# The use of an electronic alert to reduce excessive prescribing of short-acting beta$_2$-agonists for people with asthma in primary care in east London: a mixed methods study

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# Statement of originality

I, Shauna Mary McKibben, confirm that the research included within this thesis is my own work or that where it has been carried out in collaboration with, or supported by others, that this is duly acknowledged below and my contribution indicated. Previously published material is also acknowledged below.

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# Abstract

The excessive prescribing of short-acting beta$_2$-agonists (SABAs), an indicator of poorly controlled asthma and a risk factor for asthma attacks, remains problematic despite proliferating guidelines for the management of asthma in primary care. Computer decision support alerts are increasingly used to influence prescribing behaviour with guidelines recommending clinicians are alerted to excessive SABA prescribing and patients subsequently invited for a review of asthma control. The aim of this thesis was to determine the effect of an alert to reduce excessive SABA prescribing and explore the potential reasons for the alert's success or failure.

Phase 1 of the thesis involved a systematic review of the literature on the use of electronic alerts to reduce excessive SABA prescribing in primary care. Findings showed limited evidence to support the use of an alert to reduce excessive SABA prescribing when delivered as part of a multicomponent intervention in an integrated healthcare system.

Using a retrospective case-control study design, Phase 2 explored the effect of a single component alert to reduce SABA prescribing in 132 practices across three Clinical Commissioning Groups in east London. Findings showed a small, potentially clinically significant 6% reduction in repeat SABA prescribing within 12 months of the SABA alert ($P<0.001$).

Phase 3 consisted of qualitative research with asthma experts and primary care staff (n=32), to explore the use of an alert to identify excessive SABA prescribing in practice. Using the 'framework' analysis approach, findings showed varying definitions and perceptions of excessive SABA use and inconsistent alert use, influenced by suboptimal design and ambiguous action. Inconsistencies in how excessive SABA prescribing is defined, identified and managed by clinicians in practice were observed.

Findings show that alerts to improve SABA prescribing practice have potential to improve asthma management and clinical outcomes for people with asthma in primary care. Further research is required to determine the impact of an alert on SABA prescribing when optimised and delivered in a multicomponent intervention. Future alert interventions require a collaborative effort between people with asthma, general practice and wider primary care.

# External outputs and publications

Parts of this work have been presented at various national and international conferences and published in the following journals.

### Publications

*1.* McKibben, S., Bush, A., Thomas, M and Griffiths, C. 'Tossing a coin:' Defining the excessive use of short-acting beta2-agonists in asthma - the views of general practitioners and asthma experts in primary and secondary care." *npj Primary Care Respiratory Medicine* 28, 26 (2018).

2. McKibben, S., De Simoni, A., Bush, A., Thomas, M. & Griffiths, C. The use of electronic alerts in primary care computer systems to identify the excessive prescription of short-acting beta2-agonists for people with asthma: a systematic review. *npj Primary Care Respiratory Medicine* 28, 14 (2018).

3. McKibben, S., Bush, A., Thomas, M. & Griffiths, C. The use of electronic alerts in primary care computer systems to identify the over-prescription of short-acting beta2-agonists in people with asthma: a protocol for a systematic review. *npj Primary Care Respiratory Medicine* 27, 30 (2017).

### International Oral Presentations

1. McKibben S, de Simoni A, Bush A, Thomas M, Griffiths C. The use of electronic alerts in primary care computer systems to identify the excessive prescribing of short acting beta2-agonists in people with asthma at *ERS International Congress*, Milan (September 2017).

### National Oral presentations

1. McKibben S, Bush A, Thomas M, Griffiths C. A qualitative study on the use of electronic alerts to identify excessive prescribing of short acting beta$_2$-agonist (SABA) inhalers in people with asthma: the views of asthma experts and primary care staff at *Primary Care Respiratory Society UK Conference* (September 2017).

2. McKibben S, de Simoni A, Bush A, Thomas M, Griffiths C. The use of electronic alerts in primary care computer systems to identify the excessive prescribing of short acting beta2-agonists

In people with asthma: a protocol for a systematic review *at Society for Academic Primary Care Conference*, (January 2017).

3. McKibben S, de Simoni A, Bush A, Thomas M, Griffiths C. The use of electronic alerts in primary care computer systems to identify the excessive prescribing of short acting beta2-agonists in people with asthma: a protocol for a systematic review *at Primary Care Respiratory Society UK Conference* (October 2016).

**Poster presentations**

1. McKibben S, Bush A, Thomas M, Griffiths C. Evaluating the effectiveness of an electronic prescribing alert to identify high salbutamol use among people with asthma: a primary care mixed methods study. *William Harvey Day, Barts and The London School of Medicine and Dentistry*, Queen Mary University of London (September 2017).

2. McKibben S, de Simoni A, Bush A, Thomas M, Griffiths C. The use of electronic alerts in primary care computer systems to identify the excessive prescribing of short acting beta2-agonists in people with asthma: a protocol for a systematic review. *Asthma UK Centre for Applied Research Annual Scientific Meeting*, Edinburgh (November 2016).

**Collaborations**

1. Hull S, McKibben S (co-author), Homer K, Taylor S, Pike K, Griffiths C. (2016) Asthma prescribing, ethnicity and risk of hospital admission: an analysis of 35,864 linked primary and secondary care records in East London. *npj Primary Care Respiratory Medicine* 26. doi:10.1038/npjpcrm.2016.49.

2. Hull S, McKibben S, Homer K, Taylor S, Pike K, Griffiths C. Asthma prescribing, ethnicity and risk of hospital admission: an analysis of 35,864 linked primary and secondary care records in East London. (Oral Presentation) *International Primary Care Respiratory Group 8th World Conference*, Amsterdam, May 2016 and *Society for Academic Primary Care Conference*, Cambridge, January 2016. (Poster Presentation) *European Respiratory Society International Congress*, London, September 2016.

# List of abbreviations

| | |
|---|---|
| ACOS | Asthma –Chronic Obstructive Disease Overlap Syndrome |
| AED | Accident and Emergency Department |
| BDP | Beclometasone Dipropionate |
| BTS | British Thoracic Society |
| CCG | Clinical Commissioning Group |
| CDSS | Computer Decision Support System |
| COPD | Chronic Obstructive Pulmonary Disease |
| CEG | Clinical Effectiveness Group |
| EHR | Electronic Health Record |
| EMIS | Egton Medical Information Systems |
| EPS | Electronic Prescription Service |
| FEV1 | Forced Expiratory Volume in One Second |
| GINA | Global Initiative for Asthma |
| HCPs | Health Care Professionals |
| ICD | International Classification of Diseases |
| ICS | Inhaled Corticosteroid |
| IQR | Interquartile Range |
| IPCRG | International Primary Care Respiratory Group |
| LABA | Long-Acting $Beta_2$-Agonist |
| NHS | National Health Service |
| PEFR | Peak Expiratory Flow Rate |
| QOF | Quality and Outcomes Framework |
| RCT | Randomised Controlled Trial |
| SABA | Short-Acting $Beta_2$-Agonists |
| SIGN | Scottish Intercollegiate Guidelines Network |
| UK | United Kingdom |

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# Chapter 1. General Introduction

This introductory chapter provides a background to the research undertaken and reported in this thesis. Section 1.1 discusses the role of short-acting beta$_2$-agonist (SABAs) in the management of asthma, the current issues regarding the associated risks and the challenge of defining excessive SABA use. Section 1.2 discusses current SABA prescribing practice in relation to evidence-based guidelines and the varying roles of primary care staff in asthma management. Section 1.3 explores the increasing role of computer decision support system (CDSS) in the management of asthma and the associated challenges. Section 1.4 sets out the thesis structure including the research question(s), rationale and aims and objectives of the research undertaken.

## 1.1 Asthma

Asthma is a heterogeneous disease characterised by chronic airway inflammation which manifests in variable respiratory symptoms such as wheeze, shortness of breath, chest tightness, cough and expiratory airflow limitation.[1] Symptoms commonly vary over time and in intensity. When inhaled, SABAs activate beta$_2$-adrenergic receptors causing the relaxation of smooth muscle in the lungs resulting in dilation and opening of the airways providing relief of asthma symptoms.[2]

### 1.1.1 Asthma prevalence

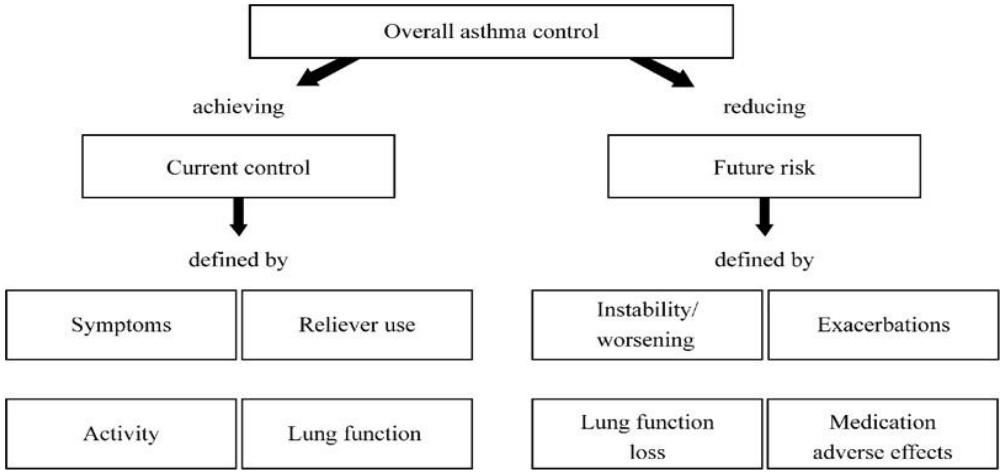
Asthma is one of the most common long-term conditions in the world. An estimated 339 million people globally are thought to have asthma, with approximately 5.4 million people in the UK affected.[3,4] Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) suggests the UK has one of the highest asthma prevalences in the world.[5] Globally an estimated 21% of adults and 14% of children experience asthma symptoms.[3,6] However in the UK, the lifetime prevalence of patient-reported symptoms suggestive of asthma is approximately 29.5 % (18.5 million people).[7] Despite recent analysis suggesting a plateau in new diagnoses of asthma particularly in children, the lifetime diagnosis and prescription of asthma-related medication in

primary care continues to rise.[8] Furthermore, research indicates a disproportionate prevalence in the burden of asthma among people of ethnic minority populations. In a review of asthma outcomes among ethnic minorities in the UK, Netuveli *et al.,* identified that people with asthma from Black and South Asian ethnic backgrounds were at substantially increased risk of hospital admission when compared to their White counterparts.[12] More recently in their research on asthma prescribing and risk of hospital admission in inner city east London, Hull *et al.,* identified that Black and South Asian ethnic minorities had a two-fold risk of being hospitalised for asthma compared to the White population.[13]

### 1.1.2 Asthma control

Asthma control is defined as the extent to which the manifestations of asthma can be observed or have been reduced or removed by treatment.[14,15] Figure 1.1 summarises Bateman *et al's.,* goals for achieving asthma control and reducing future risk.[16] Inhaled corticosteroids (ICS) are used in the management of asthma to maintain asthma control by suppressing airway inflammation and reducing airway hyper-responsiveness. SABA use is both a marker of current asthma control and future risk, with frequent and increasing use associated with poor symptom control,[17,18] increased risk of exacerbations[9,19–24] and potentially asthma-related death.[25–27] When prescribed at an appropriate strength/dose, the regular use of ICS should result in minimal to no asthma symptoms and therefore a decreased need, or ideally no need, for SABAs.[37]

Figure 1. 1 Goals of asthma management[16]



It is estimated that asthma control is suboptimal in over half of the asthma population.[28] Poor asthma control is primarily due to suboptimal management,[29,30] and is associated with a higher risk of exacerbations, increased morbidity, mortality and healthcare costs.[28,31–33,34] Research has consistently reported that both suboptimal ICS use and overuse of SABAs is associated with poor outcomes.[35] However using prescribing data to infer asthma control is problematic for a number of reasons. Prescribing data is a crude surrogate indicator of asthma control that may not accurately reflect current use. For example, despite inhaled medication being prescribed, it cannot be assumed this was dispensed from pharmacy. Furthermore actual inhaler use based on device actuation and delivered dose to the lungs cannot be captured.[36–38] Discrepancies also exist between patient-perceived asthma control and guideline-defined asthma control[28] with binary descriptors of asthma control as 'good' or 'bad', ''optimal' or 'sub-optimal' not reflective of the continuum of asthma care.[15]

### 1.1.3 Short-acting beta2-agonists and risk

The use of SABAs in the management of asthma has not been without controversy with two "epidemics" of asthma mortality attributed to the adverse effects of SABAs.[39] During the mid-1980s in New Zealand, three case-control studies reported an increased risk of death among people using the short acting $beta_2$-agonist, fenoterol.[40–42] Findings suggested an association between the dose of and cumulative exposure to beta-agonists in general, rather than the specific compound of fenoterol.[43,44,45] Between 1970 and 1992 research carried out in nine countries where fenoterol was licenced did not indicate any relation between asthma mortality and beta-agonists in general nor fenoterol in particular.[46] However in 1992, Spitzer *et al*., examined prescription records in the Saskatchewan province in Canada and found an association between inhaled beta-agonists and increased risk of death particularly among those prescribed more than two canisters per month of fenoterol or salbutamol.[27]

In 1994, a study by Suissa *et al.,* carried out in the Saskatchewan Province, concluded the association between inhaled beta-agonists and asthma mortality was observed in those using more than two SABAs per month but also with increasing use i.e. a doubling of monthly SABA use, was a major predictive factor of adverse outcomes in asthma.[26] Other studies have demonstrated that regular use of SABAs, fenoterol and salbutamol, accelerated the decline in clinical disease control and lung function.[39,47]

In the 1990s, enquiries in England and Scotland reported an association between increasing SABA use and asthma deaths. A review of 50 asthma deaths in England between 1992 and 1994 noted that those requiring two or more SABAs monthly were at increased risk [50] In a review of 95 deaths from asthma in Scotland between 1994 and 1996, the management of asthma was judged inappropriate in 41% of asthma deaths[51] with excessive repeat prescribing of SABAs implicated in both reports.

In the most recent confidential enquiry into asthma deaths in the UK, the National Review of Asthma Deaths (NRAD), further implicated the excessive prescribing of SABAs as a preventable factor in 195 asthma related deaths.[25] Between 2012 and 2013, 39% received more than 12 SABAs in the previous year, with 4% having received more than 50 SABAs in the previous year. Despite uncertainty regarding the mechanism of action, evidence suggests a risk-benefit paradox of SABAs; that despite being used to counteract symptoms of airway inflammation, SABAs may have pro-inflammatory effects that enhance, rather than reduce, airway responsiveness.[48,49] These consistent findings indicate the need for urgent action to address current prescribing practices and the provision of asthma care in the UK.

### 1.1.4 Defining excessive use

The association between SABA use, poor asthma control and risk of exacerbation varies in the reporting of the SABA threshold, language and evidence cited in the literature. National asthma guidelines devised by the British Thoracic Society in collaboration with the Scottish Intercollegiate Guideline Network (BTS/SIGN) state that *heavy* or *increasing* SABA use is a risk factor for asthma death.[52] The international Global Initiative for Asthma (GINA) strategy state that *high* SABA use is a potentially modifiable risk factor for exacerbations.[1] BTS/SIGN base use Spitzer *et al.,*[27] Suissa *et al.,*[26] and the UK enquires into asthma deaths as described in the previous section as their evidence base for recommendations[50,51,53,54] whilst GINA base recommendations on evidence from Suissa *et al*., and Turner *at al.*[26,55] BTS/SIGN define poor asthma control as SABA use of more than three times a week[52] in contrast to GINA guidelines which define poor control as use of SABA more than twice a week.[1] In comparison, the NRAD recommendations that one SABA inhaler a month, or more than six puffs a day, is indicative of poor asthma control far exceeds guideline recommended levels of SABA use indicative of sub-optimally controlled asthma.

A number of studies have identified an increased risk of asthma attack and/or hospital admission associated with SABA use at much lower levels than one inhaler a month (12 a year). Studies have suggested an increased risk associated with use of more than three SABAs a year,[56] more than four SABAs a year,[9] more than five SABAs a year,[57] more than six SABAs a year[18,58] and more than nine SABAs a year.[22] More recently Hull *et al.,* identified a progressive risk of hospital admission associated with increasing prescription of SABAs; a two-fold increase in risk of admission when prescribed more than 3 SABAs in the previous year and more than a three-fold increase in risk if prescribed more than 12 SABAs in the previous year.[13]

Studies have also stratified levels of SABA use and associated risk rather than determining risk based on definitive prescribing threshold. Schatz *et al.* derived an asthma control scale based on four levels of SABA use: between 0-2, 3-6, 7-12 and >12 SABAs a year. Patients prescribed between 3 to 6 SABAs per year were at greater risk of asthma exacerbations and poorer symptom control, with increasing risk when prescribed between 7 to 12 SABAs and more than 12 SABAs a year.[18]

In Tavakoli *et al's.,* analysis of the predictors of SABA use in asthma, they distinguished between

excessive and inappropriate SABA use, with excessive defined as using at least 12 SABAs a year whilst the inappropriate use of SABAs was interpreted in conjunction with ICS use, as >2 puffs SABAs and no ICS per week or 9 SABAs and <=100µg/day of ICS per year.[62] A recent 'Asthma Right Care' initiative from the International Primary Care Respiratory Group (IPCRG)[65] has sought to provide clarity and consistency in the messaging used to talk about SABAs. Recommendations have called for a shift to the term 'over-reliance' rather than 'overuse' or 'excessive use' as the latter holds negative connotations that may deter patients from using SABAs when clinically appropriate.

The risks of SABA use have also been defined with the co-prescribing of ICS, with the excessive use of SABAs and underuse of ICS use associated with the use of significantly more health care resources.[22] Lanes *et al.* concluded that patients who received more than one SABA prescription a month the previous year with regular use of inhaled steroids (7+ prescriptions per year), had a 60% reduction in risk of asthma death.[59] The NRAD inferred an association between the under-use of ICS and over-use of SABAs with 49 patients (38%) prescribed fewer than four ICS prescriptions in the year before death whilst 103 (80%) were issued with fewer than 12 preventer inhalers in the year before death. Furthermore, Hull *et al.,* reported the greatest burden of emergency hospital admission for asthma occurred among those prescribed less than 10 ICS inhalers a year with rising number of SABAs prescribed associated with risk of hospital admission.[13] National and international guidelines recommend SABAs are not prescribed in isolation but rather with an appropriate level of ICS to achieve and maintain control of asthma symptoms and reduce future risk.[1,52]

In an assessment of the use of primary care electronic health records in the management of respiratory disease, Ryan *et al'.,*[66] define medication prescribing and medication use as two separate variables that should be used to identify at-risk patient. This suggests that to improve overall asthma control the behaviours of both patient use and clinician prescribing of SABAs should be targeted.

## 1.2 Prescribing

The medication process in primary care is comprised of three stages; medication prescribing administration and monitoring, each involving a multidisciplinary team of professionals, informal

carers and patients.[67] Prescribing medicines is an inherently risky and often complex task,[68] described by Cribb and Barber as 'a balance between the right technical properties, what patients want and the greater good.' [69]

### 1.2.1 Prescription types

Prescribing occurs in a number of ways in general practice: as an acute prescription for a one-off provision of medicine, by repeat prescription for long-term medication use,[70,71] or by repeat dispensing commonly managed by a pharmacist.[72] Paper prescriptions, otherwise referred to as an 'FP10', are historically the most common prescription type. In 2010 the electronic prescription service (EPS) was introduced whereby a prescription is digitally signed by the prescriber and sent via a central network (the Spine) to be downloaded in pharmacy. The purpose of EPS was to improve the efficiency and safety of prescribing, to improve communication in primary care and reduce prescribing workload.[72] However the uptake of EPS has been variable with up to 70% of patients continuing to be issued prescriptions by paper.[73] Despite the purported benefits, the additional training requirements and required revision of procedures have been likely disincentives to EPS uptake.[72]

### 1.2.2 Repeat prescribing

Salbutamol is the most commonly prescribed SABA used for the relief of asthma symptoms.[74] It is the eleventh most commonly dispensed medication in England, with approximately 22 million items dispensed in 2017.[75] In a recent report on repeat prescribing in the UK, it was estimated that up to 80% of all SABAs are issued 'on repeat,' with the management of repeat prescriptions accounting for 20 per cent of a GPs workload.[76] Furthermore, the number of repeat prescriptions issued nationally is estimated to have more than doubled from 5.8 to 13.3 items per patient per annum in the past two decades.[77]

Zermansky identified three tasks in repeat prescribing; prescription production, management control (authorization, compliance, review date, flagging) and clinical control (authorization, periodic review).[79] Robust systems for safe and effective repeat prescribing are required[78] however this is problematic as repeat-prescribing systems vary between practices and require a high degree of local tailoring and judgment from frontline staff.[71,76] In ethnographic observations of receptionists in four general practices, Swinglehurst *et al.* identified repeat prescribing as a complex technology-supported social practice, with receptionists heavily involved in the production and quality and safety of repeat prescriptions.[71]

The "error" and "harm" associated with prescribing and medicines management in primary care is well documented with reducing preventable harm in repeat prescribing a patient safety priority worldwide.[80,81] The NRAD identified that of those prescribed SABA in the year before death 97% were obtained on repeat prescription.[25] This raises concerns regarding the review processes for SABA prescribing in primary care,[72] with concerns regarding the adequacy of control in the review process.[71,79] The NRAD recommended that patients who have requested the maximum number of SABA approved prescriptions are identified and invited to attend for urgent review.[25] In an e-Delphi study on the most important safety features of GP computer systems, there was consensus that practice staff should be alerted to patients either under-using or over-using their medication.[82] A systems approach that combines technology interventions, education and improvement to improve repeat prescribing at both frontline and organisational level is required but currently lacking in practice.[83]

### 1.2.3 Role of pharmacists

Almost two decades ago Zermansky highlighted the role of pharmacists in identifying and managing high risk repeat prescribing.[79] Systematic reviews of pharmacist-led interventions targeted at patients and/or prescribers have shown potential to improve medication use processes.[84,85] In the PINCER trial, general practices were allocated to either (1) simple computer-generated feedback for patients identified by at-risk prescribing (control) or (2) a pharmacist-led multifaceted intervention composed of feedback, educational outreach, and dedicated support (PINCER).[86] Findings showed that a multicomponent pharmacist-led intervention reduced a range of medication errors in general practices. Most recently, Petty highlighted missed opportunities to improve the quality and safety of repeat prescriptions across primary care,[76] yet concerns regarding the management of repeat prescribing persist and the pharmacist's role in asthma management remains underutilised.[79]

The role of community pharmacists in clinical tasks has typically been limited, due in part to national contracts which generate the majority of income from dispensing services.[76] Since 2015, NHS England initiatives have seen an increased role of pharmacists in general practice, mainly to relieve GP pressures driven by workforce changes.[87] This has increasingly involved the delegation of responsibilities for the management of repeat prescriptions and medication reviews from GPs to pharmacists. However in a recent review of pharmacist's intervention in asthma management, Crespo-Gonzalez *et al.* concluded the most common pharmacist interventions continue to be patient education and self-management rather than process interventions.[88]

In 2016, the Murray Review,[90] a review into the utilisation of community pharmacy in England identified that patients and the public still do not benefit from the full range of skills that community pharmacists possess. The review highlighted the underutilised potential for pharmacists in the management of long-term conditions including medicines management. Recommendations included the development of Medicines Use Reviews (MURs) into full clinical reviews in community pharmacy, to include on-going monitoring and follow-up of patients.[90] In Scotland, the role and responsibilities of community pharmacists has already been extended to the management of long-term conditions such as asthma. The Chronic Medications Service (CMS) involves a pharmaceutical assessment and care planning to facilitate pharmacist's monitoring and review of medications. Within the CMS, when medication is dispensed by community pharmacists details are sent to the

corresponding GP practice and the patient's Emergency Care Summary; a national shared electronic patient record system across NHS Scotland which is automatically updated.[91] This gives a more accurate picture of medication use based on items dispensed rather than prescribed.

The Pharmaceutical Services Negotiating Committee (PSNC) have proposed similar roles for community pharmacists in England.[92] This would involve pharmacists being responsible for medication adherence issues, undertaking clinical assessments, medicines reviews and checking for suspected adverse effects. In a recent Cochrane review on community pharmacist services, the impact of pharmacist's management of long-term conditions, the management of hypertension was comparable between pharmacists and GPs.[93] Such findings highlight the potential for pharmacist-led interventions in asthma management as an adjunct or alternative to GP delivered care. However, despite recommendations from the Murray Review, the absence of integrated computer systems limits the sharing of data between primary care service providers. Furthermore, pharmacist-led interventions in asthma management are likely to be dependent on funding, leadership, culture, time and the overcoming of professional boundaries between community pharmacists and GPs.

In the past two decades, the purchasing of medications online through either online pharmacies or alternative sources has become an increasingly convenient and cost saving way to obtain medications. However, there are a number of safety risks linked to the online purchase of medicines outside the traditional supply chain, including insufficient clinical supervision, monitoring and lack of continuity of care.[94] The in online purchasing of medications may therefore limit the opportunity for pharmacist-led interventions in asthma management. However, health care professionals, particularly pharmacists, are ideally positioned to influence such behaviour and reduce risk of online purchasing of medications through tailored interventions for asthma management.[94]

### 1.2.4 Evidence-based asthma guidelines

BTS/SIGN are the mainstay guidelines for asthma care across the UK.[105] However despite the increasing evidence base to guide clinical practice, including the recently published National

Institute for Health and Care Excellence (NICE) guidelines for the diagnosis, monitoring and management of asthma,[108,109] application of asthma guidelines into clinical practice remains problematic.[106,107] It is suggested that inconsistency in guideline recommendations regarding appropriate SABA use and prescribing practice sends a contradictory message to clinicians making guideline application into practice both challenging and confusing.[96] For example, BTS/SIGN recommend that SABAs should not be prescribed without an ICS, thus removing SABAs as the first step of the commonly recognised 1 to 5 stepwise approach in the pharmacological management of asthma.[52] In contrast, NICE advise that SABAs can be used in the first step as sole treatment for asthma.

Most recently, the NRAD identified a failure among clinicians to adhere to national asthma guidelines, in particular the excessive prescription of SABAs, insufficient prescription of ICS and failure to recognise patients at current and future risk of asthma attack.[25] There may be a number of reasons for poor adherence to asthma guidelines in practice including a lack of awareness, lack of guideline knowledge, disagreement with guidelines or external or practical barriers such as lack of time and limited staff resources.[96–99] Continued variability in asthma management across primary care has resulted in increasing calls for one universal guideline to provide coherent and consistent advice to clinicians to improve asthma care.[110–113] Computer decision support systems (CDSSs) in clinical practice have been recommended to increase clinician adherence to evidence-based guidelines[100,101] and to improve the overall efficiency and quality of health care.[102–104]

## 1.3 Computer decision support systems

Electronic health records (EHRs) are defined as digitised health record systems that facilitate the access, storage, display, and retrieval, printing, and sharing of patient's health care information.[114] EHRs can be integrated with computer decision support to improve the quality and safety of patient care through the use of routinely collected patient data.[115] Success of such systems is dependent on use, therefore it is important to understand how these systems work in clinical practice.[116]

### 1.3.1 Defining computer decision support

Wyatt and Spiegelhalter define CDSSs as 'active knowledge systems which use two or more items of patient data to generate case-specific advice.'[117] However defining CDSSs is challenging due to variability in the features and characteristics of such systems in practice. Over 15 years ago, in seminal research on the effective features of decision support, Bates *et al.,* defined CDSSs systems as those which provide "passive and active referential information as well as reminders, alerts, and guidelines."[118] More recent definitions increasingly reflect higher levels of technical sophistication of decision support systems.[119] In a step-by-step roadmap for using CDSSs to improve outcomes, Osheroff *et al.* define CDSSs as that which provides "clinicians or patients with computer-generated clinical knowledge and patient-related information, that is intelligently filtered or presented at appropriate times, to enhance patient care."[104] Therefore important features of such systems are not only the type of information and how it is presented but also when it is presented.

CDSSs are either systems that are stand-alone, or more recently integrated with EHRs as technological capabilities have increased. Integrated decision support uses routinely recorded clinical and demographic data to tailor and target clinician advice for specific populations and disease profiles.[66] CDSS designs range from simple to more complex systems. A simple system may present descriptive text to support clinician decision-making whilst a complex system may include patient data integrated with guidelines or protocols.[119,] CDSSs most commonly include alerts and reminders generated from electronic patient data to guide and assist clinical decision-making.[121,122] Sittig *et al.* identified the majority of CDSSs utilise simple alerts and reminders to assist with decision

making.[125] However in the literature no clear distinction is made between CDSS "reminders", "alerts", and "prompts" with these terms often used interchangeably.[122]

### 1.3.2 Features of effective computer decision support systems

James *et al.,* define effective CDSSs as those which present the right information, in the right format, at the right time, without requiring special effort."[126] Kuperman elaborates that effective CDSSs are those which utilise real time patient specific EHR data to generate alerts integrated at the point of care.[127] The importance of CDSS integration streamlined with workflow was first emphasised in Bates *et al's.,* seminal research *Ten Commandments for Effective Clinical Decision Support*.[118] When such systems use real time patient data to support clinician decision making, patient's are increasingly likely to receive more appropriate and timely care. Maviglia *et al.,* suggest that level of integration with clinical practice will determine the success of alerts but there remains limited guidance on where and how CDSSs should be integrated to improve process and patient outcomes.[128]

The clinical workflow concept has evolved from the manufacturing industry which focused on the completion of a collection of tasks to accomplish a process.[129] In healthcare, workflow describes the point at which clinicians are engaged in an activity of interest, such as prescribing medications, documenting clinical encounters and ordering investigations."[130] Thorough understanding of the clinical workflow processes and when and how to prompt clinicians within workflow strongly increases the likelihood of decision support use.[118] In a study on decision support and GP prescribing, Hayward *et al*. identified that alerts integrated in-consultation often do not align with prescribing workflow, but instead present when prescribing decisions have already been 'justified, negotiated and agreed' with the patient at various points in the consultation.[124] Consideration should be given to the technological, clinical, and socio-technical issues that influence clinical decision making when designing and implementing CDSSs.[120]

The presentation of alerts that interrupt workflow, commonly referred to as 'hard' or modal alerts, have shown a significantly higher effect on outcomes than non-interruptive (passive) reminders, soft or non- modal alerts.[122,137,145,146] In a review of the literature on drug safety alerts, van der Sijs *et al.,* recommend that to facilitate use, alerts should have high specificity and sensitivity and

minimise workflow disruption.[142] Furthermore, increased user acceptability has been observed when alert recommendations could not be ignored.[118,145] This suggests that alert success is dependent not only on when, where and how alert presents but also on the type of information displayed and the ability of the user to act on such information.

Research suggests that success of medication-related decision support is dependent on human factor design.[143] In a review of human factors in the design and implementation of medication alerts, Phansalkar *et al*, suggested that for alerts to be acted upon, they should present in a clinician's visual field, with alert size, colour, and signal words tailored to indicate level of risk.[144] Further suggestions include decision support that presents clinically meaningful, pragmatic, evidence based knowledge that can be actionable rather than ignored. [127]

### 1.3.3 Computer decision support and asthma

Several systematic and narrative reviews have highlighted the potential of CDSSs to improve clinician performance and decrease adverse patient outcomes in chronic disease management.[122,142,147–149] In particular two systematic reviews have focused on the increasing use of CDSSs to improve the management of chronic conditions such as asthma.[150,151] However, it is unclear to what extent decision support has been used to specifically reduce excessive SABA prescribing in asthma is unclear.

In a systematic review of CDSSs in the management of asthma, Matui *et al*.,[150] concluded that systems were ineffective at improving patient outcomes because they were rarely used,[153–155] and users were often not compliant with CDSS advice.[155,158] However, when systems were used, some improvement to clinical outcomes was reported. [152,156] In comparison, in a systematic review on CDSSs and asthma in primary care, Fathima *et al.,*[151] concluded that CCDSs comprised of multiple components such as reminders and education, have the potential to improve the management of asthma when compared to single-target interventions with fewer components. These findings echoed research on the effectiveness of CDSSs for other common chronic conditions such as diabetes and osteoporosis.

In a study evaluating the impact of at-risk registers for severe asthma (ARRISA), Smith *et al.*, used

alerts to identify people at risk of asthma attack.[160] Findings showed the alerts had no significant effect on asthma exacerbations, with 70% of end-users reporting that alerts had limited impact on the management of identified patients despite the wording, appearance and visibility of alerts being customised by practice. Whilst CDSSs alerts are commonly generated in electronic health records to improve high-risk medication prescribing,[68,161] the alerts in the ARRISA study were not specific to SABA prescribing. Recommendations from the NRAD report and leading asthma charity Asthma UK have called for increasing use of CDSSs in the management of asthma prescribing however the use of alerts for excessive SABA prescribing remains unclear.

### 1.3.4 Challenges

Despite advances in technology and design, concerns regarding the usability and relevance of CDSSs remain.[119] Current research gaps in CDSSs include determining optimal specificity and sensitivity of alerts, the personalisation and timing of alerts in the prescribing process and capturing appropriate outcome measures from which CDSS success can be measured.[121] Furthermore, prescribing practices are commonly based on guideline recommended 'best practice' that remain open to interpretation.[127] A predominant issue in CDSS design is clinicians being inundated with alerts of low clinical significance resulting in "alert fatigue."[142,163] Coleman *et al.,* define alert fatigue as cognitive overload and/or desentisation "resulting from alerts consuming too much time and mental energy,"[121,165] This increases the chance that prescribing alerts pertinent to patient safety or of clinical relevance will be overridden or ignored by clinicians. [142,163,164,166] For example, in a review by Van der Sijs *et al.,* clinicians overrode alerts between 49% and 96% of the time.[142] Alert fatigue is often due to the failure of CDSSs to provide patient specific guidance to clinicians at the appropriate time and using an appropriate method of display.[167] Creating a clear and concise alert that displays sufficient information, as well as facilitating appropriate action, presents many challenges as there is no one size fits all approach to decision support systems nor prescribing processes.[127]

In a review of CDSS functionalities, Jones *et al.* concluded that insufficient reporting of the implementation and context of CDSS use makes it difficult to evaluate why some interventions are successful and others are not.[168] Systematic reviews often do not differentiate one type of decision support from another making the evaluation of individual CDSS components challenging.[122,137,168,169] Furthermore, heterogeneity in study design, clinical setting, study population, software

specifications, CDSS workflow integration and process and clinical outcomes is common even when evaluating the same drug or disease.[147]

In a seminal review on the quality and safety of eHealth, Black *et al.,* reported that CDSSs vary on multiple dimensions, including levels of sophistication, detail, data source with variable integration across health services.[120,170] In a subsequent summary of the grand challenges in clinical decision support, Sittig *et al*. emphasised that CDSS use is influenced by the local contexts and healthcare settings in which they are applied.[124] The majority of CDSS evaluations originate from North America, with design and use likely influenced and facilitated by integrated healthcare organisations in an insured healthcare system.[102,103,118,122,137,167,] In contrast, the interoperability of NHS technology systems, including the integration of health and social care records, data sharing and digitisation of patient records across IT platforms has shown limited large-scale success. However, a number of local NHS clinical commissioning groups (CCGs) have successfully moved towards integrated and interoperable health care records, with success attributed to the early buy-in and involvement of clinicians and the role of digital technology in wider transformation plans.[171] The current ability of local healthcare providers to achieve such ambitious plans is however likely to be constrained by one of the most financially challenging and pressured periods in the history of the NHS.

## 1.4 Study rationale

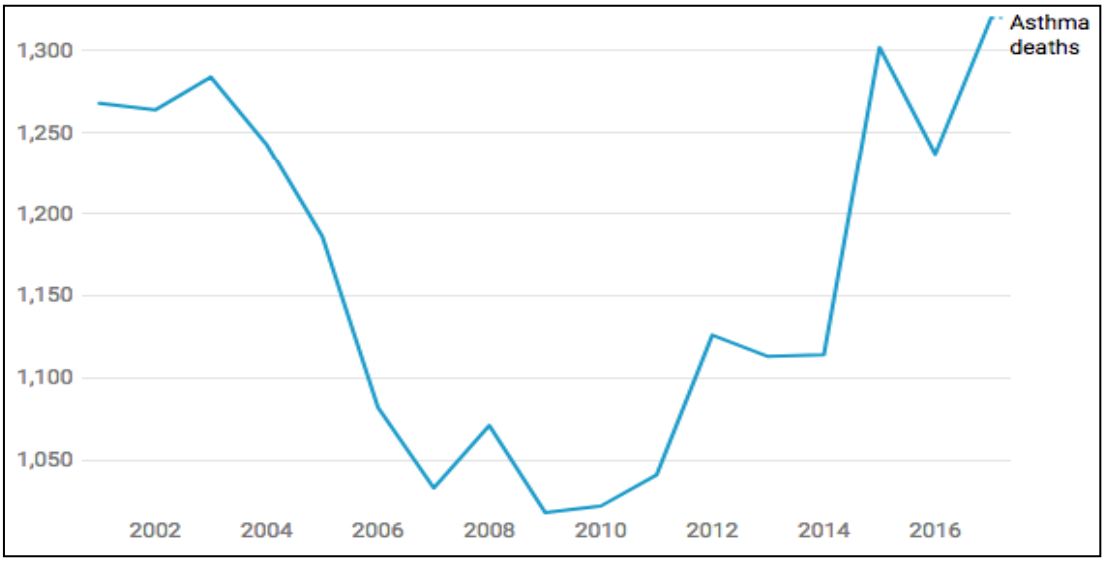
### 1.4.1 Addressing the literature

Despite an increasing number of guidelines for the management of asthma, there is no consensus definition on how many SABAs is problematic. In the literature, the reporting of "excessive" SABAs is variable in terms of quantity and associated risk. The impact of inconsistent messaging on clinician prescribing remains unclear. Furthermore, asthma management is not restricted to GPs but involves members of the wider primary care team including receptionists and pharmacists. Increasing evidence shows the potential to improve the management of asthma and prescribing practices through CDSSs alerts. However, alerts often do not align with decision-making that occurs at various points in clinician workflow. At present the evidence to support the use of alerts in SABA prescribing remains unclear.

### 1.4.2 Current problem

Recent figures indicate that asthma deaths in England and Wales are the highest on record, with an increase of more than 25% from ten years ago (figure 1.2).[172] Asthma mortality is however rare contributing to less than 1% of all deaths globally.[3] Furthermore, the accuracy of death certification was highlighted as a potential limitation of the data analysed in the NRAD report, with the cause of many deaths incorrectly coded as asthma rather than as a result of comorbid disease.[25] Whilst asthma deaths remain shocking, the reliability of data and the analysis and interpretation of asthma death statistics remains challenging.

Figure 1. 2 Trends in asthma deaths in England and Wales (1997-2017)



Source: Office of National Statistics (2018)[172]

Asthma morbidity, defined as the frequency of acute asthma exacerbations, emergency department visits and hospitalisations, remains a burden to health care services and patients.[7] A study by Partridge *et al.* estimated that 75% of hospital admissions for asthma are preventable, with poor prescribing practice a potentially avoidable contributor to both asthma morbidity and mortality.[174]

Two studies on variations in UK hospitalisation rates for asthma identified increasing rates of asthma morbidity among adults and children of Black and South Asian origin.[12,180] However, the limited number of UK studies are out-dated having taken place in the 1980-90s and inclusive of only three broad ethnic groups, namely: Whites, Blacks and South Asians. Recent research by Sheikh *et al.,* suggests that increased hospitalisations among ethnic minorities are likely due to variability in asthma knowledge and awareness, greater severity of asthma, and differences in the quality of care[181] and medication use.[182,183] Understanding such variations is challenging, as ethnic minority groups remain under-represented in asthma research.

Recommendations have called for innovative strategies for the early detection and prevention of asthma attacks in primary care to reduce asthma morbidity and the burden of disease.[7] An assessment of the impact of CDSSs on asthma mortality is beyond the scope of this thesis. However, the role of CDSSs in identifying potentially poor asthma control and the influence of CDSSs on clinician's prescribing behaviour requires further exploration.

### 1.4.3 Asthma outcomes in east London

In London, asthma prevalence is estimated to be lower than the rest of England ranging between 3.5% to 5.7% of the population.[184,185] However, in three densely populated boroughs in inner city east London, mortality from asthma is higher than that of London and England with a rate of 2.75 per 1000 asthma deaths in Tower Hamlets, increasing to 5.41 in Hackney and 5.85 in Newham (Figure 1.3).[186] London has higher hospital admission rates for asthma in comparison to the rest of England despite a lower prevalence of asthma.[184] Within London, crude hospital admission rates in the east London boroughs of Hackney, Newham and Tower Hamlets are above the London average (figure 1.4).[186] Asthma morbidity disproportionately affects people from ethnic minority backgrounds,[12] which may account for the poor asthma outcomes in the ethnically diverse and transient Inner city east London boroughs. Often concentrated in inner-city areas[175,176] ethnic minorities often have poorer continuity with healthcare providers,[177] less familiarity with primary healthcare practitioners[178] and are more likely to present to Accident and Emergency Departments (AED) as a primary source of care.[179]

Figure 1. 3 Asthma mortality rate per 1,000 deaths in east London in comparison to London and England, 2013.[186]

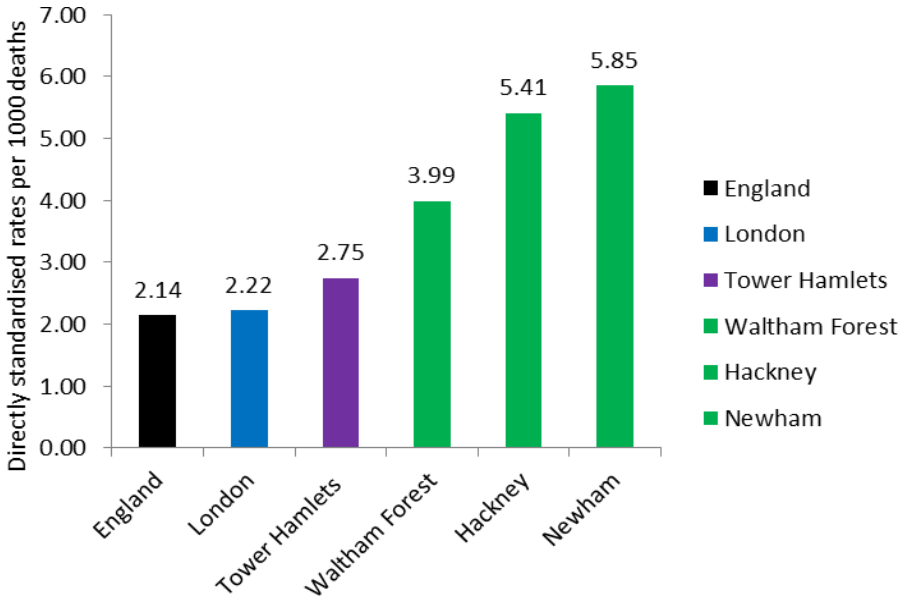
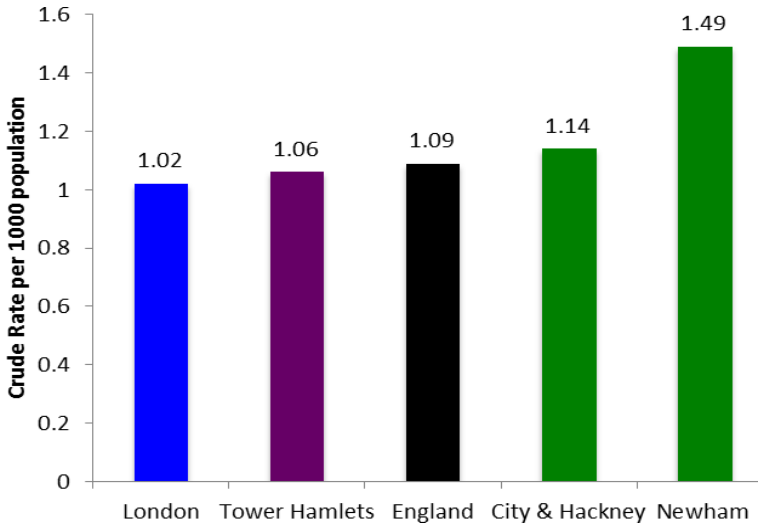


Figure 1. 4 Crude hospital admission rates in Hackney, Newham and Tower Hamlets in comparison to London and England in 2012–13.[186]




### 1.4.4 Framing the research question

The rationale for the framing of this thesis as an evaluation of an alert for "excessive" SABA "prescribing" is described below:

(i) "Excessive" SABAs: this is quantified using the pre-defined EMIS Asthma Medicines Management alert threshold of three SABAs in three month. The description of this threshold as excessive was reflective of the terminology used in the most recent evidence in the NRAD report.

(ii) SABA "prescribing": SABA prescribing is commonly used as a proxy measure of SABA use with terms often used interchangeably in the literature. This is because actual SABA use cannot be determined as it is not possible to capture device actuation and drug deposition in the lungs. For the purpose of this thesis, the term SABA "prescribing" is not used interchangeably with SABA use, as the aim of the thesis is to explore the effect of a CDSS alert intervention on clinician's prescribing behaviour.

## 1.5 Aims and Objectives

This thesis aims to address the gaps in the research in the following ways:

I. To provide a systematic overview of the literature on the use of CDSS alerts to reduce excessive prescribing of SABAs in primary care.
II. To evaluate the effect of a CDSS alert to reduce SABA prescribing and improve asthma management.
III. To explore the views of asthma experts and primary care staff regarding the use of a CDSS alert to reduce excessive SABA prescribing in primary care.

The objectives of this thesis are comprised of the following three contemporaneous stages:

Phase 1: A systematic review of the literature on the use of CDSS alerts to reduce excessive SABA prescribing and to determine the features of alert systems that have the potential to improve process outcomes for healthcare providers and clinical outcomes for people with asthma in primary care.

Phase 2: Evaluate the effect of the Asthma Medicines Management alert (SABA alert) on SABA prescribing in general practices in east London using a retrospective case-control study design, including a subgroup analysis of repeat prescribing and secondary process measures and clinical outcomes of asthma care.

Phase 3: Explore what primary care staff and asthma experts understand by excessive SABA prescribing, identify the extent to which the SABA alert is used and the factors influencing its use, and highlight the roles and relationships between primary care staff in the management of excessive SABA prescribing.

## 1.6 Structure of the thesis

Chapter 1 introduces the background to the study placing it in context within current literature, highlights the current challenges in identifying and managing excessive SABA prescribing and the potential for CDSSs to assist clinicians in practice. This is followed by an outline of the study's aims and objectives of this thesis delivered in three contemporaneous phases.

Chapter 2 sets out the methodology that has been used to inform the design of the thesis. The chapter includes a discussion of mixed-methods research traditions and the application of both quantitative and qualitative methods appplied in this thesis are described, critiqued and justified.

Chapter 3 reflects *Phase 1* of the thesis; a systematic review of the literature on the use of alerts to identify and reduce excessive SABA use. Both the systematic review protocol[188] and the review findings[189] have been peer reviewed and published prior to this thesis. Phase 1 addresses gaps in the literature regarding the use of alerts specifically for excessive SABA prescribing whilst reviewing the impact and the features associated with CDSS alert interventions.

Chapter 4 presents *Phase 2* of the thesis, a case-control study evaluating the impact of the EMIS Asthma Medicines Management alert (SABA alert) on process measures and clinical outcomes of asthma management. This includes an analysis of asthma outcomes of interest at predefined time points before and after the introduction of the SABA alert. Findings across three clinical commissioning groups (CCGs) in east London were analysed collectively.

Chapter 5 presents *Phase 3* of the thesis comprising of a qualitative study with primary care staff and asthma experts. This study provides insight on the perceptions of the problem of excessive SABA prescribing, highlighting the roles of primary care staff in the identification and management of excessive SABA prescribing. It also addresses how the SABA alert is used in practice including the influences and challenges to its use. Phase 3 provides both context and understanding to Phase 2 findings.

Chapter 6 integrates the contemporaneous findings of Phase 1, 2 and 3 of the thesis. Findings of Phase 1 (Systematic Review) and Phase 3 (Qualitative study) are discussed in relation to the findings

of Phase 2 (Quantitative study). A number of recommendations for practice are made, including discussion of recommendations of further work. The chapter finishes with an overall conclusion, summarising the thesis findings in relation to the aims of the research.

# Chapter 2. Methodology

This chapter outlines a general introduction to the methodology applied in in this thesis. Firstly, a description and rationale for the selection of a mixed methods research design is discussed to provide context to the thesis. The contribution of patient and public involvement in shaping the thesis is described prior to a description of the methods applied in this thesis. A discussion of the key philosophical assumptions underlying a particular research tradition precede the presentation and justification of the methods applied. The chapter ends with a summary of how the aims and objectives of the research project will be met whilst acknowledging some of the potential limitations of the methods to be applied.

## 2.1 General introduction to research methodology

Creswell[190] defines methodology as the framework that relates to the entire process of research, whilst the research design refers to the plan of action that links the philosophical assumptions to specific methods e.g. mixed methods. The methods can be defined as the techniques of data collection and analysis, such as a quantitative instruments or qualitative analysis of text data.[191] However, the methodology requires moving beyond descriptions of the research process instead critiquing how the research process had been generated and justified and the philosophical assumptions that underpin the methods applied.

Philosophical assumptions, described by Guba and Lincoln[192] as 'paradigms', underpin the methodological approach adopted by any researcher, depending on the researcher's ontological and epistemological standpoint. Blaikie[193] describes ontology as concerned with what exists, while epistemology refers to the possible ways of knowing what exists based on assumptions about what there is to know or can be known. Therefore, the researcher approaches a subject with a set of ideas (ontology) that determines the line of enquiry (epistemology) examined in a specific way (methodology).[192]

Health services research, is defined by Bowling[194] as "...an applied field of multi-disciplinary research concerned with the relationship between the provision, effectiveness and efficient use of health services and the health needs of the people." This type of research involves either quantitative methods, rooted in the natural sciences, qualitative methods, rooted in the social sciences, or a mixture of both approaches.[191] This chapter describes the methodology used to explore the effect of an electronic alert to reduce excessive SABA prescribing.

## 2.2 Mixed-methods research design

### 2.2.1 Defining mixed methods

Mixed methods research, defined as the collecting, analysing, and mixing both quantitative and qualitative data in a single study or a series of studies,[190] has been described as the "third methodological movement" behind that of quantitative and qualitative methods.[195] The use of mixed methods is increasing in prominence in health services research and particularly in health service evaluations.[196]

There are a number of approaches to mixed methods research based on what is being combined, when or where the combination is made and the breadth and purpose of combinations used to address the research question.[197] Mixed methods can be applied concurrently (at the same time), sequentially (one after another) or independently, with data integrated either by design, methods, interpretation and reporting or a combination of approaches.[198] The most common mixed method design types as described by Creswell & Plano-Clark[199] are presented in figure 2.1.

Figure 2. 1 Main mixed methods design types

| *Design Type* | *Variants* | *Timing* | *Weighting* | *Mixing* | *Notation* |
|---|---|---|---|---|---|
| Triangulation | • Convergence<br>• Data transformation<br>• Validating quantitative data<br>• Multilevel | Concurrent: quantitative and qualitative at same time | Usually equal | Merge the data during the interpretation or analysis | QUAN + QUAL |
| Embedded | • Embedded experimental<br>• Embedded correlational | Concurrent or sequential | Unequal | Embed one type of data within a larger design using the other type of data | QUAN(qual) or QUAL(quan) |
| Explanatory | • Follow-up explanations<br>• Participant selection | Sequential: Quantitative followed by qualitative | Usually quantitative | Connect the data between the two phases | QUAN → qual |
| Exploratory | • Instrument development<br>• Taxonomy development | Sequential: Qualitative followed by quantitative | Usually qualitative | Connect the data between the two phases | QUAL → quan |

*(Creswell & Plano-Clark, 2006)*

### 2.2.2 Philosophical basis of mixed-methods research

Mixed-methods research is not committed to any one philosophy, because one philosophy cannot account for the variety of methods used. Instead, mixed-methods research adopts a more pragmatic perspective, which is further described below.

#### 2.2.2.1 Pragmatism

Pragmatism is a middle-ground philosophy that does not seek to address a research 'truth' or abstract knowledge, but instead seeks to enhance knowledge through the direct enquiry of

research.[200] In pragmatism, there is no all-embracing worldview,[201] with Onwuegbuzie and Johnston[202] noting that a philosophical and methodological pragmatism in mixed methods involves inclusive ontological and epistemological dispositions. Creswell[191] describes these dispositions as worldviews that guide researcher in their quest of knowledge through research. The elements of each worldview position, including pragmatism, are presented in figure 2.2. In a pragmatist argument for mixed methodology in medical informatics, Scott and Briggs[203] view knowledge generation as practical rather than theoretical, with methods applied based on the ability to address the research question, rather than methods driven by ontological and epistemological assumptions. Pragmatism involves pluralism of methods that despite appearing contradictory; quantitative and qualitative methods can complement and enable one to more fully to see his or her world.[202] The plurality of methods seeks to answer questions through research to improve the world, and in the case of this thesis, the world of applied health services research.

Figure 2. 2 A summary of philosophical worldviews

| **Postpositivism** | **Constructivism** |
|---|---|
| • Determination<br>• Reductionism<br>• Empirical observation and measurement<br>• Theory verification | • Understanding<br>• Multiple participant meanings<br>• Social and historical construction<br>• Theory generation |
| **Advocacy/Participatory** | **Pragmatism** |
| • Political<br>• Empowerment Issue-oriented<br>• Collaborative<br>• Change-oriented | • Consequences of actions<br>• Problem-centered<br>• Pluralistic<br>• Real-world practice oriented |

*(Creswell, 2018)*

### 2.2.3 Strengths and weaknesses of mixed methods

Mixed methods research can utilise the strengths and counterbalance the weaknesses of quantitative and qualitative approaches when addressing complex, multifaceted issues such as health services interventions and living with chronic illness.[204] Furthermore using a mixed methods approach can provide stronger evidence for a conclusion through "convergence and corroboration" of findings.[199] One of the main criticisms of mixed methods research is that methods should not be mixed as they are belong to two separate and incompatible paradigms.[190] Combining two methods in one study can be time consuming and requires experience and skills in both quantitative and qualitative methods. Potential challenges exist in the appropriate integration of data, with difficulty in presenting the results of a mixed methods study a barrier to conducting this type of research.[205]

### 2.2.4 Rationale for a mixed methods design

This thesis was undertaken to explore the effect of an electronic alert at reducing SABA prescribing in primary care. Alerts are common features of computer decision support systems in medical informatics, defined as "the study and application of methods to improve the management of patient data, clinical knowledge, population data." [206] Medical informatics is described as a "hybrid sociotechnical field" encompassing social, technological, and cultural effects, a mixed methods approach that is not limited to one method is the most appropriate study design for research in this field.[207] In this thesis, quantitative research is used to evaluates changes in SABA prescribing and secondary clinical and process of care outcome measures following the implementation of an alert for excessive SABA prescribing across three CCGs in east London. Qualitative research is used to explore the wider issues regarding the use of an alert to identify and manage excessive SABA prescribing in primary care. A mixed methods design enables a broader understanding of the role of alerts for excessive SABA prescribing, to contribute current literature and gaps in knowledge. Therefore, the qualitative approach is used to complement the quantitative findings, to provide

insight into the use of an alert for excessive SABA prescribing that would not be reflected in a sole quantitative study design.

### 2.2.5 Application of mixed methods in this thesis

An embedded mixed methods design (figure 2.3) was applied in this thesis. This involved data concurrent data collection with the qualitative study (phase 3) supplemental to the quantitative study (phase 2). The embedded design is a mixed methods design in which one data set provides a supportive, secondary role in a study based primarily on the other data type.[190] This design is popular in the health sciences whereby quantitative and qualitative approaches are used in tandem and embed to provide new insights. The quantitative and qualitative methods were independent of one another and integrated in interpretation, in what Onwuegbuzie and Johnston[202] define as paradigmatic mixing legitimisation. This method seeks to address the challenge of competing epistemological and ontological and methodological viewpoints of qualitative and quantitative research described further in the individual sections of this chapter.

This quantitative phase of the thesis involved a retrospective case-control study to determine the effect of an alert for excessive SABA prescribing, primarily on SABA prescribing, and secondarily on the number of asthma reviews, time to asthma review, ICS, LABA and combination inhaler prescribing, exacerbations and primary care consultations. The qualitative phase of the thesis involved interviews with primary care staff and asthma experts to explore perspectives of excessive SABA use and the role of an alert to reduce excessive SABA prescribing. In addition, observations with receptionists were carried out to provide insight into the process for the repeat prescribing of SABAs and how excessive SABA prescribing may be identified at this point. Both data sets were collected and analysed concurrently, with findings integrated in the interpretation stage. In this way, the qualitative work supported the quantitative findings by providing practical context and insight into the identification of excessive SABA prescribing and the role of the alert. Greene *et al.*[208] describe such methods as complementarity (i.e., seeking elaboration, illustration, enhancement, and clarification of the findings from one method with results from the other method).

Figure 2. 3 Mixed method embedded design


*(Creswell, 2018)*

## 2.3 Patient and Public Involvement

The role of Patient and Public involvement (PPI) in applied health research is increasing. PPI involves patient's sharing their views and experiences as contributors to the research process rather than being the subject of research.[209] Patient and public contributions at an early stage can help clarify research questions and ensure the most appropriate people are involved thereby strengthening the research.[210] Early involvement of PPI, for example through the contributions of an advisory group, are more likely to have a positive impact on research compared to late involvement and contributions in an oversight capacity.[211]

Asthma UK Centre for Applied Research (AUKCAR) facilitates patient and public involvement (PPI) for researchers to ensure that research affiliated with AUKCAR remains relevant to those affected by asthma. The group is comprised of people with asthma, including parents and carers of people with asthma who can bring insight and experiences of living with asthma as well as a range of personal and professional skills from other walks of life.

### 2.3.1 Rationale

It was important that the views of people with asthma were considered in design of the project to ensure issues relevant to their asthma care were addressed. The AUKCAR PPI group were consulted to inform the content of a topic guide for qualitative interviews, to ensure the relevant

primary care staff involved in the management of SABAs were included in the study and to ensure appropriate outcomes were captured in the quantitative study.

### 2.3.2 Methods

In March 2015, an open-ended questionnaire was devised with the assistance of the AUKCAR PPI lead. The questionnaire was circulated the AUKCAR PPI group by email (Appendix 2.1). Questions focused on experiences of SABA use and NRAD[25] recommendations for an alert to identify people prescribed excessive SABAs. Completed responses were sent directly from PPI members to the lead researcher by email.

### 2.3.3 Patient and Public Involvement feedback

Responses were received from 13 PPI group members. An overview of points raised is summarised below. Responses were collated and summarised into the main points below.

**SABA use experiences**

Of the 13 responses, patients described variable use of SABA inhalers, including none, less than one SABA a month, one SABA a month or possibly more depending on symptoms. One person responded they routinely used two puffs of SABAs between two to four times a day, irrespective of symptoms, as this was how they thought it should be used, whilst another person required SABA four times a day due to severe asthma. Patients described having contact with the pharmacist, GP and/or asthma specialist in regards to SABA use, whilst the nurse was not mentioned.

**Requesting repeat prescriptions**

Responses described repeat prescriptions requests for SABAs were made in either paper or electronic format in a process that involved the GP, receptionist and pharmacy. Suggestions to improve the process through which SABAs are obtained included integrated computer systems between GP and pharmacist so that both could be alerted to high SABA use, improved GP record keeping, increased use of the comments section by patients when requesting prescriptions electronically on EMIS and the increased clinician checks on medication type and dose as not always correct.

**An alert for excessive SABA use**

An alert to identify high SABA use in primary care was welcomed. It was acknowledged that patients are often not aware of the problems of high SABA use and different clinicians may process repeat prescriptions and SABA use should be brought to their attention. It was suggested that an alert will be dependent on the on human factors such as co-operation between practice and patient, and that pharmacists should also be alerted to high SABA use, potentially through the electronic prescription service. The role of pharmacy was viewed as important as patients do not always need to attend the GP but will always need to go to the pharmacy to collect prescriptions. Pharmacy was viewed as well placed to highlight high SABA use to a patient and explain the need for review. Respondents raised questions regarding the proposed action following a SABA alert. A number of challenges were envisaged particularly with potentially limiting SABAs and the difficulty of asthma reviews.

Respondents raised questions regarding the proposed action following a SABA alert. A number of challenges were envisaged particularly with potentially limiting SABAs and the difficulty of asthma reviews:

- Potential concerns regarding the availability of SABAs for people with difficult to control asthma or under specialist care that require above normal use
- Concerns that if a GP does not prescribe SABAs following an alert the patient may be more at risk of an asthma attack than from SABA overuse
- An alert may not mean excessive SABA use due to a variety of reasons for requesting SABAs including lost inhalers, forgotten repeat prescriptions or holiday requests
- Difficulty in getting patients to attend review, patients may not understand the relevance of excessive SABA use
- Lack of available appointments at suitable times especially if a review needs to be carried out within a certain time frame from alert
- An alert needs to be supportive of users and whether the surgery can offer suitable appointments
- The alert should not be overridden until the patient has a review carried out
- SABA review should occur at annual asthma review as patients may resent having to attend

**Alerting patients**

There were a number of suggestions as to how patients could be followed up following an alert. Suggestions included contacting patients by letter, email, text message, phone call to invite for asthma review or by prescription message from GP delivered by a range of staff including asthma nurse, receptionist or pharmacist.

### 2.3.4 Implications for study

PPI feedback highlighted the variations in SABA use, methods to obtain SABAs, the potential challenges of an alert and considerations regarding the management of people identified as excessively using SABAs. The original plan for the study was to gather GP perspectives on the use of an alert to identify excessive SABA prescribing, as GPs are most likely to hold prescribing

responsibility. However, as highlighted in feedback, receptionists and in particular pharmacists played an important role in how patients currently obtained SABAs. Therefore, it was viewed as necessary to include a range of staff in qualitative study to further understand their input into the identification of excessive SABA use and to place the use of a SABA alert in a wider primary care context. The feedback also helped shape questions for the interview topic guide for primary care staff and experts including what constitutes excessive SABA use, how an alert is/could be used to identify excessive SABA use and how excessive SABA use is acted upon in practice. Furthermore, PPI feedback highlighted the importance of capturing the effect of the alert on repeat SABA prescribing in the quantitative study, rather than SABA prescribing alone.

## 2.4 Quantitative research methods

Creswell[191] defines quantitative research as the collection of data by numbers to which statistical analyses are applied to explain relationships between variables. In this section, an overview of quantitative research methodology will be described including experimental and quasi-experimental design, with a particular focus on the non-experimental technique utilised applied in this thesis.

### 2.4.1 Philosophical assumptions underpinning quantitative research

The collection and analysis of quantitative data assumes that deductive reasoning of defined concepts or hypotheses can uncover a truth or reality.[194] These assumptions represent a positivist paradigm: that which is influenced by health beliefs systems including the ontological, epistemological and methodological positions adopted by the researcher.[192] Positivism is described further in the following section.

#### 2.4.1.1 Positivism

Positivism is a scientific paradigm based on data and facts with knowledge believed to be absolute and value free.[212] The ontological position of positivism is one of realism, in which objects have an existence independent of and discoverable by the researcher.[213] The positivist epistemology is one of objectivity, with researchers impartially discovering absolute knowledge about a reality.[214] Methodological positivism refers to a concept of knowledge rooted in science,[215] however a true objective reality in applied health services research is questionable as it fails to acknowledge the context within which health services are used, as well as the person(s) using and delivering the service.[216]

### 2.4.2 Quantitative study designs

There are three main types of quantitative study designs: experimental, quasi-experimental and non-experimental. Experimental study designs commonly refer to prospective, randomised, controlled trials to determine causality between variables, in contrast to quasi-experimental study designs to determine associations between variables.[217] Experimental designs are commonly used to demonstrate the efficacy of an intervention or treatment through a focused, rigorous process to achieve scientific integrity, whilst quasi-experimental designs determine associations but not causality due to non-randomisation and are perceived as of lower scientific integrity.[217]

Non-experimental research designs are commonly observational, either prospective or retrospective and descriptive in the reporting of findings. Despite non-experimental designs generally perceived as of the lowest scientific rigor, each design has its own merits based on the appropriateness of the research design to answer the research question.

#### 2.4.2.1 Observational research

Observational research in the form of a retrospective case-control study design was applied in this thesis and is further described below.

#### 2.4.2.1.1 Observational study design

An observational study can be defined as one that observes changes or differences in one characteristic in relation to changes or differences in other characteristic(s) without interference from the researcher.[218] Whilst an experimental design provides valuable evidence about treatments and interventions, much of clinical or public health knowledge comes from measuring the effectiveness of an intervention in 'real world' scenarios at the population level through observational research.[219] A retrospective observational study design was applied to observe the effect of an alert on SABA prescribing. This involved a case-control study, which is further described below.

#### 2.4.2.1.2 Case-control studies

A case-control study involves the selection of two similar populations with shared outcomes in which one has been exposed to an intervention and one not.[218] This can include matching historical data (control group) obtained prior to the implementation of an intervention with post-intervention data (case group).[220] Matching is often based on similar population characteristics between both groups. In this thesis, case-control groups were matched on the basis of excessive SABA use.

Whilst experimental designs are viewed as the most appropriate to evaluate computer decision decision, a case-control study design is often the most feasible option for retrospective evaluations. In this thesis, a prospective evaluation was not possible and therefore the current design was most feasible method with which to address the research question. A case-control design is most useful in demonstrating the impacts of an intervention in a limited time-frame hence its use in this multi-phased thesis.[221] Furthermore, the total number of individuals required to obtain adequate power in a case–control study is often considerably less than other observational methods, for example cohort studies.[222] This was deemed an appropriate when evaluating the intervention in a population limited by geographical locality of east London.

#### 2.4.2.1.3 Electronic health records in observational research

Electronic health record (EHR) data has been used to support observational studies, either as stand-alone data or following linkage to primary research data or other administrative data sets.[223] As exposure and outcome data already exist in electronic form for those registered with a general practice, the use of EHRs for observational research purposes is increasing.[66] Large routine primary care data sets offer opportunities and sufficient power to study difficult to reach populations including ethnic minority groups.[224] However, there is wide variation in how EHR data is utilised and reported in observational research. EHR systems usually fail to capture complete and accurate clinical information at the point of care due to design limitations and inefficient use of these systems by clinicians to document clinical data.[101,225] Although EHR-derived data are convenient resources for research, they are originally collected for other purposes, and usually suffer from missing or incorrect data and potential biases which may impact on data collection and analysis.[226–228]

### 2.4.3 Statistical analyses

In applied health research normality is more often the exception rather than the norm, with non-parametric statistical tests most commonly used in non-normal data.[229] Count data, as reflected in the quantitative phase of this thesis, is commonly skewed. Histograms were used to confirm skewed distribution of SABAs and non-parametric tests were applied. Non-parametric tests place few assumptions on the data and therefore outlying observations, that may be problematic in a parametric approach, can be dealt with using non-parametric methods. Non-parametric tests however may lack power to determine an effect, particularly if the sample size is small.[230] The statistical tests applied in this thesis are described below.

#### 2.4.3.1 Median and Interquartile Range

The media and interquartile range (IQR) was reported to determine the distribution (centre and spread) for continuous variables i.e. prescribing and consultations, rather than the mean and standard deviation associated with normally distributed data. The median and IQR was calculated to compare continuous outcome measures between the case-control datasets, with the median providing a measure of central tendency and the IQR reflecting the spread of the data and variability of the sample.[231] The median (IQR) provides an overall description of prescribing and consultation data including the identification of outlying data and similarities and differences between the case and control group.

#### 2.4.3.2 Mann-Whitney U test

Unlike the parametric t-test that compares the mean of two groups when data is normally distributed, the Mann-Whitney U test was used to determine the strength of relationships between continuous variables: prescribing and primary care consultations, by comparing the medians between the case and control groups.[232–234]

#### 2.4.3.3 Chi Squared test

The Chi-squared test was used to compare the distribution of categorical variables (number of asthma reviews) between the case and control groups, to determine whether asthma reviews increased in response to the alert. However, the test does not address the potential influence of other explanatory variables on that relationship, the direction or strength of the relationship.[235]

#### 2.4.3.4 Regression analysis

Regression analysis was used to determine the relationships and strength of associations between the dependent variables and independent variables when adjusted for covariates. Using a generalised linear regression model (Poisson regression and Binary logistic regression) outcome data was adjusted for covariates including age, gender, ethnicity, control group and prescribing in the prior time-period. Whilst the Mann- Whitney U test indicates the association between groups the strength and direction of associations and confounding effects are not determined. Whilst the Mann-Whitney U test reports the positioning of data above or below the median, the magnitude of the observation is not taken into account.[236] Therefore, for outcomes of interest using count data e.g. prescribing and consultations, Poisson regression was used as it assumes a non-normal distribution of data. Binary logistic regression was used to analyse the number of asthma reviews, a dichotomous dependent variable.

### 2.4.4 Reliability, validity and rigour in quantitative research

Rigour refers to the extent to which the researchers worked to enhance the quality of the studies. In quantitative research, this is achieved through measurement of the validity (internal and external) and reliability of studies.[237] Internal validity refers to the strength by which observed results are attributable to an intervention. There are three biases commonly associated with observational studies that affect internal validity including selection bias: when the study population is not randomly sampled; information bias: inaccurate assessment of the outcome, the exposure, or potential confounding variables; and confounding bias: the exposure to a risk factor that is associated with the exposure but not the end point.[238,239] Internal validity of a study may be compromised by not having a control group or a control group that is not comparable to that of the intervention group.[240] There, in this study patients identified by the alert as being prescribing excessive SABAs (case) were compared to a population matched by excessive SABA prescribing prior to the alert (control) rather than unmatched with the general population.

Internal validity may be threatened by regression to the mean (RTM), which can be defined as a statistical phenomenon in which the distribution of a unit of observation moves towards the mean following its selection based on extreme measurement.[221] RTM may potentially influence the findings of the case-control study as SABA prescribing was captured at an excessive point.

External validity involves the ability to generalise results from the study population to the general population, to "other persons in other places at other times."[240] The most common threat to external validity in observational research comes from sample size obtained from a single geographic location or facility. This is acknowledged as a likely limitation due to the focus of the research specific to ethnically diverse population and locality. However, due to a lack of real-world RCT testing, observational studies an often have greater external validity than experimental designs as they can provide insight into real world clinical practice rather than controlled conditions of an RCT.[241]

The use of electronic health record (EHR) data poses potential threats to the validity of observational research, otherwise described as data validity; that data reflects what it claims to represent.[242] However, there are a number of issues regarding the quality of EHR data, including heterogeneity in the capture, reporting and assessment of EHR data.[243] Whilst the potential for EHR data to inform clinical decision making and real-life research in asthma has been highlighted,[66] there remains wide variation in the approaches used, with limited attention being paid to the validity of the underlying algorithms used and suboptimal reporting of studies.[244]

## 2.5 Qualitative research methods

Creswell defines qualitative research as:

*"an inquiry process of understanding a social or human problem, based on building a complex, holistic picture, formed with words, reporting detailed views of informants, and conducted in a natural setting."* (Creswell, 1994)

However, no one universal definition adequately captures the variation and complexities of qualitative research methods. Strauss and Corbin,[245] define qualitative research in terms of what it is not, for example, as that which produces findings other than through statistical analysis or quantification of numerical relationships between variables as in quantitative research. Qualitative research is often described as naturalistic and interpretative, concerned with exploring phenomena 'from the interior.'[246] In this approach, the perspectives and accounts of research participants are a starting point from which phenomenon can be explored.[247] Researchers utilise participants experiences to provide a lens to shape the understanding of the social world.[194]

Qualitative research designs can be classified into three categories: exploratory, descriptive, and explanatory research. Explanatory research use research hypotheses to specify the nature and direction of the relationships between or among variables being studied to understand why phenomena occur. Descriptive studies depict people, products, and situations using one or more guiding research questions rather than structured research hypotheses. Exploratory research seeks to create hypotheses rather than test them, instead formulating problems and clarify concepts for example in response to literature searches, focus group discussions, or case studies.[248]

The philosophical assumptions of qualitative research are described in the following section prior to a description of the methods applied the qualitative phase of this thesis.

### 2.5.1 Philosophical assumptions underpinning qualitative research

Qualitative research comprises different orientations and approaches, various intellectual and disciplinary traditions grounded, often, in differing philosophical assumptions.[249] The philosophical assumptions underpinning qualitative research are often a source of contention within the literature, with Denzin and Lincoln[192] of the opinion that no one theory or paradigm is distinctively

associated with qualitative research. Braun and Clarke[250] note there are a number of oppositional approaches within the social sciences, contrasting to the mainstream positivist empiricist research design and practice of quantitative research. These include four dominant taxonomies that underpin qualitative research: the positivist, constructivist, critical and feminist paradigms.[251] However, Barbour[252] notes that distinctions between paradigms are often not clearly defined. As it is not possible to define each paradigm within the confines of thesis, the constructivist paradigm specific to the qualitative study is further described in the following section.

#### 2.5.1.1 Constructivism

The qualitative study is contextualised by a constructivist/interpretivist paradigm. In an analysis of paradigm positions, Guba and Lincoln[253] describe the aim of constructivism as to understand. In its relation to phenomenology, constructivism assumes that people construct social reality by interpreting the world around them. Unlike the positivist philosophy predominant in quantitative research where the researcher is completely 'detached' from the tangible subject, the ontology of constructivism assumes that the researcher is actively engaged in research participant's construction of their 'social reality.'[191] As such, applied health services research involves studying the environment that both shapes and is shaped by the research participants within.[194]

Unlike positivism, the ontology (nature of social reality) of constructivism assumes that 'social reality' does not exist as a discrete, tangible, measurable 'fact,' but that individuals construct a subjective 'social reality' of multiple meanings.[191] In a constructivist epistemology, (the relationship between the researcher and the social reality they seek to know), the researcher takes into account local contexts and meanings that shape individual's reality.[254] This data is used to identify patterns of relationships and gain insight into the meanings of phenomena from the perspective of individuals.[191,194]

### 2.5.2 Exploratory research design

The aim of exploratory research is to gain an increased understanding of an issue or situation for which little is known, and from which further in-depth research may be generated.[255] Pope and May[256] describe that qualitative exploration of a topic can complement quantitative work by exploring complex behaviours, attitudes, and interactions which quantitative methods cannot. Exploratory research can be referred to as interpretive research whereby the intention is to build an understanding of an issue rather than prove a theory.[255] Constructivists do not generally begin with a theory rather they "generate or inductively develop a theory or pattern of meanings."[191] Atheoretical research in is categorised by Kelly[257] as 'generic qualitative research' with the aim of providing a surface-level analysis or general overview of a topic. Such methods are useful in health research, in particular, when examining clinical decision making by exploring both the declared and the "implicit or tacit routines and rules" which doctors use.[258] Similarly, exploratory qualitative research in this thesis enabled a broad analysis of excessive SABA prescribing in primary care including the wider issue of alerts to improve prescribing.

### 2.5.3 Sampling

Sampling in exploratory research can be defined in its broadest sense as the selection of specific data sources from which data are collected to address the research objectives.[259] Unlike quantitative research, qualitative research is more interested in understanding the complex processes behind phenomena through a detailed study of a few participants. There are a number of ways in which ways in which participants can be selected for inclusion in qualitative research. Four sampling strategies are the most commonly used in health services research: convenience sampling, purposive sampling, snowballing and theoretical sampling.[194]

Convenience sampling recruits opportunistically based on participant availability.[194] This strategy is resource-efficient, in terms of saving time, money and efforts, but may have implications for quality of data due to potential limited range of opinions.[260] Purposive sampling deliberately

selects participants who can provide insight specific to the topic of investigation or those with varied opinions to enhance the quality and depth of the data.[260] Snowballing involves recruiting participants with potential characteristics of interest based on the suggestions of others in the absence of a clear sampling strategy.[194] Theoretical sampling involves the recruitment of participants to aide theory development and refinement commonly associated with grounded theory research.[260]

#### 2.5.3.1 Sampling strategy

In exploratory research, pragmatic convenience sampling is common as researchers usually look for individuals who are knowledgeable about a topic or process in line with specific purposes in accordance with the research objective.[261]

Asthma 'experts' defined as primary or secondary care clinicians who have contributed specifically to asthma care at a national or international level were recruited by convenience sampling following research team discussion.

A pragmatic decision was made to convenience sample primary care staff specifically from Tower Hamlets CCG due to the proximity to the lead researcher due to established networks between practices and the Clinical Effectiveness Group (CEG) at QMUL. It is acknowledged that convenience sampling may limit findings give the quantitative study was carried out across three CCGs. Therefore it is possible the qualitative work may not fully reflect the reasons for alert success or failure to reduce excessive SABA prescribing. However as this was exploratory research, the findings in Tower Hamlets provide general insight into the topic of alerts to change SABA prescribing behaviour, from which specific, in-depth research may be facilitated as a standalone project rather than embedded within a quantitatively dominated mixed methods project. The purpose of qualitative research is not to determine all there is to know about topic through exhaustive sampling.[262,263] A sufficient sample size is commonly justified by data "saturation."[264] Originating in grounded theory, Glaser and Strauss[265] define saturation as something that is reached when new data fails to enhance the development of categories. Saturation has been described by Urquhart[266], as when no new codes

occur in the data. Saturation is often used as a criterion for discontinuing data collection, and/or analysis[267] and is often used by researchers as an indication of quality.[268] However, there are no specific guidelines in the literature regarding the appropriate sample size to achieve data saturation in qualitative research.[269,270]

In an analysis on data extensiveness in qualitative research, Sobal[271] argues that sample size should be guided by principles of data adequacy and appropriateness as well as analytical redundancy. However, a balance should be sought between the sample size needed to achieve information power in the thematic analysis process and ambition for a larger sample to find out as much as possible, rendering data unmanageable and incomprehensible.[263] Therefore qualitative data collection was guided by that which has already been collected and ended when the 'new' did not materially add anything to the overall story.[245]

### 2.5.4 Data collection

Qualitative research relies on textual data rather than numbers to explain phenomena.[191,194] The three main most common methods to generate data in qualitative research are through interviews, ethnography/observational research and (focus) group discussions.[272] Interviews are the most common qualitative research method. There are three fundamental types of research interviews: structured, semi-structured and unstructured.[273] Interviews generally involve more than merely asking questions to elicit the views and opinions of the participants on a one-to-one basis and may also be conducted in groups, in person, on the telephone or by video. [252,274]

Research through observation is the main approach of ethnography, which can be described as the observation of human behaviour in the natural setting.[272] Ethnography observes the sequences of human activities in a manner that is open to discovering new data, and then connects observed data to local contexts of the study.[275] The main aim of observational research in healthcare is to collect data on errors, adverse events, near misses, team performance, and organisational culture.[276]

Focus group discussion is common in exploratory health services research.[272] A focus group can be defined as any group discussion in which the researcher actively encourages and enables group interaction.[277] However, this method may not the most appropriate for accessing views or attitudes of participants due to the group setting. One-to-one interviews are better at generating and clarifying narratives than focus groups which are more suitable for studying how views are created and modified.[252]

The qualitative methods used in this thesis are described below, including justification and rationale for use.

#### 2.5.4.1 Interviews

Semi-structured interviews consist of several key questions that help to define the areas to be explored whilst allowing the interviewer or interviewee to pursue an idea or response in more detail.[273] The interview is often guided by a topic guide, with appropriate prompts to increase the depth of interaction.[194,252] Researchers conducting exploratory research usually look for individuals who are knowledgeable about a topic or process, for example experts in the field of investigation.[248] In classification as an 'expert,' it is assumed the person has specific knowledge on the research topic.[278] In an analysis of interviewing experts, Littig[278] notes that experts are those who have a certain degree of both formative and/or interpretive power.

There are three different types of expert interviews: exploratory expert interviews, systemising expert interviews and theory generating expert interviews.[278] Exploratory expert interviews as are most commonly used in a field of research with unknowns and therefore deemed appropriate this thesis to explore the use of alerts for excessive SABA prescribing.

Telephone interviews were conducted to enable access to wide range of experts both nationally and internationally that could not have otherwise been reached. Although face-to-face interviews

are the dominant interview method in qualitative research, telephone interviewing has become increasingly common.[279,280] Telephone interviews may be often viewed as inferior methods of data collection when compared to those carried out in person.[281,282] However research suggests the depth and quality of data generated by telephone does not significantly differ from those generated by face-to-face interviews.[283]

Semi-structured face-to-face interviews were carried out in-person with primary care staff, including general practitioners (GPs), pharmacists and nurses. In-person interviews gave an added advantage of referencing the alert on-screen when in interview. The term focus group has often been construed as synonymous with group interviews however they are fundamentally different in that focus group discussions rely on the interactions between participants to generate data whilst group interview involves the researcher asking group participants the same question in turn.[252] Group interviews were facilitated *via* clinical meetings where necessary, enabling primary care staff to participate in protected practice time, when they may have been otherwise unable to do so.

#### 2.5.4.2 Observations

Observations are increasingly used to understand and evaluate the delivery of a service.[284] In this study this involved observations of receptionists in the management of repeat SABA prescriptions. As identified In Chapter 1 and in PPI feedback discussed earlier in this chapter, SABAs are commonly obtained in through repeat prescribing that relies on reception staff. Observations with clinicians carry out repeat prescribing activities may provide increased understanding of the role of an alert in this process. An important advantage of observation in this context would be to overcome the discrepancy between what people say in interview and what they actually with the SABA alert.[285] However, given the variable uptake of clinician interviews, clinician observations were deemed challenging due to added time constraints in practice and the variability of repeat prescribing activities. It was anticipated that observations with receptionists as they process and manage repeat prescribing activities would be increasingly accessible partly influenced by their

non-clinical role. Such observational methods analysing the role of receptionists in repeat prescribing have been previously carried out[71] but not specifically in relation to SABAs. Receptionist observations are not intended to provide an in-depth analysis of SABA repeat prescribing but to provide a broad understanding of the identification and management of excessive SABA prescribing and when, how and by whom an alert may be used. It is envisaged that further in-depth research using different methods, for example an ethnography or comparative case study may potentially result from the findings.

An observation guide was adapted from Spradley's *9 Dimensions of descriptive observation*.[286,287] This provided a focus for observations using the domains of cultural space, objects, acts, activities, events, times, actors, goals, and feelings. These categories represent the range of what might be observed in any specific social setting, and may carry meaning for the participants in the setting.[288] Descriptive observations are usually carried out observing everything, however as the role of receptionists in the repeat prescribing of SABAs was of specific relevance to the research question, the domain of 'activities' was of particular focus during observation.

### 2.5.5 Analysis

Thematic analysis is best suited for exploratory studies investigating an area where not much is known.[289] Braun and Clarke[290] define thematic analysis as "a method for identifying, analysing and reporting patterns within data," and as one which does not require the detailed theoretical and technological knowledge of other qualitative approaches.[290,291] The Framework Method is most commonly used for the thematic analysis of semi-structured interview transcripts in applied heath research.[292] This approach was developed for applied policy research and involves five stages as described by Ritchie and Spencer:[293] Stage 1-2 Transcription and Familiarisation, Coding Stage 3-4 Developing a Framework, Stage 5 Applying the framework Stage 6 and 7 Charting and interpreting the data. Qualitative research often lacks transparency in relation to the analytical processes employed.[294,295] Therefore the framework approach was deemed appropriate for systematic analysis of data and clarity in reporting and communication of findings.[291,295] In thematic analysis,

data "saturation" can be defined as the point at which information has been exhaustively coded.[296] However it is questionable as to whether data can ever be saturated due new ways of interpretation from a range of different perspectives.

### 2.5.6 Reliability, validity and rigour in qualitative research

There are fundamental difference in the knowledge derived through a positivist and interpretivist paradigm is due to varying ontological and epistemological beliefs.[253] The traditional meaning of reliability and validity, as described in the quantitative research positivist paradigm, is not transferable to qualitative research as unlike quantitative research, qualitative research does not seek to measure.[297] Lincoln and Guba[298] conceptualise traditional quantitative terms of reliability and validity as the 'trustworthiness' of qualitative research. In this way, internal validity in quantitative research is replaced with 'credibility,' external validity with 'transferability'; reliability with 'dependability'; and objectivity with 'confirmability.'[202] A number of steps were taken to ensure the trustworthiness of the qualitative research process using the criteria created by Lincoln and Guba (1985).[298]

Credibility has been described as that which addresses the "fit" between respondents' views and the researcher's representation of them.[299] Reflections on the credibility of the qualitative research process were made using Noble and Smith's (2015) nine-step strategy for ensuring credibility.[300] These include acknowledging personal biases which may influence findings, acknowledging biases in sampling; good record keeping; comparing and contrasting similarities the data, including rich and thick verbatim descriptions of participants' accounts to support findings; demonstrating clarity in thought processes during data analysis and subsequent interpretations; engaging with other researchers to reduce research bias, respondent validation and data triangulation. To enhance qualitative research credibility, personal biases have been acknowledged through reflexivity (Chapter 6). Clarity in the thought processes during data analysis and interpretations have been demonstrated in an illustrative example of the use of the Framework Method in Appendix 5.6. Data was compared and contrasted to identify similarities and differences, for example, in definitions and perceptions of excessive SABA use. A mixture of rich and thick verbatim descriptions of participants' accounts have been analysed and reported; the coding and analytical framework was reviewed by

an independent researcher who acted as second coder.

Transferability has been defined as the degree to which, not just findings but their context, can be transferred to other contexts or settings so that the behaviour and experiences of participants become meaningful to an outsider.[298,301] This is often achieved through 'thick description' of the participants and the research process.[302] The participants and processes described in the qualitative study may be transferable to further research on alerts in primary care prescribing for asthma or other conditions, with the context of the complexities of SABA prescribing and asthma management possibly transferable to the management of other long-term conditions.

Dependability describes the stability and consistency of findings over time, in particular whether a person external to the research process would agree the process was carried out in a reasonable manner.[298] This involves the provision of a transparent research process including rationale for decisions taken including those related to sampling and reflective thoughts.[302] To ensure consistency in the research process, transcripts were coded following multiple reflections of interview audio as well as comparing and contrasting audio with the number of the interviews transcribed by Penguin Transcription services. Furthermore, an independent researcher coded three transcripts, with codes compared and the emerging themes reviewed and reflected upon over two visits.

Confirmability is concerned with the neutrality of the research process, for example that data and interpretations of the findings are clearly derived from the data and not influenced by researcher perspectives or experiences.[298,302] Whilst the use of an independent coder also influenced the confirmability of the research process, researchers are encouraged to embrace 'subjectivity' through reflexive practice, to acknowledge the emotional influence of a researcher's personal and professional background the analysis and interpretation of data.[252,303] Nowell *et al.,*[291] propose that trustworthiness of qualitative analysis be achieved through Lincoln and Guba's[298] four criteria for trustworthiness with the addition of audit trails and reflexivity. A reflexive account detailing the research student's professional and personal background and experience of the research process is documented in Chapter 6.

## 2.6 Chapter summary

In this chapter, the philosophical basis of quantitative and qualitative research in mixed methods was described. The apparent inadequacy of either quantitative or qualitative research designs to sufficiently answer applied health services research questions was highlighted in this chapter. The pragmatic advantage of mixed-methods research to harness the individual strengths, whilst overcoming the individual weaknesses of both quantitative and qualitative research, was presented. The chapter outlined the rationale for choosing a mixed-methods research design with emphasis on how individual methods were applied to address the research question. Further descriptions of the methods applied are discussed in the corresponding individual chapters in this thesis.

# Chapter 3. The use of electronic alerts in primary care computer systems to reduce excessive prescribing of short-acting beta$_2$-agonists for people with asthma: a systematic review

## 3.1 Introduction

### 3.1.1 Background

Following the National Review of Asthma Deaths (NRAD) identification that of 195 deaths from asthma between 2012 and 2013, 39% were prescribed more than 12 SABAs in the previous year whilst 4% were prescribed more than 50 SABAs in the same time period, the electronic surveillance of prescription refill frequency was recommended to alert clinicians to people with asthma prescribed excessive quantities of SABAs.[25]

Computer decision support systems (CDSSs), defined as by Wyatt and Spiegelhalter as 'active knowledge systems which use two or more items of patient data to generate case-specific advice' have the potential to influence prescribing behaviour.[117] General practice computer systems increasingly use reminders and alerts for preventative care and disease management[137,304] including more recently for asthma.[150,151]

Evidence shows that CDSSs do not consistently improve prescribing behaviour and clinical outcomes[119] and whilst CDSSs have many assumed benefits, the empirical evidence to support is often weak and inconsistent. Furthermore it is unclear to what extent electronic alerts have been used in the management of SABA prescribing and what impact, if any, they have on patient outcomes.

Representing Phase 1 of thesis, this chapter will determine the evidence for the use of electronic alerts to reduce excessive SABA prescribing in primary care, review the characteristics of interventions that have the potential to reduce excessive SABA prescribing and provide an evidence base for Phase 2 and Phase 3 of the thesis.

### 3.1.2 Review aim

This review aims to provide a systematic overview of the use of electronic alerts to identify excessive prescribing of SABAs in primary care.

### 3.1.3 Review objectives

The objectives of Phase 1 of the thesis were to:

1. Evaluate the effectiveness of electronic alerts to reduce excessive SABA prescribing in primary care by:

a) Identifying studies that used electronic alerts generated by excessive SABA prescribing

b) Establishing the impact of an alert on process outcomes for healthcare providers and clinical outcomes for people with asthma

2. Determine the features of alert systems that have the potential to improve process outcomes for healthcare providers and clinical outcomes for people with asthma by:

a) Reviewing intervention design and delivery

b) Establishing the extent of user engagement/non-engagement

## 3.2 Methods

The systematic review was registered on PROSPERO (International Prospective Register of Systematic Reviews) with identifier CRD 42016035633. Systematic review methods were documented in a published review protocol.[188]

### 3.2.1 Database selection

The literature was identified from the following database sources: Medline, Embase, Cinahl, Scopus and Cochrane Library (Cochrane Reviews, Other Reviews, Trials, Methods Studies, Technology Assessments, Economic Evaluations, Cochrane Groups).

These database sources were chosen following:

- Discussion with study supervisors and guidance from Queen Mary University Faculty Liaison Librarian for Medicine & Dentistry.
- Peer review feedback prior to the acceptance of the systematic review for publication.
- A combination of the database searches used in two previous systematic reviews on clinical decision support systems for asthma.[150,151]

### 3.2.2 Search strategies

Search terms were based on the database search methods for the Cochrane Airways Group Specialised Register. On-going and unpublished trials were searched for using the following websites. Due to variability in the design and reporting of CDSSs for prescribing practice,[164] the search strategy was deliberately broad to ensure the screening of studies with interventions that may have included yet not explicitly reported the use of a SABA alert.

### 3.2.3 Study inclusion criteria

Studies were considered for inclusion according to the PICOS criteria (population, intervention, control, outcomes and study design) which is a widely known strategy for framing a research question.

*(P) - Participants*

Studies that delivered care to adults and/or children with asthma, in a primary care setting. Primary care was defined as healthcare delivered in a community setting, most commonly in general practice, by a clinician, nurse or pharmacist. Non-clinical staff, including administrators and/or receptionists were also included.

*(I) - Intervention*

CDSSs were defined as 'active knowledge systems which use two or more items of patient data to generate case-specific advice.'[117] Studies were included if they incorporated a CDSS alert in the management of asthma. The intervention search strategy was purposely broad to facilitate screening of individual papers within which an alert triggered to excessive SABA prescribing may not have been explicitly reported. Alerts used in secondary or tertiary care, for other respiratory conditions that were not asthma were excluded.

*(C) - Comparator*

The comparator was 'usual care.'

*(O) - Outcomes*

Our primary outcome of interest was excessive SABA prescribing. Excessive prescribing of SABA was assessed on a study-defined basis. Secondary outcomes of interest included additional measures of prescribing and process of care (future SABA and ICS prescribing, ICS/SABA prescribing ratio, ICS/long-acting beta$_2$-agonist prescribing (LABA), asthma reviews), and clinical

outcomes (asthma exacerbations with/without oral steroids, unscheduled primary and secondary care asthma consultations, asthma control).

*(S) - Study design*

Randomised controlled trials (RCTs), in any language, carried out between 1990-2016, were included. The cornerstone of clinical research on interventions is generally considered that of RCTs,[305] with systematic reviews of RCTs considered the most rigorous way to evaluate intervention effectiveness.[305,306]

The decision to set 1990 as the earliest date for study inclusion was based upon a) the search dates used for previous systematic reviews on clinical decision support systems for asthma[150,151] and b) the introduction of the general practice contract in 1990, that encouraged the role of computers to facilitate the capture of care delivery data for which GPs could be reimbursed and remunerated for delivery of care.

### 3.2.4 Validity assessment

The data extraction and quality appraisal of the studies were conducted simultaneously.

Quality assessment of studies was undertaken using the Critical Appraisal Skills Programme (CASP) tool for Randomized controlled trials.[307] The Cochrane Collaboration's seven-step criteria approach for assessing risk of bias in randomised trials[308] as described in section eight of the Cochrane Handbook for Systematic Reviews of Interventions was used to assess the risk of bias of included studies. The primary researcher and second reviewer (AD) independently appraised the quality and risk of bias in the four studies included in the systematic review whilst carrying out data extraction with unanimous agreement between the two reviewers. The risk of bias is reported in section 3.3.3.

### 3.2.5 Data abstraction

Using a piloted data extraction form the primary researcher and an independent researcher independently extracted the following data from included trials: country, setting, funding, study design, healthcare professional and patient population, features of the CDSS intervention, description of the control group, outcome measures, results and risk of bias assessment. Data extraction tables were compared and discussed without disagreement. The items selected for data extraction were based on the Cochrane Collaboration data extraction form for RCTs.[309] As alerts may form part of a CDSS intervention it is important to consider other components of an intervention in which an alert may be one part.

### 3.2.6 Data syntheses

The systematic review protocol was published prior to screening studies for inclusion.[188] The protocol stated that a meta-analysis would be carried out, if possible, and heterogeneity in outcomes between studies would be determined using the I-squared statistic as described in the Cochrane Handbook for Systematic Reviews of Interventions.[309] Furthermore where possible, subgroup analyses would be performed on age categories as defined by BTS/SIGN.[52] However due to the small number of studies identified for inclusion in this review and the variability in outcomes reported it was not possible to carry out a meta-analysis and sub-group analyses. Therefore a narrative synthesis approach was followed.

### 3.2.7 Reporting assessment

The systematic review was reported using the 27 checklist items as recommended by PRISMA-guidelines.[310]

## 3.3 Results

### 3.3.1 Search results

Table 3.1 presents a breakdown of the number of studies identified from each of the electronic databases. In addition, three studies were further identified from reference lists of included studies.

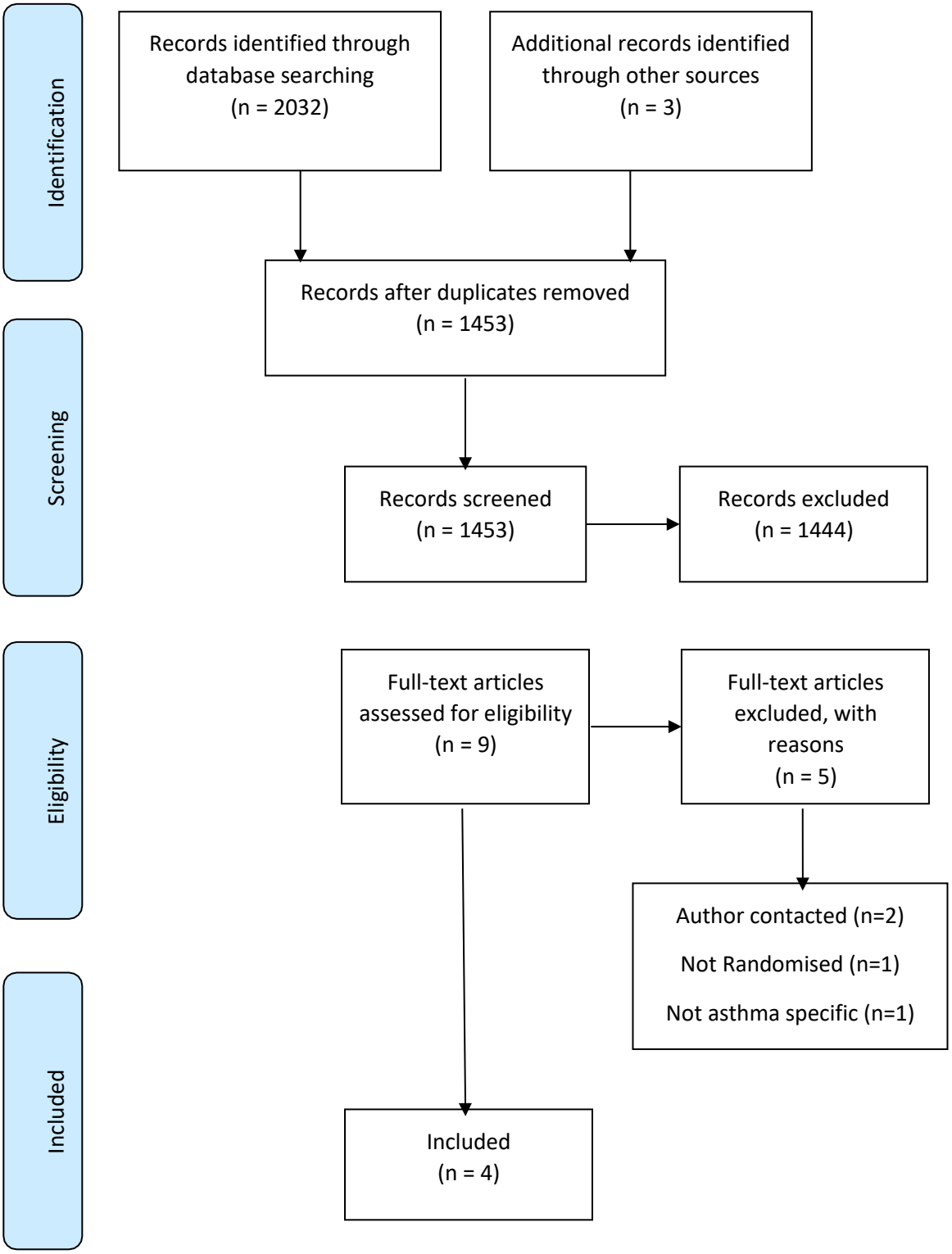
Table 3. 1 Database search results

| Electronic Database Searched | Number of identified studies |
|---|---|
| MEDLINE | 455 |
| CINAHL | 19 |
| Embase | 94 |
| Cochrane | 196 |
| Scopus | 1268 |
| Total studies from database searches | 2032 |

### 3.3.2 Study selection and exclusion

The combined database searches yielded 2032 studies with three studies from additional sources. There were 1453 studies remaining following the removal of 582 duplicates. To determine whether CDSS alerts for asthma were triggered by the prescribing or dispensing of SABAs, the titles and abstracts of the identified papers were screened. As they did not include an alert triggered on excessive SABA prescribing or dispensing, 1444 studies were excluded. The remaining 9 studies that potentially included an alert for SABA prescribing were screened by full-text. Where there was reporting uncertainty, authors of included studies were contacted by email to clarify intervention design and characteristics. 5 studies were excluded; 2 following author's intervention clarification, 1 was not randomised and 1 was not asthma specific. Figure 3.1 PRISMA flowchart details the step-by-step screening process resulting in the identification of four RCTS that met the review inclusion criteria.

Figure 3. 1 PRISMA flow chart



### 3.3.3 Validity assessment

The terms quality, validity, and bias are used interchangeably in the systematic review literature to describe methodological conditions and the appraisal of internal validity of studies.[309,311] Studies were included irrespective of quality status as studies rated as "low quality" because of methodological flaws or lack of reporting may nevertheless generate new insights whilst 'high' quality studies do not guarantee interpretation and insight to inform practice.[312] Cochrane Collaboration's assessments of internal validity of randomised trials is concerned with how well the study was designed and executed to prevent systematic errors or bias due to study design, conduct, analysis, interpretation, or reporting.[311] The risk of bias in the studies included in this review was assessed using the Cochrane Risk of Bias Tool[308] and reported in Table 3.2. All but one of the four studies included in the systematic review had low risk of bias.

Table 3. 2 Risk of bias assessment of included studies

| Study | Selection bias | Allocation Concealment bias | Performance bias | Detection bias | Attrition bias | Selective reporting | Other bias | Overall risk |
|---|---|---|---|---|---|---|---|---|
| McCowan | No | No | No | Unclear: blinding of outcome assessors not detailed | Yes: attrition rate variation was not fully explained. No intention-to-treat analysis | Unclear: no protocol | No | C-High |
| Eccles | No | No | No | No | No | No | No | A-Low |
| Zeiger | No | No | No | No | No | No | No | A-Low |
| Tamblyn | No | No | No | No | No | No | No | A-Low |

### 3.3.4 Study characteristics

Four RCTs were conducted between 2001 and 2015; two recent studies by Tamblyn *et al.* [313] and Zeiger *et al.*[314] (published in 2014 and 2015) were carried out within integrated healthcare systems in the United States and Canada respectively, whilst two older studies by McCowan[156]and Eccles[153] (published in 2001 and 2002) were carried out with the National Health Service (NHS) in the United Kingdom. Study duration ranged from between 6 months,[156] 12 months before and after,[153] 12 months[314] and 33 months.[313]

### 3.3.5 Population characteristics

Three of the four studies included people with asthma under-18 years of age. In two of the three studies the lower age for inclusion ranged from 5 years of age[313] and 12 years of age[314] whilst not reported in the third.[156] No studies stratified findings by age range. Method of defining asthma status varied between studies. In older studies by McCowan *et al.*[156] and Eccles *et al.*[153] the methods used to identify patients with asthma within an EHR were not clearly specified. This included patients on an asthma register,[156] and patients identified from computerised searches for relevant (unspecified) codes for asthma diagnosis, management, and drug treatment.[153] In the two recent studies by Tamblyn *et al*.[313] and Zeiger *et al.*[314] ICD-9 code 493 was used to determine asthma diagnosis. In Zeiger *et al.* an ICD-9 was required within at least the previous 3 years and at least one ICS dispensed in prior 6 months,[314] with health insurance a prerequisite for patients in both studies. Both study and population characteristics of studies are presented in Table 3.3.

Table 3. 3 Characteristics of included studies

| Author (year, country) | RCT Study design | Practice participation/ setting | Patient participation | Time scale | Inclusion Criteria | Exclusion criteria |
|---|---|---|---|---|---|---|
| McCowan (2001, UK) | Cluster RCT | 46 practice clusters | 447 patients | 6 months | All ages, on asthma register | Not specified |
| Eccles (2002, UK) | Cluster RCT with 2x2 incomplete block design | 62 practice clusters | 5,139 patients | 24 months 12 months baseline, 12 months | 50% of doctors using EMIS or AAH Meditel system to view clinical data/issue prescriptions during consultations | Single-handed practices |
| Zeiger (2014, USA) | Randomised stratified block design | Managed care organisation | 1,999 patients | 20 months; 8 months intervention; 12 months follow-up | Patients aged 12- 56 years with physician diagnosed asthma; (ICD-9 code 493) in previous 3 years, >=7 SABAs dispensed, continuous health-plan membership and pharmacy benefit in the prior year, >=1 ICS canister dispensed in prior 6 months | Co-morbidities: COPD, emphysema, Cystic Fibrosis, chronic bronchitis, bronchiectasis, Churg Strauss syndrome, Wegener granulomatosis, Sarcoidosis, pulmonary hypertension, steroid-dependant asthma, Omalizumab in prior 3 months, interpreter require |
| Tamblyn (2015, Canada) | Cluster RCT | 81 physician clusters | 4,447 patients | 33 months | >5 years, asthma diagnosis (ICD9 code 493), provincial drug plan insured | COPD diagnosis (ICD-9 Code: 492, 44, 496) |
| RCT, randomised control trial; COPD, chronic obstructive pulmonary disease, ICD, international classification of diseases; SABAs, short-acting beta2-agonists; ICS, inhaled corticosteroid | | | | | | |

### 3.3.6 Intervention characteristics

Table 3.4 summarises the intervention features in which an electronic alert was delivered. A multicomponent intervention was used in each of the four included studies, with an alert being one of a number of features. Methods of alerting included computerised prompts,[153,156] a 'real-time' electronic message to physicians[314] and a 'dashboard' alert.[313] No study included an electronic alert as a sole intervention.

Table 3. 4 Summary of Intervention features

| Features in addition to alert | McCowan | Eccles | Zeiger | Tamblyn |
|---|---|---|---|---|
| Guideline decision support | X | X | | X |
| Allergy Specialist referral | | | X | |
| Asthma nurse home-care monitoring | | | | X |
| Self-management plan | X | | | X |
| Patient advice sheet | X | X | | |
| Patient information letter | | | X | |

Due to the heterogeneity of CDSS design, function and reporting in the literature, a detailed description of intervention characteristics of the 4 included studies is presented in Appendix 3.1 adapted from the framework for reporting of CDSSs used by Kawamoto *et al.*[137] and the computer decision support system taxonomy used by Berlin *et al.*[315] This Includes descriptions of intervention context, knowledge source, decision support type, delivery, workflow and auxillary features of the interventions used within included studies.

#### 3.3.6.1 Context and function

The aims of the intervention in McCowan *et al*.,[156] Eccles *et al*.[153] and Tamblyn *et al.*[313] focused on the impact of an intervention on broad asthma management whilst aim of Zeiger *et al.*[314] was to reduce excessive SABA use. The alert in McCowan *et al.,* Eccles *et al.* and Tamblyn *et al.* presented in consultation whilst in Zeiger *et al.,* the clinician was alerted in 'real-time' at point of excessive SABA dispensing from pharmacy.[314] Potential barriers to the use of the intervention were reported in three of the four studies. In McCowan *et al.,* alert presentation was dependent on clinician data entry however as this was a stand-alone system separate

from the EHR double data-entry would have been required.[156] In Eccles *et al.,* alerts initially presented when a patient's EHR was entered but this was changed to presenting when a relevant morbidity code for asthma was entered.[153] However as the codes were not reported in the study there is uncertainty as to when and how an alert may have presented. In Zeiger *et al.* an electronic message within the electronic medical record system was sent to a patient's primary care provider when a patient with excessive SABA use was identified from SABA dispending records.[314] In Tamblyn *et al.,* the alert presented when a patient's EHR was entered and therefore was not specific to asthma.[313] None of the interventions in the four included studies were delivered in conjunction with behaviour change programmes.

#### 3.3.6.2 Knowledge and data source

A range of guidelines relevant at time of study, were used as the knowledge base for intervention design and delivery. This ranged from British Asthma Guidelines,[156] National Asthma Education & Prevention Programme (NAEPP) guidelines and Global Initiative for Asthma guideline[314] and Canadian consensus guidelines.[313] In one study, evidence based guidelines for asthma were developed and reported elsewhere.[153,316] In two studies alerts were driven by data derived within the patient EHR,[153,313] whilst one study relied on data being manually entered onto a separate programme.[156] In one study, the alert was generated in response to pharmacy data contained within a research data warehouse within the Kaiser Permanente integrated healthcare system.[314] In two studies generic alerts were generated in response to pre-determined scenarios within the CDSS,[153,156] whilst in the two recent studies within integrated healthcare systems, alerts were personalized to patients.[313,314]

#### 3.3.6.3 Decision support and information delivery

In McCowan *et al.,*[156] the decision support was a system based on a combination of asthma guidelines, clinical scenarios and reminders, clinical presentation as determined by the data manually entered at consultation including SABA use, would trigger a series of prompts related to scenarios predetermined within the CDSS. The decision support was delivered on a floppy disk to be installed on participants Microsoft Windows compatible computer desktop and that had to be opened separately to the EHR for use in asthma consultations

In Eccles *et al.,*[153] a CDSS provided contextualized prompts triggered when relevant asthma

codes were entered on the EHR. Asthma management and prescribing suggestions were presented based on guidelines, clinical scenarios and health record information. The CDSS was accessible from within the main computerised operating system used by clinicians however the guideline recommendations presented as a separate pathway that required clinicians to leave the EHR. It is unclear what type of information presented to clinicians within consultation or whether the recommendations prompted the clinician to access the separate pathway for the guideline. It is unclear what specific advice was presented to clinicians in regards to SABA use however the system offered suggestions for management that included prescribing recommendations.

Zeiger *et al.,*[314] used real-time identification, notification, and facilitated allergy specialist referral for excessive SABA users. The intervention was delivered within the Kaiser Permanente Southern California (KPSC) managed care organisation (MCO) that utilises integrated electronic medical record systems and an electronic registry linked to dispensing data and hospital data for health insured patients. When excessive SABA use was determined at time of dispensing, the patient's clinician was explicitly informed of excessive SABA use at that point. An electronic message was generated to the clinician with the following information:

*"Your patient (Name, MR #) was recently identified with uncontrolled asthma based on being dispensed a seventh canister of albuterol within the past year. Kaiser Permanente and other groups have documented that this amount of use of albuterol is a sign of uncontrolled asthma and is associated with an increased rate of future asthma ED visit and/or hospitalizations. "* (Zeiger *et al.* 2014, p.456, appendix E1).

The message also stated the patient had been recommended by letter to take (or restart) regular ICS. Clinicians were advised if the patient had been referred to an allergy clinic and were encouraged to contact their clinician regarding asthma care. Therefore the message to clinicians was not at point of care and did not require action as patient letter and allergy referral were facilitated within the study.

Tamblyn *et al.,*[313] used a dashboard alert (figure 3.2) that presented upon identifying a

patient's asthma as out-of-control. This was determined by daily update of SABA prescriptions dispensed and physician visit information from the regional health insurance database. The alert presented within the EHR informing clinicians of a patient's poor asthma control. The clinician could access the patient's asthma profile, enroll the patient on a home care support and monitoring programme or close the alert. The patient's asthma profile contained information on current medications, level of SABA use, respiratory-related emergency department visits, symptoms and impact on daily activities, as well as prescribing recommendations and an optional action plan. In the studies in which the intervention facilitated referral to an allergy specialist[314] and an asthma nurse home monitoring programme,[313] referral rates were not reported.

Figure 3. 2 Decision Support dashboard alert


#### 3.3.6.4 Auxillary features

User involvement in the intervention development in McCowan *et al.,*[156] consisted of a steering group consisting of GPs with an interest in asthma reviewing the project over an 18- month period. In Eccles *et al*.,[153] user involvement in CDSS design was not reported however, user feedback was obtained after 4 months of the study resulting in an alteration to the method of intervention presentation however it is not clear what type of information was obtained, how it was obtained and how it was used. A usage log within the computer recorded when the guidelines were used but reasons for (non) engagement was not reported.

In three studies patients were targeted by the intervention. In McCowan *et al.*,[156] an optional asthma action plan and advice sheet was available, whilst in Tamblyn *et al.,*[313] an asthma action plan was automatically generated by the CDSS when recommendations were accepted by a clinician however use remained at clinician discretion. This was in contrast to Zeiger *et al.*,[314] in which patient letters were generated by administrative outreach in a managed healthcare organisation removing the need for clinician action. Education and training were reported in two of the four studies. McCowan *et al.,*[156] reported that 'online help' was accessible from within the CDSS programme and an installation booklet and user guide were also provided. In Eccles *et al.,*[153] two members from Intervention practices were sent to a one-day workshop on how to use the CDSS.

### 3.3.7 Defining excessive SABA prescribing

Due to the variety of definitions of excessive SABA use identified in Chapter 1 Introduction, excessive SABA prescribing was determined by study definition. There was a lack of uniformity in the definition and description of excessive SABA prescribing between the four studies reviewed. Tamblyn *et al.*[313] defined excessive SABA use as was defined as the dispensing of more than the equivalent of 250 doses of the most commonly prescribed FABA, salbutamol 100 mcg, in a 3-month period. However, Zeiger *et al.*[314] defined excessive SABA use as the dispensing of 7 SABAs per year, equating to 4 puffs of SABA per day per year.

In both Tamblyn *et al.*[313] and Zeiger *et al.*[314] SABAs were referenced in terms of excessive use, however the aim of this review was to determine the effect of CDSS on excessive SABA prescribing. Variations in framing the problem of SABA use/prescribing was described in Chapter 1 with SABA use and SABA prescribing used interchangeably in the literature. Howwever, SABA use cannot accurately be captured and can only be assumed by SABA prescribed/dispensed data, where excessive *use* was reported, excessive *prescribing* should be assumed.

### 3.3.8 Outcomes

A summary of findings is presented in Table 3.5. A detailed description of findings by study can be found in Table 3.6.

Table 3. 5 Summary of review outcome findings

| Study Author and Year | Study-defined excessive SABA prescribing | SABA prescribing | ICS prescribing | ICS-SABA scribing ratio | ICS-LABA prescribing | Asthma reviews | Asthma Exacerbations | Asthma Exacerbation requiring oral steroids | Unscheduled primary care consultations for asthma | Unscheduled secondary care consultations for asthma | Asthma control |
|---|---|---|---|---|---|---|---|---|---|---|---|
| McCowan 2001 | | | +/- | | | +/- | + | +/- | + | +/- | |
| Eccles 2002 | | +/- | +/- | | | | | +/- | +/- | | |
| Zeiger 2014 | + | + | +/- | | + | | | +/- | | +/- | |
| Tamblyn 2015 | | | | + | | | | | | | + |
| **+** positive effect; +/- no effect; SABA, short-acting beta$_2$- agonist; ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist | | | | | | | | | | | |

Table 3. 6 Detailed description of review outcome findings

| Study | CDSS use | Process outcomes of interest | Clinical outcomes of interest | Interpretation |
|---|---|---|---|---|
| McCowan 2001 | Not reported | No between-group difference in number of patients prescribed maintenance therapy based on British asthma guidelines step; *p*= 0.51. No between-group difference in number of patients attending practice initiated asthma reviews OR 0.69 (CI 0.21-2.21). | Fewer exacerbations reported in the intervention group; 12/147 (8%) in comparison to the control group 57/330 (17%); OR 0.43 (CI 0.21-0.85). Fewer patients prescribed oral steroids for an exacerbation; 7/147 (5%) of the intervention group compared to 35/330 (11%) of the control group OR 0.42 (CI 0.14-1.29). Fewer primary care consultations initiated by patients; 22% intervention group compared to 34% control group, OR 0.59 (0.37-0.95). No between group difference in hospital admissions; OR 0 (CI 0-3.44); or emergency department visits; OR 0 (CI 0-9.16). | Of the 46 practices registered to participate, 21 were randomised but only 5 completed the trial due to software problems. Patients treated with CDSS initiated less asthma consultations and were less likely to experience an exacerbation. However it was not clear how exacerbation was defined. The CDSS was not integrated and usage rate was not captured. |
| Eccles 2002 | Median number of active interactions between groups was zero. | No between-group difference in numbers of SABA prescribed; OR 1.04 (CI 0.83-1.31).<br><br>No between-group differrence in numbers of ICS prescribed; OR 0.95 (CI 0.78-1.16). | No between-group difference in number of consultations for asthma OR 0.94 (CI 0.81-1.08). No between-group difference in number of patients prescribed oral steroids before and after OR 1.0 (CI 0.82-1.22). | Cluster study design with practices as the unit of randomisation, consisted of two arms, asthma and angina each acting as control for the opposite arm. Data analysed 12 months before and after. A high number of practices participated (62); prescribing data was obtained from 1139 patients (intervention) and 1385 (controls). Process of care data was obtained from 1200 patients treated with the intervention and 1163 controls. Intervention had no effect on process or clinical outcomes. Median intervention usage was zero. Data was analysed on an intention to treat basis. |

Table 3.6. Detailed description of findings (continued)

| Study | CDSS use | Process outcomes of interest | Clinical outcomes of interest | Interpretation |
|---|---|---|---|---|
| Zeiger 2014 | Not reported | Less patients in the intervention group dispensed excessive SABA: 50.7% vs 57.1% control group; RR 0.89, *p*= 0.007 (CI 0.82-0.97) and increased time to be dispensed SABA excessively; HR 0.80; *p*=<0.001 (CI 0.71-0.91). Greatest effects seen in those with no prior asthma specialist care. Reduction in SABAs dispensed to intervention group at 3 months *p*= 0.002, 6 months *p*= <0.001, 12 months *p*= <0.001. Increase in ICS-LABA inhalers dispensed to intervention patients without prior asthma specialist care; 3 months *p*= 0.004, 6 months *p*=<0.001,12 months *p*= 0.03. | No between group difference in number of patients with an exacerbation requiring oral steroids; *p*= 0.71, either with or without prior specialist asthma care; *p*= 0.38 vs *p*= 0.83. No between group difference in number of patients with an asthma exacerbation requiring >= two oral steroid courses; *p*= 0.55, either with or without prior specialist asthma care; *p*= 0.89 vs *p*= 0.50.No between group difference in number of asthma ED visits and/or hospitalisation; *p*= 0.96, either with or without prior specialist asthma care; *p*= 0.55 vs *p*= 0.66. | Real-time outreach intervention in the Kaiser Permanente Southern California (KPSC) managed healthcare system. Usual care included KSPC extensive integrated asthma care management. The intervention reduced excessive SABA use, and ICS/LABA use. Greatest effect was seen in the subgroup of patients without prior asthma specialist care. Physician engagement was not captured Multicomponent intervention included a clinician message, patient letter and allergy referral. |
| Tamblyn 2015 | Physicians did not use the CDSS intervention 'Asthma Decision Support' in 60.5% of consultations for patients with out-of-control asthma | Increased ICS-SABA mean ratio in the intervention group; mean difference= 0.27 *p*= 0.034 (CI 0.02–0.51); | Reduction in out of control asthma events in the intervention group rate difference -8.7/100 PY; *p*= 0.29 (CI -24.7, 7.3). Greatest effects in the sub-group with out-of-control asthma when beginning the study. Rate difference: -28.4, *p*= 0.04 (CI -55.6, -1.2); Greatest reduction in the subgroup with out-of-control asthma at beginning of the study when treated with CDS alone had Rate difference: -36.9/100 PY; *p*= 0.01. | 81 physicians were randomised to 'asthma decision support;' 2,273 patients treated with the intervention, 2174 controls. intervention increased mean ratio ICS-SABA use and reduced the rate of out-of-control episodes. Greatest effect in the subgroup of patients with out-of-control asthma at study entry treated by CDS alone. In 60% of out-of-control visits the decision support was not utilised. |
| *CI* 95% confidence intervals, *SABA* short acting beta$_2$-agonist, *ICS* inhaled corticosteroid, *LABA* long acting beta$_2$-agoinst, *RCT* randomised control trial, *I* Intervention, *C* Control, *OR* Odds ratio, *RR* risk ratio, *ED* emergency department, *PY* patients per year, *CDSS* computer decision support system, *HR Hazard Ratio* | | | | |

#### 3.3.8.1 Primary outcome

##### 3.3.8.1.1 Excessive SABA prescribing

Zeiger *et al*.,[314] reported a reduction in the number of patients being dispensed excessive SABAs ($p = 0.007$) and an increase in length of time between SABA prescriptions ($p = < 0.001$). These effects were noted in the subgroup of patients without prior asthma specialist care who received the intervention ($p = < 0.001$). Tamblyn *et al.,*[313] reported excessive SABA (expressed as fast-acting b-agonist) dispensing as a composite primary outcome, the rate of out-of-control asthma episodes, which included emergency department (ED) attendances and hospitalisations. It was therefore not possible to determine the effect of the intervention on SABAs alone.

#### 3.3.8.2 Secondary outcomes

##### 3.3.8.2.1 SABA prescribing

Zeiger *et al.,*[314] reported a reduction in the number of SABAs dispensed at 3 months ($p = < 0.001$), 6 months ($p = < 0.001$) and 12 months ($p = < 0.001$) in the subgroup of patients without prior specialist asthma care. Eccles *et al.,*[153] reported no significant effect of a computerised decision support system on SABA prescription in the 12 months before and after the intervention (odds ratio (OR) 1.04, 95% CI 0.83–1.31).

##### 3.3.8.2.2 ICS prescribing

Zeiger *et al*.,[314] reported no difference in the number of patients dispensed ICS (not as a combination inhaler), whilst Eccles *et al.,*[153] reported no difference in the number of patients prescribed ICS before and after the intervention. McCowan *et al.,*[156] reported no between-group difference in maintenance prescribing patterns and no difference in the proportion of patients classified by management step.

#### 3.3.8.2.3 ICS-SABA prescribing ratio

Tamblyn *et al.,*[313] reported an increase in the ratio of ICS-SABAs dispensed (mean difference 0.27, $p = 0.03$; 95% CI 0.02–0.51) with higher ratios reported in both subgroups of patients whose asthma was controlled and out of control at the start of the study. Zeiger *et al*.,[314] reported a controller (ICS) to total medication ratio of greater or equal to 0.5 at 3, 6 and 12 months, in particular for those without prior asthma specialist care. As the ICS to total medication ratio was calculated by the number of ICS canisters or 30-day supplies of oral controller medications dispensed, divided by the total number of controller units and SABA inhalers, it was not possible to determine the ICS-SABA ratio specifically.

#### 3.3.8.2.4 ICS/LABA prescribing

Zeiger *et al*.,[314] reported an increase in the number of patients in the subgroup without prior asthma specialist care dispensed an ICS-LABA inhaler at 3 months ($p = 0.004$), 6 months ($p = < 0.001$) and 12 months ($p = 0.03$).

#### 3.3.8.2.5 Asthma reviews

McCowan *et al.,*[156] reported no reduction in the number of patients attending practice- initiated asthma reviews. This was not reported by other studies.

#### 3.3.8.2.6 Asthma exacerbations

Exacerbations were determined by study-defined parameters, as described in the protocol. This was due to the variation in definitions of exacerbations in the literature on asthma. McCowan *et al.,*[156] observed a reduction in asthma exacerbations, with 8% of patients who received the intervention reporting an acute asthma exacerbation compared to 17% in the control group (OR 0.42; 95% CI 0.21-0.85). However, there was no difference in the use of oral steroids to manage these attacks in the intervention and control group. Zeiger *et al.,*[314] reported no difference in the numbers of patients prescribed oral steroids for an exacerbation irrespective of prior asthma specialist care status. Neither McCowan *et al.,* nor Zeiger *et al.,* explicitly defined an asthma exacerbation. Eccles *et al.,*[153] reported no difference in the numbers of patients prescribed oral steroids before and after the intervention but did not specifically report asthma exacerbations.

#### 3.3.8.2.7 Unscheduled consultations for asthma

Eccles *et al.,*[153] found no between-group reduction in the number of primary care asthma consultations, whilst McCowan *et al.,*[156] reported that patients who received the intervention initiated fewer primary care consultations (OR 0.59; 95% CI 0.37–0.95). However neither study clarified whether consultations were scheduled or unscheduled. Both McCowan *et al.,*[156] and Zeiger *et al.,*[314] reported no effect of the intervention on AED attendances or hospitalisations for asthma. Tamblyn *et al.,*[313] reported AED visits and hospitalisations for asthma as a composite outcome defined as 'rate of out-of-control asthma episodes,' therefore secondary care consultations for asthma could not be specifically determined.

#### 3.3.8.2.8 Asthma control

Tamblyn *et al.,*[313] reported a reduction in the rate of out-of-control asthma events, defined as a composite outcome of excessive SABA use, AED attendance and hospitalisations for asthma, in the sub-group of patients whose asthma was out-of-control at the beginning of the study (mean difference −28.4, $p = 0.04$; 95% CI −55.6, −1.2). When stratified by intervention component, the rate of out-of-control asthma events further reduced when patients were treated with CDSS alone (rate difference (RD) −36.9/100 per year, $p = 0.01$) in comparison to those threated with both CDSS and the asthma home care monitoring programme (rate difference -28.4, $p = 0.04$; 95% CI −55.6, −1.2).

## 3.4 Discussion

### 3.4.1 Summary of findings

Given the few studies identified, the evidence to support the use of alerts to reduce excessive SABA prescribing in primary care is limited but promising. This review found that electronic alerts, when delivered as a multicomponent intervention have the potential to successfully identify and reduce excessive SABA prescribing. The greatest effect on SABA prescribing occurred in well-resourced integrated health care systems with access to referral to multidisciplinary teams and services. None of the studies included used a SABA alert as a sole intervention.

### 3.4.2 Comparison with the literature

Our findings support previous research on the use of computer decision support for long-term conditions including asthma, chronic obstructive pulmonary disease, diabetes and osteoporosis which found that interventions consisting of multiple components are associated with greater improvement in outcomes than single-target interventions with fewer components.[130,150,317]

The McMaster group's meta-regression explored the features of CDSSs associated with system 'effectiveness'.[102] They found that stand-alone programs, for example in McCowan *et al.,*[156] as well as advice directed at both health-care practitioners and patients, and requiring users to enter an explanation for any overrides of system recommendations was associated with better patient outcomes.[102] Standalone programmes are more likely to be used in older studies such as McCowan *et al.,*[156] with more recent studies by Tamblyn *et al.,*[313] and Zeiger *et al.,*[314] using integrated CDSS to improve asthma outcomes. Matui *et al.,*[150] note that use of standalone programmes risks poor user engagement with CDSS however integrated CDSSs do not guarantee engagement, as reflected in low user rates in Tamblyn *et al.*[313] In two studies in which CDSS engagement was reported, users failed to engage with decision support,[153] whilst in another, clinicians failed to interact with the CDSS in approximately 60% of cases.[313] However it is not clear whether levels of engagement were consistent between clinicians and whether clinician interaction declined over time. There may be valid reasons to account for the variability in decision support engagement which include technical design of the CDSS, the setting in which the system is deployed and the characteristics of users and the patients treated.[119] User engagement of 40% in Tamblyn *et al.,*[313] in comparison to almost no engagement in Eccles *et al.,*[153] is likely due to the increased ease of use associated with more recent, sophisticated decision support integrated within a comprehensive EHR system that accesses pharmacy, as well as primary and secondary care data.

The two studies that showed greatest effects on outcomes of interest in this review were those carried out recently (in the past three years), in which decision support was integrated

with EHRs.[313,314] In contrast to McMaster group findings, these findings support the evidence, as described in Chapter 1, that computer decision support integrated with clinician workflow is associated with improved outcomes.[122,137,141] Zeiger *et al's.,*[314] findings that a multicomponent alert intervention can reduce excessive SABA use, supports the evidence that electronic health records and electronic messaging in an integrated health care system increases clinician adherence to evidence-based guidelines.[318] The identification and reduction of excessive SABA use in Zeiger *et al*.,[314] was facilitated by alerts that were not restricted to point-of-care presentation. Such methods of alerting may offer a solution to the dilemma that automatic provision of decision support at point of decision making neither guarantees clinician uptake or engagement[119] nor predicts improvements in process of care or patient outcomes.[102]

As described in Chapter 1, alerts integrated within EHRs may interrupt clinician workflow and result in "alert fatigue" with up to 96% of alerts over ridden or ignored.[142] Following user feedback, Eccles *et al.,*[153] altered decision support to trigger when a clinician entered a relevant morbidity code rather than being automatically activated upon entering a patient's medical record. Whilst this may have been an attempt to minimise alert fatigue it did not improve CDSS user interaction. It is likely that very low CDSS interaction reflected clinical guidelines being located in a separate system not supported within clinician workflow.

In a non-randomised study by Cho *et al*,[319] used a CDSS to classify asthma severity based on symptoms, FEV1 or PEFR and medication use, including SABAs. If asthma severity was aggravated compared to a previous visit the CDSS presented a warning message in consultation, advising that medications should be changed according to current asthma severity and that referral to an asthma specialist should be considered. The CDSS resulted in fewer prescriptions for beta$_2$-agonists (p=0.02) however it is unclear whether this was short or long acting beta$_2$-agonists or both. Furthermore the change in prescribing was not quantified and it is unclear whether the warning message contained direct advice on SABA prescribing.

In a non-controlled before and after study by Wong *et al.,*[320] notifying providers of their patients with excessive SABA use resulted in reduced SABA prescriptions. The intervention involved written or verbal confirmation by the prescriber for all new prescriptions for more than one SABA per month prior to pharmacist dispensing. Pharmacists manually alerted clinicians by fax and follow-up telephone call. This included guideline recommendations for appropriate SABA use and requested a reduction of SABA prescribed to less than or equal to one inhaler per month, if the prescriber judged it appropriate.

This resulted in a reduction in the percentage of people prescribed more than one SABA per month between year one and year two (22.9% vs 9.7%, P <0.01), with 67% receiving less than one SABA per month during year two. For example Wong *et al.*[320] highlight the potential role of pharmacists that has been absent from the four studies included in this review.

None of the four included studies reported using qualitative methods to complement intervention design despite the potential to influence intervention RCT design and delivery.[321] Such methods may optimise alert design, improve clinician interaction with decision support and aid the interpretation of results in future.

### 3.4.3 Outcome reporting

The recent Lancet commission on redefining airways disease highlighted the underutilised potential for the use of EHRs containing clinical, laboratory, and health utilisation data for asthma research in primary care.[322] However asthma clinical research often lacks standardised outcomes, with variability in clinical definitions of asthma and disease severity, control and attacks/exacerbations.[323,324] In their scoping review of defining asthma outcomes using EHR data, Al Sallakh *et al.*,[244] note that variability and underreporting make it difficult to assess the validity of studies and compare their findings. Such inconsistent definition, measurement and reporting of asthma outcomes therefore makes it challenging to determine the effects of one intervention over another in practice.

For example in two previous systematic reviews of the literature on CDSS for asthma by Matui *et al.*[150] and Fathima *et al.,*[151] the reporting of both clinical and process outcomes varied across the included studies. As described in Chapter 1 there are variations in how SABA use is defined in the literature. Definitions of excessive SABA use also varied between Tamblyn *et al.,*[313] and Zeiger *et al.*[314] as described in section 3.4.7. The reporting of inhaled steroid use varied between the studies. In Zeiger *et al.*[314] both ICS prescribing and ICS/LABA combination inhaler prescribing were captured. Whilst in Tamblyn *et al.,*[313] the ICS-to-SABA ratio was reported, in McCowan *et al.*,[156] ICS prescribing was reported by British asthma guidelines step and in Eccles *et al.,*[153] the separate prescribing of inhaled steroids and LABAs was reported.

ICS-to-SABA ratio has been used as a measure of quality of asthma care and a marker for deficits in asthma treatment and potential risk in a number of studies in the literature.[326,327] Despite identifying the excessive prescribing of SABAs and under prescribing of ICS as a marker of risk and a contributor to asthma deaths, NRAD,[25] like BTS/SIGN[52] do not specify an ICS/SABA ratio threshold as indicative of poor asthma control. Challenges are likely to arise in the accurate capture of ICS data within EHRs given the variations ICS in dose equivalence resulting from increased generic prescribing[112] and the prescribing of combination inhalers including as maintenance and reliever therapy (MART). This may present challenges for the standardisation of endpoints and comparison of outcomes between future studies.

Surprisingly asthma reviews were reported in only one of the four studies included in the systematic review despite being fundamental to asthma self-management.[325] It may be that asthma reviews are not a routinely captured outcome measure due to the challenge of translating process measures into improvements in patient outcomes.[328] In Zeiger *et al.,*[314] patients using excessive SABAs without prior specialist asthma care were invited for an allergy specialist review however only a minority of intervention patients recommended availed of the allergy review. Patients were also contacted by letter and advised to initiate follow-up with their primary care doctor however, these follow-ups were not reported.

There are wide variations in the definition and reporting of asthma exacerbations in the literature[329] and in a recent scoping review by Al Sallakh *et al*.,[244] on EHR data and asthma outcomes. There were variations in the reporting of exacerbations in the studies included in this systematic review. Zeiger *et al,*[314] defined an exacerbation as least one oral steroid course, or two or more courses with exacerbations considered distinct when separated by at least 30 days. Tamblyn *et al.,*[313] did not explicitly report asthma exacerbations as an outcome measure instead reporting on out-of-control asthma events characterized by three components: an AED attendance, hospitalization and/or excessive SABA use in the past three months. However Tamblyn *et al's.,* definition of out-of-control asthma as a composite outcome may reflect an uncertainty in defining an exacerbation as a progressive worsening of symptoms in comparison to that which requires AED attendance or hospitalization. In a review to determine a consensus definition for asthma exacerbations, Fuhlbrigge *et al.*[330] found no dominant definition of "exacerbation" in the literature but noted that the three components were

commonly used: (1) systemic use of corticosteroids, (2) asthma-specific emergency department visits or hospitalization, and (3) SABA use. However the use of oral steroids was notably absent from Tamblyn *et al's.,* definition. Fuhlbrigge *et al.,*[330] argue that each component adds independent information about a patient's underlying condition recommending that variables used to determine an exacerbation where reported as a composite outcome are also reported as single indicators. Despite two of the three components in Tamblyn *et al's* definition of out-of-control asthma reflective of Fulhbrigge's, definition of an exacerbation, exacerbation rates could not be determined due to the individual components of asthma control not fully reported. In McCowan *et al.*[156] an exacerbation was determined as such if reported by a clinician, however it was not clear how the clinician's reporting was derived. Oral steroid prescribing did not reflect an exacerbation, instead used to determine how a reported exacerbation was managed. In Eccles *et al*.[153] an exacerbation was not specifically defined however was determined by steroid prescribing before and after CDSS use.

Each of the four studies included in the systematic review included unscheduled consultations for asthma as an outcome measure. However the definition of unscheduled consultation varied across studies. Both McCowan *et al*.,[156] and Eccles *et al.*[153] reported on the number of primary care asthma consultations, however neither study clarified whether consultations were scheduled or unscheduled. Both McCowan *et al.,*[156] and Zeiger *et al.,*[314] reported and/or AED attendances or hospitalisations for asthma. Tamblyn *et al.,*[313] reported AED visits and hospitalisations for asthma as a composite outcome defined as 'rate of out-of-control asthma episodes,' as previously discussed, therefore asthma related secondary care contacts could not be specifically determined.

### 3.4.4 Strengths and limitations

As interventions to improve prescribing volumes/rates do not necessarily result in more 'appropriate' prescribing or improved patient outcomes,[119] both process and clinical outcomes were assessed in this review. Due to variations in the definition and reporting of asthma outcomes in studies using EHR data as identified by Al Sallakh *et al.,*[244] selection and reporting bias was reduced by including study defined outcome definitions in this review. Few studies met our inclusion criteria, with only one study reporting our primary outcome of interest therefore due to the limited number of published reports of randomised controlled trials in our analyses, there may be possibility of publication bias or selective reporting.

Interventions in the two older studies by McCowan *et al.,*[156] and Eccles *et al*.,[153] were poorly

described which may have limited our interpretation of the findings. We were unable to conduct a meta- analysis due to heterogeneity in intervention design and outcomes evaluated. Due to poor reporting, no conclusions could be drawn on health economic impact.

The inclusion of only RCTs is a potential limitation of this review. It has been suggested that population-based intervention studies using health information technology are less likely to be randomised.[314] This may account for the few RCTs identified for inclusion in this review (n=4). Furthermore, the design, delivery and understanding of complex interventions requires a multi-method research approach to facilitate the rigorous assessment and interpretation of results.[306] Understanding of issues pertaining to the effectiveness of CDSSs is unlikely to be achieved through analysis of RCTs alone.[331] It has been suggested that in topic areas where the number of patients is limited or the evidence is conflicting, systematic reviews offer the benefit of collating evidence from a variety of sources.[305,332] Therefore excluding non-RCTs has potentially limited our understanding of the use of CDSSs for SABA prescribing and findings should be interpreted with caution.

## 3.5 Conclusions

There is some evidence that electronic alerts integrated with EHRs and delivered as part of a multicomponent intervention can reduce excessive SABA prescribing. Due to variations in health care systems, intervention designs and outcomes measured, further research is required to determine the effects of alerts on excessive SABA prescribing in a publically funded health system. Future research should determine the point at which novel alerts will most effectively reduce excessive SABA prescribing and be accepted by users.

## 3.6 Implications

### 3.6.1 Implications for clinical practice

There is an increased focus on the digitalisation of the NHS in an attempt to improve safety and quality of care,[333] with recommendations from both NRAD and Asthma UK calling for national use of electronic alerts to identify excessive prescribing of SABAs in the UK.[25,334] Due to the few studies identified in this review, the role of alerts to reduce excessive SABA prescribing in the UK's publically funded NHS remains unclear. Integrated care can take many forms involving

collaboration between policy providers and commissioners and between service providers, however benefits arise primarily when clinical teams and services are brought together and incentives are aligned to support service improvement.[318] It is likely that a combination of design, technical capabilities and variety of intervention components, when delivered in an integrated health care system, facilitated the improvements to SABA prescribing and asthma management identified in recent studies. However due to organisational, management, policy and financial barriers and the increasing politicisation of the NHS, it remains challenging to deliver such improvements in a publicly funded health care system such as the NHS.[335]

### 3.6.2 Implications for future research

This review identifies a number of areas where potential exists and where further research is recommended. In the UK, 78% of bronchodilators are issued on repeat prescription[76] yet research fails to address the use of alerts at this point in the prescribing process. Furthermore, two studies from the UK, carried out over a decade ago, did not integrate interventions within EHRs, in contrast to more recent studies from North America. Future research should consider novel ways to deliver SABA alerts as a sole intervention and/or as part of a multicomponent intervention in primary care. Furthermore, the point in the prescribing process at which a SABA alert will have greatest impact should be explored. Interventions should be trialled both in and outside of the consultation to target clinicians and people with asthma.

Findings highlight the potential of multicomponent CDSS interventions to reduce SABA prescribing and improve asthma management. Further potential to explore the effect of a single component CDSS intervention on SABA prescribing as no such studies were identified. Given the limited number of RCTs on this topic, future study design and evaluation such not be restricted to RCTs but should include observational and mixed methods research.

Standardised methods for the design and reporting of CDSS interventions in asthma are recommended to enable a thorough evaluation of process and clinical outcomes. An explicitly defined outcome set that includes standardised endpoints, e.g., excessive SABA use and asthma exacerbations may help the translation of research findings into clinical practice. In studies using CDSSs to improve the management of asthma, asthma reviews be included as an important process outcome measure.

Findings support the recommendations of as Kawamoto *et al*.,[137] and Berlin *et al.,*[315] that studies use a taxonomy or framework to theoretically underpin the design and reporting of interventions including the implementation processes and health economics outcomes associated with CDSS-based alerts. This should include the enhanced reporting of EHR interventions through the use of the RECORD and STROBE statements[336] Future studies should consider mixed methods designs that incorporate qualitative methods before, during and/or after an RCT as recommended by O'Cathain *et al*.,[321] End-users should be involved in the design of alerts to optimise interventions purpose, usability and trial design. Such methods may help determine the barriers and facilitators to alert usage in practice, as well as assisting in the development of alerts that are transferable to the real-world clinical setting.

# Chapter 4. An electronic alert to reduce excessive prescribing of short-acting beta$_2$-agonists for people with asthma in general practice in east London: a retrospective case-control study using routine electronic health record data

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## 4.1 Introduction

### 4.1.1 Recap of context

This chapter represents Phase 2 of the thesis; a retrospective case-control study of electronic health care record (EHR) data to evaluate the effectiveness of a single component alert intervention to reduce SABA prescribing. This follows Phase 1 findings that when delivered as part of a multicomponent intervention CDSS alerts show limited potential to reduce excessive SABA prescribing. No studies in the review evaluated an alert as a single component intervention nor assessed the impact of an alert at reducing repeat prescriptions of SABAs. As such, the evidence to support alerts in the identification and management of excessive SABA prescribing remains unclear.

### 4.1.2 Asthma Medicines Management alert

In 2015, EMIS Health, national providers of general practice software systems, collaborated with Asthma UK to devise and implement an alert to improve identify and improve problematic prescribing in asthma. The Asthma Medicines Management alert* was developed to identify people prescribed excessive SABAs, high long-acting beta- agonists (LABAs) or long-acting muscarinic antagonist (LAMA) use and/or the prescribing of LABAs/LAMAs without concomitant inhaled corticosteroids (ICS) (figure 4.1). The SABA alert identifies patient's prescribed more than three SABA prescriptions in a three-month period and activates upon opening of a patient's EHR. The alert was made active in EMIS web practices on 17th June 2015. The original intention of this study had been to work collaboratively with EMIS to prospectively evaluate an alert to identify excessive SABA prescribing in primary care. However, 6 months after commencing the PhD, EMIS implemented the SABA alert resulting in the retrospective evaluation of the SABA alert as presented in this chapter.

* Referred to hereafter as SABA alert

Figure 4. 1 Asthma Medicines Management alert configuration

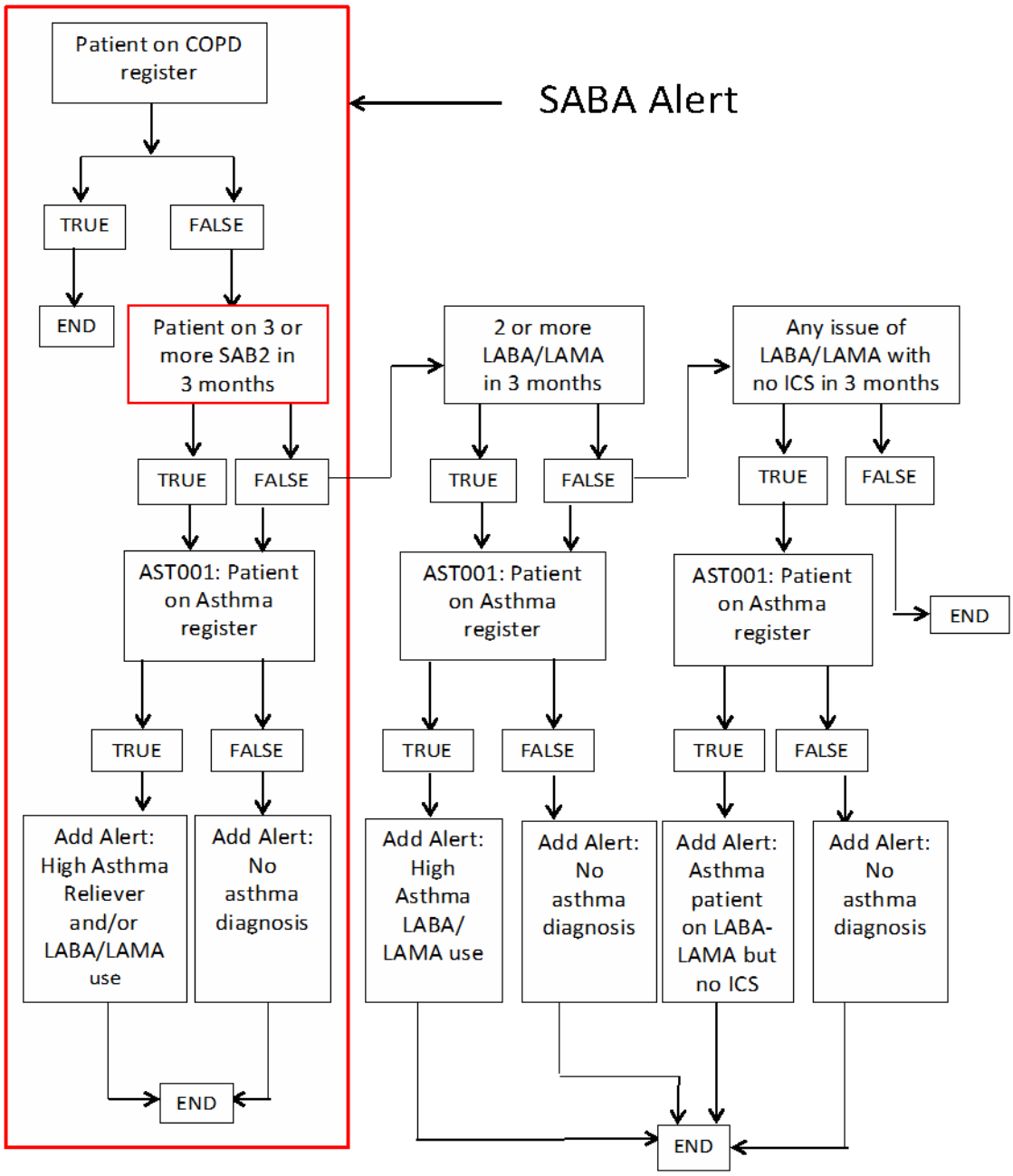
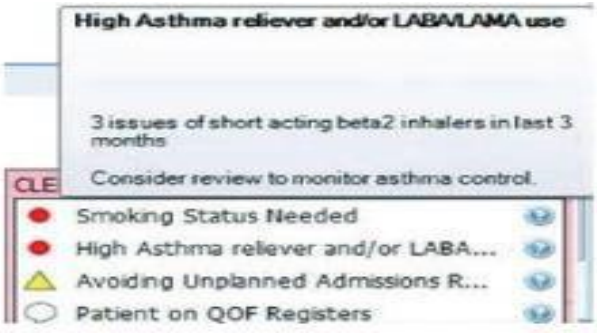


Figure 4.2 presents the SABA alert as displayed in the EHR. The SABA alert automatically presents at the bottom right hand corner of the EHR screen, in what is referred to as the 'pop- up' box or the 'QOF' box. The QOF is a pay-for-performance system incentivising disease-specific performance targets. This was introduced on 1 April 2004 as part of the General Medical Services (GMS) contract for general practice. There are currently three QOF asthma indicators that present in this box; asthma diagnosis, smoking status and annual asthma review. The QOF box is however not restricted to QOF indicators and a range of other outstanding areas of patient care present in this box and are commonly referred to as alerts, reminders, 'flags or pop-ups. Once the SABA prescribing threshold has been triggered the SABA alert remains in the QOF box until the protocol criteria is no longer met. The SABA alert was devised on the assumption that only one SABA device is issued at a time however it is not uncommon for two SABA devices to be issued per prescription.[337]

Figure 4. 2 Asthma Medicines Management alert display



### 4.1.3 Hypothesis

This study aimed to test the following hypotheses:

*The null hypothesis*
The Asthma Medicines Management alert will have no effect on SABA prescribing in the 12-months post trigger date.

*The alternative hypothesis*
The Asthma Medicines Management alert will have an effect on SABA prescribing in the 12-months post trigger date.

### 4.1.4 Aims and Objectives

The aim of Phase 2 of the thesis was to determine the effectiveness of an electronic alert at reducing SABA prescribing among people with asthma prescribed excessive SABAs in primary care.

The objectives of Phase 2 of the thesis were to:

1. Evaluate the effect of the Asthma Medicines Management alert on the primary outcome of SABA prescribing at 12 months following the alert intervention using a historically controlled case-control study design.

2. Determine the effect of the Asthma Medicines Management alert on secondary outcomes: process measures (number of asthma reviews, time to asthma review, ICS/LABA prescribing, combination inhaler prescribing) and clinical outcomes (exacerbations, primary care consultations) of asthma care.

3. Explore subgroup analyses by time point (0-3, 3-6, 6-12 months) and prescription type (acute/repeat).

## 4.2 Methods

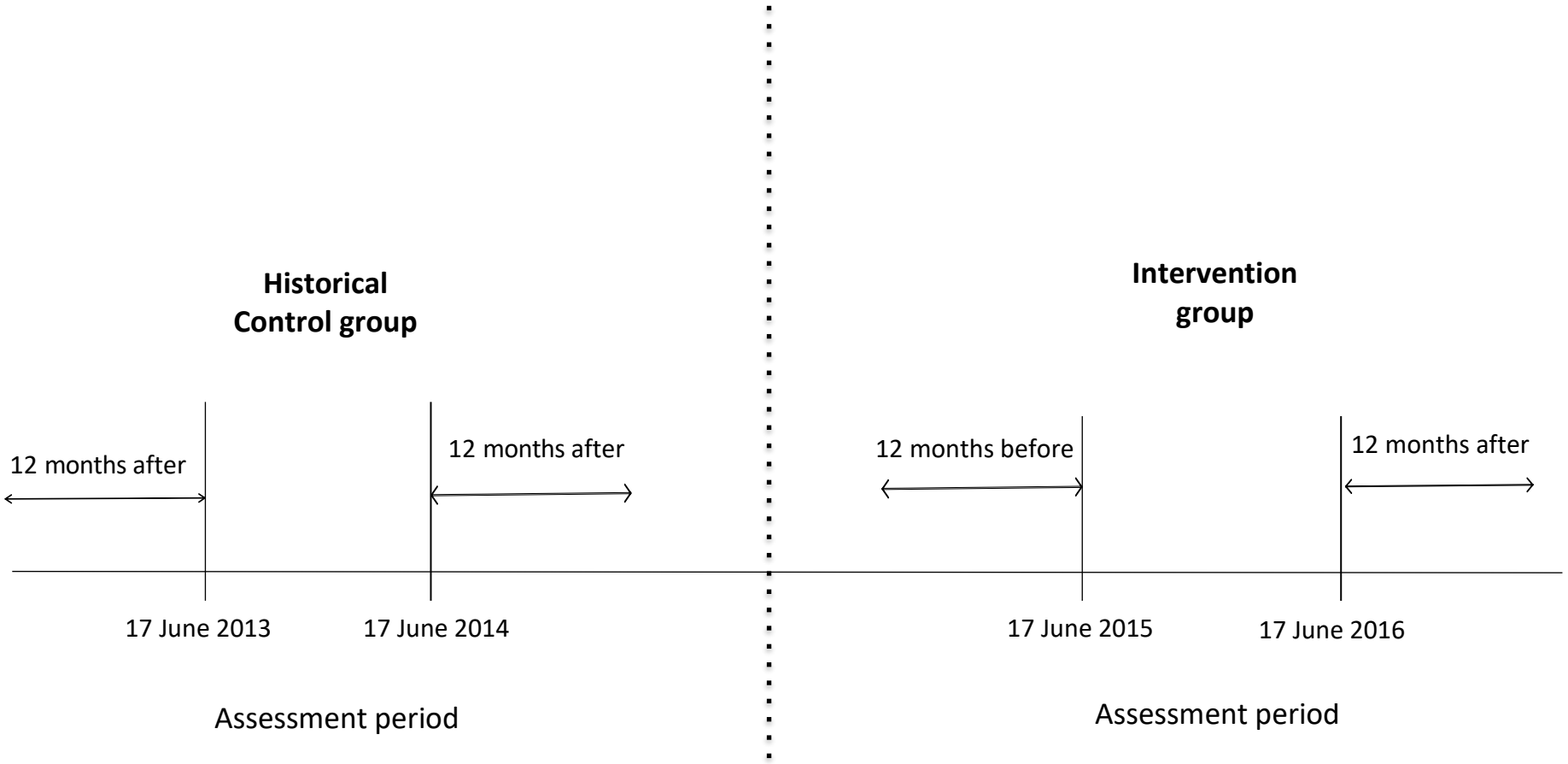
### 4.2.1 Study design

#### 4.2.1.1 Case-control study design

A case-control study design was used to determine the effects of an alert on outcomes of interest by comparing two population groups identified by excessive SABA prescribing: those identified following the implementation of an alert intervention (intervention group) and those historically matched as having been prescribed excessive SABAs prior to the alert intervention (control group). The study design is presented in figure 4.3. The choice of retrospective case-control design was influenced by two factors (1) convenience; by utilising a readily available data source in the locality within which the researcher was based, and (2) time; a prospective study would have exceeded both doctorate funding and timeframe for completion.

The intervention group were those identified as having been prescribed excessive SABAs in a 12-month period after the alert intervention (17th June 2015 to 17th June 2016) and the historical controls were those identified as having been prescribed excessive SABAs in a 12-month period before the alert intervention (17th June 2013 to 17th June 2014). The date of study entry for each patient was the date on which excessive SABA prescribing first occurred i.e. the point at which a third prescription for SABAs was generated. Patient and practice data was extracted and anonymised by the Clinical Effectiveness Group (CEG) at QMUL prior to being obtained by the researcher hence data analysis at practice and patient level was not possible. As practice characteristics were not analysed, cluster adjustment by general practice not required and a paired analysis between the intervention and control groups was not possible. Despite being identified by two distinct time-periods, patients may have been included in both intervention and control groups. This is acknowledged as a potential limitation in section 4.5.2.

Figure 4. 3 Case-control study design



#### 4.2.1.2 Sample size and power

Sample size and power was calculated using Chi-square test and interpreted using Cohen's statistical power analyses.[338] A Queen Mary University of London statistician was consulted throughout this study and assisted with power calculations.

An original power calculation was based on Hull *et al's.* study of asthma prescribing in the same three east London CCGs with a population of 35,864 asthma patients.[13] Based on approximately 30,000 patients in each arm of the study at 80% power and 5% significance, it was estimated that a very small effect size of 0.011 could be detected in the case-control study in *Phase 2* of this thesis. In clinical terms, this equated to the detection of an estimated 0.03% difference in those prescribed >3 SABAs between the intervention and control group in the 12 months following the excessive prescribing trigger. However, on further review, the inclusion criteria in Hull *et al.* were those with a QOF read code set for asthma diagnosis rather than our subset of interest; those prescribed excessive SABAs.

Following preliminary data collection, 18,244 patients met the *Phase 2* study inclusion criteria reported in section 4.2.2.3. Therefore at 80% power and 5% significance it was re-estimated that a minimum effect size of 0.02 could be detected. However following data analysis, there was a 1.69% difference in those prescribed >3 SABAs in the intervention and control group in the 12 months following the excessive prescribing trigger. This meant the actual effect size was 0.015 and when compared to the estimated power calculation, the study was underpowered at 52%.

To increase power, data was adjusted for covariates: age, ethnicity and SABA prescribing prior. Based on the evidence that each significant covariate adjusted for variation can add approximately 10% power,[339] the study was approximately powered at 82%.

Socio-economic status as determined by indices of multiple deprivation (IMD2010) was not included in covariate analysis. This has been acknowledged as a study limitation in section 4.5.2.

### 4.2.2 Study population

#### 4.2.2.1 Study setting

The study included data from 132 primary care practices using EMIS web general practice computer software in three ethnically diverse boroughs in east London: Tower Hamlets (n=37), Hackney (n=43) and Newham (n=52). This constituted a combined GP registered population of approximately 1 million. Practices were automatically included due to the data sharing agreements between general practice in east London and the Clinical Effectiveness Group (CEG) at QMUL.

#### 4.2.2.2 Patient demographics

Anonymised demographic data including age, gender and ethnicity were extracted. Ethnicity was self-reported, recorded at the practice either during registration or routine consultation. Ethnic categories were based on the UK 2011 census codes for ethnicity[340] and condensed into five major categories: White (British, Irish, other White), Black (Black African, Black Caribbean, Black British, other Black and mixed Black) and South Asian (Bangladeshi, Pakistani, Indian, Sri Lankan, British Asian, other South Asian or mixed Asian). Coding category 'other' was used to describe people who self-identify as White persons not of English, Welsh, Scottish or Irish ethnic groupings as referenced in census data. Ethnic category 'not stated' refers to unknown ethnicity or not reported/missing data. Appendix 4.1 details how the ethnicity categories were refined into the three categories used in this study.

#### 4.2.2.3 Inclusion and exclusion criteria

Four rules were generated used to search the EHR to determine patients eligible for inclusion based on the following criteria:

Rule 1: Patients aged between 5 and 75 years

Rule 2: Asthma in the previous 12 months

Patients were defined by the QOF Read code diagnosis of asthma.[341] Table 4.1 includes the expanded cluster list of codes for QOF Asthma diagnosis.

Rule 3: Prescribed at least one canister of short-acting beta$_2$-agonist (SABA) in the previous 12 months

A SABA prescription was defined as any SABA included in the Asthma Medicines Management alert protocol as listed in Table 4.2.

Rule 4: Excluding COPD

Patients who had a diagnosis of COPD as identified by the QOF Read code set[342] were excluded from the study.

Table 4. 1 Expanded QOF codes for Asthma diagnosis

| Read Code | Code description |
|---|---|
| 173A. | Exercise induced asthma |
| H3120 | Chronic asthmatic bronchitis |
| H33.. | Asthma |
| H330. | Extrinsic (atopic) asthma |
| H3300 | Extrinsic asthma without status asthmaticus |
| H3301 | Extrinsic asthma with status asthmaticus |
| H330z | Extrinsic asthma NOS |
| H331. | Intrinsic asthma |
| H3310 | Intrinsic asthma without status asthmaticus |
| H3311 | Intrinsic asthma with status asthmaticus |
| H331z | Intrinsic asthma NOS |
| H332. | Mixed asthma |
| H334. | Brittle asthma |
| H335. | Chronic asthma with fixed airflow obstruction |
| H33z. | Asthma unspecified |
| H33z0 | Status asthmaticus NOS |
| H33z1 | Asthma attack |
| H33z2 | Late-onset asthma |
| H33zz | Asthma NOS |
| H3B | Asthma-chronic obstructive pulmonary disease overlap syndrome |

Table 4. 2 Short-acting beta2-agonist inclusion

| SABA Name, Dosage and Quantity |
|---|
| Asmasal 95micrograms/dose Clickhaler (Focus Pharmaceuticals Ltd) |
| Bricanyl 500micrograms/dose Turbohaler (AstraZeneca UK Ltd) |
| Easyhaler Salbutamol sulfate 100micrograms/dose dry powder inhaler (Orion Ltd) |
| Easyhaler Salbutamol sulphate 100micrograms/dose dry powder inhaler (Orion Ltd) |
| Salamol 100micrograms/dose Easi-Breathe inhaler (Teva UK Ltd) |
| Salamol 100micrograms/dose inhaler CFC free (Teva UK Ltd) |
| Salamol Easi-Breathe Cfc-Free Breath-Actuated Inhaler 100 micrograms/puff |
| Salbulin Novolizer 100micrograms/dose inhalation powder (Meda Pharma Ltd) |
| Salbutamol Accuhaler 200 micrograms/dose and |
| Salbutamol Breath-Actuated Inhaler (Cfc-Free) 100 micrograms/dose |
| Salbutamol Breath-Actuated Inhaler (Cfc-Free) 100 micrograms/dose~(c13U.) |
| Salbutamol Cfc-Free Inhaler 100 micrograms/puff |
| Salbutamol Cfc-free inhaler 100 micrograms/puff~(c13J.) |
| Salbutamol 100micrograms/dose breath actuated inhaler CFC free |
| Salbutamol 100micrograms/dose dry powder inhaler |
| Salbutamol 100micrograms/dose inhaler CFC free |
| Salbutamol 200micrograms/dose dry powder inhaler |
| Salbutamol 95micrograms/dose dry powder inhaler |
| Terbutaline 500micrograms/dose dry powder inhaler |
| Ventolin 100 micrograms/dose Evohaler (GlaxoSmithKline UK Ltd) |
| Ventolin 200 micrograms/dose Accuhaler (GlaxoSmithKline UK Ltd) |

### 4.2.3 Study outcomes

#### 4.2.3.1 Primary outcome

*SABA prescribing*

The main outcome of interest was SABA prescribing at 12 months following the SABA alert. The definition of excessive SABA use was based on the Asthma UK Medicines Management alert definition of high SABA use as three SABA prescriptions in a three-month period. As SABA may be issued on a variety of prescription types including by acute or repeat, the date and type of SABA prescription was captured and included in sub-group analysis.

#### 4.2.3.2 Secondary outcomes

*Asthma reviews*

The number of asthma reviews and time to review were defined by the following QOF Read code set: 66YJ (Asthma annual review) 66YK (Asthma follow-up), 66YQ (Asthma monitoring by a nurse), 66YR (Asthma monitoring by a doctor), 8B3j (Asthma medication review) and 9OJA (Asthma monitoring check done).[341]

The number of asthma reviews and time to asthma review were analysed at 0-3 months and 3-6 month time points only as deemed more likely to be clinically significant than a review carried out at a later point. No review data was captured in the prior time period and therefore the potential influence of having had a review prior to the alert trigger was not explored.

*ICS, LABA and Combination inhaler prescribing*

The types of ICS, LABA and Combination inhalers included in the study are presented in appendices: ICS (appendix 4.2), LABAs (appendix 4.3) and Combination inhalers (appendix 4.4). Spacer prescriptions were not included.

Decision-making regarding the choice of inhalers for inclusion was guided by a variety of sources: (i) the British National Formulary for prescribing (ii) MIMs online; a prescribing and clinical reference for general practice, (iii) Hull *et al's* study on asthma prescribing in the same population[13] and (iv) clinical experience as an asthma health care professional.

*Exacerbations*

An asthma exacerbation was defined as any oral steroid prescription type as listed in appendix 4.5. This definition was based on Al Sallakh *et al's.*[244] scoping review of asthma outcomes using electronic health record data, which identified this as a commonly used definition of an exacerbation in a number of studies.[343–350] Oral steroid prescriptions were assumed to be prescribed for the treatment of an asthma exacerbation as prescribing for alternative purposes could not be determined in the data set. Exacerbations were primarily analysed at 0-12 months

prior and post the excessive prescribing trigger date.

*Consultations*

Primary care consultations were captured using the following consultation types readily available within the EHR: Administration note, discussion with colleague, discussion with other professional, emergency appointment, emergency consultation, extended hours consultation, externally entered note, face to face consultation, face to face consultation with relative/carer, GP surgery, home visit note, nursing home visit note, other note, telephone call from a patient, telephone call from a relative/carer, telephone call to a patient, telephone call to a relative/carer, telephone consultation, telephone triage encounter, third party consultation, urgent consultation, walk-in clinic. Asthma-specific consultations could not be determined as data is routinely coded by consultation type and not for presenting reason/condition. Primary care consultations were primarily analysed at 0-12 months post excessive prescribing trigger date but not in the prior time period.

#### 4.2.3.3 Sub group analyses

Outcomes were explored by time period 0-3, 3-6 and 6-12 months, with the exception of asthma reviews, and by acute and repeat prescription type. Subgroup analysis by various time point was deemed appropriate to account for likely regression to the mean in the 0-3 months following SABA prescribing being identified at an extreme (excessive) point.

Sub-group analysis by prescription type was explored as SABAs are commonly obtained by repeat prescription. This data would be used to complement qualitative findings of Phase 3 on the roles of primary care staff in SABA prescribing.

It was assumed that characteristics and prescribing practice between the three CCGS in east London population would be similar therefore individual CCG analysis was not required.

### 4.2.4 Data collection and management

Data collection and management was facilitated by a data analyst from the CEG at QMUL.

The CEG has data sharing agreements with general practices in Hackney, Newham and Tower Hamlets to access aggregated and anonymised patient data for research purposes. The CEG is linked with both EMIS and the NHS N3 network, the national broadband network for the NHS, enabling the CEG to search and extract general practice data. Data were extracted on secure N3 terminals using EMIS-Web and processed using Microsoft Excel and Access.

To ensure accuracy of the data, the study methods underwent multiple revisions from June 2016, supported by a data analyst, with final data extraction carried out in December 2017.

#### 4.2.4.1 Identifying alert trigger date

As the SABA alert was not coded within the EHR at time of activation, it was not possible to automatically determine patients for whom the SABA alert activated. An Excel search was written to identify patients prescribed excessive SABAs within the intervention and control group periods. Of those eligible for inclusion, patients prescribed at least 3 SABAs in a 90-day period were identified. The date on which a third SABA prescription was generated was taken as the point at which the SABA alert would have triggered for that patient and was the point from which all outcomes of interest were measured.

Data was saved and imported into Access alongside patient demographics and outcomes of interest. The SABA alert date was imported from Excel to Access. Using the anonymised patient identifier, data was merged to provide one line patient level data. All data searches were carried out by the data analyst and the searches can be found in Appendix 4.6 (intervention group) and Appendix 4.7 (control group).

#### 4.2.4.2 Inhaled steroid data

Until May 2009 all doses of ICS in the BTS/SIGN asthma guidelines were referenced against beclometasone dipropionate equivalent (BDP) given via chlorofluorocarbon metered dose inhalers (CFC-MDIs). Most recent BTS/SIGN guidelines[52] no longer refer to BDP equivalent dosage. However, there is no gold standard comparator of ICS dosage, and BDP equivalent is often used as the reference standard when comparing ICS in terms of their potency.[105]

Due to complexities of calculating BDP equivalent prescribing of inhaled steroids in clinical practice, the ICS prescribing data captured could not be analysed within the study timeframe and was therefore omitted.

### 4.2.5 Statistical analyses and reporting

Statistical analyses were performed using IBM SPSS Statistics 24. All statistical analyses were carried out and analysed by the lead researcher and checked by the QMUL statistician. The statistician provided advice regarding all statistical tests and reviewed all results.

The statistical tests applied were a result of data not normally distributed. Distribution of data was determined by reviewing frequency tables and histograms for count data. No formal test was carried out to determine distribution due to challenges of using statistical tests to determine normality in a large dataset. Non-parametric tests were used to determine the relationship between prescribing and consultations (Mann Whitney-U test) and the numbers of asthma reviews carried out in the intervention and control groups (Chi-Squared test). A mixed effects regression model was applied to collective CCG data. Prescribing and consultation data were analysed using Poisson regression, whilst a binary regression was applied to the number of asthma reviews.

The following covariates were adjusted for potential baseline imbalance: age, gender, ethnicity and prescribing in the equivalent timeframe prior to the alert (where applicable). The median (IQR) was reported alongside Mann-Whitney *P*-values as despite suggestions that the actual distribution of the data does not matter,[353] differences in spread may sometimes be as clinically important as differences in medians.[236] The relationship between independent and dependent variables is commonly misreported as causal, therefore data adjusted using regression analysis has been reported as indicative of correlation not causation.[354] The

direction and strength of effect was determined using Adjusted Beta (β*)*, Exp β (adjusted odds ratio) and the reliability of the effect determined by a 95% confidence interval (95% CI) and P- value.

Multiple testing of the primary outcome of interest SABA prescribing data was pre-specified. Subgroup analysis by time point was due to data being identified at an extreme point (excessive SABA prescribing) with regression to the mean likely in the 0-3 months following the alert. To account for multiple testing, Bonferroni adjustment was applied and the cut-off for a statistical significant effect of the intervention on SABA prescribing was reduced from $P<0.05$ to $P<0.016$.

### 4.2.6 Ethical considerations

Ethical approval was not required as aggregated, anonymised patient-level data was reported in this study. All GPs in the participating east London practices consented to the use of practice anonymised patient data through pre-existing data-sharing agreements with the CEG.

### 4.2.7 Validity and reliability of data

This study has been reported in line with the STROBE statement (Reporting of Observational Studies in Epidemiology) and the RECORD statement (Reporting of studies Conducted using Observational Routinely collected health Data.[336] Both checklists can be found in appendix 4.8.

As optimal reporting should include complete code lists, detailed algorithms and validity assessment,[244] code lists and algorithms are presented in appendices 4.1-4.7.

Quality checks were carried out manually to ensure the purported date of alert for excessive SABA prescribing was accurately captured by the Excel search. This involved reviewing the number and dates of SABA prescriptions for 100 patients prior to the date of alert trigger.

## 4.3 Results

The primary outcome of SABA prescribing in the 12 months following the alert intervention is presented below. Secondary outcomes are reported: number of asthma reviews and time to review, number of exacerbations as determined by prednisolone prescribing, and primary care consultations. Exploratory sub group analyses were carried out by time point and by prescription type. Both SABA and prednisolone prescribing were adjusted for prior and post excessive SABA prescribing trigger point. Primary care consultations and asthma reviews prior to the date of excessive SABA prescribing were neither captured nor adjusted for in both intervention and control groups. ICS, LABA and Combination inhaler prescribing data was collected but not reported for reasons explained in section 4.2.4.2. Data was adjusted for covariates: age, gender and ethnicity. Ethnicity was adjusted for collectively and reported by ethnic category where statistically significant.

### 4.3.1 Population characteristics

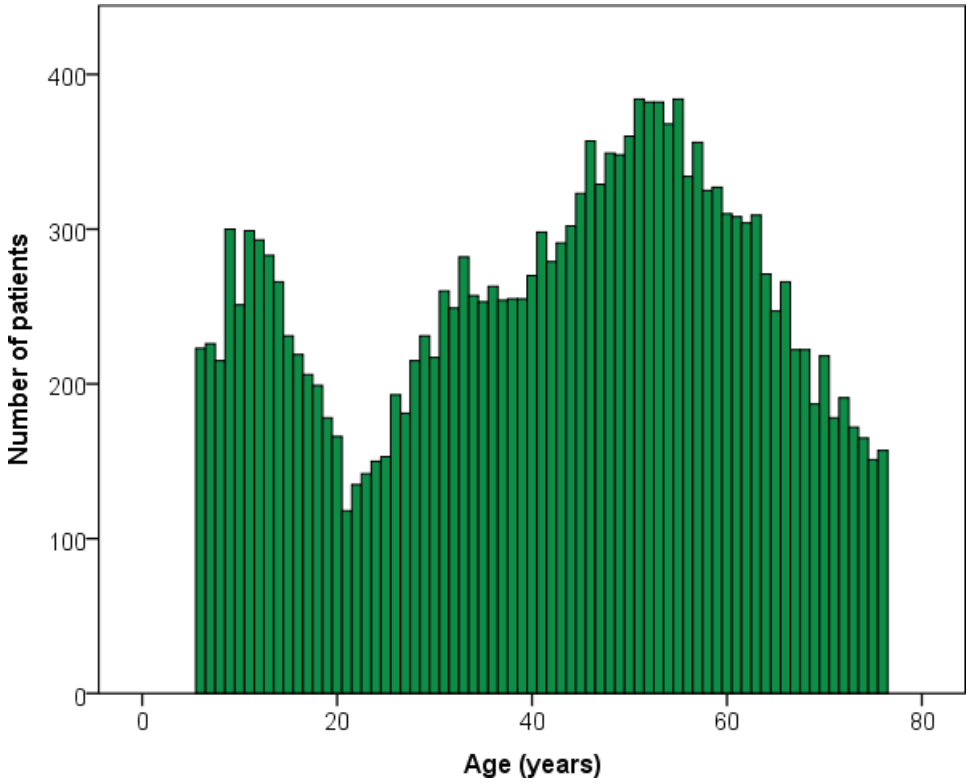
A total of 18,244 were included in the study. Table 4.3 presents a comparison of patient characteristics between the intervention and control group. Patients were evenly distributed between groups by age and ethnicity however there was a higher number of patients in the intervention than control group with more females than males.

Table 4. 3 Characteristics of included patients

| Patient demographics | | Control Group | Intervention group |
|---|---|---|---|
| Number of patients | | 8691 | 9553 |
| Age | | 41.93 (SD 19.338) | 42.17 (SD 19.344) |
| Gender | Female | 5351 (56%) | 4717 (54%) |
| | Male | 4202 (44%) | 3974 (46%) |
| Ethnicity | White | 3338 (34.94%) | 3128 (35.99%) |
| | Black | 1723 (18.04%) | 1582 (18.2%) |
| | South Asian | 3787 (39.64%) | 3401 (39.13%) |
| | Other | 445 (4.66%) | 358 (4.12%) |
| | Not stated | 260 (2.72%) | 222 (2.55%) |

The mean age of patients was 42.1 years (+/-SD 19.3). Figure 4.4 presents the age distribution of patients. There were two notable clusters of children/adolescents and older age peaking between 50-60 years, with the study population consisting of more females (55.2%) than males (44.8%). The majority of patients were of South Asian ethnicity (39.4%), followed by those of White ethnicity (35.4%) and Black ethnicity (18.1%).

Figure 4. 4 Patient distribution by age




### 4.3.2 Distribution of data

Histograms were used to review the distribution of SABA prescribing in the intervention group (figure 4.5) and control group (figure 4.6). Both histograms show uneven spread and skewed data reflective of non-normal distribution and therefore non-parametric tests were applied in this study.

Figure 4. 5 SABA distribution 0-12 months intervention group

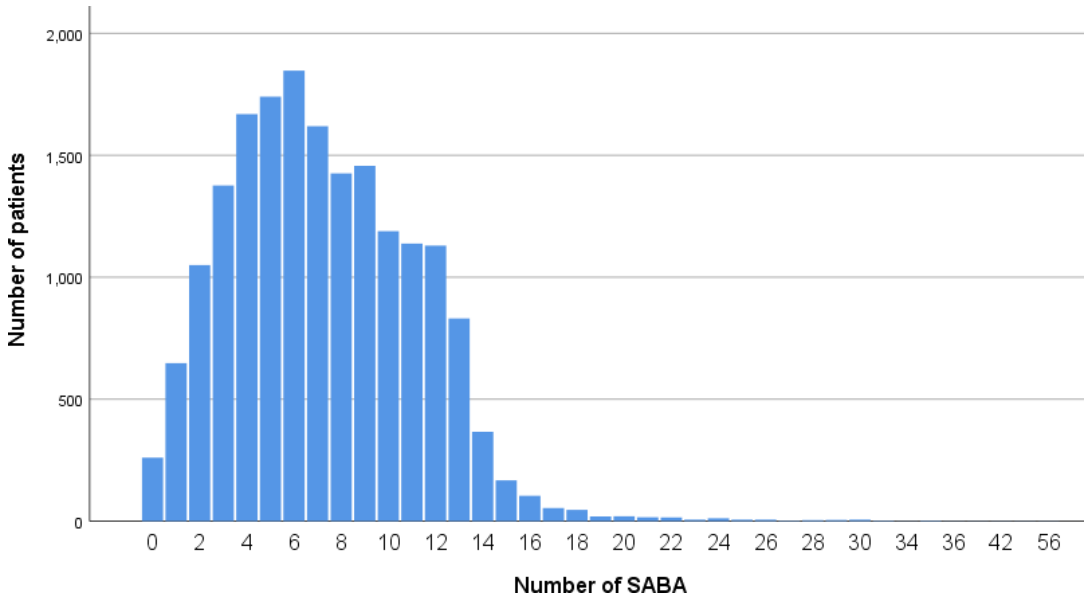
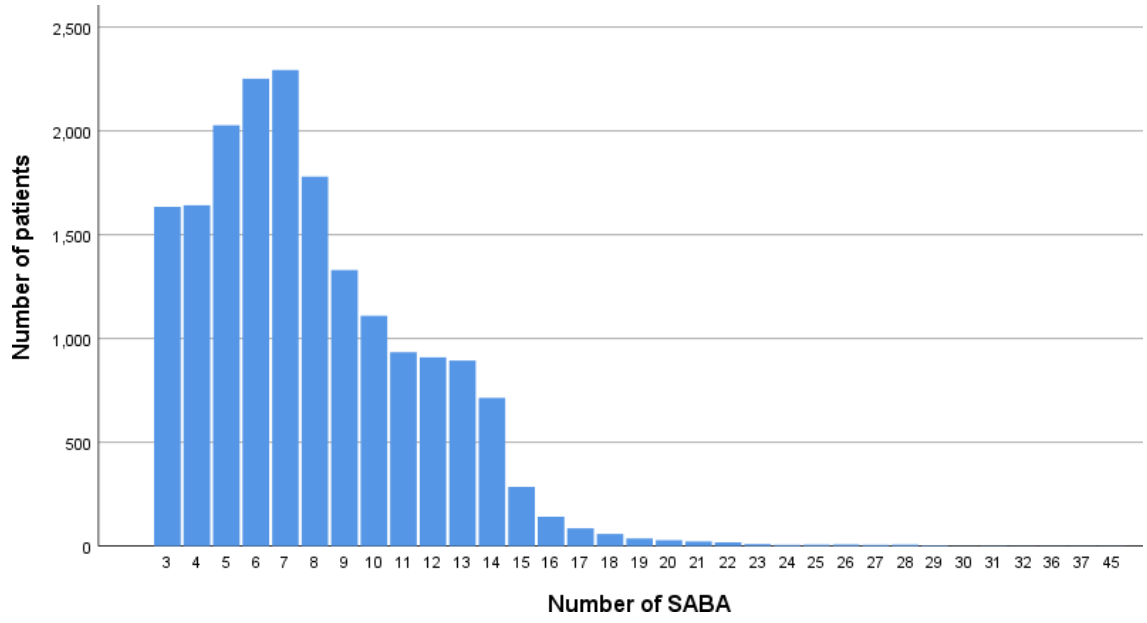



Figure 4. 6 SABA distribution 0-12 months in control group



### 4.3.3 Primary outcome

#### 4.3.3.1 SABA prescribing: 0-12 months

The median and interquartile Range (IQR) of SABAs prescribed in the intervention and control group at 0-12 months prior and post SABA prescribing trigger is presented in Table 4.4. The median number of SABA inhalers prescribed was similar between groups.

Table 4. 4 Number of SABA prescribed in the control and intervention groups at 12 months before and after the intervention group (SABA alert) and at 12 months before and after the historical control group (no SABA alert). Reported as Median and Interquartile Range (IQR).

| Number of SABA inhalers prescribed (Months) | Control group | Intervention group |
|---|---|---|
| | Median (IQR) | Median (IQR) |
| 0-12 mo nth prior | 7 (5-11) | 7 (5-11) |
| 0-12 month post | 7 (4-11) | 7 (4-11) |

A comparison between the distributions of SABAs prescribed in the 0-12 months prior and post excessive prescribing trigger between groups was carried out to determine the spread of data. This is presented in Table 4.5. In the 0-12 months prior to the SABA prescribing trigger, a greater proportion of the population in the intervention group were prescribed >12 SABA in comparison to control group, however in the 12 months post SABA prescribing trigger the opposite was observed. Furthermore a greater proportion of the intervention group were prescribed no SABAs at 0-12 months post SABA prescribing trigger when compared to the control group.

Table 4. 5 Comparison of SABA prescribing at 0- 12 months before and after the intervention group (SABA alert) and at 0-12 months before and after the historical control group (no SABA alert).

| SABA prescribing 0-12 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 3 (alert trigger) | 824 (9.5%) | 810 (8.1%) | 0.001 |
| 4-6 | 2865 (33.0%) | 3055 (30.4%) | |
| 7-12 | 3907 (45.0%) | 4447 (44.3%) | |
| >12 | 1095 (12.5%) | 1732 (17.2%) | |
| SABA prescribing 0-12 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 111 (1.3%) | 149 (1.6%) | <0.001 |
| 1-3 | 1400 (16.1%) | 1674 (17.5%) | |
| 4-6 | 2406 (27.7%) | 2850 (29.8%) | |
| 7-12 | 3851 (44.3%) | 4108 (43.0%) | |
| >12 | 923 (10.6%) | 772 (8.1%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on SABA prescribing in the 12 months post SABA prescribing trigger is presented in table 4.6. In the intervention group, SABA prescribing reduced by 7% in the 12 months following the alert (AOR 0.938, 95% CI 0.927-0.947, *P*<0.001). SABA prescribing reduced by 4% in the Black population (AOR 0.964, 95% CI 0.949 – 0.980, *P*<0.001), 3% in the South Asian population (AOR 0.972, 95 % CI 0.949–0.980, P<0.001) and by 4% in those of Other ethnicity (AOR 0.961, 95% CI 0.935–0.989, P=0.006). SABA prescribing was associated with increasing age however, despite statistical significance being achieved the small size of effect suggests a negligible association between age and SABA prescribing that is not clinically significant (AOR 1.002, 95% CI 1.002 – 1.003, P<0.001). There was no association between gender and SABA prescribing as reflected in an effect size of almost zero (AOR 0.994, 95% CI 0.983 – 1.005, *P*=0.283). Those prescribed excessive SABAs in the 12 months prior had a 7% chance of being prescribed excessive SABAs in the 12 months post prescribing trigger (AOR 1.073, 95% CI 1.072 – 1.074, *P*<0.001). There was no significant variance in SABA prescribing across individual CCGs to account for changes to SABA prescribing ($\sigma^2$ 0.001, 95% CI 0.000 - 0.005, $\sigma$= 0.333).

Table 4. 6 Poisson mixed effects model with SABA prescribing at 0-12 months as a dependent variable adjusted for covariates.[1]

| Factors | | Adjusted β[5] (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.002 (0.002 - 0.003) | 1.002 (1.002 – 1.003) | <0.001 |
| Gender[2] (Female) | | -0.006 (-0.017, 0.005) | 0.994 (0.983 – 1.005) | 0.283 |
| Ethnicity[3] | Black | -0.036 (-0.052, -0.020) | 0.964 (0.949 - 0.980) | <0.001 |
| | South Asian | -0.028 (-0.041, -0.016) | 0.972 (0.959 - 0.984) | <0.001 |
| | Other | -0.039 (-0.067, -0.011) | 0.961 (0.935 - 0.989) | 0.006 |
| | Not stated | 0.001 (-0.036, 0.037) | 1.001 (0.964 - 1.037) | 0.975 |
| SABA 0-12 months prior | | 0.071 (0.070-0.072) | 1.073 (1.072 – 1.074) | <0.001 |
| Group (Intervention)[4] | | -0.064 (-0.075, -0.054) | 0.938 (0.927 – 0.947) | <0.001 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.001 (0.000 – 0.005) | | 0.333 |

[1] adjusted for age, gender, ethnicity and SABA prescribing prior

[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.3.2 SABA prescribing: 0-3 months

The median and IQR of SABAs prescribed in the intervention and control group at 0-3 months prior and post SABA prescribing trigger is presented in Table 4.7. The median number of SABA inhalers prescribed in the 0-12 months was similar in both groups.

Table 4. 7 Number of SABA prescribed in the control and intervention groups at 0-3 months before and after the intervention group (SABA alert) and at 0-3 months before and after the historical control group (no SABA alert). Reported as Median and Interquartile Range (IQR).

| Number of SABA inhalers prescribed (Months) | Control group | Intervention group |
|---|---|---|
| | Median (IQR) | Median (IQR) |
| 0-3 month prior | 3 (3-3) | 3 (3-3) |
| 0-3 month post | 2 (1-2) | 2 (1-2) |

Table 4.8 compares the distribution of SABAs prescribed in the 0-3 months prior and post SABA prescribing trigger in the intervention and control group. In the 0-3 months prior to the SABA prescribing trigger, a higher proportion of people were prescribed between 4-6 SABAs in the intervention group than control group. However in the 0-3 months post SABA prescribing trigger, the opposite was observed with a higher proportion of the control group prescribed 4-6 SABAs than the intervention group.

Table 4. 8 Comparison of SABA prescribing at 0-3 months before and after the intervention group (SABA alert) and at 0-3 months before and after the historical control group (no SABA alert)

| SABA prescribing 0-3 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 3 (alert trigger) | 7175 (82.6%) | 7776 (81.4%) | 0.165 |
| 4-6 | 1481 (17%) | 1735 (18.2%) | |
| 7-12 | 35 (0.4%) | 42 (0.4%) | |
| >12 | 0 (0%) | 0 (0%) | |
| SABA prescribing 0-3 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 1478 (17.0%) | 1633 (17.1%) | 0.044 |
| 1-3 | 6820 (78.5%) | 7538 (78.9%) | |
| 4-6 | 377 (4.3%) | 355 (3.8%) | |
| 7-12 | 14 (0.2%) | 26 (0.2%) | |
| >12 | 2 (0%) | 1 (0%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on SABA prescribing in the 0-3 months post SABA prescribing trigger is presented in table 4.9. When adjusted for prescribing in the control group, there was a 2% reduction in SABA prescribing the 0-3 months post excessive prescribing trigger however this was not statistically significant (AOR 0.983, 95% CI 0.961-1.006, *P*=0.148). When adjusted for ethnicity, a 4% reduction in SABA prescribing was observed in the Black (P=0.026) and South Asian population (P=0.006) and an 8% reduction in those of Other ethnicity (P=0.007). SABA prescribing was associated with increasing age however, despite achieving statistical significance the small effect size suggests a negligible association between age and SABA prescribing that is not clinically significant (AOR 1.004, 95% CI 1.004 – 1.005, P<0.001).

Despite a 2% reduction in SABA prescribing among females, the relationship between gender and SABA prescribing was not statistically significant (AOR 0.979, 95% CI 0.955-1.002, *P*=0.069). Those prescribed excessive SABAs in the 0-3 months prior had a 30% chance of being prescribed excessive SABAs in the 0-3 months post prescribing trigger (AOR 1.308, 95% CI 1.291-1.324, *P*<0.001). There was no significant variance in SABA prescribing across individual CCGs to account for changes to SABA prescribing ($\sigma^2$ 0.007, 95% CI 0.001 - 0.051, σ= 0.324).

Table 4. 9 Poisson mixed effects model with SABA prescribing at 0-3 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.004 (0.004 – 0.005) | 1.004 (1.004 – 1.005) | <0.001 |
| Gender[2] (Female) | | -0.021 (-0.045, 0.002) | 0.979 (0.955 – 1.002) | 0.069 |
| Ethnicity[3] | Black | -0.037 (-0.070, -0.004) | 0.963 (0.932 – 0.996) | 0.026 |
| | South Asian | -0.038 (-0.065, -0.011) | 0.962 (0.937 – 0.989) | 0.006 |
| | Other | -0.081 (-0.140, -0.022) | 0.922 (0.869 – 0.978) | 0.007 |
| | Not stated | -0.074 (-0.152, 0.003) | 0.928 (0.858 – 1.003) | 0.061 |
| SABA 0-3 months prior | | 0.269 (0.256 – 0.281) | 1.308 (1.291 – 1.324) | <0.001 |
| Group (Intervention)[4] | | -0.017 (-0.039, 0.006) | 0.983 (0.961 – 1.006) | 0.148 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.007 (0.001 – 0.051) | | 0.324 |

[1] adjusted for age, gender, ethnicity and SABA prescribing prior

[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.3.3 SABA prescribing: 3-6 months

The median and IQR of SABAs prescribed in the intervention and control group at 3-6 months prior and post SABA prescribing trigger is presented in Table 4.10. The median number of SABA inhalers prescribed in the 3-6 months was similar in both groups.

Table 4. 10 Number of SABA prescribed in the control and intervention groups at 3-6 months before and after the intervention group (SABA alert) and at 3-6 months before and after the historical control group (no SABA alert). Reported as Median and Interquartile Range (IQR).

| Number of SABA inhalers prescribed (Months) | Control group | Intervention group |
|---|---|---|
| | Median (IQR) | Median (IQR) |
| 3-6 months prior | 1 (0-2) | 1 (0-2) |
| 3-6 months post | 2 (1-3) | 2 (1-3) |

Table 4.11 compares the distributions of SABAs prescribed in the 3-6 months prior and post SABA prescribing trigger in the intervention and control group. In the 3-6 months prior, a higher proportion of people in the control group were prescribed no SABAs prescribed in comparison to the intervention group. However in the 3-6 months post SABA prescribing trigger, the opposite was observed with a higher proportion of the intervention group prescribed no SABAs in comparison to the control group.

Table 4. 11 Comparison of SABA prescribing at 3-6 months before and after the intervention group (SABA alert) and at 3-6 months before and after the historical control group (no SABA alert).

| SABA prescribing 3-6 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 0 | 2516 (29.0%) | 2571 (26.9%) | <0.001 |
| 1-3 | 5678 (65.3%) | 6436 (67.4%) | |
| 4-6 | 473 (5.4%) | 531 (5.6%) | |
| 7-12 | 23 (0.3%) | 15 (0.1%) | |
| >12 | 1 (0%) | 0 (0%) | |
| SABA prescribing 3-6 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 1308 (15.1%) | 1544 (16.2%) | 0.002 |
| 1-3 | 6605 (76.0%) | 7282 (76.2%) | |
| 4-6 | 749 (8.6%) | 701 (7.3%) | |
| 7-12 | 29 (0.3%) | 24 (0.3%) | |
| >12 | 0 (0%) | 2 (0%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on SABA prescribing in the 3-6 months post SABA prescribing trigger is presented in table 4.12. When adjusted for the control group, SABA prescribing reduced by 4% in the 3-6 months post excessive prescribing trigger (AOR 0.955, 95% CI 0.935-0.976, *P*<0.001). SABA prescribing reduced by 5% in the Black population (P=0.001) and by 4% in the South Asian population (P=0.002). SABA prescribing was associated with increasing age however, despite being statistically significant the small effect size suggests a negligible association between age and SABA prescribing that is not clinically significant (AOR 1.002, 95% CI 1.002-1.003, *P*<0.001). SABA prescribing reduced by 1% among females in the 3-6 months post excessive prescribing trigger however this was not statistically significant (AOR 0.988, 95% CI 0.966-1.010, *P*=0.288). Those prescribed excessive SABAs in the 3-6months prior to trigger date had a 21% chance of being prescribed excessive SABAs in the 3-6 months post prescribing trigger (AOR 1.216, 95% CI 1.208- 1.226, *P*<0.001). There was no significant variance in SABA prescribing across individual CCGs to account for changes to SABA prescribing ($\sigma^2$ 0.001, 95% CI 0.000 -0.010, σ= 0.350).

Table 4. 12 Poisson mixed effects model with SABA prescribing at 3-6 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.002 (0.002 – 0.003) | 1.002 (1.002 – 1.003) | <0.001 |
| Gender[2] (Female) | | -0.012 (-0.034, 0.010) | 0.988 (0.966 – 1.010) | 0.288 |
| Ethnicity[3] | Black | -0.051 (-0.082, -0.020) | 0.950 (0.921 – 0.980) | 0.001 |
| | South Asian | -0.039 (-0.064, -0.014) | 0.961 (0.938 – 0.986) | 0.002 |
| | Other | -0.042 (-0.097, 0.013) | 0.958 (0.907 – 1.013) | 0.131 |
| | Not stated | -0.020 (-0.092, 0.053) | 0.980 (0.912 – 1.054) | 0.593 |
| SABA 3-6 months prior | | 0.196 (0.189 – 0.204) | 1.216 (1.208 – 1.226) | <0.001 |
| Group[4] (Intervention) | | -0.046 (-0.067, -0.024) | 0.955 (0.935 – 0.976) | <0.001 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.001 (0.000 – 0.010) | | 0.350 |

[1] adjusted for age, gender, ethnicity and SABA prescribing prior

[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.3.4 SABA prescribing: 6-12 months

The median and IQR of SABAs prescribed in the intervention and control group at 6-12 months prior and post SABA prescribing trigger is presented in Table 4.13. The median number of SABA inhalers prescribed prior and post SABA prescribing trigger was similar between both groups. However fewer SABAs were prescribed in the intervention group than control group in the 6-12 months post SABA prescribing trigger.

Table 4. 13 Number of SABA prescribed in the control and intervention groups at 6-12 months before and after the intervention group (SABA alert) and at 3-6 months before and after the historical control group (no SABA alert). Reported as Median and Interquartile Range (IQR).

| Number of SABA inhalers prescribed (Months) | Control group | Intervention group |
|---|---|---|
| | Median (IQR) | Median (IQR) |
| 6-12 months prior | 3 (1-5) | 3 (1-5) |
| 6-12 months post | 4 (2-6) | 3 (2-5) |

Table 4.14 compares the distributions of SABAs prescribed between groups in the 6-12 months prior and post SABA prescribing trigger. In the 6-12 months prior, a higher proportion of people in the control group had no SABAs prescribed in comparison to the intervention group. However in the 6-12 months post, the opposite was observed with a higher proportion of the intervention group prescribed no SABAs or 1-3 SABAs in comparison to the control group. Furthermore, a greater proportion of the control group population were prescribed 4-6 or 7-12 SABAs in the 6-12 months post SABA prescribing trigger in comparison to the intervention group.

Table 4. 14 Comparison of SABA prescribing at 6-12 months before and after the intervention group (SABA alert) and at 6-12 months before and after the historical control group (no SABA alert)

| SABA prescribing 6-12 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 0 | 1259 (14.5%) | 1250 (13.1%) | <0.001 |
| 1-3 | 3931 (45.2%) | 4347 (45.5%) | |
| 4-6 | 2626 (30.2%) | 2957 (31.0%) | |
| 7-12 | 858 (9.9%) | 978 (10.2%) | |
| >12 | 17 (0.2%) | 21 (0.2%) | |
| SABA prescribing 6-12 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 492 (5.7%) | 727 (7.6%) | 0.014 |
| 1-3 | 3564 (41.0%) | 4338 (45.4%) | |
| 4-6 | 3484 (40.0%) | 3490 (36.5%) | |
| 7-12 | 1124 (13.1%) | 970 (10.1%) | |
| >12 | 27 (0.2%) | 28 (0.3%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on SABA prescribing in the 6-12 months post SABA prescribing trigger is presented in table 4.15. When adjusted for the control group, SABA prescribing reduced by 9% in the 6-12 months post SABA prescribing trigger (AOR 0.912, 95% CI 0.898-0.925, *P*<0.001). When adjusted for covariates, SABA prescribing reduced by 4% among the Black population (P<0.001), by 3% in the South Asian population (P=0.001) and by 6% in those of Other ethnicity (P=0.04). SABA prescribing was associated with increasing age (AOR 1.003, 95% CI 1.002-1.003, *P*<0.001) but not gender (AOR 0.999, 95% CI 0.984 – 1.015, *P*=0.905). Despite being statistically significant, the small effect size suggests the association between age and SABA prescribing is not clinically significant. Those prescribed excessive SABAs in the 6-12 months prior to SABA prescribing trigger had a 10% chance of being prescribed excessive SABAs in the 6-12 months post (AOR 1.102, 95% CI 1.099-1.106, *P*<0.001). There was no significant variance in SABA prescribing across individual CCGs to account for changes to SABA prescribing at 6-12 months ($\sigma^2$ 0.000, 95% CI 0.000 -0.002, σ=0.446).

Table 4. 15 Poisson mixed effects model with SABA prescribing at 6-12 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.003 (0.002 – 0.003) | 1.003 (1.002-1.003) | <0.001 |
| Gender[2] (Female) | | -0.001 (-0.016, 0.015) | 0.999 (0.984 – 1.015) | 0.905 |
| Ethnicity[3] | Black | -0.043 (-0.065, -0.021) | 0.957 (0.937-0.979) | <0.001 |
| | South Asian | -0.034 (-0.051, -0.016) | 0.966 (0.950-0.984) | 0.001 |
| | Other | -0.057 (-0.096, -0.018) | 0.944 (0.908-0.982) | 0.004 |
| | Not stated | -0.010 (-0.061, 0.041) | 0.990 (0.940-1.041) | 0.706 |
| SABA 6-12 months prior | | 0.098 (0.095 – 0.101) | 1.102 (1.099 – 1.106) | <0.001 |
| Group[4] (Intervention) | | -0.092 (-0.107, -0.077) | 0.912 (0.898-0.925) | <0.001 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.000 (0.000 – 0.002) | | 0.446 |

[1] adjusted for age, gender, ethnicity and SABA prescribing prior
[2] reference males, [3] reference White population, [4] reference control group

### 4.3.4 Secondary outcomes

#### 4.3.4.1 Asthma reviews

The number of reviews and time to review were analysed at 0-3 months and 3-6 months post SABA prescribing trigger and not 6-12 months.

##### 4.3.4.1.1 Number of people having an asthma reviews at 0-3 months

The number of asthma reviews carried out between groups 0-3 months following post SABA prescribing trigger is presented in Table 4.16. There was a significant difference in the number of asthma reviews between groups, with a higher proportion of reviews in the intervention group than control group (P=0.001) (Table 4.16).

Table 4. 16 Number of people having had an asthma review in the intervention and control group at 0-3 months

| Asthma Review 0-3 months post | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| Yes | 1809 (20.8%) | 2182 (22.8%) | 0.001 |
| No | 6882 (79.2%) | 7371 (77.2%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on asthma reviews in the 0-3 months post SABA prescribing trigger is presented in table 4.17.

Table 4. 17 Binary mixed effects model with number of people having had an asthma review at 0-3 months as an independent variable adjusted for covariates[1]

| Factors | | Adjusted β (95 % CI) | Exp β / OR (95 % CI) | P-value |
|---|---|---|---|---|
| Age | | 0.005 (0.003-0.007) | 1.005 (1.003-1.007) | <0.001 |
| Gender[2] (Female) | | 0.069 (-0.003, 0.142) | 1.071 (0.997-1.152) | 0.060 |
| Ethnicity[3] | Black | 0.106 (0.003-0.208) | 1.111 (1.003-1.231) | 0.044 |
| | South Asian | 0.175 (0.090-0.261) | 1.191 (1.094-1.298) | <0.001 |
| | Other | 0.171 (0.003-0.345) | 1.186 (1.003-1.411) | 0.054 |
| | Not stated | 0.027 (0.206-0.260) | 1.027 (1.228-1.296) | 0.821 |
| Group[4] (Intervention) | | 0.114 (0.043-0.184) | 1.120 (1.043-1.202) | 0.002 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.018 (0.002 – 0.146) | | 0.348 |

[1] adjusted for age, gender, ethnicity
[2] reference males, [3] reference White population,[4] reference control group

When adjusted for the control group, the number of asthma reviews in the intervention group increased by 12% (AOR 1.120, 95% CI 1.043- 1.202, *P*=0.002). When adjusted for ethnicity, the number of asthma reviews increased by 12% in the Black population (P=0.044) and 19% in the South Asian population (P<0.001). The number of asthma reviews was positively associated with increasing age however despite being statistically significant the small effect size is likely to be clinically insignificant (AOR 1.005, 95% CI 1.003-1.007, *P*<0.001).

There was a non-statistically significant 7% increase in asthma reviews among females in comparison to males (AOR 1.071, 95% CI 0.997-1.152, *P*=0.060). There was no significant variance in number of asthma reviews across individual CCGs to account for differences in number of asthma reviews at 0-3 months ($\sigma^2$ 0.018, 95% CI 0.002 -0.146, *P*=0.348).

#### 4.3.4.1.2 Number of asthma reviews: 3-6 months

The number of asthma reviews carried out at 3-6 months following post SABA prescribing trigger is presented in Table 4.18. There was no significant between-group difference in the number of people having an asthma review at 3-6 months (P=0.370) (Table 4.18).

Table 4. 18 Number of people having had an asthma review in the intervention and control group at 3-6 months

| Asthma Review 3-6 months post | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| Yes | 1917 (22.1%) | 2160 (22.6%) | 0.370 |
| No | 6774 (77.9%) | 7393 (77.4%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on asthma reviews in the 3-6 months post SABA prescribing trigger is presented in table 4.19. When adjusted for the control group, there was a 3% statistically non-significant increase in the number of asthma reviews in the intervention group (AOR 1.028, 95% CI 0.985- 1.102, *P*=0.430). When adjusted for ethnicity, the number of asthma reviews increased by 17% in the South Asian population only (P<0.001). There was a positive association between increasing and the number of asthma reviews however despite being statistically significant the small effect size is not clinically significant (AOR 1.005, 95% CI 1.003-1.007, *P*<0.001). There was a statistically significant 12% increase in asthma reviews among females in comparison to males (AOR 1.120, 95% CI 1.042-1.204, *P*=0.002). There was no significant variance in number of asthma reviews across individual CCGs to account for differences in number of asthma reviews carried out ($\sigma^2$ 0.030, 95% CI 0.004-0.234, *P*=0.338).

Table 4. 19 Binary mixed effects model with number of people having had an asthma review at 3-6 months as an independent variable adjusted for covariates[1]

| Factors | | Adjusted β (95 % CI) | Exp β / OR (95 % CI) | P-value |
|---|---|---|---|---|
| Age | | 0.005 (0.003-0.007) | 1.005 (1.003-1.007) | <0.001 |
| Gender[2] (Female) | | 0.114 (0.042-0.186) | 1.120 (1.042-1.204) | 0.002 |
| Ethnicity[3] | Black | -0.030 (-0.123, 0.072) | 0.970 (0.884-1.074) | 0.562 |
| | South Asian | 0.158 (0.073-0.242) | 1.171 (1.075-1.273) | <0.001 |
| | Other | 0.044 (-0.136, 0.224) | 1.044 (0.872-1.251) | 0.632 |
| | Not stated | 0.203 (-0.043, 0.449) | 1.225 (0.957-1.566) | 0.106 |
| Group[4] (Intervention) | | 0.028 (-0.042, 0.098) | 1.028 (0.958-1.102) | 0.430 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.030 (0.004-0.234) | | 0.338 |

[1] adjusted for age, gender, ethnicity

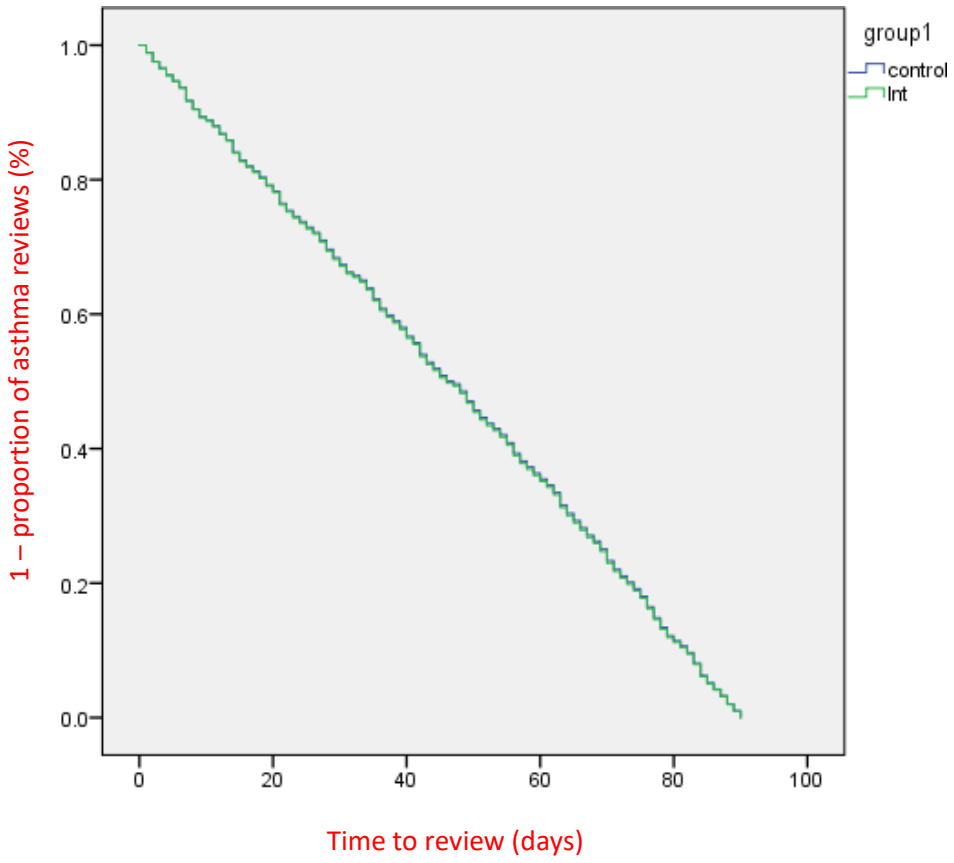
[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.4.1.3 Time to review: 0-3 months

The median time to asthma review in the 3 months post SABA prescribing trigger was 48 days (IQR 22-70) in the control group and 46 days in the intervention group (IQR 23-69). There was no significant difference in the time to review between both groups at 3 months (*P*=0.762). Figure 4.7 shows the time to review between groups at 0-3 months.

When adjusted for the control group, no effect on time to asthma review was observed in the intervention group at 0-3 months post SABA prescribing trigger (Adjusted β 0.010, SE 0.032, *P*=0.753). Neither gender (β 0.015, SE 0.033, *P*=0.635), nor ethnicity (*P*=0.856), was associated with time to review at 0-3 months. Asthma reviews occurred in those of younger age however this is likely to be clinically insignificant given the small effect size. (β -0.002, SE 0.001, *P*=0.030).

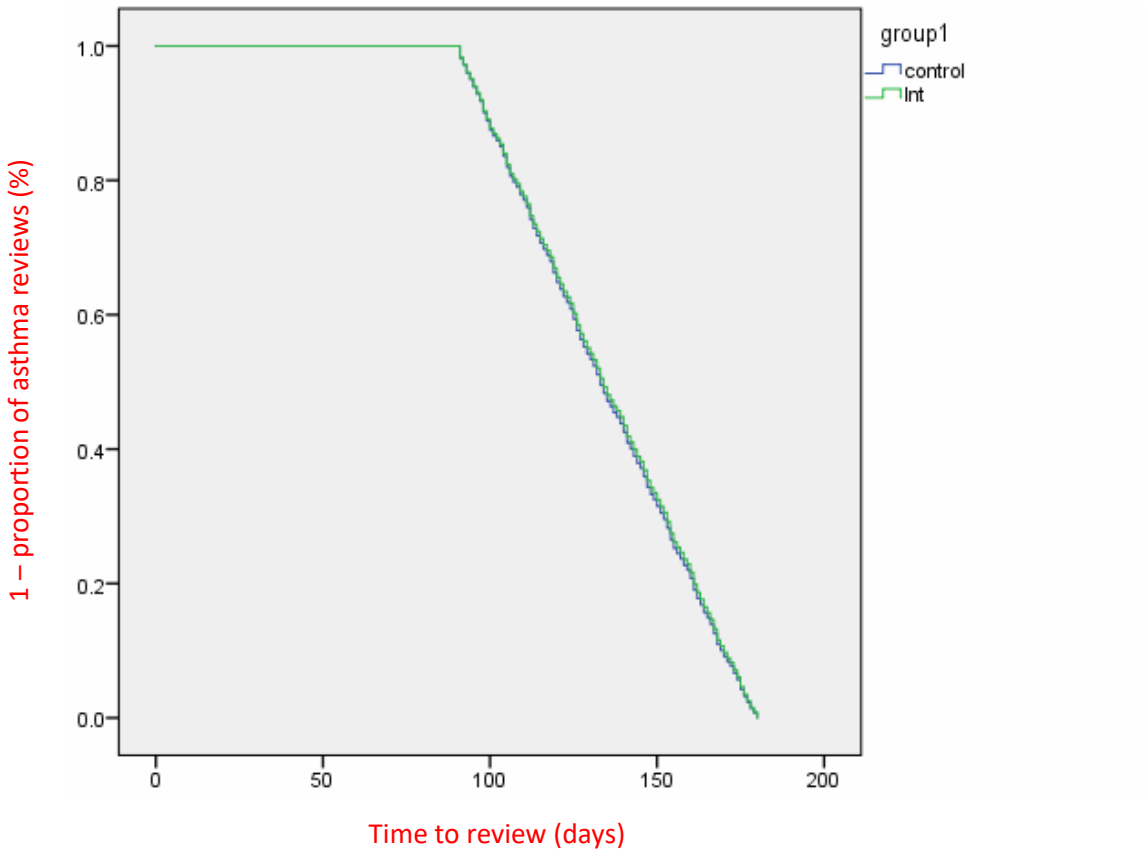
Figure 4. 7 The proportion of asthma reviews carried out in the intervention and control groups at 0-3 months using a survival mixed effects model




#### 4.3.4.1.4 Time to review: 3-6 months

The median time to asthma review at 3-6 months post SABA prescribing trigger was 133 days (IQR 112-156) in the control group and 134 days in the intervention group (IQR 112-158). There was no significant difference in the time to review between both groups at 3-6 months (*P*=0.409). Figure 4.8 shows the time to review between intervention and control group at 3-6 months.

Figure 4. 8 The proportion of asthma reviews carried out in the intervention and control groups at 3-6 months using a survival mixed effects model




When adjusted for the control group, no effect on time to review was observed in the intervention group at 3-6 months post SABA prescribing trigger (Adjusted β -0.027, SE 0.031, *P*=0.384). Neither gender (Adjusted β 0.010, SE 0.032, *P*=0.765) nor age (Adjusted β 0.001, SE 0.001, *P*=0.356) nor ethnicity (*P*=0.511) was associated with time to review at 3-6 months.

#### 4.3.4.2 Asthma exacerbations

##### 4.3.4.2.1 Prednisolone prescribing: 0-12 months

Table 4.20 compares the distribution of prednisolone prescribing between groups in the 12 months prior and post SABA prescribing trigger, with the majority of the control and intervention groups not prescribed prednisolone. Differences in prednisolone prescribing between groups in the 12 months prior to the SABA prescribing trigger was not statistically significant (*P*=0.75), however, a statistically significant difference was observed in the 12 months post (*P*=0.032).

Table 4. 20 Comparison of prednisolone prescribing at 0-12 months before and after the intervention group (SABA alert) and at 0-12 months before and after the historical control group (no SABA alert).

| Prednisolone courses prescribed 0-12 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 0 | 6835 (78.6%) | 7414 (77.6%) | 0.075 |
| 1 | 1043 (12.0%) | 1189 (12.4%) | |
| 2 | 391 (4.5%) | 421 (4.4%) | |
| 3 | 169 (1.9%) | 214 (2.2%) | |
| >3 | 253 (3.0%) | 315 (3.3%) | |
| Prednisolone courses prescribed 0-12 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 6926 (79.7%) | 7487 (78.4%) | 0.032 |
| 1 | 977 (11.2%) | 1149 (12.0%) | |
| 2 | 343 (3.9%) | 408 (4.3%) | |
| 3 | 168 (1.9%) | 177 (1.8%) | |
| >3 | 277 (3.2%) | 332 (3.5%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on prednisolone prescribing in the 0-12 months post SABA prescribing trigger is presented in table 4.21.

Table 4. 21 Poisson mixed effects model with prednisolone prescribing at 0-12 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95 % CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.014 (0.013 – 0.016) | 1.014 (1.013 – 1.016) | <0.001 |
| Gender[2] (Female) | | 0.248 (0.203 – 0.293) | 1.281 (1.225 – 1.340) | <0.001 |
| Ethnicity[3] | Black | -0.063 (-0.124, -0.003) | 0.938 (0.883 – 0.997) | 0.041 |
| | South Asian | -0.094 (-0.142, -0.046) | 0.910 (0.867 – 0.955) | <0.001 |
| | Other | -0.189 (-0.302, -0.075) | 0.827 (0.739 – 0.927) | 0.001 |
| | Not stated | -0.005 (-0.156, 0.145) | 0.995 (0.855 – 1.156) | 0.943 |
| Prednisolone 0-12m prior | | 0.111 (0.110 – 0.113) | 1.117 (1.116 – 1.119) | <0.001 |
| Group[4] (Intervention) | | -0.012 (-0.054, 0.029) | 0.988 (0.947 – 1.029) | 0.561 |

[1] adjusted for age, gender, ethnicity and prednisolone prescribing prior
[2] reference males, [3] reference White population, [4] reference control group

When adjusted for the control group, the intervention had no effect on prednisolone prescribing in the 12 months post SABA prescribing trigger (AOR 0.988, 95% CI 0.947 – 1.029, *P*=0.561). Following covariate adjustment for ethnicity, prednisolone prescribing reduced by 6% among the Black population (P=0.041), by 9% in the South Asian population (P<0.001) and by 16% in those of Other ethnicity (P=0.001). In contrast, female gender was positively associated with prednisolone prescribing (AOR 1.281, 95% CI 1.225 – 1.340, P<0.001) with those prescribed prednisolone prior to the SABA trigger 12% more likely to be prescribed prednisolone post SABA prescribing trigger (AOR 1.117, 95% CI 1.116 – 1.119, P<0.001). Prednisolone prescribing was positively associated with increasing age however despite being statistically significant the small effect size is not clinically significant (AOR 1.014, 95% CI 1.013-1.016, P<0.001). No significant variance in prednisolone prescribing was observed across individual CCGs to account for differences at 0-12 months ($\sigma^2$ 0.018, 95% CI 0.002 - 0.146, *P*=0.348).

#### 4.3.4.2.2 Prednisolone prescribing: 0-3 months

Table 4.22 compares the distribution of prednisolone prescribing between groups in the 0-3 months prior and post SABA prescribing trigger. There was no difference in prednisolone prescribing observed between groups in the 0-3 months prior (*P*=0.297) and post (*P*=0.558) SABA prescribing trigger.

Table 4. 22 Comparison of prednisolone prescribing at 0-3 months before and after the intervention group (SABA alert) and at 0-3 months before and after the historical control group (no SABA alert)

| Prednisolone courses prescribed 0-3 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 0 | 7703 (88.6%) | 8498 (89.0%) | 0.297 |
| 1 | 705 (8.1%) | 712 (7.5%) | |
| 2 | 177 (2.0%) | 213 (2.2%) | |
| 3 | 65 (0.7%) | 69 (0.7%) | |
| >3 | 41 (0.5%) | 61 (0.5%) | |
| Prednisolone courses prescribed 0-3 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 8048 (92.6%) | 8807 (92.2%) | 0.558 |
| 1 | 447 (5.1%) | 522 (5.5%) | |
| 2 | 135 (1.6%) | 145 (1.5%) | |
| 3 | 36 (0.4%) | 50 (0.5%) | |
| >3 | 25 (0.1%) | 29 (0.1%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on prednisolone prescribing in the 0-3 months post SABA prescribing trigger is presented in table 4.23. When adjusted for the control group, the intervention had no effect on prednisolone prescribing at 0-3 months (AOR 1.008, 95% CI 0.969-1.048, *P*=0.695). Following covariate adjustment, neither ethnicity nor female gender was associated with prednisolone prescribing in the 0-3 months post SABA prescribing trigger. However, prednisolone prescribing prior was associated with a 33% increase in prednisolone prescribing post SABA alert trigger (AOR 1.327, 95% CI 1.312-1.341, *P*<0.001). There was a statistically significant association between age and prednisolone prescribing (AOR 1.002, 95% CI 1.001-1.003, *P*<0.001) however the small effect size suggests the association is not clinically significant. Variance between CCGs was tested however convergence of the data in the Hessian matrix was not possible due to low numbers of prednisolone prescribed within the 0-3 months between CCGs.

Table 4. 23 Poisson mixed effects model with prednisolone prescribing at 0-3 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95 % CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.002 (0.001 – 0.003) | 1.002 (1.001 – 1.003) | <0.001 |
| Gender[2] (Female) | | 0.008 (-0.033, 0.048) | 1.008 (0.967 – 1.049) | 0.708 |
| Ethnicity[3] | Black | -0.002 (-0.059, 0.056) | 0.998 (0.942 – 1.057) | 0.955 |
| | South Asian | 0.032 (-0.013, 0.078) | 1.032 (0.987 – 1.081) | 0.165 |
| | Other | 0.065 (-0.032, 0.163) | 1.067 (0.968 – 1.177) | 0.190 |
| | Not stated | 0.069 (-0.058, 0.197) | 1.071 (0.943 – 1.217) | 0.288 |
| Prednisolone 0-3m prior | | 0.283 (0.272 - 0.294) | 1.327 (1.312 – 1.341) | <0.001 |
| Group[4] (Intervention) | | 0.008 (-0.031, 0.047) | 1.008 (0.969 – 1.048) | 0.695 |

[1] adjusted for age, gender, ethnicity and prednisolone prescribing prior
[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.4.2.3 Prednisolone prescribing: 3-6 months

A comparison in prednisolone prescribing between groups in the 3-6 months prior and post SABA prescribing trigger is presented in Table 4.24. There were significant differences in prednisolone prescribed between groups in the 3-6 months prior (*P*=0.011) and 3-6 months post trigger (*P*=0.049.) Count data indicates that in both the 3-6 months prior and post trigger less prednisolone was prescribed in the control group in comparison to the intervention group. In contrast, the proportion of the population having one or two courses of prednisolone prescribed was higher in the intervention group at both 3-6 months prior and post SABA prescribing trigger.

Table 4. 24 Comparison of prednisolone prescribing at 3-6 months before and after the intervention group (SABA alert) and at 3-6 months before and after the historical control group (no SABA alert)

| Prednisolone courses prescribed 3-6 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 0 | 8094 (93.1%) | 8804 (92.2%) | 0.011 |
| 1 | 438 (5.0%) | 540 (5.7%) | |
| 2 | 99 (1.1%) | 117 (1.2%) | |
| 3 | 29 (0.3%) | 58 (0.6%) | |
| >3 | 31 (0.2%) | 34 (0.3%) | |
| Prednisolone courses prescribed 3-6 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 7994 (92.0%) | 8707 (91.1%) | 0.049 |
| 1 | 491 (5.6%) | 619 (6.5%) | |
| 2 | 117 (1.3%) | 141 (1.5%) | |
| 3 | 53 (0.6%) | 49 (0.5%) | |
| >3 | 36 (0.4%) | 37 (0.3%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on prednisolone prescribing in the 3-6 months post SABA prescribing trigger is presented in table 4.25. When adjusted for the control group, the intervention had no effect on prednisolone prescribing (AOR 1.008, 95% CI 0.969-1.048, *P*=0.695). When adjusted for the control group, prednisolone prescribing reduced by 8% the 3-6 months post SABA prescribing trigger (AOR 0.924, 95% CI 0.890-0.960, *P*<0.001). Following covariate adjustment, a 6% reduction in prednisolone prescribing was observed among those of Black ethnicity (AOR 0.938, 95% CI 0.886-0.993, *P*=0.028) and a 10% reduction was observed among those of Other ethnicity (AOR 0.895, -95% CI 0.808-0.992, *P*=0.035). In contrast, prednisolone prescribing increased by 6% in those of South Asian ethnicity in the 3-6 months following the SABA prescribing trigger (AOR 1.063, 95% CI 1.018-1.110, *P*=0.006). There was a statistically significant increase in prednisolone prescribing with increasing age, however the extremely small effect size suggests this is not clinically significant (AOR 1.006, 95% CI 1.005-1.007, *P*<0.001). There was no association between prednisolone prescribing and gender (AOR 1.024, 95% CI 0.984-1.065, *P*=0.236). Prednisolone prescribing prior was associated with a 33% increase in prednisolone prescribing post SABA prescribing trigger (AOR 1.327, 95% CI 1.311- 1.344, *P*<0.001). CCG variance was tested however convergence of the data in the Hessian matrix was not possible due to low numbers of prednisolone prescribed in the 3-6 months between CCGs.

Table 4. 25 Poisson mixed effects model with prednisolone prescribing at 3-6 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.006 (0.005 – 0.007) | 1.006 (1.005 – 1.007) | <0.001 |
| Gender[2] (Female) | | 0.024 (-0.016, 0.063) | 1.024 (0.984 – 1.065) | 0.236 |
| Ethnicity[3] | Black | -0.064 (-0.120, -0.007) | 0.938 (0.886 – 0.993) | 0.028 |
| | South Asian | 0.062 (0.018 – 0.105) | 1.063 (1.018 – 1.110) | 0.006 |
| | Other | -0.110 (-0.212, -0.008) | 0.895 (0.808 – 0.992) | 0.035 |
| | Not stated | 0.113 (-0.011, 0.236) | 1.119 (0.989 – 1.266) | 0.074 |
| Prednisolone 3-6m prior | | 0.283 (0.271 – 0.296) | 1.327 (1.311 – 1.344) | <0.001 |
| Group[4] (Intervention) | | -0.078 (-0.116, -0.040) | 0.924 (0.890-0.960) | <0.001 |

[1] adjusted for age, gender, ethnicity and prednisolone prescribing prior
[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.4.2.4 Prednisolone prescribing: 6-12 months

Table 4.26 compares prednisolone prescribing between groups in the 6-12 months prior and post SABA prescribing trigger. There was a significant difference in prednisolone prescribed between groups in the 6-12 months post trigger (*P*=0.006) but not in the prior 6-12 months (P=0.089). The proportion of the population prescribed no courses or one to two courses of prednisolone was higher in the intervention group at both 6-12 months prior and post SABA prescribing trigger.

Table 4. 26 Comparison of prednisolone prescribing at 6-12 months before and after in the intervention group (SABA alert) and at 6-12 months before and after in the historical control group (no SABA alert)

| Prednisolone courses prescribed 6-12 months prior | Control group (N%) | Intervention group (N%) | P-value* |
|---|---|---|---|
| 0 | 7694 (88.5%) | 8328 (87.2%) | 0.089 |
| 1 | 635 (7.3%) | 788 (8.2%) | |
| 2 | 179 (2.1%) | 227 (2.4%) | |
| 3 | 81 (0.9%) | 90 (0.9%) | |
| >3 | 102 (1.0%) | 120 (1.2%) | |
| Prednisolone courses prescribed 6-12 months post | Control group (N%) | Intervention group (N%) | P-value* |
| 0 | 7520 (86.5%) | 8185 (85.7%) | 0.006 |
| 1 | 755 (8.7%) | 859 (9.0%) | |
| 2 | 218 (2.5%) | 284 (3.0%) | |
| 3 | 81 (0.9%) | 74 (0.8%) | |
| >3 | 117 (1.1%) | 143 (1.6%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on prednisolone prescribing in the 6-12 months post SABA prescribing trigger is presented in table 4.27. When adjusted for the control group, the intervention had no effect on prednisolone prescribing at 6-12 months (AOR 1.037, 95 % CI 0.980-1.099, *P*=0.200). When adjusted for covariates, an 11% reduction in prednisolone prescribing among those of Black ethnicity (AOR 0.893, 95% CI 0.821-0.970, *P*=0.008), a 18% reduction among those of South Asian ethnicity (AOR 0.815, 95% CI0.762-0.872, *P*<0.001) and a 21% reduction among those of Other ethnicity (AOR 0.791, 95% CI 0.677-0.924, *P*=0.003) was observed. Prednisolone prescribing was associated with increasing age (AOR 1.014, 95% CI 1.012-1.015, *P*<0.001), prednisolone prescribing prior (AOR 1.223, 95% CI 1.217-1.228, *P*=<0.001) and female gender (AOR 1.347, 95% CI 1.266-1.434, *P*<0.001). There was no significant variance across the three CCGs to account for differences in prednisolone prescribing in the 6-12 months post SABA prescribing trigger ($\sigma^2$ 0.003, 95% CI 0.000 – 0.031, *P*=0.408).

Table 4. 27 Poisson mixed effects model with prednisolone prescribing at 6-12 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-Value |
|---|---|---|---|---|
| Age | | 0.014 (0.012 – 0.015) | 1.014 (1.012 – 1.015) | <0.001 |
| Gender[2] (Female) | | 0.298 (0.236 – 0.361) | 1.347 (1.266 – 1.434) | <0.001 |
| Ethnicity[3] | Black | -0.113 (-0.197, -0.030) | 0.893 (0.821 – 0.970) | 0.008 |
| | South Asian | -0.204 (-0.271, -0.136) | 0.815 (0.762 – 0.872) | <0.001 |
| | Other | -0.234 (-0.390, -0.078) | 0.791 (0.677 – 0.924) | 0.003 |
| | Not stated | -0.003 (-0.204, 0.199) | 0.997 (0.815 – 1.220) | 0.979 |
| Prednisolone 6-12m prior | | 0.202 (0.197 – 0.206) | 1.223 (1.217 – 1.228) | <0.001 |
| Group[4] (Intervention) | | 0.037 (-0.020, 0.095) | 1.037 (0.980 – 1.099) | 0.200 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.003 (0.000 – 0.031) | | 0.408 |

[1] adjusted for age, gender, ethnicity and prednisolone prescribing prior
[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.4.3 Primary care consultations

##### 4.3.4.3.1 Primary care consultations: 0-12 months

Table 4.28 compares the distribution of primary care consultations between groups in the 0-12 months post SABA prescribing trigger. An increased proportion of the intervention group did not consult in the 12 months post SABA prescribing trigger in comparison to the control group. However, an increased proportion of the intervention group had between 1-3 consultations in comparison to the control group. This was in contrast to a lower proportion of the intervention group consulting between 7-10 and >10 times in comparison to the control group. The effect of covariate adjustment on primary care consultations in the 0-12 months post SABA prescribing trigger is presented in table 4.29.

Table 4. 28 Comparison of primary care consultations at 0-12 months after in intervention group (SABA alert) and at 0-12 months after in the historical control group (no SABA alert)

| Primary care consultations 0-12 months post | Control group (N%) | Intervention group (N%) | P-Value* |
|---|---|---|---|
| 0 | 3068 (35.3%) | 3647 (38.2%) | <0.001 |
| 1-3 | 3170 (36.5%) | 3476 (36.4%) | |
| 4-6 | 1298 (15.0%) | 1295 (13.6%) | |
| 7-10 | 709 (8.2%) | 701 (7.3%) | |
| >10 | 446 (5.0%) | 434 (4.5%) | |

* Derived from Mann-Whitney test

Table 4. 29 Poisson mixed effects model with primary care consultations at 0-12 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.015 (0.014 – 0.015) | 1.015 (1.014 – 1.015) | <0.001 |
| Gender[2] (Female) | | 0.284 (0.265 – 0.302) | 1.328 (1.303 – 1.352) | <0.001 |
| Ethnicity[3] | Black | -0.109 (-0.136, -0.083) | 0.896 (0.872 – 0.920) | <0.001 |
| | South Asian | 0.079 (0.059 – 0.100) | 1.082 (1.060 – 1.105) | <0.001 |
| | Other | -0.128 (-0.174, -0.081) | 0.879 (0.840 – 0.922) | <0.001 |
| | Not stated | -0.208 (-0.279, -0.137) | 0.812 (0.756 – 0.871) | <0.001 |
| Group[4] (Intervention) | | -0.083 (-0.101, -0.066) | 0.920 (0.903 – 0.936) | <0.001 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | |
| CCG Variance | | 1 | | |

[1] adjusted for age, gender, ethnicity
[2] reference males, [3] reference White population, [4] reference control group

When adjusted for the control group, an 8% reduction in consultations was observed in the intervention group in the 12 months post SABA prescribing trigger (AOR 0.920, 95% CI 0.903-0.936, *P*<0.001). When adjusted for covariates, a 10% reduction in primary care consultations among those of Black ethnicity (AOR 0.896, 95% CI 0.872 – 0.920, P<0.001), a 12% reduction among those of Other ethnicity (AOR 0.879, 95% CI 0.840 – 0.922, P<0.001) and a 19% reduction among those with ethnicity not stated (AOR 0.812, 95% CI 0.756 – 0.871, P<0.001) was observed.

In contrast an increase in consultations was associated with age (AOR 1.015, 95% CI 1.014-1.015, *P*<0.001), female gender (AOR 1.328, 95% CI 1.303-1.352, *P*<0.001) and South Asian ethnicity (AOR 1.082, 95% CI 1.060 – 1.105, P<0.001). Heterogeneity between CCGs was assumed with an estimated variance of 1.

#### 4.3.4.3.2 Primary care consultations: 0-3 months

Table 4.30 compares the distribution of primary care consultations between groups in the 0-3 months post SABA prescribing trigger. There was an increased proportion of the intervention group not consulting in the 0-3 months post SABA prescribing trigger in comparison to the control group.

Table 4. 30 Comparison of primary care consultations at 0-3 months after in intervention group (SABA alert) and at 0-12 months after in the historical control group (no SABA alert)

| Primary care consultations 0-3 months post | Control group (N%) | Intervention group (N%) | P-Value* |
|---|---|---|---|
| 0 | 4857 (55.9%) | 5646 (59.1%) | <0.001 |
| 1-3 | 3292 (37.9%) | 3348 (35.1%) | |
| 4-6 | 452 (5.2%) | 450 (4.7%) | |
| 7-10 | 76 (1.0%) | 89 (0.9%) | |
| >10 | 14 (0.1%) | 20 (0.1%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on primary care consultations in the 0-3 months post SABA prescribing trigger is presented in table 4.31. When adjusted for the control group, an 8% reduction in consultations was observed in the intervention group (AOR 0.924, 95% CI 0.895-0.952, *P*<0.001). When adjusted for covariates, an 8% reduction in primary care consultations among those of Black ethnicity (AOR 0.917, 95% CI 0.876-0.960, *P*<0.001) and a 28% reduction among those with ethnicity not stated (AOR 0.720, 95% 0.632-0.819, *P*<0.001) was observed.

In contrast an increase in consultations was associated with age (AOR 1.014, 95% CI 1.013-1.014, *P*<0.001), female gender (AOR 1.282, 95% CI 1.242-1.324, *P*<0.001) and South Asian ethnicity (AOR 1.110, 95% CI 1.071- 1.151, *P*<0.001). There was no significant variance in consultations across individual CCGs to account for covariate influence at 0-3 months post SABA prescribing trigger ($\sigma^2$ 0.017, 95% CI 0.002-0.125, *P*=0.322).

Table 4. 31 Poisson mixed effects model with primary care consultations at 0-3 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.014 (0.013 – 0.014) | 1.014 (1.013 – 1.014) | <0.001 |
| Gender[2] (Female) | | 0.249 (0.217 – 0.281) | 1.282 (1.242 – 1.324) | <0.001 |
| Ethnicity[3] | Black | -0.086 (-0.132, -0.040) | 0.917 (0.876 – 0.960) | <0.001 |
| | South Asian | 0.105 (0.069 – 0.141) | 1.110 (1.071 – 1.151) | <0.001 |
| | Other | -0.079 (-0.159, -0.000) | 0.924 (0.852 – 1.000) | 0.050 |
| | Not stated | -0.328 (-0.458, -0.199) | 0.720 (0.632 – 0.819) | <0.001 |
| Group[4] (Intervention) | | -0.079 (-0.110, -0.049) | 0.924 (0.895 – 0.952) | <0.001 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.017 (0.002 – 0.125) | | 0.322 |

[1] adjusted for age, gender, ethnicity
[2] reference males, [3] reference White population, [4] reference control group

#### 4.3.4.3.3 Primary care consultations: 3-6 months

Table 4.32 compares the distribution of primary care consultations between groups in the 3-6 months post SABA prescribing trigger. An increased proportion of the intervention group did not consult in the 3-6 months post SABA prescribing trigger in comparison to the control group, whilst a lower proportion of the intervention group consulted between 1-3 times at 3-6 months.

Table 4. 32 Comparison of primary care consultations at 3-6 months after in intervention group (SABA alert) and at 0-12 months after in the historical control group (no SABA alert)

| Primary care consultations 3-6 months post | Control group (N %) | Intervention group (N %) | P-Value* |
|---|---|---|---|
| 0 | 5172 (59.5%) | 6055 (63.4%) | <0.001 |
| 1-3 | 3043 (35.0%) | 3004 (31.5%) | |
| 4-6 | 398 (4.6%) | 414 (4.3%) | |
| 7-10 | 71 (0.8%) | 68 (0.7%) | |
| >10 | 5 (0.0%) | 12 (0.1%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on primary care consultations in the 3-6 months post SABA prescribing trigger is presented in table 4.33

Table 4. 33 Poisson mixed effects model with primary care consultations at 3-6 months as a dependent variable adjusted for covariates[1]

| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.014 (0.013 – 0.015) | 1.014 (1.013 – 1.015) | <0.001 |
| Gender[2] (Female) | | 0.279 (0.245 – 0.313) | 1.321 (1.277 – 1.367) | <0.001 |
| Ethnicity[3] | Black | -0.104 (-0.153, -0.055) | 0.901 (0.858 – 0.946) | <0.001 |
| | South Asian | 0.107 (0.069 – 0.145) | 1.112 (1.071 – 1.156) | <0.001 |
| | Other | -0.184 (-0.272, -0.096) | 0.831 (0.761 – 0.908) | <0.001 |
| | Not stated | -0.105 (-0.230, 0.020) | 0.900 (0.794 – 1.020) | 0.100 |
| Group[4] (Intervention) | | -0.101 (-0.134, -0.069) | 0.903 (0.874 – 0.933) | <0.001 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.036 (0.005 – 0.256) | | 0.320 |

[1] adjusted for age, gender, ethnicity
[2] reference males, [3] reference White population, [4] reference control group

When adjusted for the control group, a 10% reduction in consultations was observed in the intervention group (AOR 0.903, 95% CI 0.874-0.933, *P*<0.001). When adjusted for covariates, a 10% reduction in primary care consultations among those of Black ethnicity (AOR 0.901, 95% CI 0.858-0.946, *P*<0.001) and a 17% reduction among those of Other ethnicity (AOR 0.831, 95% CI 0.761-0.908,*P*<0.001) was observed. The number of consultations at 3-6 months was positively associated with increasing age (AOR 1.014, 95% CI 1.013-1.015, *P*<0.001), female gender (AOR 1.321, 95% CI 1.277-1.367, *P*<0.001) and South Asian ethnicity (AOR 1.112, 95% CI 1.071-1.156, *P*<0.001). There was no significant variance in consultations across individual CCGs to account for covariate influence at 3-6 months post SABA prescribing trigger ($\sigma^2$ 0.036, 95% CI 0.005 - 0.256, *P*=0.320).

#### 4.3.4.3.4 Primary care consultations: 6-12 months

Table 4.34 compares the distribution in primary care consultations between groups in the 6-12 months post SABA prescribing trigger. An increased proportion of the intervention group did not consult in the 6-12 months post SABA prescribing trigger in comparison to the control group. Furthermore a lower proportion of the intervention group consulted on between 1-3 occasions in the 6-12 months post SABA prescribing trigger in comparison to the control group.

Table 4. 34 Comparison of primary care consultations at 6-12 months after in intervention group (SABA alert) and at 0-12 months after in the historical control group (no SABA alert)

| Primary care consultations 6-12 months post | Control group (N %) | Intervention group (N %) | P-Value* |
|---|---|---|---|
| 0 | 5444 (62.6%) | 6125 (64.1%) | 0.012 |
| 1-3 | 2402 (27.6%) | 2552 (26.7%) | |
| 4-6 | 601 (7.0%) | 648 (6.8%) | |
| 7-10 | 194 (2.3%) | 176 (1.9%) | |
| >10 | 50 (0.4%) | 52 (0.5%) | |

* Derived from Mann-Whitney test

The effect of covariate adjustment on primary care consultations in the 6-12 months post SABA prescribing trigger is presented in table 4.35. When adjusted for the control group, a 7% reduction in consultations was observed in the intervention group (AOR 0.930, 95% CI 0.903-0.956, *P*<0.001).

When adjusted for covariates, a 12% reduction in primary care consultations among those of Black ethnicity (AOR 0.875, 95% CI 0.838-0.913, *P*<0.001), a 12% reduction among those of Other ethnicity (AOR 0.879, 95% CI 0.816-0.948, *P*=0.001) and a 17% reduction among those with ethnicity not stated (AOR 0.826, 95% CI 0.737-0.928, *P*=0.001) was observed. The number of consultations at 6-12 months was positively associated with increasing age (AOR 1.016 95% CI 1.015-1.017, *P*<0.001), female gender (AOR 1.374, 95% CI 1.332-1.417, *P*<0.001) and those of South Asian ethnicity (AOR 1.036, 95% CI 1.002-1.072, *P*=0.035). There was no significant variance in consultations across individual CCGs to account for covariate influence ($\sigma^2$ 0.040, 95% CI 0.006 - 0.286, *P*=0.319).

Table 4. 35 Poisson mixed effects model with primary care consultations at 6-12 months as a dependent variable adjusted for covariates[1]

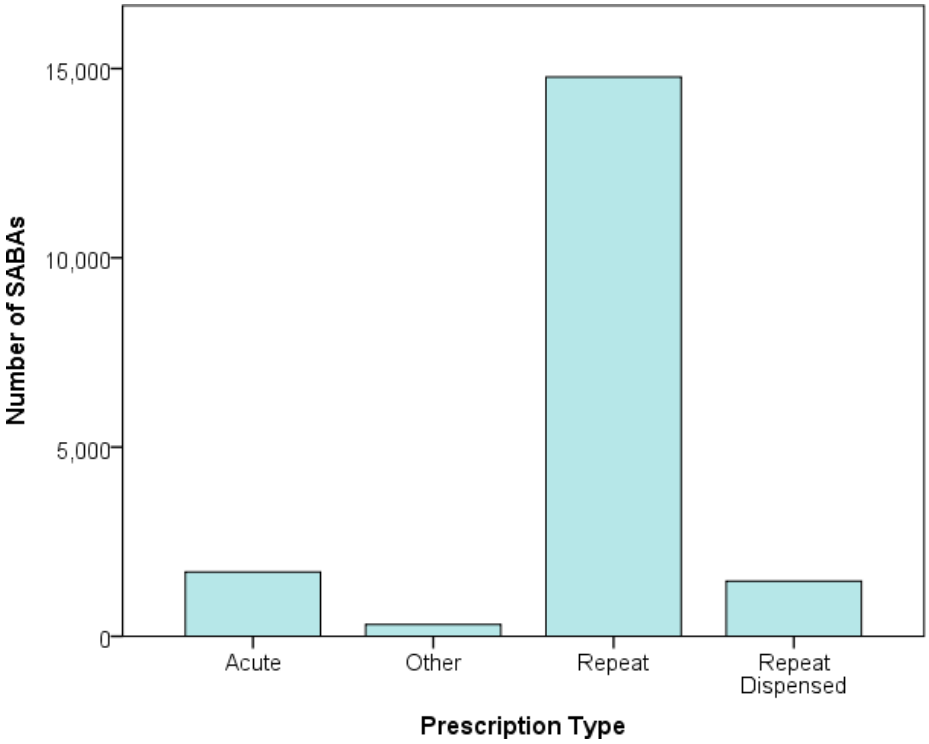
| Factors | | Adjusted β (95% CI) | Exp β / OR (95% CI) | P-value |
|---|---|---|---|---|
| Age | | 0.016 (0.015 – 0.017) | 1.016 (1.015 – 1.017) | <0.001 |
| Gender[2] (Female) | | 0.318 (0.287 – 0.349) | 1.374 (1.332 – 1.417) | <0.001 |
| Ethnicity[3] | Black | -0.133 (-0.176, -0.090) | 0.875 (0.838 – 0.913) | <0.001 |
| | South Asian | 0.036 (0.002 – 0.070) | 1.036 (1.002 – 1.072) | 0.035 |
| | Other | -0.128 (-0.203, -0.053) | 0.879 (0.816 – 0.948) | 0.001 |
| | Not stated | -0.190 (-0.305, 0.074) | 0.826 (0.737 – 0.928) | 0.001 |
| Group[4] (Intervention) | | -0.072 (-0.101, -0.044) | 0.930 (0.903 – 0.956) | <0.001 |
| Random effect | | Estimated $\sigma^2$ (95% CI) | | P-value |
| CCG Variance | | 0.040 (0.006 – 0.286) | | 0.319 |

[1] adjusted for age, gender, ethnicity
[2] reference males, [3] reference White population, [4] reference control group

### 4.3.5 Repeat prescribing

In the total study population, 81% (14,776) of SABAs were prescribed by repeat prescription in comparison to 9.3% (1,700) on acute prescription (Figure 4.9).

Figure 4. 9 Number of SABA prescribed in the total population by prescription type




Exploration of subgroup analyses by prescription type identified a 6% reduction in SABA repeat prescriptions issued in the 0-12 months post SABA prescribing trigger (Adjusted β -0.059, 95% CI - 0.047, -0.071/AOR 0.942, 95% CI 0.931 - 0.954, *P*<0.001). No effect on acute SABA prescribing was observed (Adjusted β -0.031, 95% CI 0.011, -0.074/AOR 0.969, 95% CI 0.928 -1.011, *P*=0.153).

When analysed by time point, repeat SABA prescribing reduced at 3-6 months (Adjusted β -0.050, 95% CI -0.073, -0.026/AOR 0.951, 95% CI 0.929-0.974, *P*<0.001) but not acute SABA prescribing (Adjusted β 0.021, 95% CI -0.064, 0.107 /AOR 1.021, 95% CI 0.938-1.113, *P*=0.622). A 6-1 months post SABA prescribing trigger, a statistically significant reduction in repeat SABA prescribing (Adjusted β -0.081, 95% CI -0.098, -0.065/AOR 0.922, 95% CI 0.906-0.937, *P*<0.001) and acute prescribing (Adjusted β -0.069, 95% CI -0.129, -0.009/AOR 0.933, 95% CI 0.878-0.991, *P*=0.024) was observed.

## 4.4 Summary of findings

Table 4.36 details a summary of outcomes by time point following covariate adjustment.

In the 0-12 months following the SABA prescribing trigger, SABA prescribing reduced by 6%, (AOR 0.938, 95% CI 0.927-0.947, *P*<0.001). This was reflected in a 6% reduction to repeat SABA prescribing (AOR 0.942, 95% CI 0.931 - 0.954, *P*<0.001), but not acute prescribing (AOR 0.969, 95% CI 0.928 - 1.011, *P*=0.153). No effect on prednisolone prescribing was observed (AOR 0.988, 95% CI 0.947 – 1.029, *P*=0.561), however primary care consultations reduced by 8% (AOR 0.920, 95% CI 0.903-0.936, *P*<0.001).

When explored by time point, there was no change in SABA prescribing was observed at 0-3 months post SABA prescribing trigger (AOR 0.983, 95%CI 0.961-1.006, *P*=0.148). However the number of asthma reviews increased by 12% (AOR 1.120, 95% CI 1.043-1.202, *P*=0.002). There was no change in prednisolone prescribing (AOR 1.008, 95% CI 0.969-1.048, *P*=0.695) however consultations reduced by 8% (AOR 0.924, 95% 0.865-0.952, *P*<0.001).

At 3-6 months post SABA prescribing trigger, SABA prescribing reduced by 4% (AOR 0.955, 95% CI 0.935- 0.976, *P*<0.001). When analysed by prescription type, SABA repeat prescribing reduced by 5% (AOR 0.951, 95% CI 0.929 – 0.974, *P*<0.001) but no effect was observed on acute prescribing (AOR 1.021, 95% CI 0.938-1.113, *P*=0.622). Exacerbations reduced by 8% (AOR 0.924, 95% CI 0.890- 0.960, *P*<0.001), and consultations reduced by 10% (AOR 0.903, 95% CI 0.874-0.933, *P*<0.001).

At 6-12 months post SABA prescribing trigger, SABA prescribing reduced by 9% (AOR 0.912, 95% CI 0.898-0.925, *P*<0.001). When analysed by prescription type, repeat SABA prescribing reduced by 8% (AOR 0.922, 95% CI 0.906 - 0.937, *P*<0.001) and acute SABA prescribing reduced by 7% (AOR 0.933, 95% CI 0.878-0.991, *P*=0.024). There was no change in prednisolone prescribing (AOR 1.037, 95% CI 0.980-1.099, *P*=0.200) however primary care consultations reduced by 7% (AOR 0.930, 95% CI 0.903-0.956, *P*<0.001).

Following covariate adjustment at 0-12 months post SABA prescribing trigger, SABA prescribing was associated with increasing age ($p<0.001$), Black ethnicity ($p<0.001$), South Asian ethnicity ($p<0.001$), Other ethnicity ($p=0.006$) and SABA prescribing prior *(*$p<0.001$). At 0-3 months, SABA prescribing was associated with increasing age ($p<0.001$), Black ethnicity ($p=0.026$), South Asian ethnicity ($p=0.006$), Other ethnicity ($p=0.007$) and SABA prescribing prior ($p<0.001$). At 3-6 months following the alert, SABA prescribing was associated with increasing age ($p<0.001$), Black ethnicity ($p=0.001$), South Asian ethnicity ($p=0.002$) and SABA prescribing prior ($p<0.001$). At 6-12 months following the alert, SABA prescribing was associated with increasing age ($p<0.001$), Black ethnicity ($p<0.001$), South Asian ethnicity ($p=0.001$), Other ethnicity ($p=0.004$) and SABA prescribing prior ($p<0.001$).

Table 4. 36 Summary results of adjusted analyses* by time point

| Outcomes | 0-12 months | | 0-3 months | | 3-6 months | | 6-12 months | |
|---|---|---|---|---|---|---|---|---|
| | AOR (95% CI) | P-Value | AOR (95% CI) | P-Value | AOR (95% CI) | P –Value | AOR 95% CI | P-Value |
| SABA prescribing | 0.938 (0.927-0.947) | <0.001 | 0.983 (0.961-1.006) | 0.148 | 0.955 (0.935-0.976) | <0.001 | 0.912 (0.898-0.925) | <0.001 |
| Number of asthma reviews | | | 1.120 (1.043-1.202) | 0.002 | 1.028 (0.958-1.102) | 0.430 | | |
| Exacerbations | 0.988 (0.947-1.029) | 0.561 | 1.008 (0.969-1.048) | 0.695 | 0.924 (0.890-0.960) | <0.001 | 1.037 (0.980-1.099) | 0.200 |
| Consultations | 0.920 (0.903-0.936) | <0.001 | 0.924 (0.895-0.952) | <0.001 | 0.903 (0.874-0.933) | <0.001 | 0.930 (0.903-0.956) | <0.001 |
| | | | Adjusted B (SE) | P-Value | Adjusted B (SE) | P-Value | | |
| Time to review | | | 0.010 (0.032) | 0.753 | - 0.027 (0.031) | 0.384 | | |

*adjusted for age, gender, ethnicity, prior SABA prescribing and prior exacerbations

## 4.5 Discussion

### 4.5.1 Main findings

This study demonstrates a small but potentially clinically significant 6% reduction in repeat SABA prescribing in the 12 months following the SABA prescribing alert intervention (P<0.001). This provides evidence from which to reject the null hypothesis as set out in section 4.1.3. The evidence to support a SABA prescribing alert is strengthened by the observed 12% increase in asthma reviews at 0-3 months (P=0.002), and a 4% reduction in SABA prescribing (p<0.001) and an 8% reduction in exacerbations (p<0.001) in the subsequent 3-6 months. However no change in SABA prescribing was observed in the immediate 0-3 months following the alert intervention. This may reflect a reluctance or inability among clinicians to alter SABA prescribing without first assessing asthma control and clinical need. This suggests that asthma reviews act as a catalyst for SABA prescribing change. At 6-12 months SABA prescribing reduced by 9% (p<0.001) however no change in prednisolone prescribing was observed (p=0.200). The relationship between SABA prescribing and exacerbations remains unclear. It is not possible to comment further on the relationship between these two variables without acknowledging the role of ICS prescribing which unfortunately was absent from the study. These findings highlight the importance of assessing the co-prescription of ICS and SABAs to determine inappropriate prescribing practice and potentially at-risk patients.

### 4.5.2 Strengths and limitations

#### 4.5.2.1 Strengths

This study is based on asthma cases from a multi-ethnic population of approximately one million GP-registered patients. Findings may be representative of primary care practices in ethnically diverse, inner city populations delivering care using EMIS web computer systems. Utilising the CEG data network avoided potential selective bias of practice 'opt-in.' Potential confounding effects of prescribing changes over time were considered by analysing data at three time points within a 12-month period whilst adjusting for covariates. To aide transparency and reproducibility full lists of clinical codes and algorithm to identify patient eligibility have been reported. Strengths also include the large data set and automatic data collection, with the case-control design conveniently lending itself to the data set and time available.

#### 4.5.2.2 Limitations

In the hierarchy of evidence, observational study designs such as case-control studies are commonly viewed as producing lower quality evidence than those using an RCT or cohort study design. An RCT is the recommended method to evaluate computer decision support interventions[125] however this was not possible given the intervention had already been implemented by EMIS without the researcher's knowledge. Furthermore an RCT would not have been achievable within the thesis timeframe given the volume of work required for the mixed methods concurrent phases. An interrupted time series (ITS) analysis; often used to evaluate retrospective changes to prescribing following an intervention,[356,] may have been a more appropriate design to determine changes to SABA prescribing before and after the alert intervention. However as the date and time of SABA alert activation was not coded within the EHR, a flaw in system design, it would not have been possible to identify those specifically prescribed excessive SABAs using an ITS analysis. Instead changes to SABA prescribing for the asthma population as a whole would have been captured.

It was not possible to utilise patient identifiable data for the purpose of this research as highlighted in section 4.2.1.1. page 107. Therefore patients may potentially have been included in both the case and control groups. This may have resulted in an overestimation of intervention effect given that: (1) similarities in patient characteristics in case and control groups could not be adjusted for, and (2) the positive impact of an intervention is more likely to be observed when evaluated closer to its point of implementation, particularly as the study did not extend beyond 12 months. It was not possible to capture asthma quality improvement initiatives and SABA prescribing practices at local level between 2013 and 2016. Therefore the potential influence and impact of such practices on SABA prescribing could not be accounted for.

Results were likely subject to regression to the mean (RTM) as SABA prescribing was identified at an extreme point on first measurement. Given the alert was triggered by excessive SABA prescribing in a three month period, RTM in the 0-3 months following the alert was likely. Therefore, following primary analysis of data at 0-12 months, additional time points were selected to analyse the effect of time on alert use. A non-differential bias of

SABA prescribing RTM was however observed in both the intervention and control group increasing the validity of findings compared to possible differential biases. Analysis was strengthened by the measurement of data at 3-6 months and 6-12 months to reduce the impact of RTM. Multiple testing of SABA prescribing at three time points (0-3, 3-6 and 6-12 months) in addition to analysis at 0-12 months was a potential limitation. To strengthen findings, Bonferroni adjustment was applied and the *P* value cut-off for statistical significance was reduced from $P<0.05$ to $P<0.016$. Statistically significant findings remained so following Bonferroni adjustment.

The inappropriate use of asthma medications is a major contributor to uncontrolled asthma in inner-city, ethnically diverse populations such as east London.[11,367] The interdependent relationship between ethnicity, socio-economic status and asthma prescribing has been acknowledged at various points in this thesis. However as socio-economic status was not captured in the study, it was not possible to explore the confounding effect of socio-economic status as a predictor of SABA use alongside ethnicity.

There are a number of weaknesses in the study due to the limitations of EHR data. It was not possible to determine dose equivalent prescribing of the various SABA and ICS inhaler types included in the study. Due to intervention configuration, it is possible that more than one SABA inhaler was prescribed per prescription and that number of SABA inhalers prescribed was underestimated. The SABA alert was configured to include patients on the asthma register, determined as any QOF Read code for asthma diagnosis. Such a definition included 'H3B Asthma-chronic obstructive pulmonary disease overlap syndrome' (ACOS) and as such SABA use may have been overestimated. It is also possible the SABA alert triggered on more than one occasion in the 12 months of the study however it was not possible to detect this within the data set.

Prednisolone prescribing was assumed to be for the treatment of an exacerbation of asthma but may have been prescribed for other clinical reasons. Exacerbations were not distinguished between one another, with the dose and duration of prednisolone prescribing not captured. Multiple prednisolone prescriptions within a 30-day period may have reflected the same exacerbation but were counted as separate events. Unlike prescribing outcomes, the number of consultations carried out in the prior 0-3, 3-6, 6-12 months was not captured in the dataset. As this was not adjusted for in regression analysis it may have been a potential confounder.

### 4.5.3 In relation to the literature

Of the four RCTs included in a systematic review of the literature in Phase 1 of this thesis, Zeiger *et al.,*[314] reported a reduction in the number of patients dispensed excessive SABAs (<7 SABAs per year) within 12 months following the intervention (*P*=0.007). A reduction in SABA dispensing was also observed at 3 months (*P*<0.001), 6 months (*P*<0.001) and 12 months (*P*<0.001). Findings in this study indicate that an alert intervention can reduce SABA prescribing, therefore echoing the findings of Zeiger *at al*.,[314] as reported in Phase 1 systematic review. However, the multicomponent intervention in Zeiger *et al.,* included patient referral to an allergy specialist. Interestingly, a reduction in SABA prescribing at 3 months in Zeiger *et al.*[314] coincided with earlier time to allergy specialist review, occurring an average of 36 days post excessive SABA dispensing. This was in contrast to findings in this study in which there was no effect on time to asthma review, occurring an average of 46 days following the SABA prescribing trigger. This may reflect challenges in obtaining an asthma review in primary care, when compared to quicker time to specialist hospital review in an insured healthcare system.

In Zeiger *et al.,*[314] the intervention failed to reduce exacerbations despite reducing SABA prescribing. However Zeiger *et al.,*[314] defined exacerbations as distinct episodes separated by at least 30 days, whilst no distinction was made between exacerbations in this study. Therefore multiple courses of prednisolone reported in this study may have been indicative of one exacerbation. In Zeiger et al.,[314] the lack of reduction in exacerbations was likely due to the poor uptake of allergy specialist reviews. Similarly, in this study, poor review uptake was also problematic with 77% of patients identified by the SABA prescribing trigger not having an asthma review. This highlights potential challenges in practice follow-up of patients therefore limiting the opportunity to improve asthma control and reduce risk of asthma attack. Asthma review uptake may be influenced by patient and HCP discrepancies in perceived and actual asthma control,[357,358] with patients less inclined to attend review if they perceive their asthma as well controlled irrespective of excessive SABA prescribing.

The use of CDSSs to change prescribing behaviour is challenging due to heterogeneity in the type of decision support used and the broad scope of clinical outcomes reported in the literature. Each of the four studies in Phase 1's systematic review included an alert as part of a multicomponent intervention, with no study using a single component alert intervention, such as the SABA alert. For example, the intervention in Zeiger *et al.,*[314] included communication with patients by letter, advising either to attend an allergy referral that had been automatically generated in response to the intervention or advising to initiate follow-up with their primary care doctor. A multicomponent intervention may aide the timely review of patients thereby facilitating a reduction in SABA prescribing. This offers potential explanation for the lack of effect of a sole SABA alert intervention at reducing exacerbations in the present study. A more complex intervention beyond a sole SABA alert intervention may have greater potential to improve SABA prescribing and reduce exacerbations. This may require an intervention that not only targets the prescriber at the point of prescribing, but targets and requires action from multiple members of the primary care team. Further insight as to what such an intervention may entail is explored in the qualitative research in the next phase of the thesis.

In Phase 1's systematic review, McCowan *et al*.,[156] was the only one of four studies to capture asthma reviews as an outcome measure, but found no difference in practice initiated reviews. This was likely due to the intervention not being integrated with the general practice computer system resulting in poor user engagement. Studies by Garg *et al.,*[122] Kawamoto *et al.,*[137] and Fillmore *et al*.,[141] recommend that to best influence prescribing behaviour alerts should not only be integrated with general practice software but should be aligned with workflow at point of decision-making. However as decision-making occurs at all points of workflow this may be challenging in practice.[123] In the Phase 1 study by Eccles *et al.,*[153] the alert presented centrally on the computer screen upon opening of a patient record, however following clinician feedback this was changed to present only when a relevant code was entered by clinicians. This was an attempt to minimise interruption to clinician workflow, yet no effect on SABA prescribing was observed. In this study, the SABA alert did not present at the point of prescribing but presented in the QOF box at the bottom right hand corner of the computer screen upon the opening of the patient's EHR by any member of staff.

In two studies evaluating a computerised reminder system in hospital, Dexter *et al*.,[145] and

Overhage *et al.,*[359] reported that reminders placed at the bottom of the screen for optional clinician engagement had no effect in outcomes.[359] Conversely the SABA alert in this study may have minimised alert fatigue and cognitive overload by presenting in the QOF box rather than centrally on-screen within workflow. The option to view the SABA alert at the discretion of the clinician may have increased user acceptance and recommended action. Alternatively, the position of the SABA alert in the QOF box may have dissuaded clinicians from engaging with the intervention or not being aware of its presence. In Chapter 1, Swinglehurst *et al.,*[71] described repeat prescribing as a complex process requiring collaboration between general practice staff, in particular receptionists and GPs. As the majority of SABAs in this study were obtained by repeat prescription, the influence of the variability in the roles, process and management of repeat prescriptions at practice level will be explored through qualitative research in the next phase of the thesis.

Research suggests that CDSSs not restricted to general practice can improve prescribing behaviour. In the PINCER trial[86] a computerised pharmacist-led intervention composed of feedback and educational outreach effectively reduced prescribing errors. This RCT compared pharmacists delivering computerised feedback about potential prescribing errors to GPs, in comparison to simple GP decision support for at-risk patients in general practice. In a non-controlled before and after study by Wong *et al.,*[320] pharmacists manually alerted clinicians to excessive SABA prescribing (more than 1 SABA per month) by fax and follow-up telephone call. Pharmacists provided guideline recommendations for appropriate SABA use and requested GPs reduce SABA prescribing. This resulted in 1,230 people (67%) receiving less than 1 SABA per month in the subsequent 12 months ($P<0.01$). However, this intervention had no effect on asthma hospitalisations, AED visits, and oral corticosteroid use. Wong *et al.,*[320] highlight the potential benefit of interventions in the management of asthma that engage the wider primary care team.

In Zeiger *et al*.[314] the success of the intervention at reducing excessive SABA dispensing was attributed in part to the integration of EHR, pharmacy and secondary care data in a managed health care organisation whereby the intervention was delivered in conjunction with comprehensive asthma management initiatives as standard care. In the present study, the three CCGs are among the highest QOF achieving nationally.[360] However recent evidence to support QOF indicators in the improvement of quality of care is variable. In a recent review of QOF by NHS England it was reported that indicators do not necessarily demonstrate quality of care,[363] whilst in Lester *et al's.,*[364] qualitative study with health care professionals, QOF was

perceived as a tick-box exercise. In contrast, recent evidence by Minchin *et al.*,[365] has suggested the removal of financial incentives is associated with an immediate decline in performance on quality measures and care delivery. In a recent analysis on health care improvement, Braithwaite *et al.,*[366] argued that changing behaviours of those within health care systems requires consideration of the influence of local strategies. High QOF performance in the study population is likely influenced by quality improvement initiatives facilitated by the CEG. However, the extent to which the role of the CEG influences standard asthma care in the 3 CCGs of interest in comparison to CCGs outside of inner city east London remains unclear.

Ethnic minority groups are more likely to live in deprived neighbourhoods often in inner-city areas such as the east London population included in this study. Asthma morbidity disproportionately affects people from ethnic minority backgrounds,[12] however the majority of data on asthma and ethnicity comes from the United States (US) health insured system afforded by a majority White population.[11,368,369] In the two North American studies in *Phase 1's* systematic review, the largest proportion of the study population in Zeiger *et al.*[314] was of White background, whilst in Tamblyn *et al.*,[313] ethnicity was not reported. Socio-economic status is a proxy measure for lower income, inferior housing, poor neighbourhood social structures and differential exposures to environmental risks and stressors, that are inextricably linked to ethnicity.[367] However, despite being important social determinants of health; race and socio-economic status are often overlooked in research. In this Phase 2 study in inner-city east London, the SABA alert was associated with a reduction in SABA prescribing among those of Black and South Asian ethnicity. Unfortunately as socio-economic status was not captured alongside ethnicity further research is required to explore the association between ethnicity, socio-economic status and SABA prescribing in the east London asthma population.

A study by Griffiths *et al.*,[154] carried out in the same east London population identified variability in the management of asthma between ethnicities, with the South Asian population more commonly managing exacerbations without prophylactic ICS or systemic corticosteroids. Furthermore in a recent analysis on the factors associated with consultation rates in general practice in England, Mukhtar *et al.,*[370] reported that primary care consultation rates varied by ethnicity, with patients of Asian ethnicity consulting more frequently than the White population. However, reasons to account for such findings were not explored. Similarly, this study identified an association between higher numbers of consultations and

South Asian ethnicity, in contrast to fewer consultations among with those of Black ethnicity. Further exploration is required to identify the relationship between ethnicity and asthma self-management behaviours and health beliefs among ethnic minorities that may influence the ethnic variation in outcomes identified in this study.

### 4.5.4 Conclusion

This retrospective case-control study in an ethnically diverse inner city population identified a statistically and potentially clinically significant reduction in SABA prescribing following a SABA prescribing alert intervention. This adds to the systematic review findings in Phase 1 that a single component alert intervention has the potential to reduce SABA prescribing. The reduction in SABA prescribing appears to result from asthma reviews initiated in response to the SABA alert rather than a reduction in SABA prescribing at point of alert presentation. An asthma review facilitates an in-person assessment of asthma control and management from which asthma prescribing can then be optimised. The mechanisms through which the SABA alert facilitates an asthma review, including where in workflow the alert is identified and how and by whom the alert is acted upon remains unclear. Such issues cannot be captured in quantitative data alone. Qualitative research is required to explore quantitative findings from an end-user perspective. Current findings highlight the potential of a SABA alert intervention to support primary care staff in the identification and management of patients with poor asthma control who may be at-risk.

### 4.5.5 Implications for practice and future research

Findings have identified that an alert intervention can reduce SABA prescribing however it is not clear how this reduction occurs in response to the SABA alert. Qualitative research is required to understand the socio-technical factors influencing the use of the SABA alert. This includes determining when, how and whom engages with the SABA alert in particular within the repeat prescribing process and how this translates into a reduction in SABA prescribing.

Future exploratory qualitative research should determine whether (1) the SABA alert meets the needs of end-users in practice and (2) how the alert could be optimised to improve the

identification of at-risk patients and improve asthma prescribing. The findings of the qualitative study in Phase 3, carried out contemporaneously to this study, will be used to complement the quantitative findings of this study. Furthermore findings will help optimise a future alert intervention prior to feasibility testing in a suitably powered prospective study. Furthermore, an optimised intervention should be tested in CCGs with less high performing QOF metrics to determine whether there is greater potential for improvements in SABA prescribing and asthma management than those identified in this study. Further research to determine the relationship between ICS and SABA prescribing to improve the identification of at-risk patients is required.

Heterogeneity in the reporting of asthma outcome and CDSS interventions makes it challenging to determine the effectiveness of the SABA alert in this study in comparison to similar studies using CDSS-linked EHR data. Further research is required in the standardisation of outcome measures to determine the effectiveness of CDSSs interventions for the management of asthma in primary care.

# Chapter 5. A qualitative study on electronic alerts to reduce excessive prescribing of short-acting beta$_2$-agonists for people with asthma: the views of asthma experts and primary care staff

## 5.1 Introduction

### 5.1.1 Recap of context

This chapter represents Phase 3 of the thesis, in which qualitative research was carried out with primary care staff and asthma experts to explore their views on an alert to reduce excessive SABA prescribing. The rationale was to provide context to Phase 2 findings and to provide a broad understanding of the problem and scope of an alert for excessive SABA prescribing in primary care. The chapter begins with a recap of the study rationale, and outlines the aims and specific objectives of the qualitative study. A description of the methods applied in data generation and analysis are then presented, before findings are discussed and conclusions presented.

### 5.1.2 Background

In 2015, following recommendation by NRAD[25] and leading asthma charity Asthma UK,[334] general practice computer software providers, EMIS Health, designed and implemented the 'Asthma Medicines Management alert' to identify excessive SABA prescribing in EMIS web-using primary care practices in England.

Whilst CDSSs are increasingly used to improve prescribing practice in the management of asthma, it was unclear to what extent CDSSs alerts had been used to reduce excessive SABA prescribing. In Phase 1 of the thesis, a systematic review of the evidence on the use of CDSS

alerts in asthma to reduce excessive SABA prescribing identified the potential of alerts to reduce excessive SABA prescribing when delivered as a multicomponent intervention. However, of the two studies systematically reviewed that captured user engagement, Eccles *et al.*[153] reported that engagement with the CDSS was poor with several instances of zero interaction, whilst in Tamblyn *et al.,*[313] clinicians failed to interact with the CDSS in approximately 60% of cases. These findings support the evidence that availability of CDSS do not guarantee user engagement,[119] with alerts often ignored or overridden by users.[125,142,166] In evaluations of CDSSs for the management of hypertension and diabetes in primary care, Hetlevik *et al.,*[375] reported low user engagement in 12% of case. Qualitative work reported difficulties in CDSS design and time-consuming procedures as reasons for low engagement. However, research often overlooks the relationship between system and user as a potential reason for the success or failure of CDSSs to influence prescribing behaviour.[102] This was reflected in the absence of qualitative research in Eccles *et al*.[153] and Tamblyn *et al*.[313] incorporating qualitative work within RCTs to determine reasons for low levels of engagement with CDSSs.

In Phase 2 of the study (Chapter 4), the SABA alert had a variable effect SABA prescribing across three CCGs in east London however; an observational study design alone does not help understand reasons for intervention success or failure. Few research topics in clinical decision-making can be sufficiently understood through quantitative research alone,[376] with qualitative research to complement quantitative findings increasingly recommended.[321,377] As described in Chapter 1, CDSSs should present the right information, in the right format, at the right time, without requiring special effort."[126] Yet it is unclear what users perceive as the right information, format and time for a SABA alert and how this may impact the use of the current SABA alert.

### 5.1.3 Aims and objectives

The aim of this study was to explore the views of asthma experts and primary care staff on the use of alerts, in particular the SABA alert, to reduce excessive SABA prescribing in primary care.

The objectives of Phase 3 of the thesis were to:

- Identify clinician's perceptions of excessive SABA prescribing

- Determine the role of an alert to identify excessive SABA prescribing

- Identify the factors influencing the use of a SABA alert

- Explore the roles and relationships between primary care staff in the identification and management of excessive SABA prescribing

## 5.2 Methods

Recruitment and data collection for the qualitative study took place between May 2015 and Sept 2016 as outlined in the following sections.

### 5.2.1 Research design

As discussed in Chapter 2, theory influences research design, including the development of research questions and underpins methodology thereby influencing how data are analysed and interpreted.[257,378]

According to Kelly's classification of the role of theory in qualitative research,[257] this study can be described as 'generic qualitative research' within the field of applied health research and did not use an explicit theoretical model. With respect to methodology, an empirical approach was applied to this qualitative research to generate a surface understanding of clinician's perceptions of excessive SABA use and the role of alerts in identifying excessive use. The analysis was focused on generating knowledge as a basis for provoking a wider debate about clinicians' responses to SABA use and informing future research and development of alerts to identify excessive use of SABAs in primary care.

This study was informed by background literature on the use of alerts (Chapter 1), patient perspectives from the PPI group feedback (Chapter 2), evidence on the use of alerts for excessive SABA prescribing (Phase 3) and research team experience as clinicians: the lead researcher is clinically active respiratory nurse in a tertiary referral centre and Asthma UK, one research team member who was recent editor of the UK's leading respiratory journal and two of whom contributed to NRAD.

### 5.2.2 Defining participants

Participants were classified into two groups of either primary care staff or asthma experts. Primary care staff were defined as those involved in the delivery of day-to-day asthma care in primary care either clinically as general practitioners (GPs), nurses or pharmacists, or non-clinically as receptionists. Asthma experts were defined as primary or secondary care clinicians who have contributed specifically to asthma care at a national or international level.

### 5.2.3 Sampling strategy

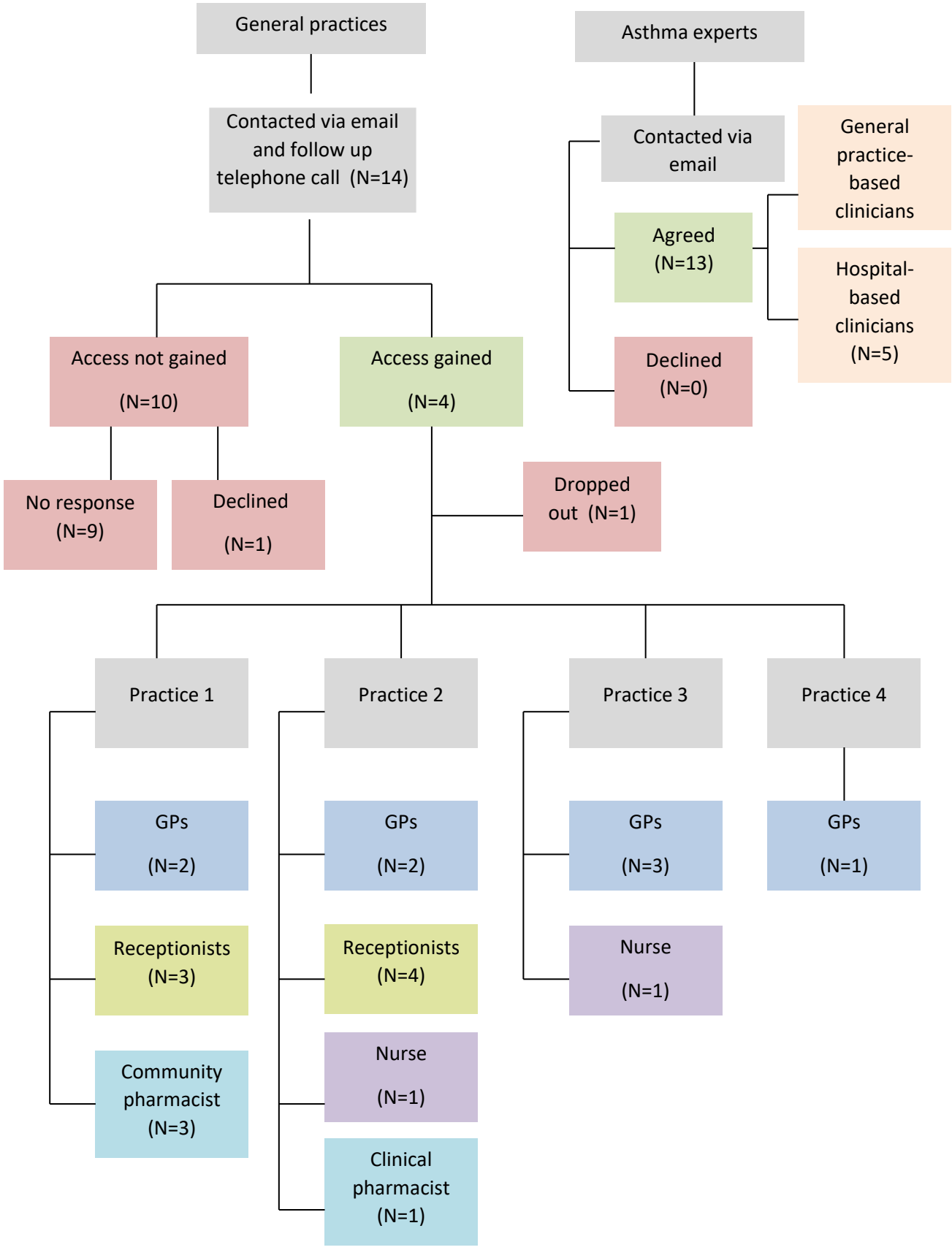
#### 5.2.3.1 Sample size

Following consideration of the issues regarding data saturation and information power, an initial approximate sample size of between 25-35 participants was suggested. This sample size was decided upon so as to not to limit the scope of the data thereby ensuring the study aims were met, yet not stretched so far as to lose significance.[267] Final sample size was based on the richness of the data as determined through a continuous process of data analysis and reflection of study aims rather than when the subjective concept of data saturation has been achieved. Concepts of data saturation and sample size in qualitative research have been discussed in Chapter 2.

#### 5.2.3.2 Participant recruitment

Participant recruitment flow chart is presented in figure 5.1.

Figure 5. 1 Participant recruitment flow chart



#### 5.2.3.2.1 Primary care staff

Primary care staff were recruited with the assistance of the Clinical Effectiveness Group (CEG) at Queen Mary University London (QMUL). The CEG is a unit funded by Clinical Commissioning Groups, GP Confederations, Public Health and research grants, to support general practices to improve care delivery and patient outcomes in primary care. Using well-established data- sharing networks, the CEG leads and collaborates on research with GP practices in east London. The rationale for sampling *via* the CEG was that practices may be more receptive to a local approach to research participation given the already established working relationship.

A purposive sample of fourteen primary care practices in the ethnically diverse borough of Tower Hamlets in east London was determined. A CEG facilitator, whose role was to liaise with practices in the facilitation of training, determined fourteen practices as research receptive to participate.

Practice managers were initially approached by a clinical lead from the CEG individually *via* email to raise awareness of the project and to invite practices to participate. The researcher initiated follow-up contact within one week by telephone call to the practice for the attention of the practice manager. If contact had not been established, a third attempt was made later that week by telephone call to the practice and an email sent to the practice manager. Receptionists and pharmacists were identified through snowball sampling within practices once access had been established. Of the fourteen practices contacted, eight GPs, two nurses, two pharmacists and seven reception staff agreed to take part (Practices 1-3). One GP (Practice 4) was recruited following referral from a participating GP in Practice 2.

#### 5.2.3.2.2 Asthma Experts

Discussion was initiated among research team members to identify clinicians who have significantly contributed to asthma care at national and international levels. The rationale for the inclusion of asthma experts is described in Chapter 2. Using purposive sampling, 13 experts were identified for study inclusion and invited *via* email to participate. Communication was initiated by team members, as expert peers, and followed up by the lead researcher *via* email.

#### 5.2.3.3 Participant characteristics

Age group, gender and field of expertise was categorised for all participants. Participant demographics are presented in Table 5.1. Of 32 participants, 8 were GPs (4 male/4 female), 13 were asthma experts (10 male/3 female), 2 were pharmacists (female), 2 were nurses (female) and 7 were reception staff (female). Participants were categorised as greater than 50 years of age (n=17), between 35-49 years (n=9) or under 35 years of age (n=6).

Table 5. 1 Participant characteristics

| Participant Number | Role | In-text identifier | Age (years) | Gender (male/female) |
|---|---|---|---|---|
| 1 | GP | GP 1 | 35-49 | M |
| 2 | GP | GP 2 | >50 | F |
| 3 | GP | GP 3 | 35-49 | F |
| 4 | GP | GP 4 | 35-49 | M |
| 5 | GP | GP 5 | <35 | M |
| 6 | GP | GP 6 | 35-49 | M |
| 7 | GP | GP 7 | 35-49 | F |
| 8 | GP | GP 8 | <35 | F |
| 9 | Nurse practitioner | Nurse 1 | >50 | F |
| 10 | Nurse | Nurse 2 | 35-49 | F |
| 11 | Community Pharmacist | Community pharmacist | <35 | F |
| 12 | Practice pharmacist | Practice pharmacist | <35 | F |
| 13 | Receptionist | Receptionist 1 | >50 | F |
| 14 | Receptionist | Receptionist 2 | >50 | F |
| 15 | Receptionist | Receptionist 3 | >50 | F |
| 16 | Receptionist | Receptionist 4 | <35 | F |
| 17 | Receptionist | Receptionist 5 | 35-49 | F |
| 18 | Receptionist | Receptionist 6 | <35 | F |
| 19 | Receptionist | Receptionist 7 | 35-49 | F |
| 20 | Expert (Primary care, UK) | Expert 1 | >50 | M |
| 21 | Expert (Hospital care, UK) | Expert 2 | >50 | M |
| 22 | Expert (Primary care, UK) | Expert 3 | >50 | M |
| 23 | Expert (Hospital care, UK) | Expert 4 | >50 | M |
| 24 | Expert (Hospital care, UK) | Expert 5 | >50 | M |
| 25 | Expert (Primary care, Int) | Expert 6 | >50 | M |
| 26 | Expert (Hospital care, EU) | Expert 7 | >50 | F |
| 27 | Expert (Primary care, UK) | Expert 8 | >50 | F |
| 28 | Expert (Primary care, EU) | Expert 9 | 35-49 | F |
| 29 | Expert (Primary care, Int) | Expert 10 | >50 | M |
| 30 | Expert (Primary care, EU) | Expert 11 | >50 | M |
| 31 | Expert (Primary care, EU) | Expert 12 | >50 | M |
| 32 | Expert (Hospital care EU) | Expert 13 | >50 | M |

### 5.2.4 Ethical considerations

Ethical approval was given by Queen Mary, University of London, Ethics of Research Committee and the Health Research Authority (appendix 5.2).

## 5.3 Data collection

Written informed consent was obtained from primary care staff (appendix 5.3) and verbally from asthma experts prior to data collection.

### 5.3.1 Interviews

An interview topic guide was constructed for use in all interviews (appendix 5.4).

#### 5.3.1.1 Primary care staff

Face-to-face semi-structured interviews were carried out by the lead researcher, with five GPs, two pharmacists, two nurses and a group discussion with three GPs in a clinical meeting. Interviews lasted no more than 30 minutes with the average length of interview 21 minutes. All interviews were audio recorded and transcribed verbatim. All observations were documented in field-notes.

#### 5.3.1.2 Experts

Semi-structured interviews were carried out by the lead researcher with thirteen asthma experts via telephone. The average length of interview was 27 minutes. Interview data was recorded on digital voice recorder and transcribed verbatim. Of the twenty-five interviews, the lead researcher transcribed fifteen interviews and ten were transcribed by Queen Mary University of London verified Penguin Transcription services. The researcher validated the transcripts completed by the transcription specialist by comparing transcripts with the original audio recording. Each interview was numbered and line numbers were added to the typed transcripts.

### 5.3.2 Observations

The lead researcher carried out non-participant observations with reception staff when processing of repeat prescriptions. This included receptionists from two practices: three receptionists from one practice (3 visits, 6.5 hours) and four receptionists from another (4 visits, 9.5 hours). Average visit length of observation per visit was approximately 2.3 hours. Visits to both practices coincided with repeat prescribing activities. An observation guide of issues to consider was adapted from Spradley's *9 Dimensions of descriptive observation*[286,287] (appendix 5.5). Repeat prescribing observations were approached, "without any particular orientation in mind, instead with the general question, "What is going on here?."[286] Initial notes were made during observations and written-up as field notes by the lead researcher who collected the data. Data was anonymised and numbered to record only the roles of the participants.

## 5.4 Data analysis

This section introduces thematic analysis using the Framework method,[293] which was the selected qualitative methodology used to answer the qualitative research question.

### 5.4.1 Thematic analysis Framework approach

The framework approach for qualitative data analysis was used to systematically organise and categorise interview data to identify emerging themes and sub-themes in the following stages: familiarisation, identifying a thematic framework, indexing, charting, mapping and interpretation.[292] The rationale for this approach has been discussed in Chapter 2.

Stage 1-2 Transcription and Familiarisation

Interviews were transcribed *verbatim* and were read and re-read several times whilst comparing to the original audio recordings to ensure transcripts remained true to individuals' accounts. This generated a broad awareness of the data. Transcripts were highlighted and notes made when points of interest or of potential significance were identified.

Coding Stage 3-4 Developing a Framework

Transcripts were coded line-by-line using a word or brief phrase to identify how the data was interpreted. Two researchers (the lead researcher and a non-clinically trained researcher) carried out independent coding of three transcripts. Following discussion at first meeting a set of codes each with a brief definition was determined. The researcher continued to code transcripts using this set of agreed codes. At the second meeting, both researchers decided that a number of codes were conceptually related and were therefore merged to form the coding framework. The interview guide was used to derive some thematic codes *a priori*; for example, the use of alerts was a predetermined code as it directly related to the research question and was an overarching question in the topic guide. However, emerging themes and subthemes were identified from the exploration of issues addressed in the topic guide.

Stage 5 Applying the framework

MAXQDA qualitative data analysis software was used to manage data.[379] The use of software facilitated the first stage of more in-depth analysis because it enabled preliminary ideas to emerge within and between data to generate initial themes. During this process some themes were merged and refined whilst some data organised into more than one category.

Stage 6 and 7 Charting and interpreting the data

Themes were generated from the data set by reviewing the framework matrix and making connections within and between categories. Central ideas embedded in the themes and subthemes were analysed to provide explanations of the data and illustrated by verbatim quotes. This included both agreeable and opposing views, to further explain the data in line with research objectives. A working example of the step-by-step process of the analysis can be found in Appendix 5.6.

## 5.5 Qualitative Results

This section reports on the four themes derived from the analysis as summarized in Table 5.2. The first theme presents how excessive SABA prescribing was defined and how the risk of excessive SABA prescribing was perceived in practice. This is followed by the second theme, which identifies the methods and challenges to the identification of excessive SABA prescribing. The third theme highlights the response to an alert for excessive SABA use in practice and describes how alert engagement and prescribing decisions are influenced. The final theme details the roles, responsibilities and relationships between primary care staff and the influence and impact on the identification and management of excessive SABA prescribing.

### 5.5.1 Summary of themes

Table 5. 2 Summary of themes and subthemes

| Theme | Subtheme *(and example of relevant quote)* |
|---|---|
| Perceptions of excessive SABA use | Defining excessive use<br>*"but then you're tossing a coin, aren't you?"* |
| | Recognising risk<br>*"until someone can prove to me, that's what we're doing"* |
| Identifying excessive use | Methods<br>"*I don't think there's a simple way of doing it"* |
| | Challenges<br>*"they're not necessarily truly high users"* |
| Using a SABA alert | Factors influencing engagement<br>*"Alert overload...which one are you going to concentrate on?"* |
| | Factors influencing action<br>*I'm issuing it this time but…"* |
| Inter-professional practice: The Three R's | Roles and Relationships<br>*"it's not like it used to be, sure it's not?"* |
| | Whose Responsiblility?<br>*"it doesn't matter what we think"* |

### 5.5.2 Theme 1: Perceptions of excessive SABA use

The theme "Perceptions of excessive SABA use" is a reflection of what GPs and experts understand by and perceive to be the risks associated with excessive SABA use in practice. The following two subthemes are described in this section:

#### 5.5.2.1 Defining excessive use

***"but then you're tossing a coin, aren't you?"***

There were wide variations in how excessive SABA use was defined by GPs and experts, with no consensus in regards to how much SABA was too much with contrasting definitions ranging from more than 12 SABAs a year to one SABA a year.

There was uncertainty among both GPs and experts in regards to the number of SABA prescribed and the duration of use over which excessive use was determined. Table 5.3 details the quantity and time frame of SABA use which GPs and experts defined acceptable with variations of between 0.5 (100 doses) and 12 SABA inhalers (2400 doses) a year.

Table 5. 3 Definitions of acceptable SABA use offered by interviewees

| SABA use threshold | General Practitioners (n=8) | Experts in general practice (n=8) | Experts in hospital care (n=5) |
|---|---|---|---|
| <3 times a week or <2 SABAs a year | 0 | 3 | 2 |
| 1 SABA a month | 1 | - | 2 |
| 1 SABA in 6 months | - | 2 | - |
| 3 – 4 SABAs a year | 1 | 1 | - |
| 12 SABAs a year | 2 | 1 | 1 |
| Unsure | 2 | - | - |
| Did not define | 2 | 1 | - |

Excessive SABA use was defined interchangeably between daily, weekly and monthly doses and/or inhaler use per month or year. Asthma experts were more likely to describe excessive SABA use by daily/weekly/monthly doses, in contrast to GPs who were more likely to refer to excessive use by inhaler quantity and how the way in which SABA use was assessed influenced perception of excessive use. One GP was surprised that what had been perceived as acceptable SABA use when quantified by inhaler count was viewed as excessive when translated into dose equivalent:

*"Yeah, I mean that's loads, isn't it, 200 [doses] a month, thinking about it, that's absolutely loads [Pause] 200, yeah. So, divided by…Yeah, I'd not thought of it actually…"* (GP 5)

GPs and experts expressed uncertainty regarding the appropriate time-period over which excessive SABA use should be determined. It was suggested that people with worsening symptoms potentially at risk might not be identified by monthly SABA use whilst people with seasonal triggers requiring increased SABA over a short time period may be inaccurately identified as using SABAs excessively:

*"One of the things we could do is when we are prescribing to be more mindful of how long we expect one inhaler to last, so is it a month or is it 3 months, which might be a more reasonable target"* (GP 1)

*"how far back do you have to go to identify an individual who's really deteriorating?...You can see the situations where patients for all sorts of independent reasons deteriorate and must use more and more bronchodilator, but that happens over a few weeks not a year or even three months"* (Expert 2)

*"do you put it [overuse] at a year or do you put it at six months? I'm not quite sure. I think twelve months gets round the seasonal problem. Six months might be more appropriate… there are reasons, over short periods of time, where people might temporarily put in their requests, and then have nothing for the rest of the year"* (Expert 3)

Whilst there was no consensus definition in how much SABA was too much, experts were more likely to quantify excessive SABA use in alignment with national and international asthma guidelines, with use of SABAs more than twice a week suggestive of poorly controlled asthma:

*"new GINA guidelines say you shouldn't use SABA more than twice a week…4 puffs a week, so one puffer a year, so tools should be used to get someone close to guideline recommended care."* (Expert 6)

There were contrasting opinions among experts, with some perceiving NRAD's definition of excessive SABA use as one SABA a month or twelve SABAs a year perceived as too high:

*"Some people think it's 12 a year so one a month, I think it would be even less, taking into account that Ventolin has 200 doses…for a month…is too much"* (Expert 11)

*"I mean that means 200 doses in 30 days which is a hell of a lot of treatment, isn't it? That's six, seven puffs a day, which is over a period of a month much too much, I think."* (Expert 2)

Whilst NRAD's recommended definition of excessive SABA use was perceived as lenient by some experts, other experts perceived national asthma guideline recommended use of SABA more than three times per week as restrictive and not realistic in practice. There was uncertainty regarding which definition was most appropriate, suggesting a lack of continuity in the evidence and application in practice:

*"I mean in an ideal world, what would you be … have your good control looks like three puffs in a week….So what's that? That's three puffs in a week and you've got two hundred [doses/year]…Yeah, I mean obviously that's silly. So twelve is actually really, setting the threshold quite high; and…it's not too low…But then you're tossing a coin, aren't you?"* (Expert 3)

*[referring to a practice nurse] "She's new to asthma and she's quite particular about guidelines, she's very like, 'This is the way it's got to be done'…which I don't think is the real world…"* (GP 3)

The choice of definition may reflect that which is transferable to practice, with NRAD's definition of excessive use as 12 SABAs a year perceived as less restrictive than guideline recommended levels:

*"We use three inhalations a week…but I think that's very stringent and that most people would go above that but that's what the local guidelines say." (Expert 10)*

Two experts questioned the evidence base for NRAD's definition of excessive SABA use, suggesting that further evidence was needed to support NRAD's findings:

*"Number one, I've not seen anything in the literature to support that [one SABA a month] and I think that is very high use."* (Expert 10)

*"…every sensible asthma doctor would think that an overuse of beta$_2$-agonists would indicate an increased risk. But is there any [epidemiological] evidence that that is the case in the UK?"* (Expert 7)

One expert supported NRAD's definition of excessive use citing epidemiological research from the Saskatchewan province in Canada that examined SABA prescribing patterns in asthma deaths over a ten-year period as *"probably not a bad place to go."* This suggests uncertainty regarding the evidence base and applicability to practice, with an assessment of excessive use variable by clinician interpretation and patient circumstance:

*"the closest model is the Saskatchewan data as a prescription database, and I seem to recall that after more than one inhaler per month on average, the curve took off…so I would have thought that's probably not a bad place to go" (Expert 4)*

*"if we want to do something now, and I think doing something now is better than just waiting and waiting…,I mean that's a subjective thing but I think twelve is as good a number as any because there is some evidence, if you like, circumstantial evidence, that that is linked to people dying from asthma…. that the figure twelve was sort of, a little bit, plucked out of the air. But nevertheless, it's a good place to start"* (Expert 3)

### 5.5.2.2 Recognising risk

***"Until someone can prove to me, that's what we're doing"***

Perceptions of the risks associated with excessive SABA use varied among interview participants, with expert's regarding GPs as less likely to be aware of the risks if not their area of specialist interest. A number of GPs described excessive SABA use as low risk, making comparisons between SABAs and drugs perceived to be higher risk such methotrexate or opiate that are associated with increased side effects and prescribed less frequently. This suggests that scale of prescribing may influence what clinicians perceive as high risk:

*"…with something like Salbutamol which is not necessarily a drug of abuse or anything"…"…codeine, tramadol, you know, higher risk drugs where we're worried about over use…"* (GP 4)

*"In terms of methotrexate, I think it's kind of life or death in terms of have they had their bloods, be aware of sore throats, whatever, but there's only about 30, 40 patients there, we've got about 800 on the asthma register"* (GP 3)

There was variation among experts regarding the type of risk associated with excessive SABA use. One expert described the risks of physiological changes to the airways as a result of excessive SABA use, whilst another expert referred to such physiological changes as 'theories' with the greatest risk of excessive SABA use not from the direct risk of SABA use but in response to uncontrolled asthma as indicated by excessive SABA use:

*"I mean clearly the review [NRAD] has highlighted a very real problem and whatever the cause or consequence, which one could argue about ad nauseam, whether the Salbutamol overuse is causing the deterioration which I think it does in some patients or whether it's just an indication of increasing severity of disease requiring other treatment, it's a combination of both no doubt"* (Expert 2)

*"…but there are other theories as well to do with beta receptor changes as a result of using too many beta agonists…ventolin is just a marker of control, ventolin doesn't kill you it just means you aren't treating the condition properly and therefore it gets out of control and I think that's the bigger picture."* (Expert 6)

A number of GPs explained that excessive SABA use might be appropriate for certain patients, for example if required for exercise, or inevitable under certain circumstances such as awaiting specialist referral:

*"he's now getting ridiculous levels of salbutamol which is quite inappropriate really but that's what he is taking until he gets reviewed by the chest physician that's what I've been giving him."* (GP 2)

*"Well, if you used it when you go for a run or if you're doing a particular sporting activity and those are planned uses then I think that's OK, it's when you find that those are insufficient that that makes me concerned. The excessive is more difficult…"* (GP 4)

There was a need for further information to appropriately assess risk, with SABA use reviewed in isolation described as less likely to be perceived of clinical concern, but instead requiring additional clinical variables:

*"the problem is that the actual patient in front of me is unlikely to be at risk of that without some other warnings or some other feature, so it makes it more difficult, I think"* (GP 4)

*"I sort of say everything is linked in so I don't want someone to just look at asthma alone, I want them to also see what else are they missing?* (GP 3)

There were conflicting opinions among experts regarding the assessment of ICS use in conjunction with SABA use in determining at-risk patients in comparison to SABA use alone:

*"In my experience it [risk] depends on the co- use of inhaled steroids in most cases...But especially the mismatch between several prescriptions of SABAs without picking up the ICS, that should trigger the red flag. So it's slightly more complex than just the number of SABA. It is in conjunction with the underuse of ICS and that's the real problem."* (Expert 12)

*"you want to monitor kids who use a lot of SABA and do not use inhaled steroids, they are at much more risk than the ones already on inhaled corticosteroids"* (Expert 13)

Opinions on the co-assessment of ICS use alongside SABA prescribing as a marker of potential risk contrasted among experts. Poor adherence to ICS treatment and the variability in quantity and duration of ICS dosing were challenges to the accurate capture of ICS use based on prescribing data and to the identification of patients potentially at risk:

*"I think the GINA guidelines for asthma now say if you require SABAs twice or more per month then you should be on an inhaled steroid. The trouble is, nobody will take an inhaled steroid, or quite a lot won't"* (Expert 5)

*"…like everywhere else in the world, people don't use inhaled corticosteroids and compliance is very poor… [this is] no different to anywhere else in the world"* (Expert 10)

*"You know, a lot of the ICS [in the] last two months, so the fact that somebody's only having six canisters in a year might actually be 100% compliant"* (Expert 3)

Due to poor-adherence to ICS treatment, two experts perceived SABA on its own as a more reliable marker of risk, rather than co-assessment of SABA and ICS use either separately or as a combined prescribing ratio:

*"I think SABA use is most important. Of course we have to measure compliance and see what people do because maybe they don't take SABA but take ICS constantly but the most important is to see the rescue medications of SABA in my view"* (Expert 9)

*"some people say ICS/SABA ratios, but I don't think that's as good because people can keep giving prescriptions for the ICS at the same time they get the SABA and not use it, and I think at the end of the day it's separate use is a good marker"* (Expert 4)

Experts described that prescribing data could not solely be relied upon to identify patients at risk. There were suggestions for prescribing data to be co-assessed with additional risk factors such as mental health and social wellbeing, as well as asthma severity:

*"the patients who have died don't just have an overuse of Beta-agonist, they have a reduced frequency of access in medical care and other psycho-social adverse factors which probably mean those patients are not going to react in the same way when they need beta-agonists more frequently than many others"* (Expert 2)

*" You may find that people who have got significant asthma and who have got it under control may be using only one inhaler but that people who have got relatively insignificant asthma and continue to use high doses of SABA who may be in fact be more at risk of death than those who are not. And that may be a very difficult thing to overcome"* (Expert 10)

### 5.5.3 Theme 2: Identifying excessive SABA use in practice

The theme *'Identifying excessive SABA use'* reflects the methods used to identify excessive SABA use in practice, how a SABA alert is positioned among these methods and the challenges impacting on the identification of excessive SABA use.

#### 5.5.3.1 Methods

***"I don't think there's a simple way of doing it"***

Three opportunities in which excessive SABA use could be identified in general practice were described; when in-consultation, when repeat prescribing or through incentivised methods such as annual asthma reviews or medication reviews.

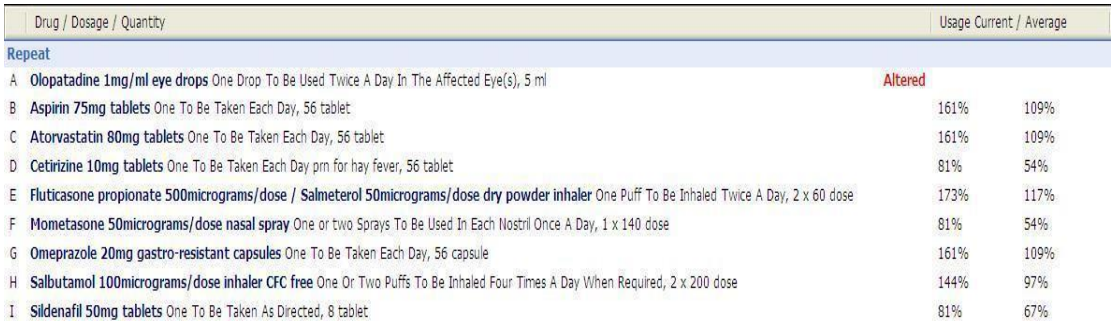
In-consultation

The identification of excessive SABA use by GPs either in a consultation involved a combination of methods: the medication current/average usage generated within the EHR that presented in the medication screen (figure 5.2), the overuse warning when issuing a prescription (figure 5.3), the SABA alert (figure 5.4) and/or by manually checking the prescribing history within the EHR.

GPs described commonly referring to the current/average medication usage feature (figure 5.2) to determine a patient's level of SABA use when reviewing medication history in consultation. Current and average usage were referred to interchangeably to determine problematic usage:

*"…you go to the medicines page like this and it's got this here that shows 'current use' and 'average'… if it's massively high, obviously it comes up in, it's already highlighted, already with the EMIS system, they've already decided their own level to flash it up in red, so you can see that's overuse" [current usage over 100%]* (GP 2)

Figure 5. 2 Medication percent usage feature

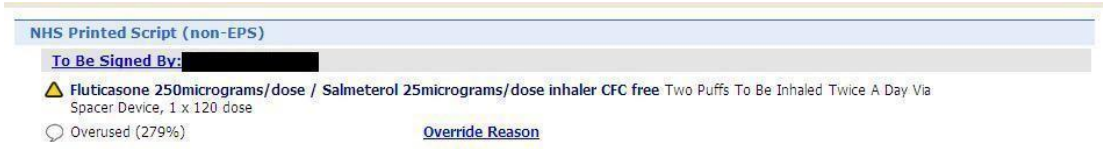


| | Drug / Dosage / Quantity | | Usage Current / Average | |
|---|---|---|---|---|
| Repeat | | | | |
| A | **Olopatadine 1mg/ml eye drops** One Drop To Be Used Twice A Day In The Affected Eye(s), 5 ml | Altered | | |
| B | **Aspirin 75mg tablets** One To Be Taken Each Day, 56 tablet | | 161% | 109% |
| C | **Atorvastatin 80mg tablets** One To Be Taken Each Day, 56 tablet | | 161% | 109% |
| D | **Cetirizine 10mg tablets** One To Be Taken Each Day prn for hay fever, 56 tablet | | 81% | 54% |
| E | **Fluticasone propionate 500micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler** One Puff To Be Inhaled Twice A Day, 2 x 60 dose | | 173% | 117% |
| F | **Mometasone 50micrograms/dose nasal spray** One or two Sprays To Be Used In Each Nostril Once A Day, 1 x 140 dose | | 81% | 54% |
| G | **Omeprazole 20mg gastro-resistant capsules** One To Be Taken Each Day, 56 capsule | | 161% | 109% |
| H | **Salbutamol 100micrograms/dose inhaler CFC free** One Or Two Puffs To Be Inhaled Four Times A Day When Required, 2 x 200 dose | | 144% | 97% |
| I | **Sildenafil 50mg tablets** One To Be Taken As Directed, 8 tablet | | 81% | 67% |

If medication use was above 200%, 'overused' would be displayed at point of prescribing (Figure 5.3). However, there was uncertainty regarding how much SABA use was reflected by overuse of 200% and how this was calculated within EMIS:

*"So…I think we have a threshold of… I'm not sure of the threshold, from memory it's about 200%, it seems quite a lot but if they're shown to be overusing on the system then that would be flagged up for the GP to authorise"* (GP 5)

Figure 5. 3 Overuse warning



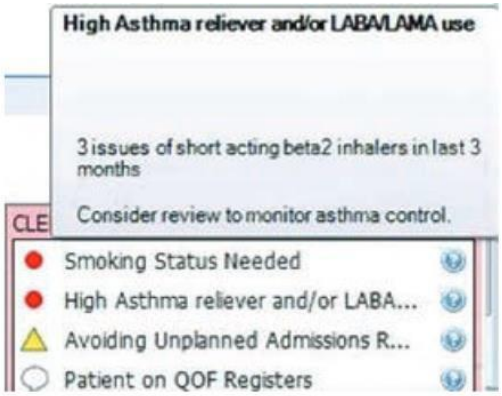

The SABA alert, evaluated in Phase 2, presented within what was commonly referred to as the QOF box 'pop up' displayed in the bottom right hand corner of the computer screen (Figure 5.4). GPs were familiar with the QOF box, and all GPs, with the exception of one, were familiar

with the SABA alert. The QOF box was perceived as a useful place for reminders relating to outstanding care for chronic disease management, for example asthma reviews, rather than high-risk issues:

*"it's a good reminder for what's outstanding for that person in their year of care"* (GP 5)

*"The QOF box where these alerts sit are just reminders really, these will be there when I am consulting with a patient, they will always be there. So whenever I see the patient or have the patient's record open I will be able to see this"* (GP 1)

Figure 5. 4 SABA alert




The medication usage feature and the SABA alert were described as prompts from which to manually check patient records for the volume and time-period of medication use. Identifying excessive SABA use required clinical interpretation that was not possible with the limited information and context presented in an alert:

*"I think what's more useful is when you right-click on the drug you can look at drug history, this is what I use more, 'cause it shows you the issue dates, so I can see that this patient's had an inhaler and they've had one in September, one in August, one in July, so they're basically requesting one every month and that gives you a much better indication."* (Clinical Pharmacist)

*"I don't think there's a simple way of doing it really, the only real way we have is of checking how many prescriptions we've done…the most efficient way we have is of looking and seeing how often someone is requesting their prescriptions"* (GP 4)

*"…here for example they are using this over 100% which is very often and then I would click into their medication list and check"* (GP 1)

## Repeat prescribing

There was a move towards electronic prescribing systems (EPS) in practices to streamline GP's access to patient data and improve the safety of prescribing. Repeat prescriptions generated in this way were referred to as an electronic 'medicines management.' GPs could assess a 'medicines management' in three formats: as a 'request', a 'request with queries' or as a repeat prescription 'awaiting signing.' GPs welcomed EPS as it integrated prescribing activities within the EHR enabling medication history to be readily viewed. GPs described assessing repeat prescriptions for SABAs in a number of ways before authorising, including checking asthma diagnosis, the frequency of request and last issue date, other medications prescribed and date of last annual asthma review. GP 1 described referring to the medication percent usage displayed within the EHR when reviewing repeat prescriptions to identify excessive SABA use:

*"So ideally, every prescription that comes in you should look at, is there a medicine review date, you should look at the use of the medication and so you know, is it overused, is it underused, is it within the authorised number of issues, all that kind of stuff which we would normally do in a medication review"* (GP 2)

*"So if it's been requested and I'm going into here (medication screen), I would go and look at when the medication was last issued because usually if they are on repeats they will have a percentage usage so we'll straightaway know if that is more than 100%, then we know they are using it often, so that is like a flag for us"* (GP 1)

However, despite efforts by practices to move towards EPS, prescribing requests by paper continued to persist:

*"I'm not sure why we even still have paper prescriptions to sign, really, we're trying to move towards the electronic workflow"* (GP 5)

*"when we did the prescribing review last year we said that everything should go through 'medicines management' but we do have prescriptions that sit in a box each day…I don't know what's happening with those"* (GP 2)

Full adoption of EPS was described as challenging, as despite the assumed benefits to both practices and patients, it was suggested that patients prefer to have choice as to how they request their medication and electronic prescribing may not be preferred by some:

*"We are positively encouraging people to go down this route, so the EPS [electronic prescription service] medicine management, but some people don't want to do it electronically straight to the chemist, they want choices. Some people for whatever reason, it comes as a paper copy"* (GP 3)

A number of GPs described the role of receptionist in highlighting SABA use concerns. Receptionists had the ability to authorise repeat prescription requests for SABAs if the prescription was within configuration parameters as set by the prescriber. If SABAs were requested more frequently than the parameters set by the clinician, there was an expectation that receptionists would raise concerns for the attention of the GP. Receptionists had the potential to identify overuse electronically at point of authorisation with 'overuse' displayed if SABA use was 200% above the configured threshold. The receptionist would send the repeat prescription for GP authorization as a 'request with queries' via the medicines management system:

(GP 8): *"Just in the screen below when you are about to authorize it, it will say 'overused' underneath"…*
(GP 6): *"So then the receptionist then has to pass it to the doctor to OK it, as they can't issue the prescription"*

The receptionist could write an electronic message in conjunction with the repeat prescription stating SABA overuse. If the request was within prescribing parameters, the receptionist could authorize the prescription and send to the GP via the medicines management system to the 'awaiting signing' inbox.

*"…so some repeats can be done by reception if they're within clinical data and med review and some cannot"* (GP 3)

For requests that came in paper format, receptionists described making handwritten, informal notes on prescriptions to highlight high SABA use for the GP's attention:

*"those sort of repeat prescriptions [paper] will be done by the front desk and they will often write, overusing, or something"* (GP 4)

Repeat prescription requests were processed by receptionists in both practices in varying ways. In one practice, a receptionist was designated with repeat prescribing duties out of patient view, whilst at the second practice repeat prescription duties were shared out between all reception staff as they carried out patient-facing duties. The aim of non-patient facing repeat prescribing was to minimise interruptions. However whilst this was done so behind a closed screen out of patient view, the receptionist was observed being interrupted by both patients and the practice manager. In contrast at the second practice, *Receptionist 4* explained that having been previously designated repeat prescribing tasks, receptionists felt pressured by patient demands to request or issue medications resulting in the repeat prescribing duties being shared among receptionists.

Despite practice protocol for repeat prescribing, receptionists were often flexible with prescription requests, making exceptions to the repeat prescribing system in order to accommodate patients. At one practice, the receptionist accepted a repeat prescription request scribbled on a piece of paper despite this being against practice protocol. When observed, paper repeat prescription requests were accepted by reception despite patient date of birth missing or incorrect spelling of the medication. On one occasion a person of ethnic minority background who spoke limited English language requested a SABA for his father on a piece of paper stating 'blue inhaler.' The receptionist, opened the patient record, identified this as a SABA, requested this electronically and it was sent to the GP for authorization. The receptionist described this as necessary to meet patient need influenced by the receptionist- patient relationship based on familiarity:

*"…we don't usually do this but the lady lost her prescription and she's a regular so we know her"* (Receptionist 3)

During interview with *GP 3*, the receptionist interrupted with a paper repeat prescription

request. The GP quickly signed and handed the paper request back to the receptionist without referring to the electronic patient record. There was inconsistency in the assessment of repeat prescriptions, with medication use not assessed prior to issue and once approved medications prescribed on repeat were only likely to be reviewed when the patient next presents in- consultation:

*"Doctors are busy and they maybe OK a prescription without thinking about when the last one was given, including SABA and have no idea how often those repeats are filled"* (Expert 6)

*"it's end of the day, boring task of clicking through loads of prescription requests…they [GPs] don't have time to check properly, it's very easy to just click 'approve'"* (Clinical Pharmacist)

## Incentivised methods

National Health Service (NHS) policy framework and local clinical commissioning groups (CCGs) incentivised targets for asthma management influenced the identification of excessive SABA use. This included financial incentivised national Quality and Outcome Framework (QOF) rewards system and Medicines Use Reviews (MURs), and local Clinical Commissioning Group (CCG) targets. QOF annual performance targets for annual medication reviews and annual asthma reviews, as well as CCG commissioned 'enhanced asthma reviews' supported at local level by the CEG.

### (i) Quality and Outcome Framework (QOF) performance

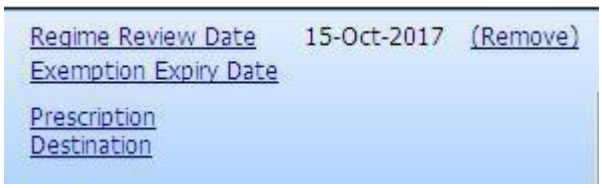
Participants described using electronic searches and templates as set by the CEG in order to identify people with asthma using high numbers of SABA as well as to identify patients eligible for QOF annual asthma review or enhanced asthma review. Search templates assisted practices to meet target driven performance indicators and safety and effectiveness measures as directed by local and national initiatives. Whilst searches relied on EHR data, clinical interpretation was necessary to determine alert relevance for individual patients:

*"The CCG have that as part of our plan for the year that we have to complete, so they [CEG} set up a search and then I've imported it to our system and run that search to keep a check on the numbers that we've done…there's a little bit of manual sifting I suppose…So the initial part we can get EMIS to do the searches for us, but then, it is manually then to look at*

*the details 'cause some of these you'll look at the patients and then when you actually click on them you'll be like, 'OK, they're palliative, they're … not appropriate to come in …' and there's reasons or different diagnoses or it's not coded properly"* (Clinical Pharmacist)

Annual medication reviews were described as a way to identify potential problems with medications, including SABAs. An annual medication review date presented in the patient record beside the QOF box at the bottom right hand corner of the computer screen and was also printed on paper repeat prescriptions (figure 5.5).

Figure 5. 5 Medication review alert




The medication review date acted as a flag for clinicians to check SABA use, particularly if the review date had been exceeded:

*"Everyone has a different view but there are several fail-safes that we've got in the system trying to mitigate the different ways of people falling through the net. The biggest thing is the reviews really...So there is a review date, which is on the prescription. If the patient has not attended and the review date has passed I can see this and I will know I need to look at those more. But even with the paper ones I tend to just double check the medications"* (GP1)

(ii) Pharmacist incentives

One expert from Europe and one UK-based pharmacist described the pharmacist's role in identifying excessive SABA use. Expert 12 described the role of alerts in pharmacy in Europe and the financial incentive for pharmacists to be responsible for the identification of excessive SABA use, in contrast to the lack of alerts in UK pharmacy:

*"it [an alert] presents at the pharmacy because it happens when the pharmacy is preparing the medication, there will be a flagging up of misuse and then the pharmacist will judge whether he needs to a make a call or not [to the GP]…it is part of their financial incentive to be guarding these potential mistakes in daily practice and get paid for it"* (Expert 12)

*"… if I click on the salbutamol that's been done, it'll tell me maybe they had it in January, March, August and October, but it won't give me any warnings. So I could, if I wanted to, I could dispense the salbutamol all day to a patient and my computer wouldn't tell me anything"* (Community Pharmacist)

A Medicines Use Reviews (MURs) was an incentivized service delivered by a pharmacist, involving the review of a patient's medication to improve medication adherence and to identify and reduce potential problems and medicines wastage. Patients eligible for MURs were identified via computerised searches in pharmacy systems and opportunistically in pharmacy at the point of patient contact:

*"…the medicine use review, it's for any patient that takes regular medicines from you for the last three months, so we have targets that we try and reach, so I'd be looking to try and find MURs but also when you're handing something out, I'll always say, 'How are you getting on with your medication?'* (Community Pharmacist)

However obtaining patient consent was a disincentive to an MUR with the principles of review deemed good practice that should be delivered routinely in pharmacy without the need for incentives:

*"I think in itself it's a very good service, but for me it's something that I would do anyway without them having … 'cause you have to sign a consent form, it's just something that I'd want … if someone isn't sure about their medication it wouldn't bother me to sit down with them. I wouldn't have to have a service that makes me do that. It's more you care about your patient."* (Community Pharmacist)

(iii) Role of incentives

One expert expressed the limited value of an alert without motivating users to respond to an alert, for example by reward or by consequence to change prescribing behaviour:

*"What you are trying to do is change behaviour, so this requires three things. Firstly motivation, either carrot or the stick, so whether getting reward for ensuring patients aren't*

*using it [SABAs] that frequently or getting punished and having to explain why people are using more and also have confidence in asthma and understand why people are using more and do something about it…An alert all by itself with no motivation and nothing to improve the doctor's confidence, it won't make any difference"* (Expert 6)

Financial incentives to identify excessive SABA use were deemed necessary for both GPs and pharmacists to prioritise and focus areas of clinical need. Performance related incentives for example the benchmarking of SABA prescribing performance to that of peers was described as an influential motivator to improve SABA prescribing. However, as *GP 4* highlights, remuneration for the additional workload associated with prescribing targets was expected:

*"I think that the minute you introduce some sort of payment metric around it you would see it go off a cliff, you know, you're paid to have your people with asthma using less than one inhaler a month, say. I think you'd see a real change in prescribing. At a very crude level GPs are self-employed businesses and for a lot of GPs it is about the bottom line. I think for a lot of practices it's about staying afloat and being sustainable and making sure that your income is sufficient to do that, so I think once you incentivise people I think that really does change practice"* (GP 5)

*"….unfortunately it has to be [incentivised] 'cause there's so much we could do, someone has to tell us where to start"* (Clinical Pharmacist)

*"there's nothing like feeling that you're doing the worst in the borough to spur you on and those sorts of opportunities where you look at it and say, so of the practices that are prescribing more than three prescriptions, because that would make you think, 'Oh, hang on, where are we, why are we so bad at this?' in the context of everyone else? …but often those things will come with a resource implication, so the reason that we're getting those things is that there's money attached to it or there is some sort of funding that has been applied to make this a priority"* (GP 4)

### 5.5.3.2 Challenges

***"They are not necessarily truly high users"***

Excessive prescribing or excessive use?

A number of challenges were described regarding the identification of excessive SABA use, in particular whether SABA prescribing data translates to *actual* overuse in patient's lives. Despite knowing how much SABA has been prescribed there was no accurate was to determine how much of the prescribed SABA was actually used. Participants described situations in which excessive SABA use based on prescription data did not automatically equate to overuse in the context of people's lives:

*"I find [the computer] it's not the most useful thing because there's so many different reasons why people would need to order medicines early or would need more, so it just happen all the time because people might have lost it or they're going on holiday for two months so they want to order a lot early…"* (GP 4)

*"…we actually did an audit in our own practice and analysed the sort of people that were on twelve SABAs, and then looked at those people, their characteristics, were they controlled or not, and what was going on…they weren't necessarily overusing SABAs but their inhalers were in about five or six different places…"* (Expert 3)

It was common for children to be prescribed multiple SABAs for school and/or family social arrangements. This made it challenging to rely on SABA prescribing data to determine excessive use particularly for children and although alerted as excessive SABA use it was not always perceived as problematic by clinicians. A number of primary care staff and experts described the practice of issuing two SABA canisters per prescription. Despite being viewed as high volume prescribing such practice was justified as necessary when considering patient circumstances and may not reflect excessive use:

*"This is quite common in paediatrics, that you have one in school, one in the school bag, one at home, one with grandma and so on. And then you might be underusing even, if it is everywhere. It might not be an indication in all cases tha it is overusing"* (Expert 7)

GP 7: *"So 4 issues means 8 because they have 2 per time, which is a lot"*

GP 6: *"Yes this is a lot…"*

Nurse 1: *"Yeah…they might not be having 2 every time…*

GP 7: *"No, all of them, it is very rare to see 1 [being issued at a time]"*

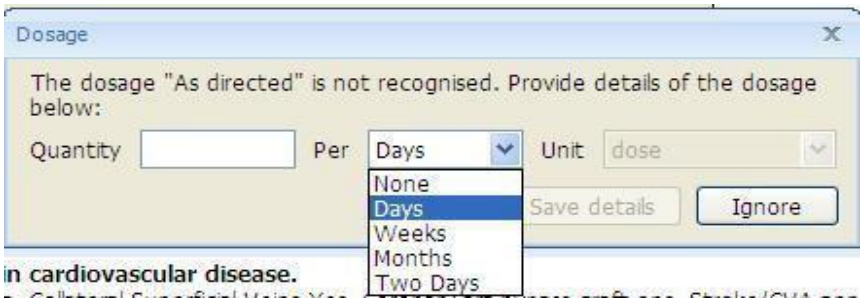
GP 6: *"We offer to 2 because they need one for school or work too"*

*"It [SABA alert] comes up quite a lot as well, quite a lot of patients, particularly children, who need quite high quantities of salbutamol…they need one for home, one for school, or they lose one, so they aren't actually using them but that would trigger off the alert as well, and they are not necessarily truly high users but have just had a high number of salbutamol prescribed. So then you are just going to ignore it [alert]"* (Nurse 1)

## EHR accuracy and clinical interpretation

Concerns were expressed regarding the accuracy of the medication percent usage feature that was generated within the EHR and aided clinician's identification of excessive SABA use. Despite being routinely used by clinicians, the percent usage displayed was dependent on how the SABA prescription was configured at point of prescribing. Configuration involved the setting of prescribing parameters, including quantity and duration of use (figure 5.6). This was used as a marker of medication compliance that presented as 'current use' and 'average use' within the medication screen of the EHR.

Figure 5. 6 Prescription configuration



Despite being commonly used by clinicians, a number of participants viewed the medication percent usage feature as an unreliable method to determine SABA overuse. This was due to variability in a) data input and b) clinician interpretation of use.

The medication percent usage displayed was dependent on data manually entered in EMIS at point of prescribing however prescription configuration was at clinician discretion with no SABA prescribing parameters within the EHR. Therefore whilst two patients may be identified as overusing SABAs (percent usage > 100%) both prescriptions may have been configured differently by volume and duration. Therefore the medication percent usage feature was described as an unreliable measure of medication use:

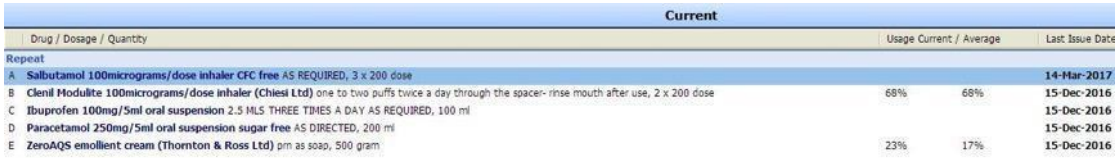
*"The excessive is more difficult, I think, 'cause you'd look on the computer screen and obviously EMIS records usage and there is a computer sort of monitoring of how quickly people are going through their inhalers. I don't think that that is incredibly accurate because it's all about the data that gets put in"* (GP 4)

*"I just think the computer systems are not always that accurate because it relies on everything being input correctly…"It [percent usage] gives a rough indication [of medication use] but I find it's not particularly accurate…"* (Clinical Pharmacist)

The use of the medication percent usage feature to determine overuse is problematic. As despite 100% compliance to medication, if the prescription was configured to four SABAs in 100 days, this would suggest excessive use. Therefore it should not be assumed that the dose and quantity of SABAs, as determined by the prescriber, was configured at an appropriate level. If no daily quantity was added, the course duration could not be automatically calculated (figure 5.7):

*"But you can leave all of that blank and if you leave all of that blank, then the computer system doesn't know what the usage is supposed to be, so it can't calculate whether they're overusing or underusing"* (Clinical Pharmacist)

Figure 5. 7 Missing medication percent usage



| Current | | | | |
|---|---|---|---|---|
| | Drug / Dosage / Quantity | Usage Current / Average | | Last Issue Date |
| Repeat | | | | |
| A | **Salbutamol 100micrograms/dose inhaler CFC free** AS REQUIRED, 3 x 200 dose | | | 14-Mar-2017 |
| B | **Clenil Modulite 100micrograms/dose inhaler (Chiesi Ltd)** one to two puffs twice a day through the spacer- rinse mouth after use, 2 x 200 dose | 68% | 68% | 15-Dec-2016 |
| C | **Ibuprofen 100mg/5ml oral suspension** 2.5 MLS THREE TIMES A DAY AS REQUIRED, 100 ml | | | 15-Dec-2016 |
| D | **Paracetamol 250mg/5ml oral suspension sugar free** AS DIRECTED, 200 ml | | | 15-Dec-2016 |
| E | **ZeroAQS emollient cream (Thornton & Ross Ltd)** prn as soap, 500 gram | 23% | 17% | 15-Dec-2016 |

Safety nets to ensure appropriate SABA use were described by the clinical pharmacist. However, as two SABA inhalers were commonly prescribed per prescription, such practice was likely to continue unless the prescription was reconfigured when being reauthorised on repeat prescription. This was observed when GP 1 opened a patient record, checked the repeat prescription configuration and reduced the quantities of SABA to be authorised from two to one SABA:

*"So when it's initially prescribed, ideally we'd have a review date set, number of authorised issues per term so the clinician's saying I'm happy for this patient to order it two times, three times, four times, before we next want to review them. Or you can put the number of days, the minimum days before they're allowed another one"* (Clinical Pharmacist)

*"So the way it is set up at the moment is 4 inhalers to be used in 100 days, normally it would be 1 or 2 inhalers in that period of time [changes number from 4 to 2]…"* (GP 1)

There were widespread variations in how the medicines percent use was interpreted and at what percent of SABA use would be of clinical concern. When asked about the point at which SABA use would be of concern, clinicians referenced the percent usage feature with wide variation in responses ranging from 120% to 600%. The following excerpts highlight clinician uncertainty when interpreting the percent use feature with EMIS:

*"If you put 120 use inhaler is going to last 60 days and they're asking for it every 30 days, then it will say that their usage is 200% and yet if they were using it 2 or 3 times occasionally, that still might not be overly concerning…o the prescription is likely to be issued unless there's something… some crazy number, so if they are 100, 150%, perhaps 200%, I suspect the prescription would be issued. If they've got 600% usage or something then you're going to query what on earth is happening with these inhalers"* (GP 4)

*"it's got this here that shows 'current use' and 'average' so we wouldn't bother really unless it was going above about 120% something like that"… "Probably about 150% you know something above that, I don't know what percentage of our patients that is already recorded at, so it's difficult for me to say really."* (GP 2)

### 5.5.4 Theme 3: Using a SABA alert

This section offers insight into what influences the use of a SABA alert. This seeks to help understand why an alert may or may not be used and how the use of the SABA alert may be increased.

#### 5.5.4.1 Factors influencing engagement

***"...which one are you going to concentrate on?"***

Alert volume

There was concern that "alert overload" made it difficult for GPs to engage with a SABA alert, resulting in the alert being ignored. One GP described scrolling through the QOF box, within which the SABA alert presents, due to the high number of reminders for outstanding issues of care requiring attention. Another GP described having to prioritise alerts due to increased workload resulting in some alerts being ignored:

***"****It comes up to here [SABA alert] for some people and they have to scroll down because there's so many [alerts]"* (GP 5)

*"people would probably ignore it 'cause if you've got alert overload, you know, if you've got 12 here, it's like which one are you going to concentrate on?"* (GP 3)

*"so they might have ten things coming up in their QOF box at the corner of the page and you just see it there [SABA alert] and you're like oh no, we can't even start to deal with all of that right now!...Which one do we pick to try and tick off that list"* (Clinical Pharmacist)

*"I know that when a patient comes in to see me and five alerts go off I think well OK, maybe I'll deal with this one but I can't deal with the other four because I haven't got half an hour with the patient*" (Expert 1)

A number of participants described the importance of setting an appropriate alert threshold to achieve a balance between alert frequency and workload. Setting the threshold appropriately was perceived as an important way to maximise alert impact and increase user engagement. If the alert threshold was set to low, thereby increasing the frequency of presentation and adding to clinician workload, there was a risk that users would become complacent to the alert. The challenge of finding a balance in the frequency of alerts was described by a number of experts in the following excerpts:

*"This [alert] could be perceived as very annoying I guess, as this hampers your daily work so I would aim at low frequency but high impact… the trick of the whole thing is that you make it not over sensitive for GPs because they will just click it away when it's always flagging up and has low specificity"* (Expert 12)

*"if you set the threshold low you will identify relatively large numbers of children which is an advantage because you won't miss anyone at risk but you will increase the numbers of alerts and the GP being confronted with those alerts might not be willing or able with time constraints, to pick up on all these and review them. So you would have to find a balance between not missing out on any kid at risk on one hand and not overburdening the GP on the other"* (Expert 13)

*"Of course a pop-up has to be a little less benign to make an impact but not so difficult that doctors are just going to ignore it completely every time because they are just too busy"* (Expert 6)

*"…it needs to be a credible thing, and needs to be visible… and not set at too low a level because, for the reasons you said; if it fires off alerts for no apparent reason then people are really gonna ignore it"* (Expert 3)

GPs described how alert engagement was influenced by the frequency of a SABA alert in comparison to alerts for other drugs. An alert for methotrexate for example, was described as low frequency and high risk, in comparison to a SABA alert described as high frequency and low risk and therefore of lower priority. As the number of people prescribed SABAs was much higher than methotrexate, SABA alerts were likely to be more frequent than an alert for methotrexate and clinicians may be less likely to respond:

*"With methotrexate we've got about, I did a search the other day, we've got about 30, 40 patients, so it's about volume as well..."I think it's kind of life or death in terms of have they had their bloods, be aware of sore throats, whatever, but there's only about 30, 40 patients there, we've got about 800 on the asthma register"* (GP 3)

"*we don't have that many patients on Methotrexate compared to Salbutamol so you're talking about a massive amount of… I think that would just irritate people and disengage them"* (GP 5)

There was concern that an increasing number of alerts for asthma could result in alerts for other long-term conditions, increasing alert volume and therefore potentially disengaging clinicians:

*"there are enough clicks in the day, because if this happens with one thing it will start to happen with others from asthma to diabetes…"* (GP 1)

*"My only worry is and it's a slight worry, is at the moment we're not getting attacked on this side, you know, so we have this, so Salbutamol is one area, let's say the same for diabetes, let's say the same for every time someone's had a stroke and they're not on aspirin and do we want an alert, if we start getting alerts on there as well, I can imagine that again, we might get ambivalent to it"* (GP 3)

*"Well, the trouble is that these systems are over-used. So if it was the only flag that appeared on people's records then obviously we'd notice it. The problem is the flags are now part of the scenery….that's the problem"* (Expert 8)

## Alert presentation

The point of alert presentation was important in achieving maximum engagement with a variety of opinions on where a SABA alert would be best positioned. A number of GPs described a preference for a SABA alert to present within the QOF box due to familiarity with the alert and engagement at GPs discretion. GP 6 and GP 7 agreed that a SABA alert was positioned appropriately in the QOF box as they expected to see alerts present there. GP 1 described the flexibility of the alert presenting with the QOF box, being able to refer to this at any point in workflow:

*"these will be there when I am consulting with a patient, they will always be there. So whenever I see the patient or have the patients record open I will be able to see this"* (GP 1)

However, a range of interview participants perceived the QOF box as not appropriate to identify excessive SABA use, as clinicians were likely to ignore the QOF box, it was suggested that a SABA alert should present centrally on-screen:

*"Because the one thing about the QOF box is it's very easy to ignore, so the central box that appears in the middle when you're doing a medication or when you're seeing that patient who has that, it would be more useful, I'm mindful of the fact that this business of clicking and saying, 'Oh, for god sake, the person hasn't come…'"* (GP 4)

*"So sometimes the popup messages that come up in the middle of the screen or when you're issuing drugs so you actually have to click on something, might get a bit more attention from people!"* (Clinical Pharmacist)

Due to the context of repeat prescribing, often carried out at end of the day when the patient was not present, there was an increased likelihood the SABA alert being ignored. A number GPs and experts suggested an alert should present when authorising repeat prescriptions, at a clinically relevant point in workflow, for maximum influence:

*"what I've heard people say is they do medicine managements in the middle of the night or last thing before they go – Their tiredness is…. Phew! Are they interested in QOF boxes? Not at all. If an alert comes and says, 'Stop, warning!' they might be more interested"* (GP 3)

*"not just as a flag down at the bottom [QOF box] because when I'm actually taking that decision I'm not even sure the flag is there on my screen when I'm dealing with an electronic prescription unless I choose to go and look. So I'm not sure that's the right place for it… [The] way to tackle this has got to be in the repeat prescribing programme because that's where the problem really arises. It's when the patient has asked for another inhaler and it's being issued as part of a repeat prescription and those come through to me to sign off...and when it comes through electronically it could at that point come through and say 'this is the fourth prescription in as many months, are you sure you are happy to give this?'* (Expert 8)

***"****I think it's in the right place apart from maybe as we were talking about at the point of repeat prescription issue, there's a process there"* (GP 5)

However in contrast, one GP described the limitations of an alert presenting when authorising repeat prescriptions due to the absence of the patient at point of decision-making:

*"Almost certainly of no value because the patient's not in front of you [at point of repeat prescribing]"* (GP 4)

When in-consultation, the presentation of the SABA alert outside workflow resulted in the alert often ignored due to limited time available in-consultation and increased demands. GPs described that due to multiple demands in-consultation, SABA use may not be of greatest importance and viewed as optional rather than essential:

*"The only thing I would say about that is that we all see them but we're just bombarded with stuff, we've got 10 minutes, someone comes in with three or four problems, we've got all of this to do already, it's just overwhelming sometimes all of the different things that…we're faced with. So sometimes as important as it may be, a salbutamol alert might be just pushed down"* (GP 5)

*"We do telephone conversations and actually even when it pops up saying, 'This young woman needs a smear,' and I will mentally prepare myself for, 'Must remember to talk about smear,' unless I talk about it right at the beginning by the end of the consultation it will have escaped my memory"* (GP 4)

*"The problem with general practice is they often come in with 2 or 3 problems and asthma may not be any of the presenting problems…and then you are trying to add it on as an extra even when you don't already have enough time"* (GP 6)

### Alert design

There were contrasting opinions among GPs regarding the type of alert design that would promote engagement. It was suggested that clinicians would not accept a hard or modal alert, similar to that of methotrexate, for excessive SABA use. Such an alert that presents centrally on the computer screen and requires interaction was perceived as likely to deter clinicians from engaging with the problem of excessive SABA use. Due to competing demands of time and workload, financial incentives for a hard alert may be required to influence engagement:

*"once again it all depends on the number of alerts that are generated because if you make it mandatory to have some sort of action and you get a lot of those alerts and GPs may be less willing to pursue on this action"* (Expert 13)

*"you've got to be a little bit careful with it, because this is much more like Big Brother looking at you and it may mean you then not get acceptance from GPs that, 'Why did you ignore it?', 'Well I don't want Big Brother breathing down my neck all the time; I don't really want this.' I think if it was really hammered down that Big Brother was watching you, then I'd say well, actually, I want some recompense for this"* (Expert 3)

It was suggested that a more targeted approach to a SABA alert was required based on a hierarchy of SABA use rather than a universal threshold. A hard alert was proposed for excessive SABA use with a soft alert viewed as more appropriate for lower levels of SABA use:

*"Well if the patient is using ten puffs a day I think that's a hard alert. I think if they are using three then maybe not"* (Expert 10)

A number of participants suggested the introduction of more comprehensive alerts to identify excessive SABA use that require less user interaction and facilitate patient engagement. Experts called for a move away from one-dimensional alerts, calling for the incorporation of features that take into account both the variability of asthma and the individual person:

*"There should be some kind of check mark box on the pop-up before you can close it that says 'have reviewed,' 'have called,' 'one for gym bag, one for home and therefore need an extra one,' something that gives the doctor an explanation which can then be reviewed if something happens, because there is a legal obligation to it as well"* (Expert 6)

*"So alerts need to somehow customised around the patient as well as the clinician"* (Expert 1)

Automated methods of communication following the identification of excessive SABA use were proposed. This included letters or prescription messages generated automatically following the triggering of a SABA alert by targeting other staff and patients to reduce workload and support action. The following excerpts describe how actions generated following the SABA alert, that inform other staff and also the patient to the problem of excessive SABA use, may enhance use of the alert:

*"If you think about the workload in general practice it's quite stressful, a lot to do, so it [alert] needs to be facilitated in a way that makes it easy for me, generates the letter for me for example, or generates the message that goes on to the prescription…An alert would come up saying 'do you want the message to appear' and it would be attached to the prescription. That means I haven't got to think, all I've got to do is say 'yes please send the message' because it takes quite a time to put messages on prescriptions and if I'm short of time it's a bit of a put off"* (Expert 8)

*"there must be some sort of automated system or automated reminder to the patient or to the clinician that no further can be issued after [an agreed number of SABAs]"* (Expert 1)

It was proposed by a number of participants that a feature that automatically invites or books patients overusing SABA for an asthma review would be advantageous. This would include the automatic form of communication with patients, either by email or text, when an alert triggered to alleviate pressures on GP time and workload. One expert proposed that patient contact was initiated to further ascertain asthma control and the need for asthma review. Such a response facilitated by an alert would streamline resources rather than inviting all alerted users to review. However the type of contact initiated would depend on patient and practice preferences and system capabilities:

*"I suppose in an ideal world to make it all fool proof would be some sort of system where it identified the patient and automatically booked them in for their asthma review or put them onto a list for somebody to call them up 'cause then we're targeting it directly"*
(Clinical Pharmacist)

*"You send an ACQ or RCP 3 questions to the patient automatically on email that the patient could send back, a lot of things could be done automatically here if you have people's emails and if it's bad then they need to come in (for review). How many automatic things can be done so the doctor doesn't have to be in the middle of it may also improve success. However not all practices have this information, my practice doesn't have the majority of email addresses for patients so it wouldn't work for me and in the UK it may probably be the same"* (Expert 6)

(GP 7): *"Could you link this alert to send a text message to the patient to advise to come to review?*
(GP 8): *"Yeah in case we forget to say"*

### 5.5.4.2 Factors influencing action

***"I'm issuing it this time but…"***

The SABA alert in its recommended action to consider asthma review, to assess control and ultimately reduce excessive SABA use. However, the opportunity to reduce SABA prescribing following the alert was dependent on type of action, the point of action and how the action was supported.

SABA prescribing decisions

There was no consensus regarding the appropriate prescribing response to the identification of excessive SABA use with suggestions that SABAs should be withheld, reduced or continue to be prescribed if excessive use was determined. Experts suggested that SABAs should be withheld by the prescribing GP or when dispensing in pharmacy:

*"In my country the GPs give a lot of important to the overuse of SABA, so what I would probably do, I wouldn't allow them to prescribe anything in asthma if the patient had more than the limit"* (Expert 9)

*"So I think that most important…could be the stopping the giving the patient in the pharmacy when they have more than the limit that we put"* (Expert 11)

*"It would be very easy to make salbutamol and terbutaline a restricted drug i.e. for the diagnosis of asthma it can't be prescribed more than so many time a year without a doctor's review"* (Expert 6)

However, in contrast to expert's opinions, GPs and pharmacists showed concern regarding the withholding SABAs being a greater risk than that associated SABA prescribing or dispensing when excessive use was identified. Such concerns appeared to be altruistic in that failing to prescribe/dispense SABAs may result in the patient having no emergency relief in the event of an asthma attack. SABAs were perceived as an essential medicine that was unethical to refuse:

*"so with all of these things whatever they might be overusing you've got to think about what are the risks of them not having it if you're not prescribing it. I mean Salbutamol is probably the best example of that, you don't want someone to have an asthma attack by refusing them Salbutamol even if their asthma isn't that controlled and they're not using the therapy appropriately, so I don't think I would ever not issue it"* (GP 5)

*"I don't think I would ever deny someone one! In the short-term if they have an asthma attack where they can't breathe, it's essentially a life-saving medication for them. I suppose it's better to save that life in the short-term and maybe keep giving it to them, even though we know that these people with poorly controlled asthma, the outcomes still aren't good longer-term but I suppose it's better than nothing"* (Practice Pharmacist)

*"Because people use it to relieve the breath, there's really almost no excuse for me to ever refuse somebody, because they end up having an asthma attack…I would not be comfortable with having a restriction on it..."* (Community Pharmacist)

Concerns regarding health care professional liability influenced decisions to issue or not to issue or dispense SABAs. The withholding of SABAs was viewed as a *"medicolegal minefield"* with concerns regarding potential litigation if a person came to harm due to not having SABAs for emergency symptom relief. Expert 12 commented that prescribing SABA in high numbers was 'clinically defendable' when made in conjunction with the assessments of ICS prescribing. This suggests clinician's concerns regarding accountability for clinical decisions to prescribe or not to prescribe SABAs:

*"It's an essential medicine. We're not gonna [sic] deny anyone it, we'd probably get sued if they then have an asthma attack"* (Community Pharmacist)

*"And this is the medicolegal … minefield. I didn't give the patient the medication because it was in the patient's best interest. The patient died because you didn't give them the medication they wanted, in his best interest – so how do you square that circle?"* (Expert 1)

*"it could be possible if you use your ICS but still need SABA inhalers maybe 2 or 3 per month, then it is clinically defendable"* (Expert 12)

GPs described that two SABA devices were commonly prescribed per prescription rather than one. Following the SABA alert, it was proposed that quantities should be reduced rather than withheld, with configuration altered from two to one SABAs per prescription. This required clinicians to input or alter the prescribing configuration, as discussed earlier in the chapter, when making or authorising prescriptions. GP 3 described that reducing the number of SABAs

was one way to ensure patients attended asthma review:

*"We do do things like for example if somebody's requesting two inhalers or we've always given them two at a time, I would have no problem in reducing that down to one inhaler and saying, 'We've reduced your quantity because we really need you to come in, before the next prescription'"* (Practice Pharmacist)

*"In fact I went around changing two Ventolin inhalers on prescriptions to one, to try and get the message that you shouldn't be using your blue inhaler unless you're out of control, and if you're out of control you should come and see me and we can talk about it"* (Expert 1)

*"We can reduce the quantity… have your review and we'll try and get your management better, it might be you don't have to use this many inhalers.' But a lot of people just want them, almost addicted"* (GP 3)

### Asthma review

GPs and experts described an asthma review as an opportunity to both confirm and explore the reasons for excessive SABA use. At the earliest opportunity of suspected SABA overuse, an asthma review was recommended to review medications, check inhaler technique, and assess patient understanding and reasons for overuse as well as developing a plan to improve asthma management:

*"But the purpose of the review is why the patient using so many. And an awful lot of people use their SABAs as a prop…and if they need a prop, find out what they need propping up for and then tackle that problem in a more appropriate manner"* (Expert 1)

*"Yeah. I think with this sort of thing you need that space, you need a dedicated piece of time to really… especially with asthma, you really need that dedicated asthma review, I think, to go through things properly 'cause I think there's massive variation on what people understand, especially about inhalers and what each one's for"* (GP 5)

Despite an asthma review being the recommended form of action in response to the alert, a number of challenges were raised regarding review availability and attendance with no clear plan on how to address these issues. *GP 3* described that timely review is not always possible due to varying appointment availability and practice resources:

*"so until you've got a good protocol and each practice will need different protocols, some are, 'See practice nurse in three weeks' time,' ours are, 'See practice nurse tomorrow,' that's how good our access is"* (GP 3)

Clinicians described the challenge of patient non-attendance for review perceiving their asthma as well controlled or not prioritised around day-to-day life:

*"But I think, I tried to act on this alert and sometimes I'm surprised because patients don't realize they are overusing because they feel their asthma is controlled by using like three inhalers per month and I explain we can change the preventer but they are not aware of that and that's why they don't come for their review"* (GP 7)

*"we had [patients] who rated their asthma as very well controlled when they were using their reliever inhaler about 10-12 times a day. So the concept of good control, or what was adequate control was very, very different"* (Expert 10)

*"I don't know why asthma in particular seems impossible to get people in for their reviews. I think a lot of them are young working people so they don't necessarily prioritise coming in for their reviews, even if they perceive that their asthma is under control, when it may not necessarily be or they're not using their inhalers appropriately, so that's another big battle, I think"* (GP 5)

Significant practice resources were required to follow up people for an asthma review, whilst generating increased workload for GPs. *GP 5* describes the additional workload following the identification of excessive SABA use whilst GP 4 highlights the challenges that such increased workload brings to general practice:

*"And to pick someone up on it at the moment that involves quite a lot of effort, so it involves dictating a letter, writing to the [patient]… or sending a task to reception to book an appointment"* (GP 5)

*"there are resource implications in that that in a small practice to commit a member of staff to doing that, writing letters to every patient, do we think that letters are the most effective way of communicating with people? Not really. We're certainly not going to commit a doctor to ringing every one of those people and saying, 'Would you like to come in?' because of the resource implication, not because it's not important"* (GP 4)

It was commonly the responsibility of other primary care staff including the receptionist, nurse and/or pharmacist to ensure that asthma reviews were offered and attended. This was often at considerable effort, involving ringing patients and sending letters. Such methods were viewed as time consuming and resource intensive, with an expectation of review to each alerted patient viewed as overstretching resources:

*"the only thing we don't do is go round their doors"* (Receptionist 1)

*"…you can do as much chasing as you can possibly do. You can ring them, I write letters to them to come in if they DNA, you know that sort of thing..."* (Nurse 2)

*"it also kills us with if you overload it [reviews], we've got patient demand there asking for access, we've got what we need to do asking for access and then you've got chronic disease access, so they don't even want to be seen but we need to see them, the asthma, the COPD, the diabetes"* (GP 3)

However, given the high levels of non-attendance for routinely offered annual asthma reviews, an additional review for excessive SABA use was regarded as challenging to deliver in practice:

*"everybody already gets an asthma review annually although many people don't take the offer of one up, and so you could, but then there are resource implications in that that in a small practice to commit a member of staff to doing that, writing letters to every patient, do we think that letters are the most effective way of communicating with people? Not really"* (GP 4)

### Repeat prescribing process

Acting on excessive SABA use identified when repeat prescribing presented a number of challenges due to the context of repeat prescribing as an the end of the day task with limited time and resources to follow-up. GP 2 described a lack of motivation when carrying out repeat prescribing, potentially resulting in inadequate assessments of medication use:

*"So all my medicines management stuff gets left to the end of the day…then it is much more difficult to follow up any kind of issues from it. So it's done at the end of the day, you are knackered, you know you just want to get home, you're not necessarily going to give it everything that you could…we know what we should do, but this is the problem at the moment in general practice, we know what we should do, we want to do what we should do, but we haven't got a hope in hell of doing it all because there is just too much pressure. So that's the kind of issues"* (GP 2)

Although reception highlighted concerns regarding potentially problematic SABA use, GP 4 described difficulty in determining potentially problematic SABA use due to the repeat prescribing process that involved a flagging of concerns by receptionists and without the patient present:

*"those sort of repeat prescriptions will be done by the front desk and they will often write, overusing, or something but in the context of current general practice, speaking honestly, it's very difficult sometimes to then drill into that and decide if there is something else that you need to be doing….it's about whether the patient's with you or are they, you know…?" So you can't read into it too much, I think without speaking to the patient and knowing the reasons"* (GP 4)

*"…the alert comes up like a pop-up but the problem can be when you cannot see the patient for days"* (Expert 11)

## Management strategy

As described by both GP 4 and expert 11, acting on excessive SABA use was challenging with no strategy for GPs, receptionists and pharmacists in responding to excessive SABA use. Expert 8 describes the lack of a clear plan for following-up of patients identified when repeat prescribing:

*" Looking at my appointment system and I have no appointments left and I'm thinking 'now what's going to happen?' Do I try to bring this person in at the end of an evening surgery because there are no appointments left and it was me who generated the request to be seen, the patient wants their inhaler by the weekend. So what's going to happen? The receptionist will say you wanted to see this patient and we've put them on after the end of evening surgery…It is not straightforward"* (Expert 8)

*GP 4* further described the challenge of navigating the repeat prescribing process with no clear guidance on how to respond to medication concerns at this point, with the system a source of frustration for both patient and prescriber:

*"And partly that's to do with the way the system works, so we deny, we refuse the prescription, the patient doesn't know that, they come in to the front desk going, 'Where's my prescription?' Reception may not… the communication between us and reception is simply, 'There's no prescription,' or maybe a scrawled note on the prescription or a computer's message saying, 'Needs to talk to doctor.' So then they'll need to make a phone call, our system is a phone call based system, so they then need to book for a phone call, by the time they're actually talking to a clinician often they're [the patient] just annoyed 'Why haven't I not got this?' and you're then having to negotiate"* (GP 4)

GPs and experts described a responsibility to find a balance between what may be clinically appropriate from a medical perspective and that was appropriate to individual patient circumstances. For example there may be many reasons why SABAs are requested for example, to circumvent the cost of individual SABA prescriptions, additional SABAs for school, home, lifestyle or family situations, or by mistake when requesting other medications. However, there was no clear pathway to help GPs manage these situations.

GP 3 reiterated clinician uncertainty on how to respond to the SABA alert commenting, "*we need to just work out in our heads what do we want to do*." Expert 7 described an absence of clear guidance and support for clinicians on how to proceed following the SABA alert which needed to be clarified:

*"What should you do then? Should you send a message to the patient to give them an appointment, should you give this information to the nurse that is supposed to call the patient to check 'how are you?' "* (Expert 7)

The absence of a plan of action was described as likely to deter clinicians from engaging with the alert:

*"the clinician needs a strategy for dealing with the problem. Alerting me to a problem is not very helpful if I don't know what to do about it….if I wasn't interested in asthma I might not know really what I'm going to do about it. And strategies for helping both in the short term, immediate moment, the moment I'm thinking 'oh I need to discuss this with the patient'* (Expert 8)

*"Something has to happen as a result of the alerts, so it's that thing about having a plan when the alert comes up"* (Expert 1)

One nurse described the variable role of reception at highlighting medication concerns, with no clear protocol on when or how this should be done. When processing repeat prescriptions, *Receptionist 3* described that despite noticing a medication review was overdue, it was outside the scope of a receptionist's role to discuss with the patient or to inform a clinician, but that *'hopefully'* a clinician would pick this up. One nurse described the receptionist's role as variable by practice priorities:

*"It's usually what's flavour of the month and there's so much overload if information that we have to, or the girls have to provide patients at the front desk, it's not always just about medications, there are other things going on as well that are priorities…a lot of the girls would mention that [SABA use] but it's not set in stone so it won't be at the top of the agenda"* (Nurse 2)

A number of experts reiterated a need to support receptionists in the identification of excessive SABA use with a plan to support:

*"There has to be a pathway about what to do with the alert when it comes up at the receptionist level perhaps when it's requested, so that somebody can have a dialogue with the patient explaining the importance of having the review rather than just say, 'You can't have any more'"* (Expert 1)

### 5.5.5 Theme 4 Inter-professional Practice: The 3 R's

The theme 'Inter-professional practice' addresses how the roles, responsibilities and relationships of primary care staff contribute to the identification and management of excessive SABA use.

#### 5.5.5.1 Roles and relationships

***"It's not like it used to be, sure it's not?"***

Receptionists

Despite an expectation among some GPs that receptionists would highlight SABA concerns, on the contrary the identification of excessive SABA use was perceived as a clinical task beyond the role of non-clinically trained staff and not something with which receptionists should be expected to engage:

*"To be honest I don't think that admin people that do scanning pay any attention to that anyway 'cause it's all really clinical stuff"* (GP 5)

*"So I can imagine reception are not looking at it enough, I'm sure if you've spoken to them they'll say they never do"* (GP 3)

(GP 7): *"I don't think the receptionists really look at what's in the [QOF] box anyway…"*
(GP 8): *"No…"*
(Interviewer): *"Should they be looking at it?"*
(GP 7): *"Probably not"*
(GP 6): *"No, No"*
(GP 8): *"It's quite medical isn't it?"*

Since the introduction of electronic prescribing, the role of receptionists in prescribing had changed. *GP 2* described the changing role of reception in highlighting medication concerns since the introduction of electronic prescribing:

*"[Reception] will highlight overuse or whatever, they would bring that up…it's not been happening as much now, but they rely on the medicines management systems and they don't flag it up any more like they used to"* (GP 2)

One expert described the changing role of reception in one European country following the introduction of electronic prescribing. A receptionist could have previously authorised a prescription that a GP would authorise, however electronic prescribing has resulted in all control of prescriptions as solely the responsibility of a GP:

"Often a patient would come to consultation with a packet of boxes and they say please renew this for me and the receptionist made the prescription and the doctor just signed, this is no more happening, because we have full electronic prescription all over Spain and a very good system…" *(Expert 11)*

When observing receptionists carrying out repeat prescribing task, two receptionists were discussing their changing role, one receptionist questioned rhetorically "*it's not like it used to be, sure it's not?.*" This reflected a sense of depreciation in their ability and experience to identify concerns or mistakes with prescriptions that was now deemed a clinical task outside their scope of practice despite routinely doing so prior to the introduction of the EHR and electronic prescribing. They described that prior to the introduction of electronic prescribing receptionists had greater 'clinical' input into the repeat prescribing process but their role to interpret and alter prescriptions had gradually declined. Receptionists spoke of contradictory expectations in their role in the management of repeat prescriptions since the introduction of electronic prescribing. This had resulted in a shift in responsibility for reviewing prescriptions from receptionists to GPs. However there remained an expectation that receptionists would continue to raise concerns regarding SABA use when requested in paper format. One receptionist described contradictory roles and responsibilities as determined by GPs, with years of experience negated with the introduction of electronic prescribing:

*"it was fine before [electronic prescribing] and they [GPs] are happy for you to do something until it goes wrong"* (Receptionist 1)

One GP suggested the potential for an increased role of receptionists in the management of SABAs that involved the triaging and signposting of patients when high SABA use was identified. This however was dependent on a GP's ability and propensity to support receptionists in an increased role:

*" that's our problem, we [GPs] haven't empowered them [receptionists]. Believe it or not that would work really… I think I'm just about… my next meeting is about empowering our reception staff and we're very good at normally doing that and I think they're actually now in a position of feeling that they could really try and get involved with patient care in more than just a, 'Let's give them an appointment, let's triage them, let's work out, signpost them,' of actually where are they in this field? And I think having teams of people… almost saying to every receptionist, before you're taking the prescription request look and see"* (GP 3)

There was a lack of continuity described in relationships between receptionists and other primary care staff. *Receptionist 1* was unaware of how GPs and pharmacists manage the repeat prescriptions initially processed by receptionist, whilst conversely, *GP 5* described uncertainty as to how receptionist process repeat prescriptions and the potential ways receptionists identify SABA overuse. In one practice, the receptionists described a number of challenges when contacting GPs about repeat prescribing issues. Methods of communication between reception and GPs were often informal and opportunistic. Receptionists previously attached hand-written notes onto a repeat prescription request by paper but these were no longer allowed as all GP communication was to be made electronically:

*"…the communication between us and reception is…maybe a scrawled note on the prescription or a computer's message saying, 'Needs to talk to doctor'"* (GP 4)

However *Receptionist 1* explained that following complaints from GPs, electronic messages were appropriate for certain, but not all, queries due to interruption in clinical practice. In one example, *Receptionist 1* explained she was no longer being able to send electronic messages to remind a GP that repeat prescriptions awaiting signing were nearing the 48 hour processing deadline. When GPs made decisions to reject medications, communication to other staff involved in the repeat prescribing process was not a prerequisite but instead at

GP discretion. *GP 1* describes the rejecting a medication without providing an explanation to reception despite being the likelihood that a patient would question this with reception, as highlighted in section 5.12.2, would likely be unhappy with decisions made:

*"that's rejected because she has requested all her medications but there's one that she got a couple of days ago so she doesn't need it. But if I wanted I could reply and leave a note to with reception and explain"* (GP 1)

However, there were conflicting opinions from allied health care professionals and reception staff regarding the potential to increased role of receptionist in the identification and management of SABA use. There was surprise from one pharmacist and one nurse in regards to current GP expectations on receptionists managing repeat prescriptions. Extending the role of reception presented potential challenges including possible confusion around the numerous types of inhalers for asthma and the competing demands on reception due to having a patient facing role and the first point of contact in practice:

*"but then receptionists might get the colours muddle up, there's always a lot of other stuff that goes on and they aren't medically trained…they could always highlight [SABA overuse] but then they have such a heavy task because a lot of things are frontline…it's alot of responsibility for people that aren't medically trained]"* (Nurse 2)

*"I think myself and other colleagues ...are just amazed that the receptionists are doing repeats and things like that"* (Clinical Pharmacist)

### Pharmacists

There were variations in the roles and relationships between pharmacists and general practice in Europe in comparison to the UK. Experts described an active role of pharmacists in Europe in identifying concerns with SABA use but also in regards to prescribing for other long-term conditions including diabetes and hypertension.

Internationally, pharmacists were described as increasingly supported and respected by GPs

in the raising of prescribing concerns. Support was also available in the form of financial incentives and integrated computer systems between pharmacy and general practice:

*"there is quite a strong link between pharmacists and GPs in Holland. In general, pharmacist will be linked to the electronic system used by GPs and usually they would have arrangements in place that would cover the over prescribing of SABA but also other issues in terms of prescribing…in respiratory they are strong but also in diabetes and cardiovascular disease and now geriatric patients, for example in decreasing the number of medications for the patient. So, a number of fields in healthcare have been claimed by pharmacists and as a result they have an increased role"* (Expert 12)

*"pharmacists play a role in the prescription refill process by identifying people being given to many SABA and deciding whether this is appropriate or not"* (Expert 6)

*"for example when a new warning comes up for people with hypertension that we must be careful because some hypertensive emergencies have happened and an alert comes from the Ministry of Health that every patient (unclear) should be checked for blood pressure frequently. The pharmaceutical people in our health service they look for the patients on this prescription and they put an email to you (the doctor) saying "please Doctor you have X number of patients on this treatment and they should be checked for their blood pressure so please make an appointment"* (Expert 11)

Pharmacy was viewed as having a prominent role in the identification and management of excessive SABA use that was presently underutilized. One of the main roles of pharmacy was to ensure that patients received safe and accurate medication, acting as a firewall to troubleshoot prescribing issues prior to medication being dispensed:

"*so that's why we are in conjunction with pharmacists because they work in a much more risk adverse situation than GPs who usually work on an 80% feasibility basis in my experience so they could now and then make the mistake of overprescribing SABA and then it is very helpful to have a different type of healthcare provider who will double check it and give you a call because this person is in a risk zone"* (Expert 12)

However pharmacy was viewed as opportune to identify excessive SABA use. There was no plan of support for pharmacists if excessive SABA use was identified with current action to dispense SABAs and signpost the patient back to general practice. However, there were calls for pharmacists to take further action such as carry out a medication use review with the patient in pharmacy. *GP 4* welcomed the increased involvement of pharmacy in asthma care, described as the 'farming out' of the GP role:

*"…they may flag it to us or more often they will tell the patient to come in and have their medication reviewed"* (GP 1)

*"So this is again the farming out of what traditionally would be a GP role, so there's nothing wrong with a pharmacist having a conversation and saying, 'You really need to go and talk to the GP,' or, 'You're ordering three a month or three every three months,' and that would be perfectly reasonable"* (GP 4)

*GP 5* proposed that rather than refer a patient back to general practice, pharmacists had a responsibility to take specific action on SABA overuse for example by reviewing a patient in a MUR:

*"I think pharmacists know how much Salbutamol they're giving to someone, so I think the more conscientious pharmacists probably do spot that and maybe that could be a cue for them to do a medication use review which they get paid for, so…"* (GP 5)

One expert commented that signposting of patients back to general practice for review was an underutilization of the role of pharmacy. *Expert 1* commented that pharmacy should be able to review and optimise medications yet due to prescribing policies the power to do so remains confined to GPs and the potential of community pharmacy is unmet:

*"the pharmacist has a prescription record of how often something's going in, so they could act as a break on it and say, 'You need to see your GP for review.' But I think that the prime role of the pharmacist is checking inhaler technique…What they're missing is they haven't got the ability or the permission to prescribe an alternative inhaler…I keep saying to loads of people, pharmacists have the ability. There are tasks which they are well suited to perform… And I think it's unlikely, unless CCG decides under some sort of patient group directive, that pharmacists can switch inhalers"* (Expert 1)

The point of contact when dispensing medication was viewed as a prime opportunity for a pharmacist to address concerns regarding SABA use, which was not possible for GPs in the process of repeat prescribing due to the patient not being present:

*"there is a role for the pharmacist because at the moment the SABA is handed over, that's the moment when you have the patient in your realm of influence."* (Expert 12)

A number of experts suggested that excessive SABA use should be identified in pharmacy at the point when SABAs are dispensed. One expert in Europe described how an alert system presented in both general practice and pharmacy, whilst two experts described the importance of such a system and what it should entail. A pharmacist should have greater responsibility for bringing concerns regarding SABA use to the GP's attention. It was perceived that an alert when dispensing SABAs was more likely to be acted upon given the challenge of responding to the high volume of alerts in general practice:

*"[an alert] presents at the pharmacy because it happens when the pharmacy is preparing the medication, there will be a flagging up of misuse and then the pharmacist will judge whether he needs to a make a call or not. The same system is actually in place in the GP's office so he could have known in the majority of cases that something is wrong but it flags up so often that in my experience usually you click that screen away because you are in a hurry to see your next patient, so that's where things go wrong"* (Expert 12)

*"Yes what could be done is that pharmacy can see all prescriptions that have been made on their register. They could then send an alert to more than one physician that this patient is collecting more than he or she is supposed to do based on individual prescriptions…And then the pharmacy would see you have collected six canisters and not two during the last month then of course if you had electronic alert system this could go to all three of the GPs telling them this patient has collected more than you have prescribed"* (Expert 7)

*"So an alert in the pharmacy that this patient has taken SABA from a different pharmacy and also to oblige them to take measures on that. This is something that depends on the health system of the country of course. And I think there must also be some connection between the different pharmacists and primary care"* (Expert 9)

There was no set method to identify excessive SABA prescribing in pharmacy. A number of factors affected the pharmacist's ability to identify excessive SABA use including the robustness of the dispensing system and the ability of the staff involved. Medication was often prepared by a non-clinically trained dispenser, with final checks carried out by a pharmacist often involving the cross checking of prescription details but not frequency of use:

*"What happens is you get a prescription in and then the dispenser will dispense it, so they'll put it into the computer, put the labels on, and then the pharmacist checks it. So I'm involved in the final checking bit, which doesn't involve looking at when they last had it, so it's relying on the fact that I checked this two days ago, why am I checking the same thing again…And if it's not me, we have five pharmacists that work within here, if it's someone else they're not gonna know that"* (Community Pharmacist)

In one European country primary care systems have moved to reduce power imbalances between pharmacy and GPs facilitated by integrated health care systems. Such systems increased community pharmacist's role in primary care and improved working relationships. However in the NHS primary care appeared to be built on hierarchies of power, as headed by GPs, which influence and determine the relationships between primary care staff. *Expert 6* reiterated the fragmented relationship and balance of power between community pharmacy and GPs in which communication initiated by pharmacists was not reciprocated by GPs:

*"when I speak with the pharmacist they say 'well I tried calling but the doctor says that's my problem, not yours so leave me alone'"* (Expert 6)

*"So I left a message with the doctor to just say, 'Are you sure you want him to be having this much, does he need to have a review?' But they never really got back to me"* (Community Pharmacist)

However *GP 1* noted inconsistent communication from pharmacists when raising concerns about SABA use. However, as described by the community pharmacist, this stemmed from a reluctance to question GP prescribing, with the GP viewed as holding responsibility for prescribing decisions, for which pharmacists were responsible for enacting:

*"it depends on the pharmacist, [contact is] not very often, but they may flag it to us or more often they will tell the patient to come in and have their medication reviewed"* (GP 1)

*"it can't be the pharmacy's' responsibility to control when they get the medication 'cause that's not our role. The doctor decides how often to give the medication... and to question a doctor sometimes … not in my experience, we've found they've been OK, but sometimes you can get people that would be like, 'Why are you asking; is it like I don't know what I'm doing?'* (Community Pharmacist)

*Expert 6* described the importance of closer working relationships with pharmacy, however the success of systems identifying high SABA use are dependent on patient relationships and a team effort that includes the patients is required. A team approach between general practice, pharmacy and the patient was essential to ensure the accurate identification of SABA overuse and to reinforce key messages regarding the significance of high SABA use as a as a marker of poor asthma control and a risk factor for asthma attack:

*"it's about the team approach with each other, it's the connection between the patient, between the clinician and the patient, the rappor…"* (Nurse 2)

*"I would think this has to be a three-way conversation between the patient and family, the pharmacist and physician…You are hoping you are going to have a relationship between the pharmacist, the patient and the doctor to ensure how the information is being tracked properly"* (Expert 6)

*"the more often the same message was delivered [to the patient] the more effect we could expect, so it would be like double root, both from the GP office and from the pharmacist"* (Expert 12)

Relationships between primary care staff and patients varied. Staff who held patient-facing roles, such as receptionists or pharmacists, were likely to have closer relationships with patients than GPs. *GP 3* described the challenge of building patient relationships whilst relying on computers, quipping that patients are likely to have a better relationship with receptionists:

*"as much as computers are very helpful, meaning the relationships of… probably the patient knows the receptionist actually now better than me because they're probably seeing them three times, they've ordered, prescribed, come in, seen Johnny, whatever…."* (GP 3)

There was a limited GP-patient relationship when requesting and obtaining SABAs through repeat prescribing. The receptionist acted as go-between for patients often relaying GP prescribing decisions. However clinical information transmitted by reception on behalf of GPs was described as a potential source of frustration for patients who often preferred to engage directly with a GP rather than non-clinical staff communicating clinical information:

*"Yeah and also patients open up to you more, they don't want a discussion with the receptionist they want a discussion with someone they see in their room on a regular basis, who they trust"* (Nurse 2)

One receptionist spoke about the difficulty of being first point of contact for patients and the challenge of meeting patient expectations. In one practice, a designated receptionist carried out repeat prescribing tasks behind shutters that acted as a barrier between patent and receptionist. On observation, both patients and the practice manager knocked on the closed shutters whilst she carried out repeat prescribing tasks interrupting the receptionist. In a second practice, receptionists shared the processing of repeat prescriptions on an ad hoc basis when concurrently carrying out general receptionist duties due to the pressure from patients when this task was done individually. *Receptionist 4* explained that repeat prescriptions could previously be left in a designated box at the reception desk but patients often had numerous questions and receptionists described feeling pressured. It was decided that rather than have a designated receptionist for repeat prescribing tasks, repeat prescriptions could be handed to any receptionist and duties shared between reception staff. Receptionists had a prominent role repeat prescribing but this came with a certain degree of pressure:

*"patients are so used to getting their own way, it's difficult to change when they've been allowed to do things a certain way for so long"* (Receptionist 3)

In both community and clinical pharmacy, intervening on excessive SABA use depended on the willingness of the patient to engage. This was influenced by the patient-pharmacist relationship, with community pharmacists often relying on opportunism and intuitive ability to determine when and how to raise issues or concerns with a patient:

*"also when you're handing something out, I'll always say, 'How are you getting on with your medication?' and that gives people a chance and they'll say really good or really bad, or they might have a particular question, and you can usually tell when someone wants to talk a little bit more"* (Community Pharmacist)

*Nurse 2* described the reluctance of patients to engage with community pharmacists on clinical matters, whilst *GP 5* reflected on the mixed patient feedback of a clinical pharmacist's

when reviewing asthma medications:

*"…what one patient may say is 'I don't want everyone to know my business,' I had that situation recently but he's happy to talk to me but not happy to talk to the pharmacist, because it's not as accepted"* (Nurse 2)

*"To be honest I had mixed feedback from patients about that, so some just didn't engage with it at all, some found it all a bit patronising 'cause they thought they can manage their asthma OK, I think some people found it useful but variability"* (GP 5)

Patients were described as having a responsibility for their own SABA use, with SABA use unlikely to change if patient behaviours cannot be changed. However, it was acknowledged that primary care staff had a responsibility to support and empower patients to take responsibility for SABA use, enabling patients to identify when asthma is not well controlled and how to act:

*"It's down to the patients responsibility as well really, isn't is, you can do as much chasing as you can possibly do. You can ring them, I write letters to them to come in if the DNA, you know that sort of thing"* (Nurse 2)

*"in the end I think we probably don't give patients enough support and responsibility that they'd be willing to take for themselves, provided they receive the right training and they should be the people who are given all the information they need and the support to be able to recognise that something's going wrong and somehow almost the alert needs to be on the inhaler itself that shines out at the patient every time they use it"* (Expert 2)

### 5.5.5.2 Who's responsible?

***"it doesn't matter what we think"***

There were varying opinions in regards to who in primary care held responsibility for SABA overuse. It was suggested that other staff members could assist in the identification and management of excessive SABA use to relieve pressures on GPs. However there was uncertainty regarding whom should take overall responsibility. *GP 3* believed the responsibility for the identification and management of SABA overuse rested with the GP but that the problem of high SABA use required a team effort to adequately address and manage the problem:

***"****Well, it could be a nurse, I mean anybody who has received the appropriate training, it could be any kind of lay person provided they're appropriately trained, but I think the issue is who takes the responsibility"* (Expert 2)

*"Definitely not them, it's me, nobody else, and as much as what I would say is I can only be as strong as the team and if we can devolve, not the responsibility but the feeding back"*
(GP 3)

*Expert 13* suggested that identification of SABA overuse is a GP responsibility, with pharmacy responsible for alerting systems potentially presenting at point of dispensing. Whilst pharmacy had a responsibility to identify high SABA use *Expert 12* explained that for systems, such as alerts, to be succe9ssful, GPs needed to retain overall responsibility with an ability to overrule pharmacists:

*"I would say the final responsibility lies with the prescriber. Certainly the pharmacy could be used as a second firewall so to speak, if before dispensing medication*
*there would be a second surveillance system popping up 'hey this patient might be at risk, please review with the prescriber' that might be useful"* (Expert 13)

*"But this is the classic mismatch about giving responsibility but not ability. [Here] the GP is still in charge because otherwise they are unlikely to accept the system, so the GP is responsible but the pharmacist is responsible for advising the GP. The GP can always overrule and can always say no if there is a special case etc, etc, "I'm doing this because of that"...using clinical insight but the pharmacist is responsible for flagging up"* (Expert 12)

Expert 9 and Expert 12 believed pharmacy had a responsibility to distribute SABAs and double- check the safety of GP prescribing, raising concerns where appropriate:

*"I think most of this responsibility lies with the pharmacist regarding the distribution. But regarding the first steps, because a patient who had to take a SABA continuously lets say, is a patient that is not well controlled, so the responsibility goes back to the doctor"* (Expert 9)

*"The majority of GPs consider the pharmacist to be in a unique position to do so [identify SABA overuse] and it means you have less of a worry as a GP you can be clinically responsible and you know you have an extra check the moment you send that prescription, by the pharmacist"* (Expert 12)

However, community pharmacist believed pharmacists were not responsible for the identification of high SABA and the flagging of concerns to GPs but rather a pharmacist was responsible for enacting GP decision-making, and did not have authority to question GP prescribing decisions:

*"The thing is, it's not something that I feel is really the pharmacy's responsibility to control how often somebody is taking the medication, 'cause we don't authorise the medication. If the doctor wants to give somebody six months, it doesn't matter what we think, then give them six months, and to question a doctor sometimes … not in my experience, we've found they've been OK, but sometimes you can get people that would be like, 'Why are you asking; is it like I don't know what I'm doing?'"* (Community Pharmacist)

GPs being solely responsible for the monitoring and identification of high SABA use, including electronic alerts, was contextualized within the current challenges of general practice:

*"Well it depends on the resources in primary care, because general practitioners have got so many other things to monitor and I think to do that and expect the GP to be responsible for that is still quite a lot"* (Expert 10)

*"If you only put the responsibility at the GP's desk, such a system will be a failure because GP's will be flagged too many times"* (Expert 12)

## 5.6 Discussion

This qualitative study explored primary care staff and experts views regarding an alert to identify excessive SABA prescribing in primary care. Four key themes were established within the present analysis that reflected the broad issues regarding an alert for excessive SABA prescribing. The four themes were: perceptions of excessive SABA use, identifying excessive use, using a SABA alert and inter-professional practice. The findings will be summarised below prior to the interpretation of findings, strengths and limitations and implications for practice.

### 5.6.1 Summary of findings

This study established that despite the evidence, discrepancies exist between how GPs and experts define excessive SABA prescribing. Excessive SABA use was more likely to be perceived as high risk if presented alongside additional risk factors rather than as a sole marker of risk. Clinicians used a combination of methods to identify excessive SABA prescribing with the SABA alert intermittently used alongside automatic EHR features and the manual checking of prescription records. The ability of the alert to influence SABA prescribing was dependent on clinician engagement with the alert and ensuing action. Findings suggest that SABA alert use was variable as the alert was not aligned with prescribing workflow, with no clear management strategy on how to respond to the SABA alert particularly when repeat prescribing.

There were conflicting views between experts and GPs regarding action following the identification of excessive SABA prescribing, with experts more likely to suggest that SABAs are withheld, whilst GPs deemed this inappropriate instead preferring to prescribe SABAs and invite patients for asthma review to assess asthma control. However, the provision of timely review following the identification of excessive SABA prescribing was challenging due to the resources required to initiate patient follow-up combined with the challenge of patient non-attendance.

Both receptionists and pharmacists were involved in the identification of excessive SABA use to varying degrees. GPs often relied on receptionists to highlight excessive SABA use when processing repeat prescriptions despite being neither a formally recognised nor supported role. In comparison to Europe, pharmacists in this study were an underutilised resource in asthma management. The need for a collective approach to the identification and management of excessive SABA prescribing across primary care was expressed among both GPs and experts but was yet to be realised in practice. Increased patient education and asthma self-management was deemed necessary for excessive SABA prescribing to be reduced rather than the sole targeting of prescribing behaviour. These findings will be further discussed in the following section and alongside findings from Phase 1 and Phase 2 of the thesis in the next chapter.

### 5.6.2 Strengths and limitations

In Chapter 2, the general strengths and limitations of qualitative research methods were reviewed. This section describes the specific strengths and limitations of Phase 3 of the thesis presented in this chapter.

#### 5.6.2.1 Strengths

One of the strengths of the qualitative findings was its inclusion of various members of primary care staff rather than GPs. This provided a broad understanding of the challenges faced in the identification of excessive SABA use in the wider context of primary care. Using what Kelly[257] refers to as generic qualitative research enabled a broad analysis of the issues surrounding the identification of excessive SABA use in practice. Conducting face-to-face interviews with GPs in practice allowed for wider discussions around the use of the EHR in identifying high SABA use. GPs were able to refer to the EHR when describing methods used to identify high SABA use was carried out in practice. Furthermore, rather than simply referring to the AUK medicines management alert, GPs were able to demonstrate the ways in which excessive use was identified within the EHR. Telephone interviews facilitated access to a wide range of experts worldwide with knowledge, experience and perspectives of a variety of healthcare systems. Observations with receptionists gave an insight into the varying processes and roles in the primary care management of SABA prescribing in real time, unlikely to be accurately captured in interview.

#### 5.6.2.2 Limitations

Although the study included a variety of primary care staff to provide broad insight into the research topic, findings are not representative of all primary care staff and experts due to the variable participant numbers. Despite a convenience sample of fourteen practices identified as likely to participate in the project, only 2 practices agreed to both clinicians and receptionists to take part, one with clinicians only and the final practice declined but one GP agreed to take part following snowball sampling. There may be a number of reasons for poor uptake; by restricting the study to a convenience sampling strategy of those who were easily accessible[380] and the challenge on clinician time during working hours. Uptake may have been higher had practices been incentivised to participate, in particular for GPs who are likely the most time deprived, financial incentives may have increased participation outside of their working day. Observations with clinicians may have provided greater insight into the role of an alert in repeat SABA prescribing however given the challenges of recruitment, interviews were judged to be more easily accessible than observations. As the study was carried out in an inner city, ethnically diverse population findings are not generalisable to wider primary care. Observations with receptionists were of limited duration and may not be reflective of the role of receptionists in other practices, whilst limited pharmacist input does not provide depth in understanding of the role of pharmacists. In utilising a 'generic qualitative research' approach in the absence of a theoretical underpinning, a larger sample size may have been required to grant sufficient information power.[262] GP interviews may not have accurately reflected the processes that GPs would adopt when prescribing SABAs in practice. Observing GPs when repeat prescribing SABAs may have helped to overcome some of these limitations however may have impacted on practice uptake. Furthermore, observations such as with receptionists may have influenced repeat prescribing practice and may lack generalisability.[381] Telephone interviews may have limited the depth and quality of data collected in comparison to face-to-face interviews.

### 5.6.3 Interpretation of findings

(i) Theme 1: Perceptions of excessive SABA use

Despite the association between excessive SABA use and risk of exacerbation and asthma related death presented in Chapter 1, inconsistencies existed among GPs and expert's understanding and application of asthma guideline evidence into practice. GPs and experts expressed conflicting opinions regarding how much SABA was too much in contrast to the most recent evidence presented in BTS/SIGN[52] and NRAD.[25] There may be a number of reasons for contrasting definitions of excessive SABA use. As highlighted in Chapter 1, there is a lack of consistency in how excessive SABA use is defined in the literature. Both NRAD[25] and BTS/SIGN[52] recommend that people prescribed more than one SABA a month (200 doses) or 12 SABAs a year, should be invited for asthma review, whilst BTS/SIGN[52] further describe that SABA use of more than three times a week (24 doses a month), at a much lower quantity of one SABA a month (200 doses a months), is a potential sign of poor asthma control. The lack of clarity and consistency in both guidelines and wider evidence to determine what constitutes 'too much' SABA has been highlighted in the recent IPCRG initiative 'Asthma Right Care' described in Chapter 1.[65]

GPs were more likely to refer to NRAD's threshold for excessive SABA use suggesting that GPs were less likely to follow guideline recommendations than experts which may reflect the challenge of guideline implementation.[382] Findings indicate that defining excessive SABA use involved a subjective balancing of the evidence with what was practical: NRAD's recommendations too lenient yet guidelines recommendations too restrictive in practice. Despite current evidence highlighted in Chapter 1,[1,25–27,52] both GPs and experts questioned the risks associated with excessive SABA prescribing particularly when SABA use was used as a sole marker of risk. GPs described a hierarchy of prescribing risk with commonly prescribed SABAs perceived low risk in contrast to higher risk, less frequently prescribed drugs such as methotrexate. The frequency of SABA prescribing may have implications for alerts as the more commonly prescribed, the more frequently an alert may present, potentially contributing to alert fatigue as has been described in Chapter 1.

GPs and experts viewed the co-assessment of ICS use in conjunction with SABA use as increasingly important in determining risk and prompting intervening action in practice. GPs and experts also described additional markers of risk such as oral steroid use, hospital admissions and emergency department attendances as necessary to identify those with current poor asthma control and at future risk. This suggests that further clinical indicators are required to identify at-risk patients and influence prescribing behaviour that may not result from an alert based on a sole assessment of SABA prescribing. A number of more targeted approach to the identification of potentially at-risk patients identified on SABA prescribing alone, have been described in the literature.

As described in Chapter 1, Schatz *et al.*[18] used a stratified approach to SABA prescribing to target patients with poor asthma control rather than determining risk based on a definitive SABA use threshold. The co-assessment of SABA and ICS prescribing as a marker of risk is reflective of NRAD's findings, implicating excessive SABA use and underuse of ICS in asthma deaths,[25] as well as reflective of Hull *et al's*[13] recommendations for the identification of those under-prescribed ICS and excessively prescribed SABAs which account for the majority of hospital admissions. Whilst CDSSs to improve clinician's adherence to guidelines offers potential to improve prescribing,[304] if clinicians do not agree with the content, for example the SABA alert threshold and/or do not perceive this threshold as indicative of risk, then the alert is unlikely to influence prescribing. The SABA alert design and factors influencing the use of an alert are discussed later in this section.

(ii) Theme 2: Identifying excessive SABA prescribing

There were two main opportunities to identify excessive SABA use either in-consultation (acute prescribing) or when repeat prescribing. The most commonly described method to identify excessive SABA use was the EHR generated medication percent usage, with the SABA alert an adjunct method rather than as the primary tool to identify problematic SABA prescribing. GPs described using the medication percent usage to identify problematic SABA use, as calculated within the EHR using the quantity, dose and time frame of use entered by the prescriber when issuing the prescription.

However, given the variability in the definitions and perceptions of excessive SABA identified in this study, it cannot be assumed that SABA prescriptions are appropriately and consistently configured to reflect guideline recommendations. Therefore people with potentially poor asthma control may not be appropriately identified in practice using this method.

When repeat prescribing, GPs did not routinely refer to the SABA alert, often relying on receptionists to highlight concerns in the absence of further clinical checks. This suggests a lack on continuity in prescribing activity in a time sensitive clinical environment. Furthermore that GPs are not adequately supported by current electronic methods to identify excessive SABA use particularly when repeat prescribing. However, it remains unclear to what extent an alert can influence repeat SABA prescribing, with Duerden *et al.,*[383] recommending that electronic methods to identify potential problems at point of repeat prescribing are explored.

It is questionable as to whether the presentation of the SABA alert in the QOF box is appropriate given that the QOF box is commonly associated with 'reminders' for incentivised quality of care indicators and administrative tasks. Furthermore, inconsistent use of the SABA alert may reflect overlap with incentivised measures such as the QOF annual asthma review, both positioned within the QOF box and with asthma review the recommended action following the alert. In an evaluation of an intervention to improve prescribing safety, Grant *et al.,*[384] reported that GPs perceived 'asthma control' as the least important safety concern due to the overlap with QOF indicators, associated with the management of long term conditions more commonly the responsibility of nurses. Furthermore positioning of the SABA alert in the QOF box with non-urgent tasks raises questions about the appropriate design and presentation of the SABA alert, the characteristics that differentiate an alert from a reminder and how such presentation influences the way in which clinicians use the SABA alert.

(iii) Theme 3: Using a SABA alert

The use of the SABA alert was dependent on two mutually existing factors: the ability of

clinicians to engage and act on the SABA alert. Engagement with the SABA alert was influenced by three factors: the volume of alerts, alert presentation and alert design. Clinicians described 'alert fatigue' from the volume of alerts presenting in practice, resulting in the prioritising of issues deemed of higher clinical importance above excessive SABA use. The reflects both the literature that a high volume of alerts deemed of variable clinical importance may result in clinician disengagement,[144] and findings of Theme 1, that alerts presented on the sole marker of SABA prescribing were not perceived as high risk and therefore less likely to be used. In the ARISSA study, alerts to identify severe asthma patient's at-risk, were based on a range of guideline criteria rather than one component of the guideline.[160] However, the at-risk alert had no effect on exacerbations with the alert design deemed a likely contributor.

CDSSs should present "the right information, in the right format, at the right time, without requiring special effort,"[126] with the literature in Chapter 1 highlighting the importance of alerts integrated both with workflow and at point of decision making.[122,123,137,141] However, in its presentation within the QOF box the SABA alert was neither aligned with workflow nor decision-making and therefore at increased risk of being over-looked. Furthermore as the SABA alert was activated when a patient's medical record was opened and not specifically at point of decision-making, engagement with the alert may be less likely. This may explain the use of the SABA alert as an adjunct method to the identification of excessive SABA prescribing. In its presentation in the QOF box with informative, optional recommendations that did not require additional user interaction, the SABA alert was representative of a 'soft' or non-modal alert design. This was in contrast to 'hard' or modal alerts for methotrexate that presented in the centre of the computer screen that required user engagement to exit the alert before progressing through the EHR. 'Soft' alerts that have optional rather than required engagement suggest non-urgency and may be likely perceived as a reminder rather than an urgent high-risk concern. It is more likely that this type of alert is overlooked rather than prioritised and therefore of limited opportunity to influence SABA prescribing behaviour.

As described in Chapter 1, an alert should consist of a signal word for example, 'information', 'warning', or 'stop' to differentiate between levels of priority, including instructions on the hazard and an explanation of consequences of the alert.[144]

However the current SABA alert fails to provide information on the risks of excessive SABA use, instruction on how to respond to the alert and the consequences of inaction, therefore offering little persuasion for clinicians to engage. The use of the SABA alert was dependent

on a number of factors including the context in which the alert presents, the type of action to be taken, how and by whom. GPs described problems on acting on excessive SABA use both in consultation and when repeat prescribing. There were challenges in-consultation due to time constraints due to the number of clinical issues that may already require attention, in addition to excessive SABA use. GPs agreed that improved resourcing of existing services was necessary to provide time for an appropriate assessment and review of asthma control and patient education. There was uncertainty regarding how excessive SABA use should be responded to particularly if identified when repeat prescribing, with no guidance for GPs or receptionists on how to respond within the repeat prescribing process. A number of experts in European and International primary care suggested SABAs should be withheld if excessive use was identified. This was in contrast to primary care staff who did not view the withholding of SABAs as an option due to concerns regarding risk of patients coming to harm and professional liability. The SABA alert did not provide advice and support for GPs on how to respond to the alert in such situations. This raises question whether the recommended action to invite patients for review is appropriate in its present form. Due to resource constraints and the already well-documented challenges of patient attendance at annual asthma review, alternative methods of reviewing patients in a timely fashion may be explored.

(iv) Theme 4: Inter-professional practice

The role of receptionists in the management of repeat SABA prescriptions is reflective of Swinglehurst *et al's*[71] findings that repeat prescribing is complex, technology-supported social practice between clinicians and receptionists. However one of the main differences between this study and that of Swinglehurst *et al*,[71] has been the introduction of the electronic prescription service. The aim of the EPS was to reduce non-clinical staff involvement by streamline prescribing to improve the processing and authorisation of prescriptions by clinicians. Despite a drive towards the EPS, variable practice uptake means that receptionists continue to process and manage repeat SABA prescriptions to differing extents. This was in contrast to the decreased role of receptionists in primary care in Europe following the introduction of electronic prescribing as described by a number of asthma experts. The variable uptake of EPS described in this study may explain the continued reliance on receptionists to raise prescribing concerns for GP's attention. However, despite the EPS, GP's described carrying out variable repeat prescribing checks prior to authorisation, often

dependent on time of day repeat prescribing was carried out and the volume of repeat prescribing requests received. As the SABA alert was not integrated with electronic prescribing workflow it raises questions regarding at what point in prescribing the SABA alert has greatest impact and on whom. The role of receptionists may vary by practice or CCG priorities as in some practices receptionists have increased ownership of QOF "pop ups."[385] Therefore, in its current presentation, it is possible the SABA alert is noted by receptionists rather than clinicians. However in observations with receptionists, none of the receptionists referred to the QOF box when carrying out either repeat prescribing tasks or patient-facing duties as this was not perceive this as part of their role.

Despite varying perceptions regarding the appropriateness of receptionists to flag SABA prescribing concerns, the receptionist's role in other areas of primary care is increasing and evolving to include the identifying and signposting of patients. Initiatives to enhance the role of receptionists including in the identification and signposting of patients eligible for screening programmes[386,387] has been recommended by the NHS England's 'General Practice Forward View.'[388] There remains potential for an increased role of receptionists in actively signposting patients with excessive SABA use for review however this requires a clear plan for the identification and management of SABA in primary care.

Both GPs and experts described a need for an increased role of pharmacists in the identification and management of excessive SABA use. This reflects on-going calls for an increased role of community pharmacists in the delivery of primary care services.[389,390] GPs and experts viewed pharmacists as a 'backstop' for prescribing safety however, the pharmacist's role in the identification of potentially problematic SABA prescribing was neither clearly defined nor supported. The action taken by pharmacists when SABA use concerns were identified, involved the dispensing and signposting of patients back to general practice for asthma review. This is reflective of the literature in Chapter 1 that described the challenge of intervening in prescribing decisions downstream rather than upstream at point of prescribing.

Furthermore, this highlights a lack of clear support for community pharmacists in the management of SABA prescribing, reflective of the underutilisation of community pharmacy described in Chapter 1. Despite the Murray Review[90] identifying an increasing potential for community pharmacists in the management of long-term conditions in England, such initiatives have not been forthcoming. The Murray Review[90] described the potential for MURs

to be extended to full clinical reviews in community pharmacy,[89] with pharmacists in Scotland already managing long term conditions such as asthma through the CPRS service.[391] However study findings showed no supported mechanism by which pharmacists could identify and respond to excessive SABA prescribing. Furthermore, pharmacist's signposting of patients back to general practice may intensify rather than resolve the challenge of timely patient review, by failing to address the problem at point of identification, with a number of GPs and experts suggesting pharmacists should be able to act on problematic SABA use for example through a medication review in pharmacy.

GPs described prescribing SABAs irrespective of the identification of excessive SABA use due to concerns of withholding SABAs without first reviewing the patient. Recent evidence has demonstrated the effectiveness of community pharmacists at improving outcomes for people with asthma through the delivery of asthma specific reviews. In the UK, a study of a community pharmacy asthma review service (CPARS)[392] and the Italian Medicines Use Review (I-MUR) service[393] identified the potential for asthma reviews to be delivered by pharmacists rather than in general practice. In a proof-of-concept study, patients who had not attended for annual asthma review were identified in general practice and referred to CPARS. Twenty-seven patients were reviewed by pharmacists using the structured SIMPLES review technique[394] in addition to standard MUR questions. In the three months following review the number of patients requesting 2 and 3 SABAs decreased, with an increase patients requesting 1 SABA and an increase in preventer inhalers. CPARS reduced general practice time and resources required to follow-up patients for review, issues identified by GPs in this study as problematic following the SABA alert. The absence of linked pharmacy and general practice records, and the inability of pharmacists to change medications were described as limitations to CPARS. These issues were also expressed as potential limitations by number of experts in this study when discussing the increased role of community pharmacists in the management of excessive SABA use.

Due to the inability of pharmacists to change prescriptions, pharmacists delivering CPRAS referred patients to general practice if changes to medications were required. This echoes current practice of community pharmacist's signposting patients to general practice if concerns with SABA use were suspected. However in CPARS patients signposted back to

general practice had an allocated review unlike current practice.

Initiatives such as CPARS offer community pharmacists the potential to intervene and triage patients for the more appropriate utilisation of both general practice resources and enhanced utilisation of community pharmacy. It was not possible to determine if the costs associated with patient referral back to general practice in CPARS were offset by improved quality of life, reductions in hospitalisation, and unplanned GP visits following the community pharmacy service. However, the RCT tested I-MUR service[393] demonstrated the potential effectiveness and cost-effectiveness of community pharmacy medication reviews. Other RCT tested interventions delivered in pharmacy show improvements in asthma control, medication adherence, inhaler technique[395] and reductions in SABA use.[396–398] The methods by which patients eligible for pharmacist-intervention are identified varies, with eligible patients most commonly identified by pharmacists or through audit searches in general practice for pharmacist follow-up.[392,393] The real-time identification of patients in response to a CDSS alert aligned with GP prescribing workflow has yet to be explored.

However pharmacist-GP relationships may not be well established in primary care and may require an overcoming of inter-professional barriers.[68,399,400] A number of international experts described the increasing role of pharmacists in the management of asthma in Europe in comparison to England. Experts described the pharmacist's role as being supported at both local and national and local level, with working relationships based on mutual respect supported by clear channels of communication. The lack of consistency or support for the identification and management of excessive SABA use across primary care identified in this study is likely to reflect contrasting infrastructure, roles and relationships in primary care nationally in comparison to internationally. It is likely that success of the I-MUR study[393] at improving asthma control and adherence was due to a significant cultural shift in the roles of Italian community pharmacy to more patient-centred and clinically orientated role as supported by the Italian Government/Ministry of Health. It is therefore questionable to what extent the Murray Review recommendations are likely to improve the management of long-term conditions if implemented in silos in primary care given the continued absence of a national strategy for respiratory disease in England. In the absence of integrated computer systems, pharmacists are is limited in their ability to make clinical decisions and remain dependent on relationships with general practice.[399]

Both GPs and experts described the need for increased patient responsibility in asthma self-

management to reduce excessive SABA use. GPs described it challenges in responding to excessive SABA prescribing, influenced by patient's lack of awareness regarding asthma control and patient expectations, particularly when repeat prescribing, as the patient is not present. As described in Chapter 1 there is discrepancy in what patients perceive by well controlled asthma, often tending to believe their asthma is under control even despite frequent symptoms, regular SABA use, or having had an acute exacerbation within the last year.[28,401,402] Inconsistency between patients' perceptions of their asthma as being well controlled in relation to asthma guideline definition of asthma control is an international issue.[403–406] Therefore, rather than targeting clinician behaviour alone, interventions should attempt to understand and address patient treatment beliefs and perceptual barriers to medication use.[407]

## 5.7 Conclusion

This study provides insight into the role of an alert to reduce excessive SABA prescribing in primary care. Whilst GPs and experts were receptive to an alert for excessive SABA prescribing, the impact of an alert was likely to be limited for a number of reasons including the variable definitions and perceptions of excessive SABA use in contrast to the SABA alert, inadequate alert design and presentation to facilitate engagement and action and lack of management strategy to support the use of the SABA alert. This was representative of the absence of a strategy for the identification and management of excessive SABA use in wider primary care.

Divergent perspectives among GPs and experts on excessive SABA prescribing and associated risks, in contrast to asthma guidelines, suggests that an alert based solely on SABA prescribing alone may not be appropriate method to identify people with asthma potentially at risk. Current methods used to identify excessive SABA prescribing in practice are inconsistent and unreliable. The SABA alert was aligned neither with prescribing workflow nor with point of

decision-making and therefore of limited influence to change prescribing behaviour. There was an expectation that receptionists and pharmacists would identify SABA prescribing concerns yet this role was neither formally recognised nor supported in primary care.

There is a lack of management strategy to support GPs in responding to excessive SABA prescribing identified when the patient is not present at point of repeat prescribing. An alert should be optimised using additional risk factors for a targeted approach to the identification of patients at potentially at risk. An alert should be aligned with repeat prescribing workflow and designed to facilitate engagement and action as part of a collaborative approach to the identification and follow-up of at-risk patients across primary care.

## 5.8 Recommendations for practice

The findings of this chapter raise a number of issues for consideration in regards to the identification and management of excessive SABA prescribing and the use of an alert in primary care. Clarity and consistency is required in how excessive SABA prescribing is defined and framed by clinicians delivering asthma care at local, national and international levels, and how excessive use is defined and framed between HCPs and patients. This should form part of wider discussion regarding increased education and awareness aimed at change attitudes towards the risk of excessive SABA use and towards overall management of asthma.

This requires action in two ways: (1) clarification regarding the configuration of SABA prescriptions to raise awareness among GPs when prescribing or a restriction on the number of SABA devices that may be configured per prescription. However, any changes to SABA prescribing should be clearly explained to the patient and may be prescribed at GP discretion. (2) Future SABA alerts should be optimised within prescribing workflow, with a hard alert more likely to be accepted if additional clinical indicators are used to identify at-risk patients. Routine searches of EHRs for at-risk patients may not identify patients in timely fashion and do not have the opportunity to influence clinician prescribing behaviour.

Findings suggest that an alert should facilitate and support both engagement and action if it is to influence SABA prescribing behaviour. Alternative ways to facilitate asthma

reviews should be explored to ensure people at risk have their asthma control. This will require clearly defined roles and responsibilities in the identification and management of potentially at-risk patients across primary care supported by a clear process for action at local level. However, at national level, the UK is experiencing an unprecedented crisis in the provision of primary care primarily due to underfunding of services. To enable those in primary care to deliver safe and effective asthma care, staffing, workload and resource constraints should be addressed as a matter of urgency.

# Chapter 6. General Discussion

## 6.1 Recap of the thesis aim

The overall aim of the project was to explore the use of an electronic alert to identify excessive SABA prescribing for people with asthma in primary care in east London.

The main objectives of the study were as follows:

Phase 1: To systematically review the literature on the use of CDSS alerts to reduce excessive SABA prescribing for people with asthma in primary care and determine the features of alert systems that have the potential to improve process outcomes for healthcare providers and clinical outcomes for people with asthma.

Phase 2: To evaluate the impact of the Asthma Medicines Management alert to reduce SABA prescribing and secondary process measures and clinical outcomes of asthma care within general practices in east London.

Phase 3: To explore the views of primary care staff and asthma experts on how they define and perceive excessive SABA prescribing, the role of an alert to identify excessive SABA prescribing, the factors influencing the use of an alert and the roles and relationships between primary care staff in the management of excessive SABA prescribing.

## 6.2 Recap of thesis findings

In Phase 1 (Chapter 3), the systematic review of the literature identified limited evidence that when delivered as a multicomponent intervention in an integrated health care system, alerts may potentially reduce excessive SABA prescribing.[189] The greatest effect on SABA prescribing occurred when clinicians were alerted to excessive SABA prescribing outside of prescribing workflow when facilitated by intervening actions including referral to an allergy specialist and a patient information letter in an integrated health care system.[314]

In Phase 2 (Chapter 4), a single component alert intervention resulted in a small but potentially clinically significant reduction in SABA prescribing in the 12 months following the SABA alert. The alert had no effect on exacerbations but a reduction in primary care consultations was observed. Exploratory subgroup analysis identified a reduction in repeat SABA prescribing, with variable effect by CCG and time frame.

In Phase 3 (Chapter 5) four themes regarding primary care staff and asthma expert's views on a SABA alert were identified. These include Theme 1: *Perceptions of excessive SABA use,* Theme 2: *Identifying excessive SABA use* Theme 3: *Using a SABA alert* and Theme 4: *Inter-professional practice*. Theme 1 identified varying definitions of excessive SABA use and application of guideline evidence on the risks of excessive SABA use among clinicians. Theme 2 established the SABA alert as one of a number of informal methods, inconsistently used by clinicians, to identify excessive SABA use. Theme 3 determined the SABA alert did not align with repeat prescribing workflow with no clear pathway of action to support its use. Theme 4 highlighted an absence of clearly defined roles for receptionists and pharmacists in the identification of excessive SABA use.

## 6.3 Addressing gaps in the literature

This thesis responds to two gaps identified in the literature as described in Chapter 1. Firstly, recommendations have called for clinicians to be alerted to the excessive prescribing of SABAs in primary care but the evidence supporting alerts in this context is unclear. Secondly, the literature on the use of alerts to change prescribing behaviour has focused on the presentation of alerts at point of decision making when in consultation but not when repeat prescribing.

The systematic review in Phase 1 of the thesis addressed the first gap in the literature, identifying that an alert delivered as multicomponent intervention can reduce excessive SABA prescribing. However, none of studies included repeat SABA prescribing as an outcome measure. Phase 2 of the thesis addressed the second gap in the literature, reporting a small reduction in repeat SABA prescribing following the use of a single component alert intervention. Further analyses indicate that a reduction in SABA prescribing is a result of asthma reviews generated in response to the alert rather than a direct result of the alert at influencing prescribing behaviour at the point of prescribing.

## 6.4 Integration of findings

In this section, the findings of Phases 1, 2 and 3 of the thesis are presented and discussed in relation to the gaps in literature identified in Chapter 1. More specifically, Phase 1 and Phase 3 findings will be discussed in relation to the findings of Phase 2 to explore the potential reasons for variability of the effect of the alert on SABA prescribing and to understand how the alert may have influenced repeat prescribing behaviour.

### Defining excessive SABA use

Chapter 1 highlighted variations in the literature on how the problem of SABA use is framed in practice. This included variations between national asthma guidelines definition of poor asthma control as 6 puffs of SABAs per week in contrast to NRADs definition of excessive SABA use as more than 1 SABA inhaler a month or alternatively 6 puffs daily, approximately 7 times higher than guideline recommended levels. A number of studies have used a targeted approach to the identification of poor asthma control and risk by capturing ICS prescribing in conjunction with SABA prescribing rather than SABA use on its own as a marker of risk. In the systematic review of the literature in Phase 1 (Chapter 3), two of the four studies variably defined excessive SABA use. In Tamblyn *et al.*[313] excessive SABA use as was defined as more than the equivalent of 250 doses in a 3-month period (2.7 puffs daily) whilst Zeiger *et al.*[314] defined excessive SABA use as seven SABAs per year equating to (four puffs daily). Both definitions were higher than national guideline recommended use for the identification of poor asthma control but less that the daily dose equivalent identified by NRAD as a risk factor for exacerbation and asthma related death.

In Phase 3 theme 1 *Perceptions of excessive SABA use,* clinicians quantified excessive SABA use by differing thresholds. Experts more likely to define problematic SABA use in accordance with guideline recommendations whilst GPs were more likely to define in accordance with higher threshold of NRAD. Theme 1 further identified that irrespective of evidence, a number of GPs and experts did not equate excessive SABA use as high risk. Additional risk factors such as ICS use, exacerbations, hospitalisations and AED were perceived necessary, in association with SABA use, to determine risk. This raises questions regarding both a lack of awareness among

GPs of the guideline evidence for excessive SABA use and the suitability of an alert to identify poor asthma control based on one component of current asthma control rather than components of future risk and overall asthma control. Findings highlight the challenge of setting an alert threshold with which GPs will respond as if end users do not perceive the alert as indicative of excessive SABA and high-risk use, then it is unlikely to influence SABA prescribing behaviour.

In Phase 1 of the thesis, the intervention in Zeiger *et al.,*[314] was triggered on excessive SABA use alone, and resulted in a reduction in SABA prescribing for patients without prior specialist asthma care. This raises questions as to how an intervention based solely on excessive SABA use reduced SABA prescribing, whilst in Phase 3 clinicians did not perceive excessive SABA use as high risk when presented alone. This was likely due to the alert in Zeiger *et al.,*[314] forming part of a multicomponent intervention in an integrated health system that facilitated a specialist allergy referral and placed responsibility on patients rather than clinicians alone. Clinicians were alerted to the problem of excessive SABA use in real-time based on dispensing data for information purposes only and did not attempt to influence prescribing behaviour at point of decision making. Through an allergy review and patient education, the multicomponent intervention sought to optimise asthma management and improve asthma control resulting in decreased need for symptom relief in turn reducing clinician SABA prescribing. In this way, the intervention in Zeiger *et al.,*[314] negated the problem identified by Hayward *et al.,*[124] in Chapter 1, that alerts often do not present within prescribing workflow at and therefore have limited influence on decision making.

Chapter 1 highlighted the interchangeable language in the literature used to describe problematic SABA use as overuse, inappropriate use, high use and excessive use. In its current format, the SABA alert described the threshold of three SABAs in three months as high use. SABAs are commonly framed in terms of 'use' as determined by prescribing data, yet in Phase 3, clinicians expressed concern that excessive use based on prescribing data may not be reflective of actual use. As patient's SABA 'use' is dependent on what has been prescribed, framing the problem as SABA use appropriates blame to the patient, maintaining reinforcing clinician power in what Bourdieu describes as the social institutions of medicine.[408,409] A shift in language from SABA 'use' to 'prescribing' refocuses responsibility of the problem upon clinicians who facilitate excessive use through prescribing. Patient SABA use and clinician SABA prescribing are not mutually exclusive with changing the behaviours of both patients and clinicians required to improve asthma management and patient outcomes. However this

raises questions regarding how alert semantics may influence how clinicians engage with the problem in practice. It is important to consider not just how SABA use is quantified but how the language used to describe and define the problem shapes meaning and influences how the SABA alert may be used.

## Defining an alert

Chapter 1 highlighted that no clear distinction is made between CDSS features such as "reminders", "alerts", and "prompts," with terms used interchangeably in the literature. In Phase 1, each of the studies systematically reviewed used different terminology to describe CDSS components, with both McCowan *et al.,*[156] and Eccles *et al*.,[153] referencing the use of prompts whilst Tamblyn *et al*.,[313] and Zeiger *et al.,*[314] referred to alerts. The prompts used in Eccles *et al.,*[153] and McCowan *et al.,*[156] offered suggestions to clinicians on how to respond when in consultation, similar to the SABA alert evaluated in Phase 2, that recommending the patient was invited for asthma review. However, the alerts in Tamblyn *et al.,*[313] and Zeiger *et al.,*[314] went beyond suggestions, instead facilitating actions to improve asthma control. In Tamblyn *et al*.,[313] an alert enabled clinician access to an asthma profile with the option to enrol patients in a home care nurse-monitoring programme, whilst in Zeiger *et al*.,[314] both patients and allergy department were alerted to excessive SABA use as well as clinicians, to facilitate referral and inform/educate patients. This suggests that an alert is inherently different from a prompt or reminder based on the actions generated. This suggests the SABA alert was akin to reminder rather than an alert in its recommendation for review rather than facilitating action for review. These issues are explored further below.

## Using an alert

Phase 3 interviews support the differentiation of alerts from prompts or reminders. In Phase 3 Theme 3 *Using a SABA alert,* two key features distinguished an alert from a prompt or reminder: engagement and action.

The importance of both alert engagement and action and how this relates to the SABA alert

are discussed further below.

### *Engagement*

The literature in Chapter 1 described that CDSSs do not guarantee user engagement, with alerts often ignored or overridden by users. In Phase 1 of the thesis, two of the four studies included in the systematic review captured CDSS user engagement, with one reporting that engagement with the CDSS was poor with several instances of zero interactions, whilst the other reported clinicians failed to interact with the intervention in approximately 60% of cases. However, neither study explored the potential reasons for poor engagement. In Phase 3 of this thesis qualitative findings showed that clinicians did not routinely use the SABA alert and it was often ignored when prescribing. As discussed in Chapter 1, workflow commonly refers to processes or activities carried out in consultation however CDSS use is dependent on the 'thought-flow' (clinical decision-making) and the 'workflow' (the clinical pathway) that often occur at different points when prescribing in consultation or in repeat prescribing activities outside of consultation. Phase 3, Theme 3 *Using a SABA alert* identified that engagement with the alert was dependent on alert presentation, alert design and alert volume. Yet, in its presentation within the QOF box, the alert is not conducive with both thought-flow and work-flow. Such failure is a result of alert design but also a result of 'thought-flow' limited by 'work-flow' time constraints in primary care consultations.

Furthermore, the QOF box is commonly associated with reminders for administration tasks or outstanding issues for routine care in the management of chronic conditions. The SABA alert presentation, coupled with design as a non-modal or soft alert with optional rather than essential engagement, is likely to reinforcing existing attitudes from Phase 3 Theme 1, that excessive SABA use is non-urgent and a low risk concern. As SABA alert design and presentation is not conducive to thought-flow or workflow, this may explain why in the qualitative study in Tower Hamlets, clinicians did not routinely use the SABA alert, as reflected in the very small reduction in SABA prescribing in exploratory analysis in this CCG in Phase 2 of thesis.

### *Action*

Phase 3 Theme 3 identified that use of the SABA alert was dependent on the type of action, the point of action and the support for action. An asthma review was the recommended action following the SABA alert, with clinicians describing the need for asthma review prior to changing SABA prescribing. In Phase 2 of the thesis, a lack of increase in the number of reviews and time to review in the 3 months following the SABA alert is likely dependent on practice follow-up and review availability as well as patient attendance, which the alert fails to address. Phase 3 Theme 3 highlighted that point of action was challenging if excessive use was identified when repeat prescribing, outside of consultation, as the patient was not present. In Zeiger *et al.,*[314] in Phase 1, clinicians were alerted to excessive SABA use outside of consultation*,* however success of the intervention was likely due to the additional components supporting action by alerting both allergy services and patients, rather than an alert requiring solely clinicians action.

As described in Chapter 1, the ARISSA study of at-risk register alerts for severe asthma failed to reduce exacerbations. Despite the intervention consisting of an at-risk alert customised to practices and supported by education and training, the alert had limited influence on receptionist's ability to prioritise appointments for patients identified as at-risk. Smith *et al.,*[160] suggest the lack of reduction in exacerbations was due to combination of training and electronic flagging of at-risk patients. However, the study did not explore the time between alert presentation and review, the components of review and by whom reviews were carried out. If timely reviews do not occur following the alert, opportunities to maximise management and improve outcomes are delayed.

Phase 2 of the thesis, the greatest reduction in SABAs coincided with asthma review however the lack of a clear plan of action on how to proceed following the identification of excessive SABA use, particularly when repeat prescribing, was described as challenging due to general practice capacity and workload. The findings of Phase 2 and the ARISSA study[160] highlight the potential challenge of providing reviews in general practice in response to an alert and may explain the variability in the number of reviews carried out across CCGs.

In contrast the ELECTRA study,[410] an RCT of a specialist nurse intervention for high-risk asthma patients in Tower Hamlets and Newham consisted of review of at-risk asthma patients in a specialist nurse-led clinic. This included educational outreach and promotion of

asthma guidelines to primary care clinicians. In contrast to the challenge of reviewing patients following the SABA alert in Phase 2 and 3 of the thesis, patients in the ELECTRA study[410] were reviewed immediately by a specialist nurse after at-risk status was identified, resulting in delayed presentation for unscheduled care and a reduction in exacerbations. In Phase 1, Zeiger *et al.,*[314] a multicomponent intervention including an alert that presented to clinicians outside of workflow reduced excessive SABA prescribing, despite only 30% of the intervention patients availing of an allergy review. The delivery of a multicomponent intervention in both Zeiger *et al.*[314] in a managed health care organisation and the ELECTRA study in the NHS[410] was facilitated by increased resource availability beyond that of routine NHS primary care. Furthermore the qualitative findings in Phase 3 identified a desire among clinicians to be supported in both the identification of at risk patients and management of asthma across primary care. This suggests that a combination of approaches targeting clinicians, primary care staff and patients may have greater potential to reduce SABA prescribing than a prescribing alert solely targeting clinicians.

SABA prescribing

Phase 3 Theme 2 *Identifying excessive SABA use* highlighted the varying role of receptionists in the repeat prescribing process in the practices in Tower Hamlet. As highlighted in Theme 4 *Interprofessional practice,* there was variable expectation and contrasting opinion among clinical staff that receptionists could and should raise SABA prescribing concerns with GPs. Furthermore, receptionists were not observed engaging with the QOF box where the SABA alert is positioned, instead associating the QOF box with clinical issues beyond the scope of their role. Therefore it remains unclear how the SABA alert that is not positioned within repeat prescribing workflow influenced SABA prescribing. It may be that other staff such as receptionists responded to the SABA alert when managing repeat prescriptions rather than clinicians at point of repeat prescribing. As described in Chapter 1, receptionists contribute to the quality and safety of repeat prescribing and often have increased ownership of 'clinical' issues presenting within the QOF box. This may result in receptionists having an increased awareness of and engagement with the SABA alert, passing on concerns to prescribers rather than the alert influencing behaviour at the point of prescribing. As repeat prescribing is often adapted to local contexts and the receptionists role is likely to vary with differences in receptionist's roles identified in the two practices in which observations were made.

As described in Chapter 1, the introduction of EPS intended to streamline the process by which GPs received, authorised and communicated repeat prescriptions may have reduced informal role of receptionists in highlighting prescribing concerns to improve the safety of repeat prescribing. However, the uptake of EPS was variable and repeat prescription requests by paper remained. In both Theme 2 and Theme 3 clinicians described an intermittently assessing repeat prescriptions prior to authorisation, with varied engagement with the QOF box at this point. It may be that uptake of EPS varied between practices however this was not captured in Phase 2 evaluation of the SABA alert. Furthermore, Chapter 1 highlights the increasing role of clinical pharmacists in the identification and management of repeat prescribing in primary care with clinical pharmacists delegated responsibilities for the management of repeat prescribing. However, it is not clear to what extent clinical pharmacists were employed in general practices across CCGs. In a recent analysis on health care improvement, Braithwaite *et al.*[366] argue that changing behaviours in health care requires consideration of local contexts including the repeat prescription process and how and by whom asthma reviews are followed by and delivered. National distribution of the SABA alert in EMIS practices fails to consider the influence of local contexts on SABA alert use. As the qualitative study in Phase 3 of the thesis involved limited research in three primary care practices in Tower Hamlets and did not include practices in Newham where the effects of the greatest effects SABA alert were observed, it was not possible to determine the influence of local context on the use of the SABA alert.

## 6.5 Overall recommendations for practice

- **Clarity and consistency**

Urgent action is required to change attitudes and perceptions towards problematic SABA use among those involved in the delivery of asthma care at all levels. This should involve three areas: clarity of the evidence on how much SABA is too much, support for the application of evidence into practice, and uniformity in the language used to frame the problem in practice. This should include one UK national asthma guideline to provide clear and consistent advice to clinicians in the primary care management of asthma and the identification of at-risk patients. A combined effort of both top-down and bottom-up approaches is required to change perceptions around SABAs. This should be supported by a national strategy for respiratory disease in England that prioritises asthma care. Findings of this thesis support bottom-up approaches such as the recent IPCRG Asthma Right Care Slide Rule pilot initiative,[65] described in Chapter 1, that seek to increase awareness, challenge attitudes and educate both primary care staff and patients on guideline-based evidence of excessive SABA use and the associated risks. Clearer and consistent use of language and messaging is required to appropriately distinguish between chronic ongoing excessive SABA use as a marker for poor asthma control and a risk factor for adverse outcomes in contrast to excessive SABA use in the management of acute asthma attacks. Failure to do so raises the risk that both health care professionals and patients fail to identify poor asthma control, whilst creating a reluctance to use salbutamol in appropriate situations.

- **Distinction between alerts and reminders**

Findings of this thesis recommend a differentiation between alerts and reminders in practice. When determining whether to implement an alert or reminder, consideration should be given to the intended target, point of presentation, time of present, level of engagement and action required. An alert should be reserved for clinical concerns that require HCP engagement, presenting centrally on screen, aligned to workflow at point of decision-making for which action is required and supported.

In contrast, reminders/pop ups/flags should be reserved for non-urgent concerns that may be addressed by HCPs and non-clinical staff, which do not require alignment with workflow or decision-making and for which engagement and action is optional. Distinctions are needed in the design of CDSSs to promote consistency in practice to reduce alert fatigue and promote engagement and action where it is appropriate.

- **Alerting to at-risk patients**

An alert to identify potentially at risk patients should utilise additional markers of risk rather than SABA use alone. In the absence of linked EHRs to capture secondary care asthma related data, prescribing data should be used to identify ICS underuse and excessive SABA use. Additional risk factors such as asthma-related hospitalisations and AED attendance data should be captured in primary care systems for a targeted approach to the identification of at-risk patients.

- **Alert design and presentation**

Findings of this thesis recommend the optimisation of the design and presentation of an alert to identify patients with poor asthma control who may be potentially at-risk. As SABAs remain the most commonly prescribed inhaler for asthma issued on repeat prescription, alerts should be aligned with clinician's repeat prescribing workflow. Rather than presenting within the QOF box, an alert should contain the three features as recommended by Phansalkar *et al*.,[144] including a signal word to determine the purpose of the alert, a description of the risks of underuse of ICS and excessive use of SABAs and an explanation of consequences of the alert. This should provide clarity for users and enable prioritisation of the alert.

- **Action**

An alert should go beyond information instead facilitating action for review following alert presentation. Without action, the alert merely serves as a reminder. As the majority of SABAs are issued by repeat prescription, an alert should facilitate action at this point. Following the challenge of timely review of patients in general practice identified in Phase's 2 and 3 of this thesis, an alert should facilitate a structured review that is not restricted to general practice. The role of community pharmacists in the structured delivery of asthma review, for example

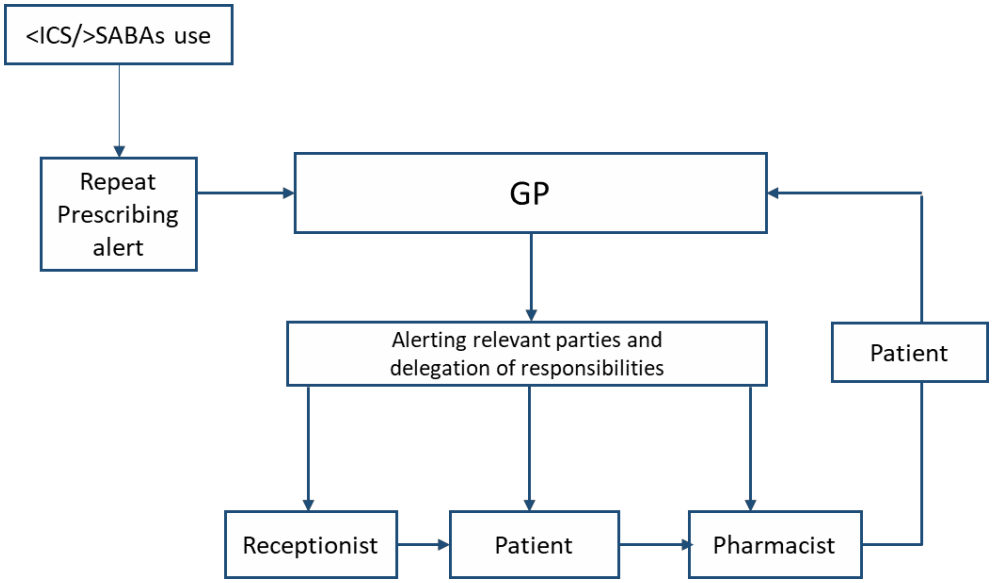
using the SIMPLES[394] approach, as part of a multicomponent intervention, should be explored. A suggestion for a multicomponent alert intervention across primary care is further described below.

- **Multicomponent alert intervention**

Findings suggest that success of an alert to reduce excessive SABA prescribing is dependent timely review of patients. As Phase 3 identified apprehension among GPs and pharmacists to withhold SABAs, an alert should enable the prescriber to generate a pharmacist-delivered asthma review upon the patient's SABA collection at pharmacy. In response to Phase 3 Theme 4 findings, the ownership of an alert should be a GP responsibility with GPs communicating the need for review to the receptionist, the pharmacist and the patient in real-time response to the alert (figure 6.1). Such action addresses both the challenge of patient follow-up in general practice whilst addressing the current underutilisation and lack of guidance for community pharmacists in the management of excessive SABA use. This also offers an alternative to the current signposting of patients from pharmacy back to general practice for review.

Following alert presentation at point of repeat prescribing, an electronic message may be sent to pharmacy using the "message to dispenser" field on the left hand side of EPS. This can provide patient specific information for the attention of the pharmacist. This should be documented on the patient's EHR so the receptionist is aware in the event of patient queries. This information should also be relayed to the patient so they are informed that an asthma review is required in pharmacy prior to SABA being obtained. If poor asthma control is identified following pharmacist's review, an urgent review should be scheduled with a GP. The potential for such an intervention should be further explored with community and CCG pharmacists and Internet pharmacy providers such as Pharmacy2U.

Figure 6. 1 Multicomponent alert intervention




- **Adapation at local level**

Implementation of a multicomponent alert should be tailored to the local area in which it is applied rather than a one-size-fits-all approach at national level. Primary care is increasingly influenced by local cultures, relationships and management that may vary by practices and/or CCG. The implementation of an intervention will require support at all levels. Therefore it is recommended that to increase acceptability, primary care staff should be central in the planning phase to identify and address potential challenges to delivery, to clarify staff roles and responsibilities and to strengthen channels of communication between primary care staff and patients. This thesis has highlighted the need for continuity of care in prescribing and asthma management. At local level there remains potential to enhance asthma management through multidisciplinary working across primary care, in particular through pharmacists working in general practice.

- **Standardised coding and reporting**

Homogeneity in the defining and reporting of asthma outcomes within EHR studies is required. As identified in Phase 1, this includes standardisation in asthma outcomes including

how outcomes are defined and captured in EHR based evaluations. Variations make the design, implementation and evaluations of EHR interventions challenging due to the lack of comparability between studies. This further supports recommendations by Al Sallakh *et al.,*[330] for improvements in the capturing and coding of asthma-related data at the point of care and reporting clarity among studies using EHRs using the RECORD Statement.

## 6.6 Discussion of further work

- **Optimising alert specificity**

**(i) Defining ICS/SABA parameters**

The relationship between patient demographics and varying SABA and ICS parameters associated with AED visits and hospitalisation data will be explored within the same dataset to determine an appropriate ICS/SABA prescribing threshold for optimisation of an alert intervention.

**(ii) Predicting inhaled steroid use**

In primary care data sets the use of ICS and combination inhaler data is commonly captured by inhaler count data despite variations in strength and potency. As acknowledged in Phase 2 of the thesis, it was not possible to include an analysis of ICS and combination inhaler prescribing data due to the challenges of calculating BDP equivalent prescribing in routine primary care data.

In response to the problem identified, data mining algorithms were developed in the course of this thesis to aide the translation of ICS prescribing to BDP equivalent dosing. The rationale was to standardise prescribing data within the EHR, to provide a targeted approach to the identification of problematic prescribing care and potentially at-risk patients in primary care.

Matching algorithms that can detect the name of the ICS or collective ICS medication, the

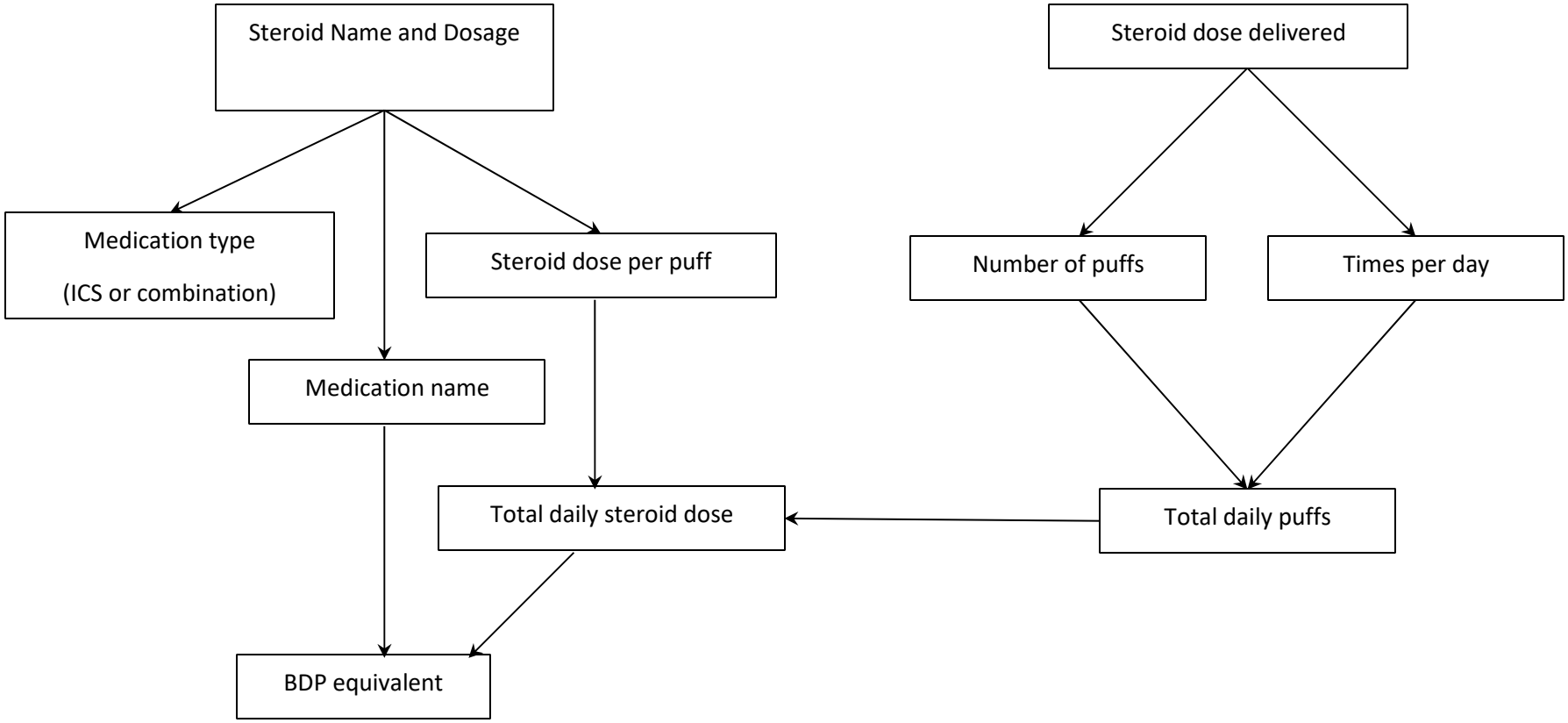
individual dose of the ICS and collective therapy and the number of times the dose is prescribed daily were developed. The algorithm translates ICS to BDP equivalent dose using *R* language software and guidance on steroid dosage from NICE.[108] Although dosages are not strict equivalences they may be used as a guide to similar clinical effectiveness (see figure 6.1 for algorithm pipeline).

Over 65 algorithmic rules were created in order to convert raw routine steroid prescribing data into BDP equivalent from primary care data. These rules can be used to create three new variables and return these in an excel format that can be used for further analysis (see table 6.1). The predictive sensitivity and specificity for the algorithms requires further testing. Further research is required to determine how the calculation of BDP equivalent corticosteroid prescribing to SABA prescribing impacts on the identification and management at-risk patient patients in primary care.

Table 6. 1 Output variables from inhaled steroid data mining algorithm

| Steroid Name | Dose | BDP equivalent |
|---|---|---|
| Beclometasone 200mcg | 2 puffs twice daily | 800 |
| Fluticasone 125mcg | 2 puffs twice daily | 1000 |
| Beclometasone + formoterol 100/6mcg | 2 puffs twice daily | 1000 |
| Budesonide + formoterol 320/6mcg | 2 puffs twice daily | 1600 |

Figure 6. 2 Inhaled steroid beclometasone dipropionate (BDP) equivalent algorithm



### (iii) Determining optimal workflow presentation

Whilst the ideal alert should demonstrate the following characteristics: provision of the right (correct) information, to the right person, in the right format, through the right channel, and at the right time,[114] the correct workflow must first be defined. As the majority of SABAs are issued on repeat prescription both inside or outside of consultation, the system capabilities for alerts presenting within repeat prescribing workflow will explored in collaboration with the CEG.

- **Feasibility of pharmacist review**

Following an exploration for the potential of alerts aligned with repeat prescribing workflow, the acceptability and feasibility of pharmacists in delivering an asthma review to patients identified by a repeat prescribing alert as potentially at risk. The feasibility of both paper and electronic repeat prescribing requests will be explored. This will include a review of the channels of communication between pharmacy and GPs that could be utilised in the delivery of a multicomponent intervention. This will involve a review of EPS use and capabilities as it is currently unclear the extent to which EPS supports reverse flow for messages from dispensers to prescribers. This work will add to the body of recent evidence assessing the increased role of pharmacy in the management of asthma and in particular the delivery of asthma reviews. Pharmacist's training needs will be identified prior to intervention delivery. Unlike recent studies, this work will explore the feasibility of a review in response to the real time identification of potentially at-risk patients at point of repeat prescribing rather than the identification of patients by general practice audit searches or opportunistic identification in pharmacy described in Chapter 1 section 1.2.3. Further research is required to determine the role of online pharmacies in excessive SABA prescribing including the current or potential methods to identify and manage excessive SABA prescribing through online platforms.

- **Patient input**

Further research should include interviews and/or focus groups with patients identified by excessive SABA prescribing to explore SABA use and asthma management from the patient perspective. This will support the design and development of interventions for healthcare

professionals to improve asthma prescribing, management and support for people with asthma. Exploration of the feasibility and acceptability of patients being alerted to excessive SABA use and having a review delivered by a pharmacists prior to SABA dispensing is required.

## 6.7 Critical appraisal of the research process

The specific strengths and limitations of the three Phases of the thesis have been discussed in Chapter 3 (Phase 1), Chapter 4 (Phase 2) and Chapter 5 (Phase 3) respectively with each phase contributing to the literature on the use of an alert for excessive SABA prescribing in primary care. A mixed methods study design enhanced this thesis through three Phases that complement and converge. Firstly, the qualitative findings of Phase 1 (Chapter 3) and Phase 3 (Chapter 5) complemented the quantitative findings of Phase 2 (Chapter 4) by providing an understanding for the variable impact of a SABA alert across the 3 CCGs included in the study. Secondly, both quantitative and qualitative methods converged in this chapter, with qualitative data used to corroborate and confirm findings.[285] A mixed methods approach utilised the views, perceptions and experiences of primary care staff to provide understanding for the effect of the SABA alert on primary and secondary outcomes. Addressing the research question using mixed methods enhanced the credibility of the research process to strengthen the overall thesis outcome.[286]

In terms of limitations, it was not possible to determine potential reasons for the variable effect of the intervention between practices, as qualitative work was carried out in Tower Hamlets only. A sequential mixed methods approach would have been more appropriate with qualitative work influenced by quantitative findings, for example, qualitative work in both Newham and Tower Hamlets may have explained why SABA prescribing reduced in one CCG but not the other. The concurrent mixed methods approach rather than a sequential mixed methods approach was applied due to project time constraints. The original proposed thesis was to collaborate with EMIS health to develop and pilot an alert for excessive SABA prescribing. However EMIS implemented an alert nationally in June 2015 prior to collaboration and the thesis plan evolved to an evaluation project facilitated by CEG. To adequately capture 12 months intervention and follow-up data, Phase 2 data could only be extracted towards the latter part of the final year of the project. Furthermore, the alert implemented by EMIS was not coded for evaluation therefore a number of meetings over

2016-2017 were required to ensure robust methods and extraction of data were applied to meet the study aims and in a suitable format for statistical analysis.

Findings are neither comprehensive nor irrefutable evidence of the structures and processes for SABA prescribing/repeat prescribing in primary care given the limited variety in the numbers of primary care staff included. Pharmacists were recruited by affiliation with practices. However, the involvement of primary care staff was restricted despite initial access gained. For example, access was gained in practice 3 and 4 (Figure 5.1 Participant recruitment flow chart) for interviews but not reception staff. Furthermore, access to the one community pharmacist was gained through strong relationships with Practice 1 however this was not reflected in the additional 3 practices. Some of the issues raised by primary care staff included conjectures about the roles of other staff in the prescribing process. Such issues can only be sufficiently addressed by involving these staff members directly, which may not have been sufficiently captured in this thesis, in particular the role of pharmacists. Flexibility and adaptability was required in data collection to accommodate GPs. This resulted in a discussion with clinicians within a clinical lunchtime meeting due to time constraints in practice. Challenges in primary care recruitment experienced in this study reiterate Riis *et al's*.,[287] process evaluation of the recruitment process in primary care that calls for a more systematic approach to support the recruitment of healthcare professionals in research. The study included only primary care staff and not patients as PPI members are not research participants but advisors. To deliver the project within time frame, people with asthma were not included as active research participants however patients should be incorporated into subsequent research to optimise and enhance the credibility of a future intervention.

## 6.8 Reflexive practice

This section provides a reflexive account detailing the lead researcher's professional and personal background and experience of the research process. As described in Chapter 2, it is recommended that researchers acknowledge and embrace the 'subjectivity' that may influence the research process including] personal and professional backgrounds.[288]

The researcher is a registered nurse held two clinical nursing positions during the research process: as a specialist respiratory and allergy nurse in a tertiary care centre and as an asthma nurse specialist at Asthma UK. The lead researcher had neither professional experience of primary care nor experience with EHR records including electronic alerts but was familiar with concerns in both practice and the literature regarding excessive SABA use. The lead researcher's role was explicit at all points of the data collection process. In the literature, the influence of researcher identity on the research process, in particular health research is commonly undertaken by clinically trained researcher interviewing health care professional peers.[411] A shared identity may increase the openness of HCPs being interviewed, however there is potential for responses to be researcher-led rather than being participant driven. There is a possibility that responses of clinically trained participants may not have been fully expressed assuming the lead researcher had 'insider' knowledge of the topic being researched, and due to apprehension of having one's practice judged. Furthermore, the researcher not having a primary care background may have resulted in interview probing and missed opportunities in direction of questioning due to a lack of understanding of primary care roles and organisational structures. However in contrast given the researcher had no vested interest in primary care risk of bias in line of questioning may have been reduced.

## 6.9 Overall conclusion

Four years after NRAD recommendations, findings of this thesis indicate a continued complacency and uncertainty among healthcare professionals in regards to excessive SABA use. Despite promising reductions in excessive SABA prescribing, an alert focusing solely on clinician's prescribing behaviour fails to address how decisions to prescribe SABAs are influenced in practice and the complexity of asthma management in primary care. Strong leadership is required to promote consistent application of the evidence base for SABA use and to challenge the ways in which health care professionals think about asthma. Clear and consistent guidance on excessive SABA use is required, with further research needed on how this can be translated into practice. This thesis provides a base for alert optimisation to meet the needs of primary care and the challenges of asthma management. This should involve an intervention that supports both the identification and follow-up of potentially at-risk patients that is not limited to SABA prescribing. This will require a collaborative effort involving people with asthma and wider primary care to help identify those with poor asthma control who are at increased risk of asthma attacks.

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# Appendices

*[Intentionally left blank]*

Appendix 3. 1 Detailed intervention characteristics

| Features of CDSSs | McCowan | Eccles | Zeiger | Tamblyn |
|---|---|---|---|---|
| Context | | | | |
| Clinical setting | Primary Care (NHS) | Primary care (NHS) | Primary Care (Kaiser Permanente Managed Care Organisation) | Primary Care (Insured Health care system) |
| Clinical task | Asthma management | Asthma management | SABA use | Asthma management |
| Unit of optimization | Process and patient outcomes | Process and patient outcomes | Process and patient outcomes | Process and patient outcomes |
| Relation to point of care | In-consultation | In-consultation | Non-specific | In-consultation |
| External behavior modification programs | Not reported | Not reported | Not reported | Not reported |
| Potential barriers | Double data entry required | Method of intervention trigger | None identified | Non-asthma specific consultation |
| Knowledge and data source | | | | |
| Clinical knowledge source | British Asthma Guidelines | Study developed guidelines | National Asthma Education & Prevention Programme/Global Initiative for Asthma | Canadian consensus guidelines |
| Data source | Manually entered | Electronic health record | Research data warehouse | Electronic health record |
| Data coding | Not reported | Not reported | Not reported | Not reported |
| Degree of customisation | Generic | Generic | Personalised | Personalised |
| Update mechanism | Not reported | Not reported | Not reported | Not reported |

| Decision Support | McCowan | Eccles | Zeiger | Tamblyn |
|---|---|---|---|---|
| Type of system | *Asthma Crystal Byte*<br>Computer decision support based on asthma guidelines, clinical scenarios and reminders. | *Computer decision support system (CDSS)*<br>Asthma management and prescribing suggestions based on guidelines, clinical scenarios and health record information | *Real-time outreach*<br>Real-time identification, notification, and facilitated allergy specialist referral for excessive SABA users. | *Asthma Decision Support (ADS)*<br>A dashboard alert, decision support for evidence-based asthma management and asthma home care and monitoring programme. |
| Reasoning method | Not reported | Not reported | Not reported | Not reported |
| Alert activation | Specific presentation complaints or features would trigger a series of prompts based on a previously determined protocol, which would have included a warning for SABA overuse. | Contextualised prompts including management suggestions were triggered when an asthma morbidity code was entered. | An electronic message within the electronic medical record system was sent to a patient's primary care provider, once-only, when a patient with excessive SABA use was identified. | Alert automatically activates upon opening the medical record of a patient with out-of- control asthma. Out-of-control asthma defined as having had an ER visit or a hospitalisation for respiratory-related problems in the past 3 months and/or the excess use (>250 doses dispensed) of fast-acting b-agonist (FABA) in the past 3 months. |
| Clinical urgency | Not reported | Not reported | Not reported | Not reported |
| Recommendation explictness | Explicit | Explicit | Explicit | Explicit |
| Logistical complexity | Simple | Simple | Simple | Simple |
| Response requirement | None | None | None | None |

| Information delivery | McCowan | Eccles | Zeiger | Tamblyn |
|---|---|---|---|---|
| Delivery format | Electronic | Electronic | Electronic | Electronic |
| Delivery mode | Voluntary | Voluntary | Voluntary | Voluntary |
| Integration | No-the programme was delivered on a 3 ½ inch floppy disk to be installed on participants Microsoft Windows compatible computer desktop to be used for asthma consultations. | No-the CDSS was a programme accessible from within the main computerised operating system of the two suppliers. The guideline was a separate pathway within the clinical system. | Yes-the asthma out-reach used the standard Kaiser Permanente Southern California (KPSC) electronic medical record system and electronic registry that allows physicians access to dispensing data and hospital data in a managed care organisation (MCO). | Yes-the ADS can be accessed from a tab in the electronic health record for intervention physicians or from the dashboard alert, when it appears. |
| Explanation availability | The research team constructed non-judgemental feedback and management suggestions based on British Asthma Guidelines but it is not clear if the rationale behindrecommendations was presented to physicians. | It was unclear whether clinicians were informed of the guideline evidence when recommendations were presented or whether the recommendations prompted the clinician to access the separate pathway for the guideline. | Physicians- 'Kaiser Permanente and other groups have documented this amount of albuterol is a sign of uncontrolled asthma…'<br>Patients- 'Kaiser Permanente and other groups have shown that care by allergists helps to improve asthma control'; 'too much use of [reliever] may indicate your asthma control could be better.' | Dashboard alert: 'since the last time you accessed the record, new information is available.' Decision support for evidence-based asthma management: provides physicians with access to Canadian asthma guidelines, including translation into assessment tools and recommendations. |
| Provision of a recommendation not just an assessment | Prompts included e.g. 'check inhaler technique,' 'review compliance,' 'consider increasing dose of preventer inhaler.' | The system offered suggestions for management including prescribing. | Included recommendations for treatment e.g. commence preventer medication, physician contact and allergy referral. | Patient specific recommendations generated. |

| Information delivery | McCowan | Eccles | Zeiger | Tamblyn |
|---|---|---|---|---|
| Recommendations executed by noting agreement i.e. click 'OK' | Not reported | Not reported | Not applicable | Dashboard alert- 'Click here to enrol your patient in the Asthma Assist Program immediately'; 'update suggested treatment'; 'proceed with changes.'<br>Decision support- patient specific recommendations generated and once selected, prescriptions and action plans where automatically generated. |
| Request documentation of reasons if CDSS recommendations not followed | Not reported | Not reported | Electronic message was sent to physicians informing of the patient's uncontrolled asthma status but did provide recommendations for the physician to act upon. | The dashboard alert could be exited however no further information was reported. |
| Interactive delivery | Yes | Yes | Not applicable | Yes |
| Additional clinical data entry not required | No- the system used data entered on a specialised data entry screen. | Yes-the system anticipated clinicians' requirements by using the information contained within a patient's computerised record. | Yes-patients were identified using computer algorithm data collected in the KPSC research data warehouse. No clinician input was necessary. | Yes-patient's asthma control was determined dynamically, based on a daily retrieval of newly dispensed prescriptions and physician visit information from the provincial health insurance databases at the Regie de l'assurance maladie Quebec (RAMQ). |

| Workflow | McCowan | Eccles | Zeiger | Tamblyn |
|---|---|---|---|---|
| System user | General practitioner | Doctor or nurse | Physician | Physician |
| Target decision maker | General practitioner | Doctor or nurse | Physician and patient | Physician |
| Data input intermediary | General practitioner | Doctor or nurse | Not required | Not required |
| Output intermediary | Not required | Not required | Not required | Not required |
| Workflow integration | Intervention software ran alongside practice software | To access guidelines the clinical system had to be exited | Generated within KPSC electronic medical record system | Integrated with clinician workflow |
| Auxiliary features | | | | |
| Local user involvement in development process | The Asthma Crystal Byte software was designed and developed by a project team, reviewed over an 18 month period by a steering group; 'The General Practitioners in Asthma Group.' | Not reported | Not reported | Not reported |
| Provision of decision support to patients as well as providers | Customised self-management plans and patient advice sheets | Not reported | Physicians were contacted by electronic message and patients by letter | Asthma action plans were automatically generated when recommendation accepted |

Appendix 4. 1 Ethnicity coding categories

| 9S and 9i Read Codes | Read Text | 2011 Census Category | National Statistics 16+1 | NS 16+1 text | Final coding categories |
|---|---|---|---|---|---|
| 9i0 | British or mixed British | 9i0 | 1. British or Mixed British | British or Mixed British | White |
| 9S1 | Ethnic White | 9i0 | 1. British or Mixed British | British or Mixed British | White |
| 9S10 | Ethnic White British | 9i0 | 1. British or Mixed British | British or Mixed British | White |
| 9S14 | Ethnic White British Other | 9i0 | 1. British or Mixed British | British or Mixed British | White |
| 9i9 | Bangladeshi or British Bangladeshi | 9i9 | 10. Bangladeshi or British Bangladeshi | Bangladeshi or British Bangladeshi | South Asian |
| 9S8 | Bangladeshi | 9i9 | 10. Bangladeshi or British Bangladeshi | Bangladeshi or British Bangladeshi | South Asian |
| 9iA | Other Asian | 9iA | 11. Other Asian | Other Asian | South Asian |
| 9iA1 | Other Asian Punjabi | 9iA1 | 11. Other Asian | Other Asian | South Asian |
| 9iA2 | Other Asian Kashmiri | 9iA2 | 11. Other Asian | Other Asian | South Asian |
| 9iA3 | Other Asian East African Asian | 9iA3 | 11. Other Asian | Other Asian | South Asian |
| 9iA4 | Other Asian Sri Lankan | 9iA4 | 11. Other Asian | Other Asian | South Asian |
| 9iA5 | Other Asian Tamil | 9iA5 | 11. Other Asian | Other Asian | South Asian |
| 9iA6 | Other Asian Sinhalese | 9iA6 | 11. Other Asian | Other Asian | South Asian |
| 9iA7 | Other Asian Caribbean | 9iA7 | 11. Other Asian | Other Asian | South Asian |
| 9iA8 | Other Asian British | 9iA8 | 11. Other Asian | Other Asian | South Asian |

| | | | | | |
|---|---|---|---|---|---|
| 9iA9 | Other mixed Asian | 9iA9 | 11. Other Asian | Other Asian | South Asian |
| 9iAA | Other Asian or Asian unspecified | 9iAA | 11. Other Asian | Other Asian | South Asian |
| 9SA6 | Other Ethnic E African Asian / Indo-Carib | 9iA3 | 11. Other Asian | Other Asian | South Asian |
| 9S and 9i Read Codes | Read Text | 2011 Census Category | National Statistics 16+1 | NS 16+1 text | Final coding categories |
| 9SA7 | Other Ethnic Indian sub-continent | 9iA | 11. Other Asian | Other Asian | South Asian |
| 9SA8 | Other Ethnic Other Asian | 9iA | 11. Other Asian | Other Asian | South Asian |
| 9SH | Other Ethnic Asian | 9iA | 11. Other Asian | Other Asian | South Asian |
| 9iB | Caribbean | 9iB | 12. Caribbean | Caribbean | Black |
| 9S2 | Ethnic Black Caribbean | 9iB | 12. Caribbean | Caribbean | Black |
| 9iC | African | 9iC | 13. African | African | Black |
| 9S3 | Ethnic Black African | 9iC | 13. African | African | Black |
| 9S44 | Black other African country | 9iC | 13. African | African | Black |
| 9SA5 | Other Ethnic African | 9iC | 13. African | African | Black |
| 9iD | Other Black | 9iD | 14. Other Black | Other Black | Black |
| 9iD0 | Somali | 9iD0 | 14. Other Black | Other Black | Black |
| 9iD1 | Nigerian | 9iD1 | 14. Other Black | Other Black | Black |
| 9iD2 | Black British | 9iD2 | 14. Other Black | Other Black | Black |
| 9iD3 | Black mixed | 9iD3 | 14. Other Black | Other Black | Black |
| 9iD4 | Black other | 9iD4 | 14. Other Black | Other Black | Black |
| 9S4 | Black other non-mixed | 9iD | 14. Other Black | Other Black | Black |
| 9S41 | Black British | 9iD2 | 14. Other Black | Other Black | Black |
| 9S42 | Black Caribbean / W.I. / Guyana | 9iD | 14. Other Black | Other Black | Black |
| 9S43 | Black North African / Arab / Iranian | 9iD | 14. Other Black | Other Black | Black |

| | | | | | |
|---|---|---|---|---|---|
| 9S45 | Black E African / Indo-Caribb | 9iD | 14. Other Black | Other Black | Black |
| 9S46 | Black Indian sub-continent | 9iD | 14. Other Black | Other Black | Black |
| 9S47 | Black other Asian | 9iD | 14. Other Black | Other Black | Black |
| 9S48 | Black other | 9iD | 14. Other Black | Other Black | Black |
| 9S5 | Black other mixed | 9iD | 14. Other Black | Other Black | Black |
| 9SA3 | Other Ethnic Caribbean Is. / W.I. / Guyana | 9iD | 14. Other Black | Other Black | Black |
| 9SG | Other Ethnic Black | 9iD | 14. Other Black | Other Black | Black |
| 9iE | Chinese | 9iE | 15. Chinese | Chinese | Other |
| 9S9 | Chinese | 9iE | 15. Chinese | Chinese | Other |
| 9iF | Other | 9iF | 16. Other | Other | Other |
| 9iF0 | Other Vietnamese | 9iF0 | 16. Other | Other | Other |
| 9iF1 | Other Japanese | 9iF1 | 16. Other | Other | Other |
| 9iF2 | Other Filipino | 9iF2 | 16. Other | Other | Other |
| 9iF3 | Other Malaysian | 9iF3 | 16. Other | Other | Other |
| 9iF4 | Other Buddhist | 9iF4 | 16. Other | Other | Other |
| 9iF5 | Other Hindu | 9iF5 | 16. Other | Other | Other |
| 9iF6 | Other Jewish | 9iF6 | 16. Other | Other | Other |
| 9iF7 | Other Muslim | 9iF7 | 16. Other | Other | Other |
| 9iF8 | Other Sikh | 9iF8 | 16. Other | Other | Other |
| 9iF9 | Other Arab | 9iF9 | 16. Other | Other | Other |
| 9iFA | Other North African | 9iFA | 16. Other | Other | Other |
| 9iFB | Other Mid Eastern (excl. Isreali, Iranian, & Arab) | 9iFB | 16. Other | Other | Other |
| 9iFC | Other Isreali | 9iFC | 16. Other | Other | Other |
| 9iFD | Other Iranian | 9iFD | 16. Other | Other | Other |

| | | | | | |
|---|---|---|---|---|---|
| 9iFE | Other Kurdish | 9iFE | 16. Other | Other | Other |
| 9iFF | Other Moroccan | 9iFF | 16. Other | Other | Other |
| 9iFG | Other Latin American | 9iFG | 16. Other | Other | Other |
| 9iFH | Other South & Central American | 9iFH | 16. Other | Other | Other |
| 9iFJ | Other Mauritian / Seychellois / Maldivian / St. Helena | 9iFJ | 16. Other | Other | Other |
| 9iFK | Other unspecified | 9iFK | 16. Other | Other | Other |
| 9SA | Other Ethnic non-mixed | 9iF | 16. Other | Other | Other |
| 9SA1 | Other Ethnic British Specific Minor. | 9iF | 16. Other | Other | Other |
| 9SA2 | Other Ethnic British Unspecific Minor. | 9iF | 16. Other | Other | Other |
| 9S and 9i Read Codes | Read Text | 2011 Census Category | National Statistics 16+1 | NS 16+1 text | Final coding categories |
| 9SA4 | Other Ethnic N African Arab / Iranian | 9iFA | 16. Other | Other | Other |
| 9SAA | Other Ethnic Greek / Greek Cypriot | 9iF | 16. Other | Other | Other |
| 9SAB | Other Ethnic Turkish / Turkish Cypriot | 9iF | 16. Other | Other | Other |
| 9SAC | Other Ethnic European | 9iF | 16. Other | Other | Other |
| 9SAD | Other Ethnic EEC | 9iF | 16. Other | Other | Other |
| 9SC | Vietnamese | 9iF0 | 16. Other | Other | Other |
| 9SJ | Other Ethnic | 9iF | 16. Other | Other | Other |
| 9iG | Not stated | 9iG | 17. Not Stated | Not Stated | Not Stated |
| 9SD | Patient refused | 9iG | 17. Not Stated | Not Stated | Not Stated |
| 9SE | Not Recorded | 9iG | 17. Not Stated | Not Stated | Not Stated |
| 9SZ | Ethnic groups NOS | 9iG | 17. Not Stated | Not Stated | Not Stated |
| 9i1 | Irish | 9i1 | 2. Irish | Irish | White |
| 9S11 | Ethnic White Irish | 9i1 | 2. Irish | Irish | White |
| 9SA9 | Other Ethnic Irish | 9i1 | 2. Irish | Irish | White |

| | | | | | |
|---|---|---|---|---|---|
| 9i2 | Other White | 9i2 | 3. Other White | Other White | White |
| 9i20 | White English | 9i20 | 3. Other White | Other White | White |
| 9i21 | White Scottish | 9i21 | 3. Other White | Other White | White |
| 9i22 | White Welsh | 9i22 | 3. Other White | Other White | White |
| 9i23 | White Cornish | 9i23 | 3. Other White | Other White | White |
| 9i24 | White Northern Irish | 9i24 | 3. Other White | Other White | White |
| 9i26 | White Cypriot | 9i26 | 3. Other White | Other White | White |
| 9i27 | White Greek | 9i27 | 3. Other White | Other White | White |
| 9i28 | White Greek Cypriot | 9i28 | 3. Other White | Other White | White |
| 9i29 | White Turkish | 9i29 | 3. Other White | Other White | White |
| 9i2A | White Turkish Cypriot | 9i2A | 3. Other White | Other White | White |
| 9S and 9i Read Codes | Read Text | 2011 Census Category | National Statistics 16+1 | NS 16+1 text | Final coding categories |
| 9i2B | White Italian | 9i2B | 3. Other White | Other White | White |
| 9i2C | White Irish Traveller | 9i2C | 3. Other White | Other White | White |
| 9i2D | White Traveller | 9i2D | 3. Other White | Other White | White |
| 9i2E | White Gypsy Romany | 9i2E | 3. Other White | Other White | White |
| 9i2F | White Polish | 9i2F | 3. Other White | Other White | White |
| 9i2G | White Estonian | 9i2G | 3. Other White | Other White | White |
| 9i2H | White Russian | 9i2H | 3. Other White | Other White | White |
| 9i2J | White Kosovan | 9i2J | 3. Other White | Other White | White |
| 9i2K | White Albanian | 9i2K | 3. Other White | Other White | White |
| 9i2L | White Bosnian | 9i2L | 3. Other White | Other White | White |
| 9i2M | White Croatian | 9i2M | 3. Other White | Other White | White |
| 9i2N | White Serbian | 9i2N | 3. Other White | Other White | White |

| | | | | | |
|---|---|---|---|---|---|
| 9i2P | White Former Yugoslavia | 9i2P | 3. Other White | Other White | White |
| 9i2Q | White Mixed Irish & Other | 9i2Q | 3. Other White | Other White | White |
| 9i2R | White Other European | 9i2R | 3. Other White | Other White | White |
| 9i2S | White Mixed | 9i2S | 3. Other White | Other White | White |
| 9i2T | White Unspecified | 9i2T | 3. Other White | Other White | White |
| 9S12 | Ethnic White Other | 9i2 | 3. Other White | Other White | White |
| 9S13 | Ethnic White Scottish | 9i21 | 3. Other White | Other White | White |
| 9i3 | White and Black Caribbean | 9i3 | 4. White + Black Caribbean | White + Black Caribbean | Black |
| 9SB5 | Other Ethnic Black Caribbean & White | 9i3 | 4. White + Black Caribbean | White + Black Caribbean | Black |
| 9i4 | White and Black African | 9i4 | 5. White + Black African | White + Black African | Black |
| 9SB6 | Other Ethnic African & White | 9i4 | 5. White + Black African | White + Black African | Black |
| 9S and 9i Read Codes | Read Text | 2011 Census Category | National Statistics 16+1 | NS 16+1 text | Final coding categories |
| 9i5 | White and Asian | 9i5 | 6. White + Asian | White + Asian | South Asian |
| 9SB2 | Other Ethnic Asian and White | 9i5 | 6. White + Asian | White + Asian | South Asian |
| 9i6 | Other mixed | 9i6 | 7. Other Mixed | Other Mixed | Other |
| 9i60 | Other mixed Black and Asian | 9i60 | 7. Other Mixed | Other Mixed | Other |
| 9i61 | Other mixed Black and Chinese | 9i61 | 7. Other Mixed | Other Mixed | Other |
| 9i62 | Other mixed Black and White | 9i62 | 7. Other Mixed | Other Mixed | Other |
| | | | | | |
| 9i63 | Other mixed White and Chinese | 9i63 | 7. Other Mixed | Other Mixed | Other |
| 9i64 | Other mixed Asian and Chinese | 9i64 | 7. Other Mixed | Other Mixed | Other |

| | | | | | |
|---|---|---|---|---|---|
| 9i65 | Other mixed or mixed unspecified | 9i65 | 7. Other Mixed | Other Mixed | Other |
| 9S51 | Black other Black and White | 9i62 | 7. Other Mixed | Other Mixed | Other |
| 9S52 | Black other Black and Asian | 9i6 | 7. Other Mixed | Other Mixed | Other |
| 9SB | Other Ethnic mixed | 9i6 | 7. Other Mixed | Other Mixed | Other |
| 9SB1 | Other Ethnic Black and White | 9i62 | 7. Other Mixed | Other Mixed | Other |
| 9SB3 | Other Ethnic mixed White | 9i6 | 7. Other Mixed | Other Mixed | Other |
| 9SB4 | Other Ethnic other mixed | 9i6 | 7. Other Mixed | Other Mixed | Other |
| 9i7 | Indian or British Indian | 9i7 | 8. Indian or British Indian | Indian or British Indian | South Asian |
| 9S6 | Indian | 9i7 | 8. Indian or British Indian | Indian or British Indian | South Asian |
| 9i8 | Pakistani or British Pakistani | 9i8 | 9. Pakistani or British Pakistani | Pakistani or British Pakistani | South Asian |
| 9S7 | Pakistani | 9i8 | 9. Pakistani or British Pakistani | Pakistani or British Pakistani | South Asian |
| 9i | Incomplete | 9i | Unclassified | Unclassified | Not Stated |
| 9S | Others | Others | Unclassified | Unclassified | Not Stated |
| 9i00 | White British | 9i0 | 1. British or mixed | British or Mixed British | White |
| 9S and 9i Read Codes | Read Text | 2011 Census Category | National Statistics 16+1 | NS 16+1 text | Final coding categories |
| 9i10 | White Irish | 9i1 | 2. Irish | Irish | White |
| 9i25 | Ulster Scots - ethnic category 2001 census | | | | White |
| 9S42-1 | Black Caribbean | | | | Black |
| 9S43-1 | Black North African | | | | Black |
| 9S43-2 | Black Arab | | | | Black |
| 9S45-1 | Black East African Asian | | | | Black |

| | | | | | |
|---|---|---|---|---|---|
| 9SA4-1 | North African Arab (NMO) | | | | Other |
| 9SAA-1 | Greek (NMO) | | | | Other |
| 9SAA-2 | Greek Cypriot (NMO) | | | | Other |
| 9SAB-1 | Turkish (NMO) | | | | Other |
| 9SAB-2 | Turkish Cypriot (NMO) | | | | Other |
| 9SI | Irish traveller | | | | White |
| 9S42-2 | Black West Indian | | | | Black |
| 9S42-3 | Black Guyana | | | | Black |
| 9SA3-3 | Guyana (NMO) | | | | Black |
| EMISNQNE35 | | | | | Not Stated |
| PCSDT4523_13274 | | | | | Not Stated |
| SITE1AS1 | | | | | Not Stated |
| SITE1BR1 | | | | | Not Stated |
| SITE1BR2 | | | | | Not Stated |
| 9SA4-2 | Iranian (NMO) | | | | Other |

Appendix 4. 2 Inhaled corticosteroids for inclusion

| Steroid 60 puffs Name, Dosage and Quantity |
| --- |
| Flixotide 100micrograms/dose Accuhaler (GlaxoSmithKline UK Ltd) |
| Flixotide 500micrograms/dose Accuhaler (GlaxoSmithKline UK Ltd) |
| Flixotide 50micrograms/dose Accuhaler (GlaxoSmithKline UK Ltd) |
| Fluticasone 100micrograms/dose dry powder inhaler |
| Fluticasone 250micrograms/dose dry powder inhaler |
| Fluticasone 500micrograms/dose dry powder inhaler |
| Fluticasone Propionate Dry Powder Breath-Actuated Inhaler 500 micrograms |
| Fluticasone propionate 100micrograms/dose dry powder inhaler |
| Fluticasone propionate 250micrograms/dose dry powder inhaler |
| Fluticasone propionate 500micrograms/dose dry powder inhaler |
| Steroid 100 puffs Name, Dosage and Quantity |
| Beclometasone 200micrograms/dose dry powder inhaler |
| Steroid 120 puffs Name, Dosage and Quantity |
| Flixotide 250micrograms/dose Evohaler (GlaxoSmithKline UK Ltd) |
| Fluticasone 125micrograms/dose inhaler CFC free |
| Fluticasone 250micrograms/dose inhaler CFC free |
| Fluticasone 50micrograms/dose inhaler CFC free |
| Steroid 200 puffs Name, Dosage and Quantity |
| Asmabec 100 Clickhaler (Focus Pharmaceuticals Ltd) |
| Beclometasone Breath-Actuated Inhaler (Cfc-Free) 100 micrograms/actuation |
| Beclometasone Cfc-free inhaler 100 micrograms/actuation~(c66W.) |
| Beclometasone 100micrograms/dose breath actuated inhaler CFC free |
| Beclometasone 100micrograms/dose inhaler CFC free |
| Beclometasone 200micrograms/dose dry powder inhaler |
| Beclometasone 50micrograms/dose inhaler CFC free |
| Clenil Modulite Cfc-Free Inhaler 100 micrograms/actuation |

Appendix 4.2. Inhaled corticosteroids for inclusion (continued)

| Steroid 200 puffs Name, Dosage and Quantity |
|---|
| Clenil Modulite Cfc-free inhaler 100 micrograms/actuation~(c66d.) |
| Clenil Modulite Cfc-Free Inhaler 200 micrograms/actuation |
| Clenil Modulite Cfc-Free Inhaler 250 micrograms/actuation |
| Clenil Modulite Cfc-Free Inhaler 50 micrograms/actuation |
| Clenil Modulite 100micrograms/dose inhaler (Chiesi Ltd) |
| Clenil Modulite 200micrograms/dose inhaler (Chiesi Ltd) |
| Clenil Modulite 250micrograms/dose inhaler (Chiesi Ltd) |
| Clenil Modulite 50micrograms/dose inhaler (Chiesi Ltd) |
| Easyhaler Beclometasone 200micrograms/dose dry powder inhaler (Orion Pharma (UK) Ltd) |
| Qvar 100 Autohaler Cfc-Free Breath-Actuated Inhaler 100 micrograms/dose |
| Qvar 100 Autohaler (Teva UK Ltd) |
| Qvar 100 inhaler (Teva UK Ltd) |
| Qvar 100micrograms/dose Easi-Breathe inhaler (Teva UK Ltd) |
| Qvar 50 Autohaler (Teva UK Ltd) |
| Qvar 50 inhaler (Teva UK Ltd) |
| Qvar 50micrograms/dose Easi-Breathe inhaler (Teva UK Ltd) |

Appendix 4. 3 Long-acting beta2-agonist inhalers for inclusion

| Long–acting beta2-agoinist Name, Dosage and Quantity |
|---|
| Foradil 12microgram inhalation powder capsules with device (Novartis Pharmaceuticals UK Ltd) |
| Oxis 6 Turbohaler (AstraZeneca UK Ltd) |
| Oxis 12 Turbohaler (AstraZeneca UK Ltd) |
| Formoterol Dry Powder Inhaler 12 micrograms/actuation, 60 dose |
| Formoterol 6 micrograms/dose dry powder inhaler |
| Formoterol 12micrograms/dose dry powder inhaler |
| Serevent 50micrograms/dose Accuhaler (GlaxosmithKline UK Ltd) |
| Salmeterol 50micrograms/dose dry powder inhaler |
| Salmeterol 50 microgram inhalation powder blisters |
| Atimos Modulite |
| Formoterol 12micrograms/dose inhaler CFC free |
| Formoterol Dry Powder Inhaler 12micrograms/actuation, 120 dose |
| Formoterol Easyhaler 12micrograms/dose dry powder inhaler (Orion Pharma (UK) Ltd) |
| Serevent 25micrograms/dose Evohaler (GlaxoSmithKline UK Ltd) |
| Serevent 25micrograms/dose inhaler (GlaxoSmithKline UK Ltd) |
| Salmeterol 25 Micrograms/dose inhaler |

Appendix 4. 4 ICS/LABA Combination inhalers for inclusion

| Compound 120 puffs Name, Dosage and Quantity |
| --- |
| Budesonide 100micrograms/dose / Formoterol 6micrograms/dose dry powder inhaler / |
| Budesonide 200micrograms/dose / Formoterol 6micrograms/dose dry powder inhaler |
| Budesonide And Formoterol Dry Powder Inhaler 100 micrograms + 6 micrograms/actuation |
| Budesonide And Formoterol Dry Powder Inhaler 200 micrograms + 6 micrograms/actuation |
| DuoResp Spiromax 160micrograms/dose / 4.5micrograms/dose dry powder inhaler (Teva UK Ltd) |
| Fluticasone 125micrograms/dose / Formoterol 5micrograms/dose inhaler CFC free/ |
| Fluticasone 125micrograms/dose / Salmeterol 25micrograms/dose inhaler CFC free / |
| Fluticasone 250micrograms/dose / Formoterol 10micrograms/dose inhaler CFC free |
| Fluticasone 250micrograms/dose / Salmeterol 25micrograms/dose inhaler CFC free/ |
| Fluticasone 50micrograms/dose / Formoterol 5micrograms/dose inhaler CFC free / |
| Fluticasone 50micrograms/dose / Salmeterol 25micrograms/dose inhaler CFC free / |
| Fluticasone And Salmeterol Cfc-Free Inhaler 125 micrograms + 25 micrograms/actuation/ |
| Fluticasone And Salmeterol Cfc-Free Inhaler 250 micrograms + 25 micrograms/actuation / |
| Fluticasone And Salmeterol Cfc-free inhaler 250 micrograms + 25 micrograms/actuation~(c1Dw.) / |
| Fluticasone Propionate And Salmeterol Cfc-Free Inhaler 125 micrograms + 25 micrograms/actuation / |
| Fluticasone Propionate And Salmeterol Cfc-Free Inhaler 250 micrograms + 25 micrograms/actuation / |
| Fluticasone Propionate And Salmeterol Cfc-Free Inhaler 50 micrograms + 25 micrograms/actuation |
| Flutiform 125micrograms/dose / 5micrograms/dose inhaler (Napp Pharmaceuticals Ltd) |
| Fostair 100micrograms/dose / 6micrograms/dose inhaler/ Fostair 200micrograms/dose/6micrograms/dose inhaler (Chiesi Ltd) |
| Seretide 125 Evohaler (GlaxoSmithKline UK Ltd) / Seretide 250 Evohaler Cfc-Free Inhaler / Seretide 250 Evohaler (GlaxoSmithKline UK Ltd) /Seretide 50 Evohaler (GlaxoSmithKline UK Ltd) |
| Symbicort 100/6 Turbohaler (AstraZeneca UK Ltd) / Symbicort 200/6 Turbohaler (AstraZeneca UK Ltd) |

Appendix 4.4. ICS/LABA Combination inhalers for inclusion (continued)

| Compound 30 puffs Name, Dosage and Quantity |
| --- |
| Relvar Ellipta 92micrograms/dose / 22micrograms/dose dry powder inhaler (GlaxoSmithKline UK Ltd) |
| Compound 60 puffs Name, Dosage and Quantity |
| Budesonide 400micrograms/dose / Formoterol 12micrograms/dose dry powder inhaler Fluticasone 100micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler Fluticasone 250micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler Fluticasone 500micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler Fluticasone And Salmeterol Dry Powder Inhaler 500 micrograms + 50 micrograms/actuation Fluticasone propionate 100micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler Fluticasone propionate 250micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler Fluticasone propionate 500micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler Fluticasone Propionate And Salmeterol Dry Powder Inhaler 500 micrograms + 50 micrograms/actuation Seretide 100 Accuhaler (GlaxoSmithKline UK Ltd) /Seretide 250 Accuhaler (GlaxoSmithKline UK Ltd) Seretide 500 Accuhaler Dry Powder For Inhalation /Seretide 500 Accuhaler (GlaxoSmithKline UK Ltd) Symbicort 400/12 Turbohaler (AstraZeneca UK Ltd) |

Appendix 4. 5 Oral steroids for inclusion

| Oral Steroid Name, Dosage and Quantity |
| --- |
| Prednisolone 2.5mg gastro-resistant tablets |
| Prednisolone 5mg gastro-resistant tablets |
| Prednisolone 25mg tablets |
| Prednisolone 1mg tablets |
| Prednisolone 2.5mg tablets |
| Prednisolone 5mg/5ml oral solution unit dose |
| Prednisolone 20mg tablets |
| Prednisolone 10mg tablets |
| Prednisolone 15mg/5ml oral solution |

Appendix 4. 6 Patient eligibility searches: Intervention group

| Rule 1 | If Rule Passed : **Goto Next Rule** | If Rule Failed : **Exclude from final result** |
|---|---|---|

Include **Patients** with **Patient Details** where:
the **Date of Birth** is after or on 17-Jun-1940 and before or on 16-Jun-2011

| Rule 2 | If Rule Passed : **Goto Next Rule** | If Rule Failed : **Exclude from final result** |
|---|---|---|

**Must have**

Include **Patients** with **Clinical Codes** where:
the **Clinical Code** is
Asthma resolved, Asthma resolved, Asthma (excluding Acute exacerbation of asthma)
, Chronic asthmatic bronchitis, Exercise induced asthma or Asthma-chronic obstructive pulmonary disease overlap syndrom
and the **Episode (First, New...)** is all values (excluding Review and End)
and the **Date** is before or on the search date
Ordering by **Date** select the latest
and check that:
the **Clinical Code** is
Asthma (excluding Acute exacerbation of asthma), Chronic asthmatic bronchitis, etc...
and the **Date** is before or on the search date

**And**

Include **Patients** with **Medication Issues** where:
the **Drug** is Selective Beta2-Adrenoceptor Stimulants (excluding Pirbuterol, Reproterol Hydrochloride, Rimiterol Hydrobromide, Tulobuterol Hydrochloride, Indacaterol 150microgram inhalation powder capsules with device, Indacaterol 300microgram inhalation powder capsules with device, Onbrez Breezhaler 150microgram inhalation powder capsules with device (Novartis Pharmaceuticals UK Ltd), Onbrez Breezhaler 300microgram inhalation powder capsules with device (Novartis Pharmaceuticals UK Ltd), Olodaterol 2.5micrograms/dose solution for inhalation cartridge with device CFC free, Striverdi Respimat 2.5micrograms/dose solution for inhalation cartridge with device (Boehringer Ingelheim Ltd), Spiolto Respimat 2.5micrograms/dose / 2.5micrograms/dose solution for inhalation cartridge with device (Boehringer Ingelheim Ltd) and Tiotropium bromide 2.5micrograms/dose / Olodaterol 2.5micrograms/dose solution for inhalation cartridge with device CFC free), Other Adrenoceptor Stimulants (excluding Isoetarine Hydrochloride and Isoprenaline Sulfate), Anticholinergic Bronchodilators (excluding Oxitropium Bromide, Spiolto Respimat 2.5micrograms/dose / 2.5micrograms/dose solution for inhalation cartridge with device ( Boehringer Ingelheim Ltd) and Tiotropium bromide 2.5micrograms/dose / Olodaterol 2.5micrograms/dose solution for inhalation cartridge with device CFC free), Theophylline Derivatives (excluding Choline Theophyllinate), Compound Bronchodilator Preparations (excluding Franol tablets (Sanofi), Franol Plus tablets (Sanofi), Indacaterol 85micrograms/dose / Glycopyrronium bromide 54micrograms/dose inhalation powder capsules with device and Ultibro Breezhaler 85microgram/43microgram inhalation powder capsules with device (Novartis Pharmaceuticals UK Ltd)), Corticosteroids For Inhalation (excluding AirFluSal Forspiro 50micrograms/dose / 500micrograms/dose dry powder inhaler (Sandoz Ltd)), Drugs For Prophylaxis Of Asthma (excluding Isoprenaline Sulfate), Rybar Inhaler, Sodium Chloride Nebuliser solution 0.9 %, 2.5 ml single dose unit, Saline 0.9% nebuliser liquid 2.5ml Steri-Neb unit dose ampoules (Teva UK Ltd), Adrenaline Acid Tartrate Inhaler 280 micrograms/puff, Medihaler-Epi Inhaler 280 micrograms/puff, Adrenaline Min-I-Jet Injection 1 mg/1 ml, Alupent Refill Aerosol inhalation 750 mcg/metered inhalation, Alupent Aerosol 0.75 mg, Orciprenaline Sulfate Aerosol 0.75 mg, Orciprenaline Sulfate Refill 750 micrograms/dose, Nucala 100mg powder for solution for injection vials (GlaxoSmithKline UK Ltd), Mepolizumab 100mg powder for solution for injection vials or Omalizumab
and the **Date of Issue** is after 12 months before the search date
and the **Date of Issue** is before or on the search date

| Rule 3 | If Rule Passed : **Exclude from final result** | If Rule Failed : **Goto Next Rule** |
|---|---|---|

Include **Patients** with **Clinical Codes** where:

the **Clinical Code** is Chronic obstructive pulmonary disease resolved, Chronic obstructive pulmonary disease (excluding Smokers' cough, Chronic tracheitis, Acute exacerbation of chronic obstructive airways disease, Chronic obstruct pulmonary dis with acute lower resp infectn and Chron obstruct pulmonary dis wth acute exacerbation, unspec), Chronic bronchitis (excluding Smokers' cough, Chronic tracheitis and Acute exacerbation of chronic obstructive airways disease), Emphysema, Mild chronic obstructive pulmonary disease, Moderate chronic obstructive pulmonary disease, Severe chronic obstructive pulmonary disease, Very severe chronic obstructive pulmonary disease, End stage chronic obstructive airways disease, Asthma-chronic obstructive pulmonary disease overlap syndrom, Other specified chronic obstructive airways disease (excluding Chronic obstruct pulmonary dis with acute lower resp infectn and Chron obstruct pulmonary dis wth acute exacerbation, unspec), Chronic obstructive airways disease NOS, Chronic emphysema due to chemical fumes, Obliterative bronchiolitis due to chemical fumes, [X]Other emphysema, [X]Other specified chronic obstructive pulmonary disease or Eosinophilic bronchitis

and the **Episode (First, New...)** is all values (excluding Review and End)

and the **Date** is before or on the search date

Ordering by **Date** select the latest

and check that:

the **Clinical Code** is Chronic obstructive pulmonary disease (excluding Smokers' cough, etc...

**Rule 4** **If Rule Passed : Include in final result** **If Rule Failed : Exclude from final result**

Include **Patients** with **Medication Issues** where:

the **Drug** is Salbutamol (excluding Asmaven Tablets 2 mg, Asmaven Tablets 4 mg, Combivent inhaler ( Boehringer Ingelheim Ltd), Cobutolin Tablets 2 mg, Cobutolin Tablets 4 mg, Combivent Nebuliser solution, Libetist Oral solution 2 mg/5 ml, Salbutamol Injection 50 micrograms/ml, Salbutamol 500micrograms/1ml solution for injection ampoules, Salbuvent Injection 50mg/ml, Salbuvent Injection 500mcg/ml, Salbuvent Injection 50mcg/ml, Salbutamol 5mg/5ml solution for infusion ampoules, Salbulin Liquid 2 mg/5 ml, Salbutamol 5mg/2.5ml nebuliser liquid unit dose vials, Salamol Nebuliser solution 2.5 mg/2.5 ml, Salbutamol Nebules 0.1 %, Salbutamol 2.5mg/2.5ml nebuliser liquid unit dose vials, Salbutamol 5mg/ml nebuliser liquid, Salbuvent Respirator solution 5mg/ml, Salbutamol Sf syrup 2 mg/5 ml, Salbuvent Solution for intravenous infusion 1mg/ml, Salbutamol Spandets 8 mg, Salbutamol Sr Spandet(s) 8 mg, Salbutamol 4mg modified-release tablets, Salbutamol 8mg modified-release tablets, Salbutamol 2mg/5ml oral solution sugar free, Salbutamol Syrup 1 mg/5 ml, Salbutamol Syrup 2 mg/5 ml, Salbuvent Syrup 2mg/5 ml, Salbulin Tablets 2 mg, Salbulin Tablets 4 mg, Salbutamol 2mg tablets, Salbutamol 4mg tablets, Salbuvent Tablets 2 mg, Salbuvent Tablets 4 mg, Salamol 2.5mg/2.5ml nebuliser liquid Steri-Neb unit dose vials (Teva UK Ltd), Salamol 5mg/2.5ml nebuliser liquid Steri-Neb unit dose vials (Teva UK Ltd), Ventolin Injection 50 micrograms/ml, Ventolin 500micrograms/1ml solution for injection ampoules (GlaxoSmithKline UK Ltd), Ventolin 5mg/5ml solution for infusion ampoules (GlaxoSmithKline UK Ltd), Ventolin 2.5mg Nebules ( GlaxoSmithKline UK Ltd), Ventolin 5mg Nebules (GlaxoSmithKline UK Ltd), Ventolin 5mg/ml respirator solution (GlaxoSmithKline UK Ltd), Ventolin Spandets 8 mg, Ventolin 2mg/5ml syrup (GlaxoSmithKline UK Ltd), Ventolin Tablets 2 mg, Ventolin Tablets 4 mg, Volmax 4mg modified-release tablets (GlaxoSmithKline UK Ltd), Volmax 8mg modified-release tablets (GlaxoSmithKline UK Ltd), Kentamol Inhaler 100 micrograms/dose, Salbutamol 4mg modified-release capsules, Salbutamol 8mg modified-release capsules, Ventmax SR 4mg capsules (Chiesi Ltd), Ventmax SR 8mg capsules (Chiesi Ltd), Maxivent 2.5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Ashbourne Pharmaceuticals Ltd), Maxivent 5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Ashbourne Pharmaceuticals Ltd), Combivent nebuliser liquid 2.5ml UDVs ( Boehringer Ingelheim Ltd), Salapin 2mg/5ml syrup (Pinewood Healthcare), Salbutamol 2.5mg/2.5ml / Ipratropium bromide 500micrograms/2.5ml nebuliser liquid unit dose vials, Ipramol nebuliser solution 2. 5ml Steri-Neb unit dose vials (Teva UK Ltd), Novolizer Salbulin Inhalation Cartridge + Device 100 micrograms/dose, Novolizer Salbulin Inhalation Cartridge Refill 100 micrograms/dose, Salbutamol 2.5mg/2. 5ml / Ipratropium bromide 500micrograms/2.5ml nebuliser liquid ampoules, Salipraneb 0.5mg/2.5mg nebuliser solution 2.5ml ampoules (Actavis UK Ltd), Salbutamol 2.5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Galen Ltd) and Salbutamol 5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Galen Ltd)), Ventolin (excluding Ventolin Injection 50 micrograms/ml, Ventolin 500micrograms/1ml solution for injection ampoules (GlaxoSmithKline UK Ltd), Ventolin 5mg/5ml solution for infusion ampoules (

injection ampoules (GlaxoSmithKline UK Ltd), Ventolin 5mg/5ml solution for infusion ampoules (
GlaxoSmithKline UK Ltd), Ventolin 5mg/ml respirator solution (GlaxoSmithKline UK Ltd), Ventolin Spandets 8 mg, Ventolin 2mg/5ml syrup (GlaxoSmithKline UK Ltd), Ventolin Tablets 2 mg and Ventolin Tablets 4 mg) , Bricanyl (excluding Bricanyl 500micrograms/1ml solution for injection ampoules (AstraZeneca UK Ltd), Bricanyl 5mg/2ml Respules (AstraZeneca UK Ltd), Bricanyl 10mg/ml respirator solution (AstraZeneca UK Ltd), Bricanyl Respirator solution 2.5 mg/ml, Bricanyl Respules 2.5 mg/ml, Bricanyl 1.5mg/5ml syrup ( AstraZeneca UK Ltd), Bricanyl 5mg tablets (AstraZeneca UK Ltd) and Bricanyl 2.5mg/5ml solution for injection ampoules (AstraZeneca UK Ltd)) or Terbutaline Sulfate (excluding Bricanyl Expectorant Elixir, Bricanyl 500micrograms/1ml solution for injection ampoules (AstraZeneca UK Ltd), Bricanyl 5mg/2ml Respules (AstraZeneca UK Ltd), Bricanyl 10mg/ml respirator solution (AstraZeneca UK Ltd), Bricanyl Respirator solution 2.5 mg/ml, Bricanyl Respules 2.5 mg/ml, Bricanyl 1.5mg/5ml syrup (AstraZeneca UK Ltd), Bricanyl Compound Tablets, Bricanyl 5mg tablets (AstraZeneca UK Ltd), Bricanyl SA 7.5mg tablets ( AstraZeneca UK Ltd), Monovent 1.5mg/5ml syrup (Sandoz Ltd), Monovent Tablets 5 mg, Monovent Sa Tablets 7.5 mg, Terbutaline 500micrograms/1ml solution for injection ampoules, Terbutaline 10mg/ml nebuliser liquid, Terbutaline Sulfate Respirator solution 2.5 mg/ml, Terbutaline Sulfate Respules 5 mg/2 ml, Terbutaline Respules 5 mg/2 ml, Terbutaline 1.5mg/5ml oral solution sugar free, Terbutaline 5mg tablets, Terbutaline 7.5mg modified-release tablets, Bricanyl 2.5mg/5ml solution for injection ampoules ( AstraZeneca UK Ltd), Terbutaline 2.5mg/5ml solution for injection ampoules, Terbutaline Nebulisation single dose unit 5 mg/2 ml and Terbutaline 5mg/2ml nebuliser liquid unit dose vials)
and the **Date of Issue** is after or on 17-Jun-2015 and before 17-Jun-2016

Appendix 4. 7 Patient eligibility searches: Control group

| Rule 1 | If Rule Passed : **Goto Next Rule** | If Rule Failed : **Exclude from final result** |
|---|---|---|

Include **Patients** with **Patient Details** where:
the **Date of Birth** is after or on 17-Jun-1938 and before or on 16-Jun-2009

| Rule 2 | If Rule Passed : **Goto Next Rule** | If Rule Failed : **Exclude from final result** |
|---|---|---|

**Must have**

Include **Patients** with **Clinical Codes** where:
the **Clinical Code** is
Asthma resolved, Asthma resolved, Asthma (excluding Acute exacerbation of asthma)
, Chronic asthmatic bronchitis, Exercise induced asthma or Asthma-chronic obstructive pulmonary disease overlap syndrom
and the **Episode (First, New...)** is all values (excluding Review and End)
and the **Date** is before or on the search date
Ordering by **Date** select the latest
and check that:
the **Clinical Code** is
Asthma (excluding Acute exacerbation of asthma), Chronic asthmatic bronchitis, etc...
and the **Date** is before or on the search date

**And**

Include **Patients** with **Medication Issues** where:
the **Drug** is Selective Beta2-Adrenoceptor Stimulants (excluding Pirbuterol, Reproterol Hydrochloride, Rimiterol Hydrobromide, Tulobuterol Hydrochloride, Indacaterol 150microgram inhalation powder capsules with device, Indacaterol 300microgram inhalation powder capsules with device, Onbrez Breezhaler 150microgram inhalation powder capsules with device (Novartis Pharmaceuticals UK Ltd), Onbrez Breezhaler 300microgram inhalation powder capsules with device (Novartis Pharmaceuticals UK Ltd), Olodaterol 2.5micrograms/dose solution for inhalation cartridge with device CFC free, Striverdi Respimat 2.5micrograms/dose solution for inhalation cartridge with device (Boehringer Ingelheim Ltd), Spiolto Respimat 2.5micrograms/dose / 2.5micrograms/dose solution for inhalation cartridge with device (Boehringer Ingelheim Ltd) and Tiotropium bromide 2.5micrograms/dose / Olodaterol 2.5micrograms/dose solution for inhalation cartridge with device CFC free), Other Adrenoceptor Stimulants (excluding Isoetarine Hydrochloride and Isoprenaline Sulfate), Anticholinergic Bronchodilators (excluding Oxitropium Bromide, Spiolto Respimat 2.5micrograms/dose / 2.5micrograms/dose solution for inhalation cartridge with device ( Boehringer Ingelheim Ltd) and Tiotropium bromide 2.5micrograms/dose / Olodaterol 2.5micrograms/dose solution for inhalation cartridge with device CFC free), Theophylline Derivatives (excluding Choline Theophyllinate), Compound Bronchodilator Preparations (excluding Franol tablets (Sanofi), Franol Plus tablets (Sanofi), Indacaterol 85micrograms/dose / Glycopyrronium bromide 54micrograms/dose inhalation powder capsules with device and Ultibro Breezhaler 85microgram/43microgram inhalation powder capsules with device (Novartis Pharmaceuticals UK Ltd)), Corticosteroids For Inhalation (excluding AirFluSal Forspiro 50micrograms/dose / 500micrograms/dose dry powder inhaler (Sandoz Ltd)), Drugs For Prophylaxis Of Asthma (excluding Isoprenaline Sulfate), Rybar Inhaler, Sodium Chloride Nebuliser solution 0.9 %, 2.5 ml single dose unit, Saline 0.9% nebuliser liquid 2.5ml Steri-Neb unit dose ampoules (Teva UK Ltd), Adrenaline Acid Tartrate Inhaler 280 micrograms/puff, Medihaler-Epi Inhaler 280 micrograms/puff, Adrenaline Min-I-Jet Injection 1 mg/1 ml, Alupent Refill Aerosol inhalation 750 mcg/metered inhalation, Alupent Aerosol 0.75 mg, Orciprenaline Sulfate Aerosol 0.75 mg, Orciprenaline Sulfate Refill 750 micrograms/dose, Nucala 100mg powder for solution for injection vials (GlaxoSmithKline UK Ltd), Mepolizumab 100mg powder for solution for injection vials or Omalizumab
and the **Date of Issue** is after 12 months before the search date
and the **Date of Issue** is before or on the search date

| Rule 3 | If Rule Passed : **Exclude from final result** | If Rule Failed : **Goto Next Rule** |
|---|---|---|

Include **Patients** with **Clinical Codes** where:

the **Clinical Code** is Chronic obstructive pulmonary disease resolved, Chronic obstructive pulmonary disease (excluding Smokers' cough, Chronic tracheitis, Acute exacerbation of chronic obstructive airways disease, Chronic obstruct pulmonary dis with acute lower resp infectn and Chron obstruct pulmonary dis wth acute exacerbation, unspec), Chronic bronchitis (excluding Smokers' cough, Chronic tracheitis and Acute exacerbation of chronic obstructive airways disease), Emphysema, Mild chronic obstructive pulmonary disease, Moderate chronic obstructive pulmonary disease, Severe chronic obstructive pulmonary disease, Very severe chronic obstructive pulmonary disease, End stage chronic obstructive airways disease, Asthma-chronic obstructive pulmonary disease overlap syndrom, Other specified chronic obstructive airways disease (excluding Chronic obstruct pulmonary dis with acute lower resp infectn and Chron obstruct pulmonary dis wth acute exacerbation, unspec), Chronic obstructive airways disease NOS, Chronic emphysema due to chemical fumes, Obliterative bronchiolitis due to chemical fumes, [X]Other emphysema, [X]Other specified chronic obstructive pulmonary disease or Eosinophilic bronchitis

and the **Episode (First, New...)** is all values (excluding Review and End)

and the **Date** is before or on the search date

Ordering by **Date** select the latest

and check that:

the **Clinical Code** is Chronic obstructive pulmonary disease (excluding Smokers' cough, etc...

**Rule 4** **If Rule Passed : Include in final result** **If Rule Failed : Exclude from final result**

Include **Patients** with **Medication Issues** where:

the **Drug** is Salbutamol (excluding Asmaven Tablets 2 mg, Asmaven Tablets 4 mg, Combivent inhaler ( Boehringer Ingelheim Ltd), Cobutolin Tablets 2 mg, Cobutolin Tablets 4 mg, Combivent Nebuliser solution, Libetist Oral solution 2 mg/5 ml, Salbutamol Injection 50 micrograms/ml, Salbutamol 500micrograms/1ml solution for injection ampoules, Salbuvent Injection 50mg/ml, Salbuvent Injection 500mcg/ml, Salbuvent Injection 50mcg/ml, Salbutamol 5mg/5ml solution for infusion ampoules, Salbulin Liquid 2 mg/5 ml, Salbutamol 5mg/2.5ml nebuliser liquid unit dose vials, Salamol Nebuliser solution 2.5 mg/2.5 ml, Salbutamol Nebules 0.1 %, Salbutamol 2.5mg/2.5ml nebuliser liquid unit dose vials, Salbutamol 5mg/ml nebuliser liquid, Salbuvent Respirator solution 5mg/ml, Salbutamol Sf syrup 2 mg/5 ml, Salbuvent Solution for intravenous infusion 1mg/ml, Salbutamol Spandets 8 mg, Salbutamol Sr Spandet(s) 8 mg, Salbutamol 4mg modified-release tablets, Salbutamol 8mg modified-release tablets, Salbutamol 2mg/5ml oral solution sugar free, Salbutamol Syrup 1 mg/5 ml, Salbutamol Syrup 2 mg/5 ml, Salbuvent Syrup 2mg/5 ml, Salbulin Tablets 2 mg, Salbulin Tablets 4 mg, Salbutamol 2mg tablets, Salbutamol 4mg tablets, Salbuvent Tablets 2 mg, Salbuvent Tablets 4 mg, Salamol 2.5mg/2.5ml nebuliser liquid Steri-Neb unit dose vials (Teva UK Ltd), Salamol 5mg/2.5ml nebuliser liquid Steri-Neb unit dose vials (Teva UK Ltd), Ventolin Injection 50 micrograms/ml, Ventolin 500micrograms/1ml solution for injection ampoules (GlaxoSmithKline UK Ltd), Ventolin 5mg/5ml solution for infusion ampoules (GlaxoSmithKline UK Ltd), Ventolin 2.5mg Nebules ( GlaxoSmithKline UK Ltd), Ventolin 5mg Nebules (GlaxoSmithKline UK Ltd), Ventolin 5mg/ml respirator solution (GlaxoSmithKline UK Ltd), Ventolin Spandets 8 mg, Ventolin 2mg/5ml syrup (GlaxoSmithKline UK Ltd), Ventolin Tablets 2 mg, Ventolin Tablets 4 mg, Volmax 4mg modified-release tablets (GlaxoSmithKline UK Ltd), Volmax 8mg modified-release tablets (GlaxoSmithKline UK Ltd), Kentamol Inhaler 100 micrograms/dose, Salbutamol 4mg modified-release capsules, Salbutamol 8mg modified-release capsules, Ventmax SR 4mg capsules (Chiesi Ltd), Ventmax SR 8mg capsules (Chiesi Ltd), Maxivent 2.5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Ashbourne Pharmaceuticals Ltd), Maxivent 5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Ashbourne Pharmaceuticals Ltd), Combivent nebuliser liquid 2.5ml UDVs ( Boehringer Ingelheim Ltd), Salapin 2mg/5ml syrup (Pinewood Healthcare), Salbutamol 2.5mg/2.5ml / Ipratropium bromide 500micrograms/2.5ml nebuliser liquid unit dose vials, Ipramol nebuliser solution 2. 5ml Steri-Neb unit dose vials (Teva UK Ltd), Novolizer Salbulin Inhalation Cartridge + Device 100 micrograms/dose, Novolizer Salbulin Inhalation Cartridge Refill 100 micrograms/dose, Salbutamol 2.5mg/2. 5ml / Ipratropium bromide 500micrograms/2.5ml nebuliser liquid ampoules, Salipraneb 0.5mg/2.5mg nebuliser solution 2.5ml ampoules (Actavis UK Ltd), Salbutamol 2.5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Galen Ltd) and Salbutamol 5mg/2.5ml nebuliser liquid unit dose Steripoule vials (Galen Ltd)), Ventolin (excluding Ventolin Injection 50 micrograms/ml, Ventolin 500micrograms/1ml solution for injection ampoules (GlaxoSmithKline UK Ltd), Ventolin 5mg/5ml solution for infusion ampoules (

injection ampoules (GlaxoSmithKline UK Ltd), Ventolin 5mg/5ml solution for infusion ampoules (
GlaxoSmithKline UK Ltd), Ventolin 5mg/ml respirator solution (GlaxoSmithKline UK Ltd), Ventolin Spandets 8 mg, Ventolin 2mg/5ml syrup (GlaxoSmithKline UK Ltd), Ventolin Tablets 2 mg and Ventolin Tablets 4 mg) , Bricanyl (excluding Bricanyl 500micrograms/1ml solution for injection ampoules (AstraZeneca UK Ltd), Bricanyl 5mg/2ml Respules (AstraZeneca UK Ltd), Bricanyl 10mg/ml respirator solution (AstraZeneca UK Ltd), Bricanyl Respirator solution 2.5 mg/ml, Bricanyl Respules 2.5 mg/ml, Bricanyl 1.5mg/5ml syrup ( AstraZeneca UK Ltd), Bricanyl 5mg tablets (AstraZeneca UK Ltd) and Bricanyl 2.5mg/5ml solution for injection ampoules (AstraZeneca UK Ltd)) or Terbutaline Sulfate (excluding Bricanyl Expectorant Elixir, Bricanyl 500micrograms/1ml solution for injection ampoules (AstraZeneca UK Ltd), Bricanyl 5mg/2ml Respules (AstraZeneca UK Ltd), Bricanyl 10mg/ml respirator solution (AstraZeneca UK Ltd), Bricanyl Respirator solution 2.5 mg/ml, Bricanyl Respules 2.5 mg/ml, Bricanyl 1.5mg/5ml syrup (AstraZeneca UK Ltd), Bricanyl Compound Tablets, Bricanyl 5mg tablets (AstraZeneca UK Ltd), Bricanyl SA 7.5mg tablets ( AstraZeneca UK Ltd), Monovent 1.5mg/5ml syrup (Sandoz Ltd), Monovent Tablets 5 mg, Monovent Sa Tablets 7.5 mg, Terbutaline 500micrograms/1ml solution for injection ampoules, Terbutaline 10mg/ml nebuliser liquid, Terbutaline Sulfate Respirator solution 2.5 mg/ml, Terbutaline Sulfate Respules 5 mg/2 ml, Terbutaline Respules 5 mg/2 ml, Terbutaline 1.5mg/5ml oral solution sugar free, Terbutaline 5mg tablets, Terbutaline 7.5mg modified-release tablets, Bricanyl 2.5mg/5ml solution for injection ampoules ( AstraZeneca UK Ltd), Terbutaline 2.5mg/5ml solution for injection ampoules, Terbutaline Nebulisation single dose unit 5 mg/2 ml and Terbutaline 5mg/2ml nebuliser liquid unit dose vials)
and the **Date of Issue** is after or on 17-Jun-2013 and before 17-Jun-2014

Appendix 4. 8 The Reporting of Observational Studies in Epidemiology (STROBE) and the Reporting of studies Conducted using Observational Routinely collected health Data (RECORD) statement

| | Item No. | STROBE items | Location in manuscript where items are reported | RECORD items | Location in manuscript where items are reported |
|---|---|---|---|---|---|
| **Title and abstract** | | | | | |
| | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found | Chapter 4 | RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included.<br><br>RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract.<br><br>RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract. | Chapter 4 |
| **Introduction** | | | | | |
| Background rationale | 2 | Explain the scientific background and rationale for | Chapter 4: Section 4.1 | | |

| | | | | | |
|---|---|---|---|---|---|
| | | the investigation being reported | | | |
| Objectives | 3 | State specific objectives, including any pre-specified hypotheses | Chapter 4: Section 4.1.4 | | |
| **Methods** | | | | | |
| Study Design | 4 | Present key elements of study design early in the paper | Chapter 2: section 2.4.2; Chapter 4: Section 4.2 | | |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Chapter 4: section 4.2.1 and 4.2.2 | | |
| Participants | 6 | *(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study* - Give the eligibility criteria, and the | (a) Chapter 4: section 4.2.2 | RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided.<br><br>RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. | Section 4.2.1 and 4.2.2; appendix 4.6 and 4.7 |

| | | | | | |
|---|---|---|---|---|---|
| | | sources and methods of selection of participants<br><br>*(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case | (b) Chapter 4: matching inclusion criteria section 4.2.2.3 and numbers section 4.3.1 | RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage. | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. | Chapter 4: section 4.2.3 | RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided. | Chapter 4; Explanation see section 4.2.3 |
| Data sources/ measurement | 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Chapter 4: section 4.2.3 and appendices 4.1 – 4.7 | | |
| Bias | 9 | Describe any efforts to address potential sources of bias | Chapter 2: Section 2.4.4 | | |
| Study size | 10 | Explain how the study size was arrived at | Chapter 4: section 4.2.1 | | |

| | | | | | |
|---|---|---|---|---|---|
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | Chapter 4: Section 4.2.5 | | |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding<br>(b) Describe any methods used to examine subgroups and interactions<br>(c) Explain how missing data were addressed<br>(d) *Cohort study* - If applicable, explain how loss to follow-up was addressed<br>*Case-control study* - If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy<br>(e) Describe any sensitivity analyses | Section 4.2.5 | | |
| Data access and cleaning methods | | .. | | RECORD 12.1: Authors should describe the extent to which the investigators | Chapter 4: section 4.2.2. and |

| | | | | | |
|---|---|---|---|---|---|
| | | | | had access to the database population used to create the study population.<br><br>RECORD 12.2: Authors should provide information on the data cleaning methods used in the study. | section 4.2.4 |
| Linkage | | .. | | RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided. | N/A |
| **Results** | | | | | |
| Participants | 13 | (a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed)<br>(b) Give reasons for non-participation at each stage.<br>(c) Consider use of a flow diagram | Chapter 4: section 4.3.1 | RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram. | Chapter 4: section 4.2.1.1 |
| Descriptive data | 14 | (a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on | Chapter 4: section 4.3.1 | | |

| | | | | | |
|---|---|---|---|---|---|
| | | exposures and potential confounders<br>(b) Indicate the number of participants with missing data for each variable of interest<br>(c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount) | | | |
| Outcome data | 15 | *Cohort study* - Report numbers of outcome events or summary measures over time<br>*Case-control study* - Report numbers in each exposure category, or summary measures of exposure<br>*Cross-sectional study* - Report numbers of outcome events or summary measures | Chapter 4: Section 4.3.1 | | |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Chapter 4: section 4.3 and 4.4.1 | | |

| | | | | | |
|---|---|---|---|---|---|
| | | (b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | | | |
| Other analyses | 17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | Chapter 4: section 4.4 | | |
| **Discussion** | | | | | |
| Key results | 18 | Summarise key results with reference to study objectives | Chapter 4: section 4.4 and 4.5 | | |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Chapter 4: section 4.5.2 | RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported. | Chapter 4 section 4.5 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant | Chapter 4: Section 4.5 | | |

| | | | | | |
|---|---|---|---|---|---|
| | | evidence | | | |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Chapter 4 section 4.5 | | |
| **Other Information** | | | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | | | |
| Accessibility of protocol, raw data, and programming code | | | | RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code. | N/A |

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

Appendix 5. 1 Patient and Public Advisory Group questions


Using too many blue inhalers may mean that asthma is not well controlled and that people may be at high risk of an asthma attack and may end up in hospital. To avoid this, when too many blue relievers (blue inhalers) are prescribed, an alert may appear in the GP computer to warn that a person needs to have an asthma review as they may be at high risk of having an asthma attack. As an alert may impact on how many relievers a person may be prescribed it is important to get the patient and public perspective on how you feel about this and an alert. Your feedback will help focus the questions for primary care staff and may help inform a patient focus group.

| Question | Response |
|---|---|
| What are your thoughts about an alert in GP practices that identifies when patients have been prescribed too many blue inhalers? | |
| An alert will be triggered when patients have been using too many blue inhalers and are at high risk of an asthma attack. The patient will be invited for Asthma Review. Do you think there would be any problems with this? If so, please explain. | |
| What do you feel would be the best way to 'alert' the patient that they have been using too many blue inhalers and are required to attend review? | |

| Question | Response |
|---|---|
| How many blue inhalers do you, or the person you care for, use in a month? | |
| Has anyone told you or the person you care for that you are using too many blue inhalers? If so, what was done about it? | |
| Have you obtained blue reliever inhalers by repeat prescription, either for yourself or the person you care for? If so, please tell me what process you go through. | |

What suggestions would you have to improve the repeat prescription process?

Finally, if a focus group was conducted what other questions do you believe would be important to ask? Thank you

Email: s.m.mckibben@qmul.ac.uk
Shauna McKibben - Postgraduate Research Student
Asthma UK Centre for Applied Research/Queen Mary University London

Appendix 5. 2 Queen Mary Ethics of Research Committee correspondence


Queen Mary, University of London, Room W121
Queen's Building
Queen Mary University of London Mile End Road
London E1 4NS

Queen Mary Ethics of Research Committee

c/o Professor Chris Griffiths
Room 1.21 - Centre for Primary Care
Queen Mary University of London Yvonne
Carter Building
Turner Street
Mile End Road, London

27th September 2017

To Whom It May Concern:

Re: QMREC2061a –The use of electronic alerts to identify excessive prescribing of short acting beta$_2$-agonists for people with asthma in primary care: a mixed methods study.

I can confirm that Shauna McKibben has completed a Research Ethics Questionnaire with regard to the above work, and also referred to; and taken advice on, Health Research Authority guidance. N.B. This liaison having taken place prior to the commencement of any analyses.

The result of which was the conclusion that her proposed work does not present any ethical concerns; is extremely low risk; and thus does not require the scrutiny of the full Queen Mary Research Ethics Committee.

Yours faithfully

Ms Hazel Covill – QMERC Administrator

Covill Research Ethics Administrator
Tel: +44 (0) 20 7882 7915

Appendix 5. 3 Consent Form

Queen Mary University of London

Asthma UK Centre for Applied Research

## Consent form

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: Evaluation of an electronic alert to identify the excessive use of short acting beta2-agonist (SABA) inhalers in patients with asthma: a qualitative study of the views of primary care staff.

Thank you for agreeing to participate in this research. The person organising the research must explain the project to you before you agree to take part.

If you have any questions please ask the researcher before you decide to take part.

You will be given a copy of this Consent Form to keep and refer to at any time.

- *I consent to the processing of my personal information for the purposes of this research study which may include anonymised audio recording and/or handwritten observations taken by the researcher. I understand that such information will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998.*
- *I consent to anonymised audio and/or handwritten observations being used as part of a doctorate degree (PhD) and may contribute to research papers published in an academic journal.*
- *I understand that if I decide at any other time during the research that I no longer wish to participate in this project, I can notify the researchers involved and be withdrawn from it immediately*

**Participant's Statement:**

I_____agree that the research project named above has been explained to me to my satisfaction and I agree to take part in the study.

Signed: Date:

**Investigator's Statement:**

I_____confirm that I have explained the nature and demands of the proposed research to the participant.

Signed: Date:

**Contact:** Shauna McKibben **Email**: s.m.mckibben@qmul.ac.uk

Appendix 5. 4 Interview topic guide

| **Topic guide for interviews** | |
|---|---|
| **Topic** | **Questions and prompts** |
| Identifying and managing high SABA use | How would you define excessive SABA use? Excluding pre-exercise use. PROMPT: volume and duration, evidence e.g. National Review of Asthma Deaths, BTS/GINA guidelines, other research |
| | How do you identify patients prescribed high numbers of SABA inhalers? PROMPT: methods: computerised/manual and context, task: consultation/repeat prescribing, workflow |
| | What happens if high SABA prescribing is identified? PROMPT: type of action, challenges to action, who is involved |
| | Who is involved in identifying and managing high SABA use? PROMPT: the role of reception, pharmacy, nurse, patient |
| Alerts to identify high SABA use | What are your thoughts on an alert to identify patients being prescribed excessive SABA? PROMPT: current EMIS medicines management alert |
| | How do you use this alert? PROMPT: In what context, how do you respond |
| | How could the alert be improved? |
| Additional questions for primary and secondary experts | What are your thoughts on recommendations for electronic surveillance of SABA prescribing in primary care practices? PROMPT: National Review of Asthma Deaths, current EMIS medicines management alert |
| | How do you feel this could best be done? |
| | What do you view as challenges to such a system? How could these challenges be overcome? |
| | Who should such a system involve? |
| | How should the success of such a system be measured? |

Appendix 5. 5 Observation guide

| **Observation guide for reception staff** | |
|---|---|
| **Categories** | **Issues to consider** |
| **Space:** Layout of the physical setting when repeat prescribing; rooms, space | What is the general environment in particular the area in which repeat prescribing tasks are carried out? What aspects of the space facilitate/hinder monitoring of prescribing? Why? How is the room/area laid out? How does receptionist's personal space correlate with professional space in repeat prescribing tasks? Do people consider the impact of space of relevance to the task of repeat prescribing? |
| **Staff:** People involved in repeat prescribing and interactions | Who are the different actors? Age, gender, ethnicity, profession? How do they interact with each other? Who speaks to whom and for how long? What is the hierarchy? With what other staff do they discuss tasks? Do staff have multiple roles? How do they demonstrate what role they are playing at any one time? What behaviours make their role/status apparent? |
| **Activities:** Type of activities including but not limited to repeat prescribing tasks | What activities do staff have responsibility for? Who decides what activities they do? Is their behaviour different from what they say their activities are? What activities are considered more important than others? Are some activities 'performed' more than others? Are there visible and invisible activities? What is the gravity of acts in repeat prescribing? E.g. clinical input, decision making, assessment, interpretation |
| **Objects:** Computers, furniture etc. in repeat prescribing | What objects are involved in repeat prescribing? Are there 'unofficial' objects that people use? How do people use them? What significance is attached to them? Are all objects understood and used in the same way? What objects help or hinder repeat prescribing? |
| **Time:** The sequence of events of repeat prescribing | What is the sequence of events in repeat prescribing tasks? Who decides on sequencing? Is timing considered important? By whom? For what reasons? Who controls the timing of events? What happens if a sequence is interrupted? |
| ***Goals:*** What are staff attempting to accomplish when managing SABA repeat prescriptions | What are explicit and implicit goals? Personal and group goals? How are goals decided upon? What is the work people do to achieve goals? How do goals change over time? What happens if goals aren't achieved? What is considered success? How is success celebrated? |

Appendix 5. 6 Illustrative Example of the use of the Framework Method

The following is an illustrative example of the use of the Framework Method used in Chapter 5 "A qualitative study on the use of electronic alerts to identify excessive prescribing of short acting $beta_2$-agonist (SABA) inhalers in people with asthma: the views of asthma experts and primary care staff."

In this study, we used semi-structured interviews and observations to collect data from 32 participants including clinicians (GPs and asthma experts) nurses, pha rmacists, reception staff. Using the Framework Method themes were developed inductively from the experiences and views of interviewees. This working example demonstrates how the Framework method was used to critically explore participant responses, identify deviant cases and interpret themes. The following is an example to illustrate how the Framework method was applied during this study.

*Section 1: Transcription*

Of the 25 audio recorded interviews 15 were transcribed by the researcher and 10 were transcribed by a by a transcription specialist from Penguin Transcription services, as recommended by Queen Mary University of London. The researcher validated transcripts by comparing the completed transcript against the audio recordings. Each interview was numbered and line numbers were added to the typed transcripts. Any initial notes made during observations were written-up into detailed field notes by researcher who collected the data. Data was anonymised and numbered to record only roles of the participants.

*Section 2: Familiarisation with the interview*

The researcher thoroughly read and re-read each transcript, and listened back to the audio- recorded interviews to become familiar with the whole data set. Initial impressions were documented for example where participants expressed exceptionally strong or contrasting views. One such example was a pharmacist who believed it was not their responsibility to refuse to dispense salbutamol inhalers that were prescribed by the GP. Yet it was suggested by

a number of asthma experts that pharmacists had a responsibility to do so. Familiarisation through reading and making notes in this way also enabled us to find our way easily around hundreds of pages of transcript later in the analysis.

*Section 3: Coding*

Coding was carried out by the researcher and supported by a second coder. Both the researcher and second coder independently coded the same three transcripts. Segments of interest within the text were assigned a label or code alongside notes and ideas, including questions raised, ideas to explore or patterns emerging. An excerpt of open coding from one interview is included below. The participant, a GP, describes the role of reception staff could be expanded to support GPs in identifying and managing high SABA use and how this could be done. The researcher's underlining emphasises data of potential relevance to the research question and of issues to consider further.

**Coding example:** GP 3

*Coding labels*

Checking for overuse; alert

Power

Future role/ responsibility

Receptionist role, clear plan

Repeat prescribing

Action,

Team-work

Repeat prescribing system

157 So I can imagine reception are not looking at it enough, I'm sure if you've spoken to them they'll say

158 they never do and we haven't… that's *our* problem, we haven't empowered them. Believe it or not that

159 would work really… I think I'm just about… my next meeting is about empowering our reception staff

160 and we're very good at normally doing that and I think they're actually now in a position of feeling

161 that they could really try and get involved with patient care in more than just a, 'Let's give them an

162 appointment, let's triage them, let's work out, signpost them,' of actually where are they in this field?

163 And I think having teams of people… almost saying to every receptionist, before you're taking the

164 prescription request look and see…So that's me with this alert but then they could also be before

165 you're printing off if it's a repeat, have a look at this alert, which I think you're talking about would

166 flash up. And then in my head, and it depends if we want to be paperless or not, it would be great if

167 they could almost stamp the prescription or do something saying, 'Doctor beware,' because if they

168 don't issue it, then again, we're getting a clog going on but they need to be just highlighting to us

169 'cause we will then be signing it and not going into the alert

*Notes and Ideas*

What is the role of reception? GP expectation? Do reception want to be empowered?

GP responsible for receptionist role; expanding role; utilizing reception; increasing role in patient care

Team work or reception work?

Receptionist checking alert, applying clinical judgement? Increased role in decision making

*Section 4: Developing a working analytical framework*

After two researchers had each open coded the same three transcripts, we met to discuss coding progress. One full working day was spent reviewing the three transcripts. Discussion included why each section had been coded as such, why it had been interpreted as meaningful and what it told us about the identification and management of high SABA use in primary care and the role of alerts in this process. There was significant overlap in how researchers coded text, however, sometimes interpretations of the content was expressed in different ways. For example risk was coded in the text as of ''risk categorisation' by one researcher and 'recognising the risk' by the other. Following discussion it was agreed to label this code as 'recognising risk', as shown in table A, to reflect participant's interpretation of risk rather than determined by others.

The initial framework underwent a process of application and refinement until the research questions aims were met and further data was not contributing any new data to address the research question. The analytical framework was repeated by the primary researcher until additional data collection was unlikely to generate new findings. This was influenced by no new codes emerging and no new definitions of high SABA use being introduced. The framework was discussed at a second meeting including codes and initial interpretations and no new codes were added to the framework. The final framework consisted of 7 sub-codes clustered into four themes. The following example shows how the analytical framework was refined for Theme 1.

**Initial coding**

| Initial codes | Subcode |
|---|---|
| Defining overuse | Volume and time frame |
| | EMIS alert |
| | SABA per prescription |
| | Doses |
| | Percentage use |
| | Challenges |
| Risk categorisation | Level of risk |
| | Assessing risk |
| | SABA volume |
| | Evidence |
| | Other drugs |
| SABA Prescribing | Prescription type |
| | System |
| | Volume and time frame |
| | Assessment |
| | Challenges |
| Methods | Percentage use |
| | Colour |
| | Medication review |
| | QOF box |
| | EMIS alert |
| | Manual |
| | Practice initiatives |
| | Incentivised methods |
| | Challenges |

**Revised coding**

| **Themes** | **Codes** | *Description* |
|---|---|---|
| Perceptions of excessive SABA use | Defining excessive use | How high use is defined and perceived in relation to evidence |
| | Risk perceptions | The perceived risk of high SABA and how the risk is contextualized by other drugs and evidence |
| Identifying excessive use | Methods | The methods used to identify high SABA use and the influences on identification |
| | Challenges | The human and systems factors influencing the identification of high SABA use |

*Section 5: Applying the analytical framework*

The final analytical framework was applied to each transcript using MAXQDA 2018. In practice, this meant importing transcripts to the software for indexing. The lead researcher systematically went through each transcript, highlighting each meaningful passage of text and selecting and attaching an appropriate code from the final analytical framework. Below is an excerpt from GP 4's transcript in which the participant discussed high SABA use. The example below shows the application of the analytical framework to a transcript for GP 4, using only codes from the 'Identifying excessive SABA use' theme.

32 So excessive is harder to define over concerning, so I'd start with if
33 you're using it as prescribed, so twice a day, and you're not needing to
34 use it on, well, if you used it when you go for a run or if you're doing a

Defining excessive

35 particular sporting activity and those are planned uses then I think
36 that's OK, it's when you find that those are insufficient that that makes
37 me concerned.

Risk perceptions

37 The excessive is more difficult, I think, 'cause you'd look on the
38 computer screen and obviously EMIS records usage and there is a sort
39 of monitoring of how quickly people are going through their inhalers.

Methods

40 I don't think that that is *incredibly* accurate because it's all about the
41 data that gets put in. If you put 120 use inhaler is going to last 60 days
42 and they're asking for it every 30 days then it will say that their usage is
43 200% and yet if they were using it 2 or 3 times occasionally, that still
44 might not be overly concerning.

Challenge

*Stage 6: Charting data*

Once data had been coded using the framework, data was imported by theme from MAXQDA into Microsoft Excel. Data was presented by participant and code, and summarised it using verbatim words and inserted it into the corresponding cell in the matrix. Software enabled quick and easy retrieval of indexed data for specific codes within each transcript. Once the data was coded using the analytical framework, we summarized the data in a matrix for each theme using Microsoft Excel. Table 1 documents the charting of codes from the Themes 'Perceptions of excessive SABA use' and 'Identifying excessive SABA use' into a matrix, with page and line references.

**Table 1. Charting data into the Framework matrix**

| | Defining excessive use | Risk perceptions | Methods | | Challenges |
|---|---|---|---|---|---|
| GP 3 | "Anyone who has more than 12 short-acting agonists a year, SABAs a year, should be highlighted" *[p1, 15-17]* | "I think it's no way on the same level. With methotrexate we've got about, I did a search the other day, we've got about 30, 40 patients, so it's about volume as well, so I don't think it is… *[p11, 274-277]* | "We are positively encouraging people to go down this route, so the EPS medicine management, but some people don't want to do it electronically straight to the chemist, they want choices" *[p8, 192-196]* | "The QOF box works for me but I'm aware I'm the partner, the overseer, I'm the one that's got that eye." *[p15, 400-401]* | '"cause they're probably just taking it with a panic attack rather than 'cause they've got a genuine asthma" *[p11, 272-273]* |
| GP 4 | "if you're using it as prescribed, so twice a day, and you're not needing to use it on… Well, if you used it when you go for a run or if you're doing a particular sporting activity and those are planned uses then I think that's OK" *[p2, 33-37]* | "the actual patient in front of me is unlikely to be at risk of that without some other warnings or some other feature, so it makes it more difficult, I think" *[p5, 121-125]* And the vast majority of our patients who have asthma are unlikely to come to significant harm from it and it's balancing those two priorities, which is challenging, I think" *[p4, 115-117]* | "So either it comes as a paper prescription that we'll sign or medicine management on the computer" *[p6, 160-161]* | "you'd look on the computer screen and obviously EMIS records usage and there is a computer sort of monitoring of how quickly people are going through their inhalers" *[p2, 38-40]* | "I don't think that that is incredibly accurate because it's all about the data that gets put in" *[p2, 41-42]* |
| Expert 8 | "A well-controlled asthmatic shouldn't need more than one every six months so twelve a year is quite a high threshold." [p7, 291-293] | | "So the receptionist sort of deals with the paper-work side if you like but it has to come through to me to sign either on paper or increasingly these days almost electronic" *[p4, 147-149]* | "The electronic prescribing bit is sort of separate to the patient record...it will tell me when the last prescription was but it wont tell me the ones before" [*p7, 302-307]* | "So the first thing I would say is to check the default setting, I don't think EMIS has got it in quite the same way, that is it set to one" *[p5, 214-215]* |
| Pharmacist 1 | "The one we've got set up at the moment is more than six relievers in a year, so that'd be one every two months" *[p4, 123-125]* | | "I tend to do the ones [repeat prescriptions] where the doctor's on holiday or annual leave or not in that day and I get the extra ones. They come to me by default" *[p9, 317-321]* | | "I just think the computer systems are not always that accurate because it relies on everything being input correctly" *[p10, 357-362]* |

Stage 7: interpreting the data

Themes were generated from the data set by reviewing the matrix and making connections within and between participant and categories. The generation of Theme 1 'Perceptions of excessive SABA use' and Theme 2' Identifying excessive SABA use' has been documented in this illustrative example (table C). This process was influenced both by the original research objectives and by new concepts generated inductively from the data. One of the research questions in the topic guide enquired how excessive SABA use was identified in practice. However this was interpreted in the context of the wider data to determine significance to the research question. Ideas were generated and explored beyond descriptive data to determine inks between data, as well as deviant cases, to develop explanatory themes.

Whilst the methods used to identify high SABA use was of key importance when addressing the research question, it became apparent from the data that a number of issues influence and impact on the ways in which excessive SABA use was identified. For example, the code 'Defining excessive SABA use' highlighted the methods used in practice and was conceptually related to 'Risk perceptions' which together formed the overarching category named 'Perceptions of excessive SABA use.' Whilst the codes 'Methods' and 'Challenges' formed the theme 'Identifying excessive SABA use.'

- Defining excessive use

High SABA use will be identified based on how one perceives high use. However there were variations between participants in regards to what constituted high use. For example there was contrasting opinions between experts and GPs regarding the definition of high use; **"anyone who has more than 12 short-acting agonists a year, SABAs a year, should be highlighted"** ***[GP 3 p1, 15-17]*** in contrast to **"a well-controlled asthmatic shouldn't need more than one every six months so twelve a year is quite a high threshold." [Expert 8, p7, 291- 293].**

- Risk perceptions

This suggests a lack of certainty in how high SABA use is interpreted raising questions regarding the impact on variable interpretations of high use and associated risk. It is questionable as to whether those who define high use as 12 or more SABAs a year perceive high use as low risk. *GP 3* described high use as 12 SABAs a year and did not perceive high use as problematic without further evidence: **"so don't think it is [of concern]… It would be if, and touch wood it hasn't happened, you know, if we'd had an asthma death or lots of hospital admissions"** ***[p11, 274-277]***

- Methods

Prescriber's views on high SABA use and the associated risk, combined with varied methods to obtain SABAs, may result in inconsistent identification of high SABA use. As GP 4 explains**, "once the prescription is done there is no review process…well, the next time will be when they next have a clinical encounter" (p6, 175-177).** Furthermore there is no one standardised way of managing repeat prescriptions as GP 2 describes **"when we did the prescribing review last year we said that everything should go through medicines management but we do have prescriptions that sit in a box each day…I don't know what's happening with those."**

The methods used to obtain SABAs i.e. electronic or paper prescription, influence how high use is identified in practice. When SABAs were requested on repeat prescription *GP 1* describes checking the EHR to identify the extent of high use: **"I would go and look at then the medication was last issued because usually if they are on repeats they will have a percentage usage so will straightaway know if that is more than 100%, then we know they are using it often, so that is like a flag for us."** In contrast, GP 4 describes manual checking the EHR as computerised indicators for usage were unreliable: **"I don't think there's a simple way of doing it really, the only real way we have is of checking how many prescriptions we've done…"** This raises questions about the reliance on computers to identify high SABA use, suggesting that the ways in which high SABA use is established depends on both human and systems factors.

- Challenges

Human and systems factors presented challenges to the identification of high SABA use. For example whilst GPs relied on EHR systems to identify and present high use to the clinician, the EHR system relied on clinician data input to do so: **"I don't think that that is incredibly accurate because it's all about the data that gets put in" [GP 4, p2, 41-42].**

Whilst electronic methods to identify high SABA use are increasingly relied upon the usefulness will depend on the context in which it presents, for example when repeat prescribing the patient is not present and can restrict response: **"…the alert comes up like a pop-up but the problem can be when you cannot see the patient for days" (Expert 11)**

Despite the computer system identifying a patient as overusing SABAs, clinicians respond to overuse in different ways based in their interpretations of high use. In the following, *GP 4* describes high SABA use as open to interpretation and would continue to prescribe based on his own interpretations: **"So the prescription is likely to be issued unless there's something… some crazy number, so if they are 100, 150%, perhaps 200%, I suspect the prescription would be issued. If they've got 600% usage or something then you're going to query what on earth is happening with these inhalers."**

<u>Points for further consideration</u>

Why does GP 4 suspect the prescription would still be issued? What influences the perception of high SABA use as low risk? What type of action occurs when high SABA use is identified? How might an alert assist with this?