 16 years and one 14 years following parental consent). Fourteen participants were not contactable.

Adherence to the prescribed regimen

Telephone follow-up revealed that six (7%) patients had not taken their medicine. Two parents/carers were concerned about side effects (macrogol and topical corticosteroid), two had not required their medicine (chlorphenamine, pizotifen and sumatriptan), one patient refused to be administered a macrogol suspension and one patient was concerned about how nifedipine would interact with her other medicines.

I read the leaflet that it came with then decided to try naturally. I haven't started her on it yet. They said that she wasn't drinking enough. I pushed the fluids, she's been better than she was. It can cause diarrhoea and I didn't want to send her the other way…
Parent of Patient 18 (macrogol)

I haven't been taking it because I couldn't find out if it was compatible with my other medicines. I'm doing my exams at the moment, I didn't think it would be very smart to take them.
Patient 46 (nifedipine)

Thirty-two (40%) participants admitted to occasionally forgetting to administer/take a dose of medicine. Four (5%) participants had purchased medicine compliance aids.

We were advised to take it with or after food. If I'd forgotten I didn't know if I could then give it and so I would miss the dose and give his next one. Parent of Patient 61 (ursodeoxycholic acid)

I don't find it difficult to stick to the plan because I know we have to stick to it because it's for his eyes. A bit inconvenienced… it blows his weekend out. We give it on a Saturday morning so we can do something on a Friday night if we want to. I sometimes forget the folic acid as he has three days off when he's on the methotrexate. Parent of Patient 20 (methotrexate)

Eighteen (22.5%) participants intentionally omitted doses. These were due to adverse effects (5, 27.8%), concurrent acute illness (3, 16.7%), timing of administration (3, 16.7%), the desire to look up more information before starting the medicines (2, 11.1%), incorrect use (2, 11.1%), child declining to take (1, 5.6%), a mother not wanting their child to have the medicine as, although not used for this indication, they were an antidepressant (1, 5.6%) and ran out of supplies (1, 5.6%).

He was poorly once and was taking Calpol, Nurofen and antibiotics. So, I stopped giving it then as I thought it was a bit much.

Parent of Patient 100 (ranitidine)

Only the first night because of reading the side effects. My husband looked on the internet. Then we read the information the doctor gave us and realised it was more related to children and my husband was much happier so we gave it. Parent of Patient 56 (desmopressin)

Seeking further information

Twenty-six (30.2%) participants sought further information about their medicine. Twenty-two participants (84.6%) searched the internet, two (7.7%) asked a friend/relative, one (3.8%) asked other parents and one (3.8%) had looked in the British National Formulary.

Participants sought further information to: find out about side effects (13, 50%), general interest (5, 19.2%), reassurance about the appropriateness of treatment (4, 15.4%), research a specific query (3, 11.5%) and check that there were no interactions with concomitant medicine(s) (3, 11.5%).

I'm giving something new. I want to know what side effects there are. [Patient 6] is on lots of medicines, she's having seizures and I want to see how it interacts with the others, I don't want to make these worse. Parent of Patient 6 (levomepromazine)

Basically, is that the right drug? Is it common to use it at this stage? Parent of Patient 75 (azathioprine)

Concerns and further questions

Twenty-four (30%) participants who had taken/administered their medicine had some concerns. These related to side effects (10, 41.7%), efficacy (6, 25%), administration (4, 16.7%) and other concerns (4, 16.7%). Other concerns were the: perceived stigma of taking an antidepressant, impact of a friend questioning the choice of therapy, anticipated repeat prescription problems through the general practitioner (GP) and advice provided by a pharmacist.

There was one thing. My friend works in a hospital, I'm not sure

what she does, but when she saw what [Patient 11] was on she said that they'd been told to stop using them. I don't know why that is. Parent of Patient 11 (piroxicam)

Administration issues

Issues regarding administration were experienced by 21 (26.3%) participants. These were issues concerning: dislike of the taste/smell (11, 52.4%), timing of administration (3, 14.3%) and the impact of autism/learning difficulties (2, 9.5%). Other (5,23.8%) experiences included the: manipulation of a tablet to obtain a part-dose, problems extracting a tablet from a blister pack, fear of an inhaled spacer device, absence of a bottle adapter and swallowing difficulties.

It was difficult to find a suitable time as needed to be taken on an empty stomach an hour before food. She took it at school as there's no afternoon break. In the morning she has breakfast, then there's lunchtime. When she comes home she has an evening meal and then she's tired and it's time for bed. Parent of Patient 23 (lansoprazole)

He's got a new spacer now as he couldn't cope with the big one. It scared him. He's got a smaller one with bears on it now which is fine from the GP. Parent of Patient 33 (beclomethasone inhaler)

Adverse effects

While cause and effect was not established, adverse effects were reported by 29 (36.3%) participants (Table 3).

Upper abdominal pain under her rib cage for three weeks, periodic headache, exhausted, very, very tired, her menstrual cycle has gone haywire. She's been off school for three weeks. I'm desperate to find out the cause to alleviate her symptoms. My head tells me it's the side effects from the drug… Parent of Patient 15 (ciclosporin)

I was told one of the side effects was increased appetite. But her

appetite is much greater now. I didn't realise just how much it would increase. Parent of Patient 30 (pizotifen)

Table 3 Reported Adverse Effects

Therapeutic Use	Medicine	Number of Patients Reporting Effect	Reported Adverse Effect(s)
Eczema	Topical corticosteroid	1	Staining of clothing.
	Hydroxyzine	1	Drowsiness
Allergy	Fluticasone	2	Nose bleed, sore throat
Urinary Frequency/Enuresis	Oxybutinin	2	Drowsiness, dry mouth.
	Tolterodine	2	Drowsiness, dry mouth, constipation, abdominal pain.
Migraine/Headache	Pizotifen	3	Behavioural changes, constipation, increased appetite.
	Propranolol	1	Fatigue
Gastro-Oesophageal Reflux	Ranitidine	1	Vomiting
Epilepsy	Levetiracetam	2	Behavioural changes
	Acetazolamide	1	Behavioural changes
	Lamotrigine	1	Suicidal ideation
Constipation	Marogol	1	Diarrhoea
Rheumatic diseases	Nifedipine	1	Nausea, dizziness.
	Hydroxychloroquine	1	Abdominal pain.
Immunosuppression	Azathioprine	2	Blacking out/fainting, hairloss.
	Ciclosporin	1	Abdominal pain, headache, fatigued, changes to menstrual cycle.
	Methotrexate	1	Abdominal pain.
Other	Amitriptyline	1	Drowsiness
	Atorvastatin	1	Jaundice
	Enalapril	1	Dry cough
	Itraconazole	1	Abdominal pain.
	Propranolol	1	Coldness of the extremities

Further supply issues

Twelve (15%) participants experienced difficulties obtaining further supplies. Forty-seven participants (58.8%) had sufficient supplies from the hospital and 21 (26.3%) obtained further supplies from their GP. The problems experienced by participants included: delays in posting out clinic letters to the GP (4, 33.3%), insufficient information on the letter for a repeat

prescription (3, 25%), insufficient quantities prescribed by the GP (2, 16.7%), misreading of a letter by the GP (1, 8.3%), cancellation of a follow-up outpatient appointment where a repeat prescription was to be provided (1, 8.3%) and confusion due to a therapy substitution by the hospital pharmacy which did not then match the information in the clinic letter (1, 8.3%).

Yes, there was some confusion between the doctors. The hospital hadn't written to the GP, the letter hadn't been sent so I had to phone the consultant who organised the letter. Missed a week of the antibiotic. Parent of Patient 26 (co-trimoxazole)

Ran out of tablets. The doctor said to take the course and we'll see you back. Out-patient on 8th June cancelled by the hospital and arranged for much later in August. Had to phone up and get it brought forward. The doctor said to take it for 6 weeks. We only had a 4-week supply. Parent of Patient 45 (amitriptyline)

DISCUSSION

Patients have a right to decide not to take their medicine and may have different views about risks, benefits and side effects.[15] In this current study, 6/86 (7%) participants had not started their medicine and 18/80 (22.5%) participants had intentionally omitted some doses. Therefore, some are reviewing the initial therapy decision and others are making treatment changes without consulting a healthcare professional. Shared decision-making between clinicians and patients about treatment choice is important.[16] Poor communication may lead patients to obtain information outside of a consultation with a healthcare professional.[17]

Overall participant reported adherence in this study was comparable with that published in the paediatric literature.[18, 19] Four (5%) participants had purchased medicine compliance aids. Due to a lack of beneficial outcomes with the use of compliance aids the UK Royal Pharmaceutical Society recommends original pack dispensing with appropriate pharmaceutical care including clinical medication review.[20]

A recent systematic review identified a number of findings that contribute to explaining treatment adherence in paediatrics.[2] Including beliefs about the condition or treatment, treatment regimen and child resistance. Findings from the present study were consistent with these. For example, 3/86 (3.5%) participants decided against treatment, 21/80 (26.3%) experienced issues with administration including the taste/smell of the medicine and timing of

administration. While the systematic review[2] focused on long-term conditions it did not identify when during treatment these themes occurred. This current study found that they can occur within the first 6 weeks after starting a new medicine.

A study of adult patients prescribed a new long-term medicine found that once a patient has experienced their medicine, they gain some knowledge of what it does and new questions arise.[5] The current study has shown that children and their parents/carers have similar experiences after the first few weeks of therapy. This is illustrated by 26/86 (30.2%) participants researching further information about their new medicines, 24/80 (30%) having concerns or further questions and 29/80 (36.3%) possibly experiencing an adverse effect to treatment.

Twenty-one (26.3%) parents/carers had difficulties administering the medicine to their child. In adults, oral solid dosage forms are mostly acceptable. However, potential paediatric patients may include neonates, toddlers, young children and adolescents, and hence will have widely varying needs.[21] A change in formulation is currently excluded from triggering an NMS consultation.[22] Any future paediatric medication review should include changes in formulation as a trigger for a medication review.

Current evidence suggests that when patients move between care providers the risk of miscommunication and unintended changes to medicines is a significant problem.[23] This current study suggests that this is an issue in paediatrics with 12 (15%) participants experiencing problems arranging a repeat supply with seven (58.3%) due to a miscommunication.

A systematic review of interventions to improve the safe and effective use of medicines by consumers identified a scarcity of evidence in children/young people.[24] The benefits of a medication review through the NMS have been appraised.[7] The NMS appraisal identified a variety of factors impacting on adherence including forgetfulness, beliefs about treatment necessity, stigma, lack of peer/family support, lack of knowledge, side effects, fear of dependency, regimen complexity, inability to use the formulation and access to medicines. Each of these factors was identified in this current study. The NMS applies a structured approach to identifying and resolving these issues.[7, 22] However, it may not be available to children and is not available to their parents/carers.[6]

The results of this current study suggest that paediatric patients and their caregivers may benefit from some support initiative after the first few weeks of treatment with one option

being an NMS type intervention. In addition to medication review a number of other initiatives may further support patients realising the benefits of their medicines. These include fostering better partnerships with patients, the use of telephone helplines for information on medicines, developing specific internet support websites and improvements to how different healthcare professionals collaborate together.[13]

The limitations of this study include sample size which was relatively small, specialist paediatric centre setting which may limit how generalisable the results are and the restriction to English language speakers.

CONCLUSION

Paediatric patients and their parents/carers experience a range of issues during the first 6 weeks after starting a new medicine. Intervention at this stage may provide useful support to both the patient and their parent/carer. Further research is required to determine the type of intervention and how it could be integrated in to practice to optimise paediatric medicine use.

What is already known on this subject?

- Little is known about the experiences of paediatric patients, and their parents/carers, during the first few weeks after a child has started a new medicine.
- Adult patients have been shown to experience a number of issues following the initiation of a new medicine.

What this study adds?

- This study has shown that children, and their parents/carers, experience a range of issues during the first 6 weeks after starting a new medicine.
- These issues include concerns/questions, information requirements, adverse effects, arranging further supplies and adherence.
- Interventions to support medicine taking during this period may optimise medicines use in this group of patients.

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Competing Interests

None declared.

Ethics Approval

The study was approved by Yorkshire and Humber—Sheffield, UK, National Research Ethics Service 24/09/14 (REC reference 14/YH/1086, IRAS project ID 148123).

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Appendix XXV Study 1 conference poster 1

Appendix XXVI Study 1 conference poster 2

Appendix XXVII Study 1 conference poster 3

Appendix XXVIII Study 2 published paper

CHILDREN/YOUNG PEOPLE TAKING LONG-TERM MEDICATION -A SURVEY OF COMMUNITY PHARMACISTS' EXPERIENCES IN ENGLAND

Key Words

Community Pharmacy, Medication Review, Chronic Medication, Pharmaceutical Care, Prescribed Medicines

Word Count

Abstract = 253, manuscript = 2729

ABSTRACT

Objectives

To determine whether community pharmacists undertake medication reviews with children/ their carers, and to identify the type of medication-related experiences presented to them when a child is taking long-term medication.

Methods

A 13 question semi-structured survey was posted to 354 England-based community pharmacists with telephone follow-up/repeat mailing of non-responders. Participants were asked about their practice as a community pharmacist over the preceding 12 months to children/young people, or their carers, taking long-term medication. The questionnaire covered: medication-review, reported adherence, information requests, adverse effects, administration and obtaining medication supplies. The data were analysed using SPSS version 22 and NVivo version 10.

Results

The response rate was 76/354 (21.5%). Eighteen (23.7%) respondents had undertaken a Medicines Use Review (MUR) and 22 (28.9%) a New Medicines Service (NMS) medication review with a child/ their carer. Participants reported that patients/their carers had presented to them with non-adherence including stopping medication (24, 31.6%) and changing the dose (28, 36.8%). Respondents were directly asked about the indication (59, 77.6%), dose regimen (63, 82.9%), administration (64, 84.2%) and adverse effects (58, 76.6%) of prescribed medication. Respondents reported patients/carers experiencing difficulties

obtaining medication from their community pharmacy (47, 61.8%) and patients' general practitioners declining to prescribe a medication recommended by a specialist (27, 35.5%).

Conclusions

MUR and NMS reviews are utilised by community pharmacists in children/their carers. The medication-related experiences presenting to community pharmacists could fall within the purview of a medication review (MUR or NMS). There is scope to further extend this service to this group of patients/carers.

Keywords

Community Pharmacy, Medication Review, Chronic Medication, Pharmaceutical Care, Prescribed Medicines

INTRODUCTION

It has been reported that patients who are prescribed self-administered medication typically take about half their doses and consequently efforts to assist patients with adherence might improve the outcomes of medication use[1]. Barber *et al* in a study of patients newly started on chronic medication found that they quickly became non-adherent and identified a number of medication-related problems and information needs[2]. These included adverse effects, concerns about taking a new medication, difficulty in swallowing the medication and remembering the regimen.

In children, medication adherence may be influenced by a number of factors: parents/carers beliefs about the condition, the treatment regimen, child resistance, relationships within families, desire to preserve normal life and input from health professionals[3]. A recent study of the experiences of medication-related issues encountered by parents/carers of paediatric liver transplant patients found that they had problems obtaining their medication, encountered difficulties with administration and experienced adverse effects[4]. Improving adherence to medication regimens has been shown to improve disease outcomes in children[5-7].

In England two funded structured medication review services are available through community pharmacy to support patients taking medication -the New Medicines Service (NMS) and the Medicines Use Review (MUR) services[8, 9]. These aim to improve patient engagement with their medication, increase adherence to the prescribed regimen, reduce waste and reduce adverse drug reactions[8, 9]. Patients are eligible to access the NMS if they have been newly prescribed medication for hypertension, asthma/chronic obstructive pulmonary disease, type II diabetes or prescribed antiplatelet or anticoagulant therapy[8].

The MUR has been established for patients taking multiple medications[9]. Seventy percent of MURs should be undertaken in patients in one of the following target groups: those taking medication classified as high risk e.g. anticoagulants and diuretics, medication for respiratory and cardiovascular conditions and those recently discharged from hospital with changes to their medication[9]. However, these services are only available to patients who are themselves judged competent to consent to the service and are not available to carers on behalf of others[9, 10]. Children/young people may therefore be excluded if they cannot consent or through not being in one of the target medication groups.

The rationale of medication review is likely to apply to children with chronic diseases[11]. This view is supported by the recent recommendation from the English National Institute for Health and Care Excellence (NICE) that further research is needed on medication review in children, including minimising medication-related problems[12].

In order to explore the concept of a paediatric medication review in community pharmacy, this current research was undertaken to determine whether community pharmacists are undertaking medication reviews with children/young people or with their parents/carers. In addition, this study sets out to identify the type of paediatric medication-related experiences that are presented to community pharmacists by children/young people and/or their patients/carers when taking long-term prescribed medication.

Aim of the Study

To determine whether community pharmacists undertake medication reviews with children/young people or their parents/carers and to identify the type of medication-related experiences that are presented to community pharmacists when a child/young person is taking long-term prescribed medication.

Ethics Approval

Ethical approval was obtained from Aston University Life and Health Sciences Ethics Committee study number 823, 14/10/15.

METHOD

Setting

England based community pharmacists.

Participant Recruitment

The National Health Service Business Services Authority (NHSBSA) ePACT system was accessed to identity the addresses of all community pharmacies that had dispensed prescriptions from a single specialist UK paediatric hospital during the period November to December 2015. This enabled the targeting of community pharmacies that were known to have previously dispensed a prescription for a child.

Data Collection

Permission was obtained from the superintendent pharmacists of the UK large chain community pharmacies to post a questionnaire to their stores identified from the NHSBSA ePACT system. Smaller chain and independently owned pharmacies were not approached in advance of the questionnaire being posted.

A pre-piloted 13 question semi-structured questionnaire, participant information leaflet and pre-paid return envelope were posted by the study Principal Investigator (PI) to all community pharmacists identified from the NHSBSA ePACT system. Telephone follow-up of all non-responders was undertaken following one week after the original return date by the study PI. Non-responders were asked if they would like to take part in the study and offered the opportunity to complete the questionnaire by telephone or receive a further postal questionnaire.

Participants were asked about their practice as a community pharmacist over the preceding 12 months to children/young people aged under sixteen years, or their carers, taking long-term medication. For the purposes of this study long-term medication was defined as taking, or expected to be taking, one or more medications for a period of six weeks or more. The questionnaire covered the following topics: medication-reviews, reported adherence, information requests, adverse effects, administration and obtaining medication supplies. The questions were developed by the authors based on the aspects covered by the NMS and

MUR services, previous published experiences[2, 3, 4, 13] and the authors' knowledge of managing medication use in paediatric patients.

Data Analysis

The quantitative results were coded and analysed using descriptive statistics (counts/frequency). The Statistical Package for Social Sciences (SPSS) version 22 was used to analyse the quantitative data. The qualitative responses were listed, grouped by similar/related theme and analysed using thematic analysis. NVivo version 10 was used to analyse the qualitative data.

RESULTS

Recruitment

An overall response rate of 76/354 (21.5%) was achieved (Figure 1). Thirteen (3.7%) respondents declined to take part in the study. Ten cited time constraints, one respondent was not interested in taking part, one felt that they did not see enough paediatric patients to contribute to the study and one respondent advised that their branch was run by a different pharmacist each day.

See Figure 1: Participant Recruitment

Demographic Information

The year of registration of respondents ranged from 1970-2015 (Table 1). Respondents worked between fourteen and seventy hours per week (mean 43.1 hours) in community pharmacy.

The type of pharmacy that respondents mostly practiced in is included in Table 1. Thirty-nine (51.3%) respondents described their employer as a 'large national chain', nineteen (25%) a small chain of less than 50 stores, fourteen (18.4%) a small independent, two (2.6%) a medium size chain of more than 50 stores and two (2.6%) a combination of more than one employer.

The average number of prescription forms overseen each month ranged from 950 – 13,000 with a mean of 5064.1. Five (6.7%) respondents did not answer this question. The majority of respondents (56/76, 73.7%) encountered children taking long-term medication in their practice at least once a week, eleven (14.5%) encountered them once a month and nine (11.8%) every three months or less.

Medication Review

Respondents were asked if they had undertaken a medication review with a child/young person or their parent/carer. Eighteen (23.7%) respondents advised that they had undertaken an MUR, twenty-two (28.9%) an NMS medication review and sixteen (21.1%) any other form of medication review.

Those respondents who had not undertaken a medication review in this group were asked for their reasons why. The most commonly cited reason for not undertaking an MUR or NMS consultation with a paediatric patient/carer was due to the perceived difficulties around taking consent (42, 55.3%) and a lack of formal reimbursement for undertaking an MUR or NMS review with the parent or carer of a child/young person (22, 28.9% for MUR and 19, 25% for NMS). Seven (9.2%) respondents listed that they were not confident in their ability to undertake a review of a child's medication. The ability of a child to engage with a medication review was mentioned as a barrier by six (7.9%) respondents:

> "*Have to judge if they can understand your counselling and are capable of putting this in to action. Have carried out MUR on patients 14, 15, 16 years old but not younger."* Respondent 124

A further four (5.3%) respondents observed that the child is not always present when a prescription is collected. Three (3.9%) felt that there was insufficient time to undertake a medication review.

Adherence to Prescribed Medication

Respondents were asked what experiences had been personally reported to them by a child/young person or their parent/carer relating to adherence (Table 2).

Respondents were asked to cite any additional reasons personally presented to them by children/young people, or their parents/carers, why they had been unable to adhere to the prescribed regimen. These were the impact of adverse effects (6, 7.9%), lack of efficacy (4, 5.3%), taste (3, 3.9%), concerns about a dose being too high (1, 1.3%), the impact of being a working parent (1, 1.3%) and the inconvenience of taking medication to school. (1, 1.3%)

Information Requirements

Respondents were also asked what information had been personally sought from them by children/young people or their parents/carers regarding long-term medication (Table 2).

Other information requested by patients or their parents/carers included the duration of treatment (3, 3.9%), interactions between medications (2, 2.6%), changes in brand/manufacturer/packaging (1, 1.3%), safety of the medication (1, 1.3%), if the medication

was the most appropriate for the condition being treated (1, 1.3%) and using a medication at school (1, 1.3%).

> "*Information request regarding the timing of doses (i.e. was it necessary to take a supply to school), whether to take it with or after food, could the taste be improved, potential side effects to look for and tell school about.*" Respondent 83

In one (1.3%) respondent's experience, they felt that information about side effects was not generally provided by the prescriber:

> "*Patients (young patients) and their carers are usually more concerned with side effects of medication as opposed to the indication and administration as they have this explained more thoroughly by the doctor.*" Respondent 162

Reported Experiences with Medication Use

Respondents were asked what experiences had personally been reported to them by children/young people whilst taking long-term medication or by their parents/carers (Table 3).

Two (2.6%) respondents had additionally reported problems with the use of 'specials' (unlicensed medicines manufactured to meet the needs of an individual patient):

> "*[Family doctor]/Commissioning bodies reluctant on cost basis to prescribe specials – often referred back to the hospital pharmacy*." Respondent 179

> "*Issues with [family doctor] wanting to prescribe cheaper tablet version of medication, asking patients/parent to crush tablets rather than prescribe the more expensive liquid versions.*" Respondent 306

DISCUSSION

This study has demonstrated that community pharmacists are utilised as a resource for medication taking through their direct contact with children or their parents/carers. The medication related interactions could fall within the remit of a structured medication review.

The limitations of this study include a small sample size which may have been improved further through utilising more than a single reminder and an on-line survey option. Also the targeted mailing of community pharmacists identified from a tertiary hospital ePACT data rather than all community pharmacists may limit the generalisability of the results.

Due to the low initial response all non-responders after the initial mailing were actively telephoned as an attempt to increase response rate. With the exception of thirteen potential participants all others agreed to participate in the research suggesting that there were no objections due to the study topic.

The type of community pharmacy employer was representative of the national picture with 53.9% of respondents working in a large national or medium size chain of pharmacy. A U.K. General Pharmaceutical Council registrant survey identified that 51% of pharmacists are employed by a large or another community pharmacy multiple[14].

The current guidance around undertaking MUR and NMS consultations requires these to be undertaken directly with the patient[9,10]. This does not preclude the inclusion of children/young people if they are competent to consent but it does exclude their parents/carers[9, 10]. A recent review of the literature did not identify any published research relating to medication review in children[15]. Yet this study found that around a fifth of respondents were undertaking medication reviews in this cohort. The finding that the main reason for not undertaking a medication review related to the perceived difficulty in gaining consent is worthy of investigation. Further support for pharmacists around the consent taking process could be provided by professional bodies such as the Great Britain based Royal Pharmaceutical Society (RPS). The requirement for these services to be targeted at patients taking specific medications, not all of which will apply to children/young people, may further restrict access to the service.

Whilst most respondents had not completed a medication review in a child they had encountered a number of paediatric related medication experiences presenting to them in their practice that could benefit from such a review. These included adherence, information needs, adverse effects, formulation issues and obtaining further supplies. The England based Pharmaceutical Services Negotiating Committee (PSNC) could help enable change to formally allow parents/carers to access the current medication review services for support with their child's medication.

A study of adult patients prescribed a new chronic medication found that once a patient has experienced their medication, they gain some knowledge of what it does to them and new questions arise[2]. The information gap created when patients have experienced their new medication may lead to inappropriate non-adherence. In this current study, respondents reported that patients, or their parents/carers, had informed them that they had either themselves, or through a decision made by a parent/carer, stopped treatment or changed the dose without first having sought advice from the prescriber. Overall, these intended changes to adherence were reported by respondents more frequently than forgetting a dose. Research is required to further explore intended non-compliance in this group.

When asked about the sort of information that had been requested by patients or their parents/carers, more than three quarters of respondents indicated that they had been personally asked about each of: the indication, dose, administration and adverse effects of a medication being taken by a child. Current information resources on using medication in children aimed at patients and parents/carers are available from www.medicinesforchildren.org.uk. This is a partnership programme between the Royal College of Paediatrics and Child Health, the Neonatal and Paediatric Pharmacists Group (NPPG) and Wellchild [16]. However, it is not known how this resource is utilised by community pharmacists and greater promotion to this group by the NPPG and RPS may be beneficial.

Respondents reported a number of challenges that children or their parents/carers presented to them during treatment including: administration difficulties, difficulties obtaining further supplies, adverse effects and the patient's family doctor being unwilling to prescribe a hospital recommended medication. The difficulties experienced obtaining further supplies of a medication and with administration may be more specific to paediatrics [13,17]. Most of the experiences described in this present study fell under the current purview of medication review services in England[8,9].

Medication review is an established part of community pharmacist activity in England[18] and is becoming more common across Europe[19]. A review of interventions to improve the safe and effective use of medication by consumers identified a scarcity of evidence in children and young people[20]. An extension of current medication review services to children and their parents/carers would provide an interaction with the community pharmacist to discuss medication. Indeed, this contact may be the first point at which a healthcare professional has the opportunity to intervene in the optimisation of medication use in this group of

patients/carers. The findings of this present study support increasing the access of current medication review services to children, young people or their parents/carers.

Further Work

Continuing research has three main themes: to evaluate the potential benefits of medication review in the paediatric group, to explore how the daily lives of paediatric patients and their parents/carers impacts upon medication use and to explore the decision making process that leads to intended non-compliance

CONCLUSION

Around a quarter of community pharmacists are undertaking a structured medication review with children/young people or their carers. Community pharmacists are utilised as a resource regarding long-term prescribed medication use by children or their parents/carers. These interactions with community pharmacists could fall within the purview of a medication review and hence there is scope to extend this service to this group. Further work is required to determine how community pharmacists could be further utilised in supporting children/young people, and their carers, with their medication of which one intervention could the introduction of a paediatric medication review.

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CONFLICTS OF INTEREST

Nil.

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Figure 1: Participant Recruitment

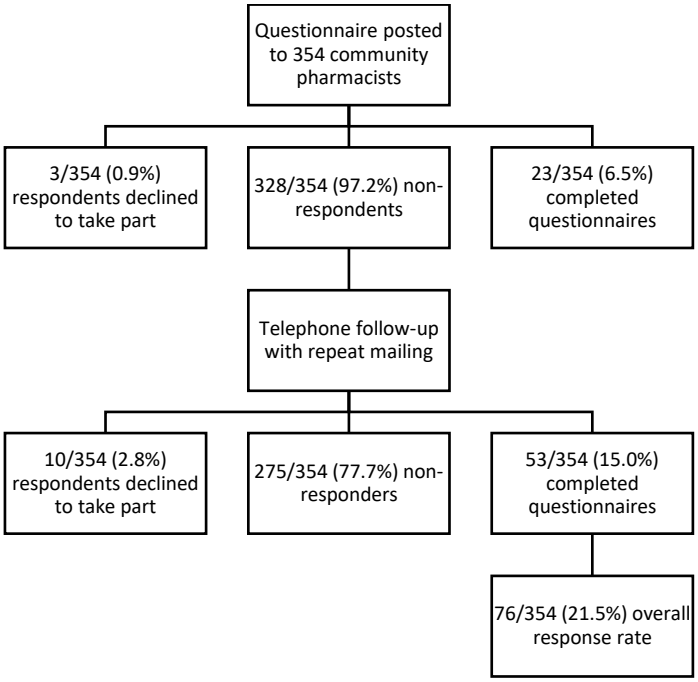


Table 1 Year of Registration and Type of Pharmacy in Which Respondents Practiced

		N (%)
Year of Registration	>2011	24 (31.6%)
	2006-2010	17 (22.4%)
	2001-2005	6 (7.9%)
	1996-2000	7 (9.2%)
	1991-1995	5 (6.6%)
	1986-1990	4 (5.3%)
	1981-1985	7 (9.2%)
	1976-1980	4 (5.3%)
	1970-1975	2 (2.6%)
Type of Pharmacy Mostly Worked In	High street pharmacy in a large town/city	26 (34.2%)
	Pharmacy in a small town/suburb	21 (27.6%)
	Health centre based pharmacy	15 (19.7%)
	Supermarket pharmacy	3 (3.9%)
	Healthy living pharmacy	2 (2.6%)
	A combination of the above	9 (11.8%)

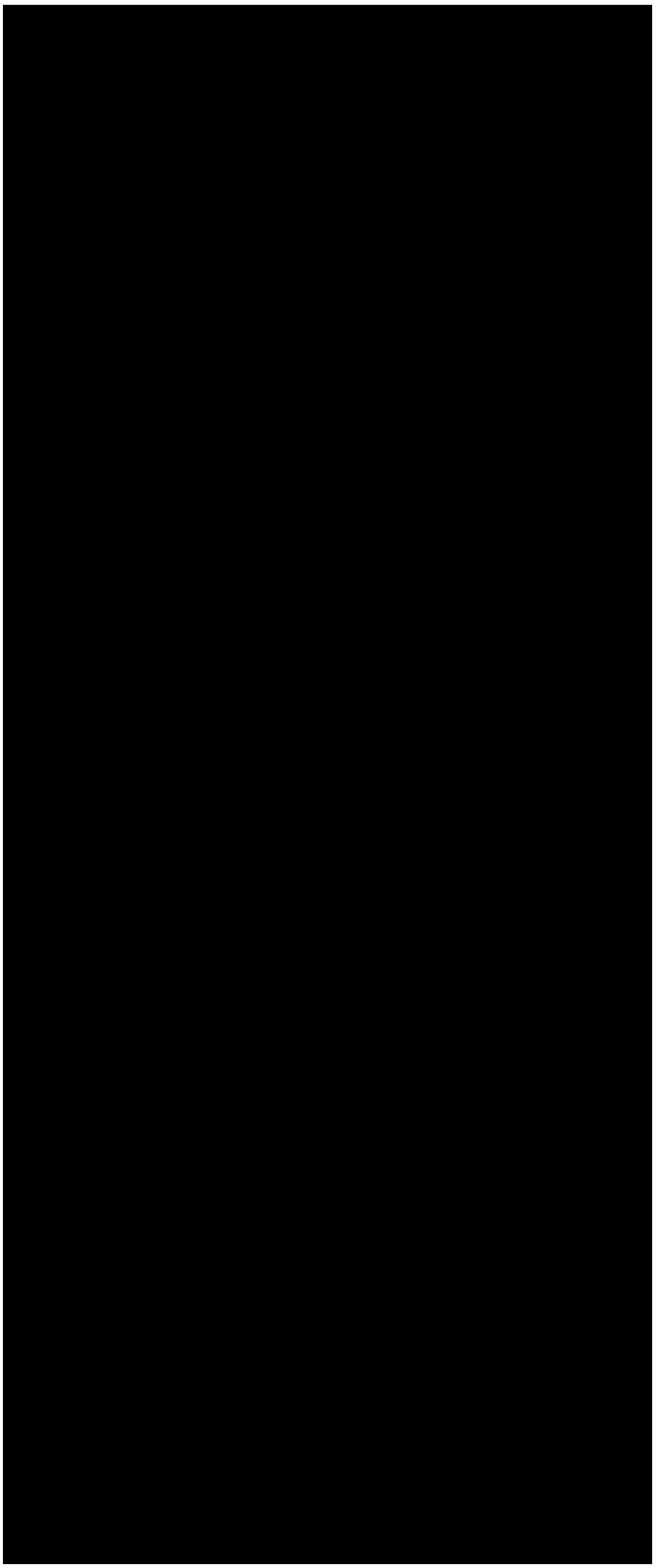
Table 2 Experiences Personally Reported to Respondents Relating to Adherence and Information Requests by Children/Young People or their Parents/Carers

Experiences of Adherence and Information Requests	Number of respondents citing reported experience (%)
The Patient/carer had forgotten to take/administer a dose.	36 (47.4%)
The patient/carer had decided to stop taking/administering the medicine without informing the prescriber.	24 (31.6%)
The patient/carer had decided to reduce the dose taken/administered without informing the prescriber.	19 (25%)
The patient/carer had decided to increase the dose taken/administered without informing the prescriber.	9 (11.8%)
Information on how to take/administer the medication.	64 (84.2%)
Information on the dose regimen.	63 (82.9%)
Information on the prescribed indication for the medication.	59 (77.6%)
Information on the adverse effects of the medication.	58 (76.6%)

Table 3 Medication-Related Experiences Personally Reported to Respondents by Children/Young People or their Parents/Carers

Reported Experience	Number of respondents citing reported experience (%)
The patient/carer was experiencing administration difficulties.	51 (67.1%)
The patient/carer was experiencing difficulties obtaining supplies of the medicine from a community pharmacy.	47 (61.8%)
The patient had experienced adverse effects.	39 (51.3%)
The patient's General Practitioner was unwilling to prescribe a hospital recommended medicine.	27 (35.5%)
The patient/carer was experiencing difficulties obtaining supplies of the medicine from a hospital pharmacy.	10 (13.2%)
The patient/carer was experiencing difficulties obtaining supplies of the medicine from a homecare provider.	7 (9.2%)

Appendix XXIX Study 2 conference oral presentation

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Appendix XXX Study 3 published paper

The Treatment-Related Experiences of Parents, Children and Young People when a Child/Young Person Takes Regular Prescribed Medication

Introduction

Efforts to assist patients with adherence might improve the benefits of prescribed medication [1]. In children, adherence may be influenced by parents'/carers' beliefs about the condition, regimen, child resistance, daily life and health professional influence [2].

Taking medication has been shown to place a burden on patients' daily lives including the routine of taking medication, monitoring and travelling [3,4]. The formulation, quantity, packaging, brand, adverse effects and negotiating the healthcare system add to this burden [3]. The stigma from family and friends associated with taking medication may add a psychological burden and influence patients' beliefs about medication [3].

The experiences of children, and families, taking medication have been described for asthma [5,6], diabetes [6], cystic fibrosis [7,8], attention deficit hyperactivity disorder [9], inflammatory bowel disease [10], diabetes [11] and post-transplant patients [12,13]. Challenges were described around medication use in school, taking in front of peers, social activities, regimen rigidity, reliance on family and adherence. The desire to achieve normality in adolescents can lead to patient-initiated changes to their medication [14].

Treatment burden can lead to poor adherence, waste and poor outcomes [15]. Minimally disruptive medication tailored to the realities of patients' daily lives could greatly improve quality of life [15]. For children and young people, understanding how medication taking affects daily life may help identify opportunities for optimising use.

Aim of the Study

To explore the treatment-related experiences when children and young people take regular prescribed medication

Ethics Approval

Approved by the West of Scotland Research Ethics Committee 16/3/17, reference 17/WS/0038.

Method

Setting

This study was undertaken at Birmingham Children's Hospital -a UK paediatric hospital.

Participant Recruitment/Selection

Purposive sampling by ward pharmacists of in-patients aged up to 18 years who had been taking two or more prescribed medications concurrently at home, prior to admission, for six weeks or longer. Each participant was provided with an information sheet. Participants who wished to join the study were identified to JA who took consent. Consent was taken from the patient's parent/carer who acted as the study participant if the child was under 16 years old or the patient if aged 16 years or older. Children under 16 years were encouraged to take part in the study and assent was taken based on their understanding.

Twenty-four participants were recruited into the study - eight from each age group 0 - 5, 6 - 10 and 11 – 18 years to provide a breadth of experience across the full childhood age range. The study was not offered to non-English speakers due to the short time opportunity to arrange an interpreter.

Data Collection

Face-to-face semi-structured interviews, with pre-piloted questions, were recorded and transcribed verbatim. The interviews took place during the patient's in-patient stay and were undertaken by JA, a pharmacist not involved in the care of the study patients. The questions covered in the interviews were identified through a literature review (Figure 1). Demographic/background information recorded included the patient's age and usual medication.

Fig.1 Interview Questions

Interview Topic: The Medication Regimen

Question set:

- Tell me about your daily regime of taking/administering medication.
- What changes have you had to make to your daily life to take in to account taking medication?
- What changes have you had to make to the medication regimen to fit it around your daily lives? Have you adjusted the schedule yourself?
- What aspects of medication taking are the most challenging? How have you solved these challenges?
- Have you sought the advice of a healthcare professional for help with your medication taking schedule?
- Do you use any aids to help with remembering to take/administer medication?
- How has medication impacted on you/your child's family life and social life for example, holidays and visiting family/friends?
- Have you looked up any further information about the medication yourself? Where did you look? What did you wish to find out?

Interview Topic: Medication Formulation and Packaging

Question set:

- Have you experienced any problems with administering/taking the medication? For example, size of the tablet, taste or preparation to get the prescribed dose? How have you managed to get around this?
- Is the number of doses difficult to manage? How have you managed to get around this?
- Does the packaging that the medication comes in cause you any difficulties? How have you got around this?
- Have you experienced any problems if the brand/manufacturer of your/your child's medication changes?
- What written instructions were you provided with about your medication? Were they useful? Would you have liked any additional information?
- If the dose changes, when/how do you usually get told about this? Do you receive any written information?

Interview Topic: Managing Supplies of Medication

Question set:

- Have you encountered any difficulties obtaining prescriptions or supplies of medication for you/your child?
- On average, how much time do you spend dealing with the healthcare system around medication? For example, arranging supplies.
- Have you ever received inadequate or conflicting information about your medication?
- Is the way that information is provided to you about medication suitable? For example, face-to-face with the prescriber, pharmacist or nurse.

Interview Topic: Adverse Effects

Question set:

- Have you/your child experienced any side effects from the medication?
- How did the side effect affect you/your child?
- Did you know what to do?
- Was it something that you knew could happen?
- Had anyone spoken to you about the side effects?

Interview Topic: Other Experiences

Question set:

- Are there any other challenges around medication that I have not mentioned that you would like to raise?

Data Analysis

The interview transcripts were analysed using NVivo version 11. Thematic analysis was undertaken by JA using the 6 phases described by Braun and Clarke [16]. The themes identified were independently reviewed by KAW and DRPT.

Results

Twenty-three parents and one 16-year-old patient consented. Assent was taken from 5 patients who contributed to the interviews with their parents. Two were aged 11 years, two 14 years and one 15 years.

In total 166 prescribed medications were taken by patients at home (Table 1). The number of medications prescribed for each patient ranged from 3 to 15 (mean 7, mode 5).

Table 1. Type of Prescribed Medication

Medication	**Number Prescribed**
Vitamin and mineral supplementation	18
Antiepileptic	17
Treatment of gastro-oesophageal reflux disease	12
Inhaled bronchodilator	11
Treatment of constipation	11
Prophylactic antibiotics	9
Analgesia	8
Inhaled corticosteroid	6
Oral corticosteroid	6
Antiemetic	5
Nebulised sodium chloride	5
Oral antihistamine	4
Emollient	4
Pancreatin	4
Insulin	3
Nasal corticosteroid	3
Nebulised antibiotic	3
Nebulised DNase	3
Oral bronchodilator	2
Leukotriene antagonist	2
Other medications	30

Participants described many experiences of how taking medication impacted on their lives. These have been summarised into common themes. Participants identified additional experiences that were not part of the original interview framework. These included: the rigidity that parents demonstrated around dose times, managing dose changes in school, the internet as an information resource and for liaising with other parents and the influence of medication labelling.

The Timing of Doses

Participants experienced challenges around the timing/frequency of doses. A four-times-daily regimen was the most difficult to adhere to due to the time available within daily activities. Participants described extending the duration of their day, arranging doses around meals/other medication and maintaining a precise time gap between doses.

"We have to keep the gaps in-between equal, night-time especially because she has to have one at midnight, one at 2am then she's due one at 6am. I have to stay up late until 2 o'clock and then I sleep after I've given her medicine." [Father of Patient 20 prescribed oral omeprazole, erythromycin, dexamethasone, glycopyrronium and co-trimoxazole.]

To make the medication regimen fit around daily life participants adjusted the timing of medication or daily activities. Establishing a routine was identified as important. Few participants sought advice about their medication schedule from a healthcare professional. Others sought advice on changing the timing of medication. This included adjusting the times away from the hospital administration times. Two participants had changed the regimen themselves.

Medication at School

Participants described their experiences of medication at school. Whilst some had positive experiences others avoided the need to administer at school. Difficulties included educating teachers, administration in front of peers, transporting medication, limitations on frequency of administration and arranging additional medication for storage at school. School staff were unable to administer updated doses of medication following a verbal instruction of a dose change when medication was labelled with the previous dose.

> *"If she's gone to an out-patient appointment and her doses have changed she'll have an old packet that hasn't been labelled properly. Then I'm saying to [the school] the doses have changed. The school say 'well we can't give it because the dose that we've got is incorrect'. Then I'm waiting a week for the prescription to come or potentially two weeks for a letter from the hospital to get to the GP and then the GP to write out a new dose of medication. Quite often I'll have to keep her off school because they can't give the new dose."* [Mother of Patient 21 prescribed oral desmopressin, levothyroxine, hydrocortisone and subcutaneous somatropin.]

Medication Adherence

Many participants cited remembering to give their child's medication as their biggest challenge. Strategies employed to reduce the risk of unintended non-adherence included a mobile phone alarm, placing medication where it was visible, home-made chart/administration record and verbal reminders. A number of participants had purchased medication compliance aids. A second checking process had been adopted by one participant to reduce the risk of error.

> *"I've had to put a list, like a checklist, on my fridge to make sure that I know I gave it him as well. I didn't before and I used to feel like I was forgetting so I wrote it down so I know I gave it him."* [Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine, pancreatin, nebulised sodium chloride, salbutamol and colistimethate.]

> *"My husband and I always check them together to make it easier. In the past my mum did because she was a nurse and she taught me to double check which is brilliant because there have been times when I've been tired..."* [Mother of Patient 9 prescribed via gastrostomy senna, Movicol®, paracetamol, carbamazepine, levetiracetam, omeprazole, buccal midazolam, inhaled oxygen, rectal phosphate and sodium citrate.]

Medication Information

Participants found the information provided with their medication useful. Some described their experiences of receiving information about dose changes in clinic. This was provided verbally, with insufficient time for participants to write down, or with a hand-written note that was difficult to read.

> *"That's how we had to learn how to increase the dose. It was just a little scribble on a piece of paper from the consultant at first and the actual letter comes about three weeks later. I hope that when it finally comes through I've read this squiggle correctly and remembered what he said in clinic."* Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Few participants felt that they had received inadequate or conflicting information. Others believed that they were not told enough about access to medication outside of the hospital, how to use their medication, adverse effects or the type of medication prescribed.

"We have some people telling us it's really bad for him to be on [steroids]. When he's older he's going to suffer with his bones. When we went to the 'out-of-hours' at [the local hospital] it was one of the doctors there. So, we listen to him and then we're told we need [the steroids by the respiratory team] so I'm like what do I do?" [Mother of Patient 17 prescribed oral theophylline and montelukast. Inhaled salbutamol and Seretide®. Intranasal fluticasone.]

Participants commonly researched further information about their medication using the internet. This was for general interest, assurance, alternative treatment options, how to use their medication and information on adverse effects. Other participants avoided using the internet through fear of finding out something of concern.

"At the end of the day we are responsible for [Patient 1]. I have researched them, I don't understand half of it, but I've got an understanding to maybe ask the right questions and just check because we are responsible for him and we've not had anyone who's on regular medicines in the family." [Mother of Patient 1 prescribed oral Movicol®, cetirizine, theophylline, hydrocortisone (intramuscular if required). Inhaled salbutamol and Seretide®. Intranasal fluticasone.]

Participants recounted experiences of using on-line support groups. Whilst helpful for some they created uncertainty for others through reading other patients' experiences and advice from 'expert parents'. One parent utilised a Facebook page for epilepsy and found that the reassurance provided reduced the need to contact the medical team.

"I've joined a parenting group and I thought it would be nice to talk to other parents in the same position. They were saying things like if you give too much Creon then it will do this, you need to provide this sort of thing. I ignored it in the end and thought it's probably best not to listen to you. Listen to the professionals." [Mother of Patient 14 prescribed oral multivitamins, vitamin E, ranitidine and pancreatin, nebulised sodium chloride, salbutamol and colistimethate.]

"Different heart mum's groups. They'll say they were on captopril but now they're on something and I'm like, well, what's that then? Is it like captopril? Why is your daughter now taken off captopril and put on to this one and I'm thinking can't [Patient 15] be taken off captopril and put on this one?" [Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.]

"I joined a parents' for epilepsy Facebook. Sometimes you just think the doctor only has so much time with you and they have so much information that they can give you. It can be quite lonely out there when you don't know what you're doing. Reading about her hair falling out and the other mums and dads are saying it's fine…it will grow back it's not forever, she's not going to end up completely bald. It can be reassuring." Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Medication Formulation and Packaging

Child resistance due to taste, colour, tablet size, refusal and disliking inhaler devices were cited. The ease of tablets compared with liquid formulations was mentioned.

"It takes a lot more time to deal with liquids because you have to keep drawing them up. If I'm late for school, I can just grab a tablet and quickly take it. But when it comes to liquid I had to stay over a bit longer and draw it up. It's more convenient with it being tablets." [Patient 2 prescribed oral phenoxymethylpenicillin, folic acid, paracetamol, ibuprofen and morphine sulphate.]

Parents used a variety of methods to aid their child's medication taking. These included: distraction, tasting medication to empathise with their child, taste masking and changing the formulation.

Some participants had experienced difficulties with medication packaging and expressed concern about waste when receiving large bottles. Labelling caused some anxiety. A 'cytotoxic' label caused one participant to decide against taking their medication. An 'unlicensed medication' label on a bottle of phenobarbital caused concern.

"I think the other thing was his phenobarbital coming with a great big label on saying 'unlicensed medicine'. My mum saw it and she was like 'oh my gosh! what are they doing?'." [Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).]

Few participants described challenges if the manufacturer of their medication changed. Others described uncertainty about whether they were receiving the correct medication, difficulty remembering the name, intolerance of alternative brands and the inconvenience of

requiring refrigerated storage depending on the brand dispensed.

> *"We have to try and keep to the same brand but we've found a lot of community pharmacists give us a different brand. Now the GP puts it on the prescription. Epilim liquid and syrup get interchanged. The syrup isn't good for her teeth, it's quite sugary and quite thick to [administer] to her. We do find one week we'll get liquid and another we'll get syrup."* Mother of Patient 24 prescribed oral sodium valproate, carbamazepine and inhaled salbutamol.

Travelling with Medication

Administering medication was considered awkward in the presence of other people.

> *"We're in a café and we're drawing up meds and everyone's looking at you thinking 'what are they doing!'. Especially when you're out and about that's the worst."* [Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.]

Transportation was described as a problem for daily travel and holidaying. Particular problems were with refrigerated medication and large bottles. Some participants had purchased oral syringes with caps to carry doses. One participant risked the period of time that their refrigerated medication was transported at room temperature. Other participants used medication compliance aids for holidays and described using ice blocks to keep medication cool. Some participants avoided going on holiday due to the perceived difficulties over transporting and accessing medication.

> *"Holidays is a hard one. When we got there we had a cold bag with ice packs in it and obviously the ice packs were melting and we had to stop and get ice from different shops. We had to stop at three different stops to get ice to cool his medicines down which was really hard. It was so hot the ice was melting and then when I got there the labels had come off!"* [Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.]

Managing Supplies of Medication

Participants who received their medication through the hospital described the ease of receiving a prescription in an out-patient clinic and their medication from the hospital pharmacy. Those receiving medication through their GP highlighted community pharmacy

prescription collection services and on-line ordering as useful. However, a number of participants described some difficulties obtaining medication in primary care. These were: the GP declining to prescribe, unavailability in community pharmacy, difficulties with the repeat prescription process and delayed communication between hospital and GP. Participants described the advanced planning that they undertook to maintain medication supplies.

> *"Initially yes, it was a very big problem. Trying to get the GP to prescribe something that's not listed in his bog standard BNF was a big issue. He refused to prescribe anything so now I literally don't go to the GP.* [Mother of Patient 18 prescribed oral sirolimus, mycophenolate, sodium bicarbonate, D-mannose and sodium feredetate.]

> *"There's certain meds the GP won't prescribe. They're like, 'well, hang on they shouldn't be on that med anyway'. That's the way they see it. Even the digoxin, when we brought the forms to the GP after he got discharged he was looking at it and like 'Really! Is he on that!? Are you sure!?'."* [Mother of Patient 15 prescribed oral captopril and inhaled salbutamol.]

The time taken to arrange supplies of medication focussed around two themes - ordering frequency and the time it took for the prescription and supply. In particular, having to frequently arrange supplies of medication due to a lack of synchronisation. This required ordering at least one medication weekly.

> *"The phenobarbital in particular. We were told that we could order it and obtain it within 48 hours. But subsequently actually we need 10 days. We've never run out but there was once in particular it was really challenging."* [Mother of Patient 11 prescribed oral phenytoin, vigabatrin, levetiracetam and ranitidine (previously phenobarbital).]

Adverse Effects

Half of participants had experienced adverse effects ranging from diarrhoea to thrombocytopenia. Most had been informed by the healthcare team, other parents or through self-research. Most participants sought advice from nurses within their specialty. Mild side effects were managed by participants.

Discussion

This study has identified many challenges that children, young people and their parents experience when a child or young person is taking regular prescribed medication. Similar experiences to those in the published literature were described including adherence, regimen inflexibility, impact on social activities, travelling with medication, administration at school and arranging repeat supplies. In addition, this study has identified how parents interpret dosing instructions, challenges around implementing dose changes in school and concern about medication waste.

The timing of doses and their impact on daily life was notable. The difficulty of the regimen has been shown to affect adherence in paediatrics improving once a routine is established [2]. In this current study participants had similar experiences but required support with the timing of administration, especially limiting this to waking hours. There are opportunities for this during the prescribing consultation, dispensing and medication review.

Challenges were identified with medication taken at school reflecting those previously described including access to medication and not wanting to take in front of peers [6,17,18]. Despite there being national guidance on medication in schools in the UK [19] and USA [20] poor experiences remain. A survey in Finland found inconsistencies in local school policies on medication [21]. This current study additionally identified difficulties around implementing dose changes. Information on changes to medication may be enhanced through the electronic transfer of clinic letters to GPs [22] and through direct electronic referral from hospital to community pharmacies [23]. Further work is required to support patients taking medication in school through better collaboration with healthcare professionals.

The most challenging aspect about having a child on medication was remembering to administer. The consequences of poor adherence are well established [1,2]. A number of strategies were employed to aid adherence including compliance aids. The evidence base for medication compliance aids is limited and indicates a lack of patient benefit [24]. However, participants highlighted the additional benefit of compliance aids when transporting medication. This study highlights the importance of individualising patient care including considering the daily routine of each family.

Participants described receiving insufficient information in clinic verbally and through hand-written notes. The quality of instructions provided about medication influences adherence [1]. Healthcare practitioners may also influence adherence through patient engagement with

conversations about medication [25]. Patients and parents require clear documentation of medication regimens.

Most participants looked up further information about their medication using the internet in accordance with published studies [26,27]. Consultations with healthcare professionals are constrained by time [26]. A consequence of this is the desire to seek further information as explained by participants in this current study. However, poor interpretation of information about medications could lead to poor compliance [28]. A quality assessment tool may help children and parents to assess online information [28]. There is an opportunity at the points of prescribing and dispensing to 'sign-post' people to quality assured internet sites.

Some participants accessed on-line parent support groups which is observed in parents/patients with long-term conditions [26 – 28]. Some found these groups informative whereas others found they raised more questions and disliked the 'expert parent' approach. Further research has been suggested around how pharmacists may support patients using the internet for medication information [28].

The absence of child friendly formulations was problematic. To optimise the use of currently available formulations, training in swallowing medication could be provided by healthcare professionals which has previously proved successful [29].

Participants expressed concern about wasted medication. In the UK approximately £300 million of NHS prescribed medication is wasted annually [30]. A recent study identified that more than 33% of medication returned to Dutch community pharmacies was preventable [31]. Globally, the total amount of medication consumed will increase by about 3% through 2021 with spend approaching $1.5 trillion [32]. Therefore, initiatives that have been described to reduce waste [30] will be of increasing importance. This study confirms that medication waste is evident in paediatrics with parents expressing concern. There are opportunities for pharmacists to reduce waste through medication review.

Travelling with medication and taking medication outside of the home proved challenging. Parents were making decisions around the stability of medication out of the fridge and usual packaging. This current study identified that more support and advice is required for parents/patients travelling with medication.

Challenges were described arranging supplies of medication in primary care as previously described [33]. These remain problematic for parents and patients who may not be informed

of these potential problems. Contact between the hospital and the patient's GP to agree the supply route should take place at the earliest opportunity. Better integration of pharmacists and GP working can optimise medication supply including synchronising repeat medications [34]. Timely transfer of information is recommended as a standard for good medicines optimisation [35].

Participants reported adverse effects from their medication. Treatment side effects have been shown to be a factor in non-adherence in paediatrics [2]. Parents and patients should be informed about potential adverse effects, their management and how to seek advice. There remains further opportunity to understand how patients and parents would like to be informed about adverse effects.

The strength of this study is the detailed insight into how medication taking in children impacts on daily life from the perspective of the parent and/or the patient. The results from the study can be incorporated in prescribing and dispensing consultations to further optimise medication use. These findings may also be incorporated in a formal paediatric medication review with individual patients/parents.

Study limitations include the possibility of participants providing answers that they perceived to be acceptable. Consistency of the interview process was maintained with one researcher undertaking all interviews. The interviews took place whilst the patient was an in-patient which may have influenced how participants prioritised their experiences. Undertaking the research at a single UK institution may limit the generalisability of the results. Whilst healthcare systems differ between countries, many of the experiences investigated are likely to be similar.

Conclusion

Parents and patients experience many challenges with their medication. This study has identified the following opportunities for healthcare professionals to contribute towards the optimal use of medication in paediatric patients:

- Engagement with patients and parents regarding medication choice/regimen to ensure treatment is achievable within their daily lives.
- Better collaboration with schools regarding patients' medication especially when changes are made to treatment.

- Provision of clear instructions regarding changes that patients/parents are expected to make to current treatment.
- Sign-posting to quality assured internet sites about medication.
- Provide support to children to swallow solid dose forms.
- Ensure medication quantity is optimised to reduce waste.
- Early collaboration between hospital and primary care health providers to agree medication supply.

Minimally disruptive medication tailored to the realities patients' daily lives could greatly improve quality of life [15]. This current study has identified how medication taking affects daily life when children and young people take regular medication.

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Conflicts of Interest

The Authors have no conflicts of interest to disclose.

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Appendix XXXI Study 4 conference poster