A 360-DEGREE APPRAISAL OF THE BARRIERS TO MEDICATION ADHERENCE IN PAEDIATRIC PATIENTS WITH LONG-TERM ILLNESS

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ABSTRACT

Research indicates that paediatric medication adherence in long-term conditions is often sub-optimal and can be affected by a range of developmental, social and family factors. However, little is known about children's medication-taking experience. The aim of this research was to identify the most common barriers to adherence from the perspective of three different groups: the medicine-taker, the medicine giver and the healthcare professional (HCP). A further aim was to evaluate the role of community pharmacists in supporting paediatric patients with long-term medication needs.

Study one conducted a systematic review of seven databases from January 1995 to 2016, yielding 18 studies that used self-report methods to identify barriers to medication adherence in children and adolescent, aged 5-18 years with long-term conditions. The common barriers were a lack of caregiver and healthcare support, medication regimen complexity, forgetfulness, medication side-effects and concerns about medication need and efficacy. Stigma was the only condition-specific adherence barrier for children and adolescents with HIV, all other barriers were uniform across conditions.

Study two used a Delphi method with paediatric healthcare professionals (N=23) to prioritise adherence barriers in current clinical practice. Agreement was rated on a 5-point scale, the mean and standard deviation was used to determine consensus between participants to each adherence barrier. The main observed barriers to adherence were the need for constant reminders from caregivers to ensure medication was taken, medication-taking fatigue, medication taste and increased responsibility for medication-taking. The results indicated that there is a variation between the barriers identified through paediatric self-reports and what is observed by healthcare professionals in practice.

Study three used a retrospective questionnaire to identify caregivers (N=52) barriers to medication administration and their opinions of community pharmacists. Common barriers identified were their child's heavy reliance on them to ensure medication was taken, frustration and fatigue from having to take regular medication and their child's increased responsibility for medication-taking. Caregivers were generally positive about the support they received from the pharmacist to care for their child with long-term medication needs and would welcome medication reviews and information sessions with the pharmacist to help with their child's adherence.

Study four utilised a prospective observational design with 15 community pharmacies to evaluate the number and nature of paediatric queries that pharmacists received relating to long-term conditions over 4-weeks. Results indicated that asthma was the most queried condition. Caregivers often needed help with inhaler use, symptom management and understanding the long-term use of inhaled steroids. The barriers to effectively managing paediatric issues were the inability to communicate with the caregiver and child together and caregiver beliefs. Pharmacists believed that the introduction of medication reviews and information sessions with caregivers and their children could be effective measure to improve paediatric adherence.

In conclusion, it may be suggested that there are commonalities in the adherence barriers experienced between children, adolescents and caregivers. However, the terms used to describe adherence barriers may change based on the perspective and therefore are perceived differently. Healthcare professionals only had partial awareness of the adherence barriers paediatric patients and caregivers experience. Furthermore, advanced community pharmacy services should be extended to include paediatric medicine to determine their effectiveness in reducing paediatric adherence barriers.

Table of Contents

List of Tables

List of Figures

List of abbreviations

CASP	*Critical Appraisal Skill Programme*
GPhC	*General Pharmaceutical Council*
GP	*General Practitioner*
HbA1c	*Glycated haemoglobin*
HAART	*Highly active antiretroviral therapy*
HBM	*Health Belief Model*
HCP	*Healthcare professional*
HIV	*Human immunodeficiency virus*
IBD	*Inflammatory bowel disease*
ICS	*Inhaled corticosteroids*
MUR	*Medication use review*
NHS	*National Health Service*
NICE	*National Institute of Clinical Excellence*
NMS	*New Medicines Service*
OTC	*Over the counter*
PBC	*Perceived behaviour control*
SCD	*Sickle cell disease*
SD	*Standard deviation*
TPB	*Theory of Planned Behaviour*
TRA	*Theory of Reasoned Action*
T1DM	*Type 1 Diabetes Mellitus/ Insulin dependent diabetes mellitus*
T2DM	*Type 2 Diabetes Mellitus/ Non-insulin dependent diabetes mellitus*

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Declaration

I declare that the research contained in this thesis, unless otherwise formally indicated within the text, is the original work of the author. The thesis has not been previously submitted to this or any other university for a degree, and does not incorporate any material already submitted for a degree.

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Chapter 1 Introduction

1.1 Justification of research

This research intends to fill a knowledge gap by extending the current understanding of medication adherence barriers in long-term conditions to children, as well as adolescents. Furthermore, this research will aim to identify how different groups of people that are involved in paediatric care (the patient, caregiver and healthcare professional), perceive and experience medication-taking adherence barriers, therefore providing an understanding of the similarities and differences between groups.

In addition, as there is currently no commissioned community pharmacy service to support paediatric patients taking medication for long-term conditions and their caregivers, the attitudes of caregivers regarding community pharmacists will be investigated.

1.2 Medication Adherence

Adherence is described as "the extent to which a patient's medication taking coincides with an agreed-upon prescribed treatment" [1]. The failure to adhere has been strongly associated with poor disease control, poorer quality of life, condition complications, increased healthcare costs, greater morbidity and increased risk of mortality [2]. Non-adherence can be categorised as either intentional or unintentional, with unintentional non-adherence referring to a failure to adhere due to factors such as forgetfulness and poor understanding of their treatment instructions and factors which are not in their control, such as the inability to open medication packets. It is regarded as a passive cause of non-adherence. This differs from intentional non-adherence, which relates to an active decision-making process leading to medication not being taken as prescribed. Reasons may include avoidance of adverse effects of medication, scepticism about the need for medication,

beliefs regarding the severity of the condition or fear of stigma associated with the condition and/or medication [3].

Evidence indicates that adherence in paediatric patients, defined as a person aged up to 19 years of age [1], with long-term conditions ranges from 43% to 100%, with an average of 58% [1, 4]. This suggests that over half of children and adolescents requiring prescribed medication are not gaining the full benefits from their treatment.

1.3 Terminology

A long-term or chronic condition such as asthma and diabetes is classified as such due to its long duration, slow progression and need for drug therapy to achieve long-term control [5, 6]. The management of a long-term condition relies heavily on the ability of an individual or caregiver to manage the day-to-day responsibilities that come with that condition, such as medication-taking, lifestyle modifications, regular self-care tasks and maintaining regular contact with their healthcare providers [7].

The earlier widespread use of the term "compliance" has now been superseded with the more relevant term "adherence". Compliance is defined as "the extent to which a patient's behaviour matches the prescriber's recommendations", implying that compliance does not involve patient input into the treatment decision-making process [8]. Healthcare professionals are now working towards achieving a patient-centred approach, which considers patient preferences, needs and values in order to make clinical decisions. The use of the term "adherence" is therefore more appropriate, as it refers to treatment recommendations that have been formed in agreement between the patient and prescriber. Three types of non-adherence have been identified: unintentional – a belief that recommendations are being followed; unplanned – an intention to follow recommendations but cannot; and intentional – a belief that the medication is the wrong course of action [9].

"Persistence", is defined as "the duration of time from initiation to discontinuation of treatment" [10]. However, during this time, any amount of medication could be taken; therefore there is the possibility of a person being non-adherent, yet persistent with their treatment, as a patient can take either more medication than is prescribed or less, resulting in the medication-taking behaviour not being reflective of the intended prescribed instructions and defining it as non-adherence. However, the act of medication-taking has not stopped therefore, the patient is still persistent.

Finally, "concordance" describes the consultation process between patient and prescriber, defining a consultation which is based on shared decision-making and is reflective of both the prescriber's recommendations and patient preference [8], thus it is inclusive of a patient-centred approach [9]. Non-concordance can occur if there is a failure to establish a relationship of shared decision-making between the prescriber and patient, which may be a cause of non-adherence to medication, i.e. the failure to act in accordance to the prescribed treatment regimen, leading to poor medication-taking behaviour [8, 9].

1.4 Methods of measuring adherence

Rates of adherence vary greatly depending on the patient group, condition type and the measurement method used. Several methods of measuring adherence exist to identify and understand medication-taking behaviours. Direct methods of measuring adherence include drug assays from blood or urine samples and patient observations. Whilst these techniques offer accuracy, they are expensive to implement and invasive. Alternatively, several indirect measures are available and choice is dependent on validity, ease of use, patient group, literacy level and reliability. Indirect methods include self-reported measures of adherence, pill counts, prescription refill rates, patient diaries and electronic monitoring devices.

Self-report measures are a common choice as they offer the advantage of being cheap and easy to use, however the potential lack of willingness of participants to disclose information can distort the results, as well as the accuracy and validity of the measure [11, 12]. Commonly used self-report measures include the *Morisky Medication Adherence Scale* (MMAS-4/MMAS-8) [13], which is frequently used due to its simplicity, speed, ease of scoring, applicability to a broad range of patient populations and its ability to identify barriers to non-adherence which relate to forgetfulness and adverse effects. The MMAS is also easily used in patients with low literacy levels, as is the *Self-efficacy for Appropriate Medication Use self-reporting method* (SEAMS) [12]. The SEAMS is a 13-question method incorporating questions relating to self-efficacy, but in comparison to the MMAS, it takes slightly longer to score. The *Brief Medication Questionnaire* (BMQ) originally developed for hypertensive patients, is a self-report method for assessing barriers to adherence via structured questions regarding aspects of the patient's regimen, beliefs and recall. Therefore, it aims to determine the specific cause of nonadherence. However, the scoring system is more complex than the MMAS and is not ideal for patients with lower levels of literacy [12]. Like the BMQ, the *Hill-Bone Compliance Scale* is for hypertensive patients but it cannot be generalised to other conditions due to its specific design for hypertension. Equally, the Medication Adherence Rating Scale (MARS) is specifically for patients with chronic mental health illnesses and cannot be generalised to other conditions.

Additional indirect methods include Medication Event Monitoring Systems (MEMS) where a microelectronic chip is located in medication bottle caps, registering the date and time of bottling opening. However, each time the bottle is opened it does not necessarily equate to medication intake and can be easily manipulated to show higher adherence [14]. Due to the high cost of the device, it is not always favoured over the cheaper alternatives, such as self-report scales. Furthermore, a meta-analysis which compared the accuracy and

internal validity between the MEMS and self-report measures found them to be comparatively equal in terms of determining rates of adherence, suggesting that self-report measures provided good estimations of adherence with much lower cost implications when compared to MEMS [15].

The pill counting method of measuring adherence is cheap and easy but is liable to overestimations, due to their failure to assess if medication is actually taken [14]. Patient diaries require patients to remember to fill them in and if forgetfulness is a cause of non-adherence, diary entries may also be sporadic. Furthermore, patient diaries and pill counting measures are liable to the 'Hawthorne' effect [16], whereby patients may show increased adherence, as they are aware of the observations being made.

1.5 Background of long-term conditions in paediatric populations

Throughout this thesis, the term 'child' will be referred to those aged five to twelve years and 'adolescent' will refer to those aged thirteen to eighteen years. The term 'paediatric' will encompass both age groups.

The most common long-term condition to affect children in the UK is asthma, with 1.1 million children currently receiving treatment [17]. Asthma is one of the major causes of hospital admissions and Accident and Emergency (A&E) attendance, with approximately 70% of these related to preventable factors such as improper inhaler technique and failure to attend review appointments that are designed to assess asthma control and review medication [17, 18]. This high use of emergency care services due to poor asthma control is despite the existence of the National Institute of Clinical Excellence (NICE) quality-standards of treatment and recommendations for primary care healthcare professionals to put in place services to provide an integrated approach to manage patients with respiratory disease.

Other common conditions to affect children and adolescents are inflammatory bowel disease, including Crohns's disease and ulcerative colitis. This affects approximately 60,000 children and adolescents in the UK [19]. The condition relies on several lifestyle changes such as dietary modifications and exercise to be adhered to, in addition to medication to limit the number of inflammatory exacerbations.

Furthermore, epilepsy requires long-term medication as part of its treatment and affects 34,000 children and adolescents in the UK who are currently receiving anti-epileptic medication [20].

Type 1 diabetes mellitus (T1DM) in the UK affects around 26,500 children and young people aged up to 21 years. In addition, type 2 diabetes mellitus (T2DM) affects approximately 500 children and adolescents [21]. Although elevated blood glucose levels define both conditions, the treatment and consequences of non-adherence significantly differ. T1DM must be controlled with insulin injections to replace insulin that the body cannot produce and non-adherence or omission of injections leads to diabetic ketoacidosis and hospitalisation. This is compared with T2DM, which may be initially controlled with diet, lifestyle modifications and oral medication. Non-adherence in T2DM will result in rising blood sugars but the immediate impact is less severe, compared to non-adherence to insulin replacement injections in T1DM. Diabetes management for both T1DM and T2DM includes several components to ensure strict glycaemic control and to limit the risk of long-term complications such as nephropathy, neuropathy, retinopathy and cardiovascular disease. The current NICE guidelines outline a patient-centred approach to tailoring treatment plans inclusive of education, diet modification, self-care, medication adherence and self-monitoring to reduce the impact of the condition on future health [21]

Lastly, human immunodeficiency virus (HIV) affects approximately 1200 children in the UK. The long-term management of HIV is with a medication regimen known as 'highly

active antiretroviral therapy', (HAART), a medication regimen which requires a strict 80% minimum adherence to reduce mortality, viral load and reduce the potential of drug resistance occurring [22].

1.6 Factors impacting adherence in paediatric populations

1.6.1 Patient-centred factors

1.6.1.1 Age, gender, ethnicity and socio-economic status

Age has been shown to be an important risk factor to adherence in several studies, due to the developmental changes that take place during adolescence [23-25]. The progression from childhood into adolescence has been shown to result in declining rates of medication adherence [23]. The outcome of a longitudinal study of 193 children with T1DM observed a significant association between age and diabetic control. An increase in age from childhood into adolescence saw a reduction in adherence and higher HbA1c (glycated haemoglobin) levels; a marker of average plasma glucose concentrations over a specified timeframe [23-25].

Similarly, a longitudinal cohort study of 142 participants aged either 7 or 13 years old with T1DM over 4 years, found that HbA1c control significantly decreased over the 4 years of the study, specifically from the age of 13 to 16 years old. This was linked to physiological and social changes that occur in adolescence [26, 27]. Even though diabetic knowledge increases in adolescence, there is still a decline in glycaemic control and overall adherence. Results of these studies indicate that other aspects of cognitive thinking and rationale influence adherence. The period of adolescence is a time for identity formation, obtaining independence and cognitive maturation, including autonomous decision-making [28]. The incorporation of a chronic condition into this already complex developmental stage could make adherence tasks increasingly difficult to manage [28, 29]. This is further supported

by the results of a study in which 106 participants aged 8-16 years with asthma had their medication adherence electronically measured over one month and showed a steep decline in mean adherence from age fourteen. Reduced adherence to medication occurred even though there was an increase in asthma knowledge and responsibility for asthma related tasks, which increased with age [23].

Although these studies highlight the effect of age on knowledge, responsibility and cognitive thinking to adherence from childhood to adolescence, they do not attempt to understand the barriers to medication adherence and how they change with age. Therefore, there is a gap in the literature which needs to identify child and adolescent perceived medication adherence barriers and understand how they change with age across a range of long-term conditions.

The role of gender in medication adherence has produced conflicting results and the reason for this remains unclear. Gender has not been shown to affect adherence to asthma medication and HIV treatment [23, 30, 31]. However, other studies have shown that females have significantly lower adherence to HIV medication [32] and males have lower adherence to diabetic medication [33].

Patients from ethnic minority backgrounds, specifically black Africans and South Asians in America and Europe, frequently display lower rates of adherence when compared with Caucasians [23, 34, 35]. The disparities displayed between ethnic groups have often been linked to socio-economic difference [36, 37], low levels of parental education [36], housing quality [38], language barriers [25] and family income [38]. A study of children with asthma has shown ethnicity to be an independent risk factor for non-adherence, resulting in lower rates of adherence to inhaled corticosteroids (ICS) [39].

1.6.1.2 Mood

Negative mood states such as depression and anxiety have been shown to negatively affect adherence, in adult and paediatric populations. This is due to depression causing feelings of hopelessness and reduced optimism, which leads to reduced belief in the benefits of medication-taking and poorer adherence [40, 41]. Depression also causes social withdrawal leading to isolation from family and peers and a reduction in the amount of support received to manage a long-term condition, which can make the daily management of medication-related tasks more difficult [41]. A person with a long-term condition and depression is three times more likely than a non-depressed person with a long-term condition to be non-adherent to medication-taking and the prescriber's recommendations [41].

1.6.1.3 Cognitive functioning

Executive functioning and autonomy are thought to develop with age [42, 43]. Executive functioning, defined as the ability to organise, plan, problem solve and self-regulate behaviour, has been linked to medication adherence [43, 44]. It has been predominantly investigated in children with diabetes, who must acquire the ability to set goals, organise numerous treatment tasks and show flexibility to adapt aspects of treatment, such as insulin units and has been shown to be positively associated to adherence and glycaemic control [43, 45].

Furthermore, studies have shown that responsibility for T1DM related tasks shifts from the caregiver to their child between the ages of nine to eleven. During this time, parental autonomy support decreases as the child assumes more responsibility and autonomy. This has been shown to decrease blood glucose monitoring, suggesting that children and adolescents still need ongoing support from caregivers [43, 46].

1.6.1.4 Beliefs about medication

Beliefs about medication can be predictive of the strength of intention to adhere to medication treatment in adult patients, caregivers of children and paediatric patients [47-49]. Beliefs provide the basis of a positive or negative attitude towards behaviour [50]. Therefore, beliefs regarding medication are a highly effective way of predicting medication-taking behaviour. Negative beliefs regarding medication necessity and medication efficacy have been linked to lower adherence rates in children and adolescents [49]. Beliefs regarding medication concerns, such as concerns about adverse effects or the long-term effects of medication, have been shown to be negatively associated to medication adherence, particularly when concerns about medication outweigh the beliefs of medication necessity [51, 52].

1.6.1.5 Illness perception

The way in which an illness or condition is perceived by a patient can have a big impact on their emotional state, decision-making processes and can also predict whether specific health behaviours will be performed [53]. An individual's illness perception is deemed as a five dimensional representation of mental and personal ideas: identity of illness, causes, consequences of illness on aspects of life, course of illness and illness control [53]. Studies have shown that adolescents who perceive their illness as severe have fewer concerns regarding medication side-effects and fears regarding potential medication dependence, as the necessity of medication outweighs the negative aspects of the medication treatment [54]. Reports from parents have also shown that a higher disease severity is predictive of better adherence to medication in inflammatory bowel disease [55]. However, there is also a need to address this from the perspective of paediatric patients, to understand how their beliefs and perceptions impact medication-taking behaviour and how, or if it differs from

caregivers beliefs. Having a better understanding of paediatric health beliefs can help to target patient interventions and improve health behaviours.

1.6.2 Family interaction, support and caregiver beliefs

1.6.2.1 Maternal depression

The impact of maternal depression has been shown to negatively affect a child's medication adherence [56], through the hindrance of a mother's ability to provide optimum levels of care due to feelings of negativity and helplessness, leading to an impaired ability to perform daily tasks, inclusive of medication administration tasks [57].

A cohort study of 158 mothers of children with asthma highlighted that maternal depression was related to increased reporting of their child's asthma interfering with daily activities [57]. Adherence to asthma medication was five times more likely to be reported as being problematic and mothers were four times more likely to report their child having forgotten to take their medication when compared with non-depressed mothers [57].

1.6.2.2 Family cohesion, family functioning and a chaotic household

Family cohesion has been defined as the level of support, helpfulness, shared affection and care among family members [58]. Children are initially reliant on their family to assume responsibility for condition-related management tasks [59-61]. However, family support and cohesion have shown to be positively associated with adherence across ages and conditions. Parental involvement through providing support in blood glucose monitoring has shown to be positively associated with better glycaemic control and lower HbA1c levels in 10–15 year olds [59, 62]. Similarly, a cross-sectional study of 126 adolescents with asthma aged 13-20 years showed that family support was positively associated with asthma control [63, 64].

Family functioning relates to factors such as family conflict, responsibility for care-related tasks and perceptions of supportive parental behaviour, therefore encompassing aspects of family cohesion. Diabetic control has often been related to family functioning at meal times [65, 66]. Meal times involve a variety of tasks relating to diabetic management, such as blood glucose monitoring, insulin administration, dietary awareness and measured carbohydrate intake [65, 66].

In addition to family cohesion and family functioning, there has been some focus on addressing the role and impact of a chaotic household on treatment adherence [67]. A chaotic household has been defined as an "economical measure of environmental confusion in the home exemplified by background factors such as noise and crowding" [67]. A disorganised home environment is a risk factor and strongly predictive of poor glycaemic control as measured by HbA1c results [67, 68]. It is thought that a chaotic household can potentially exacerbate an already negative parenting style and may negatively influence those children who need parental guidance and support with their diabetic management tasks [61, 67]. This was seen in a prospective cohort study of 104 children and adolescents with T1DM aged 1-13 years old. There was a significantly negative relationship between household chaos, adherence and glycaemic control [67]. Another study of 224 children and adolescents aged 8-18 years old with T1DM and their parents identified a link between treatment adherence and one vs. two-parent households. It was found that a one-parent household was related to lower rates of adherence and HbA1c control which may stem from an increase in parenting stress [69].

1.6.2.3 Support

The degree of support received from family, friends and healthcare professionals has been shown to significantly affect treatment adherence and subsequently treatment outcomes [70]. During adolescence there is greater reliance on peer support when compared to childhood, as children are still heavily reliant on their caregivers [71]. However, contrary to this, there is evidence to show that even during adolescence the positive role of family support does have a positive impact on adherence, compared to adolescents that do not receive positive family support [59-61]. Supportive families encourage their child's beliefs about their ability to self-care and by supporting beliefs regarding the efficacy of treatment to manage their long-term condition [72].

Peer support has shown to reduce stress, leading to increased metabolic control in T1DM [73]. However, peer support has not been shown to effect medication adherence and does not reduce medication adherence difficulties, but rather offers a more supportive role [73], that helps with disease adaptation and emotional well-being [74]. Support from peers has been shown to be effective in areas relating to exercise adherence, emotional support and blood glucose testing [74]. Treatment tasks such as insulin injecting are usually done in private and perhaps subject to less peer involvement [74]. Family members are more closely involved in certain aspects of care, such as medication administration and dietary aspects as this takes place predominantly in the home setting.

Support received from healthcare team members is also highlighted as a contributing factor to adherence and condition management [75]. Previous studies have found that a lack of support from healthcare teams was a factor in non-adherence [1, 28, 76, 77]. A study of 58 adolescents with T1DM assessed the role of support from healthcare teams and its link to adherence [75]. The results identified that a non-supportive healthcare team was a significant indicator of poor treatment management. Furthermore, decreased support from

a healthcare team increased emotional distress and HbA1c and decreased appointment attendance, blood glucose testing, diet and medication adherence. Adolescents who reported that their healthcare team 'nagged' them, were shown to have lower adherence and appointment attendance [75]. Further research in these areas found that implementing a collaborative method of managing a long-term condition, improved treatment adherence [78].

1.6.2.4 Caregiver beliefs

As caregivers assume responsibility of treatment-related tasks for young children, their beliefs, knowledge and understanding affects the extent to which caregivers adhere to their child's medication treatment. Parents of 67 children with asthma aged 3-7 years old were asked about their beliefs regarding their child's prescribed preventer asthma medication. Seventy-five percent of parents believed that the medication was a necessity in ensuring their child's good health. An increased parental necessity belief about medication was shown to be related to increased adherence to treatment [79, 80]. The 34% percent of parents with concerns about medication were significantly more likely to report lower adherence to their child's medication. In situations where caregivers concerns outweigh their beliefs about medication's necessity, there is a need to dispel misconceptions and information gaps through better education and targeting of groups that are at risk of poor adherence, to prevent caregivers from withholding their child's medication doses [80].

1.7 Behaviour models designed to understand health behaviour

To understand and explain health-related behaviour, the Health Belief Model (HBM) was developed in the 1950s [50]. It was initially used to try to explain why people failed to engage in health programmes that were designed to detect and prevent diseases. This was

modified in later years to understand medication-taking adherence in illness [50, 81], exercise behaviour in T2DM [82] and healthy eating habits [83]. The HBM is based on the understanding that health behaviour results from several subjective components: perceived severity, perceived susceptibility, benefits and barriers to treatment, and cues to action. Its application has shown that medication adherence can be improved by physicians, through education-led interventions that focus on perceived benefits and external cues [84-86]. For instance, providing education about the condition, its dangers if not managed properly, negative outcomes of terminating medication and educating about the positive effects of maintaining medication adherence were all seen to greatly improve adherence in hypertension patients, when compared to a control group, 69% vs 36% adherence rate respectively [84, 87].

Later, the 'Theory of Planned Behaviour (TPB)', was designed from an adaptation of the 'Theory of Reasoned Action (TRA)', which proposed that an individual's behavioural intention is a precursor to performing a specific behaviour [84]. Behavioural intention is influenced by two aspects: by an individuals' attitude towards the behaviour in question and a belief that it will lead to either a positive or negative outcome. Secondly, intention is mediated by subjective norms, referring to social pressures and the perceptions of significant others towards the behaviour, and if they deem it to be something that is positive or negative [88]. The TPB has been used to determine behavioural intention and behaviour outcomes in many areas such as, health screening [89], healthy eating [90, 91], medication taking [92] and smoking behaviour [93].

The concept of Perceived Behavioural Control (PBC), which is also a component of the TPB, refers to the perception of the ease or difficulty of performing a particular behaviour, and the belief about whether or not there are necessary opportunities and resources to perform the behaviour [94]. A greater amount of resources and opportunities an individual

has available to them leads to an increased perception of the ease with which the behaviour can be performed, resulting in the PBC being high for that behaviour. The initial TRA deemed intention to be a strong determinant of behaviour, whereas the TPB views intention and perceived behavioural control as two separate factors that could each influence and predict behavioural outcomes independently. PBC is thought to impact on behaviour directly, if PBC is deemed strong enough.

These social-cognitive models have predominantly been used to give insight into complex health-behaviour patterns of adults [84, 86, 95], but have seldom been applied to paediatric health-behaviours. Paediatric health-behaviour has additional complexities due to the influence of caregivers and developing cognitive maturity of the child to understand and rationalise why medication related behaviour is important.

Depending on the stage of cognitive development the child may not be able to understand the benefits or need for treatment. This means that they may not understand the perceived susceptibility or benefit aspect of the HBM, or the attitudes for the TPB. A child's understanding of their condition is influenced by their level of cognitive ability, therefore depending on their developmental stage they may be unable to comprehend the necessity of medication, logically think about risks of non-adherence or appreciate disease complications. The influence of parental attitudes and their health beliefs are highly influential on their child as it determines their motivation to adhere, rather than their child's, especially at a young age [96]. Therefore, the value that a family places on medication and treatment is an important component of understanding paediatric adherence [97].

Health-behaviour models for paediatric use need to account for age, beliefs, psychosocial and mental changes that take place and the shift in responsibility for medication administration, as well as familial influence.

1.8 The role of pharmacists in improving paediatric medication adherence

The NHS Community Pharmacy Contractual Framework currently offers two advanced services to help patients better understand and safely use their medicines, these services are the Medication Use Review (MUR) and New Medicines Service (NMS). The MUR service is for adults already taking medicines(s) for a long-term condition and its purpose is to improve adherence, improve patients understanding of their medication and to identify medication side-effects and propose solutions, if appropriate [98]. In comparison, NMS is designed for adult patients prescribed a medicine to manage a long-term condition for the first time. The purpose of the service is to provide support and promote self-management, improve patient understanding of their medication and condition, address medication side-effects and attempt to manage adherence difficulties early on [99].

Medicine management and addressing patient care needs in paediatric medicine requires significant support and input from healthcare professionals [100, 101]. Common issues that are known to affect paediatric medication adherence are medication side-effects [30], forgetting [102] and medication beliefs [23]. These adherence issues have the potential to be addressed by healthcare professionals. The accessibility and familiarity of pharmacists within the community could offer the potential to help children, adolescents and their families to address issues and concerns.

Existing literature examining the role of pharmacists in paediatric medicine have predominantly focused on hospital pharmacist interventions in improving paediatric medication prescribing, rather than focusing on improving adherence to medication [103, 104]. Hospital-based studies have identified that pharmacists have a positive role in ensuring appropriate prescribing and reducing patient harm by reviewing medication charts, with pharmacist interventions having a positive effect on patient care and treatment outcomes [104, 105].

However, patients and their carers that are not in a hospital setting still require access to additional accessible support systems to discuss treatment, concerns and have a healthcare professional to review regimens. Therefore, there is a gap in the literature which needs to be addressed to assess the contribution that community pharmacists can make in improving paediatric adherence. There is also a need to understand caregivers' opinions of community pharmacists, to determine if community pharmacists would be well-received to deliver advanced paediatric services to children and their families.

1.9 Aims of the research project

The causes of non-adherence, both perceived and experienced have been attributed to a diverse number of barriers. In the current literature, these include the nature of the condition, complexity of treatment regimen, family relationships, caregivers' beliefs about medication and condition and children's cognitive, physical and psychosocial developmental stages. The identification of these barriers has been important in predicting potential adherence outcomes. However, no study has provided a broad appraisal of the barriers to medication adherence over multiple long-term conditions and identified if adherence barriers are condition specific and how they change with age. Understanding the age-association is important in addressing how medication-taking difficulties change over time and can help to develop age appropriate interventions, treatment strategies and support systems.

Furthermore, no study has compared how the experience and perception of barriers to paediatric medication-taking differ between the patient, caregiver and the healthcare professional. Understanding this can help to create an awareness of how adherence barriers change depending on who is asked and the importance of gaining the right perspective to appropriately identify adherence problems and create treatment plans.

The NHS Community Pharmacy Contractual Framework and NICE quality standards provide a set of guidelines to help improve the quality of patient care with long-term conditions [106]. Currently, there is a lack of focus on providing dedicated community pharmacy based services to paediatric patients. The role of community pharmacists in offering advanced paediatric services to address medication issues and improve adherence to families of children taking medication for long-term conditions has not been evaluated. Thus, there is a need to identify the need for such services within community pharmacy and to evaluate the opinion of caregivers towards community pharmacists in relation to paediatric medication.

The aims of this research are three-fold:

I. To appraise the barriers to medication adherence across multiple long-term conditions.

II. To investigate the barriers to medication adherence from the patient, caregiver and healthcare professional perspectives, to better understand the commonalities and difference between the groups.

III. To evaluate the potential role of community pharmacists in providing support to paediatric patients and their caregivers with long-term conditions.

Chapter 2 Paediatric self-reported barriers to medication adherence in long-term illness: a systematic review of literature

The initial chapter identified numerous patient-centred factors, social factors and family factors that affect medication adherence. The chapter also identified that there is a lack of research that addresses adherence barriers from the perspective of children and adolescents and how these change with age. Therefore, this study will aim to review literature to collate the barriers to medication adherence based on child and adolescent self-reports.

2.1 Introduction

The nature of a long-term condition requires regular engagement in multiple health-related behaviours such as, medication adherence, lifestyle modifications and appointment attendance. Research suggests that almost half of the paediatric population with long-term conditions exhibit low adherence to medication taking [1], and even lower adherence to lifestyle modifications. For example, 17% of paediatric patients report adhering to exercise regimens and 22% report adhering to dietary plans in T1DM and T2DM [53]. Non-adherence can negatively affect health, well-being and increase the cost of care [107].

Both experienced and perceived barriers to adherence have been investigated across multiple long-term conditions [1, 108-110] and from differing viewpoints; such as patients [111], caregivers [112, 113] and healthcare professionals [114], with results often showing causes of poor adherence relating to medication beliefs, adverse effects and treatment complexity [29]. However, there is a lack of uniformity and consistency in the aims and ages addressed in the studies to properly understand the adherence barriers to medication-taking in children and adolescents. In particular, there is a poor understanding of the adherence barriers specifically from the viewpoint of children and adolescents relating to

their medication-taking experience and perception. The findings from these studies aid healthcare teams by enabling them to have a better understanding and awareness of factors that potentiate adherence problems. This facilitates their ability to identify patients experiencing problems or likely to experience problems and intervene accordingly to prevent worsening symptoms or poor disease control.

Currently, there are a limited number of systematic reviews that have aimed to collate the barriers to medication adherence in the paediatric population. The existing reviews are based on adolescent experiences, with none based on understanding the experiences of children. [108, 109]. One systematic review addressed barriers to medication adherence in adolescents aged 12 to 20 years old, through a combination of self- and parental-reported barriers to medication adherence. This review found that the common barriers to adherence were the dislike of medicine taste, forgetfulness, belief that the medication was ineffective, denial about having the condition, medication which was complicated or difficult to use, inconvenience of taking medication, interference that medication causes with activities, fear of side-effects, embarrassment, laziness and negativity toward health care providers [108]. Another review collated the self-reported barriers to medication adherence in adolescent's aged 13-19 years [109]. The major themes identified as barriers to adherence were relationships with peers, parents and healthcare professionals, forgetfulness, organisation, medicine complexity, financial costs and the need for independence and normality [109]. Although both reviews are informative in understanding the barriers to adherence and health behaviours, they failed to address the medication-taking experience of children. Children may still require significant input from their caregivers and are known to have less autonomous control, compared to adolescents [115]. However, the experience that children have of medication-taking is still important to understand, as it

forms a complete understanding of paediatric medication-taking behaviour and how it changes from childhood to adolescence and the factors that influence change.

Allowing children and adolescents to report on their own medication-taking behaviour allows for their perception of the impact of their condition on their day-to-day activities to be understood and compared with other age groups, the potential for comparison with other age groups is important to understand the changes that occur over time and how these can be better targeted in practice. Self-reports also enable a better understanding of their concerns and motivations, something which may not be easily or accurately conveyed by others, namely caregivers. As children become older and more independent, parental reports may become less accurate due to increased autonomy, independence and responsibility that their children acquire [116]. Furthermore, there is evidence to suggest that children can complete age-appropriate health questionnaires from as young as five, as well as describe their emotions and perceptions [117, 118].

The aim of this systematic review was to collate the findings from research studies regarding the barriers to medication-taking adherence in a paediatric population from the perspective of children and adolescents, with the following aims:

I. To identify the barriers to medication adherence in paediatric patients aged 5-18 years old with a long-term condition based on literature which uses self-reporting research methods.

II. To identify any condition specific barriers to adherence

2.2. Method

The current systematic review has followed the methodological and format guidance proposed by Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [119], Critical Skills Appraisal Programme (CASP) [120] and Cochrane [121].

2.2.1. Eligibility criteria

The following criteria were used to identify and select all relevant studies for inclusion into the review.

Inclusion:

1. Participants aged between 5 and 18 years.
2. Participants taking medication for a minimum of 6 months for a long-term medical condition.
3. Studies using self-report research methods to identify barriers to medication adherence.
4. Data are solely representative of the child or adolescent – i.e. no mixed data from child and caregiver reports.
5. Publications from January 1995 to January 2016.
6. Studies which published in English.

Exclusion:

7. Intervention studies, systematic reviews and meta-analyses.

2.2.2. Information sources

An extensive search of published literature was carried out using the following electronic databases from January 1995 to January 2016; PubMed, COPAC, Web of Science, CINAHL, PsychINFO, Embase and Proquest hospital collection. The databases were last accessed on 17th November 2016.

2.2.3. Search terms

The general search terms utilised when searching each database were variations of the following: (*adherence OR compliance) AND (child OR adolescent OR paediatric OR pediatric OR children) AND (chronic illness OR condition OR long-term) AND barriers AND medication.* The search terms were adjusted to account for American and British spelling variations and the search strategy used both MeSH and non-MeSH terms.

2.2.4. Study selection

Abstracts identified through the database searches and deemed relevant were read for applicability. Relevant studies were obtained and examined against the inclusion/exclusion criteria.

2.2.5. Data collection

All studies which matched the inclusion/exclusion criteria had the following data extracted and tabulated (Table 2.2): author(s), sample characteristics (age range and average age of sample, clinical condition and sample size), type of self-report method used, study design, barriers to medication adherence – qualitative studies had findings stated descriptively and as percentages for quantitative studies.

2.3. Critical appraisal

A quality appraisal was conducted to assess whether the studies included in the review had addressed the research question(s) using rigorous and reliable research methods. A quality checklist used was based on the guidance provided by CASP [120] and Cochrane [121]. The quality assessment criteria focused on four main elements: validity, generalisability of the data, reliability of the research process and objectivity, the criteria consisted on a 15-point checklist (Appendix A) by which each study was assessed. Studies which scored 8 points or more (56%) were deemed of high quality [122]. Lower quality studies were not excluded from the review as the data produced can be insightful, despite the lack of clarity of the methods used [121].

Eight of the eighteen studies included in the review used a qualitative methodological design to identify barriers to medication adherence, carrying-out either focus groups or semi-structured interviews.

Six qualitative [123-128] and five quantitative studies [129-133] recruited participants through condition-based clinics or during scheduled follow-up appointments. Although a practical method of recruitment for the target audience of the research, there is increased likelihood that those children and caregivers that often miss appointments or never attend will be poorly represented, further reducing the generalisability of data and their barriers to adherence not well understood. One qualitative study recruited patients from a hospital emergency department, therefore potentially skewing the sample towards children who are poorly managing the condition and low adherers to medication [134].

Another qualitative study recruited participants through mass invitations from community pharmacies, therefore encouraging a wider demographic for participation [135]. Similarly, a quantitative study mailed all patients registered at an inflammatory bowel disease (IBD)

clinic, therefore targeting even those children and families that may usually miss their follow-up appointments [136].

Four quantitative studies used participants who had previously been involved in similar research studies, therefore introducing bias into the sample as they could potentially be aware of the aims and nature of the research [24, 25, 137, 138].

Four studies included caregivers into the studies [24, 126-128]. Three of these studies interviewed caregivers and children separately and one conducted a combined semi-structured interview [127]. Although, the researcher aimed for this to encourage discussion between caregiver and child, the limitations of such a method can potentially lead to children deferring to their parents for answers and opinions. Furthermore, there may be views or experiences children may not wish to share in front of their caregiver, therefore limiting the openness and truthfulness of responses.

One study utilised two types of focus group methods; face-to-face and online. The online focus group offered greater anonymity, therefore allowing participants to be more open about their adherence experience and difficulties. However, there was less interaction between participants in the online focus group, as participants did not have to be online at the same time, leading to delayed reaction and response times to the posted comments. In comparison, the traditional face-to-face focus group was more interactive and provided an opportunity for participants to engage with one another in a controlled setting [135]. The use of a face-to-face and online focus group was an effective way to gather information from both introvert and extrovert participants.

The sample size of the eight qualitative studies ranged from 2 to 40 participants. The small sample sizes limits generalisability of the data to larger populations. However, two studies achieved data saturation, thereby indicating that sufficient sampling had taken place and the data obtained were sufficient for the research question under investigation as no new

data was being collected [127, 135]. The size of the quantitative studies ranged from 38 to 232 participants. None of the studies performed sample size calculations to determine what the optimal sample size should be for the study. A small sample size limits the generalisability of the results and undermines the true effect of statistically significant findings.

Generalisability is limited in nine studies due to a lack of ethnic diversity. Five studies mainly consisted of a white population [123, 125, 130, 131, 138], two studies had mainly a black demographic [126, 137] and two with a largely Caucasian Dutch demographic [25, 135]. Additionally, the socioeconomic status of one study consisted of mainly middle and upper-middle class families [131], therefore the diversity of the population was poorly represented.

All qualitative studies conducted a thematic analysis of data, which was coded and emerging themes identified.

Despite recruitment bias, sample size and demographic limitations, the overarching themes identified as barriers to medication adherence were similar across the studies, these included forgetting, side-effects of medication, perceived lack of benefit or need for medication and organisation problems.

2.4. Results

2.4.1. Study selection

An in-depth search of 7 databases produced 4527 results of published studies. Where possible MeSH terms were used to refine the searches, and exclude publication types (systematic reviews and meta-analysis), age groups and clinical conditions (acute conditions). From these results, 445 potentially relevant studies were selected for abstract analysis; any that were duplicated or that did not meet the inclusion criteria were eliminated. The full text of 111 studies was assessed and 93 were discounted, each for a specific reason in accordance with the inclusion criteria, resulting in 18 studies left for inclusion, Figure 2.1.

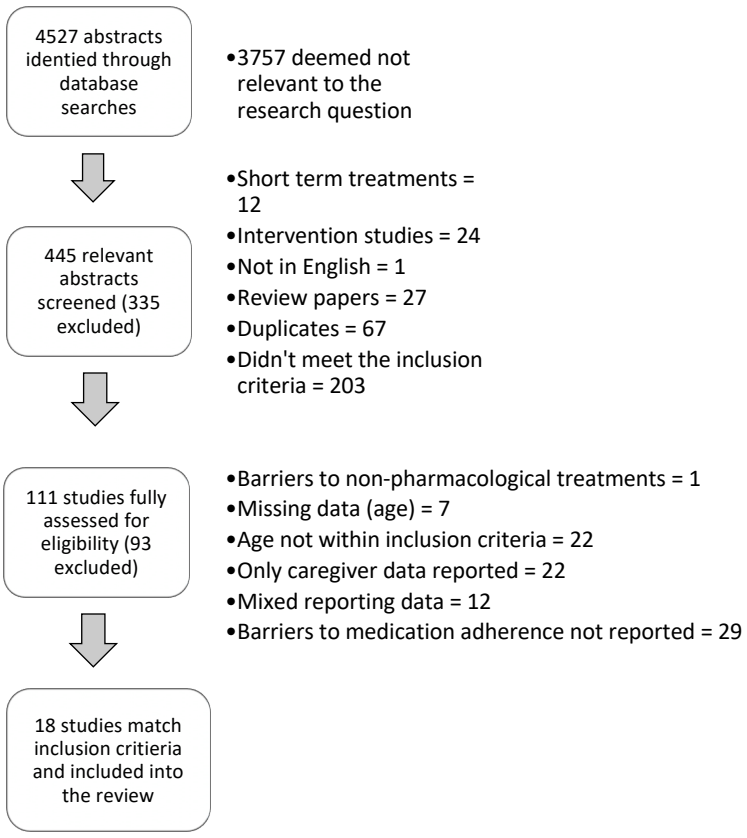

Figure 2. 1 Flow diagram to show the screening process and identification of relevant studies for inclusion

2.4.2. Sample and participant characteristics

The total number of participants included in the review was 1287, ranging across five conditions. The majority of studies were representative of three conditions: asthma, Human Immunodeficiency Virus (HIV) and inflammatory bowel disease (IBD), with one study each representing sickle cell disease (SCD) and post-organ transplant (heart) (Table 2.1).

Table 2. 1 Sample and participant characteristics

Condition	Respiratory conditions	HIV	Inflammatory bowel disease	Post-organ transplant	Sickle cell disease	Total
Total number of studies	7	5	4	1	1	18
Total number of participants in all studies	576	402	278	2	31	1289
Participants in questionnaire studies	384	285	183	-	31	883
Participants in focus group and semi-structured interview studies	192	117	95	2	-	406
Age range	6-18	8-18	9-18	16-18	13-18	

2.4.3. Rates of adherence

Ten of the 18 studies measured the rate of medication adherence. The overall adherence rate ranged from 24% to 80%.

The 'adherence rate' referred to in the studies has been defined as the percentage of doses taken by the patient over a specified time frame, divided by the prescribed doses, multiplied by 100, to achieve a percentage rate of medication adherence. Apart from one study that measured adherence on a Likert scale ranging from zero to ten, with ten representing all doses taken as prescribed.

The specified time over which the adherence rate has been calculated varies in each study. A three-day time frame was used in two studies [129, 137], as was a retrospective seven-

day account in two further studies [133, 138]. Three studies used a retrospective one month account [24, 123, 131]. A single study assessed daily use of medication over a one year period [25]. A further two studies did not include the time frame used to calculate the adherence rate within the methodology [132, 136].

The main method of assessing adherence was using self-report questionnaires, with only one study using an electronic measure [123]; an electronic monitor was used to assess adherence to steroid-containing inhalers. This recorded the date and time of an apparent inhalation.

Table 2. 2 Study characteristics

Author	Age range (mean)	Clinical condition	Sample size	Adherence measure	Patient related factor to non-adherence	Adherence rate	Percentage of participants citing each adherence barrier (%)	Significant findings	Quality rating
[136] Kitney, L 2009	9-18 (13.2)	Inflammatory bowel disease	119	Self-report questionnaire	-forgot -too busy -feel sick with prescribed vitamins -enemas are uncomfortable -swallowing difficulty -feeling better -too much medication	80%	56.3% 55.6% 24% 18.2% 17.8% 16.0% 13.4%	Nonadherence greater in older teens, 14.6 vs 13 years P=0.04 Nonadherence is greater in those with a longer disease duration, 5 vs 3.1yrs P=0.004	High
[138] Gray, W. 2012	13-17 (15.5)	Inflammatory bowel disease	79	Semi-structured individual interview	-forgot -wasn't home -regimen interferes with activities -ran out of medication -hate the taste -not feeling well -refused to take -don't think the medication is necessary -hard to swallow -side-effects -fell asleep/sleeping -tired -too busy -pharmacy ran out of medication -didn't get repeat prescription -too lazy -lost medication	8.63 out of 10	84.8% 43.0% 34.2% 15.3% 12.7% 12.7% 11.4% 10.1% 7.6% 6.4% 3.9% 3.9% 2.6% 1.3% 1.3% 1.3% 1.3%		High
[131] Greenley, R. N 2010	11-18 (15.1)	Inflammatory bowel disease	64	Self-report questionnaire	-lack of time -feeling well -belief that medication is ineffective -side-effects -pharmacy barriers -insurance barriers	65%	33% 16% 14% 14% 8% 5%	Significantly fewer barriers experienced on monotherapy vs multi-therapy P=0.03 Significant less barriers when daily frequency of medication ≤1 vs ≥ 1 P=0.01	High
[127] Hommel, K. A 2011	13-17 (15.75)	Inflammatory bowel disease	16	Semi-structured individual interview	-general forgetfulness and forgetting due to activities -Swallowing difficulties -too many pills cause routine difficulties and reduced motivation -parental nagging -immediate vs. long term perceived benefits -embarrassed in front of others	Not recorded			High

Table 2.2 (Continued)

Author	Age range (mean)	Clinical condition	Sample size	Adherence measure	Patient-related factor to non-adherence	Adherence rate	Percentage of participants citing each adherence barrier (%)	Significant findings	Quality rating
[129] Khan, M 2009	10-18 (9.9)	HIV	127	self-reported adherence via a 3-day recall questionnaire every 3 months	-forgetting -pharmacy issues -difficulties in taking the drug -run out of medication -other	30%	11% 9% 7% 6% 9%	Adolescents (>13) were significantly less likely to reach undetectable viral loads then children under 13 years due to lower adherence rates (P=0.025)	High
[137] Chandwani, S 2012	13-18	HIV	108	Face-to-face interviews	-forgot -away from home -fell asleep -busy -a change in daily routine - “others don’t notice if I don’t take my medication” -too many pills -to avoid side-effects -felt good -ran out of pills -was sick -depressed -trouble with food recommendations -drunk -drug toxicity	72% for ≤16 years and 59% for ≥ 17 years old	**≤16 yrs** / **≥17 yrs** 52.7% / 53.8% 51% / 44.2% 50.9% / 42.3% 43.6% / 50% 38.2% / 26.9% 23.6% / 32.7% 23.6% / 32.7% 16.4% / 33.3% 23.6% / 25% 25.5% / 21.2% 20% / 25% 18.2% / 21.2% 16.4% / 19.2% 1.8% / 13.5% 3.6% / 3.8%		High
[24] Buchanan, A. L 2012	8-18 (12.8)	HIV	120	Self-report questionnaire	-felt good -can’t keep medication down -forgot -to avoid side-effects -refusal to take medication -couldn’t get medication -did not refill prescription -schedule interference -away -change in daily routine -slept through dose time -too much medication -felt sick -multiple caregivers -busy with other things -toxicity -issues to take as directed -depressed -other children will see	51%	Percentage for each barrier not reported in study	Younger children aged 8-12 years showed significant agreement on barrier ‘busy with other things’ (P=0.05) when compared to 12-18 year olds. Older children aged 12-18 years reported ‘forgetting’ more often than younger children aged 8-12 years old. (P=0.04)	High

Table 2.2 (Continued)

Author	Age range (mean)	Clinical condition	Sample size	Adherence measure	Patient-related factor to non-adherence	Adherence rate	Percentage of participants citing each adherence barrier (%)	Significant findings	Quality rating
[139] Johnston Roberts, K. 2005	7-12 (9.5)	HIV	9	In-depth, face-to-face interviews	-busy with daily routine or busy engaged in fun activities -forgetting -fall asleep before evening dose or slept through morning dose -nausea -vomiting -diarrhoea -bad taste -tablet is too big -hard to swallow -missed doses when out in public or amongst peers and family to keep HIV/AIDS status a secret -embarrassment "medication is a daily reminder of having HIV/AIDS and just want to feel 'normal' so feel low in mood and don't want to do anything"	Not recorded			High
[133] Estripeaut, D 2016	12-18	HIV	38	Questionnaire	-Forgetting	32%	70%		Low
[124] Edgecombe, K 2010	11-18	Uncontrolled severe asthma	22	In-depth semi structured interview	-Needing parental reminders -Forgetfulness -Perceived lack of effect of medication -Cannot be bothered -Conflict with other priorities -Adverse effects from medication	Not recorded	Percentage for each barrier not reported in study		High
[135] Koster, S. E 2015	12-16	Asthma	21	Focus groups	-Forgetting; in a hurry to get to school, forgot more during weekends and school holidays, busy with other things. -difficulty in taking medication outside of home -Doubting necessity of medication	Not recorded	Percentage for each barrier not reported in study		High

Table 2.2 (Continued)

Author	Age range (mean)	Clinical condition	Sample size	Adherence measure	Patient-related factor to non-adherence	Adherence rate	Percentage of participants citing each adherence barrier (%)	Significant findings	Quality rating
[132] Logan, D 2003	11-18	Asthma	152	Self-report questionnaire	-medication causes changes to my body that I don't like -implication of the regimen on daily life -side-effects -medication causes physical pain and discomfort -difficult to understand instructions -can't remember everything to manage the illness -confused if regimen changes -organisation difficulty -anxiety/nerves -planning difficulty -time consuming to manage regimen -doctors are too busy to talk about illness and regimen -refusal to give up time with peers to manage regimen -don't trust Dr/nurse -want to forget about illness -get treated like a child by the Dr -don't want friends to know - "none of my friends have to deal with this, so why do I" -"my family doesn't understand what it's like to live with my illness	27%	Percentage for each barrier not reported in study	Older teens significantly reported more barriers to adherence when compared to younger participants.	High
[123] Naimi, D. R 2009	15-18 (16)	Asthma	40	Observational cohort study Mixed method: Qualitative: 2 semi-structured face to face interviews conducted 1 month apart and analysed for themes. Quantitative: electronic monitoring of inhaler use	-forgot due to difficulty in organising time and setting priorities -bad taste -too much medication to take -felt well so didn't take dose -no symptoms, so not used -not efficacious -lost inhaler -ambivalent about results -away from home and forgotten medication -medication doesn't help -felt medication is not necessary -embarrassed to use medication in front of friends -fear of addiction to medication -bad effect on appearance (acne/height) -conflict at home	43%	55% 45% 33% 32.5% 20% 20% 22.5% 18% 17.5% 15% 15% 7.5% 7.5% 5% 2.5%	Younger participants had better adherence than older participants P=0.01	High

Table 2.2 (Continued)

Author	Age range (mean)	Clinical condition	Sample size	Adherence measure	Patient-related factor to non-adherence	Adherence rate	Percentage of participants citing each adherence barrier (%)	Significant findings	Quality rating
[25] van Dellen, Q. M 2008	7-17	Asthma	232	Mixed methodology; face-to-face interviews and self-report questionnaires	-annoying to take medication -ICS makes me fat -ICS makes me short for my age -lack of self-efficacy	46%	Percentage for each barrier not reported in study	children with well controlled asthma show significantly poor adherence than children with not well controlled asthma (P<0.001) children with high self-efficacy showed significantly better adherence than children with low self-efficacy (P<0.001) children that received positive stimulation from parents to use ICS show significantly better adherence than those children that received less positive stimulation (P<0.001)	High
[134] Penza-Clyve, S. M 2004	9-15 (11)	Asthma	36	Focus groups Results coded into categories and subcategories	-just don't want to take medication -engaged in another activity that they did not want to interrupt -parental nagging -too busy -too tired -no asthma symptoms -forget -away from home -forgot if already taken the dose -embarrassed to use inhaler in front of peers -feel interrogated by peers to explain their medication	Not recorded	Percentage for each barrier not reported in study		High

Table 2.2 (Continued)

Author	Age range (mean)	Clinical condition	Sample size	Adherence measure	Patient-related factor to non-adherence	Adherence rate	Percentage of participants citing each adherence barrier (%)	Significant findings	Quality rating
[130] Modi, A. 2006	6-13 CF (10.1) Asthma (9.7)	Cystic fibrosis & Asthma	73	Mixed methodology: -Face to face interviews -daily phone diary over 2 days -self-report questionnaire -electronic monitoring over 3 months	Cystic Fibrosis: -oppositional behaviours to nebuliser -forgetting short term MDI -time management difficulties for antibiotics -difficulty swallowing antibiotics -forgetting antibiotics -bad taste of short tern MDI Asthma: -forgetting ICS -forgetting short term MDI -time management for ICS -oppositional behaviours to ICS -bad taste of short term MDI	Not recorded	 40% 27% 25% 25% 25% 18% 68% 42% 22% 22% 17%		High
[126] Modi, A. C 2009	13-18	Sickle cell	31	Self-report questionnaire	Pain management (n=25) -forgot or lost -taste or side-effects -desire to be normal Oral antibiotics (n=6) -taste or side-effects -difficulty swallowing -desire to be normal -medication efficacy Hydroxyurea (n=2) -Forgetting or lost Transfusion (n=9) -treatment pain or discomfort - side-effects -multiple medications Vitamins and minerals supplements (n=13) -forgotten or lost -taste aversion or side-effects Chelation therapy (n=5) -treatment pain or discomfort -forgetting or lost Hydration treatment (n=13) -taste aversion or side-effects -time management	Not recorded	 58% 38% 25% 50% 33% 33% 33% 100% 33% 22% 22% 58% 33% 50% 43% 31% 23%		High

Table 2.2 (Continued)

Author	Age range (mean)	Clinical condition	Sample size	Adherence measure	Patient-related factor to non-adherence	Adherence rate	Percentage of participants citing each adherence barrier (%)	Significant findings	Quality rating
[125] McAllister, S. 2006	12-18	Post-heart transplant	2	Mixed methodology cross sectional design. Quantitative: self-report questionnaire. Qualitative: interview with open ended questions.	-felt well/felt good/felt healthy -medication taking takes too much daily scheduling -difficulty in swallowing -presence of side-effects -negative cosmetic and physiological changes -stress/depression/psychological issues -medication has a negative impact on social events -don't want to take medication in front of people	Not recorded	Percentage for each barrier not reported in study due to small sample size		High

2.4.4. Demographics

Age was reported as a significant predictor to adherence in two studies [123, 136], commonly finding that increasing age was related to lower adherence. In an IBD study, non-adherent adolescents were observed to be significantly older than adherent adolescents, mean age of 14.6 vs. 13.0 years old (P=0.04) [136]. Similarly, a study of adolescents with asthma found that older participants had lower adherence than younger participants, P=0.01 [123]. Age was also seen to be predictive of determining viral loads; adolescents aged over 13 years with HIV had higher viral loads due to lower rates of adherence, when compared to those aged under 13 years [129]. Additionally, duration of condition was significantly associated with lower adherence, with a mean disease duration of 5.0 vs. 3.1 years showing higher rates of non-adherence (p=0.004) [136].

2.4.5. Self-reported barriers to medication adherence

The self-reported barriers presented below fall into seven categories.

2.4.5.1. Forgetting

Forgetting to take medication was the most commonly reported cause for non-adherence across all studies and conditions.

In IBD studies, adolescents who reported forgetting to take medication also stated this as the primary cause for poorly managing their treatment. Forgetting was reported for various reasons such as changes between home and school routines, as well as taking part in extracurricular activities. Participation in extracurricular activities was reported to make adherence difficult, especially to medication regimens that require multiple daily dosing. This was reportedly due to difficulties in prioritising daily tasks and medication related tasks [127].

This is similar to findings from the asthma studies, which found that forgetting resulted from poor time management, it was also the most commonly reported reason for adherence problems [134]. Additionally, non-intentional forgetting resulted from the absence of experiencing any active asthma symptoms leading to forgetfulness to take preventer asthma medication [123, 134, 136].

HIV studies also found that forgetting to take medication was the most commonly reported barrier in all five studies [129, 133, 137, 140], with one study showing that forgetting to take medication was an issue for up to 70% of adolescents with HIV [133]. Furthermore, forgetting was reported to be a significant factor to non-adherence in those aged 12-18 years, who reported forgetting more often than children aged 8-12 years old (P=0.04) [24]. The same study also recognised that children who shared responsibility with their caregiver reported 'forgetting' and 'busy with other things' significantly more often than children whose caregiver was fully responsible for their medication, P<0.001 and P=0.05 respectively [24].

2.4.5.2. Stigma

The negative stigma associated with HIV led to some children feeling that their antiviral medication needed to be concealed in public and from their peers, resulting in medication-taking avoidance behaviours, this is in addition to these children also feeling embarrassed by their HIV condition [128]. Being embarrassed to take medication in front of peers or in public was also an issue expressed by 7.5% of adolescents with asthma [123, 132, 134] and adolescents with IBD [127]. Stigma was not reported in other conditions in this review.

2.4.5.3. Medication beliefs

The discontinuation of medication due to doubts regarding medication effectiveness and a belief that medication is not necessary was reported in four studies as a barrier to medication adherence by 10% to 14% of participants in two IBD studies [131, 138]. This was also highlighted in two asthma studies; with the perceived lack of medication effectiveness as a reason to not take medication as prescribed [123, 124].

2.4.5.4. Side-effects

The experience of medication side-effects was a common theme across all conditions. Two studies reported between 6.4% – 14% of adolescents with IBD not taking medication because of side-effects [131, 138]. Four HIV studies included in the review reported that the avoidance of side-effects was the cause for medication non-adherence [24, 128, 133, 137]. This is similar to 38% of adolescents with sickle cell disease reporting side-effects as a cause for non-adherence [126]. Similarly, asthma medication can cause side-effects such as acne, height restriction and weight changes and are reported causes of non-adherence in three asthma studies [123, 124, 132].

2.4.5.5. Taste and formulation issues

The perceived poor taste of medication and difficulties in swallowing tablets and/or capsules was an issue in four studies [125-128]. Non-adherence ranged from 7% to 18% in IBD studies [136, 138], 17% to 45% non-adherence in asthma studies [123, 130] and between 30 to 50% non-adherence due to taste aversion and swallowing problems for oral antibiotics [126].

2.4.5.6. The role of family and healthcare professionals

The experience of children and adolescents relating to the input and support of caregivers is mixed. Parental nagging was a barrier towards medication taking mentioned in a focus group study of children and adolescents aged 9 to 15 years old with asthma [134] and in a semi-structured interview of adolescents aged 13 to 17 with IBD. Nagging was deemed to have a negative influence to medication taking [127]. Conversely, an interview study involving adolescents with uncontrolled asthma found a lack of parental reminders for medication taking as a barrier to adherence [124]. The involvement of multiple-caregivers was also deemed to be a negative factor [24].

Parental confidence in the medication and course of treatment, plus encouragement for the use of inhaled corticosteroid (ICS) inhalers for asthma was a significant predictor to whether or not their child used their ICS medication [25].

Furthermore, in one asthma study the feeling of distrust towards their doctor was related to some adolescents not adhering to their medication. They also felt treated as a child and that the doctors were too busy to talk about their medication or condition [132].

2.4.5.7. Lifestyle impact

Medication regimens causing time constraints and interfering with daily life was commonly reported across all IBD studies, ranging from 33% to 56% [127, 131, 136, 138].

Young children aged 8 to 12 years old with HIV showed significant agreement on the barrier ‘busy with other things’ as a reason for poor adherence when compared to adolescents aged 12-18 years old, (P=0.05) [137]. A HIV study based on an in-depth interview with children aged 7 to 12 years old found several themes that impacted medication adherence such as, being busy, engaged in activities or sleeping through morning doses [128]. This is similar to asthma studies, which found that a lack of

motivation was a barrier to adherence, often due to being busy engaged in other activities and not wanting to stop tasks to take medication or because medication times conflicted with activities and daily tasks [124, 130, 132, 134, 135]. Annoyance of having to take medication for asthma and feeling burdened by a their medication regimen was also reported [134].

2.5. Discussion

The findings of this review have identified factors that contribute to low rates of adherence in children and adolescents based on self-report of their own medication-taking behaviour. The most common barriers to medication non-adherence were forgetfulness, beliefs about medication, side-effects, the role of family and HCPs and the impact of medication taking on lifestyle. These barriers were consistent across different conditions and age ranges. Many findings of this review have been previously identified as factors that have a negative impact on adherence. However, this review has identified adherence barriers by synthesising findings from studies with children and adolescents with long-term conditions and using self-reports. Previous reviews have predominantly focused on adolescents, whereas this review is inclusive of a wider age range, therefore extending the understanding of medication barriers to children.

The most common reason reported for non-adherence was forgetting. Unintentional non-adherence in paediatric patients that experience organisational and time management difficulties has been linked to poor executive functioning [43]. Executive functioning is the term used to encompass cognitive skills such as organisation, planning, problem solving, memory and rationalisation [141]. Cognitive skills are expected to improve with age, leading to an expectation that there would be a reduced presentation of barriers linked to forgetfulness and regimen management difficulties such as planning and problem solving. However, this review has shown that 'forgetting' was a common barrier to adherence across all age ranges but more common in older children. Significant results identified that 13-18 year olds reported 'forgetting' as a barrier more often than 8-12 year olds (49% v 29%) [24].

Forgetfulness has multiple causes which can often be interconnected. As children reach adolescence their social habits and interests begin to change, leading them to spend less time at home and increasing time spent engaged in social or independent activities [28].

When daily planning fails to include medication taking, this can be a potential cause for increased forgetfulness as no provision has been made for taking medication when away from home. Furthermore, being 'busy' was negatively associated with adherence and occasionally expressed as a reason why forgetfulness occurred. Being 'busy' also includes time spent involved in activities and being away from home. Tiredness, resulting from daily activities, or general medication-taking fatigue, can lead to a lack of motivation to take medication [28].

The perceived lack of medication benefit can be described as an intentional form of non-adherence, because if it is thought that the medicine does not work, it will not be taken [30]. A perceived lack of efficacy requires a review of the way a patient takes their medication, to ensure it is taken correctly, to provide the desired therapeutic effect. There is also a need to improve patient knowledge of the medication and treatment. This is to improve the patients understanding of the intended outcomes, purpose of the treatment and to manage patient expectations [30]. In addition, the patient may have a poor clinical response to the medication and would need to discuss this with the prescriber to decide an alternative treatment choice [30]. However, in patients that are well-controlled or experiencing minimal symptoms, medication may not be providing added benefit or visible and quantifiable change. In such cases, medication non-adherence may not be intentional. Instead, forgetfulness due to the absence of a perceived need may result in less importance being placed on medication-taking.

The experience of medication side-effects was expressed across conditions. It can often be a leading cause of intentional non-adherence due the additional negative burden that the

presence of side-effects places on an individual [29]. Medication side-effects can prevent the patient from achieving either symptomatic relief or maintaining prophylaxis [142]. Furthermore, side-effects to medication reduces belief in the treatment and increases distrust of the healthcare team [143].

The taste of medication was a common barrier to adherence and was often reported by children and adolescents in this review. Approximately 50% of adolescents with sickle cell disease expressed that the taste of oral antibiotics was a barrier to adherence [126]. Past research has shown strong evidence for the relationship between unpleasant tasting oral formulations and medication adherence in children, especially towards oral antibiotics [144]. However, with an absence of formulations specifically designed for children's palatability and ease of administration, prescribers are limited in their prescribing choices [145]. Caregivers, therefore may be forced to administer medication in a manner which is unintended by the manufacturers (unlicensed), such as crushing tablets or mixing medication with food or drink [146].

Conditions such as HIV are unduly subject to the negative effects of stigma, for this reason families, children and adolescents may be inclined to hide their status and/or medication taking in front of others due to the fear of being seen and asked about their medication [147, 148] as was seen in two of the HIV studies [24, 128]. Furthermore, research has identified that children with asthma view themselves as being different due to their asthma condition, leading to them carrying out normalisation strategies so they can integrate with their peer groups [149]. Therefore, the use of asthma medication leads to some children and adolescents feeling a sense of embarrassment, especially when they are required to use their asthma medication in front of their peers, as it is deemed as an activity which is not normal occurring within their peer groups [123, 132, 134]. For this reason, interventions requiring children to bring a friend to jointly receive information regarding medication and

the condition could be a way to make a child feel more comfortable, confident and empowered to take their medication [150].

Other issues such as being busy, lacking motivation and the interference of medication-taking with daily life were all negatively associated to adherence in studies. Existing research supports this as studies show a negative association between children and adolescents with long-term conditions and quality of life [151, 152]. There is unwillingness to prioritise and plan medication-related tasks around other activities and commitments.

In this review, one asthma study identified that children who reported receiving positive reinforcement from their parents to use their ICS inhaler had significantly better adherence than parents who did not reinforce their child to use their inhaler [25]. Extensive research has shown that parental concerns are inversely associated to medication adherence, such that, as concerns are increased, adherence to medication is decreased [51, 52, 153]. Conversely, a higher perceived parental belief regarding the necessity of medication is associated to treatment adherence [154]. Studies have also indicated that adolescents form their own opinions about the concerns and need for medication [23]. This may increase the number of responses in studies which relate to the concerns about medication efficacy [123, 124, 131, 138].

Research also suggests that a positive and collaborative relationship between the patient, their families and healthcare provider enables families and their child to better manage self-care tasks [155]. Understanding patient preference, their lifestyle and problem solving medication- or condition-related issues creates trust and a platform on which a long-term condition can be effectively managed [156, 157]. Furthermore, offering children and caregivers assistance through condition-specific education programmes [158] and support

networks [158, 159], aims to improve adherence by increasing self-care resources and knowledge to manage their condition.

In this review, non-adherence was also caused by distrust and a poor patient-prescriber relationship [132]. Replacing the un-cooperative nature of regimen planning with a more supportive and collaborative method, has been shown to increase the level of support felt, leading to improved adherence [78]. This suggests that in order to improve how adolescents feel about their healthcare team, more time needs to be invested in ensuring they are confident with their treatment and feel as though they will be supported by their healthcare team. This can be done by improving communication and creating mutually agreed care-plans between the patient and their healthcare teams.

2.5.1. Limitations

The studies reviewed in this systematic review incorporated both qualitative and quantitative studies, varying in condition, severity, regimen and age range to provide a broad representation of medication adherence barriers in children and adolescents however, several limitations exist.

Firstly, the barriers identified are similar across studies but the representation of some barriers are overly represented due to the amount of quantitative studies often asking the same range of questions, such as those that examine the issues of side-effects, formulation problems and issues surrounding regimen routine and organisation. In contrast, qualitative studies can reveal in-depth personal issues affecting the patient, allowing for themes to emerge that are not seen in quantitative studies, but are of high importance and significance to understanding medication-taking behaviour. Thus, important factors relating to adherence are under-represented and overlooked. For example, conflict at home [123] and parental nagging [127] addressed in semi-structured interviews as barriers to

adherence, neither of which were highlighted in quantitative studies and are important issues which would warrant further understanding about their impact on the child and on adherence. The negative psychological impact of having to take anti-viral medication for HIV in children was discussed in a face-to-face interview [128] and can help HCPs provide better, tailored care, including mental-health support [158] to young patients living with long-term conditions. Furthermore, the severity, treatment regimen and range of problems experienced can vary between each patient, even within the same condition; meaning that different factors will be of varying importance to each patient due to their subjective nature. However, this review has collated and provided an overview of all the self-reported barriers to adherence, rather than just providing a summary of the most common barriers. Therefore, this provides a broader understanding of adherence barriers and avoids excluding under-represented, but significant barriers.

Themes derived from qualitative research are dependent on the researcher's interpretation, data analysis process and how the categories and subcategories are chosen. The lack of uniformity in data analysis across qualitative studies can make the comparison of themes and subcategories difficult [160].

Self-report methods tend to suffer from some inherent disadvantages such as desirability issues, where participants want to provide answers which portray them in a positive light or answer in a way in which they believe the researchers are wanting them to [161, 162]. In comparison, the advantages offered by self-reports is the quantifiable nature of the data and in-depth collection of data relating to experience, knowledge, emotions and opinions from open-ended questions in qualitative studies, as well as understanding the relationships between multiple variables for a specific cohort of participants. They also offer the potential to be easily revised to offer applicability to people of differing ages, literacy levels and conditions.

2.5.2. Further research directions

As a lack of support was expressed by several studies as a dominant cause of being a barrier to adherence, the role of community based services should be evaluated to understand the active role they have in supporting paediatric patients with long-term conditions. Furthermore, the experience of healthcare providers in encountering adherence barriers is important, as the information that a patient and carer may divulge to their healthcare provider may not be an accurate account of actual adherence, therefore the need to understand the variation and commonalities in the expression of barriers between child, caregiver and healthcare provider is needed. This will enable healthcare providers to better understand the adherence problems and strategically formulate solutions to improve adherence.

This review has identified some important themes affecting adherence based on self-reports of children and adolescent regarding their own medication taking behaviours in long-term conditions. As this research seeks to appraise the multiple factors affecting adherence, the views of caregivers and healthcare professionals are valuable in achieving this. Caregivers primarily manage and administer medication to their child until they begin to assume responsibility for these tasks. A caregivers insight would permit a better understanding of what problems they experience. The comparison between caregiver and child can identify how problems are differently experienced, prioritised and the prevalence of barriers between the groups. Similarly, understanding a healthcare professional's experience of adherence barriers could be limited to what the caregivers or child tells them, which may be different from the true nature of the problem. Therefore, by understanding what is seen in practice could guide our understanding of how caregivers and patients discuss their problems in a clinical setting.

2.6. Conclusion

The barriers to adherence are uniform across conditions, except for ‘stigma’ which was a specific barrier identified for children and adolescents with HIV. This review highlighted the need for better relationships between patients, families and healthcare providers to provide safe platforms in which patients feel able to discuss their treatments, concerns and overcome the inherent often associated with medication-taking.

2.7. Summary of findings

Eighteen studies across five conditions had an adherence rate range from 24% to 80%. The most commonly reported barriers to medication non-adherence were forgetfulness, beliefs about medication, side-effects, the role of family and HCPs in providing support and the impact of medication taking on lifestyle.

Chapter 3 Patient-barriers to adherence in current clinical practice: a consensus study using healthcare professionals

The systematic review of literature reported in Chapter 2 identified several common barriers to medication adherence based on child and adolescent self-reports. This chapter will determine the extent to which paediatric adherence barriers are seen in current clinical practice by healthcare professionals involved in paediatric care.

3.1 Introduction

Patient-identified adherence barriers are numerous [29, 107] and associated with intrinsic factors such as attitudes, health beliefs, self-efficacy and extrinsic factors, for example, familial and healthcare support systems [163]. Collation of these barriers can enable healthcare professionals to better understand the patterns of non-adherence and promote better and timely identification, discussion and resolution with the patient and their families [164]. In the absence of open and honest discussions between the patient, families and their healthcare team there is a limit to how successfully adherence barriers can be identified and overcome. It is known that patients have reservations in admitting their non-adherence or difficulties with adherence to their prescriber, as they feel it is not something which they are able to address in consultations or because of fear of judgement [68]. This can be due to prescribers not initiating a conversation focusing on adherence, either due to lack of time in consultations or due to poor communication [165, 166].

Prescribers tend to define treatment problems in terms of diagnosis, achieving treatment outcomes and if outcomes are not being achieved then to identify, understand and address these causes. Whereas the patient is more likely to view problems in the context of symptoms, emotional distress, concerns and difficulties in carrying out health-related behaviours [157]. Currently, there is an absence of research which helps to understand the

extent to which healthcare professionals observe barriers to paediatric medication adherence. A better understanding of observable barriers in current practice can help determine which barriers can be more easily addressed because of better awareness and which barriers are equally important, but not observable and require further probing by the healthcare teams to determine if they could be problematic to medication adherence. Furthermore, this study will enable a comparison to be made between the barriers which healthcare professionals observe in practice and those which are commonly reported barriers to adherence by children and adolescents in self-report studies (Chapter 2).

As the systematic review identified that a lack of support from healthcare professionals was one of the causes for poor adherence, understanding the healthcare professionals experience of adherence barriers in current practice will help to identify why this is the case. It can also provide a better awareness of the disparities in experience between the patient and the healthcare professional. Little is known about how well paediatric self-reported adherence barriers translate in practice and if healthcare professionals see the same barriers to adherence as are described by patients in their self-reports. If healthcare professionals do not understand barriers to adherence, this could impact on the treatment choices made and reduce the potential to resolve adherence problems due to the lack of awareness.

The involvement of healthcare professionals in research has been shown to provide positive contributions to clinical research, leading to changes to current practice being implemented to improve patient care. This has been achieved through evaluating services and clinical practice [167, 168], in the implementation of interventions [169] and in understanding patient experience of healthcare services and healthcare staff to improve patient experience [170, 171].

Delphi consensus studies are an effective method to establish an agreement of opinions on a defined topic in situations where there are inconsistencies and contradictions between results of published literature [172] or, when large amounts of information have been collected by multiple research methods [173]. The establishment of agreement – how much an individual agrees to a statement and consensus – the level of agreement participants have with each other is achieved by recruiting participants within a chosen field of expertise to form a convergence of opinion on a specific topic. The method of using multiple rounds of questionnaires and feedback allows for items under review to be validated and ranked, until consensus is formed. The panel remains anonymous to each other throughout the study, therefore eliminating the formation of group conformity on opinions, which can appear in group discussion techniques [174]. The potential to contact participants via email is another beneficial element to the study design as it improves the ease in which questionnaires can be completed and returned, as well as eliminating geographical restrictions and increasing participant recruitment [175, 176].

The traditional Delphi technique consists of an initial open-ended question phase, which forms the initial item pool, based on the answers provided by the panel. The answers are accumulated and circulated to the panel for any additional commenting. All the items are then placed into a questionnaire format and answer options are based on a Likert-scale. After each round, answers are ranked and fed back to the panel for agreement or further comment. This provides a format for the subsequent questionnaire rounds. However, it is accepted in the literature that the Delphi process can be modified by excluding the initial open-ended questionnaire phase if a suitable systematic review has been conducted and the data is relevant to the intended aims of the Delphi study [177].

In the current study, the initial item pool is guided by the systematic review in Chapter 2, which focused on identifying medication barriers in paediatric long-term conditions, via

self-report methods. The purpose of this study was to form a quantitative measure from qualitative analysis and to understand the extent to which patient-identified barriers are prevalent in current practice.

Effective patient care and successful intervention in long-term conditions entails healthcare being delivered by an organised multi-disciplinary care team; often inclusive of nurses, doctors and pharmacists. Each profession offers a different knowledge base, range of skills and prioritise aspects of patient care differently [156]. Therefore, the inclusion of varied healthcare professionals into this study offers the ability to determine if uniformity in the expression of patient-identified barriers to adherence exists within clinical practice across varying disciplines. This also has added benefit when creating interventions to improve paediatric adherence allowing the same intervention models to be easily applied and used across multiple settings by multiple healthcare professionals.

This study aimed to determine which paediatric-identified barriers to adherence are observed in current clinical practice by healthcare professionals. Gaining an understanding of how different groups prioritise or observe adherence barriers, provides a better platform from which interventions and changes to treatment can be formulated. It can also enable caregivers and HCPs to find ways to reduce these barriers and methods to modify medication-taking behaviour. Understanding the HCPs experiences of the barriers to medication adherence provides awareness of the barriers they often come across and therefore have the potential to address in practice. Healthcare professionals prescribe, administer, manage or provide medication, therefore their understanding and awareness of medication-taking barriers, including those which are not observable to them, is important. Knowing the common and important barriers to paediatric adherence can allow for changes to the way interactions with patients and their families takes place.

Using the findings from an initial systematic review (Chapter 2), the aim of this study was to;

I. Identify which paediatric-identified barriers to medication adherence are most often experienced in practice, by establishing consensus between healthcare professionals with experience of paediatric medicine.

II. Compare the difference in frequency between HCP and paediatric reported barriers to medication adherence.

3.2. Method

3.2.1. Design

A two-round iterative Delphi process was implemented via email, whereby participants remained anonymous to each other throughout the study. Round-one required participants to rank their agreement to statements in the questionnaire using a 5-point Likert scale (*5=always* and *1=never*) (Appendix B) and add any additional comments that they wished to contribute. A 5-point Likert scale was used to determine which barriers to adherence were most commonly observed by healthcare professionals in a practice-based setting. The numerical values associated to the categorical response scale were derived from existing literature which ranks the responses from 1-5 [178, 179]. The results were summarised and the mean calculated. The second-round questionnaire was used to form a level of consensus to the results of round-one and a further chance to add any additional comments. The second questionnaire (Appendix C) presented statements to the participants in rank order from highest to lowest mean value.

The statements included in the questionnaire related to medication adherence barriers, which were derived from the results of an earlier systematic review of literature that was used to identify and collate the barriers to adherence based on self-reports of children and adolescents aged between 5-18 years old with long-term conditions. Those barriers which were related to adherence and frequently mentioned as barriers to poor adherence were include into the consensus questionnaire.

3.2.2. Piloting

The questionnaire was completed by two pharmacists and a doctor known to the researcher to evaluate the time taken to complete, and to determine if the instructions and language used throughout the questionnaire was clear and concise. As a result of piloting the

questionnaire, minor typographical errors and the wording of some adherence statements was corrected to clarify their meaning.

3.2.3. Participants

The participant panel consisted of 23 healthcare professionals comprised of pharmacists, nurses and doctors from primary and secondary healthcare services, all with a background in paediatric medicine.

Participants were deemed eligible for inclusion if they (i) were fluent in written and verbal English, (ii) had a role or experience in prescribing, administering and supplying medication to paediatric patients or had an active role in overseeing the administration of medication to children.

Recruitment took place through email invitation via a representative at each of the following healthcare services; Great Ormond Street Hospital, London; Royal Alexandra Hospital, Brighton; East Kent Hospitals University NHS Foundation Trust, Ashford: Queensway surgery, Southend; Quality of Life Medical centre, London and The Royal College of Nursing specifically the Child and Young People: Specialist Care Forum.

Prior to email invitations being sent it was confirmed that emails would only be sent to those healthcare professionals with the relevant experience in working in paediatric medicine, therefore expertise was confirmed prior to invitation. As outlined in the 'participant information leaflet' (Appendix B) – those who completed the initial, phase one questionnaire had provided consent to be part of the study and subsequent rounds.

3.2.4. Procedure

Questionnaire one: Ranking statements to form agreement

The questionnaire was emailed to the representatives and forwarded to potential participants. Participants were asked to rank how often they had experienced each of the twenty barriers to impact adherence on a 5-point Likert scale; *5=always, 4=very frequently, 3=often, 2=seldom* and *1=never*. The participants were asked to return the questionnaire to the email address provided (Appendix B).

Questionnaire two: Determination of consensus to results

The mean rating was calculated for each statement and statements placed in descending order from the highest mean. This formed the second-round questionnaire and was sent to the participants to rate their agreement with the results. An additional comment box was provided for participants to express their opinions or to provide justification for their level of agreement with the results (Appendix C).

3.2.5. Ethical approval

An application for ethical approval to carry out the consensus study was submitted to the ethics committee of the School of Pharmacy and Biomolecular Science at The University of Brighton. Approval to conduct this study was granted on 9th February 2016 (Appendix D).

3.2.6. Data analysis

'Agreement' refers to the extent to which participants agree to observing an adherence barrier in practice, it can be assessed using mean, median or mode calculations. 'Consensus' is a term used to ascertain the level of agreement participants have with each other and is calculated as a standard deviation (SD) [176, 180, 181]. The mean was

calculated for each adherence statement and used to determine the extent of agreement participants had to each statement. The standard deviation was also calculated for each statement and used to assess the degree of dispersion from the mean, thus the smaller the SD the greater level of consensus between participants for each statement [179]. A mean of 3.00 and above demonstrated a strong agreement level of participants to the statement and it is regularly seen in practice, whereas a score of 2.49 and below was a weaker level of agreement and suggests that this statement is less often seen by HCPs in practice. Adherence barriers which are neither common or uncommon/no agreement and there is a variation in how often the barrier is seen in practice by HCP were deemed at mean values 2.50-2.99. A standard deviation of 1.00 or less was used as it shows that there is little variance around the mean, limits the variability of opinion, participants agree and have formed a strong consensus to the statement. Therefore, the collective opinion is centred up to 1.00, if a larger SD was used then this would increase the variability of opinion around the mean and not form a strong consensus. Furthermore, the mean was used to determine agreement of participants to adherence statements as the mean of the groups ratings has shown to result in less statistical error when compared to using the median or interquartile ranges [182]. Therefore, the use of SD is a method of providing an indication of dispersion around the calculated group mean for each statement.

3.3. Results

Twenty-three healthcare professionals participated in phase-one, there was a loss of eight participants after phase-one of the study, resulting in 15 participant responses at phase-two. Results of the phase-one questionnaire can be seen in Table 3.1. Participants ranked the statement 'need of constant reminders from parents and/or caregivers to take medication' as the most common barrier to adherence seen in current practice. The first ten barriers in Table 3.1 have a mean value of 3.00 or above, suggesting that participants had formed strong agreement and those barriers are most commonly seen to affect adherence in current practice. Participants ranked 'not having a friend to talk to about their medication and/or condition' as the least often seen barrier to contribute to adherence, with a mean value of 2.00. Three barriers; 'taste of medication', 'feeling upset and frustrated with having to take regular medication' and 'parental views on the child's medication', have a mean of 3.00 or greater and a SD of >1.00. This indicates that participants agreed with the statement being a frequently observed adherence barrier but consensus is not achieved and there is a difference in opinion regarding barrier ranking. The greater SD value could also be due to not all participants providing a ranking for the statement, therefore increasing the data spread around the mean. Additional participant comments stated that patient age, comorbidities, parents not giving medication to their child and incorrect asthma devices being used were adherence barriers that they observe, in addition to the ones listed.

Twelve respondents (80%) at phase-two agreed with the results of phase-one, Table 3.2. Two participants rated moderate agreement, with one participant expressing the opinion that children and adolescents 'feeling that their medication is not helping them feel better' should occupy the first position within Table 3.1; as the most important factor to non-adherence. As 80% agreement was reached with minimal further commenting, therefore the study was terminated after two rounds.

Table 3. 1 Results of phase one Delphi questionnaire

Factor affecting adherence	Mean rating (highest to lowest)	Standard deviation (SD)	No. of participants that provided a rating for each factor
Needing constant reminders from parents/caregivers to take medication	3.65	0.76	23
Becoming tiresome of taking long term medication	3.52	0.97	23
Taste of medication	3.43	1.17	22
Becoming more responsible for their own medication	3.39	0.92	23
Children's activities or social events	3.26	0.90	23
Forgetting	3.17	0.87	23
Parental views on the child's medication	3.17	1.52	21
Feeling upset and frustrated with having to take regular medication	3.13	1.23	22
Refusal to take medication	3.04	0.95	23
Difficulty in sticking to a fixed medication schedule	3.00	1.02	22
Busy with other things	2.87	0.85	23
Difficulty in swallowing medication	2.87	0.90	23
Avoiding side-effects	2.70	1.04	23
Other people noticing them taking their medication	2.61	1.17	21
Not knowing how and when to take their medication	2.57	0.71	23
Having too many pills	2.35	0.76	23
Feeling that their medication is not helping them feel better	2.30	1.00	22
Dose avoidance	2.22	1.18	21
A child's satisfaction with its healthcare team	2.22	1.28	21
Not having a friend to talk to about their medication/condition	2.00	0.98	21
Other: Wrong device in asthma patients	0.22	1.02	1
Other: Teenage/adolescent poor compliance problem	0.22	1.02	1
Other: age; younger age more compliant	0.17	0.82	1
Other: comorbidity affect/influence drug intake	0.17	0.82	1
Other: Parents not giving medication	0.13	0.61	1

Table 3. 2 Level of consensus to results of phase one

Level of agreement	% (no. of participants)	Comments to non-agreement
Agree	80% (12)	-
Moderately agree	13.3% (2)	Belief that "feeling that their medication is not helping them feel better" should occupy the first position in the rankings. As a patient, will not take his/her medication if he/she feels that it is not working.
Neutral	6.6% (1)	-
Moderately disagree	-	-
Disagree	-	-

3.4. Discussion

A consensus study was used to prioritise known barriers to paediatric medication adherence to understand their prevalence in current practice based on the experience and awareness of healthcare professionals.

The main barrier observed by HCPs to adherence was 'needing constant reminders from parents/caregivers to take medication'. The need for reminders may suggest that children and adolescents either forget to take, are late to take their medication or do not take their medication, leading caregivers to perceive that they need to provide reminders to their children to take their medication. It is normally assumed that caregivers are responsible for administering medication to young children. Therefore, caregivers that need to provide their children with reminders may suggest that these children have assumed some or all responsibility for their medication and the caregiver has less control. The systematic review (Chapter 2) identified that children and adolescents most often reported forgetfulness as a barrier to medication taking. However, in a practice setting, where caregivers and children may attend appointments together, HCPs may become aware of adherence problems if caregivers mention that they are having to provide their child with reminders or if they know their child is non-adherent. Studies considering the impact of parental reminders on adherence have reported mixed findings. Some studies have indicated that children would like reminders so that they do not forget to take their medication, whereas other studies have shown that parental reminders can be perceived as 'nagging', which has been negatively associated to adherence [127, 134].

Furthermore, depending on the perspective, a barrier to adherence may be viewed differently by different people. Such that, from a child's perspective, they may have simply forgotten to take their medication; a caregiver may interpret their child forgetting as a need to offer reminders, which may be conveyed as nagging by their child and to a HCP it may

translate as the “child needs parental reminders”, therefore, it is mostly commonly seen in practice. It could also suggest that the caregiver has more input than their child to speak about their issues and concerns, if so, consultations need to be more patient-focused.

The barriers ‘children’s activities and social events’ and ‘forgetting’ were ranked fifth and sixth. In comparison to the systematic review, ‘forgetting’ was the most common barrier to adherence based on paediatric self-reports. However, for these barriers to be known to the HCP, the patient or caregiver needs to openly admit that this is the issue, as it is not an observable barrier.

If healthcare professionals do not ask, patients are less inclined to freely offer the information [183]. A study of patients prescribed cardiovascular medication showed that 61% of patients rarely or never discussed their medication adherence with their doctor. Therefore, this results in a failure to identify and address poor adherence. Furthermore, 67% of the patient’s doctors were not aware of how often their patient missed doses of their medication because they had never discussed this [184]. Hence, self-report studies can be beneficial as they can offer a personal insight into patient medication-taking behaviours, as they offer the opportunity to anonymously share their experiences.

The second most commonly observed barrier to adherence was ‘becoming tired of taking long-term medication’. Medication-taking fatigue is common in patients who are required to take medication on a long-term basis [185]. In young children who may lack the ability to comprehend why they must take medication daily, it adds to the difficulty a caregiver may have to maintain adherence, particularly if it leads to a child’s refusal to take medication. Medication-taking fatigue can result in children not wanting to take medication, becoming frustrated and stop taking medication. Healthcare professionals may recognise this when their patient’s condition worsens or they become increasingly symptomatic and if the caregiver highlights this.

Increasing medication-taking responsibility has been associated with lower adherence due to increased forgetting, poor planning and poor ability to manage condition-related tasks [23]. As the patient increases in age, the barrier 'becoming more responsible for their medication taking' may become apparent either through the caregivers account, reduced medication requests and with an increase in acute symptoms and treatment needs.

The impact of parental views on adherence was ranked seventh, indicating that HCPs see parental beliefs regarding their child's medication as having a negative impact on their child's medication adherence. Parents may express their concerns to the HCP, then the HCP must have that discussion with the parent, to discuss concerns and make shared decision on how to best manage their child's condition and treatment. Existing studies have shown that when parental beliefs regarding necessity and perceived benefits of medication are positive, their children show better adherence than those parents with negative views or greater concern regarding medication [52, 153].

Healthcare professionals frequently experienced the barrier, 'refusal to take medication', which was ranked ninth. In comparison, refusal to take medication was only mentioned in two studies in the systematic review [24, 138]. Refusal to take medication may be related to other barriers, such as, poor medication taste or medication-taking fatigue. Increased age and increased autonomy which leads to refusal to take medication could relate to a form of intentional nonadherence. Furthermore, there may be a reluctance to admit refusal to take medication to a HCP.

Medication taste was also a highly-ranked factor in affecting adherence, consistent with the systematic review findings, which found this to be a frequent patient-identified problem. Problems with medication taste have been shown to lead to refusal to take medication [186], which could support results of the factor 'refusal to take medication'. In contrast to the systematic review finding, swallowing difficulties was frequently mentioned as a factor

to negatively affect adherence, this was ranked low by HCPs, suggesting that it is not a barrier they often come across. The ranking may be affected by the disciplines that the healthcare professionals work in, particularly if their specialised area does not involve the administration of oral medication.

The barrier 'having too many pills', referring to regimen complexity and/or dosage frequency commonly appeared as barrier to medication adherence in the systematic review. However, participants rated this factor as being less commonly seen in practice as a barrier to adherence. Conflicting results may be due to prescriber's beliefs regarding the need for the medication, rather than understanding the patient's view-point relating to the difficulties they face in managing a multi-drug regimen. Although, some conditions may require multi-drug regimens to be followed such as HIV and cystic fibrosis, to maintain symptom control and prevent disease progression, regimen complexity is still a significant factor to non-adherence [187-189].

Non-adherence to 'avoid side-effects of medication' was ranked in the lower half of Table 3.1, suggesting that this is not often seen in practice as a barrier to adherence. Side-effects to medication were one of the main barriers to adherence in the systematic review. This suggests that children and adolescents are reporting medication side-effects to a greater extent than the HCPs are aware of. This may lead to HCPs not accurately understanding why their paediatric patients are non-adherent. Evidence shows that the presence of/or concerns about side-effects leads to doses being altered or missed, resulting in sub-optimal adherence [190]. However, healthcare professionals would only be aware of this aspect if patients were to discuss the presence of/or concerns regarding side-effects with their healthcare team. Without the awareness of side-effects being a causative barrier to adherence, HCPs are unable to adjust doses or change the medication to help the patient. The importance of understanding the patient-HCP points-of-view to create treatment plans

which are reflective of both sides. This has shown to increase patient satisfaction and ability to cope with their condition and commit to their treatment [191].

3.4.1. Limitations

Due to the two-phase feedback process, there is a risk of fewer responses after each phase, therefore reducing the ability to form consensus due to fewer participants. The Delphi technique traditionally uses between three to four iterative rounds; this study reduced the phases to two. This minimises the non-response rate due to the inherent time consumption the study takes, as well as the limited time healthcare professionals have in which to part-take in studies which extend over prolonged periods of time. The use of a two-phase study design has been successfully used numerous times in research; therefore, the quality of the results is not diminished from using a shortened version [172, 173, 175]. Additionally, email communication was used to increase the ease and speed of data collection. Furthermore, a diverse range of professionals were used but all with expertise in the paediatric medicine, therefore broadening the knowledge base and experience based on the varying degrees of patient engagement.

Participants were provided with a list of known medication adherence barriers to rank, although this limited HCPs from independently generating their own list of barriers to answer the research question, they were provided with the opportunity to make any additional comments or add adherence barriers not already present, at each stage of the study. These can be seen in Table 3.1, where five additional barriers were added and Table 3.2, in which one participant commented on the results of the phase-one questionnaire.

Furthermore, the twenty statements used in the study have significant overlap and are interlinked. Therefore, if one barrier has a lower ranking, a similar barrier may be ranked higher due to the overlap and similarities.

3.5. Conclusion

This study set out to identify which paediatric-identified barriers to medication adherence are most often experienced by HCPs in current practice. Based on the findings, there are variations between the barriers that paediatric patients identify through self-reports and what is either discussed with the HCP, or observable in practice. This identifies the need make HCPs more aware of the common barriers reported by children and adolescents, so that these can be addressed in practice.

3.6. Summary of findings

Healthcare professionals ranked the need for constant reminders from caregivers to take medication, becoming tiresome of taking long-term medication, medication taste, increased responsibility for taking medication and social activities as commonly observed barriers to non-adherence in clinical practice. Barriers less frequently observed were difficulty in swallowing medication, too much medication, medication side-effects, busy with other things and feeling that medication is not helping.

Chapter 4 Caregivers perceived barriers to paediatric medication adherence in long-term illness and their opinion of the role of community pharmacists

The previous chapter used a Delphi study with 23 healthcare professionals to identify that HCPs most commonly observed the barrier 'needing constant reminders from parents/caregivers to take medication', to paediatric adherence in clinical practice. This chapter will determine medication adherence barriers from caregivers' experience and their past experiences with community pharmacists relating to their child's medication.

4.1. Introduction

Caregivers are central to ensuring medication adherence for their children with long-term medical conditions, especially when children are too young to assume responsibility [151]. Caregivers' medication giving behaviour is driven by multiple factors, such as concerns and beliefs about medication, their ability and willingness to administer medication to their child and their perception of how severe their child's condition is, therefore the need for medication [80, 153, 192]. There is evidence to suggest that when perceived medication necessity outweighs concerns about medication, medication adherence will be high [52]. In situations where concerns and misconceptions about medication are the underlying cause of intentional non-adherence, healthcare professionals such as pharmacists have a prominent role in understanding and dispelling caregivers concerns and opinions. To change opinions and promote medication use, attitudes towards medication use are important to consider, specifically in African and South Asian minority groups, who display greater belief in alternative therapies and lack trust in pharmaceutical treatments [193]. In conditions such as asthma, safety concerns regarding the long-term use of inhaled corticosteroids are important barriers to adherence which require input from a HCP to

dispel misconceptions and to help caregivers manage and incorporate medication tasks into daily life [112].

Caregivers have been shown to experience at least one adherence barrier when administering medication to their child with IBD [194]. These included, being away from home and not having any medication, the medication regimen interfering with daily activities and their child's refusal and/or defiance to take medication [194]. Caregivers of children with asthma have been identified adherence barriers as, forgetting to give medication to their child and their child's reaction to being given medication [151, 195]. Furthermore, a systematic review of caregivers barriers for children 12 years and younger, found that caregivers concerns about medication effectiveness and side-effects, medication complexity and the time-consuming nature of treatment were barriers to adherence, across five long-term conditions [196]. However, studies have not investigated caregiver barriers to adherence in children and adolescents with long-term conditions. The current study will aim to understand caregiver barriers to adherence and investigate how they change with age and condition.

Caregivers have been shown to overuse emergency services and increase the use of medication when their child is experiencing an increase in acute symptoms, in order to manage and improve symptoms. Just over 13% of caregivers would seek help or advice from their doctor in acute situations [197]. As community pharmacists are easily accessible and can offer advice to caregivers on how to avoid exacerbations and manage their child's symptoms [57, 197], it is valuable to understand caregivers experiences and opinions towards community pharmacists.

Caregivers have concerns about their child's medication [8], as well as difficulties in managing and administering medication [130, 198]. Understanding their perception and experience of adherence barriers can aid the development of targeted clinical services to

help reduce problems in medication-administration and minimise concerns. Furthermore, by understanding the caregivers opinion of community based pharmacists, it can give an indication as to how well paediatric medication services in community pharmacies will be received.

This study aimed to investigate the following:

I. To understand the barriers to paediatric medication adherence based on caregivers experience.

II. To understand caregivers opinions and experiences of the community pharmacist's ability to help support them with their child's long-term medication.

III. To determine which service(s) caregivers think should be introduced within the pharmacy to offer support to them and their child for their long-term condition management.

4.2. Method

4.2.1. Study design

A cross-sectional retrospective questionnaire design was used, this consisted of 4 sections intended for caregivers of children with a long-term condition to share their experience of administering medication to their child and of their experience as caregivers of using community pharmacy services.

4.2.2. Piloting

The questionnaire was completed by four caregivers of children with a long-term condition that were known to the researcher to evaluate the time taken to complete the questionnaire, and to determine if the language and instructions used throughout the questionnaire were clear and easy to follow. Feedback indicated that that layout and Likert scales were easy to follow and complete. However, some questions needed re-wording to make them easier to understand. Minor typographical errors were also corrected.

4.2.3. Participants

Participants had to be aged over 18 years and either be the primary caregiver or one of the main caregivers to a child or children aged between 5 and 16 years, with a long-term medical condition that requires on-going medication for its management. The caregiver had to be fluent in spoken and written English.

Caregivers to children with severe learning disabilities were excluded from the study. Consent was assumed on completion of the questionnaire. Participants were offered the chance to enter a prize draw for a £50 gift voucher. All data was handled confidentially in accordance to the University of Brighton data protection policy.

4.2.4. Questionnaire design

The questionnaire was separated into the following four sections (Appendix E);

Section A: Identified the child's conditions, number of prescribed medicines, age and gender.

Section B: Identified the caregivers relationship to the child and the level of education completed.

Section C: Determined the frequency with which caregivers' experience barriers to medication adherence on a 5-point Likert scale (*5=always* and *1=never*). The items selected for inclusion were based on common adherence problems identified through paediatric self-reports (Chapter 2). It was presented to caregivers to identify if they encounter the same issues as their child.

Section D: Aimed to understand the caregivers' opinions of community pharmacists and to rate their previous experiences with pharmacists, which was related to their children's condition or medication, on a 5-point Likert scale (*5=agree* and *1=disagree*).

4.2.5. Procedure

Recruitment took place via a large multiple-chain pharmacy. Permission was sought form head office prior to contacting individual pharmacy managers in the London, Kent and the South East of England areas. Twenty-five pharmacy managers were contacted about the study, fifteen managers agreed to take part and questionnaires were distributed through these pharmacies.

Initially, questionnaires were offered to all patients collecting prescriptions or receiving over-the-counter services by the pharmacist. This approach generated few responses as the pharmacist was restricted by time or management duties. To improve the response rate, the questionnaires and information sheets were attached to all prescription bags pending

collection. This reduced the demand on the pharmacist and allowed greater distribution of questionnaires. This method generated more responses than the initial approach but responses were still low. A display was created at each front-of-house service counter. Pharmacy counter-staff distributed questionnaires either at the point of prescription collection, point of sale or to walk-in customers waiting for prescriptions as counter-staff have the greatest contact with the public, compared with other staff members.

Secondly, an online version of the questionnaire was created using Bristol Online Survey and placed onto the forum section of netmums.com and mumsnet.com.

4.2.6. Ethics

An application for ethical approval to carry out the study was submitted to the ethics committee of the School of Pharmacy and Biomolecular Science at The University of Brighton. Approval to conduct this study was granted on 13th September 2016 (Appendix F).

4.2.7. Data analysis

Descriptive statistics such as percentage, mean, median, standard deviation and inter-quartile ranges were calculated to determine the levels of endorsement of the potential barriers to adherence and to determine caregiver attitudes towards community pharmacists. Thematic analysis was used for open-ended questions relating to caregiver experience. Thematic analysis provides the ability to code, categorise and identify similar response types [199]. This aides the identification of which pharmacy services caregivers believe would help them better care for their child, what common problems caregivers encounter when administering medication to their child and understand why caregivers have previously had to seek assistance from the pharmacist regarding their child's medication.

The Kruksal Wallis test was performed for multiple group comparisons of Likert scale data. As the data from caregivers regarding pharmacy experience and adherence problems was rated on a Likert scale, it is assumed that it does not fit a normal distribution curve and it is assumed that the data is nonparametric. The Kruksal Wallis test was used because there was a need to determine if there is a statistical difference between two or more groups of an independent variable [200, 201]. The Mann Whitney U statistical test was used for bi-group comparisons, such as two independent groups on a dependent variable, such as gender [202]. Spearman's Rank correlation coefficient ranks values of each variable and was used to determine a positive or negative correlation between two variables [203].

4.3. Results

4.3.1. Sample demographics

The total sample consisted of 52 caregivers. As seen in Table 4.1, the caregivers were predominantly mothers (82.7%) and over half (55.8%) had completed an undergraduate degree or higher. The majority of caregivers' children were boys (61.5%) and the overall mean child age was 10 years, standard deviation (SD) = 3.3. The mean number of prescribed medicines taken by each child was 2, range 1-5 medicines and a mean condition duration of 2.8 years, range 1-4 years. The most common long-term condition amongst children and adolescents was asthma (34.6%), followed by ADHD (13.5%).

Table 4. 1 Caregiver and child demographics

Child gender (N=52):	**Caregiver relation to child:**
Female: (20) 38.5%	Mother: (43) 82.7%
Male: (32) 61.5%	Father: (3) 5.8%
	Other: (6) 11.5%
Age of child:	
Mean age of child = 9.9 years	**Education level of caregiver:**
Mean age of females = 10.1 years	Postgraduate qualification: (12) 23.1%
Mean age of males = 9.8 years	Undergraduate degree: (17) 32.7%
5-8 years: (20) 38.5%	A-levels: (10) 19.2%
9-12 years: (18) 34.6%	GCSEs: (6) 11.5%
13-16 years: (14) 26.9%	No qualifications: (6) 11.5%
	No answer: (1) 1.9%
Child's long-term condition:	
Asthma: (18) 34.6%	Mean number of prescribed medicines per child = 2.1
ADHD: (7) 13.5%	Average condition duration = 2.8 years
Diabetes mellitus: (6) 11.5%	
Eczema: (6) 11.5%	
Other: (15) 28.8%	

4.3.2. Adherence barriers experienced by caregivers

As seen in Table 4.2, caregivers reported their child as being heavily reliant on them to ensure medication was taken (71.2%), as the most common barrier to adherence. Just over half of caregivers reported their children feeling upset and frustrated with needing to take medication regularly (52%), as the second highest barrier to medication-taking. Forty-six percent of caregivers reported that their child had some responsibility for the medication-

taking. Other frequent barriers were the tiredness of taking long-term medication (46.1%); avoidance (40.4%) and refusal (32.6%) to take medication were also common barriers to adherence reported by caregivers. Twenty-five percent of caregivers reported that their opinion of their child's medication would determine if they would administer it to them or not and 23.1% reported that as their child become more responsible for their medication-taking, they missed more doses. Caregivers rated the item 'I don't always know how and when to give my child their medication', as the least frequent barrier to adherence (3.8%).

Table 4. 2 Caregivers rating to adherence items affecting their child's medication administration

Adherence item	Caregivers rating 'often', 'very frequently' and 'always', %(n)
My child is heavily reliant on me to ensure their medication is taken	71.2 (37)
My child feels upset and frustrated with having to take regular medication	52.0 (27)
My child has some responsibility over their medication	46.2 (24)
My child is tired of taking long term medication and doesn't take it	46.1 (24)
My child avoids taking their medicine	40.4 (21)
My child refuses to take medication	32.6 (17)
My opinion of my child's medication will decide if I give it to them or not	25.0 (13)
As my child becomes more responsible for their own medication they miss more doses	23.1 (12)
My child has a friend to talk to about their medication/condition	23.1 (12)
My child's activities or social events leads to medicine not being taken	23.1 (12)
My child doesn't like the taste of the medicine and doesn't take it	21.1 (11)
Other people noticing my child taking their medicine leads to missed doses	17.3 (9)
I'm sometimes busy with other things	15.4 (8)
If my child has difficulty swallowing medication then I don't give it to them	15.3 (8)
Medicine is not taken so that side-effects to the medication can be avoided	11.5 (6)
I find it difficult to stick to my child's fixed medication schedule	11.5 (6)
I sometimes forget to give my child their medicine	7.7 (4)
I need constant reminders to give my child their medication	7.7 (4)
I feel that my child's medication is not helping them feel better then, I do not give it to them	7.6 (4)
My child has too many pills to take and doesn't take all of them all the time	7.6 (4)
Medicine is not taken so that the medication doesn't affect my child's physical appearance	5.7 (3)
I don't always know how and when to give my child their medication	3.8 (2)

Statistical analysis indicated that a child's gender was significantly associated with how much responsibility they had over their medication, with females having more responsibility than males (mean 3.15 v 2.16, p=0.02). Females were not significantly older than males (p>0.05) Age was positively correlated with responsibility for medication management; as age increased the responsibility for medicines also increased (r=0.51, p < 0.01). Reliance on the caregiver to ensure medication was taken had a negative age association, therefore, as age increased there was less reliance on the caregiver, (r=-0.44, p=0.001).

The duration of the condition was significantly associated with the item 'other people noticing my child take their medicine leads to missed doses'; with a stronger endorsement of the barrier for children and adolescents diagnosed for less than a year, compared to those that had been diagnosed for between one and two years (r= -0.099, p=0.01). Furthermore, an increase in the duration of the condition (r=0.326, p=0.02) had a significant, positive correlation with children assuming more responsibility for their medication taking, independent of age.

The number of medicines a child or adolescent was prescribed was significantly associated to the barrier 'as my child becomes more responsible for their own medication, they miss more doses', (r=0.400, p=0.003). Therefore, as the number of prescribed medicines increases, it was positively correlated with an increase in missed medication doses as children and adolescents assume more responsibility for their medication-taking.

Furthermore, children and adolescents that were prescribed two medicines had more responsibility for their medication than those children and adolescents taking only one medicine (r=0.333, p=0.02).

Caregivers of children taking three medicines were significantly more likely to have increased difficulty in adhering to their child's fixed medication schedule. This was significant when compared to children taking one or two medicines (r=0.352, p <0.05).

4.3.3. Caregivers experience of using pharmacy services

The overall opinion and experience that caregivers had of community pharmacists was positive, Figure 4.1. Caregivers who had sought advice from the community pharmacist about their child's medication agreed (84.6%) that they found the pharmacist to be helpful and supportive to their needs and that they had received enough support to be able to care for their child (71.1%). Caregivers also believed that community pharmacists had the knowledge and skill set to help them with their child's medication problems (80.8%). Sixty-nine percent of caregivers felt confident in asking the pharmacist for advice about their child's medication. However, if caregivers were experiencing difficulties with administering medication to their child, only 55.8% of caregivers felt that the pharmacist would know what to do and could be asked for advice. Just over half of caregivers (51.9%) would see the pharmacist before the GP if they had questions about their child's medication.

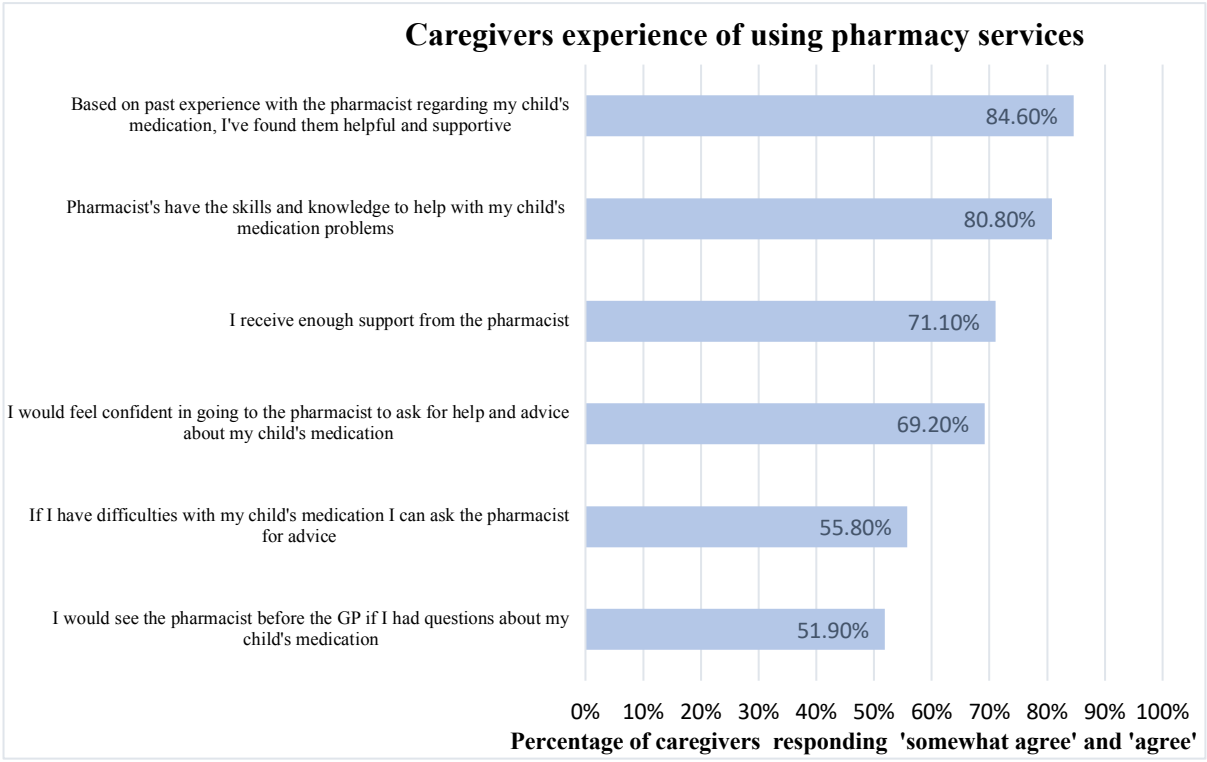

Figure 4.1 Representation of opinions and experiences of caregivers using community pharmacy services for their child's long-term medication needs

As the number of medicines increased, caregivers felt less confident about asking the pharmacist for advice relating to their child's medication (r=-0.375, p=0.006). Additionally, as the number of prescribed medicines increased, caregivers felt that they received less support from their pharmacist to care for their child (r=-0.296, p=0.022). Caregivers that experienced daily problems with their child's medication adherence were more positive about the skills and knowledge a pharmacist has (r=0.285, p=0.001) and caregivers also had greater confidence in seeing the pharmacist regarding their child's medication problems (r=0.402, p=0.001), when compared to caregivers that experienced problems less frequently. Caregivers experiencing daily problems were also more likely to seek help from their pharmacist before visiting the GP (r=0.178, p=0.01).

Pharmacy services that caregivers suggested could be introduced in the community pharmacy, to improve adherence and reduce caregiver and patient difficulties are presented in Table 4.3.

Table 4. 3 Pharmacy services to improve paediatric adherence based on caregivers opinions

Category	No. of participants	Description/ example quotes from caregivers
Medication reviews/help with medication use	11	- "finding an easier way to use an inhaler" - "How to manage an asthma attack" - "Making my child comfortable discussing IBS as is currently very embarrassed" - "Help with using spacers with inhalers" - Help with getting child to take medication - Help to plan when to give medication/medication timing - Asthma review, peak flow monitoring and checking technique
More information about condition or medication	11	- Information sessions or mother's groups - More information on natural remedies/alternative medicines and treatments - Discussion about medication choices
Increase ease of medication availability	5	- "reminders of when medication is expected to run low based on dosage".
Adherence aids	1	Pill boxes

The main recommendations were for services that would focus on helping caregivers with effective use of medication and devices, such as creams, inhalers and spacers. Furthermore, caregivers also suggested introducing information sessions and providing information regarding, alternative and natural treatments.

4.4. Discussion

Results of this study indicate that caregivers perceive their children to be heavily reliant on them to ensure medication is taken. Results have also shown that as child age increased, it was positively correlated with amount of responsibility assumed. This is comparable to results from existing studies, in which children and adolescents with asthma began taking some responsibility for their medication from the age of seven. At this age children had assumed up to 20% of responsibility, this increased to 50% by age eleven, with full responsibility by age nineteen [204]. This suggests that there is a gradual shift from caregiver to child. However, studies have shown that although children and adolescents begin to assume responsibility for their medication, they still require input from caregivers to help them manage and to provide support [42].

A longer condition duration has been associated with lower adherence rates in conditions such as asthma, epilepsy and diabetes after approximately three and a half years of diagnosis [107]. In this study, children who were diagnosed for less than a year had missed more doses based on caregiver-reports, compared to children who had a longer condition duration. This is consistent with previous research of children with epilepsy, which identified that difficulty in establishing a medication routine within the first six months of newly initiated treatment resulted in 60% non-adherence [205]. Reasons for non-adherence have been associated to parental stress [193, 206], difficulty in organising a medication routine [207] and symptomatic relief [206]. Furthermore, caregivers in this study had difficulty in maintaining an effective medication routine if their child was taking three medicines or more.

In this study, more medication was reported to be missed during the first year of diagnosis compared to children and adolescents with a longer condition duration, due to 'other people noticing' medication being taken. Studies support that the time after the initial

diagnosis of a condition and the continual need to take medication is a change for the caregiver and their child. Normalising a medication-taking routine is an important factor to good adherence [149]. In conditions, such as asthma, children and adolescents feel embarrassed to use their medication in front of peers, in public and don't like to carry it with them as it is inconvenient, therefore the medication is not taken [107, 134, 208].

In the current study, caregivers' reports identify that duration of condition is significantly associated with increase in responsibility for medication taking. Increased responsibility also led to more missed dose, especially if they are taking more than one medicine, this may be due to difficulties in organisation and prioritisation of medication into daily life. There is increased difficulty in adolescence, due to increased independence and social changes [23].

The experience of medication barriers in caregivers mainly focuses on issues such as tiredness of taking medication, their child's frustration, refusal and avoidance of medication taking in this study. The level of responsibility their child has also negatively impacts adherence. From a caregiver perspective, the impact of medication on physical appearance is of lesser importance. Caregivers also deem swallowing difficulties of pills to a far less importance compared with children and adolescent self-reports, where difficulties in swallowing medication are reported as a major issue.

Overall, caregivers were marginally positive regarding the support they received from the pharmacist. Positive relationships between patient, healthcare professional and family are known to be effective in achieving medication adherence in paediatric care [29, 101]. Pharmacists who are involved in paediatric intervention studies have positively contributed to optimising therapy and reducing medication side-effects for patients with a long-term condition [156, 209]. For children, studies have shown that interventions which teach them

about their medication, by adapting education programmes for their developmental and providing parental education, improve adherence [210].

In this study, caregivers believe that their children are heavily reliant on them to take their medication, which is similar to the consensus of healthcare professionals identifying that children and adolescents need constant reminders from their caregivers to take their medication.

This study contributes an understanding of caregivers opinions towards community pharmacists and pharmacist's current ability to help caregivers in managing their child's long-term medication needs. The study also adds an understanding of the potential pharmacy services which could be introduced to help improve adherence, based on caregiver needs.

4.4.1. Limitations

The sample size for the study was small due to the limited number of pharmacies which took part in the study, therefore reducing the number of potential responses. The questionnaire length and number of overlapping questions can lead to respondent fatigue. Furthermore, the same theme of adherence barriers was used across studies, however, caregivers did have the opportunity to add additional adherence barriers and comment if they needed.

There is a risk of bias in this study, as caregiver were recruited from pharmacies and asked about their opinions of pharmacists. This may lead to participants responding in a more positive manner. Future studies can minimise the risk of bias by recruiting participants from a different setting.

4.5. Conclusion

Pharmacists were thought to be able to provide support to caregivers of children with long-term conditions; however more emphasis needs to be placed on helping those caregivers that face persistent or multiple problems with their child's medication. Medication complexity is an issue for caregivers and then their children once they assume responsibility for their medication, therefore there is a need to work with families to reduce the medication-taking burden.

4.6 Summary of findings

The age of the child and duration of the condition were positively correlated with caregivers' children achieving more responsibility for their medication taking. More non-adherence to medication occurred in the first year of diagnosis and multi-drug regimens led to increased non-adherence and difficulty with maintaining a routine.

Caregivers experiencing daily adherence problems with their child were more positive about community pharmacists and marginally more likely to seek help from the pharmacist before the GP. Caregivers suggested services which focused in providing more information about medication and conditions would help them manage with their child's medication better, as well as services which review medication use to ensure proper use.

Chapter 5 The role of community pharmacists in supporting caregivers of children with a long-term illness

The previous study used caregiver reports to identify the difficulties they have with medication adherence, express their opinions regarding community pharmacists and the services which they believe would help them with their child's medication. This study will use community pharmacists to observe paediatric medication queries and identify which paediatric pharmacy service could improve adherence.

5.1 Introduction

There is increasing emphasis on the introduction and delivery of patient-facing services in primary care [211]. This is to allow for early detection of adverse effects to medication, adherence difficulties and to address patient concerns. This ensures timely problem-solving and may involve changing prescribed medication to more suitable alternatives. Additionally, this promotes adherence and reduces medicine waste [212]. On initiation of newly prescribed treatment, patient-centred services enable easy access to information and healthcare professionals, to ensure patients and carers are provided with enough support to empower self-care, self-efficacy and to better manage long-term conditions [213].

Pharmacists are advantageously placed within the community to offer support and guidance relating to the treatment of minor ailments, healthy living and the management of long-term conditions. The availability of advanced pharmacy services such as Medication Use Reviews (MUR), New Medicines Service (NMS) and annual flu vaccination service for adults with long-term conditions facilitates a pathway to engage in conversations about medication problems and discuss medication appropriateness based on patient preference, symptoms and lifestyle. A patient-centred approach to medicines management creates an

environment which allows pharmacists and patients to discuss and understand the purpose of prescribed medication, promote adherence and understand the patient's needs and expectations from their treatment [214].

Effective self-management of a long-term condition involves behaviour change, such as dietary modifications, and/or the additional learning of new behaviours, such as the act of medication-taking or blood glucose testing in T1DM. Adherence to treatment is dependent on several factors, some of which include health beliefs, ease of medication use and effective communication with health care professionals [215]. Pharmacy based services such as MURs and NMS are currently accredited for adult patients on long-term medication. The absence of nationally accredited services available for children on long-term medication and/or their caregivers provides fewer opportunities for this patient group to access the same targeted care.

The aim of the present study is to determine the extent to which caregivers and/or their children use the resources offered by community pharmacies to help them with their medication needs and long-term condition. Also, to identify their potential to optimise paediatric care in the absence of nationally accredited services.

The purpose of evaluating the role of community pharmacists is to determine if there is a potential and if there is patient/public acceptance to provide a patient-centred service that increases patient choice. Also, if improving access to services will result in improved adherence through an uptake of service use by providing a service which targets a known group of patients with poor adherence to long-term medication. Furthermore, if there is a potential to reduce hospital admissions and helps to decide if a public health paediatric service in community pharmacy will deliver a positive experience and outcome.

This study aimed to assess how frequently caregivers and patients seek help and advice from the pharmacist regarding paediatric medicine. This will help identify which common

problems require pharmacist input and at which point caregivers, children and adolescents will see the pharmacist.

The study aimed to address the following:

I. To evaluate how often pharmacists are approached with paediatric medicine related queries over a period of four weeks.

II. To identify common barriers which prevent pharmacists from effectively managing paediatric medicine queries.

III. To understand which services can be implemented within community pharmacies to better address adherence issues and support families.

IV. To assess the role of community pharmacists in supporting caregivers and their children with a long-term condition.

5.2 Method

5.2.1 Study design

This was a prospective observational study carried out over a period of four continuous weeks and took place in community pharmacies across London and South East England. Participants were community pharmacists and they were required to record all paediatric medication related queries relating to long-term conditions. Permission to contact pharmacists of a large multiple pharmacy chain was sought prior the commencement of the study, as well as owners of independent pharmacies. Pharmacists in the London, Kent and the South East of England areas were contacted and informed about the study, those who expressed an interest and agreed to participant in the study were sent the questionnaires and participant information sheets.

5.2.2 Piloting

The evaluation questionnaire was completed by two pharmacists not involved in the study. This was to provide feedback on its wording, clarity of instructions and ease of layout. Based on feedback received, minor typographical errors were corrected. The instructions provided were clear and the layout was easy to follow.

5.2.3 Participants

Pharmacists were considered eligible for inclusion into the study if they were GPhC registered and currently a manager of a community pharmacy.

5.2.4 Questionnaire design

The questionnaire was divided into four sections and consisted of a query log and four questions (Appendix G).

Query log

To determine the extent to which caregivers seek community pharmacists in resolving medication and condition related issues and/or in providing general condition related advice, pharmacists were asked to record all queries from caregivers or patients. This included the nature of the query i.e. what the query was about, demographics: age and sex of child, person making the query, medication or condition the query related to, if advice was provided and what it was.

Pharmacists confidence in paediatric medicine knowledge

One item measured pharmacist confidence in paediatric medicine knowledge. Pharmacist were asked to rate, their overall, general confidence in managing paediatric queries on a 5-point Likert scale; *confident, fairly confident, unsure, somewhat confident* and *not confident*. The numerical values associated to the categorical response scale were derived from existing literature which ranks categorical responses from 1-5 [178, 179]. One open-ended question asked pharmacists about their opinion regarding the public perception of pharmacists regarding paediatric medicine knowledge.

Issues and service implementation

Pharmacists were asked by two opened-ended questions about the challenges they face when dealing with paediatric queries and what services they believe should be introduced within pharmacies, to help caregivers and their children to reduce adherence issues and improve self-care.

Demographics

Pharmacist demographics were collected at the end of the study, this included: gender, ethnicity, age and years in practice.

5.2.5 Procedure

Recruitment took place via a large multiple-chain pharmacy and an independent pharmacy. Permission was sought form head office prior to contacting individual pharmacy managers in the London, Kent and the South East of England areas. Thirty pharmacy managers were contacted about the study, fifteen agreed to take part.

Pharmacists were instructed to maintain a record of all paediatric medicine or condition related queries they were asked by paediatric patients and/or caregivers about their child aged between 5-16 years. All acute medicines and self-limiting conditions not related to their long-term condition were excluded from being recorded in the log, any present at the time of data analysis were ignored. All queries were logged for a period of four continuous weeks after which they were collected by the researcher. A four-week time period was used to firstly minimise the burden on the pharmacist from a longer duration study and secondly, a shorter period may not have been enough to generate data, as the study took place over the Christmas period.

5.2.6 Ethical approval

An application for ethical approval to carry out the study was submitted to the ethics committee of the School of Pharmacy and Biomolecular Science at The University of Brighton. Approval to conduct this study was granted on 13th September 2016. (Appendix H)

5.2.7 Data analysis

All qualitative data generated was thematically analysed and categorised according to the emerging themes. A percentage calculation was performed to assess the confidence level

of pharmacists in managing queries, patient and pharmacist demographics. The queries from the query log were grouped into conditions and thematic analysed.

5.3 Results

5.3.1 Demographics

Fifteen pharmacists participated in this study, 14 of whom worked in a large multiple pharmacy chain and one in an independently-managed pharmacy. The pharmacist's demographics are reported in Table 5.1. The majority of pharmacists were female (73%) and over half were of Asian ethnicity (53%). Their years of practice experience since qualification ranged between 18 months and 12 years. Most pharmacists were 26-35 years old (80%), while 7% were under 26 and 13% were aged between 36-45 years old.

Table 5. 1 Pharmacist demographics

	N/ (%)
Gender:	
Male	4 (27)
Female	11 (73)
Age (years):	
<26	1 (7)
26-35	12 (80)
36-45	2 (13)
Ethnicity:	
White – British/Irish/European	5 (33)
British Asian/Asian	8 (53)
British Black/black – African/Caribbean	2 (13)
No. of years in practice:	
<3	4 (26.6)
3-5	4 (26.6)
6-9	4 (26.6)
>10	3 (20)

5.3.2 Queries

The total number of queries pharmacists received were 36, with each pharmacist receiving an average of two queries and range 0-10 queries. The children's age ranged from 5 to 14 years old. Sixty-four percent (23) of queries were for children aged between 5-10 years and 36% (13) for children and adolescents aged 11-14 years. Results showed 50% (18) of the queries were for boys, 33% (12) for girls and on six occasions (17%) the gender of the child was either not recorded or not asked by the pharmacist. The most commonly queried condition over 4-weeks was asthma (15), Table 5.2.

Table 5. 2 Summary of patient related factors

Condition queried over 4-weeks	**N/ (%)**
Asthma	15 (42%)
Eczema/dermatitis	8 (22%)
Attention deficient hyperactive disorder (ADHD)	4 (11%)
Diabetes (T1DM)	3 (8%)
Other	6 (17%)
Patient Demographics	
Male	18 (50%)
Female	12 (33%)
Unknown	6 (17%)
Child age (years):	5-14 (range)
5-10	23 (64%)
11-14	13 (36%)
Demographic of persons making a query	
Mother	22 (61%)
Father	2 (6%)
Parent (unknown if mother or father)	7 (19%)
Parent and child (patient)	4 (11%)
Child/adolescent (patient) alone	1 (3%)

5.3.3 Pharmacist log of paediatric medicine queries

As can be seen in the Table 5.3, caregiver queries predominantly focused on four areas: how and when to take medication, caregiver concerns, managing exacerbations of the condition and side-effects to medication. The queries relating to asthma were about how to use inhaler devices (5), dosage frequency (3), parents concern (3) about inhaled corticosteroid use and management of symptoms (2) and side-effects (1). The second most common condition was eczema (8), with most queries relating to the management of exacerbations (5). Three of the queries related to T1DM regarding insulin storage, requesting an emergency supply of medication and help to fix a blood-testing monitor.

Eighty-six (31) percent of queries were made by parents alone; 61% (22) were mothers and 6% (2) were fathers. Children accompanied their parents on 4 occasions (11%) and only on one occasion did the patient come alone (3%) for OTC advice which was subsequently related to side-effects of incorrect inhaler use for asthma management.

Four of the 15 pharmacists returned blank query logs, stating that no queries were made for long-term conditions, only for acute medication such as antibiotics. Two of the blank logs

were from pharmacists working in pharmacies located within the same building as a GP surgery. One pharmacist returned a query log for queries all relating to children under the age of five; ages not included in the study inclusion criteria so the results were not included.

Table 5. 3 Paediatric queries received by pharmacists over 4-weeks

Medication/condition	*Age/gender*	*Relation*	*Query*	*Intervention/advice*
Asthma				
Beclomethasone 50mcg inhaler	7/M	Parent	Dosage frequency	Not using enough for symptom control, advised twice daily use
Salbutamol 100mcg inhaler	12/M	Parent	Dosage frequency concerns	use only when required
Salbutamol	9/M	Parent	Over usage of inhaler as symptomatic	Inhaler technique + GP referral for potential need of ICS inhaler
Clenil 50mcg/asthma	6/M	Mother	How and when to use inhaler + concerned about steroid use.	Inhaler technique with spacer + dose instructions. Discussed ICS concerns, counselling provided.
Beclomethasone	12/M	Mother	Concerned about steroid use	Discussed ICS concerns, counselling provided.
Ventolin inhaler/asthma	10/M	Mother	Concerned inhaler isn't working as symptomatic	Checked inhaler technique + GP referral
Becotide inhaler/asthma	7/F	Parent	Child feeling breathless, using maximum daily dose	GP referral
Asthma	11	Parent and child	Child needed help with inhaler use	Technique shown
Ventolin inhaler/asthma	5/M	Parent	Parent didn't know how to use inhaler and the spacer	Technique shown
Ventolin inhaler/asthma	8/F	mother	How to use inhaler	Technique shown
Seretide inhaler/asthma	14/F	Patient	Patient presented with candidiasis infection of the mouth and throat	Checked her inhaler technique, corrected technique. Advice on oral hygiene, OTC medication provided.
Asthma	6/F	Mother	How to use spacer device	Technique shown
Asthma	7/M	Mother	Concerned about using steroid inhaler	Discussed ICS concerns, counselling provided.
Asthma	6/F	Mother	How to use inhaler	Technique shown
Asthma	13/M	Mother	Flu jab inquiry	Advice provided
Eczema/dermatitis				
Eczema	12/M	Patient and parent	Flare up on arms and legs	Checked for infection, sold hydrocortisone cream, advised on emollient use
Eczema	6	Parent	Flare up, increase in dry skin	Advised to increase use of emollients
Emollient cream/dermatitis	7/F	Father	How to use cream and intended benefits	Counselled on how to apply and manage condition
Ketoconazole shampoo	8/F	Mother	Adverse effect	Expected side effect but if persists or too strong see GP
Eczema	6/F	Mother	Flare up under both knees	Referred and use of emollient
Eczema	13/M	Mother and patient	Flare on both arms and hands	Emollients and referred
Eczema	5/F	Mother	Flare up; red, itchy rash	Emollients and referred
Eczema	7F	Mother	Attempted to buy steroid cream for daughter	Stopped, emollients given instead and referred to GP

Table 5.3 (Continued)

Medication/condition	*Age/gender*	*Relation*	*Query*	*Intervention/advice*
Diabetes				
Insulin/T1DM	12	Patient and parent	How to store insulin	Advice provided
Insulin/T1DM	13/M	Father	Ran out of insulin	Emergency supply given
T1DM	13/M	Mother	Glucometer fault	Fixed
ADHD				
Peadasure shakes/ADHD	7/M	Mother	Methylphenidate side-effects + advice on meal replacement drinks	Had a joint discussion with parent and telephoned GP to discuss best option for her child and assess his needs.
Circadin 2mg tablets/ADHD	6	Mother	Formulation query	GP referral
Omega-3/ADHD	11/M	Mother	If omega-3 will help her son to concentrate	Mixed evidence but can try as no clinical risk
Concerta/ADHD	13/M	Mother	Ran out of medication	Referred to out of hours' doctor
Other				
Desmopressin	10/M	Mother	Can I double the dose to make it work better?	Not to increase. If no improvement in symptoms must see prescriber to discuss dosage. Advised of dangers to adjust dose without medical assistance.
Calceos tablets/Crohns disease	10/M	Mother	Medication side-effects and child doesn't like the formulation.	Advised to split the dose to twice a day rather than single dose. If no improvement, see GP for alternative.
Genotropin GoQuick 12mg syringe	9	Mother	How to order medication	Advice provided
Glycerol suppositories/IBD	5/F	Mother	Concern about GP prescribing decision	Checked for safety and advised on medication need
Cefalexin/allergies and skin conditions	5/F	Mother	Related to the product ingredients	Safety checked and advice provided
Epilepsy	14	Parent	Medication side-effects	GP referral
4 blank logs and 1 with queries for children outside of the inclusion age range				

5.3.4 Pharmacists confidence

Pharmacists predominantly felt 'fairly confident' (53%) in their ability to problem solve paediatric medication related queries. A further 27% of pharmacists felt 'confident', 13% were 'somewhat confident' and 7% felt 'unsure' in their confidence of managing paediatric queries.

5.3.5 Pharmacists self-perception of their paediatric knowledge

Pharmacists thought they would be deemed knowledgeable in the public's opinion (87%) about paediatric medicines as compared with adult medicines, Table 5.4. However, pharmacists also commented that they felt that although they were deemed knowledgeable, it was mainly limited to minor ailments, over the counter medication and commonly prescribed medication; but to a lesser extent regarding unlicensed or specialised medication and uncommon medical conditions.

Table 5. 4 Pharmacists self-perception of their paediatric knowledge

No. of participants	Are pharmacists deemed knowledgeable about paediatric medicine?	Additional comments
13 (86.6%)	**Yes**	- For OTC questions and minor ailments - We can help manage a condition, but limited to due to age restrictions - We can be a good source of information. - If we know the parents, then they are more likely to come see us with their children - Not for specialised treatments - Parents generally concerned about child safety
1 (6.6%)	**No**	
1 (6.6%)	**Possibly**	-Depending on the type of drug

5.3.6 Barriers to managing paediatric queries

Several different barriers were reported to have been encountered by pharmacists when attempting to manage paediatric queries, Table 5.5. The most common barriers expressed were a lack of time and inability to communicate with the patient, the parents were also a barrier to effective query management. Timing issues were a problem for two pharmacists, which meant they were unable to commit enough time to talk at length with the patient and their caregivers. The inability to speak to the child directly was also an issue for pharmacists who would prefer to interact with the child as well as the parent (2); however, only on 11% of occasions did children accompany their parent to the pharmacy. One pharmacist found that medication taste and the lack of alternative flavours or formulation to help the patient or caregiver in administering medication was a barrier to adherence. In

addition, parents were deemed as barriers, specifically their pre-conceived ideas and lack of trust towards the pharmacist, especially when dealing with less common medical conditions and treatments. Furthermore, parent's negative views of the pharmacist's ability to help meant that some parents were seen to bypass the help that pharmacists could provide; instead opting to see their GP as a first-line measure.

Table 5. 5 Barriers to dealing with paediatric medicine queries

Pharmacist barriers	**N/ (%)**
Timing and communication issues	
Can't communicate directly with the patient	2 (11.1%)
Not able to commit enough time to talk to child or parent	2 (11.1%)
Role of parents	
Parents don't trust pharmacist's advice	2 (11.1%)
Parents have their own opinions and presumptions	2 (11.1%)
Parents worry so much about their children they go straight to the GP	1 (5.5%)
Unlicensed/licensing issues or specialised medication	
Parents don't trust pharmacist or GP when child is under specialist care	1 (5.5%)
No dose in BNF for unlicensed medication so must rely on advice from consultant prescriber	1 (5.5%)
Lack of confidence when patient is under specialist care due to concern about giving wrong advice	1 (5.5%)
Extreme age restrictions for OTC medication	1 (5.5%)
Paediatric versus adult medication	
Having to double check more compared to adult queries, because of age and weight	1 (5.5%)
Pressure to check appropriateness and suitability of paediatric medication	1 (5.5%)
Other	
Not receiving complete information about the severity of the condition	1 (5.5%)
Contacting prescribers in the event of queries	1 (5.5%)
Taste barriers as there are few alternatives	1 (5.5%)
Not knowing full patient history	1 (5.5%)

5.3.7 Service provisions

Sixty-one percent (9) of pharmacists believed that paediatric medication reviews, counselling services, or the extension of current MUR and NMS services, to allow caregivers to consent to pharmacists speaking to their children, either alone or with their caregiver, would enable pharmacists to better support their paediatric patients, Table 5.6.

Table 5. 6 Services which could be offered to improve paediatric adherence

Services suggested	N/ (%)
Counselling and advice services for patients and caregivers – for newly prescribed and existing medication treatment	9 (56.25%)
Education programmes	2 (12.5%)
Improving knowledge of administration and available formulations	2 (12.5%)
Creation of CPDs or database for more information regarding the use and administration of unlicensed medication	1 (6.25%)
Compliance aids for children	1 (6.25%)
Increased paediatric training for pharmacists during university	1 (6.25%)

Other recommendations suggested that greater emphasis should be placed on paediatric medicine management during the pharmacy degree, so that pharmacists would be better equipped to problem-solve in practice. Compliance aids, education programmes and more accessible knowledge of unlicensed medication administration were also suggested as methods to improve adherence.

5.4 Discussion

The results of this study indicate that caregivers do seek advice from pharmacists relating to their child's long-term condition. Queries from caregivers mainly focused on four areas: how and when to take medication, caregivers concern about medication, managing exacerbations of the condition and side-effects to medication.

Caregivers most commonly queried how and when to give medication to their child. In this study, children were predominantly aged between 5 to 10 years old and medication administration responsibility is still likely to lie with the caregiver [216]. Therefore, caregivers administering new medication for either new or existing conditions need additional support to correctly and safely give medication to their child.

Concerns about medication side-effects were not limited to a specific medication or condition. Caregivers sought advice regarding medication side-effects and how to manage them. In comparison to the systematic review in Chapter 2, non-adherence due to medication side-effects was reported in twelve studies (60%) and was a major cause of medication avoidance. The results from the current study are supported by existing literature which identified that caregiver concerns about medication commonly occur across a range long-term conditions and are often regarding the perceived effectiveness of their child's medication and concerns about medication side-effects [196].

The consensus study with healthcare professionals in Chapter 3, rated that non-adherence due to side-effects of medication was not a common adherence barrier observed in practice. This may be due to side-effects being self-limiting or the patient and carer may seek advice from other health professionals, such as community pharmacists [217]. Therefore, side-effects may be resolved before they attend their appointments or they are not addressed because issues such as medication side-effects are not discussed at appointments.

Pharmacists in this study had minimal interaction with children or adolescents and mainly engaged with parents, as parents were not accompanied by their children to the pharmacy on a regular basis. As caregivers are primarily responsible for their child's medication when the child is young, children may be deemed to not have the capacity to understand the information provided by healthcare professionals, therefore are not present at the pharmacy with their parent [196, 218]. Additionally, caregivers may seek to alleviate their own concerns about their child's medication or look for support to ensure their child's condition is managed, therefore, caregivers may visit the pharmacist to address their issues and the presence of their child may not be necessary.

Pharmacists suggested that advanced pharmacy services could help with adherence difficulties as it would allow for time to be dedicated to speaking in-depth with caregivers and their children about medication use and allow for a discussion in which concerns and potential problems can be managed. However, pharmacists also reported a lack of confidence to deal with specialised and unlicensed medication. This led to concerns about providing caregivers with incorrect information and advice. Their lack of confidence and their perceived inability to help caregivers to the standard they wish to, may have also resulted in their belief that the public perception of pharmacists is less well regarded when it's relating to more specialised medication. The results of this study are similar to an existing study which also found that pharmacists' confidence in providing public health services was low, due to lack of time, resources and an expectation that service users would have negative feedback [219], however, there was public satisfaction regarding the health-care services provided by pharmacists. This is similar to the opinions caregiver had of community pharmacists in Chapter 4, which were positive about the pharmacists' ability to help them with their child's medication. Therefore, further work may consider

investigating why pharmacist's self-perception and confidence is low compared to caregiver and public opinion.

Although the number of queries received by pharmacists over a four-week period were few, the nature of the queries, such as questions about dosing, medication use and managing acute symptoms can be overcome by simple interventions. The clinical support that caregivers need can be easily fulfilled by pharmacists when dispensing a new medication or by having targeted paediatric services. This can reinforce the caregivers and child's knowledge, reinforce the need for medication, ensure proper use of medication and identify family factors which may lower adherence [217, 220].

The use of public awareness campaigns targeting caregivers and their children with long-term medication could encourage them to visit the pharmacy to review their medication, raise awareness about paediatric medication issues and signpost pharmacies as a place where caregivers and their children can receive healthcare support [221]. Caregivers primarily collect their child's medication and frequently engage with the pharmacist [218]. Caregivers view community pharmacists as easily accessible with the ability to provide information and the potential to simplify information, so their child can understand information that their doctor sometimes complicates too much for the child to understand properly [218, 220]. Therefore, pharmacists are in a prime position to offer paediatric services.

Receiving information about a newly prescribed medication promotes good adherence [222], however only a certain degree of information is retained following a consultation and only 64% of patients retain all the basic information provided by the practitioner regarding a new prescription [223]. In situations where patients and their caregivers need additional advice and support, pharmacists are able to reaffirm information and provide additional counselling.

5.4.1 Limitations

With the limited number of pharmacists, locations and by focusing on a single-service, it is difficult to generalise the findings of this study to other aspects of pharmacy practice. Furthermore, during busy times in the pharmacy, there is potential for entries to be missed, resulting in incomplete entries. This was identified as a limitation based on feedback from the pharmacists involved in the study. Furthermore, the written account may be too brief in relation to the encounter, especially if there is not enough time to write the query.

However, the exploratory findings of the study add to the understanding of the problems of managing adherence issues in community pharmacies and highlight the issues that pharmacists have and possible services which can limit adherence problems.

5.5 Conclusion

Pharmacists need to utilise methods to increase engagement with caregivers and their children taking long-term medication. Achievable strategies involve making the public aware of the pharmacist's valuable role in paediatric medication management. The establishment of accredited schemes to provide counselling and/or review services to families will dedicate time to ease concerns, improve understanding and knowledge of medication and make clear the benefits of medication adherence on long-term condition management. However, on a basic level, pharmacists need to become more visible and engage more when dispensing new medication to ensure children and their caregivers are able to understand when and how to take their medication.

5.6 Summary

Caregivers most commonly sought advice from the pharmacist regarding inhaler use, medication dosage and to discuss their concerns regarding their child's medication. Pharmacists lacked confidence in dealing with specialised or unlicensed medication queries. A lack of time with the patient and caregiver to discuss issues and caregiver opinions were barriers to pharmacists adequately managing paediatric queries.

Introducing pharmacy services that would focus on providing counselling and advice to paediatric patients and their caregivers was thought to be a potential method to help combat medication adherence issues.

Chapter 6 General discussion

The primary aim of the current research was to extend our understanding of adherence barriers from the perspective of adolescents to children. A further aim was to form an appraisal of the paediatric medication adherence barriers across multiple long-term conditions from the perspective of the patient, the caregiver and the healthcare professional. This was to identify the most common barriers to adherence and to better understand the commonalities and differences between the groups. Another aim was to evaluate the potential role of community pharmacists in providing support to paediatric patients and their caregivers based on caregiver opinions.

The main findings of this research suggest:

I. There is a lack of commonality in the barriers to adherence, either experienced or perceived between the patient, caregiver and healthcare professionals within this research. The healthcare professionals in the Delphi study observed a small proportion of the barriers experienced by caregivers and paediatric patients.

II. Almost 85% of caregivers found pharmacists to have been helpful and supportive in relation to their child's medication and over half of caregivers would see the pharmacist before the GP. Furthermore, over 40% of caregivers would welcome the introduction of information sessions or medication reviews to help with their child's medication issues and management.

III. Community pharmacists most commonly advised caregivers on correct medication administration techniques, managing symptoms and side effects and caregiver concerns. The implementation of paediatric medication

reviews and counselling services for both the caregiver and their child were thought to be interventions which could offer opportunities to reduce adherence issues. The implementation of paediatric medication reviews and counselling services for both the caregiver and their child were services suggested by 56% of pharmacists as interventions which could offer opportunities to reduce medication adherence issues.

6.1 Summary of studies

Study one was a systematic review and included eighteen studies to collate the barriers to paediatric medication adherence using child and adolescent self-reports, across long-term conditions. The review identified several common issues to adherence such as forgetfulness, particularly in children aged over 12 years. This was attributed to daily schedule changes between home, school and extra-curricular activities. Difficulties in organisation and prioritisation for multidrug and/or multiple daily dosing regimens led to missed medication doses. Patient belief that the medication was not efficacious and/or was not needed was a cause of non-adherence. This was related to a lack of perceived clinical benefit of the medication. The experience of medication side-effects was a common cause for non-adherence across all conditions. In addition, the taste of the medication and difficulties in swallowing solid, oral formulations such as tablets and capsules, led to dose avoidance. A distrust of doctors and a feeling that they do not treat their adolescent patients appropriately for their age was a cause of appointment avoidance and poor adherence. Furthermore, a lack of parental support, belief and confidence in their child's treatment was believed to cause poor adherence. A single condition-specific barrier to medication adherence was 'stigma', associated with HIV leading to non-adherence to HIV medication.

Study two used the Delphi technique with healthcare professionals to identify the most commonly observed causes of medication non-adherence in children and adolescent with long-term conditions, as observed from their current clinical practice. The most common observation was that children and adolescents needed constant reminders from their caregivers to take their medication. Medication-taking fatigue, medication taste and an increased the level of responsibility a child or adolescent has for their medication-taking were perceived to be causes of poor adherence. Furthermore, extra-curricular school activities, social events, forgetfulness and parental views regarding medication, were barriers to adherence that healthcare professionals regularly observed. Factors such as the number of medicines and medication efficacy were not regularly observed in practice, however, these were important reasons for non-adherence in the systematic review based on child and adolescent self-reports.

Study three used a cross-sectional design to investigate the barriers to paediatric medication adherence based on caregivers' experience. The questionnaire also evaluated the opinion of caregivers towards community pharmacists and their ability to help caregivers with their child's long-term medication.

The common barriers to adherence, based on caregiver experience, were the heavy reliance by their children on them to ensure that their medication was taken, their child's negative feelings towards taking long-term medication, an increase in their child's responsibility for their medication-taking and their child experiencing medication-taking fatigue. In addition, caregivers' opinion of pharmacists based on past interactions was positive. They felt that pharmacists were helpful, supportive and had enough knowledge to help them with their child's medication.

The final study was an observation study involving community pharmacists. The study sought to understand the frequency and nature of paediatric queries received by pharmacists over a 4-week period. This was to evaluate how often paediatric patients and caregivers used pharmacists to seek help and advice regarding their medication. Furthermore, the pharmacist's opinion was sought to determine their views regarding the introduction of advanced paediatric medication services.

The most commonly occurring queries related to asthma and inhaler techniques, symptom control, how to manage side-effects of their medication, inhaler dosage queries and parental concerns regarding medication and/or the condition. Other common queries were regarding skin disorders such as eczema and how to manage exacerbations of the condition.

Pharmacists felt that a lack of time, caregiver opinions and misconceptions and specialised paediatric treatments were barriers to effectively dealing with paediatric medication queries. Pharmacists suggested that advanced services such as medication reviews for paediatric patients and their caregivers could improve adherence. This is because time could be committed to having proper discussions between the pharmacist, patient and caregiver, as well as looking as looking at appropriateness of prescribing.

6.2 Discussion of findings

The barriers to adherence are numerous and varied from each perspective: the patient, caregiver and the healthcare professional. It may be suggested that the barriers to medication adherence are interlinked, Figure 6.1. The data to produce Figure 6.1 was derived from the results of Chapter 2, Chapter 3 and Chapter 4. The barriers to adherence within the 'Child and adolescent' circle were based on the data in Chapter 2. Specifically, the seven categories that the self-reported barriers were assigned into and the common barriers within each of the seven categories (page 48-52). The barriers to adherence within the 'Healthcare professional' circle was based on the results from Chapter 3. The barriers to adherence with a mean rating of 3.0 and above were included in this circle (Table 3.1). The 'Caregivers' circle is derived from the data in Chapter 4 (Table 4.2) and the barriers with up to 25% caregiver rating of 'often', 'very frequently' and 'always'.

A busy lifestyle involving activities and social events can interrupt the normal routine of medication taking, therefore leading to delays in taking medication or missing the dose entirely. Furthermore, a lack of support and organisational difficulties were common issues for children and adolescents. Support from caregivers to self-care has been shown to be linked to better adherence [42, 46], therefore in situations where this is lacking, it may lead to difficulties in children and adolescents attempting to organise their own treatment. Poor organisation could be another cause of non-intentional forgetfulness, whereby doses are missed due to poor planning, particularly for treatments that require multiple drugs or multiple daily dosing.

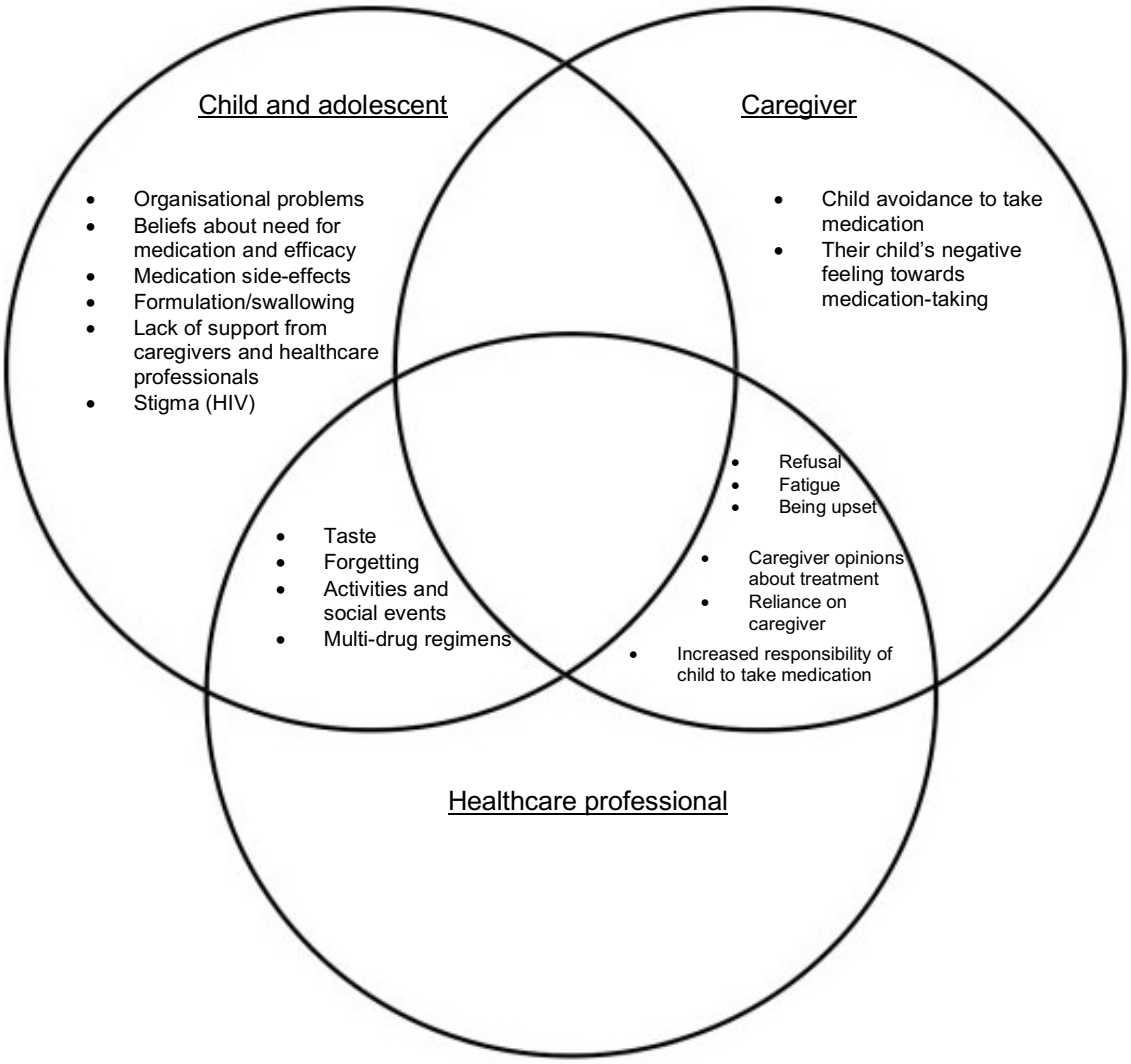

Figure 6. 1 A Venn diagram showing the relationship between the similarities and differences of the most commonly experienced, perceived and observed barriers to paediatric medication adherence in children, adolescents, caregivers and healthcare professionals

Intentional forgetfulness or avoidance of medication-taking is a reasoned choice to not perform a behaviour and can result from several of the main self-reported barriers to adherence by children and adolescents. As seen in Chapter 2, self-reports commonly showed that medication taste and swallowing difficulties with oral medication were reasons for non-adherence. These barriers can make medication-taking difficult, which

negatively impacts adherence [144, 224]. Therefore, to minimise the difficulties the choice is made not to take the medication.

Side-effects can also have a negative impact and lead to intentional forgetfulness, as the concern about medication side-effects becomes greater than the perceived benefit of medication-taking [52]. Patients experiencing negative effects from the medication may experience a loss of confidence in the treatment. Therefore, if medication is not taken, the side-effects can be avoided. The lack of efficacy, either real or perceived, leads to a belief that the medication is not beneficial. If it is thought that the medication does not seem to work then it will not be used as there is no motivation to be adherent.

In comparison, caregivers perceived barriers to adherence as their child's refusal and negative emotions towards medication-taking, as seen in Chapter 4. However, this could be due to the formulation or taste of medication, as was self-reported by children and adolescents in Chapter 2.

Furthermore, the reliance of younger children on caregivers was a barrier to adherence as well as increasing responsibility for medication-taking as children become older. This may suggest that even with increasing age and responsibility, the child still wants or needs caregiver input. This also relates to child and adolescent self-report findings in Chapter 2, which found a lack of caregiver support as a barrier to adherence.

Therefore, it can be suggested that the barriers to adherence do overlap, or that there could be commonalities between caregivers and children and adolescents, but as the perspective is changed, the term used to describe the barriers to adherence may differ and therefore be perceived as different.

An alternate explanation for the differences in expression between the studies may be related to the age of children and adolescents. The caregivers' children in this study were younger in age compared to the participants in the systematic review, who were

predominantly adolescents, therefore potentially already more independent and autonomous, experiencing different adherence problems, compared to children.

Healthcare professionals (HCPs) were seen to partially observe adherence barriers in caregivers and in their paediatric patients. HCPs observed that formulation issues and multi-drug regimens were problems to adherence, as well as the impact of lifestyle on medication-taking in children and adolescents. They also observed that caregivers experience their child refusing to take medication, medication-taking fatigue and increasing responsibility for medication-taking as adherence barriers. Caregivers' opinions of medication were not only a barrier to adherence for healthcare professionals, but also the findings from Chapter 5, in which pharmacists also express caregivers' opinions as a barrier towards adequately addressing adherence barriers. Furthermore, caregivers self-reported in Chapter 5 that their opinion of their child's medication would determine if they would give their child medication or not.

Caregivers voicing their opinions or concerns about their child's medication needs to be addressed in a manner that enables HCPs to successfully overcome their problems or ease their concerns. However, there is a need to create an environment in which the patient can do this and address some of their adherence issues, particularly issues such as side-effects to medication, formulation problems and their beliefs. Existing evidence shows that caregivers of children with long-term medication needs vary in the information they require from their healthcare provider. Caregivers often felt that they received inadequate information, therefore suggesting that healthcare professionals may need to personalise the information they provide, based on the requirements of the caregiver [225].

However, as seen in Figure 6.1, there are no adherence barriers which are common between all three groups, therefore, when medication treatment decisions are made, not all

concerns, ideas and opinions may be considered. However, a possible explanation for there being a lack of common adherence between the groups may be because of the settings used to collect data.

The HCPs participating in the Delphi study (Chapter 3), were predominantly in secondary care or from condition specific clinics, therefore may see patients with more severe conditions and therefore have more problems. In contrast, the caregivers were from a community based setting and therefore, may have children with less severe conditions. The children and adolescents participating in the studies included in the systematic review (Chapter 2) were also mostly recruited from their specific condition-related clinics, with increased severity and as a result have more adherence barriers.

Therefore, future work should consider using the same setting for all three groups and form comparisons of the adherence barriers.

In this research, no adherence barrier was common between all three groups, especially between caregivers and children and adolescents. This highlights the need to have better communication between groups, so that there is better awareness of the barriers that each person faces, particularly within the same household. This is to promote a more cohesive partnership and support between caregiver and child. A healthcare professional's ability to provide adequate information, interpersonal sensitivity, and partnership-building are associated with more truthful adherence reporting, better adherence, greater satisfaction, and more positive evaluations of health care quality [68]. In addition, as HCPs deem caregivers opinions and views to be barriers to adherence, more work in this area is needed to determine why caregiver views are restricting proper adherence resolution and what can HCPs do to effectively work through caregiver concerns.

An intervention study trialled aspects of 'Social Learning Theory' to improve adherence in children with asthma, the study used strategies such as, enhancing self-efficacy, improving

problem-solving, self-monitoring and goal-setting [226]. The study showed a 90% increase in children appropriately using prescribed medication. The underutilisation of medication decreased by 100% and an 87% decrease in children not using their medication at all. The study also showed that individualised interventions can significantly improve adherence. Although it was conducted in a home-based environment, similar education based services can be implemented in a community setting, along-side or by extending existing services.

6.3 Implications of the research and further work

This research recommends the introduction and evaluation of community-pharmacy based paediatric services which focus on reviewing and educating both paediatric patients and their caregivers on new and existing medication. Any new service should focus on reducing patient's and caregiver's concerns, discussing implications of medication-taking on lifestyle, reducing administration difficulties and helping with strategies to improve medicines management in the adolescent patient.

The commissioning of new NHS services is a pivotal way of ensuring that healthcare professionals are providing services that are meeting the current needs of the population and can improve the quality and outcomes of patient care [211, 212, 221]. Over the last decade, the predominant focus of newly commissioned services has been to encourage patients with long-term conditions to manage their medication appropriately and for healthcare-professionals to minimise adherence-related issues, manage inappropriate prescribing to vulnerable patients and to limit the experience of adverse effects. The delivery of these services has commonly been from community pharmacies, due to their unique placement within the community and pharmacists being part of a patient-centred profession with expertise in medicines. Advanced pharmacy services such as Medication Use Reviews (MUR) have been shown to be beneficial in increasing patient education,

minimising hospital admissions and reducing costs through reducing medication waste [98, 227]. Studies have shown that pharmacist-led interventions in adults with long-term conditions have successfully identified medication and lifestyle problems [211, 212, 221]. Interventions that provide education, counselling and monitoring can significantly improve adherence [156, 228, 229]. Focusing on specific conditions, community pharmacist-led interventions have shown improvements in adherence in adult patients with hypertension [230], asthma [231] and T2DM [232]. Furthermore, healthcare professionals can also offer support to patients that have difficulties in remembering to take medication and/or need additional support to manage their condition. The use of text messaging has been used as a simple and effective way to deliver reminders and support messages to children and adolescents with type 1 diabetes mellitus, if forgetting is an issue [233]. The deliverance of social and familial support is also effective in overcoming conflict and promoting strategies with which families can work cohesively [61, 68].

The management of long-term paediatric conditions such as asthma and diabetes are highlighted in detail by NICE guidelines. These guidelines highlight the importance of involving families and caregivers in supporting their children to manage their treatment effectively [18, 21]. Furthermore, they outline the role of healthcare professionals in ensuring that there are appropriate and patient-focused services available and care provided by multidisciplinary care teams. Considering this, it is surprising that there are no nationally accredited advanced pharmacy care services, which are specifically tailored to paediatric patients and their caregivers. In contrast, there are numerous studies highlighting the effectiveness of pharmacist interventions in a hospital setting. These interventions have focused on reducing prescribing errors [234, 235] optimising treatment [236] and educating caregivers to improve medication adherence [237].

Therefore, further work in this area should focus on constructing a pilot study to evaluate the outcomes of a paediatric medication service on improving adherence, reducing barriers to medication adherence and defining the role of community pharmacists in supporting paediatric care. In addition, due to the number of queries caregivers had regarding asthma inhalers and symptoms, any piloted service should have a strong focus on asthma. The aim of the service should be to improve asthma control, avoid hospitalisation risk and systemic corticosteroids need due to poorly controlled asthma [238].

Furthermore, these results have a relevance to paediatric secondary care services, as healthcare professionals only observed some adherence issues in practice, with barriers significant to adherence in adolescents potentially being missed. A review of the consultation technique between healthcare professionals, the patients and the caregivers should be conducted to determine the strategies used to identify adherence issues and the intervention methods used to address them.

6.4 Limitations of the research

A main limitation of this research was the low sample size, specifically in Chapter 4, where data collection was limited due to the number of pharmacies willing to participate. Therefore, finding statistically significant relationships within the data was more difficult.

The barriers and factors used to address adherence issues were the same across studies. Although this offered consistency and made comparisons easier, many adherence items overlapped and may have caused participant fatigue from answering too many similar questions.

Furthermore, many long-term conditions were under-represented by this project, either because of a lack of existing studies specific to this area to include in the systematic review or because of the low percentage of children and adolescents in the population with a

specific condition, therefore making it difficult to capture this when the studies were active. Therefore, this limits the generalisation of the findings across conditions, although the initial aim of the study was to filter and identify adherence barriers generally across various long-term conditions.

Although the research was aiming to extend the understanding of medication adherence barriers in children, there was insufficient published literature that included self-reported barriers in children. This resulted in a greater proportion of adolescent studies being eligible for inclusion in the systematic review (Chapter 2). Therefore, the results cannot be generalised to the child population.

6.5 Conclusion

This research has provided a comparative overview of how different perspectives can impact the way paediatric adherence barriers are seen, experienced and potentially addressed. Exploring the communication techniques between the healthcare professional, patient and caregiver may be effective in identifying areas of improvement. Furthermore, piloting an extension of the current medication review services to paediatric medicine may address some of the known adherence barriers and improve medication use and promote better health outcomes.

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Appendices

Appendix A: Critical appraisal tables for Chapter 2

Criteria	Edgecoo mb	Koster	Hommel	Penza-Clyve	Naimi	Johnston -Roberts	McAllister	Modi '09	Estripeuat
Clear statement of research aims	N	Y	Y	Y	N	Y	Y	Y	N
Justification of research design chosen	N	Y	Y	Y	N	N	Y	N	N
Research process is logical and/or reliable	Y	Y	Y	Y	Y	Y	Y	Y	N
Methodological rigor Inc. use of validated scales/self-reports	Y	N	Y	Y	Y	Y	Y	Y	N
Outline of a well conducted and accurate sampling strategy	Y	Y	Y	N	Y	Y	Y	Y	N
Refusal and withdrawal of participants stated.	Y	N	Y	N	Y	N	Y	N	N
Rigorous and detailed data collection process	Y	Y	Y	N	Y	N	Y	Y	N
Rigorous and detailed data analysis	Y	Y	Y	Y	Y	Y	N	Y	Y
Clear statement of findings	Y	Y	Y	Y	Y	Y	Y	Y	N
The data is representative of the views of the participants	Y	Y	Y	Y	Y	Y	Y	Y	N
Findings are transferable or there is generalisability to other specific settings?	N	N	N	N	N	N	N	N	N
Researcher bias and influences have been considered?	Y	Y	Y	Y	Y	N	N	N	N
There Is enough reporting detail?	Y	Y	Y	Y	Y	Y	N	Y	Y
Conclusion is detailed and fits the data	Y	Y	Y	N	Y	Y	Y	Y	Y
Conclusion considers existing assumptions, current relevance and future research direction?	Y	N	Y	N	Y	Y	Y	Y	Y
Comments									Unknown how questionnaire was developed or how random selection was done
High/Low quality	High	High	High	High	High	High	High	High	Low

Criteria	Kitney	Greenley	Gray	Van Dellen	Buchanan	Modi '06	Khan	Chandwani	Logan
Clear statement of research aims	Y	Y	Y	Y	N	Y	Y	Y	Y
Justification of research design chosen	N	N	Y	Y	N	N	N	N	N
Research process is logical and/or reliable	Y	Y	Y	Y	Y	Y	Y	Y	Y
Methodological rigor Inc. use of validated scales/self-reports	Y	Y	Y	Y	Y	Y	Y	Y	Y
Outline of a well conducted and accurate sampling strategy	N	Y	Y	Y	Y	Y	N	N	Y
Refusal and withdrawal of participants stated.	N	Y	Y	Y	N	Y	N	Y	Y
Rigorous and detailed data collection process	Y	Y	Y	Y	Y	Y	Y	Y	N
Rigorous and detailed data analysis	N	Y	Y	Y	Y	Y	Y	Y	Y
Clear statement of findings	Y	Y	Y	Y	Y	Y	Y	Y	Y
The data is representative of the views of the participants	Y	Y	Y	Y	Y	Y	Y	Y	Y
The findings are transferable or there is generalisability to other specific settings? (Validity of the findings/generalisability)	N	N	N	Y	Y	N	N	N	Y
Researcher bias and influences have been considered?	N	N	N	N	N	N	N	N	Y
There Is enough reporting detail?	Y	Y	Y	Y	Y	Y	Y	Y	Y
The conclusion is detailed and fits the data	Y	Y	Y	Y	Y	Y	Y	Y	Y
The conclusion considers existing assumptions, current relevance and future research direction?	Y	Y	Y	Y	Y	Y	Y	Y	Y
Comments									
High/Low quality	High	High	High	High	High	High	High	High	High

Appendix B: Participant information sheet and phase 1 Delphi questionnaire for Chapter 3

University of Brighton

Information sheet

You are invited to take part in a research study aiming to identify important patient related factors in paediatric adherence. Before you decide whether or not to take part, please read the following information. If you have any questions, please do not hesitate to contact the research team using the contact details provided at the end of this information sheet.

What is the purpose of the study and why should I take part?
We are particularly interested in finding out about children's medication taking behaviour and understanding what affects medication adherence. As vital members of the healthcare service, you are in an excellent position to help us and your participation will be greatly valued.

Who can take part?
If you are a qualified Nurse, Doctor or Pharmacist that has experience of delivering medication to children or overseeing the administration of medication to children with long term medical conditions.

How long does it take and what do I have to do?
We are running a Delphi exercise with a panel of experts and would like you to give us your opinion on a number of statements relating to paediatric adherence. There will be up to 3 rounds of questionnaires, you will receive feedback after each round is completed. The first questionnaire will take approximately 10 minutes to complete and there are 23 questions overall. After each round the questionnaire will become shorter and quicker to complete. If you do not wish to answer a certain question, please leave this blank. All correspondence is via email, so you will not meet other members of the panel.

If I agree to complete the questionnaire now, can I still change my mind?
Participation is voluntary and you are free to withdraw at any time. In this case, simply do not submit the questionnaire. Any unfinished questionnaires will be discarded.

Will my answers and identity be anonymous and confidential?
Yes. All responses will be anonymised before being summarised and used. The completed questionnaire will only be seen by the researcher and research supervisors, who will keep your individual responses confidential.

Are there any risks involved in taking part?
There are no identified risks involved if you chose to take part in this study. However, if you experience any negative emotions and feelings, we recommend that you stop filling in the questionnaire and withdraw your participation. If you wish to speak to someone, then please contact the researchers on the contact details provided below.

What will happen to the results of the research study?
The results of the study will be used to further develop the research project and the results will feature in a final report which will be submitted to the University of Brighton for educational purposes. As the answers

you provide are anonymous, you will not be identifiable in any written work at any stage of the research.

What if there are any problems?

If you have a concerns or complaints about any aspect of this study, please speak to the researcher Nafeesa Ullah (N.Ullah1@uni.brighton.ac.uk) or the research supervisor, Dr Angela Macadam (A.Macadam@brighton.ac.uk) who will do their best to answer your questions.

Contact Details: The University of Brighton, School of Pharmacy and Biomolecular Science, Huxley Building Room 608, Moulsecoomb, Lewes Road, BN2 4GJ

The following pages contain a number of statements relating to children with long term medical conditions, requiring on-going treatment with medication e.g. asthma and diabetes.

Each statement has been identified in research literature as a factor which influences medication adherence in children. Please read each statement and rate how frequently you see such factors influencing adherence in your professional experience of working with children with long-term medical conditions.

(5) Always
(4) Very frequently
(3) Often
(2) Seldom
(1) Never

Please answer each question as best as you can, if there are any questions that you do not wish to answer or are unsure about, then you may leave these blank.

Factors influencing adherence in children	**Always (5)**	**Very frequently (4)**	**Often (3)**	**Seldom (2)**	**Never (1)**
Children's activities or social events					
Other people noticing them taking their medication					
Becoming more responsible for their own medication					
Avoiding side-effects					
Avoiding effects of medication to their physical appearance					
Becoming tiresome of taking long term medication					
Dose avoidance					
Forgetting					

Not knowing how and when to take their medication					
Busy with other things					
Difficulty in sticking to a fixed medication schedule					
Needing constant reminders from their parents/caregivers to take their medication					
Difficulty in swallowing medication					
Having too many pills					
Taste of medication					
Heavy reliance on their parents/caregiver to ensure medication is taken					
Feeling upset and frustrated with having to take regular medication					
Refusal to take medication					
Having a friend to talk to about their medication/condition					
Feeling that their medication is not helping them feel better					
A child's happiness with its healthcare team					
The level of responsibility children have over their medication					
Parental views strongly impacting whether or not a child takes their medication					

Thank you very much for your time in completing this questionnaire. Please return it to Ms. Nafeesa Ullah at N.Ullah1@uni.brighton.ac.uk

Appendix C: Results of phase 1 Delphi and phase 2 questionnaire for Chapter 3

University of Brighton

Questionnaire 2

Thank you very much for completing the first questionnaire and telling us your experiences of what affects adherence in children. We collected responses from 23 healthcare practitioners and have summarised their ratings below. The factors with the highest ratings (indicating more of you seeing it in practice) are now at the top of the list and those rated as the least often seen at the bottom.

Factors influencing adherence in children	**Mean rating**
Needing constant reminders from parents/caregivers to take medication	3.65
Becoming tiresome of taking long term medication	3.52
Taste of medication	3.43
Becoming more responsible for their own medication	3.39
Children's activities or social events	3.26
Forgetting	3.17
Parental views on the child's medication	3.17
Feeling upset and frustrated with having to take regular medication	3.13
Refusal to take medication	3.04
Difficulty in sticking to a fixed medication schedule	3.00
Busy with other things	2.87
Difficulty in swallowing medication	2.87
Avoiding side-effects	2.70
Other people noticing them taking their medication	2.61
Not knowing how and when to take their medication	2.57
Having too many pills	2.35
Feeling that their medication is not helping them feel better	2.30
Dose avoidance	2.22
A child's satisfaction with its healthcare team	2.22
Not having a friend to talk to about their medication/condition	2.00
Other: Wrong device in asthma patients	0.22
Other: Teenage/adolescent poor compliance problem	0.22

Other: age; younger age more compliant	0.17
Other: comorbidity affect/influence drug intake	0.17
Other: Parents not giving medication	0.13

Please indicate your level of agreement with the order of these factors in predicting adherence to medication in children using the scale below.

Please tick in the appropriate box to indicate how much you agree with the order of factors:

Agree	Moderately agree	Neutral	Moderately disagree	Disagree

If you have rated your agreement as either 'neutral', 'moderately disagree' or 'disagree', please could you tell us why?

Thank you very much for your time in completing this questionnaire. Please return it to Ms. Nafeesa Ullah at N.Ullah1@uni.brighton.ac.uk

Appendix D: Ethical approval letter for Chapter 3

School of Pharmacy &
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9 February 2016

APPLICATION FOR ETHICAL APPROVAL FOR PROJECT PROPOSAL

The validation of patient centred factors known to impact medication adherence in paediatric populations.
The School Ethics Committee has approved the above application. There are no ethical issues with this proposal.

Yours sincerely

Dr Anna Guildford

Chair, School of Pharmacy and Biomolecular Sciences Research Ethics Committee.

Appendix E: Participant information sheet and questionnaire for Chapter 4

University of Brighton

Information sheet

You have been invited to take part in an exciting research study about your experiences of caring for a child who needs regular medication. Before you decide whether or not to take part, please read the following information. If you have any questions, please do not hesitate to contact the research team using the contact details at the end of this information sheet.

What is the purpose of the study and why should I take part?
We are interested in finding out about children's medication taking behaviour and your thoughts on pharmacy services. Your participation will be greatly valued and will help us to gain knowledge of medication taking habits and trends in children.

Who can take part?
If you are the caregiver of a child aged between 5 - 16 with a long-term medical condition which needs regular medication.

Who cannot take part?
If your child has a severe learning disability, unfortunately you will not be able to take part but we thank you for your interest.

How long will the questionnaire take?
It will take approximately 5 minutes to complete this questionnaire, some questions are very quick to answer, while others may take some thought. If you do not wish to answer a certain question, please leave this blank. There are 4 brief parts to the questionnaire.

If I agree to complete the questionnaire now, can I still change my mind?
Yes, participation is voluntary and you are free to withdraw at any time. Simply do not submit the questionnaire, any unfinished questionnaires will be discarded.

Will my answers and identity be anonymous?
Yes, your answers are completely anonymous – the researcher will not know who has completed the questionnaire. The completed questionnaire will only be seen by the researcher and research supervisors.

Are there any risks involved in taking part?
It is possible that in reflecting on your experiences you may have some negative emotions and feelings. If you feel yourself becoming distressed, we recommend that you stop filling in the questionnaire and withdraw your participation. If you wish to speak to someone about the questionnaire, then please see the onsite Pharmacist or contact the researchers on the contact details provided below.

What will happen to the results of the research study?
The results of the study will be used to further develop the research project and the results will feature in the final report. As the answers you provide are anonymous, you will not be identifiable in any written work.

What if there are any problems?

If you have a concerns or complaints about any aspect of this study, please speak to the researcher Nafeesa Ullah (N.Ullah1@uni.brighton.ac.uk) or the research supervisor, Dr. Angela Macadam (A.Macadam@brighton.ac.uk) who will do their best to answer your questions.

Contact Details:

The University of Brighton, School of Pharmacy and Biomolecular Science, Huxley Building Room 608, Moulsecoomb, Lewes Road, BN2 4GJ

Please detach this sheet and keep it for your future reference

A brief questionnaire to understand caregivers experience of giving medication to children and of their opinions of community pharmacists

This questionnaire is made up of four parts and is aimed to find out your experiences of giving medication to your child. It may take 4 or 5 minutes to complete all the questions, however, if there are any questions that you do not understand or do not wish to answer, you may leave these blank.

If you have more than one child with a long-term illness, you may complete a questionnaire for the child you believe has more problems with their medication or you may do a questionnaire for each child, the choice is entirely yours.

Part A: This part is to get to know your child a little better

A1. How old is your child? _____

A2. What gender is your child?
☐ Male
☐ Female

A3. What medical condition does your child suffer from? _____

A4. How long have they had this condition?
☐ Less than a year
☐ 1-2 years
☐ 3-4 years
☐ 5 years or more

A5. How many different medicines does your child take on a daily basis for this condition?
☐ 1
☐ 2
☐ 3
☐ 4
☐ 5 or more

Part B: This part is to get to know you a little better

B1. What is your relationship to the child? _____

B2. What is the highest level of education you have completed?
☐ GCSE/O-level
☐ A-levels
☐ Undergraduate degree
☐ Post-graduate qualification
☐ No qualifications/schooling not completed

Part C: The following questions are about your experiences of giving medication to your child

C1. On the scale below, please rate how frequently you experience problems when giving your child their medication.
☐ On a daily basis
☐ On a weekly basis
☐ On a monthly basis
☐ No problems experienced

C2. What are the main problems you encounter when giving your child their medication?

C3. Below is a list of some commonly experienced problems that caregivers face when giving medication to their children, please read each statement and rate how frequently you experience each factor with your child.
Please answer each question as best as you can, if there are any questions that you do not wish to answer or are unsure about, then you may leave these blank.

Factors influencing adherence in children	**Always (5)**	**Very frequently (4)**	**Often (3)**	**Seldom (2)**	**Never (1)**
My child's activities or social events leads to medicine not being taken					
Other people noticing my child taking their medicine leads to missed doses					
As my child becomes more responsible for their own medication they miss more doses					
Medicine is not taken so that side-effects to the medication can be avoided					
Medicine is not taken so that the medication doesn't affect my child's physical appearance					
My child is tired of taking long term medication and doesn't take it					

My child avoids taking their medicine					
I sometimes forget to give my child their medicine					
I don't always know how and when to give my child their medication					
I'm sometimes busy with other things					
I find it difficult to stick to my child's fixed medication schedule					
I need constant reminders to give my child their medication					
If my child has difficulty swallowing medication then I don't give it to them					
My child has too many pills to take and doesn't take all of them all of the time					
My child doesn't like the taste of the medicine and doesn't take it					
My child is heavily reliant on me to ensure their medication is taken					
My child feels upset and frustrated with having to take regular medication					
My child refuses to take medication					
My child has a friend to talk to about their medication/condition					
I feel that my child's medication is not helping them feel better and I do not give it to them					
I'm happy with my child's healthcare team					
My child has some responsibility over their medication					
My opinion of my child's medication will decide if I give it to them or not					

Part D: Your experience of community Pharmacists

D1. What service would you like community pharmacists to offer within the pharmacy to caregivers like yourself or to children with long-term medication and illness, so that it helps you or your child to manage better?

D2. Remembering back to the last time you had to ask the pharmacist about your child's medication, can you please state what this was relating to?

D3. Below is a table of what your general pharmacy experience has been like, please answer as honestly as possible.

	Agree (5)	**Somewhat agree (4)**	**Unsure (3)**	**Somewhat disagree (2)**	**Disagree (1)**	**Not applicable**
I've spoken to the pharmacist about my child's medication before and found them helpful and supportive						
If I had questions about my child's medication, I would see the pharmacist before my GP						
I would feel confident in going to the pharmacist to ask for help or advice about my child's medication						
If I have difficulties with giving my child their medication, I feel that I could ask the pharmacist for advice because they would know what to do						
I think that pharmacists have the skills and knowledge to help me if my child had problems with their medication						
As a caregiver, I feel that I receive enough support from the pharmacist to be able to care for my child						

Thank you for your time in filling in this questionnaire and taking part in this research. Your time is greatly valued.

You may hand your questionnaire back to the pharmacy team or use the addressed envelope provided, should you wish to post it back.

£50 AMAZON VOUCHER PRIZE DRAW

For your chance to win a £50 Amazon voucher, please fill in your details below. Your details will only be used to inform you if you have won, otherwise your details will be confidentially discarded.

Name:

Telephone number/Email address:

Appendix F: Ethical approval letter for Chapter 4

School of Pharmacy &
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Huxley Building
Moulsecoomb
Brighton BN2 4GJ

pabs.ethics@brighton.ac.uk

13th September 2016

APPLICATION FOR ETHICAL APPROVAL FOR PROJECT PROPOSAL
Caregiver's barriers to paediatric medication adherence in long-term illness and their opinion of the role of community pharmacists

The School Ethics Committee has approved the above application. The committee had the following comments for your consideration:

- The project, but would benefit from a revision of its grammar and writing fluency.
- Confidentiality is assured by anonymous questionnaires. Customers can add personal detail for inclusion in a prize draw but these details will be separated from the questionnaire and placed into a ballot box so to maintain anonymity. Alternatively they can choose to send back the full questionnaire with attached details, but this will identify the volunteers and break confidentiality. Suggest removing the option of postage or prize entry by post?

You may now start your project.

The End date for your project is **31st January 2017**. If, towards the end of your project, you realise it will over-run you must apply for an extension, allowing plenty of time for ethics approval.

Yours sincerely,

Dr Anna Guildford

Chair, School of Pharmacy and Biomolecular Sciences Research Ethics Committee.

Appendix G: Participant information sheet and query log for Chapter 5

Information sheet

University of Brighton

Dear Pharmacist,

You have been invited to take part in a study to evaluate the role of community pharmacists in supporting paediatric patients with long-term medication and their caregivers.

Before you decide whether or not to take part, please read the following information. If you have any questions, please do not hesitate to contact the research team using the contact details at the end of this information sheet.

What is the purpose of the study and what do I need to do?
We are interested in finding out how often pharmacists are asked to provide advice and support on paediatric medicine related issues. You are kindly asked to record all the paediatric medicine related queries that you receive for patient aged between 5-16 years old, over a period of 4-weeks.

How long will the study last?
The study is intended to be done over a continuous 4-week period.

If I agree to complete the study now, can I still change my mind?
Yes, participation is voluntary and you are free to withdraw at any time. Simply do not send the evaluation form back, any unfinished evaluation forms will be discarded.

Will answers and identity be anonymous?
We recommend that you keep all information that you enter into the log anonymous, so that patients or carers cannot be identified. We also do not need names of the pharmacists taking part, therefore your identity will also be anonymous.
The completed forms will only be seen by the researcher and research supervisors.

Are there any risks involved in taking part?
No risks have been identified, however, all pharmacists are advised to work according to the SOPs which have been put in place in your store.

What will happen to the results of the study?
The results of the study will be used to further develop the research project and the results will feature in the final report. As the answers you provide are anonymous, no persons will be identifiable in any written work.

What if there are any problems?
If you have a concerns or complaints about any aspect of this study, please speak to the researcher Nafeesa Ullah (N.Ullah1@uni.brighton.ac.uk) or the research supervisor, Dr. Angela Macadam (A.Macadam@brighton.ac.uk) who will do their best to answer your questions.
Contact Details: The University of Brighton, School of Pharmacy and Biomolecular Science, Huxley Building Room 608, Moulsecoomb, Lewes Road, BN2 4GJ

Please detach this sheet and keep it for your future reference

University of Brighton

A service evaluation study: A Pharmacists log of paediatric medication queries over a 4-week period

This study is to ascertain the level of paediatric medication related queries, specifically for patients aged 5-16, with long-term illness that you encounter. These queries can come from parents, caregivers or patients themselves.
In the table below, please record all queries that you receive over the next 4-weeks.

Date	Medication(s) and condition the query is related to	Age and gender of child if known	Nature of the query	Who is making the query? (patient, parent, etc.)	Intervention or advice provided

1. Thinking about the queries you get asked, what is the greatest barrier you face when trying to deal with these paediatric medicine related issues?

2. How confident do you feel when giving advice related to paediatric medication?

- ☐ Confident
- ☐ Fairly confident
- ☐ Unsure
- ☐ Somewhat confident
- ☐ Not confident

3. What service(s) could community pharmacists offer to caregivers of paediatric patients in order to reduce adherence issues and/or other regimen related problems?

4. Do you think that community pharmacists are thought of as being knowledgeable enough about paediatric medicines in the same way as adult medication by the public?

Thank you for your time and participation

Appendix H: Ethical approval letter for Chapter 5

pabs.ethics@brighton.ac.uk

13th September 2016

APPLICATION FOR ETHICAL APPROVAL FOR PROJECT PROPOSAL

Evaluating the role of community pharmacists in supporting paediatric patients with long-term illness and their caregivers.

The School Ethics Committee has approved the above application. There are no ethical issues with this proposal.

The End date for your project is **16th October 2016**. If, towards the end of your project, you realise it will over-run you must apply for an extension, allowing plenty of time for ethics approval.

Yours sincerely

Dr Anna Guildford

Chair, School of Pharmacy and Biomolecular Sciences Research Ethics Committee.