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Understanding and Managing Polypharmacy in Patients with Asthma: A Mixed Methods Study

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Co-Supervisors: Prof. Stuart Anderson & Dr Kathrin Cresswell & Ms Alpana Mair

Thesis submitted in fulfilment of the requirements for the research degree of PhD Precision Medicine
Edinburgh University
2022
Declaration

I declare that this thesis has been composed solely by myself and that it has not been submitted, in whole or in part, in any previous application for a degree. Except where stated otherwise by reference or acknowledgement, the work presented is entirely my own.
# Abbreviations

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<td>ACE</td>
<td>Angiotensin-converting enzyme</td>
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<tr>
<td>ACCORD</td>
<td>Academic and Clinical Central Office for Research and Development</td>
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<tr>
<td>ADR</td>
<td>Adverse Drug Reaction</td>
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<td>ADRN</td>
<td>Administrative Data Research Network</td>
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<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
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<td>ALHS</td>
<td>Asthma Learning Health System</td>
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<td>ANOVA</td>
<td>Analysis of Variance</td>
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<td>AUKCAR</td>
<td>Asthma UK Centre for Applied Research</td>
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<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>BNF</td>
<td>British National Formulary</td>
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<td>BTS</td>
<td>British Thoracic Society</td>
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<td>CHI</td>
<td>Community Health Index</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<tr>
<td>DOB</td>
<td>Date of Birth</td>
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<tr>
<td>eDRIS</td>
<td>electronic Data Research and Innovation Service</td>
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<td>EMIS</td>
<td>Educational Management Information System</td>
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<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>FEV₁</td>
<td>Forced Expiratory Volume (in one second)</td>
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<td>GERD</td>
<td>Gastroesophageal Reflux Disease</td>
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<tr>
<td>GGC</td>
<td>Greater Glasgow and Clyde</td>
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<td>GINA</td>
<td>Global Initiative for Asthma</td>
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<td>GP</td>
<td>General Practitioner</td>
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<td>HAART</td>
<td>Highly Active Anti-Retroviral Therapy</td>
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<td>HCP</td>
<td>Healthcare Professional</td>
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<td>ICD-10</td>
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<td>ID</td>
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<td>IRR</td>
<td>Incidence Rate Ratio</td>
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<td>IRAS</td>
<td>Integrated Research Application System</td>
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<td>KDE</td>
<td>Kernel Density Estimates</td>
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<td>LRSNS</td>
<td>Lothian Research Safe Haven</td>
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<td>MDT</td>
<td>Multidisciplinary Team</td>
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<td>MUR</td>
<td>Medicines Use Review</td>
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<td>National Health Service</td>
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<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
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<td>NSAID</td>
<td>Non-steroidal Anti-inflammatory Drug</td>
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<td>NUTS3</td>
<td>Nomenclature of Territorial Units for Statistics 3</td>
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<td>OID</td>
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<tr>
<td>PBPP</td>
<td>Public Benefit and Privacy Panel for Health and Social Care</td>
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<td>PCRS</td>
<td>Primary Care Respiratory Society</td>
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<td>PINCER</td>
<td>Pharmacist-led Information technology Intervention for the reduction of Clinically Important Errors in medicines management</td>
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<td>Abbreviation</td>
<td>Full Form</td>
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<td>RCGP</td>
<td>Royal College of Physicians</td>
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<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
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<td>SIMD</td>
<td>Scottish Index of Multiple Deprivation</td>
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<td>SiMPATHY</td>
<td>Stimulating Innovation Management of Polypharmacy and Adherence in the Elderly</td>
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<td>SMRs</td>
<td>Structured Medication Reviews</td>
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<td>SMR</td>
<td>Scottish Morbidity Record</td>
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<tr>
<td>START</td>
<td>Screening Tool to Alert to Right Treatment</td>
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<tr>
<td>STOPP</td>
<td>Screening Tool of Older Persons Prescriptions</td>
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<tr>
<td>UK</td>
<td>United Kingdom</td>
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<td>UR6</td>
<td>The 6-category Scottish Government Urban Rural Classification Scale</td>
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<td>US</td>
<td>United States</td>
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<tr>
<td>VPN</td>
<td>Virtual Private Network</td>
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Abstract

Introduction
Problematic polypharmacy, where patients are prescribed multiple medications that are not therapeutically beneficial and can cause unnecessary and potentially harmful adverse drug reactions, can be mitigated using medication reviews. Polypharmacy can occur in patients with asthma taking multiple types of inhalers and medications for their asthma. They often have other medicated comorbidities, particularly those with difficult-to-treat or severe asthma. We have limited knowledge of the trajectory of polypharmacy management in patients with asthma. Therefore, it is imperative that we gain a better understanding of asthma polypharmacy management to control inappropriate polypharmacy given asthma’s association with polypharmacy and multimorbidities (where patients develop two or more co-morbidities concurrently). This study explored how existing polypharmacy management techniques may have impacted inappropriate polypharmacy generally and, specifically, in patients with asthma to provide a lens into how we might revise future medication management procedures, guidelines and resources in polypharmacy and asthma healthcare practice.

Methods
This mixed methods study included qualitative interviews focused on medication management processes and issues to provide a broader understanding of asthma polypharmacy that informed quantitative data analysis. The interviews were conducted to identify differences between general polypharmacy and asthma polypharmacy. Recruitment involved purposive and snowballing techniques to ensure a diverse population and reach saturation in responses. Two cohorts were questioned regarding polypharmacy treatment management and barriers involved in its implementation. The first focused upon healthcare professionals (HCP) (n=21) with a polypharmacy specialisation. Five GPs, four consultants and twelve general practice and hospital pharmacists were interviewed. The second study focused on asthma HCPs (n=32). Eight GPs, eight asthma specialist consultants, nine pharmacists and seven nurses were interviewed. To determine the extent to which the interviews captured wider clinical practice, quantitative analysis explored pattern changes in a retrospective longitudinal data set containing Scottish asthma patient records (n = 671,238; 51.12% women) from 2009 to 2017 using R studio. The data was stratified by multimorbidity, age, socioeconomic background and gender. Differences in deprescribing and hospital admissions due to adverse drug reactions were also analysed.

Results
The GPs interviewed noted that, in general polypharmacy, structured medication reviews occurred less frequently than informal medication reviews, due to time constraints. However, amongst patients with asthma, asthma annual reviews were strongly adhered to and contained a medication review though polypharmacy was not a specific focus. HCPs noted that roles and the allocation of responsibilities when conducting medication reviews, repeat prescription monitoring and deprescribing in primary and secondary care were not well-defined, reflecting confusion about which HCPs were charged with these ‘responsibilities’. Specialist nurses in asthma and pharmacists felt less confident than physicians in removing medications lest their patients’ symptoms or illness returned and preferred lowering dosages instead by stepwise deprescribing as noted in asthma guidelines for inhaled and oral steroids.
Interprofessional communication between primary and secondary care was very limited, particularly regarding patient medication changes. The dataset analysis revealed that the onset of asthma polypharmacy typically occurred at 50-59 years of age but arose at a younger age (40-49) amongst those from lower socioeconomic backgrounds, especially men. Polypharmacy also coincided with increased levels of multimorbidity. These patterns were also identified by HCPs in the interviews. Since 2012, polypharmacy has steadily decreased and deprescribing gradually increased – coinciding with the introduction of the Scottish Polypharmacy Guidance, which offers detailed advice on conducting medication reviews and deprescribing. Stepping down medication was found to be more prevalent than outright removal, (also confirmed in the interviews). Patients taking 15+ medications had the highest levels of hospital admissions across all patients over the age of 50, particularly between ages 70 and 90, possibly due to increased frailty. Though overall prescribing/deprescribing patterns broadly followed Tudor Hart’s inverse care law, whereby, access to care by different social demographics is inversely proportional to need, deprescribing of medications over time observed in the 5-9 medication category was irrespective of social class, age and/or gender. The widely observed differential access to care flagged by Tudor Hart appeared to be eroded by the increased engagement of older frail patients across the board (regardless of demographic) with healthcare services.

**Conclusion**

Current polypharmacy policies target frail over-75s with polypharmacy. Polypharmacy seemingly decreased amongst this demographic suggesting that their increased engagement with health services due to their frailty increases their opportunities to have a medication review. However, polypharmacy is often experienced by those significantly younger than 75, particularly, we have shown, amongst younger multimorbid patients from lower socioeconomic backgrounds (especially men). This, the study suggests, may be because of their lower engagement with healthcare services. Targeting demographics with less interaction with healthcare services could advance polypharmacy mitigation/management. The potentially low levels of deprescribing observed confirms HCP acknowledgement that structured medication reviews are occurring less frequently and systematically than suggested by policy (though they occur under certain contingencies such as the asthma annual review). The continuing high level of hospital admissions amongst patients prescribed 10+ medications calls into question the adequacy of medication reviews performed for at-risk patients requiring polypharmacy management. Clarifying the function and roles associated with medication reviews across care systems could enhance the discovery of inappropriate polypharmacy in patients and prevent unnecessary drug related hospital admissions.

Undertaking mixed methods analysis, involving both detailed qualitative interviews and large-scale quantitative modelling, presents challenges to the researcher in terms of both the scale of research work and the range of tools and skills that need to be deployed. It does, however, offer important additional insights – particularly in this case the opportunity to link HCP perceptions about care processes with more general modelling of patient morbidity patterns and engagement with health services that are not necessarily apparent to respondents involved.

**Lay Summary**
Patients with asthma can be prescribed multiple inhalers and medications, particularly if they have severe asthma. Being diagnosed with other diseases in addition to their asthma can cause an increase of the medications prescribed. However, it can be harmful if patients are prescribed multiple treatments that they do not need. To prevent the prescription of medications that could potentially cause harm, patients need to have these medications checked or removed from their prescriptions. This study aimed to understand how multiple medications prescribed to patients with asthma are managed and removed by healthcare staff and how it affects these patients.

Healthcare staff were interviewed on how they check their patients’ medications and if they encounter issues when managing these medications. UK doctors and pharmacists with experience in managing inappropriate medication use were recruited. General practitioners (GPs), asthma specialist consultants, hospital and general practice pharmacists and nurses with experience with patients with asthma were interviewed for comparison. Also, patterns in prescriptions were investigated from asthma patient records in Scotland between the years 2009 to 2017.

In the interviews, GPs admitted to having a quick look over their patients’ medication lists because they lacked time, rather than having in depth discussions with their patient about their treatment. Only patients with difficult illnesses were transferred to a pharmacist for an in-depth discussion about their medications. Patients with asthma were provided an annual asthma review but this only involved discussions about asthma medications. However, healthcare staff were confused about which of their colleagues should manage and remove multiple medication use. They were also unsure about who was responsible for checking repeat prescriptions. Similarly, it was found that there was very little communication between GP surgeries and hospitals, particularly in patient medication changes. This lack of communication meant that healthcare staff would not know the reason behind specific medication changes. Nurses specialists, in asthma, and pharmacists were more reluctant than GPs and asthma specialists to remove medications due to their patients’ illness returning. It was confirmed in the patient prescription analysis that lowering medication dosage was preferred more than removing medication. Men in poorer areas showed high numbers of medications in their 40s, particularly if they had additional diseases including asthma. However, dosage changes and/or removal occurred despite a persons’ economic background, age or gender which could provide an alternative to the theory suggesting that patients most in need do not receive the care that they need.

Visiting health services frequently means that patients are more likely to have their medications checked, particularly in the over 75s. However, this study shows that patients with asthma younger than 75 have high numbers of medications and targeting patients with asthma with less interactions with healthcare services could improve medication management. Medication checks do not seem to be happening as regularly as suggested by healthcare policy because healthcare staff have ever-growing workloads, except for annual asthma reviews which have detailed instructions on their use.

The pressure put on doctors, nurses and pharmacists to complete these medication reviews in addition to their existing workloads needs to be taken into consideration by future policymakers. Creating clear roles and responsibilities for staff who may attempt to carry out medication reviews within healthcare services could make it easier to
discover inappropriate medications and prevent unnecessary drug related hospital admissions.

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Chapter 1

1.1 Introduction

Polypharmacy is defined as when a patient is prescribed multiple medication, usually five or more medications. This can cause the prescription of medications that are not therapeutically beneficial for patients and can trigger unnecessary and potentially harmful adverse drug reactions (ADRs). Therefore, health policy interventions seek to mitigate it. This thesis reports a mixed methods study of polypharmacy which sought to characterise the factors giving rise to inappropriate pharmacy and the opportunities to better manage polypharmacy. This chapter will introduce key topics discussed in the thesis, provides some background to the terminology used throughout and describes the structure of the thesis.

1.2 Background
1.2.1 Introduction to Polypharmacy

Medication is the most common healthcare intervention for many acute and chronic conditions and generates the third highest cost of health expenditure\textsuperscript{1,2}. The definition of polypharmacy means ‘many medications’ but the specific number of medications that are considered to constitute polypharmacy remains unclear. In the literature, polypharmacy has been defined varyingly as involving patients taking between two to over 10 medications concurrently\textsuperscript{3}. However, polypharmacy has been described as an individual that prescribed five or more medications at any given time with ten or more medications being regarded as ‘excessive’ or ‘hyperpolypharmacy’ \textsuperscript{1,2,4–7}. Polypharmacy has been used both as a positive and negative term. Historically, it was viewed as something that should be avoided, as polypharmacy was often associated
with, and seen as a sign of, poor prescribing quality, the cause of increased unplanned hospitalisations, ADRs, poor adherence, and, in turn, a lower quality of life than patients taking less medications\textsuperscript{8–14}. However, currently, polypharmacy is considered therapeutically beneficial when multiple medicines suit an individuals’ needs\textsuperscript{1,4,15}.

Polypharmacy can be distinguished in two ways; appropriate polypharmacy and problematic polypharmacy\textsuperscript{1,16}. Appropriate polypharmacy is displayed when drugs assigned to the patient achieve their specific therapeutic purpose and reduce the risk of ADR’s while the patient adheres to their full prescription\textsuperscript{17}. There are various conditions where the use of three or more drugs would be beneficial in the treatment of the disease in question. For example, myocardial infarctions require four different classes of drug (anti-platelets, statins, angiotensin-converting enzyme (ACE) inhibitors and beta blockers) as a secondary prevention. Diabetes mellitus is treated with several drugs at once. Tuberculosis treatment combines three or four medications to prevent the emergence of resistant mycobacteria. Helicobacter pylori requires three drugs to remove the bacteria from the stomach and the Highly Active Anti-Retroviral Therapy (HAART) regimen used to treat Acquired Immune Deficiency Syndrome (AIDS) also requires three or four drugs\textsuperscript{18}. When patients are prescribed the optimised combination of medicines which in this case would be appropriate polypharmacy, this will allow for the best outcomes in terms of optimising health and prolonging of the patient’s life. In contrast, inappropriate polypharmacy is present when one or more of the medications prescribed to the patient are no longer needed, due to failure to achieve their therapeutic aim, and there is no evidence based indication that the medication is required and there is an extremely high risk of ADR’s\textsuperscript{1,19}. The danger associated with inappropriate polypharmacy can be illustrated by example that if a patient takes eight medicines simultaneously, each of which has a 5% chance of an
ADR occurring, the overall risk of this patient suffering an ADR becomes 34%, which is a very high percentage possibility\textsuperscript{18}. A survey of General Practitioners (GPs), community and clinical pharmacists and gerontologists conducted in the Netherlands, focusing on elderly patients in primary care that were taking four or more drugs, discovered that, in 96 patients, there were 457 instances of inappropriate prescribing in one year. It was deemed that 60% of these medications were either not beneficial, given in the wrong dosage or wrong duration, or were not judged for appropriate use in elderly people\textsuperscript{20}.

Currently, polypharmacy is defined by crude numbering systems but a patient being prescribed five or more medication does not indicate that the patient has inappropriate polypharmacy. A patient could be taking five medications and require every single medication indicating that they have appropriate polypharmacy but the opposite could be true. Patients who possess excessive polypharmacy (where they are prescribed ten or more medications) could be a stronger indicator for inappropriate polypharmacy. Again, we cannot be certain that those ten medications are not therapeutically beneficial for the patient. Therefore, inappropriate polypharmacy requires stronger detection than combining all patients with a specific number of medications as having polypharmacy. Current polypharmacy guidance, therefore, focuses on balancing risk and quality of life rather than simply locating the inappropriate polypharmacy and removing it\textsuperscript{1}. Once the appropriate medication has been identified, the benefit versus risk analysis of the possible inappropriate medication can be completed\textsuperscript{15,16}. This evaluation of medication is known as a medication review and will be discussed further in the chapter. What, also, needs to be avoided is undertreatment. Patients with polypharmacy could find that their prescription is appropriate in that they require all the drugs prescribed to them but that they have been prescribed a lower dosage than
they need. HCPs should ensure that patients are treated with the optimal dosage particularly with drugs with narrow therapeutic ranges such as anti-epileptics\textsuperscript{21,22}.

Issues regarding compliance arise particularly amongst patients taking copious amounts of medications. Patients with excessive polypharmacy could find taking their medication burdensome as they have to remember to take every treatment. They, also, have to consider when to take each medication and to be aware of consuming foods or other medications that could cause an adverse reaction to their medication. This poses a concern if the patient does not consider a medication to be important or beneficial for them and could cease adhering to a medication to make things easier for them. Complex medication regimens and polypharmacy in patients has been found to negatively impact compliance and adherence and can cause a treatment burden\textsuperscript{23}. Good adherence has been defined in patients with asthma as around 80\% of patients adhering to their treatments\textsuperscript{24}. In a study of older patients with polypharmacy, only 19.3\% of patients were compliant with their treatment regimens dropping to half that if they took 10 or more medications\textsuperscript{25,26}. Around 40\% of the patients had poor adherence to at least one drug class and this rose to 50\% when patients were taking four or more different drug classes\textsuperscript{25,26}. The lowest adherence was found in patients with asthma and Chronic Obstructive Pulmonary Disease (COPD)\textsuperscript{25,26}. Therefore, these surprisingly low levels of adherence indicate that patient compliance is a major issue and could be an additional factor to be addressed by HCPs when evaluating polypharmacy in their patients.

\textbf{1.2.2 Introduction to Multimorbidity}

The types of patients who usually fall under the polypharmacy category, whether appropriate or inappropriate, are often patients with multi-morbidities, which is defined as the occurrence of two or more long-term chronic or acute diseases and medical
conditions, and/or older patients (who are often targeted due to ‘frailty’ which represents a ‘clinically recognised state of increased vulnerability’\(^1\), resulting from ageing) or patients who are approaching the end of their lives\(^1,7,16,27\). Several studies and guidelines focus on polypharmacy in the elderly population but not in those with multiple morbidities\(^{10,28–33}\). However, evidence based randomised controlled trials rarely include elderly and multimorbid patients in their analyses despite their being potentially those who would most to benefit from clinical trials. This is due to physiological decline, causing the inability for the body to handle adverse reactions, that can occur more readily in the elderly population increasing the potential harm in older people\(^2,7,19\). A longitudinal observational cohort study conducted in Germany, investigating the association of polypharmacy with frailty in older participants, reported frailty in 8.9% of their participants and a further 9.3% becoming frail within three years\(^7\). This indicates that frailty and polypharmacy could go hand in hand with frailty worsening as polypharmacy continues to be left unmanaged. Polypharmacy has emerged as an area of concern as we begin to focus on the ageing population and the problems of the chronically ill (especially marginalised users not knowledgeable in health lifestyles or those with poor health literacy). Furthermore, frailty and multimorbidity go hand in hand with people aged 65 or older having two or more long term conditions, rising to three or more conditions by the age of 75\(^1\).

However, multimorbidity is not just an ‘older person’s’ issue. Multimorbidity is a feature of cohorts with chronic disease but does not solely affect elderly people, many younger people have multimorbidity as well\(^{34}\). A significant proportion of multi-morbid patients are younger than 65 years, particularly in the most deprived populations where multimorbidity, on average, arises 10 to 15 years earlier than in the most affluent populations\(^1,16\). A cross-sectional study in Japan determined that almost 30% of
multimorbid patients were between the ages of 18 and 65. This prevalence increased to almost 63% in those older than 65. Furthermore, it has been shown that nearly two-thirds of patients with physical–mental health comorbidity were younger than 65. At present, it is estimated that around 50 million European Union (EU) citizens have multi-morbidities. Patients with multi-morbidities tend to visit the hospital more frequently and for longer periods of time, use a greater range of healthcare services and, in countries worldwide, spend significantly more on their health than those with a single condition. However, having multimorbidities does not imply that a patient has inappropriate polypharmacy. Patients with multimorbidities can have appropriate prescriptions. A well-managed patient profile of a patient with multimorbidities should include a patient with medications that match their individual diagnosed co-morbidities and improve their quality of life. Diagnoses of comorbidities should be regularly checked in relation to these medications to prevent overprescribing.

1.2.3 Polypharmacy Interventions

Addressing polypharmacy highlights ways in which current health services are failing and how medical intervention can be improved. Therefore, a holistic review of an individuals’ medication is needed regarding knowledge and understanding of medication safety, drug efficacy and applicability of the drugs in order to establish whether polypharmacy is appropriate or inappropriate. To manage polypharmacy, a system(s) will need to be created by enhancing the care of multimorbid patients through monitoring the benefit and risks of medications while attempting to decrease inappropriate polypharmacy. New guidelines across the EU have been developed to manage polypharmacy. The Scottish Government Polypharmacy Guidance has been created precisely for inappropriate polypharmacy detection and medication management. The guidance introduces a 7 step process of how HCPs can assist
patients with polypharmacy and how best to determine the requirement of the medication for those at-risk\(^1\). The most recent version of this guidance aims to target patients of high deprivation and high levels of multi-morbidity, as well as to patients with frailty. In addition to creating a polypharmacy guidance, the Scottish Government has developed a new Polypharmacy app which provides the guidance for medical professionals on their mobile phones\(^1\). Additionally, the Stimulating Innovation Management of Polypharmacy and Adherence in the Elderly (SIMPATHY) consortium has conducted an analysis of polypharmacy initiatives in the EU and models of tackling change in polypharmacy management\(^2\). They identified that several governmental bodies in the Netherlands, Catalonia, Germany, Portugal and Northern Ireland have created their own reports and/or guidelines\(^2\)-\(^4\). The main focus of the new guidelines introduced over the EU were either medication reviews, prescription reviews and/or treatment reviews. Poland has created a board with the aim to develop a model and strategy on polypharmacy management in the elderly\(^4\). In Sweden, clinical pharmacists implemented thorough medication reviews on elderly hospitalised patients\(^4\). Hopefully, with the assistance of these guidelines and the app, HCPs can monitor the drugs assigned to their patients, assess each drug and its necessity to improve their patients' health.

The Scottish Polypharmacy Guidance 7 Steps

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<td><strong>Aims</strong></td>
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### Effectiveness

**Step 4:** Are therapeutic objectives been achieved?

### Safety

**Step 5:** Does the patient have ADR or is at risk of ADRs?

### Cost-effectiveness

**Step 6:** Is drug therapy cost effective?

### Adherence/Patient centeredness

**Step 7:** Is the patient willing and able to take drug therapy as intended?

Figure 1.1 shows the '7-step process' to manage polypharmacy found in the Polypharmacy Guidance app as indicated by the Scottish Government.

#### 1.2.4 Medication Review

Medication reviews, where the patient is involved in decisions regarding medication use, is deemed essential in prescribing by recent healthcare policy, particularly in polypharmacy\(^1\),\(^{31}\),\(^{42}\). Prescribing cascades, where medication is prescribed to alleviate adverse events but is then not removed once the ADR has been treated, could be the cause of some polypharmacy\(^{19}\). Patients may not wish to be taking multiple medicines or may prefer a certain treatment over another. Also, it is known that individuals that, previously, received benefit from their prescribed medications may cease to receive said benefit after a certain point in their treatment but their treatments are not always stopped once this point is reached\(^{16}\). Often, patients are prescribed (and may continue to take) medications that cause adverse effects and where the harmful effects of the drug are perceived to counter the beneficial elements\(^{15}\),\(^{16}\). Medication reviews could assist patients displaying these features. An effective medication review should discuss questions such as; why the therapy was prescribed, was this medication prescribed to counteract the ADR of another drug, is the drug continuing to benefit the patient, are there any non-pharmacological alternatives available?, as similarly
indicated in the Scottish Governments 7-step medication review process\textsuperscript{1,19}. It is important that patients are given ample information to enable them to take their medication effectively and safely\textsuperscript{21}. Furthermore, a new app by the Scottish Government, a shared decision-making tool, that both HCPs and patients can access which allows for a discussion, between the patient and HCP, on their medication and their opinions on their individual medication treatment. This initiative demonstrates the shift in patient-centred care that is beginning to be seen worldwide\textsuperscript{2,8,15}.

1.2.5 Polypharmacy in Patients with asthma

Asthma is a condition in which polypharmacy can occur with an individuals' treatment of their asthma alone\textsuperscript{37}. Furthermore, patients with asthma are expected to receive an annual asthma review in which they have a review of their asthma symptoms, possible confirmation of their asthma diagnosis via lab tests, e.g., Spirometry and their Forced Expiratory Volume (in one second) (FEV\textsubscript{1}) levels checked, a de facto medication review, treatment burden such as inhaler technique are checked, concluding with an asthma action plan (a self-management plan for the patient to follow at home and intended to aid their understanding of their treatment(s))\textsuperscript{43}. This is a shared decision-making exercise which is carried out, mainly, with the practice nurse and/or practice pharmacist, although it is also sometimes conducted by GPs as well\textsuperscript{44}. However, annual asthma reviews seem to only focus on the patient’s asthma and not their other comorbidities, treatment and other possible concerns.

Polypharmacy in patients with asthma can occur easily as most patients with asthma have multiple inhalers and, if their asthma is difficult-to-treat or severe, they may be taking steroids or other medications\textsuperscript{45,46}. Difficult-to-treat asthma is uncontrolled asthma independent of treatment, whereas severe asthma is a subsection of difficult-
to-treat asthma which is dependent on high doses of treatment and/or multiple treatments\textsuperscript{47}. Studies involving polypharmacy and the associated multi-morbidities rarely mention asthma and if mentioned, asthma is noted as a secondary or even tertiary condition\textsuperscript{48,49}. This view of asthma is consistent throughout medicine and the literature. In polypharmacy literature, asthma is not considered as seriously as other co-morbidities and, therefore, is not focused on as much as other diseases\textsuperscript{50,51}. However, asthma is uniquely situated in polypharmacy as being a respiratory condition associated with other comorbidities, such as rhinitis, anxiety and depression and cardiovascular conditions\textsuperscript{52–54}.

Within asthma treatment, there are multiple actors involved across several forms of care. More specifically, asthma is viewed as a condition primarily led by nurses in both primary and secondary care\textsuperscript{55}. However, doctors and pharmacists are still heavily involved in asthma patient treatment. In primary care, GPs and nurses mainly deal with asthma annual reviews, whereas GPs and pharmacists deal with medication reviews\textsuperscript{56}. However, this is changing with more nurses and pharmacists becoming independent prescribers\textsuperscript{55,57,58}. Moreover, in secondary care, pharmacists and nurses are heavily involved in asthma patient treatment and, regularly, liaise with specialists to discuss the patient and their individual treatments\textsuperscript{59}. As there are many actors involved in this treatment process, an understanding of how these actors communicate and transfer information regarding the patient, their medications and their needs could be advantageous to comprehend for application in future polypharmacy management in patients with asthma\textsuperscript{60}. In secondary care, there has been an increase in multidisciplinary teams that discuss polypharmacy management in patients with asthma with doctors, pharmacists, nurses and other HCPs such as physiotherapists and
others that may be required\textsuperscript{61–63}. In primary care, it is commonplace for GPs, nurses and pharmacists to discuss patient treatment\textsuperscript{64,65}. However, these discussions are not well understood on how HCPs bring polypharmacy, multimorbidity and deprescribing into the equation when providing asthma care.

1.3 Structure and Scope of the thesis

The second chapter contains a literature review of the research that focuses on polypharmacy management, particularly in relation to asthma and multimorbidity. The review offers much-needed context into asthma and polypharmacy treatment with a focus on the stakeholders involved in providing polypharmacy and asthma management. A focus on the separation between asthma treatment management and additional co-morbidity management is discussed in detail. The interprofessional collaboration involved in exchanging information across primary and secondary and how it affects the conduct of medication reviews is also discussed.

The third chapter explores the methodology. The mixed methods study comprising of two qualitative interviews; one interviewing HCPs with general polypharmacy experience and the other interviewing HCPs specialising in asthma. Polypharmacy management in patients with asthma and general patients presenting with polypharmacy were compared. Quantitative data taken from asthma care records from a seven-year period, 2009-2017 were analysed. Obtaining ethical approval and methodological issues are also discussed. This chapter also highlights the aims and research questions in relation to the methodologies used.

Chapter four discusses the first round of qualitative interviews conducted recruiting physicians and pharmacists from primary and secondary care within the United
Kingdom (UK). HCPs were interviewed on polypharmacy, guidelines, medication reviews, barriers to deprescribing and interprofessional relationships.

Chapter five includes the second round of interviews with specialist nurses in asthma, pharmacists, specialists and GPs. HCPs were interviewed on how asthma treatment factors in polypharmacy and whether they take multimorbidities and other medication into consideration in addition to their patients’ asthma. Medication reviews and its links to annual asthma reviews and interprofessional relationships were also explored in the interviews. The quantitative analysis conducted in chapters six and seven was guided by the issues and understanding of polypharmacy gained from responses from the interviews in chapters four and five.

The sixth chapter contains the examination of polypharmacy prescribing patterns by quantitative analysis of the number of medications prescribed over a seven-year period from an Asthma UK prescribing dataset. The multimorbidities associated with specific polypharmacy patterns and stratifications in the prescribing data were determined. Both polypharmacy and multimorbidity patterns were stratified by age, gender, body mass index (BMI) and smoking status and socioeconomic background. Mortality rates were analysed over time and stratified by socioeconomic background.

Chapter seven investigates hospital admissions and deprescribing observed in the prescribing data. Hospital admissions caused by ADRs were analysed by level of polypharmacy. Deprescribing was analysed by separating patients with at least one medication stepped down and one medication fully removed. Hospital admissions and
deprescribing patterns were, also, stratified by age, gender and socioeconomic background.

To conclude, chapter eight discusses the key findings, the links to previous research, the strength and limitations, the clinical and research implications and future work that can be guided from this body of work.

Chapter 2 - Literature Review

2.1 Introduction

In this chapter, I will discuss the processes involved in primary and secondary care prescribing, asthma in relation to polypharmacy and multimorbidity, power dynamics in interprofessional relationships, polypharmacy demographics and multimorbidity, medication reviews, repeat prescribing and the gaps needing to be filled in the literature.

2.2 Polypharmacy demographics and multi-morbidity

Among the research conducted in elderly patients with polypharmacy, certain demographic patterns were observed. A study in Sweden revealed that potential inappropriate drug use was detected more in elderly women, between the ages of 75-89, than in elderly men\textsuperscript{29}. This was explained as possibly due to the fact women are more likely to report their health conditions and use healthcare services more than men\textsuperscript{29}. This was, further, confirmed by a survey of prescription and non-prescription
of medication use in ambulatory adults conducted in the United States (US) which found that 57% of women aged 65 years or older took at least five medications and 12% took, at least, 10 medications\textsuperscript{66}. Additionally, low educational attainment is associated with higher levels of polypharmacy, excessive or otherwise, again, especially in women\textsuperscript{28}. In a rare study of medication data and patient interviews, an English study discovered an association between obesity and alcohol consumption being linked with higher levels of polypharmacy in patients older than 50 years of age\textsuperscript{14}. Furthermore, discussions surrounding polypharmacy and race has yet to be delved into with great depth. One study in the US reported that black Americans had less polypharmacy than white Americans\textsuperscript{67}. Furthermore, in certain Asian cultures, there is a propensity to look to the GP for medication regardless of their indications, the 'pill for every ill' ideology. More recent evidence could be compiled for the demographics of patients presenting with polypharmacy as current research, though existing, is limited. Also, these higher levels of polypharmacy may not be beneficial and, so, defining the type of polypharmacy these patients have could change the demographics of the aforementioned patients.

In Spain, it was found that polypharmacy decreased between 2011 and 2015, however, this could have been due to the Spanish National Health Service (NHS) no longer reimbursing medications from 2011 which could account for their decrease rather than polypharmacy lowering\textsuperscript{68}. Agur et al., discovered that in Scotland, women were more likely to experience multimorbidities than men\textsuperscript{69}. An interesting observation was discovered in another study conducted in Spain on the links between multimorbidity, polypharmacy and ADRs found that their results suggest that the effect of age on the occurrence of ADRs may disappear when multimorbidity is considered\textsuperscript{70}. Therefore, this study suggests that ADRs and multimorbidity are linked but that age
does not have an actual effect on multimorbidity and ADRs. This is quite a controversial finding as brings into question what occurs first. Multimorbidity causes an increase in medications prescribed in patients and increased polypharmacy causes increased levels of ADRs. This study suggests that multimorbidity causes increased ADRs, but what causes multimorbidities? Age, lower socioeconomic backgrounds, susceptibility to poor health that may or may not be linked to factors involving age or poverty level. According to this study, increasing age is not a factor which leaves only poverty level, extenuating social circumstances usually related to poverty level such as poor housing, education and health literacy and susceptibility to poor health outcomes (which is usually in healthcare linked to age)\textsuperscript{70}. In contrast, however, this could be linked to patients within these lower socioeconomic backgrounds displaying higher levels of multimorbidity, polypharmacy and ADRs at a younger age.

A study in Scotland focusing on the association between COVID-19 to polypharmacy found that severe COVID-19 was associated with polypharmacy but could not be easily explained by the existence of multimorbidities in these patients\textsuperscript{71}. This suggests that multimorbidity, though commonly associated with polypharmacy, does not necessarily cause a pre-disposition to additional comorbidities or disease diagnoses. They, also, discovered that COVID-19 was strongest in those without a hospital diagnosis that suggested they were at a high risk of disease. This highlights that without being seen by HCPs, patients can be more at risk to diseases if they do not attend healthcare services. Furthermore, this study found that the association between patients prescribed non-cardiovascular drugs and COVID-19 was higher in those younger than 75. This could also be due to these patients attending health services less frequently than patients over 75. Another UK wide study on multimorbidity and COVID-19 revealed that increasing polypharmacy and multimorbidity, particularly
cardiometabolic conditions were associated with COVID-19\textsuperscript{72}. They were also more likely to be male, non-white, from lower socioeconomic backgrounds, be current/former smokers and have a high BMI. Patients with 10 or more medication were two times more at risk that patients taking 4 to 6 medications. This study only featured patients between 48-84 years of age which removes quite a large chunk of the population to analyse associations with age, particularly as patients over the age 84 are most likely pre-disposed to COVID due to frailty and, also, the removal of younger patients from lower socioeconomic backgrounds who are more susceptible to multimorbidity were also not included\textsuperscript{72}. Additionally, it was found that during lockdown, there was an increase in prescriptions and dispensations\textsuperscript{73}. This suggests that during lockdown, repeat prescriptions were heavily utilised and that, subsequently, inappropriate polypharmacy could have increased in this time due to GP surgeries being overwhelmed with work and unable to check these prescriptions.

Depression, in polypharmacy and multimorbid patients, seems to be a common co-morbidity. Rhee et al., found that patients with polypharmacy were more likely to be prescribed two or more anti-depressive medications\textsuperscript{74}. These prescriptions could have been due to multiple cognitive issues and possibly, sleep related issues such as sleep disturbances. The PACSim study in England projected how future multimorbidity would appear in patients over 65 in 2035\textsuperscript{75}. They observed that patients with 4 or more disease would quadruple from the 2015 levels by 2035 and that 2 or more of these comorbidities would be linked to cognitive/mental health, such as dementia and depression\textsuperscript{75}. If the levels of multimorbidity, particularly 4 or more comorbidities, were to increase to that degree in future, polypharmacy in those cases would become an inevitability even if one medication was prescribed per comorbidity. This means that
future planning for healthcare should factor in multimorbidity and polypharmacy management. One way could be to find non-pharmacological interventions for these morbidities or attempting early diagnosis of co-morbidities. However, this is easier said than done. If patients have multimorbidities, this could cause more patients to attend healthcare services for each of their morbidities causing a strain on the NHS and increasing workloads. This would create additional time constraints which would affect the ability of HCPs to conduct medication reviews to locate other ways to prevent polypharmacy which could cause more patients with polypharmacy and/or, also, this could affect the frequency of disease diagnosis possibly meaning that patients have (multiple) undiagnosed comorbidities.

Furthermore, if patients receive any non-pharmacological interventions that suits their lifestyle in tandem or instead of their medications would indicate a well-managed patient. In certain cases, non-pharmacological therapies in older people can be as beneficial as pharmacological treatment to treat co-morbidities but are known to not be sufficiently used in clinical practice due to lack of evidence\textsuperscript{76,77}. In contrast, a poorly managed patient with multimorbidity would be a patient with several medications for each of their comorbidities. Also, they may have medications that have been forgotten about for previous symptoms where no diagnosis, or misdiagnosis, of a comorbidity occurred or medications to alleviate the effects of another treatment\textsuperscript{38}. No evaluation of the patient’s lifestyle or circumstances may have occurred and, therefore, their regimen is standardised and not personalised\textsuperscript{78}. A study in Australia indicated that, in patients with multimorbidity, polypharmacy was an issue as patients who were aged 40 years and above were ten times more likely to be prescribed four or more medications on a daily basis\textsuperscript{37}. A shift in the literature needs to occur with research focusing on both multi-morbidity and polypharmacy in younger patients as many
articles simply exclude younger multi-morbid patients from their analyses. This exclusion, also, causes younger people to fail to qualify for interventions aimed at people with multiple chronic conditions as these inventions are typically targeted for older adults.

Polypharmacy is an indicator for multimorbidity, which translates to the need for the careful management of complex conditions, medication regimens and possible poor medications management. Patients with multimorbidity are highly likely to be faced with fragmented healthcare and instructions that are conflicting which can make it more challenging for them to adhere to their medication list and understand the instructions provided to them causing them to be alienated from their own personal medication regimen. For doctors, the difficulties associated with multimorbidity have been emphasised due to the ‘industrialisation of medicine’ and the issues this ‘industrialisation’ has caused in the management of patients with multiple medical problems. The ‘industrialisation of medicine’ has caused healthcare to turn into an industry where everything is rightly or wrongly scrutinised and the division of labour and specialisation for HCPs has made it difficult for patients with multimorbidity to receive the correct care they need for all their co-morbidities. Chronic disease management is beginning to be improved with national guidelines being implemented in disease specific clinics, such as GP practices offering diabetes management clinics.

The introduction of the Quality and Outcomes Framework (QOF) in England has allowed for the consistent discovery of diagnoses of many important chronic health conditions. This means that the coding of important diseases is likely to occur in participating practices and, as GP records in the UK are all computerised, will allow
for records to be easily understood when codes are added. Polypharmacy is an important consequence of following guidelines in people with multimorbidity\textsuperscript{39}. This may become a problem, however, when an individual is diagnosed with multiple relatively unrelated conditions who will, then, possibly experience the burden of polypharmacy. Therefore, interventions will need to be created to reduce this burden by reducing adverse events, improving prescribing quality and reducing expenses\textsuperscript{82}. The downfall of QOF is that it is a pay for performance instrument which has a points system and rewards GP surgeries with ‘good practice’\textsuperscript{83}. This could cause doctors to just follow the framework for the monetary and reward gain rather than for the patients’ benefit and could cause greater inequalities in unincentivized areas of health care. Consequently, in the first year of its implementation, practices serving lower socio-economic populations received less financial remuneration than practices in more affluent areas which, to be fair, is in keeping with the frameworks original mission of improving health outcomes than tackling health inequality. However, within three years, the achievement gap between practices had significantly lessened, narrowing from 4\% to 0.8\% in median achievement\textsuperscript{83}. Despite this gap decreasing, health inequalities should be targeted in future schemes, whether they are pay for performance or otherwise, as poorer areas seem to suffer the most with poorer healthcare and, in turn, poorer quality of life.
One cannot discuss improving healthcare in Scotland without mentioning the Inverse Care Law. The Inverse Care Law describes when ‘the provision of good medical care tends to vary inversely with the need for it in the population served’\textsuperscript{84}. It directly deals with the clinical encounter and the doctor-patient relationship\textsuperscript{34}. This law is of particular importance in Scotland as Scotland has the lowest life expectancy for women in Western Europe and the second lowest for men. Furthermore, there is an ever-widening gap between the health status of the rich versus the poor. 21\% of the Scottish population in lower socio-economic areas have limiting long-term illnesses compared with 8.5\% in more affluent areas\textsuperscript{85}. The majority of healthcare is provided through primary care in Scotland, 90\% of the activity from the NHS is from GPs, nurses and other allied HCPs. A study of 3,044 patients from 26 practices in the west of Scotland showed that patients in more deprived areas had worse long-term health, more long-term illness/disability and more multimorbidity (defined as two or more long-term conditions)\textsuperscript{85}. Moreover, the burden of poorer health and multimorbidity in lower socioeconomically deprived areas results in high demands on primary care and
creates a causal pathway to poorer access to care, less time available to be spent with
the doctor and possible higher GP stress. Additionally, they detailed that there is an
association between lower socio-economic status, multimorbidity and psychological
distress. This could be attributed to their inability to speak to their HCP when required
and at length, however, this needs to be evaluated further for better understanding.
We also need a better understanding that can be linked to the HCPs’ point of view
such as how do doctors deal with and manage additional stress. Secondary care is
displayed in the emergency services but, sadly, they are a poor substitute for the
personalised integrated primary care that patients with co-morbid conditions require.
It has been shown that many patients with chronic problems would rather see their
own trusted doctor than by any other doctor, these patients may be able to witness an
improved level of care if continuity in doctor consultations are added. These
healthcare inequalities should be taken into consideration when implementing
medication reviews and other polypharmacy reviews. What is needed by both the
patient and doctor is time. Time to discuss issues in more depth when in consultation.

Health inequalities, polypharmacy and multimorbidity are guided by governmental
policy. However, as of February 2022, the National Institute for Health and Care
Excellence (NICE) guidelines on multimorbidity and polypharmacy, under medicines
optimisation, were withdrawn to make room for a 5-year strategy after COVID. The
national Overprescribing guideline was introduced in England in September 2021 as
a replacement for the now defunct NICE guidelines. However, currently, the
Overprescribing guideline refers to most of the topics mentioned in the NICE
guidelines so the removal of these guidelines to publish a review prior to the
introduction of new and improved guidelines seems counter-intuitive. Granted, the
current way guidelines are created force doctors and patients to read two (or
sometimes more) separate documents for every condition the patient has: disease
guidelines and polypharmacy/multimorbidity guidelines. Furthermore, the clinical
implementation of these guidelines are quite low with lack of resources, lack of
awareness and lack of acceptance to the recommendations being the main reasons
for this. One way to improve this would be to create one ‘mega’ guideline linking both
(or several) topics, however, this could quickly become too many pages to read,
difficult to understand or difficult to utilise in a clinical setting. Therefore, even although
cross-referencing guidelines could be unreadable, using electronic formats that show
different recommendations based on demographic and clinical information provided
through screening questions or coded data may improve implementation by HCPs.
More simplistic versions of this could be created as a starting point with the guideline
becoming more complex as versions are developed further. Creating this systematic
and appropriate cross-referenced guideline could at least relieve some of the
treatment burden from the GPs shoulders making their normal everyday tasks easier.

2.3 Asthma in relation to polypharmacy

Inhaled treatment is the preferred medication for patients with asthma. Commonly,
short-acting β2 agonists known as relievers and/or inhaled corticosteroids are used as
‘preventer’ medications. Relievers cause smooth muscle relaxation and dilation of
the airways and ‘relieve’ symptoms whereas preventers stop swelling and
inflammation in the airways to ‘prevent’ asthma symptoms. Isidoro-Garcia et al.,
highlighted that polypharmacy is ‘almost constant’ in asthma treatment with multiple
steroids, both inhaled and oral, can be simultaneously prescribed, particularly in
severe or difficult to treat asthma. Also, as patients with asthma commonly have
additional comorbidities, therefore, pharmacological interactions in medications need
to be factored into asthma treatment. In Sweden, a cross-sectional study with 437
asthmatics with allergic multimorbidities found links asthma with anxiety, depression and allergy. This study was limited by mainly focusing on allergic multimorbidity and no other co-morbidities\textsuperscript{92}. Patients with severe asthma have more multimorbidities prevalent that other patients with asthma. Tools such as the Asthma Control Test and Asthma Control Questionnaire are used to evaluate asthma control by describing symptoms\textsuperscript{93,94}. However, these tools fixate on asthma issues and do not utilise a multidimensional approach to asthma of risk factors and other comorbidities.

Furthermore, comorbidities in patients with severe asthma may cause symptom overlap and can be associated with poor disease control, diagnoses and worse asthma outcomes\textsuperscript{95}. Comorbidities associated with severe asthma are other respiratory diseases, obesity, Gastroesophageal Reflux Disease (GERD) and cardiometabolic diseases. A study in France conducted with elderly female asthmatics found that most women had at least one medication in their prescription list that was not asthma related\textsuperscript{96}. The women in the study were found to have links between multimorbidity and disease severity. Polypharmacy in these patients was associated with poor asthma prognosis. Therefore, multimorbidity, and the related polypharmacy, seems to be an unmet factor and need in future asthma management. Furthermore, another way in which polypharmacy and asthma are ideally situated is the link between deprescribing and asthma treatment plans. An important way to handle inappropriate polypharmacy in patients is to use medication reviews to monitor medication lists to determine the best treatments for the individual patient\textsuperscript{32}.

If a medication review is conducted per guidelines, deprescribing is the next step, if appropriate. Deprescribing involves weighing the benefits and risks of a treatment in
a patients’ medication list and, usually, in the first instance, stepping down non-beneficial medication and, subsequently, aiming to remove the medication from the patients medication list. The way in which asthma treatments are prescribed are indicated by a step wise approach in official asthma guidelines. This stepwise approach allows for asthma treatments alone to be de-escalated with ease. Additionally, this stepwise approach is reviewed within the annual asthma review. However, again, the issue with patients with asthma and polypharmacy concerns their other morbidities and other treatments that they are prescribed. This stepwise approach is not transferred to other treatments as either they are not included within the annual asthma review or the guidelines for other treatments are under other disease guidelines, which may not be dealt with in a stepwise manner.

Bloom et al., revealed in their analysis of stepping down asthma medication, GP surgery doctors, nurses and community pharmacists very infrequently discussed or attempted to step down medication. They found that most doctors and nurses would only step down because they wanted to ‘reduce medication burden’ or because guidelines had told them to. However, these same HCPs stated that they were only aware of the guidelines and only a select few had seen the guidelines. This suggests that, despite the knowledge that the guidelines exist, most of these HCPs did not go out of their way to discover what the guidelines informed them to do. Asthma HCPs mainly noted that they ‘sometimes’ or ‘often’ completed annual asthma reviews and only the participants with specialised medication training were more likely to decrease medication. This further suggests that asthma reviews do not happen annually, or indeed as frequently, as noted by asthma guidelines. Mes et al., in their review of pharmacists and asthma medication adherence, found that most effective
interventions addressed the perceptions and practicalities that affected individual motivation and ability to adhere medications. Bloom et al. further noted that barriers to stepping down medications focused on lack of feasibility, poor awareness of procedures, lack of self-confidence and fear or concerns about who was responsible for stepping down. This highlights areas that may need targeting for future improvements to asthma medication management.

2.4 Medication Reviews

In March 2021, NHS England decommissioned Medicines Use Reviews (MURs), where medicines reconciliation occurred in community pharmacy, and moved to guiding HCPs to conduct Structured Medication Reviews (SMRs), along with shared decision making in patients, for implementation in primary care. Shared Decision Making, where discussions occur in clinical settings with patients about their medical care and/or treatment, has been proposed to allow patients to understand their values and preferences while having evidence-based information regarding their medication outcome probabilities, harms and benefits. Shared decision making and/or discussions with patients usually go hand-in-hand with medication reviews. However, a study in hospital medication reviews found that 70% of doctors thought medication reviews facilitated shared decision making but 77% of patients felt the care they received was paternalistic. People with high levels of literacy, usually from higher socio-economic backgrounds and have high levels of educational attainment, commonly excel in utilising shared decision making to their advantage. Patients with lower socio-economic status risk alienation and being underserved with these decision-making schemes, increasing health inequalities.
Approximately 80 million Americans are deemed to have limited health literacy and may, therefore, be saddled with worse health outcomes\textsuperscript{107}. A study conducted by Drake et al., showed that enhanced knowledge, participation in decision making, a willingness for collaborative decision making and informed choice occurred in their analysis of shared decision making in men with prostate cancer\textsuperscript{108}. However, another study claimed that Drake’s results were overinflated\textsuperscript{102}. The improvement of health and computer literacy to facilitate enhanced shared decision between HCPs and patients should be a consideration in the developmental stages of creation of systems. Existing decision making programmes should adapt to prevent the risk of further health inequalities to accumulate for example, using simpler language, avoiding complex medical terminology and using simple layouts and formats\textsuperscript{102,109}. Shared Decision Making could be a means for doctors, and the medical field in general, to empower patients who are normally disengaged to comprehend their health a little better.

Furthermore, there have been other initiatives to lessen the possible inappropriate polypharmacy. The ‘Choosing Wisely’ campaign in the US and Canada was recently developed to change clinician behaviour to align with best practice by having them stop various interventions that were not evidence-based. The necessity of the campaign was to improve patients’ health, free from harm or duplicate procedures the patient had previously received\textsuperscript{110}. Choosing Wisely aims to have medical organisations determine tests, procedures or interventions that are commonly used in their speciality. These tests are, then, complied into lists and a top five of these interventions will be indicated as having questionable use. This list will, then, be disseminated and will trickle down into careful conversations between the patient and doctor about the appropriateness of the use of an intervention, allowing for shared decision making to occur. Choosing Wisely’s key aim is to change prescribing culture
similar to the polypharmacy guidance and medication review app implemented by the Scottish Government. This initiative has been implemented by 60 specialist societies in the US and has, also, been extended into countries such as Australia, Germany, Italy, Japan, Switzerland, the Netherlands and in the UK by the Academy of Medical Royal Colleges, the coordinating body for the 23 medical royal colleges and faculties in the UK and Ireland\textsuperscript{110}. Choosing Wisely and the Polypharmacy guidance are moving away from this ‘doctor knows best’ rhetoric and moving into a new ‘patient understands what works for them best’ rhetoric also known as person-centred care. This gives an insight into the way modern medicine and prescribing is changing. However, as Choosing Wisely in England has no incentivisation, doctors are more likely to push for the QOF quotas rather than focus on an open discussion with their patients’ treatment options.

Shared decision-making, particularly in relation to polypharmacy, works synchronously with person (or patient)-centred care. There are four pillars to person-centred care; treat people with dignity, compassion and respect, provide coordinated care support and treatment, offer personalised care and enable people to recognise and develop their abilities\textsuperscript{111}. In medication reviews, the core of person-centred approaches according to Health Education England are “values, core communication and relationship building skills, conversations to engage people, conversation to enable and support people and conversations with people to manage the highest complexity and significant risk.”\textsuperscript{112} In polypharmacy, the person-centred approach is a combination of both clinical HCP perspective and patient perspective with a strong emphasis on medication reviews being a collaborative experience to inform decisions around prescribing and de-escalating treatments\textsuperscript{113}. This collaborative approach can allow for medication reviews to be much more individualised and possibly ensure the
removal (or introduction) of medication can be done in a safe, effective and co-
ordinated manner. Therefore, HCPs with the right expertise can undertake
medication reviews with the idea of addressing polypharmacy issues in the context of
the patients’ overall health goals.

A review in interventions in primary care to reduce ADRs and hospital admissions
found that most studies in medication reviews were conducted involving pharmacists,
then nurses and doctors had the least amount of studies involving a medication
review. This could reveal that pharmacists are the HCP considered in research
circles to be the ones related to medication reviews followed by nurses. GPs were
seemingly the least associated with conducting medication reviews.

The burden of ADRs on the NHS is considerably high and are a major point of
contention for HCPs. Morbidity, mortality and extra costs are the result of such a
burden. The consumption of multiple medications, specifically drug-drug
interactions) has always been viewed as a major cause of ADRs and, in turn, hospital
admissions. In a study conducted by Pirmohamed et al., it was discovered that
16.6% of ADRs were due to interactions. Non-steroidal anti-inflammatory drugs
(NSAIDs) and diuretics were most commonly found to cause such interactions. Also,
Aspirin was implicated in causing 18% of ADR admissions with gastrointestinal
bleeding as the most common adverse effect. These results are in keeping with other
literature in this area. However, as many of the aforementioned drugs have
proven benefit for patients, reducing the burden of ADRs and improving the
benefit/harm ration of drugs need to be achieved. Though, one issue is
reductions in high-risk prescribing are slow or minimal. There should be better
methods that HCPs can identify patients at high-risk of ADRs and, in association, avoid preventable hospital admissions to minimise dangers to patients\textsuperscript{118}.

One approach could be by identifying, through personalised medicine, whether the patient is absolutely required to take all their prescribed drugs. Analysing how a person's genes affect how they respond to medications has become a way in which we can prevent ADRs from occurring in a more person-centred and adaptive way. This process is known as pharmacogenomics. Two reports from NHS England and both the Royal College of Physicians and British Pharmacological Society indicate how this process is achieved\textsuperscript{120,121}. By analysing an individuals' genetic makeup, we can understand their response to specific drug types. From this analysis, we can determine the optimal drugs and doses that could best alleviate a patients’ symptoms. This personalised approach can save the time needed to adjust patients’ medications and/or dosages to discover the best treatment for that individual patient. There are tests for genetic variants in relation to determining potential ADRs in patients, however, whole genome sequencing is constantly developing and is not yet widely available\textsuperscript{122}. Implementing pharmacogenomics testing is perceived as being potentially costly despite the potential cost-saving effects of patients need to visit their HCP less\textsuperscript{123}. Due to there being limited information on pharmacogenomics in the online tools and systems used daily by prescribers, this makes it difficult to introduce on a wider scale\textsuperscript{121,123}. Therefore, continued utilisation of prescribing and de-escalating treatments to determine what works for patients will suffice until we can target these issues,
2.5 Deprescribing

Once inappropriate polypharmacy has been revealed post-medication review, deprescribing will be the next step. Deprescribing is a term that is used to refer to the stopping or reduction in dose of prescribed medications. Eliminating drugs that are unnecessary, may improve one of the negative effects of polypharmacy; poor adherence. Recently, deprescribing has been associated with negative connotations with patients and, in turn, the term de-escalating is becoming more common. Consequently, despite the primary aim of polypharmacy reviews are to achieve clinical benefits, deprescribing can deliver reduced economic costs, inconvenience and medical waste. Patients on a stabilised medication regimen with fewer medicines could potentially visit their health professionals less, reducing the burden on healthcare services. Moreover, a reviewed medication list with ADRs taken into consideration will allow for fewer unscheduled hospital admissions due to ADRs. However, unsafe deprescribing can cause a ‘withdrawal reaction’, where the removal of a medication can lead to a physiological response. Also, pharmacokinetic and pharmacodynamic changes can occur, particularly in elderly patients.

In recent years, it has been noted in the literature that there are two types of deprescribing, reactive and proactive. Reactive deprescribing occurs when a patient has had a visible reaction to their medication, whereby, they have an adverse drug reaction that may or may not result in a hospital admission. In ‘reaction’ to the noticeable effect the medication has on the patient, the medication is removed almost immediately after discovery from a patients’ prescription. Proactive deprescribing occurs when the patient displays no visible adverse reaction to a specific medication but the HCP will ‘proactively’ look at a patients’ prescription and decide
based on an evaluation of benefit versus risk whether the medication is therapeutically beneficial to the patient or if they should deprescribe the medication\textsuperscript{126,127}.

Furthermore, an analysis of other social factors in the patients’ life and environment can also be factored into the decision to deprescribe. In proactive deprescribing, the patient can either have their medication weaned off by way of dose lowering or they can have their medication removed as soon as possible depending on what the HCP views as best or patient preference if shared decision making has occurred. HCPs will commonly prescribe medications and will not remove them unless they frequently check their patients’ medications or perform some form of a medication review. A US study on proactive deprescribing in veteran patients showed that patients were rarely recommended to have medications deprescribed but placed great importance in discussing their medications with their HCPs and felt these discussions would foster the relationship with their healthcare provider despite possible disagreements on suggested changes\textsuperscript{126,130}.

The suggestion to deprescribe medications by stepwise approach is not a new one. The American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity, and many others suggest stepwise approaches\textsuperscript{100,131}. However, issues with compliance can be seen regardless of medication review and/or proposing deprescribing of medications. It is known that the more medications a patient is prescribed, the less likely they are to adhere to their treatment, particularly in older adults\textsuperscript{132}. Patients, in general, report a dislike in taking medications (especially in multiple quantities) and are often uncomfortable with the number of drugs they take\textsuperscript{8}. Consequently, improving adherence to long-term medications is a priority for policy makers, researchers and HCPs alike. Polypharmacy and adherence go hand-in-hand.
Non-adherence to medicines causes similar harmful effects as inappropriate polypharmacy does; higher risk of ADRs, increased emergency hospital visits, lower quality of life and augmented health costs\(^{133}\). However, identification of non-adherence in patients is challenging and involves many healthcare players. Reasons for non-adherence in the elderly has been associated with patient factors (mental and physical health), medication factors (complicated dosing schedules) and healthcare provider factors (poor patient-HCP relationships)\(^{132}\). Therefore, targeting these factors may have a bigger effect on health than improving specific medical therapies\(^{132}\). Medication reviews and, subsequent, deprescribing might boost patient morale and, in turn, targets the healthcare provider factors and, possibly, medication factors, but it still does not guarantee patient adherence to medicines. The creation of a decision support system/app that includes patients may alleviate elements of patient factors in non-adherence.

The use of tools like the Beers Criteria and Screening Tool of Older Persons Prescriptions (STOPP) or Screening Tool to Alert to Right Treatment (START) for medication appropriateness was noted by a randomised controlled trial suggesting that they contributed to fewer falls, hospital admissions and episodes of delirium\(^{134}\) but that they seem to have no clinical benefit to date\(^{135}\). Another trial suggested that the tool was linked to the reduction of ADRs\(^{136}\). It could be intimated that polypharmacy tools that target patients, particularly elderly patients, might need improvement or their clinical benefit needs to be determined in future research.

2.6 Repeat Prescribing
Repeat prescribing may contribute to polypharmacy, particularly inappropriate polypharmacy by allowing errors to go undetected in automated or semi-automated
prescriptions and, possibly, furthering preventable hospital admissions. A study in receptionists’ involvement in the monitoring of repeat prescriptions at four different GP surgeries observed that HCPs do not have the only involvement in repeat prescriptions with receptionist and administrative staff contributing to quality and safety in repeat prescriptions\textsuperscript{137}. They played a role in ‘bridging the gap between idealised assumptions’ about interactions built into electronic health records and repeat prescription routines. They, also, found that in all four surgeries, receptionists were unofficially in charge of getting doctor’s to sign off on repeat prescriptions which the receptionists found hard to do or they would send an email to the GP asking if the repeat prescription was ok to send off\textsuperscript{137}. The study suggested that there was ‘no best way of running repeat prescribing’ due to the certain components of the repeat prescribing routine working best in some practices versus others. This study highlights that repeat prescribing heavily involves receptionists though, officially, they do not bear the responsibility of these repeat prescriptions. It is the GPs’ responsibility to check the repeats that pass through and, based on the difficulty to obtain signatures or in cases where the receptionist received an affirmative response to sending repeats via email, this suggests that these checks are inadequate.

It was found in another study that the prevalence of one prescription item containing a prescribing and/or monitoring error was 4.9% and that most of these errors were minor\textsuperscript{138}. A minor error consisted of a low score on the study specific possibility of risk scale. Another study evaluating 97 GP practices on repeat prescription errors in New Zealand found, when auditing the practices, that there was poor concordance where practices were over-prescribing medications not on the practice agreed list\textsuperscript{139}. The study highlighted that the automation of repeat prescriptions, though a time-saver,
caused errors. Missing medications, prescriptions not being ready on time, wrong patient/wrong dosages and patients being overdue for a medication review were common errors that occurred. In terms of error detection, it seemed that only pharmacists or the patient themselves noticed there were errors. This could, possibly, suggest that doctors do not notice medication errors in repeat prescriptions. The reasons for this could be doctors simply being too busy with consultations or that they are not in charge of monitoring repeat prescriptions beyond the evaluation entailed in a medication review. However, this study may not have reported the incidences in which GPs themselves noticed errors focusing more on the pharmacist and patient perception. Therefore, GPs may notice repeat prescription errors and this study has suggested otherwise.

Repeat prescriptions are deemed to be difficult for patients to obtain whilst being an area in which surgeries seem to forget people are on long term repeats exacerbating the existence of prescribing cascades. Wilson et al. called for the now widely adopted reduced dosage units of a 28 day supply between each prescription for ease of patient access but this could be problematic as it could increase the volume of repeat prescriptions at GP surgeries causing increased workloads for auditors of these prescriptions and possible increase opportunity for prescribing cascades to occur. However, on the other hand, a shorter time frame might allow easier removal for prescriptions that were ineffective or harmful.

2.7 Prescribing Processes

Medical optimisation ensures ‘people get the right choice of medicines, at the right time, and are engaged in the process by the clinical team’141. However, the application
of this is more difficult to achieve. Hospital prescribing consists of staff organised into care teams for patients, usually multidisciplinary or contained staff from similar roles. According to studies, some teams can be hierarchal in nature and organisation, where seniority or experience of the employee is of high importance. These teams plus the HCP-patient relationship and evidence-based medicine, where the best evidence is utilised in decisions made about an individual patients care\textsuperscript{142}, are influential on prescribing practice. This hierarchal system causes issues when junior doctors, nurses or pharmacists wish to deal with a prescription that they deem inappropriate from a senior doctor/consultant. Hospital prescribing etiquette seems to consist of reluctance to changing another staffs’ prescribing decision, avoid making prescribing decision outwith your immediate team and only alter inappropriate prescribing decisions\textsuperscript{143}. Hospital doctors in prescribing usually deal with checking medication lists, checking for any drug-drug interactions and providing diagnoses. Pharmacists on the prescribing team usually deal with medicines reconciliation by way of structured medication review, correcting incorrectly prescribed medicine, monitoring repeat prescriptions and if they have an area of specialisation, they can only prescribe new medicines in that specific area. Doctors in hospital are not as involved in medicines reconciliation as pharmacists and, to a lesser extent, nurses. Similar to pharmacists, nurses usually have an area of expertise in which they conduct their prescribing\textsuperscript{57,144}. For example, specialist nurses in asthma can initiate respiratory medicines, monitor repeat prescriptions, provide patient education in how to use medications such as teaching correct inhaler techniques, make recommendations and conduct asthma reviews\textsuperscript{145,146}. Patients in secondary care encounter prescribing as and when their ill health causes them to be admitted to hospital other than when receiving repeat prescriptions\textsuperscript{147}.
In primary care, patients must make an appointment to see their HCP in order to receive care. GPs are responsible for initial diagnoses, medication reviews, checking for any drug interactions and building rapport with their patients. This extends to practice pharmacists who conduct detailed structured medication reviews to make sure that everything is correct in patient prescriptions and future repeat prescriptions. The role of practice nurses in prescribing is to conduct more disease specific reviews, be involved in medication reviews but to a lesser capacity than pharmacists and, sometimes, GPs. Also, practice nurses assist patients in adherence techniques. Pharmacists can be involved in adherence techniques but nurses seem to more involved in patient education in both primary and secondary care. The context of prescribing both general practice and hospital between HCPs depend on proximity and communication between prescribers. There are issues with interprofessional communication in both care types that require improvement. However, it seems that hospitals provide a more ideal location for medication reviews than primary care as everyone can be found on the same place and the addition of having added time with the patient than short consultation times in general practice. Therefore, improving the feasibility of medication reviews in short consultation times plus improving communication between prescribers and care systems could improve prescribing decisions and the ability to challenge colleagues prescribing decisions.

Reeve notes that UK doctors feel that they do not possess the skills or confidence to robustly defend their clinical judgement if/when they go beyond protocol decisions. She reports that professional training and assessment fixates on what the person knows rather than make use of this knowledge to make tailored decisions. This could cause the continuation of issues such as inappropriate polypharmacy as doctors, seemingly, do not feel confident to use their own judgement in clinical decisions or
reversals of wrongful or harmful prescribing. The All-Wales Medicines Strategy Group Polypharmacy guidance and other stepwise approaches to polypharmacy attempt to rectify this\textsuperscript{152}. Reeve mentions, however, that these guidelines do not ensure that understanding the patient’s experience is used to guide choices that occur in the use of evidence-based medicine\textsuperscript{151}.

Furthermore, a study in the US evaluating the feasibility of polypharmacy management in a 15-minute GP consultation highlighted the difficulties of determining the efficacy of a specific medication to subsequently suggest the deprescription of said medication\textsuperscript{153}. Providing features such as medication reconciliation, where HCPs get an accurate list of the medications a patients’ takes, properly assessing pharmacovigilance and monitoring drugs prescribed, searching for drug-drug interactions (DDIs), determining efficacy and suggesting alterations or removal of potentially harmful medications are complex processes in polypharmacy management. The authors suggest that simply implementing some of the elements of polypharmacy management in this the short 15 -minute window is better than nothing. The 2015 Commonwealth Fund observed that GPs in the UK spend even less time with their patients at an average of around 10 minutes. That is an incredibly short time to discuss the matter at hand, any issues with the GP and/or the GP having a quick informal look at the patients’ medication list, let alone suggesting to deprescribing medication in a stepwise manner. It could be argued that even implementing just one of the features of polypharmacy management as noted in the US study would be difficult to achieve in 15-minutes.
Prescribing decisions are a complex process. HCPs decisions are multifactorial with prescribers adopting several strategies when making prescribing decisions and critical heuristics in their duties conducting patient treatment. The main model used in polypharmacy management is Knapp and Oeltjen’s simplistic model of the benefit/risk model where demographic variables are taken into consideration with disease severity, benefits and side effects of medication and HCP specialty as other factors to consider\textsuperscript{154}. Raisch’s model where individual practice and thought affect prescribing decisions and organisational structure of healthcare services are also important in prescribing decisions. Patients factors were, also, deemed to influence HCP prescribing decisions as well as psychosocial factors such as stress\textsuperscript{155}. Gallan’s model of prescribing incorporates previous prescriptions, the perceived need for therapy by way of medication decisions and outcomes after prescribing\textsuperscript{156}. Current prescribing decisions integrate multiple theoretical frameworks entailed in these models.

To improve prescribing decisions, educating HCPs and equipping prescribers with these skills is imperative. It has been found that the UK is the least restrictive place in Europe in terms of legal authority to prescribe\textsuperscript{157}. Therefore, non-medical prescribing, where prescribing is conducted by any HCP that is not a doctor, aims to increase continuity of care, reduce waiting times, improve access to medicines and enhance utilisation of human and economic resources.\textsuperscript{157} A Scottish study on non-medical prescribing interprofessional education to HCPs, it was found that interprofessional collaboration and teamwork improved due to the intervention and that HCPs valued the knowledge and skills shared. In another study educating nurses and midwives about prescribing, it was discovered that their increased knowledge, status and experience in prescribing enhanced their confidence in their prescriptive authority\textsuperscript{158}. Furthermore, a multidisciplinary study on education in the context of medication review
and deprescribing, pharmacy students viewed medication review as linked to adherence and patient understanding while medical students perceived medication reviews as focusing on drug interactions\textsuperscript{159}. These final year students, also, stated they would have a lack of confidence removing any medications without an experience member of staff to assist them\textsuperscript{159}. Therefore, these studies indicate that education is heavily related to improving interventions in prescribing providing HCP with the confidence to correctly prescribe or deprescribe to supply patients with the level of care that they need.

Patients rely on HCPs to correctly diagnose and prescribe the right medicine and this continues with polypharmacy, where it is the HCPs responsibility to remove medications when they are no longer effective. Elements of HCPs prescriptions are functions that patients have no control over such as HCPs analysis of drug characteristics or the benefit risk ratio. Agency for patients in prescribing decisions can cause the HCPs to perceive patient’s expectations, if requesting a specific medication, a social pressure on them. In contrast, patients can perceive GPs advice regarding removal of prescriptions negatively as a cost-saving measure, etc\textsuperscript{160}. In UK GP surgeries, it was observed that prescribing is influenced by patient pressure and characteristics such as socioeconomic background, practice culture and shared beliefs and utilisation of guidelines\textsuperscript{161}. The perceived increase in problematic polypharmacy and the importance of patient centred safe prescribing were, also, an influence.

There has been a shift in recent years in healthcare to have a more personalised approach to patient treatment. Personalised care refers to patients having autonomy regarding their own treatment plans and delivery, based on their individualised
experiences, strengths and needs. Social prescribing has been a possible solution, particularly after COVID, to allow a more holistic approach to healthcare which signposts patients to community organisations and other non-medical sources of support\textsuperscript{162}. The existence of holistic self-management hubs for patients could alleviate pressure on HCPs in general and allow for improved use of consultations times as community groups can complement medical treatment\textsuperscript{163}. This can assist both in general prescribing and in polypharmacy management by way of providing increased time for medication reviews and medication reconciliation. It could, also, present a more effective way of reducing workloads for HCPs that seems to be a point of contention for shifting workloads between HCPs.

\textbf{NHS England Comprehensive Care Model}
Figure 2.2 taken from the 2020 Personalised Care report from NHS England.
2.8 Organisation of care and Healthcare Interprofessional Relationships

Polypharmacy management is dependent on multiple forms of healthcare systems collaborating to improve patient care. However, this is difficult to do when taking into consideration ambiguities and tensions about roles and allocations of responsibilities between different specific professional groups and local organisations which differ in their resourcing, expertise and professional status. This organisation of care can also contribute to perceived power imbalances between HCPs. Two-way communication and cooperation between team members are likely to be affected by the social power of the members. Social power is defined as the ability for people to change the behaviour of another by conforming to the first person(s). It is unwise to believe that bringing professionals together allows for ‘collaboration’ to occur\textsuperscript{164}. Trust is a key factor that needs to be established before said collaboration can begin. For example, a pharmacist could conduct a medication review with a patient and deems a certain treatment inappropriate for the patient. Yet, this drug was prescribed by the patients’ GP. There may be conflicting issues as other HCP do not want to challenge the doctors’ role\textsuperscript{165,166}. The lives of patients depend on good interprofessional collaboration. This may seem obvious but lack of communication and awareness have been shown to lead to lack and/or decrease of participation in interprofessional conduct\textsuperscript{167}. Also, views of an individual HCPs’ competency in their work is, also, used in the ability to trust their colleague\textsuperscript{64}. Furthermore, role clarity is imperative for team members to be aware of what to expect from each other. When roles are not explicitly defined, collaborative teamwork is challenged as issues of competency would appear\textsuperscript{165}. In a study interviewing nurses and pharmacists regarding medication reviews and the power dynamics when suggesting a therapy should be removed or justified in a patients’ medication regimen, nurses and pharmacists were able to
understand each other when learning and discussing each other’s individual role in the medication review\textsuperscript{165}. However, when passing this information on to the doctor, while allowing the doctor to argue why the patient was prescribed a certain drug in the first place, felt that the doctors were ‘headstrong’ in their medication choices. Nevertheless, nurses and pharmacists did agree that it was imperative that they have the doctors involvement in the medication review due to increased long term experience and knowledge of the patients\textsuperscript{165}.

The key factor to power dynamics in healthcare is the patient experience of the impact of these interprofessional relationships. It is believed that in shared decision making, while the patient does not work with HCPs per se, they are deemed to be one of the actors in the interprofessional relationship team\textsuperscript{164}. Therefore, patients with multimorbidity and/or polypharmacy should be allowed to be part of the ‘team’. One study indicated that having a pharmacist on a team of doctors had a positive impact on patient care, continuity of care and led to better decision making\textsuperscript{165}. This emphasises that a holistic approach to healthcare for patients can, also, be transferred to the healthcare services. While there is much research into interprofessional relationships in healthcare, in general, the sensitive relationships that exist during medication reviews could be researched further with particular focus on patient experience.

These interprofessional relationships are even less understood between primary and secondary care, particularly when the fragmentation of care exists, and specialists and GPs do not wish to be seen to be contradicting each other or getting involved in each other treatment choices and/or decisions.\textsuperscript{168–170} Prescriber professional background was a factor with nurses being viewed as more single disease driven, pharmacists
being willing to handle two or three co-morbidities and GPs were viewed as generalists who focused on everything\textsuperscript{171}. Furthermore, prescribers had mixed views on the potential of practice-based pharmacists to handle underlying workforce issues in general practice by shifting work classically given to GPs to pharmacists. This shows that, despite the current move to increase pharmacists’ roles and responsibilities in general practice, HCPs are sceptical about the effectiveness of this movement.

Several policy guidelines in the UK have been shifting workloads from GPs to pharmacists and nurses to alleviate pressure on GPs, however, there is limited evidence on the perspective of HCPs into how effective these workload shifts are. The Clinical Pharmacists in General Practice pilot conducted by NHS England was introduced to reduce the pressure on GPs by giving pharmacists a bigger role in patient safety and quality of care\textsuperscript{172}. Several studies have monitored patients’ views on these task shifts with reported positive patient satisfaction in nurses taking jobs classically meant for GPs\textsuperscript{173,174}. In contrast, Officer and McBride-Henry found that patients are unable to position specific roles to specific HCPs to evaluate and articulate their views in changes of responsibilities in healthcare. Patients were deemed to have limited awareness of the training and contribution and value nurses and pharmacists have in relation to GPs. They suggested that barriers in healthcare caused by practice hierarchies such as certain HCPs not being notified of certain results, inadequate follow up care due to GPs only having access to discharge information and ‘behind-the-scenes’ politics between HCPs were all visible to patients. Therefore, there seems to be a long way to go in terms of sharing roles and functions between HCPs that are interlinked to interprofessional relationships and communication. Openness to sharing knowledge and fostering a collaborative culture between these HCPs could improve
existing issues in workload and could shape prescribing in way which reduces problematic variation in prescribing.

**WHO Key Steps for ensuring medication safety**

![WHO Key Steps for ensuring medication safety](image)

Figure 2.3 was taken from the World Health Organisation (WHO) report Medication Without Harm and depict the key steps for ensuring medication safety\(^{175}\).

### 2.9 Gaps in the literature

Medication reviews and their barriers of implementation are well documented in the literature. However, the ease of access and opportunities for certain polypharmacy and multimorbid patients is not well researched. There is a focus on older people, particularly frail elderly patients, who are more likely to visit the healthcare services for many reasons associated with failing health and increased likelihood of hospitalisation which could trigger a medication review. The analysis of opportunities for access to medication review by way of comparing the access to healthcare services for older patients with polypharmacy versus younger patients, particularly from lower
socioeconomic backgrounds, access to medication reviews have not been investigated in the current literature. Opportunities to improve healthcare services for medication reviews, interprofessional relationships and the facilitation of improved communication between HCP and patient and by way of clearer and detailed notes on prescribing decisions across primary and secondary have been analysed but not the opportunity for at-risk patients to receive medication reviews when they are not regularly visiting their HCP.84,166,170,176,177.

Another gap in the literature can be found in deprescribing analysis. The social factors affecting general prescribing, polypharmacy and multimorbidity are discussed in detail in the literature. Barriers that affect deprescribing from both HCPs perspective and patient perspective are also discussed in several studies. However, how deprescribing manifests itself in patients presenting with polypharmacy across different age groups, socioeconomic background and gender is unclear. Some studies focusing on a specific drug being deprescribed have been analysed by age group such as bisphosphonate deprescribing stratified by older patients with dementia where it was found that deprescribing was uncommon and associated with poor disease prognosis.178. Furthermore, a review was conducted in gender differences in deprescribing patterns but this article did not contain any detailed information of levels of deprescribing per gender and only highlighted existing issues within gender in polypharmacy, where women have higher levels of polypharmacy.179. The literature seems to focus on how to improve deprescribing without determining the societal implications of deprescribing once achieved.

Furthermore, few studies have solely focused on asthma in relation to polypharmacy. Literature discussing asthma in relation to multimorbidity is quite prevalent within the
research. Additionally, studies that analyse polypharmacy do sometimes include asthma as a comorbidity but they are not the main focus of the research. Articles that do discuss polypharmacy in asthma focus on inhaler polypharmacy without including multimorbidity, the elderly and paediatric population, investigate polypharmacy through an ADR lens or severe asthma. Furthermore, due to asthma guidelines and protocol focusing on stepping down medication, there is limited research fully removing medications in patients with asthma. Therefore, analysis needs to be conducted in asthma patients presenting with polypharmacy, particularly in younger patients over 18, and deprescribing levels in this population.

2.10 Conclusion

The context of primary and secondary care prescribing, asthma in relation to polypharmacy and multimorbidity, organisation of care in interprofessional relationships, polypharmacy demographics and multimorbidity, medication reviews and repeat prescribing were discussed in this literature review. The gaps in the literature reveal that this study should focus on the stratification of deprescribing levels to determine which social factors affect deprescribing patterns, providing more information on asthma and the context of polypharmacy management in asthma patients presenting with polypharmacy and concentrating on the opportunity for younger multimorbid patients with polypharmacy to access structured medication reviews.
Chapter 3 - Methodology

3.1 Introduction

This chapter introduces the mixed methods utilised in this research. How ethical approval was obtained and reflexivity was accounted for is mentioned below. The research strategy, qualitative interviews, quantitative data analysis, aims and research questions for the study are all contained in this chapter.
3.2 Research Strategy

The study design sought to determine the most effective combination of research methods in which to gain a better understanding of polypharmacy. Polypharmacy is a multifactorial occurrence in medicine with many actors participating in both its occurrence and mitigation. To capture insights into the different aspects of polypharmacy prescribing and deprescribing, a mixed methods study design was utilised. This was done to encapsulate polypharmacy by using data analysis methods to model prescribing and treatment processes at scale and qualitative methods to highlight practices giving rise to this. The social processes involved while navigating the management of patients’ treatment through medication reviews and/or shared decision making are important to comprehend, to gain an understanding of polypharmacy treatment and to improve these systems to be better carried out in future. How HCPs notice polypharmacy, consider whether the patient has inappropriate polypharmacy, attempts to deprescribe or step-down medications and discovering potential barriers from patients are required to be considered by the HCP. Having a better grasp of the way HCPs handle patients presenting with polypharmacy, what are the common issues that patients face and how HCPs deal with these issues could be utilised to improve these interactions for both the patient and the HCP. Using a mixed methodology allowed for a wider range of evidence to be collected than using a single methodology to gain a better understanding of polypharmacy and to benefit from an awareness into the changes that have may have possibly occurred in polypharmacy levels over the years. Therefore, the aim was to use qualitative methods to understand how polypharmacy is managed from the HCP perspective to inform the social side of polypharmacy and quantitative methods to inform whether polypharmacy in the data confirms how it is being viewed by the public.
eye in healthcare. The qualitative interviews focused on medication management processes and issues to provide broader understanding of asthma polypharmacy that informed the quantitative analysis. Qualitative research provides a picture of the complex processes involved in polypharmacy but does not offer a generalised applicability and outcomes of these processes like quantitative methods can. Similarly, quantitative research can provide key insights into the outcomes of polypharmacy but not the processes. Moreover, qualitative research can help to guide the analysis of the quantitative portion of study by hypothesising about processes involved in polypharmacy and the quantitative methods provide the statistically factual evidence in the real world. Therefore, this is mainly to answer whether the interview answers reflect and explain what is portrayed in the dataset to develop a rich and robust understanding of polypharmacy. Do the views of HCPs showcase real prescribing patterns in reality and in the dataset?

However, issues with ethical approval caused the research plan to diverge from its original path. Gaining access to the 10-year longitudinal prescribing data that was necessary for the quantitative research turned out to be highly challenging to obtain due to the Lothian Research Safe Haven (LRSH) viewing the sample size as too large and were unwilling to allow access to very large datasets. Therefore, a cross-sectional study was recommended. The LRSH conditionally offered to provide access to prescribing data from the year 2009 in the Lothian region alone. Once this access was to be granted, the researcher would be required to re-apply for access to another year in the same region depending on the analysis of the original 2009 dataset. This would force the quantitative research to become a cross-sectional study rather than a longitudinal study. However, this would be incredibly time-consuming and provided no
guarantee that access to another year of prescribing data would be provided. This would change the research design of this study drastically and would cause the sample size to be exceedingly small both in terms of location and time period. The action of considering other forms of prescribing data produced significant delays in the research plan. Fortuitously, an Asthma UK study in Scotland was identified which had achieved access to prescribing data in people with asthma within a 7-year period. The resulting addition to the research team of this asthma study caused a shift in focus in the research. Conversations were had with Hillary Pinnock and Bruce Guthrie on the implications of changing the research focus to asthma. It was noted that the consequence of focusing on a particular disease such as asthma would provide the research with a trajectory and purpose that was missing from the original proposal. Furthermore, it would not alter the focus in terms of research design as it provided an opportunity for accessing longitudinal large-scale data in Scotland. Additionally, the literature review demonstrated that the examination of patients with asthma and their links to polypharmacy have not been greatly explored. Therefore, polypharmacy in patients with asthma became the new focus of the analysis. Furthermore, the qualitative research had an emphasis on interviewing HCPs on polypharmacy within the field of asthma.

3.2.1 Rationale for the Mixed Methodology

3.2.1.1 Social Processes of Polypharmacy and Interprofessional Relationships
While there is much research into interprofessional relationships in healthcare, in general, the sensitive relationships that exist during medication reviews could be researched further. Medication reviews focus on optimising treatments from a patients’ medication list and can confirm that the present prescriptions are accurate and optimal. However, little is known on the outcome of these reviews. Also, whether
there are issues or concerns between these professionals when deprescribing is not well researched. Furthermore, very few articles have investigated the views of HCPs about patients with polypharmacy\textsuperscript{64,190}. Qualitative studies investigating interprofessional relationships and HCP perceptions have usually been achieved by either conducting interviews or surveys on their views on the topic. Therefore, semi-structured interviews was judged to be appropriate to understand polypharmacy and gain an insight into polypharmacy treatment, approaches to deprescribing and medication reviews, and the potential for disagreements to occur when interacting with other HCPs. In healthcare, there is the patient side of the interaction and the patient facing side of the interaction. Hence, understanding how the patient perceives their polypharmacy would be beneficial. Health practitioners have extensive experience of prescribing and are likely to have reflected upon the factors giving risk to polypharmacy and, therefore, are particularly informative respondents.

Moreover, this study endeavours to determine their treatment of patients presenting with polypharmacy, the consideration of the patients’ co-morbidities (and if this alters their treatment trajectory for individual patients), the barriers they face when attempting to deprescribe and the potential for misunderstandings to arise when interacting with other HCPs when conducting reviews of medication. An understanding of how HCPs interact in medication reviews could provide indicators of how medication reviews could be better conducted and improve healthcare services for patients with polypharmacy.

\textbf{3.2.1.2 Changes in Rationale due to Ethical Approval Issues} Due to the pragmatic decision to alter the trajectory of the study design to be limited to the dataset only containing patients in Scotland with asthma, the rationale for the
study was now modified. It was discovered that polypharmacy in patients with asthma is an untapped area of research. Patients with asthma are unusual in the sense, that some patients have polypharmacy due to their asthma medications alone. Moreover, patients with asthma are required to have an asthma annual review in which their asthma medication in analysed, as their asthma medication should be appropriate. This could mean that the analysis for inappropriate and appropriate polypharmacy in patients with asthma could be easier to analyse. However, whether medication reviews are conducted additionally, in patients with asthma, are more unclear from the existing literature. Furthermore, respiratory conditions can be associated with other comorbidities, such as heart disease and anxiety/depression and analysis into these comorbidities and their subsequent treatment could be valuable to recognize. Thus, analysis in the severity of asthma and its possible associations with other comorbidities and, in turn, higher levels of polypharmacy could enhance understanding of both asthma and polypharmacy from this study. This amendment of rationale would be required to be extended to both the qualitative and quantitative areas of research.

3.2.1.3 Changes in Qualitative Study Design due to Ethical Approval Issues
The study design now aimed to focus on HCPs working in asthma. The central themes of understanding the polypharmacy in their patients, focusing on multimorbidity, conducting medication reviews, shared decision making and deprescribing in patients and the barriers associated and the interprofessional relationships in healthcare with polypharmacy remained unchanged. Conversely, these themes would need to be adjusted to focus on patients with asthma and care and take into consideration the literature into patients with asthma and polypharmacy. Around 7 asthma focused HCPs within the University of Edinburgh were approached to have an informal
exploratory discussion on issues with asthma treatment they considered to be important or worthy of further research. These conversations guided the research design for the asthma HCP interviews. Furthermore, the semi-structured questions that would be asked to HCPs would need altering. Hence, the questions were changed to ask more questions regarding specific asthma treatment and can be found in the chapter 5. Polypharmacy with an asthma focus was the main theme in the asthma questions. Questions surrounding polypharmacy due to asthma treatment alone, the severity of asthma and its connections to comorbidities, medication reviews and their associations to asthma annual reviews, the management of long-term prescribing of irregular oral steroids and possible suggestions to improve asthma treatment were added. Additionally, the inclusion and exclusion criteria were changed; the inclusion criteria would now include any HCPs, doctors, nurses, and pharmacists, in Scotland and England who worked with patients with asthma or specialised with patients with asthma, the exclusion criteria would include any HCPs that did not work with patients with asthma in the last year.

3.2.2 Aims and Research Questions

The general overarching aims of this research is to better understand prescribing in the context of polypharmacy in patients with asthma and inform attempts to reduce inappropriate polypharmacy. The individual aims and research questions for each methodology is as follows:

3.2.2.1 Qualitative Research Questions

This study sought to answer the following questions:
1. What are the clinical, procedural and social factors giving rise to polypharmacy, medication reviews and deprescribing in patients with asthma and polypharmacy?

2. What are the social interactions between patients and healthcare professionals that occur, both in patient care and interprofessionally, of prescribing/medication reviews/deprescribing in asthma and polypharmacy healthcare practice?

3. How do the current context(s) of medication reviews in asthma healthcare settings deal with patients with asthma and polypharmacy and how can they be improved from having a clearer view of the interactions and communications involved in managing polypharmacy in these patients?

3.2.3.2 Qualitative Research Aims
Therefore, the aims of the qualitative research are:

- To understand the how HCPs manage polypharmacy in patients with asthma by gaining an understanding of how they start, review and monitor medication;
- To comprehend the social interactions occurring between HCPs and patients when prescribing/reviewing medications/deprescribing in patients with asthma to improve shared decision making in healthcare from the HCP perspective;
- To understand the interpersonal communication involved in polypharmacy management between HCPs and the potential utilisation of healthcare information such as guidelines used by asthma HCPs,
- This knowledge will guide and aid interpretation of the quantitative analysis of the prescribing data.
Furthermore, the general aims of this research were to explore how medical care is given to patients with asthma and polypharmacy to provide a lens into how we might revise future medication management procedures, guidelines and resources in polypharmacy and asthma healthcare practice.

3.2.3.3 Changes in Quantitative Study Design
Due to the amendment of rationale from general patients presenting with polypharmacy to patients with asthma, this was required to be extended to both the qualitative and quantitative areas of research. The quantitative research design would, naturally, automatically be changed as any data that would be obtained regarding polypharmacy patterns over time, deprescribing changes and analysis into multimorbidity would all be stratified by the overarching asthma condition. Moreover, the dataset did not contain care home residency information and, therefore, this could not be examined per the previous study design plan. However, there was now a disconnect between the initial qualitative analysis which had been conducted in polypharmacy in general, that occurred prior to this data access. Therefore, the qualitative research design would need to be drastically revised and would see the biggest change. Furthermore, the original programme to analyse the data was to use SPSS but the program used within the safe haven was R. Therefore, R was utilised for the data analysis of the prescribing dataset.

3.3.2.4 Quantitative Research Questions and Aims
The quantitative research questions are:

1. How does polypharmacy emerge in patients in Scotland presenting with polypharmacy and asthma within the prescribing dataset?
2. What are the demographics of patients presenting with polypharmacy and asthma and how are they linked to multimorbidity, age, sex and lower socioeconomic background?

3. Can we ascertain any longitudinal patterns within asthma prescribing data by analysing medication prescriptions and de-prescriptions over time in patients with asthma?

Moreover, the aims of the quantitative portion, examining the scale of polypharmacy in patients with asthma in Scotland, endeavours to answer, in relation to the qualitative research, are:

- To study the degree to which longitudinal analysis of prescribing data could inform us about the levels of polypharmacy in patients with asthma over time and the trajectory of polypharmacy,
- To determine the demographics (age, gender, socioeconomic background) of patients presenting with polypharmacy and asthma;
- To ascertain any patterns in cases where polypharmacy is mitigated and cases where polypharmacy is prolonged through analysis of medication prescription/deprescription and possible signs of multimorbidity- with a view to better target interventions to identify and manage polypharmacy.

3.2.3 Prescribing Data Analysis

To gain an understanding in prescribing, deprescribing and repeat prescriptions, analysing prescribing data would provide real-world analysis of the levels of polypharmacy over time. There is a lack of research conducted in prescribing data within the UK from the year 2010. Therefore, this research aims to analyse prescribing data to explore polypharmacy in a longitudinal manner from 2010 onwards.
Polypharmacy will be defined as those 5 or more medications every 6 months. This research will focus on age categories, particularly in those from lower socio-economic backgrounds with polypharmacy at a younger age. The analysis will focus on patients under the age of 75 as older patients are quite commonly the focus in polypharmacy literature. Patients between the ages of 30 and 65 are not focused on and many have levels of polypharmacy that could be alarming and possibly better understood. In relation to younger patients, there will be a particular focus on multi-morbidities as higher amounts of polypharmacy coincide with greater levels of multi-morbidities in patients as this is less comprehended in the literature. Furthermore, examining whether deprescribing numbers have changed with time will be important to learn, particularly since in the introduction of the polypharmacy guidance in Scotland. Additionally, inspecting the levels of polypharmacy and deprescribing in patients with hospital admissions could point to the correlation between polypharmacy and hospital admissions.

3.3 Ethical Approval
3.3.1 Initial Applications for Ethical Approval
To conduct a mixed methods study, ethical approval was required to be obtained for both the qualitative and quantitative elements. First, ethical approvals from the university were obtained and, subsequently, approvals from the IRAS and local NHS sites were applied for.

3.3.1.1 Qualitative Ethical Approval
To conduct the interviews initially, ethical approval for the study was obtained from the University of Edinburgh Social and Political Science Ethics Committee. Once this approval was acquired, sponsorship from the ACCORD team was applied for. The ACCORD team at the university aided in applying for official study approval from the
Once the qualifying documents required had been completed, an IRAS application, the protocol, organisational information documents, participant information sheet and informed consent form and the email template to be seen to potential participants, the application was approved. Additionally, ethical approval was granted from the Edinburgh Medical School Research Ethics Committee as human subjects were involved in the interviews. The informed consent form sent to each participant indicated these ethical approvals. The risks associated to the participants were minimal.

3.4.1.2 Quantitative Ethical Approval

After a few months of enquiring after datasets that have longitudinal prescribing dataset within Scotland, an asthma dataset was discovered. This asthma dataset was a dataset created by Asthma UK Centre for Applied Research named the Asthma Learning Health System (ALHS) and contained various datasets including, prescribing, and dispensing data, dosage data, demographic data (Nomenclature des Unités territoriales statistiques 3 (NUTS3), Urban Rurality 6 (UR6) and Scottish Index for Multiple Deprivation (SIMD) levels noted), hospital and accident & emergency admission data, general practice data, Scottish Morbidity Record (SMR) data, educational attainment data and census data, with a filtered sample size of around 1% of the population of Scotland with a diagnosis of asthma. The dataset spanned between the years 2009 to 2017, which would allow for the longitudinal analysis that this research was designed to complete. The dataset was obtained from half a million patients recruited from 75 general practices in Scotland. An existing study team, mainly consisting of one PhD student, was currently working on this dataset. To obtain access to this dataset, an application had to be sent to the Public Benefit and Privacy
Panel for Health and Social Care (PBPP). In this application, my name was added to the study team who had already obtained existing access. This whole process was expeditiously carried out and access to the asthma UK datasets were obtained within 2 months of the application being sent to the PBPP. Access was granted in July 2019 after the completion of a course on data safety and confidentiality (Safe Users of Research Data Environment) provided by the Administrative Data Research Network (ADRN). The dataset could only be accessed through the Edinburgh Safe Haven portal hubs at the Bioquarter which required two-factor authentication. Due to lockdown caused by the COVID-19 pandemic, special access was approved and granted for home use via VPN.

**Research Design and Analysis Plan**

![Diagram showing research design and analysis plan]

Figure 3.1 shows the order and change of research design and analysis.
3.4 Qualitative Study
3.4.1 Qualitative Study Design

The study design for both arms of the interviews was developed with the research questions in mind. The design adopted was semi-structured interviews with doctors, nurses, and pharmacists across both primary and secondary care on polypharmacy. A semi-structured interview method was selected to allow for guideline questions to be asked but questions could be adapted to fit the participant based on their healthcare setting or profession or dependent on their previous answers to the questions. The questions selected were developed using the aims and research questions as a guide aided by the gaps in the literature and can be found in chapters 4 and 5.

3.4.1.1 Interview Recruitment
Healthcare professionals from Scotland and England were recruited. The different guidelines and ways of working between the countries added complications to the recruitment. Attempting to get roughly equal numbers from both countries to allow for effective comparison; establishing frames of reference on these differing guidelines and taking care to evaluate HCPs from both countries in tandem to compare both countries and their healthcare systems added complexity to recruitment and interviewing. HCPs were recruited from both primary and secondary care to evaluate the distinct elements in the treatment of patients in both care systems. Interviewees were recruited based on whether they were a practising HCP or had been practising in the last year. Possible interviewees were contacted via email with a participant information sheet explaining what was entailed in the interviews and a consent form requiring a signature from the participant (Appendix 1). An email template was created that would be sent to every possible interview candidate. The inclusion criteria for recruitment were practising doctors, nurses and pharmacists from both Scotland and
England across primary and secondary care who are familiar with polypharmacy and its processes within the last year in any capacity and in any age group. Recruiting patients from both Scotland and England was done to have a working comparison between the two countries. As near as Scotland and England are to each other, their respective healthcare systems differ slightly due to healthcare in Scotland being a devolved power. Healthcare systems in the UK are not universally the same or even similar across the different countries. In fact, in England alone, healthcare electronic prescribing systems can vary by county. Thus, to capture how differently polypharmacy is dealt with across Scotland and England could be advantageous to comprehending polypharmacy in two different healthcare landscapes. Also, it was preferable that they had experience working with patients with polypharmacy within one year prior to the interview. To include a wider range of HCPs, the goal was to select HCPs from a range of different specialities or working in a more general context in healthcare settings. The exclusion criteria were HCPs that were not doctors, nurses or pharmacists, any HCPs outwith Scotland and England, and any HCPs that were not familiar with polypharmacy or medication reviews. Any non-NHS staff were, also, excluded.

A snowballing technique was used in this study by asking participants if they knew of any other possible participants within the criteria. This technique was used to allow for easier recruitment and to ensure that participants did fulfil the inclusion and exclusion criteria’s ahead of the interview itself. Saturation was reached when no new information was revealed in the responses of the HCPs. A minimum of three people from each profession were required to conduct evaluations. This was to prevent any participants identities being accidentally revealed or deduced. Participants were encouraged to conduct this research as part of their work time;
however, interviews would be conducted outside working hours, if need be. Interviewees were able to view the questions beforehand, at their request.

3.4.1.2 Recruitment of Qualitative Study with Polypharmacy Healthcare Professionals

The participants were intended to be recruited within a 3-4-month period. Initially, networking at scientific conferences and internet searching to find candidates that would fit the criteria required would be the main form of recruitment strategy utilised. However, to ensure that convenience sampling and uneven access did not unduly narrow the range of responses, emails were sent to selected governing bodies such as PCRS to increase the chances of uptake by participants. One HCP assisted the researcher by posting on an online forum for HCP in the asthma network of the NHS to determine if more leads could be found. Participants were recruited through networking at scientific conferences and internet searching to find candidates that would fit the criteria required. These participants were emailed asking if they would wish to participate in the study with a participant information sheet explaining what was entailed in the interviews. It was anticipated that approximately 20-30 participants would be recruited for this study and the final number was 21, as determined by saturation 191,192.

3.4.1.3 Recruitment of Qualitative Study with Asthma Healthcare Professionals

The goal was to recruit patients within a 6-month period. However, when beginning to recruit interviewees, the COVID-19 pandemic occurred. This caused the recruitment period to be extended, due to the main participants that would be recruited for this study were essential workers and were, also, respiratory staff, an area of medicine highly required during the pandemic. Therefore, as recruitment was quite slow due to
this the study lasted 2 years. Interviewees were approached by email per the previous qualitative study. Emails were sent to governing bodies, such as Asthma UK, British Thoracic Society, Chest, Heart and Stroke Scotland, Primary Care Respiratory UK and the Scottish Practice Nurse forum, that deal with asthma and/or respiratory conditions to determine if members of such societies wished to be included in these interviews. In addition, Twitter was used to advertise the study.

3.4.1.3 Informed Consent
To confirm that participants wished to be included in the study, a participant information sheet and informed consent form was created (Appendix 1). The information sheet aimed to include the inclusion and exclusion criteria’s and provided the possible interviewees with information on the study, what would be required of them as the participant and how the information they provided would be used. Also, information on how the data they provided would be stored and future possible uses for this data. The informed consent sheet notified participants that their responses would be recorded. The participant information sheet and informed consent form were sent to the participant to peruse prior to agreeing to be interview and to be signed if agreement to both being interviewed and to the information contained within the document. The limitations of gaining consent were participant feeling pushed to participate in the study when contacted by email. The wording on the email and consent form attempted to prevent this coercion from happening. Participants were permitted to consider the information sheet for an infinite period of time as long as it is signed and sent prior to interview. Participants could request a copy of the interview questions prior to the interview itself.
3.4.1.4 Reflexivity

Reflexivity poses a challenge when conducting qualitative research\textsuperscript{193}. The researcher has a background in pharmacology and has no experience working within the NHS as any of the HCPs noted, unconscious bias was attempted to be limited as the researcher was not influenced with previous experiences with working or dealing with these types of HCPs personally. This provided the research a ‘clean state’ of which to view the HCPs and only base their views on the current literature that exists in this area. The interview questions were all modelled in a way that would make minimal assumptions on the behaviour of the HCPs and to endeavour to not guide the participants into the presumed answers that the researcher may have considered to be true themselves.

The researcher was aware of assumptions that could occur regardless of experience with the NHS and knowledge of the topic at hand. Researchers have their own personal opinions and experiences usually associated with their age, gender, social class, health status and other social characteristics that can taint their qualitative analysis in social science\textsuperscript{194}. Therefore, having an awareness of your own personal biases, particularly in healthcare, where everyone has had an encounter with health services at any given point in their life. Additionally, regularly keeping notes during interviews to pay particular attention to not bring the researcher’s own personal thoughts into the research. Furthermore, the participants were aware of the researcher’s background and would provide additional context for processes that would occur to assist the researcher in their analysis.
The disadvantage of not having experience working with the NHS and bringing that experience to the table is that it could cause blind spots in the research where the researcher did not know of all the contexts of the healthcare situations. In these situations, I researched the contexts of prescribing well ahead of time and as mentioned before, additional contexts were either provided by the participants or I would ask further questions beyond the set questions if needed to provide wider background knowledge to eliminate any blind spots to successfully answer the research questions. Therefore, I was aware of their possible influence on the questions asked and used this knowledge to improve the depth and credibility of the results/analysis.

Reflexivity occurred through both arms of the interviews, once with the asthma HCP interviews and once with HCPs with polypharmacy expertise. The interview guides for both studies were checked and questions were selected to be semi-structured to allow participants to provide answers as they saw fit. As time went on and patterns were beginning to emerge, the researcher took particular care to not guide the participants into providing an answer that could have been deduced from previous answers by utilising reciprocity, by sharing feelings and experiences to enhance the interviews, but not commenting on previous findings to the participants. GPs, nurses and pharmacists were all asked the questions in the exact same format to make sure that there were no assumptions or pre-conceived notions on what their roles were, despite the researcher being aware of how their roles are different. Furthermore, the researcher attempted to not overly control the interviews but merely probe for meanings in the responses.
3.4.1.5 Data Collection
All interviews were conducted with the researcher and the interviewee. No other persons were involved in the interview process. Collected data was in the form of audio-recording that was to be transcribed. All interviews were recorded unless the participant did not wish to be recorded, in which case, their responses will be noted. Each interview took between 20-60 minutes. Audio-recordings were conducted via telephone recording on an encrypted university laptop. Prior to the pandemic, all interviews were conducted via telephone, however, following the pandemic all interviews were conducted over teams or zoom. Due to the recording element of the study, the audio of the participant was recorded and not the video for confidentiality purposes. This recording is automatically saved on a university server per the rules on end-to-end encryption. The audio-recordings were transcribed by a third-party transcriber. Any anecdotal stories were anonymised by the participants themselves, by mentioning only the gender or age of their patient when taking about them, and could, therefore, still be used in the analysis. Any personal information recorded was immediately edited out prior to being sent to the transcriber. All recorded material will be erased after publication of the thesis, following final approval by research committee, ensuring that all responses were confidential. All audio-recordings were anonymised by allocating each recording with a code prior to being sent to the transcriber for security purposes. The transcriber site, also, used SSL encrypted software to prevent identification and for the safe keeping of documents. Once the audio was transcribed and checked, the recordings were deleted immediately. These responses were, then, transcribed, anonymised and the participants could, also, request the transcribed document if they wished to correct any responses they wished to change. No data analysis or personal data will be transferred to any external individuals or organisations.
The qualitative study design with asthma HCPs was based on the initial qualitative study design with participants being general polypharmacy HCPs with the only change being in the inclusion and exclusion criteria and the questions posited to the participants, so the data collection design remained unchanged.

All participants were aware that this study would be used towards a PhD study. Therefore, some participants assumed that there was an advanced level of knowledge of the subject being interviewed. Others, however, would explain answers more in depth and they were unsure of the level of knowledge of the interviewer. Prior to the interview, the participants did not know the background education of the researcher, but some did ask at the end of interviews if the researcher was a pharmacist. This was a common assumption made. Furthermore, issues in reflexivity could be seen here as with all research there is a level of bias caused by your own level of knowledge and experience. This was attempted to be limited, however, by endeavouring to both conduct the interview without comparing to other interviews or showing surprise at negative cases. Conscious probing was carried out to encourage participants to explain their thoughts in more detail without veering off wildly from the semi-structured questions.

3.4.1.6 Data Analysis
The qualitative research sought to achieve ethnographic insights. The recordings were transcribed, anonymised, and imported to NVivo (Version 12) for analysis. The interviews were analysed thematically. Notes were taken immediately post-interview to aid interpretation of the responses. Transcripts were read and coded with use of both inductive and deductive frameworks\textsuperscript{196}. Inductive coding was used to assist in combining the views of the healthcare professionals and discovering emerging
themes. Each line of the transcribed text was coded manually, line by line. The interviews were analysed in batches of five participants initially to verify whether all the questions being asked were appropriate, if there was any missing information, to determine as and when saturation was being reached and allowing analysis time before moving on to additional participants. Furthermore, the first five participant interviews were analysed with an initial coding framework. A coding framework was then created from this rough code to be used on the remainder of the participants. Once the responses had been coded with the initial coding framework, the interviews were looked at a second time to modify the coding framework and to develop themes within the code. Once emerging themes were noted, deductive techniques were used to develop a cohesive argument which informed the coding framework from the literature already examining similar ideas. Codes were connected using various subthemes and issues. They were also divided into several sub-sections to allow for better organisation and utilisation for analysis of results. Once coding framework was created, previously coded transcripts were reanalysed which any changes made to the code. This helped the coding remain consistent throughout the analysis. To continue the dialogue on communication between HCPs, the work organisations and relationships between HCPs in primary care alone, secondary care alone and across care systems were analysed.

Negative cases were noted by searching for confirming statements to the ‘expected’ result and comparing to disconfirming statements. Negative cases influenced the data saturation in the study in the following way. When a negative case was observed, future responses were noted for all negative cases as a differing statement to the expected result. Thus, the coding scheme was modified to reflect these statements.
Once the analysis and the coding were completed, if the negative cases outnumbered the expected results, they were included as their own result within both the code and the final data analysis. The initial anticipated result was noted for comparison. Negative cases were specifically highlighted in the code to be used and inserted in the final analysis to be explained with the other standard analysis.

3.5 Quantitative Study
3.5.1 Quantitative Study Design
3.5.1.1 Data Analysis

The research into polypharmacy aimed to be a longitudinal study. Most analysis into polypharmacy is cross-sectional and discovering how polypharmacy has altered over a natural progression of time rather than considering two isolated periods of time were considered more conducive to providing a strong correlation to the study hypothesis. The aim was to evaluate data from a ten-year period, 2009 to the present day. As no analysis has been published exploring prescribing data from 2010 until the present day in the UK, this creates a knowledge gap in polypharmacy patient analytics that can be tapped into\textsuperscript{16}. The prescribing data will be stratified according to certain factors such as age, gender, comorbidity, and socioeconomic background with a focus on younger patients with multiple morbidities. This stratification of data will allow for a richer dataset to be created to analyse polypharmacy.

Furthermore, patterns in the data were examined such as locating deprescribed medicines and possible prescribing cascades, though it was difficult to associate deprescribing with medication review. The analysis of this data developed as the research progressed and patterns began to reveal themselves. This involved additional or different stratification factors depending on the data itself. These three
cohorts of patients presenting with polypharmacy (as mentioned above) were linked and compared to the exposures of interest; Age, Gender, Co-morbidity, Socio-economic Background, Ethnic Group and Care Home Residency. Therefore, statistical analyses will be conducted. At this stage, the exact statistical analysis to be utilised in this research are undetermined but examples of possible analysis that may be used is logistic regression to examine associations in the datasets\textsuperscript{197}. This analysis will be conducted using R studio. Prescribing cascades will be more difficult to determine but will be identified by cross-referencing patient morbidities and their associated medication list. Any disconnection will be analysed for possible prescribing cascades.

Once patterns are obtained from the prescribing data, ‘hot spots’ began to show themselves as areas of polypharmacy that needed to be targeted. These ‘hot spots’ were used to determine whether these elements of polypharmacy have been properly dealt with in the polypharmacy review process and if the review needs improving. If so, the data obtained was used to suggest changes in the guidance changes in the Scottish Polypharmacy Guidance and other possible guideline designs to better fit with likely issues and demands. Furthermore, improving our knowledge of polypharmacy could assist healthcare systems in general.

The Data Source was the prescribing and SMR data. There were no exclusion or inclusion criteria other than all resident adults in Scotland who have polypharmacy linked to multimorbidity. The aim was to focus on individuals with 5 or more drugs prescribed at any given time but lower volumes of drugs per individuals were still evaluated. Three levels of polypharmacy, <5, between 5-9, and ≥10 drugs will be analysed. Polypharmacy was defined as counting individual drug names based on the
presence of distinct drug classes via drug class definitions in the British National Formulary (BNF). Subsections of the BNF describe multiple drugs that are commonly prescribed together. Multimorbidity was defined as an individual with 2 or more conditions at any given time based on the definitions described from ICD-10 codes. Furthermore, BNF classes associated with certain diseases were counted via the prescribing data. There was no follow up as this was not a study where comparison is needed. Additionally, multimorbidity was, also, be counted via the prescribing data to allow the correlation between multi-morbidity and polypharmacy to be examined. This clinical outcome of disease was ascertained by the linkage of high levels of drug prescription and the correlation attached with individuals with multiple diseases. Therefore, the time points at which an individual was diagnosed with certain diseases will be helpful.

3.6 Summary

A mixed methods research strategy was developed to gain an understanding of polypharmacy treatment and deprescribing. The qualitative method utilised was an ethnographic semi-structured set of interviews to obtain insights into HCP perspectives of their handling of patients presenting with polypharmacy, conducting medication reviews and shared decision making, deprescribing and the barriers it creates and the difference in interprofessional relationships when dealing with patients presenting with polypharmacy. The quantitative method was a longitudinal study of prescribing data to observe changes in polypharmacy prescribing and deprescribing over time with more detailed analysis into associations with certain demographics, multimorbidity and repeat prescriptions. Issues with obtaining access to the Lothian Research Safe Haven prescribing data and the literature gap in patients presenting
with polypharmacy with this specific comorbidity caused the focus of the research to shift to analysing these patterns in polypharmacy in patients with asthma.

The revised aims of this research were to study the extent to which longitudinal prescription data analysis could inform us about the levels of polypharmacy in patients with asthma over time and the trajectory of polypharmacy, identify patterns in cases where polypharmacy is mitigated and cases where polypharmacy is prolonged. The non-clinical outcomes of interest were comorbidities that are associated with persistent polypharmacy in patients with asthma - with a view to better targeting interventions to identify and manage polypharmacy in future. Furthermore, the wider aims of this research were to improve the understanding of how polypharmacy can be controlled in patients with asthma and the potential influence of healthcare information such as guidelines and tools used by asthma HCPs, and the analysis of the population data in refining the healthcare application of the polypharmacy approach, decisions in patients and measure the changes of levels of polypharmacy over time.

**Chapter 4**

4.1 Introduction
The purpose of this chapter is to introduce the first qualitative study discussed in the previous methodology chapter exploring HCP’s views on polypharmacy and whether medication reviews and better HCP interactions could allow for better deprescribing. This approach allowed for a more effective understanding of HCPs experiences with patients with polypharmacy and provided a way to develop theory from the data to improve how HCPs deal with patients presenting with polypharmacy and, in turn, how patients presenting with polypharmacy can benefit with improvements to the current
system. The qualitative analysis used for the data obtained in this study was a mixture
of deductive and inductive techniques. The research design, including the
methodology, study participants, procedures, analysis technique and ethical issues
are also discussed in this chapter.

4.2 Methodology

A qualitative design was used in this case to hear first-hand from HCPs who work
regularly with patients presenting with polypharmacy. As this study aimed to examine
the experiences of HCPs and their views on polypharmacy, a qualitative approach was
the most appropriate choice.

4.2.1 Study Participants

The sample was drawn from a population of HCPs, i.e. doctors and pharmacists who
have experience working with patients presenting with polypharmacy for at least one
year. The recruited doctors could either be specialists in hospital or general
practitioners, while the pharmacists were either hospital pharmacists, independent
prescribers or community pharmacists. HCPs were recruited from both primary and
secondary care to evaluate the distinct elements in the treatment of patients in both
care systems.

4.2.2 Data Collection

All interviews were recorded using voice memos to capture all research thoughts
during the interviews. Table 1 shows the standard questions that the HCPs were
asked. Questions were selected to provide a better understanding of polypharmacy and medication reviews. Also, questions were adapted for the individual HCP, as in hospital pharmacists were asked slightly altered questions to fit their environment compared to GPs etc.

Each interview took place within a single interview session. Interviews were carried out between March 2019 to July 2019 via telephone interviews. The interviews lasted between 25-60 minutes with the first half discussing their experiences with polypharmacy and the second half discussing their experiences with medication reviews and interactions with other members of staff.

Table 4.1 Interview Questions
Table 4.1 shows questions asked to interviewees. Questions were adapted for individual HCPs and responses were audio-recorded.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
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<tbody>
<tr>
<td><strong>Polypharmacy</strong></td>
<td>Before we get started, I was wondering if you could give me a brief overview of your experiences with patients with polypharmacy? In particular, your experiences with patients with appropriate polypharmacy vs. inappropriate polypharmacy?</td>
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<td></td>
<td>In your opinion, why do you think inappropriate polypharmacy arises? Why may it be unevenly distributed across populations?</td>
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<td></td>
<td>How do you think inappropriate polypharmacy could be minimised?</td>
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<td></td>
<td>Do you think that repeat prescriptions play a role in inappropriate polypharmacy? And if so, how?</td>
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<tr>
<td><strong>Medication Review</strong></td>
<td>In regard to minimisation of inappropriate polypharmacy, can you tell me about your experience of reviewing medications for patients with polypharmacy (compared to other medication reviews)? And do you use any specific disease or polypharmacy guidelines for guidance (such as Scottish Government’s Polypharmacy Guidance)?</td>
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<td></td>
<td>Could you talk me through how you come about reviewing a patients’ medication list? (how often, within/outside consultations and patient involvement?) Are there any triggers?</td>
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<td></td>
<td>How difficult is it to deprescribe? And what are the barriers you face when you do try to deprescribe?</td>
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<td></td>
<td>In your opinion, what is the most important component(s) to a medication review?</td>
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<td>Which patients do you think would benefit from regular medication reviews?</td>
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<td></td>
<td>Are there any patients you think do not receive medication reviews that should? Say lost to follow-up or go missing?</td>
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<tr>
<td><strong>Healthcare Professional Relationships</strong></td>
<td>Do you think that medication reviews should be improved/enhanced? If so, what do you think is missing or could be developed further?</td>
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<td></td>
<td>Are there any other staff involved in medication reviews in your practice/hospital?</td>
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<td></td>
<td>Has there been any misunderstandings or issues that have arisen regarding medication reviews with other members of staff? If so, could you elaborate on what those issues were?</td>
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<td></td>
<td>Whose job do you think it is to conduct medication reviews?</td>
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</table>

Table 4.1
All participants were anonymised and numbered for the sake of publication of results. The naming system was as follow; P for pharmacist or D for a doctor, followed by a unique number. Their gender and the country in which they practice was also noted. All future intercepts of interview text in the results section will follow this naming structure.

4.3 Results
In total, twenty-one participants were interviewed for this study. Of the participants, nine were doctors (43% of the sample) and twelve were pharmacists (57% of the sample). Table 4.2 shows the demographics of the twenty-one participants.

<table>
<thead>
<tr>
<th>Characteristics</th>
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<tbody>
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<td>Pharmacists (n=12)</td>
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<td>Sex</td>
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<td>Female</td>
<td>10</td>
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<td>Job Role</td>
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<td>Hospital</td>
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<td>Scotland</td>
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<td>England</td>
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<tr>
<td>Doctors (n=9)</td>
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<td>Geriatrics</td>
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<tr>
<td>Clinical Pharmacology</td>
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<tr>
<td>Asthma</td>
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<tr>
<td>Location</td>
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<tr>
<td>Scotland</td>
<td>4</td>
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<tr>
<td>England</td>
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</tbody>
</table>

Table 4.2 shows demographics of the twenty-one participants for the study. All respondents were anonymised.
Four main themes were identified; the organisation of medication reviews, the ease of deprescribing, the interactions between pharmacists and doctors in both primary and secondary care when conducting medication reviews and how medication reviews can be improved.

4.3.1 The organisation of medication reviews

4.3.1.1 GP surgery medication reviews

The organisation of medication reviews differs based on how they are conducted. In GP surgeries, NHS guidelines require that patients over the age of 75 have an annual medication review. However, due to GP workloads, this guideline is not always followed as closely as it should. Some GPs stated that every time a patient came in to see they would have a quick look over the patient’s medication list to check everything was in good working order. Their notes in the patient medical list would alert them to any drugs needing follow-up. Thus, this would be applied to the analysis of repeat prescriptions. GPs, also, stated that their expertise would allow them to notice high risk medications in the patient’s medication list. How effective these scans of patient medication lists are to be debated as things can easily be missed in a more opportunistic review.

‘Ok, so at one level I'm seeing a list of requested prescriptions on a month, two-monthly basis depending how long a prescription is, so on one level I've got a chance to intervene if something's looking really odd at that point, that doesn't mean to say I'm going to go into the notes and have a real look at it but it does mean I'm going to scan that list and think you know, spot anomalies.’

D2 in primary care, Female, Scotland

Pharmacists explained that this type of medication review is called a Level one medication review, an opportunistic look over the patient’s medication lists. This
medication review would turn into a level two review if it was a more in-depth paper review of the medications with a look at hospital admissions, lab results, etc. A level three medication review is a medication review with shared decision making where the patient is involved in the discussion of the medication list.

‘So, I think the first one is just you know, like an opportunistic review where you might just look at the list of medicines a patients on, and I think second review is with the records but not with the patient and level three is with the patient, the records and a list. Because obviously if you're just reviewing a list of medicines it's just pointless because you don't even know that the patients taking all that supposed medicine if you don't talk to them anyway.’

P4 in primary care, Female, England

Pharmacists in primary care are expected to carry out detailed structured medication review in comparison to GPs. Pharmacists in primary care conduct medication reviews simultaneously similarly and differently to GPs. Pharmacists are, also, given a list of patients to review. However, pharmacy technicians are more likely to conduct a level one medication review. Whereas the pharmacist will conduct level two medication reviews and upwards. Therefore, any patients transferred to (experienced) pharmacists would ‘trigger’ this kind of review. Also, some pharmacists mentioned that they would visit some patients’ homes as part of the review process. How GPs would trigger a structured medication review, other than in older frail patients, that they conducted themselves were less clear.

4.3.1.2 Hospital medication reviews
Hospital pharmacists and doctors agreed that with every hospital admission, a medication review would be conducted post medicine reconciliation. This would be one of the ‘triggers’ for a medication review. Hospital pharmacists agreed that medication reviews in hospitals were easier to conduct due to the availability of all medical teams being in the same place at the same time.
‘We have got two methods of identifying patients that we focus our medication, our comprehension review on. So, we either are in the practice and we get a referral because a patient’s been discharged from hospital and there’s a bit of a meds reconciliation type problem that prompts the comprehensive med review, and that’s usually referred from somebody else in the practice.’
P5 in Hospital, Female, England

Furthermore, HCPs agreed that a deterioration of a patient’s condition would be a trigger for a medication review.

‘So, medicines reviews need to be prompted, potentially at trigger points, so at admission to hospital, an acute deterioration, something like that, that would make you think to look at this patient in more detail...So it’s a case of making that decision of the healthcare professional as to what’s right and what’s appropriate.’
P6 in Hospital, Female, England

However, what would trigger a shift from a level two medication review to a level 3 discussion with the patient was less clear. Most HCPs would talk with their patient if they thought their medication list may indicate risk of harming them in some way or a lack of compliance in the patient.

‘I guess if I thought there was a safety issue. If it was going to actually be causing potential harm in particular with high-risk drugs... If I see a change in compliance which could indicate symptoms are perhaps getting worse and I’m a bit concerned about the patient I would ask the patient to contact me to have a wee discussion about their medication. If I see monitoring is not being done I could maybe contact the patient and find out why they are not coming in and try and emphasise to them the importance of monitoring, why we do that... I think it’s quite important just to make sure people are okay, they are stable, and they can have a discussion potentially stopping if appropriate.’
P7 in Hospital, Female, England

4.3.2 The ease of deprescribing

Most of the interviewees stated that, overall, patients want to be prescribed less medications. The interviewees viewed less medications as a way to improve the patients’ satisfaction in their medication list, less confusion about the medication they were taking and improved adherence.
‘I’ve always discussed it with the patient so they understand why something is not going to be there. They’re usually very happy because usually each contact with the doctor usually for them means an extra tablet, so with me it usually means either you stay the same or less, so they’re actually very pleased when I say, ‘We’re going to take something off you.’ ‘That’s good!’ So they’re usually quite happy.’

D3 in Hospital, Male, England

However, five interviewees explained that some patients fear changes in their medication list and deprescribing would cause, initially, more confusion rather than less. Though, all interviewees agreed that explaining your thought-process to the patient would alleviate some of this initial confusion and would help to ease deprescribing.

‘Some of the patients do not wish their medication to be changed, are quite frightened of having changes but I would say most of them are actually because we’re looking at the frail elderly, most of them are quite happy, if you explain the reasoning behind… well actually they’re quite happy to be taking fewer meds full stop but particularly if you explain the reasoning behind it, you’re not just stopping it because they’re old and frail, you’re stopping it because actually it increases the risk of X, Y or Z and they’ve already had the long-term benefit from it. Once you’ve explained that to them, they tend to be quite happy about stopping it.’

P8 in primary care, Female, England

When deprescribing, all the interviewees used a benefit versus risk analysis of the patient’s medication. If the risks outweighed the benefits, the HCP would proceed to attempt to deprescribe, either removing the medication altogether or looking for more non-medication interventions for the patient.

‘I think nowadays we’re actually far more realistic about how we treat patients, but in the past when we had GP contact and QOF patients were treated to target, they were on the four antihypertensives and relatively high doses of these to treat - I think now we’re actually being more realistic and looking at what are the risks versus the benefits.’

P9, Female, Scotland

4.3.2.1 Barriers to deprescribing
Half of the interviewees stated that the training of both doctors and pharmacists did not allow for the ability to evaluate, with ease, what medications should be deprescribed. These interviewees believed that training or improved guidelines should be provided to allow HCP to understand when it is appropriate to deprescribe.

‘I think the other problem is we don’t really know what the best way to deprescribe is, so there’s lots of research but actually in terms of how do you do deprescribing, how do you best inform the patient, how do you do the decision making, we don’t know the answers to those questions and there’s lots of resources out there but they’re not always very well shared. So obviously you’ve got your polypharmacy guidance in Scotland, the RPS guidelines, there’s a new de-prescribing network in England that’s going to be launched at the beginning of June but the people that are on the ground, I don’t think that they know a lot about those resources or know how to access them or use them so I think that’s a problem that needs tackling as well.’
P4 in Hospital, Female, England

When it comes to the patient, as many patients presenting with polypharmacy who undergo medication reviews are frail with cognitive impairment, there are many times the shared decision making cannot occur with the patient themselves but with a carer instead. All the interviewees acknowledged that carers are more worried about the patient and are less likely to be willing to deprescribe on the patients’ behalf.

‘I think it becomes tricky when the patient doesn’t have capacity because I think the patients are more open to stopping things than their relatives and carers are, so I think their relatives and carers feel more - you know when they’re making a decision on behalf of the patient I think they find that difficult and they’re probably a bit more risk adverse than the patient themselves would be. So, I try to get around that by saying ‘well what would your relatives have wanted if they could speak, rather than what do you want’ because I don’t think they’re the same thing in a de-prescribing consultation.’
P4 in Hospital, Female, England

Furthermore, three interviewees noted that HCPs fear the backlash they may receive from the patient or the carer to deprescribing and, therefore, to prevent this issue, they will not deprescribe at all.

‘often if we’re dealing with elderly people, particularly confused elderly people it isn’t just the case of you have to do a review, you have to do it with a family
member as well because you know you are concerned because it may have nothing to do with it but you know, you decide to stop someone’s aspirin and two weeks later they have a stroke, you know? It may have had absolutely nothing to do with what you’ve just done but it’s you know, you have to be sure that you’ve got family with you on this because doctors do worry, they worry about getting sued and maybe they worry about being accused of bad practice and in some ways the easy thing to do is to just follow the guidelines, foolishly rather than stand out against it.’

D1 in primary care, Male, Scotland

4.3.3 Interactions between Healthcare Professionals during medication reviews

In primary care, GPs and pharmacists usually communicate about specific patients and prescribing decisions, particularly if flagged in medication reviews by the pharmacists and vice versa. Therefore, GPs and pharmacists work together often when conducting medication reviews. Pharmacists did mention that they were challenged on their changes to a medication list, however, this would be more a rare occurrence and would happen even less frequently based on the experience of the pharmacist.

‘I think it’s really variable, in my experience it depends on the competence and experience of the pharmacist. So I can think of an example of a practice that I’ve got where the pharmacist is really capable, really competent and…is a prescriber, so actually that scenario, they stop the drugs themselves and then will communicate with the GP, ‘I’ve taken the decision to stop this,’ but they have pharmacies working with them that aren’t prescribers… I think when you’ve got newer pharmacists going in it takes a period of time before they gain that credibility with the GP, and only when they’ve got that does the GP then start to more and more often not question the decision and follow the advice that’s been given.’

P3 in Hospital, Female, England

In terms of the interaction between hospital doctors and GPs, regularly, when prescribing or changing prescriptions hospital doctors will write a letter to inform the GP of these changes but rarely do these changes meet with disapproval.

‘I do some prescribing obviously for, usually for short term things, but I tend to ask the GP to prescribe the long term things. And then I guess minimising,
making sure that the letters are clear, and making sure that we try and verify what they’re actually on each time we see them until we are minimising polypharmacy.’
D4 in Hospital, Male, Scotland

However, in terms of avoiding disapproval, a few of the interviewees mentioned that more junior members of staff are much less willing to broach the subject of deprescribing because they feel that they do not have the experience or authority to deprescribe, particularly in situations where an experienced doctor has prescribed the initial medication.

‘So actually, there is a real problem to deprescribing and a real problem is that actually people don’t feel empowered to do it and then in a hospital setting, of course, it’s like you’ve come in for your broken leg, actually, I would just like to see your broken leg, the rest of you can stay at home, I don’t want to know anything about any of your other conditions or medicines because I’m far too busy to even think about it. And that might be absolutely genuine, or it might be a junior doctor or a junior clinician who goes, actually, this is beyond my competence, I don’t know why this was prescribed. So, if you’re asking me why inappropriate polypharmacy happens, it happens for all those reasons, I don’t why it was prescribed so, therefore, how can I possibly deprescribe it?’
P12 in Hospital, Female, England

Furthermore, all interviewees discussed their concerns that, in regards medication reviews, their workloads were heavy as is and to conduct regular medications reviews would be an additional strain on them. Therefore, some of the respondents suggested that training different types of HCPs such as pharmacy technicians to conduct medication reviews to ease the burden on overworked members of staff who classically deal with medication reviews. This would allow for issues to be flagged up earlier and high-risk medications and interactions in a patients’ medication list could be dealt with earlier if escalated to the proper member of staff regardless of expertise and/or department.

‘Obviously, we think pharmacists, we’re the experts in medicines, so. Whether you’re hospital or whether you’re community, we all have a part to play in medication review. It’s also about educating and promoting medication review amongst GPs, even specialist nurses and things like that, who are prescribing
themselves, more and more so nowadays. Yeah, we all have responsibility, all healthcare professionals about performing that review… I don’t think it necessarily should be exclusively pharmacy.’

P10 in Hospital, Male, England

4.3.4 How medication reviews can be improved

Most of the interviewees viewed medication reviews as an exercise that could be improved. Most believed that patient-centred reviews are the future of medication reviews. Understanding patients’ perspective is key as it will be them that have the choice of whether to adhere to their medication list.

‘So I think there is loads and loads of work that needs to be done on medication reviews. Defining it, describing what good looks like, understanding what it is like to be a patient is part of it, assessing it, you know, do we make part of the peer review part of revalidation, somebody watching you with a patient, you know, those sort of things – there’s loads...’

P3 in Hospital, Female, England

Moreover, half of the interviewees believed that their computer systems should be coded with alerts for when to conduct medication reviews, when medications are high risk and when to follow-up patients.

‘I think maybe putting in a plan so that the system can then prompt a review might help, and then of course once people have been prescribed things I think the idea of having an annual review especially for older patients over a certain age is a very good one, and we should find ways of how we can do that.’

D3 in Hospital, Male, England

In addition, it goes without saying, it should seem, that patients are at the centre of medication reviews and hence, should most likely, always include some form of shared decision making. However, usually patients come into the clinic or hospital, take their medication and leave, it is merely their medications that are looked at and nothing else. Therefore, several of the respondents mentioned that a more holistic approach
to medication reviews and in overall patient care. Social and economic factors that affect each individual patient should be considered in a medication review. This will allow HCPs to understand the patient more and determine whether they can manage with the number of medications they have been prescribed.

‘If you think about it 80% of anybody’s health is not something the NHS can do much about, so if you’ve got COPD and your rented accommodation is damp, that’s housing services needing to batter your landlord about the head because we can change your medication all we want but it won’t make a jot of difference to you because your house is damp… it’s about relationship stuff, it’s about you know I’ll sit in a consultant room because I did anticoagulation clinics and you can get five minutes in and the patients walking out the door before they actually ask you the thing that’s really bothering them. But once they trust you, once you’ve got a relationship then that makes it a lot easier, it’s recognised that they’re agitated about something and it’s not what they tell you, but also they’ve got the trust that you’re not going to report them to social services because of whatever they say or that you can actually do something, or that you just care.’

P11 in primary care, Male, England

4.4 Discussion

Fundamentally, the most important part of polypharmacy, medication reviews and possible deprescribing is the patient. How patients were treated in the past with their medications is only significant if we focus on how we can improve the current system.

To see improvements in patient centred treatment, we must speak to the two sides of the interaction, the patient themselves to discover the issues that affect them and their possible co-morbidities and the HCPs with their concerns and dilemmas when dealing with patients and conducting medication reviews. Therefore, this analysis hopes to provide some possible solutions to the concerns that the HCPs are facing and how fixing these issues can be translated into patient treatment.
4.4.1 Patients presenting with polypharmacy
In the results section, it was discussed that patients who are older and frail are more likely to experience polypharmacy. This is corroborated in the literature as many studies have been conducted on elderly and frail patients, in regard to, polypharmacy. Additionally, many guidelines that have created for the specific use for patients presenting with polypharmacy have focused on the frail and elderly. These patients are more likely to have carers or family deal with their medication. Carers and family members, however, were discussed in a less than positive light by most of the interviewees due to their perceived over-cautious nature to viewing the patients’ health. Carers and family members have been included in guidelines previously but, perhaps a more comprehensive guideline would be better if created for those patients who are unable to converse with their HCP.

Furthermore, patients with multimorbidities obviously will experience polypharmacy as they will require treatment(s) for each individual condition that they have. However, due to the individualistic nature of our health service with the specialisations found in secondary care and other divisions of labour throughout the NHS, patients will see a specialist for each condition that they suffer from. Each specialist that they visit could potentially prescribe them a new medication. There is a possible disconnect between these specialists and the patient. This is linked to the suggested holistic view of peoples’ medications.

However, patients from lower socio-economic backgrounds who develop morbidities at a younger age due to their lifestyles require medication reviews for their polypharmacy in addition to older, frail patients. Patients from lower socio-economic backgrounds, however, may feel that they are not included in discussions about their,
health. Health illiterate patients, commonly from lower socioeconomic backgrounds are more likely to be more compliant and less likely to challenge health professionals to explain the basis for prescriptions. Therefore, they may feel marginalised and feel like HCPs do not actually care about their health and well-being. To develop on what the interviewers mentioned, training HCPs in medication reviews and polypharmacy is key, but, more importantly, patients need to feel valued and not just ‘another patient’ coming through the doors. Motivational interviewing was mentioned on occasion by some respondents. Allowing for patients to feel like they are at the centre of their care and are freely available to question their HCP is key. A study in Spain discovered that motivational interviewing reduced medication errors in patients over 65 with polypharmacy. There are many guidelines on how to deal with patients presenting with polypharmacy and, more recently, some guidelines on how to deprescribe. But information sheets and online resources empowering patients and actual shared decision-making medication reviews are relatively in their infancy, particularly in patients from lower socioeconomic backgrounds who are less likely to be health literate. The target, both socially and in healthcare, are the same people.

4.4.2 Barriers to deprescribing
The main barriers to deprescribing mentioned by the interviewees focused on HCPs themselves. Granted, respondents mentioned that they were afraid of the backlash to their suggesting to deprescribe treatments and that the patient and carer have a belief in the value of taking medications to improve their health is another concern. However, most HCPs talked about issues with deprescribing from a place of worry. Some HCPs were worried that if they removed a medication from a patients’ medication list and another HCP (usually higher up) disagreed with this change in medication. Some felt that they were not confident enough to deprescribe and that other junior members of
staff felt the same due to lack of knowledge or training on how to deprescribe. This was, also, perpetuated by pharmacists who felt lower in the scheme of hierarchy when dealing with doctors. This was a concern accentuated by a lack of evidence that deprescribing influences patient health and wellbeing.

Deprescribing is a relatively new concept. Deprescribing has been considered as a process that should be treated alike to prescribing a new drug. Therefore, as prescribing is an ongoing process, where multiple factors are assessed such as adverse drug reaction and wariness of the introduction of high-risk medications, so is deprescribing. However, deprescribing offers an unusual issue that prescribing a new medication does not. When a HCP prescribes a new drug, the responsibility lies with the prescriber. However, when the time comes to deprescribe this medication, it might not be the prescriber who has the responsibility to deprescribe the drug. This was another barrier noted by several of the interviewees; that they are unwilling or afraid to remove a medication from a medication list prescribed by another member of staff. This seemed to be less of an issue if the deprescriber was not familiar with the prescriber, but in hospital settings where they may interact with other disciplines, they were far less willing to deprescribe as it may cause misunderstandings in the work environment. Hospital HCPs, particularly pharmacist, were afraid to disrupt the hierarchy equilibrium and, therefore, would avoid deprescribe another colleagues’ prescribing decision. Perhaps, a more multi-disciplinary approach to deprescribing may need to occur to avoid these types of misunderstandings.

4.4.3 Improving Medication Reviews
Medication reviews have been utilised in the healthcare profession for several years now. However, it is well known that there are flaws in the current arrangements. The
conception of what is involved in a medication review varies wildly between different HCPs in this study alone. Some consider a glance at a patients’ medication enough for a review, whereas others only consider a full structured medication review with shared decision making as a true medication review. Polypharmacy guidelines have tried to shift away from the ‘glance at a patients’ medication list’ to shared decision making as the focus. This signals a change in the way healthcare is now viewed. In the past, the apparent priority was to make life easier for the HCP, whereas now there is a clear shift towards a more patient centred approach. As shared decision making is a relatively novel concept, it will be a few years yet until we reap the benefits that it may impact on healthcare and patient-centred care. Consequently, it was almost universally acknowledged by all the interviewees that patients should be the priority in medication reviews. From a HCP perspective, it is easier said than done to make medicine more patient-centred. The main issue is that HCPs have heavy workloads and time constraints do not allow for lengthy shared decision-making meetings with every patient they encounter. Therefore, there needs to be systems in place, to allow HCPs to conduct their jobs in a way that both benefits the patients and themselves. It was suggested by some interviewees that training other members of staff such pharmacy technicians and the like could be trained on polypharmacy and medication reviews. Another suggestion was training HCPs better, in regards, polypharmacy and medication reviews in general. However, this does not target the issue with time constraints and workload issues. This may be an issue that will never be fully resolved but if we could ease the burden on HCPs, it could be reflected in healthcare in general as there could be less of a burden of patients, if time management was targeted.
4.4.4 Strengths and Limitations

The strengths of this study lay in comparison of two geographical areas, Scotland and England. Furthermore, comparing both primary and secondary care along with hearing the perspectives from both doctors and pharmacists allowed for a wider outlook on polypharmacy treatment and management. It provided, despite small sample sizes, the experiences of two different prescribers in two different contexts and increases knowledge on the subject at hand. Furthermore, it allows for a discussion to be had about the interprofessional communication between prescribers both in primary and secondary care.

This study focused on HCPs who have, at least, a years’ experience working with patients with polypharmacy. The findings in this study, therefore, allowed for a more targeted (and possibly biased) response, as most of the HCPs were highly experienced with polypharmacy and for some it was one of their specialities. This caused an issue with the results of this study as it contained the results of people very familiar with polypharmacy. Therefore, there could be gaps in this study analysis, that could be improved. Conducting more interviews with HCPs understanding the real-world applications of polypharmacy guidelines, medication reviews and deprescribing could be very informative.

One limitation could be related to possible interviewer and unconscious bias. As far as I am aware, I attempted to not ask any leading questions or provide my experiences while conducting interviews. Some of the interview questions themselves did contain some bias in their wording, particularly in the question “What factors do you feel many contribute to inappropriate polypharmacy?”. I sought to compensate for this in the
analysis of the interviews by attempting to be unbiased in my overall evaluation of the interviews but this may have altered the responses in some of those categories. However, as much as one can try to prevent bias from occurring, it can be unconsciously done, particularly in negative cases. However, another limitation would be the small sample of HCPs with polypharmacy experience. Working from the results of this study and based off what is known in the literature about polypharmacy, talking to HCPs who are, perhaps, less familiar with polypharmacy and medication reviews would be beneficial.

4.4.5 Future Work

In future research, more detailed analysis on how GPs conduct their medication reviews beyond an opportunistic look at patient medication list could be analysed. Furthermore, stratifying the HCP by morbidity may also be helpful as it focuses on a key issue in polypharmacy; multimorbidities. Furthermore, how multimorbidities are dealt with by HCPs who specialise in a specific co-morbidity would be interesting to analyse to determine whether they consider other co-morbidities when dealing with a persons’ medication list. Asthma is co-morbidity that is not regularly discussed alongside polypharmacy in the literature. In addition, as asthma affects younger members of the population, on average, this will be beneficial to analyse a dataset that impacts younger patients based on the lack of focus of some guidelines on younger patients with polypharmacy\textsuperscript{214}. Asthma also disproportionately affects people from lower socio-economic backgrounds as it can be exacerbated by certain living conditions\textsuperscript{37,215}. Therefore, in the next chapter, interviews conducted with HCPs who are asthma specialists will be analysed. Furthermore, there seemed to be a focus on conducting medication reviews on older frail patients, in future analysis, how
medication reviews are conducted in younger patients, particularly from lower socioeconomic backgrounds requires investigating. Future studies in patients from lower socio-economic backgrounds with a more holistic approach to their healthcare could be an option as they may be more able to converse with their HCP and detail concerns to improve the current system.

4.5 Conclusion

To conclude, four main themes were identified in this chapter; the organisation of medication reviews, the ease of deprescribing, the interactions between pharmacists and doctors in both primary and secondary care when conducting medication reviews and how medication reviews can be improved. It was found that medication reviews involved looking briefly at patients’ medication lists and was more commonly utilised by GPs and hospital doctors, whereas it was deemed the pharmacist’s role to conduct structured medication reviews in both primary and secondary care. Deprescribing was limited in medication reviews, particularly from the perspective of pharmacists due to lack of confidence and fear of getting involved in another’s prescribing decision. Focusing on multimorbidities and how polypharmacy is managed in a specific morbidity could provide more information and context on how polypharmacy management techniques are carried out by HCPs without explicit polypharmacy experience.
Chapter 5

5.1 Introduction

This chapter endeavours to continue the qualitative research discussed previously. This chapter aims to focus on HCPs with asthma expertise or specialisations and their unique views on polypharmacy. This investigation provided a more detailed insight into asthma and polypharmacy care and how polypharmacy is perceived by asthma HCPs. The differences between how medication reviews and deprescribing comes about in asthma care were explored and areas where polypharmacy management in asthma care can be developed were documented. Furthermore, how interpersonal relationships between patients and HCPs and interprofessional relationships between HCPs within asthma care transpire were examined. This study is discussed in the chapter by way of explaining the research design, how study participants were recruited, the interview analysis, strengths and limitations and potential future work.

5.2 Methodology

A qualitative design was used in this case to hear first-hand from HCPs who work regularly with patients with asthma. As this study aimed to examine the experiences of asthma HCPs and their views on polypharmacy, a qualitative approach was the most appropriate choice.
5.2.1 Study Participants

HCPs, i.e. doctors, pharmacists and nurses who have experience working with patients with asthma for at least one year were included in the sample. The recruited doctors could either be specialists in hospital or general practitioners, while the pharmacists and nurses were either hospital based, primary care or integrated care based. Their experiences with polypharmacy were not noted prior to the interview as this might have skewed the results to show a more positive distribution of polypharmacy analysis, however the participants did know that the interview was about polypharmacy and asthma which may have caused participants with more involvement with polypharmacy to be willing to partake. Interviewees were purposively sampled to include HCPs from a range of different experiences and contexts. Furthermore, the demographics of the areas that the HCPs came from were noted to allow for a broadly representative sample distribution, i.e., urban vs rural. Furthermore, the genders of the HCPs were also noted to provide additional context. It was anticipated that approximately 20-35 participants would be recruited for this study and the final number was 32, as determined by saturation.

5.2.2 Data Collection and Analysis

Semi-structured interviews were conducted as the data collection method. As Chapter 4, all interviews were recorded using voice memos to capture all research thoughts from the researcher during the interviews. Table 1 shows the standard questions that the HCPs were asked. Questions were designed to provide a better understanding of the origins of polypharmacy and the possible role of medication reviews in mitigating
this. Also, questions were adapted for the individual HCP, as in hospital pharmacists were asked slightly altered questions to fit their environment compared to GPs etc.

Each interview took place within a single interview session. Interviews were carried out between October 2019 to November 2021. The interviews lasted between 20-60 minutes with the first half discussing their experiences with polypharmacy and the second half discussing their experiences with medication reviews and interactions with other members of staff.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypharmacy</td>
<td>Before we get started, I was wondering if you could give me a brief overview of the patients you encounter and do they have polypharmacy?</td>
</tr>
<tr>
<td></td>
<td>Of these polypharmacy patients, do they have polypharmacy due to their asthma medications alone or do they have additional co-morbidities?</td>
</tr>
<tr>
<td></td>
<td>When you go about prescribing a new medication to a patient, do you take their other co-morbidities or the other medication they are on into consideration?</td>
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<tr>
<td></td>
<td>Do you see any patterns of demographics in these patients with comorbidities and asthma? Which comorbidities do you see commonly?</td>
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<tr>
<td></td>
<td>Do you use any guidelines in your day-to-day practice?</td>
</tr>
<tr>
<td>Asthma Treatment Burden</td>
<td>Do you see a correlation in how severe a patients' asthma is versus how many comorbidities they have?</td>
</tr>
<tr>
<td></td>
<td>Do you encounter a treatment burden with asthma patients, where they find it difficult to use their medications? If so, how so you assist patients with this burden? Make it easier for them to take their medications?</td>
</tr>
<tr>
<td></td>
<td>In regard to polypharmacy that is caused by asthma medication alone, how so you manage the prescription of irregular oral steroids?</td>
</tr>
<tr>
<td>Medication Reviews</td>
<td>How do you manage peoples' medications?</td>
</tr>
<tr>
<td>Shared Decision Making and Deprescribing</td>
<td>Do you have discussions with patients about their medications in a shared decision-making way?</td>
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<td>-----------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
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<tr>
<td></td>
<td>Do you ever step down or deprescribe medications? If so, how do you go about deprescribing?</td>
</tr>
<tr>
<td></td>
<td>Do you find that there are any barriers to deprescribing or stepping down medications in asthma patients?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Healthcare Professional Interactions</th>
<th>Other than via a person's CHI number and drug history is there a link between yourselves and (other HCPs depending on participant)? How do you ensure that information is passed between each other?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Do you interact with any other members of staff when prescribing or deprescribing medications for patients? Are there any differences of opinion?</td>
</tr>
<tr>
<td></td>
<td>Do you think that there are any ways to improve prescribing, treatment and deprescribing in asthma patients?</td>
</tr>
<tr>
<td></td>
<td>Anything else you want to add that we haven't covered?</td>
</tr>
</tbody>
</table>

Table 5.1 shows the interview guide. These questions were adapted depending on the individual healthcare professional and their experiences.

All participants were anonymised and numbered for the sake of publication of results. The naming system was as follows; P for pharmacist or GP for general practitioner, N for nurse and S for specialist, followed by a unique number. Their gender and the country in which they practice was also noted. All future intercepts of interview text in the results section will follow this naming structure.

**5.3 Results**

Thirty-two HCPs, 8 general practitioners, 8 asthma specialists, 9 pharmacists and 7 specialist nurses in asthma were interviewed for this study. The demographics of the
participants is noted in table 2. Participants were either from primary care, secondary care or worked in both care types named integrated care. There were six themes that developed through this study; polypharmacy in asthma and its relationship to comorbidities and asthma severity, repeat prescribing and treatment burden and the associated education of patients, the use of guidelines in asthma treatment, the feasibility of medication reviews and HCP responsibility, deprescribing in asthma and its barriers for implementation, and interprofessional relationships across primary and secondary care in asthma.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
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</thead>
<tbody>
<tr>
<td>Pharmacists ((n=9))</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
</tr>
<tr>
<td><strong>Job Role</strong></td>
<td></td>
</tr>
<tr>
<td>Primary Care</td>
<td>4</td>
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<tr>
<td>Integrated Care</td>
<td>5</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td></td>
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<tr>
<td>Scotland</td>
<td>4</td>
</tr>
<tr>
<td>England</td>
<td>5</td>
</tr>
<tr>
<td>Doctors ((n=16))</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11</td>
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<tr>
<td>Female</td>
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<tr>
<td><strong>Job Role</strong></td>
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</tr>
<tr>
<td>General Practice</td>
<td>8</td>
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<tr>
<td>Hospital</td>
<td>8</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td></td>
</tr>
<tr>
<td>Scotland</td>
<td>7</td>
</tr>
<tr>
<td>England</td>
<td>9</td>
</tr>
<tr>
<td>Nurses ((n=7))</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
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<tr>
<td>Female</td>
<td>5</td>
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<tr>
<td><strong>Job Role</strong></td>
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<tr>
<td>General Practice</td>
<td>3</td>
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<td>Hospital</td>
<td>4</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td></td>
</tr>
<tr>
<td>Scotland</td>
<td>3</td>
</tr>
</tbody>
</table>
Table 5.2 shows number of Asthma HCPs interviewed, their location and which form of care that the interviewees work in.

5.3.1 Polypharmacy in asthma and its relationship with comorbidities and asthma severity

HCPs noted that polypharmacy in asthma can be heavily defined by additional comorbidities. Common morbidities seen in patients with asthma by the HCPs were COPD, anxiety and depression, cardiovascular issues, obesity, diabetes, and rhinitis. Similarly with patients presenting with polypharmacy seen across the different disease categories, polypharmacy was seen more frequently in older patients with multimorbidity.

“...I see lots of patients who are on polypharmacy, so they are on very easily a number of medications, and quite often it’s not all because of asthma, it is because of other comorbidities. The reason why we call it severe asthma or difficult asthma is, there is always a question whether they do have asthma or not”
S1, Scotland, Male

“I tend to see…the older group, who have multiple morbidities, but often asthma merging into COPD with some lack of reversibility and then the kind of cardiometabolic syndromes that go alongside that often. So, people who are perhaps a little bit overweight or obese, who have cardiovascular diabetes, hypertension associated. They are often the more challenging group to manage.”
GP1, England, Male

When asked about the correlation between asthma severity, polypharmacy and its correlations with comorbidities, some HCPs had either not given it a much thought or did not see that there was a correlation. It was uncertain if asthma HCPs do factor these comorbidities into their treatment plans when assessing their asthma. Furthermore, it was, also, unclear if the severity of asthma is linked to increased or exacerbated additional comorbidities based on HCP responses.
“I don’t know I can’t say, as a definite trend. Unfortunately, what happens is that you then always think about the last difficult patient, don’t you? The last difficult patient, they stick in your mind and you’re thinking- You’re thinking about their multi-morbidities and their comorbidities…But I’m not sure you can necessarily generalise it out to it relating to their asthma necessarily.”

P1, Scotland, Male

“I’ve never thought about it but I can definitely see that because I’ve worked in other places where we don’t have- Patients wouldn’t be quite so severe and I think, I think definitely that is something that if you think about it you do see, but it would make sense really.”

P2, Scotland, Female

However, most HCPs believed that there was a strong correlation between asthma severity and comorbidities translating to higher levels of polypharmacy.

“I would say yes, I think there’s a strong link between the severity in somebody’s asthma and comorbidities” specifically anxiety related.”

N1, England, Male

When asked if asthma HCPs take these comorbidities into consideration when treating their patients, there were differing opinions based on the HCP. General Practitioners would always respond affirmatively, to look at their patients in general terms. Nurses and pharmacists would admit that they would always try to remember to look at their patients’ other medications and comorbidities but that sometimes they would forget. Specialists, as expected, were the least likely to look at their patients’ other medications and comorbidities, though some did confirm that they paid attention to their patient in case of contraindications in relation to their patients’ asthma medications. This finding suggests that the more specialised the role of the HCP, the narrower their scope of both treatments and conditions. More specialised HCPs stated that they take other patients’ treatment into consideration as they viewed this as standard practice but it is, also, not in their interest to state that they might not be
adhering to this protocol. Furthermore, discovering the exact context of how specialised HCPs factor in other comorbidities merits further investigation.

“Yeah, absolutely. So, even if a patient comes to me with, say they’ve got epilepsy or some other complication, I still make a note of whatever medication they’re on, other health needs.”
N2, Scotland, Female

“I hope so. [laughs] I hope so, yes. I think I do. One of the things is, it’s easier to do that as a GP than it is to do it in hospital because of the prescribing system.”
GP2, Scotland, Male

“So the kind of medications that we prescribe are essentially asthma medication, so yes, we do take them into account, but most of our medication we can prescribe, in the majority of our patients, it’s mostly inhaled corticosteroids, and there are not very many patients where that would be contraindicated, I would have thought. But yes, we do look at it, if there is any reason for which they can’t take that, yes.”
S1, Scotland, Male

The HCPs who worked in multi-disciplinary teams (MDT) enjoyed the communication that occurred when they would look at the patients’ medications and comorbidities and would hear from other departments and staff with a different skillset and expertise to their own. They viewed MDT’s as an opportunity to understand other HCP and department opinions. HCPs with MDT experience felt that disagreements rarely occurred as an open discussion about patient treatment would be had and HCPs would come to treatment decisions collaboratively. HCPs considered MDTs a valuable experience which improved their interprofessional relationships with other colleagues.

5.2.2 The use of guidelines in asthma treatment
Asthma treatment is profoundly influenced by the use of guidelines. This was, also, apparent in the HCP responses. They would commonly reference using the BNF, BTS/SIGN, NICE or GINA guidelines as a guide for their asthma treatments.
“Yes, I try, I tend to use the BNF mostly for, I know there is the BTS and I’m aware of the asthma guidelines, so I do use the guidelines, you know I don’t feel sort of bound by guidelines, so you know if someone, everyone is different.”
GP3, England, Male

However, a small number of the HCPs would mention that they were not limited by the guidelines and, in some cases, they would question the guidelines and prioritise their own experience rather than be constricted by the guidelines. This view was taken by doctors, GPs or specialists, but this view was rarely mentioned by nurses or pharmacists. Nurses and pharmacists with less experience were more likely to use guidelines more religiously as they felt more professionally committed to the guidelines and were more likely to go ‘by the book’, whereas experienced doctors felt that they had more cognitive authority to question guidelines than the other HCPs.

“So I use prescribing guidelines, but I have to say, this is going to sound incredibly big headed, but I would challenge guidelines, so a local guideline, I’m far less likely to use local guideline because I’ve had lots of run-ins with local guidelines people in the past and I often don’t believe in them”
GP5, England, Male

All HCPs identified that guidelines were too generalised and that they would pay attention to the individuals’ needs rather than using the guidelines verbatim. As using asthma guidelines was considered as using disease guidelines, HCPs would also mention using other disease guidelines as well when viewing their patients’ other comorbidities or medications. They regarded this as looking at their patients in a more holistic manner rather than just focusing on their patients’ asthma. However, only four HCPs, two pharmacists and two GPs, mentioned looking at prescribing guidelines and
only one pharmacist mentioned eyeing polypharmacy guidelines but only using it as a prompt rather than an actual guidance for their prescribing. Therefore, using individualised disease guidelines was the main form of guideline usage but prescribing guidelines were not used regularly, if at all. Asthma HCPs seemed accustomed with disease guidelines and were more inclined to use them due to this familiarity. As the polypharmacy guidelines were quite new in comparison, their implementation was seemingly not as widespread. The Scottish Polypharmacy Guidance was not mentioned by an HCP in Scotland but by a pharmacist in England.

“we’ve got very good local asthma and COPD guidelines so I use them all the time. Well, as in I mean they’re imprinted on my brain so I use them all the time. Hypertension guidelines, that’s kind of been imprinted on my brain as well….And I use guidelines all the time when I’m working on wards. So, yes. Well, I mean, specific to polypharmacy, no…”
P6, England, Female

“we have done some work around polypharmacy where we basically, it’s not quite as comprehensive as say a therapeutic guideline but we have, we do prompt to for example Scottish polypharmacy guidance…”
P5, England, Female

5.3.3 Repeat prescribing, treatment burden and the associated education of patients
Treatment burdens arise when a patient does not know how to, or is unable to, take their medications effectively, usually due to their medication regimen being too complex\(^\text{220}\). Instructions associated with certain treatment regimens can also be difficult for patients to follow. This can cause medication to be less effective and, in turn, patients do not see the full therapeutic benefit of their treatments. This can negatively affect patient adherence levels. In general, there is a treatment burden in most disease types and is associated with compliance, however, with asthma the treatment burden is exacerbated by the difficulty connected to using an inhaler. The
most common way the HCPs mentioned improving this treatment burden in patients was to educate the patient on inhaler technique.

“Yes, there’s a huge treatment burden with what we expect of our patients and I’d love to sit at the end of the corridor, as patients leave the clinic and say, [0:09:57] “Can you just tell me what you’ve made of what the doctor or the nurse has explained to you about this new inhaler that they expect you to take? And how can you actually do that? Is that going to work for you?””
GP3, England, Male

“I don’t know what it is but I think a significant proportion of people with asthma still don’t use their inhalers correctly.”
GP4, Scotland, Male

“They get seen by an asthma nurse specialist who does the education and the inhaler technique and things like that and make sure that they’re actually using the device appropriately.”
N2, Scotland, Female

Treatment burdens issues were usually revealed in the annual asthma review or in regular medication reviews with a discussion with the patient. These treatment burdens were usually discovered by the nurse as it would be flagged up in the annual asthma review where asthma management plans would be created with the nurse and patient in a shared decision manner. The discovery of these burdens would trigger a deeper discussion to be had with the patient. Nurses would utilise this opportunity to educate the patient on inhaler technique and would recommend them YouTube videos or apps such as the Right Breathe app to assist patients with taking their medications correctly.

“I would usually write down a personalised asthma management plan for them. I direct them to watch YouTube videos, on how to use their inhaler and I’ll sit with them in surgery and bring up the YouTube video and watch it with them and then there’s also an App that I use called ‘Right Breathe’…”
N3, England, Female
In relation to treatment burden, patients with asthma were usually prescribed irregular oral steroids when they suffered from a severe asthma attack. However, a treatment burden can be, further, placed on the patient when these steroids are not removed from the patients’ medication list and are kept via repeat prescription.

“I don’t personally do regular. It’s a major bugbear of mine that people have them on repeats... So, for people with asthma not everybody with asthma will have a course of steroid tablets at home. For those that are appropriate they might and I think people who are engaging, they have a management plan and they understand what they’re doing and when.... I have a big issue with steroids being on repeats.”
N3, England, Female

It was unanimously agreed by all the HCPs that patients with asthma and (also mentioned) COPD should not be on long term oral steroids and that they should only be prescribed steroid as and when they needed them for a short duration. These short-term steroids were called ‘rescue packs’ but even these short steroids could find themselves on a patients repeat medication list. Particularly, during COVID, the monitoring of oral steroids and, in turn, repeat prescriptions, according to the HCPs, were inadequate, at best.

“I think we should all become oral corticosteroid stewards and ensure that we’re much more mindful about who we give steroids to, when we give steroids to, you know, they should be much better objective markers before we prescribe steroids to patients with asthma and COPD, rather than a sort of blasé giving of steroids which occurred incredibly often over Covid, because obviously, patients weren’t even being assessed”
N4, Scotland, Female

Furthermore, most HCPs believed that to prevent this treatment burden associated with irregular oral steroids, patients should be prescribed biologics and they should be weaned off oral steroids. Oral steroids are supposed to only be given as a short course
for one week in patients with asthma. However, regularly steroids are found in patients repeat prescriptions as long-term inappropriate polypharmacy. Therefore, oral steroids should be targeted by asthma HCPs for deprescribing or a replacement should be found. Biologics, such as Omalizumab, a monoclonal antibody, are preferable to oral steroids as they utilise specific biomarkers to reduce asthma exacerbations in severe asthmatics with less of the side effects and withdrawal symptoms.

“we have a very clear protocol for withdrawing all steroids and those initiated on biologics. It’s so clear that the Nurses run it independently.”
S2, England, Male

However, this proved to be a difficult task for these HCPs as they considered that patients who had been on a repeat prescription of steroids for years would be incredibly difficult to target for biologics treatment. This would be, further, compounded by the withdrawal effects caused by the removal of oral steroids.

“They’ve been on the (oral) steroids for years, so it’s hard to get them off. So that’s a really difficult situation…”
S3, Scotland, Male

The treatment burden linked to oral steroids touches on a concern within healthcare: the overuse of repeat prescriptions. Monitoring of repeat prescriptions should be regularly checked at least once a year to prevent inappropriate polypharmacy and prescribing cascades. HCPs gave mixed responses, in regards the monitoring of repeat prescriptions in their practices regardless of care system, they either remarked that there were systems in place for checking repeat prescriptions or there was none. Those who mentioned that a system was in existence either noted that their practice had a flagging system that would inform them when a person was over-ordering
product via a percentage overuse, or their practice had repeat prescribing policy that helped them monitor their patients repeat prescriptions.

“We’ve got our repeat prescribing policies and procedures in place, we try and have the correct training for repeat staff, so, when they order a repeat prescription, they’re aware to look out for any over-ordering. Managing things on repeat or acute, you’ve got set timed intervals on the repeats as well, so, you can set it for a certain amount of time, and reauthorisation dates”
P3, Scotland, Female

“The system will say, requested 400% of what they should be, so it flags up quite quickly if people are needing medication early.”
GP5, England, Male

The other response given by the remaining HCPs was that there was no practice monitoring system and that repeat prescriptions were not checked as regularly as they could be. Coincidentally, these HCPs viewed that there should be a system in place created by the practice itself or that there should be a flag within an electronic healthcare system that could uniformly notify them of over-ordering across care systems.

“The practice I work in hasn’t, historically, had amazing auditing for monitoring of chronic disease...And I think people always struggle a little bit with how to monitor those, because the easy way to do it is to take them all off repeat and then – but that generates a huge volume of work”
GP6, Scotland, Female

This lack of a monitoring system was viewed as a major failing by all HCPs. HCPs acknowledged the connotations that would occur in patients’ medication lists if they were left on certain medications for long periods of time without this being flagged up or checked in some way causing a cycle of inappropriate polypharmacy left unchecked. These HCPs recognised that a lot more work needed to be done to
prevent the over-use of repeat prescriptions and that this would be a problem for the foreseeable future if a standardised system or guideline on repeat prescriptions was not created for all HCPs to use in locations that did not have an existing system in place. A further issue of this lack of monitoring system for repeat prescriptions is that it throws into question whether or not HCPs actually perform their annual medication reviews as these flags for repeat prescription could be naturally detected in a medication review.

5.2.4 The feasibility of medication reviews and HCP responsibility
Asthma HCPs were expected to conduct asthma annual reviews. In general, polypharmacy guidelines suggest that structured medication reviews should be conducted annually as well, if performed. Nurses and specialists across care types responded that they would conduct medication reviews and asthma reviews simultaneously, to combine their workload. However, they noted that the medication reviews they would perform would not be in the form of a structured medication review but that they would eyeball the persons’ medication list, focussing on their asthma first and then considering their other treatments. Therefore, in patients with asthma, it seemed that a medication review was only prompted due to an annual asthma review. However, polypharmacy is, most generally, defined as 5 or more medications every 6 months, so having a structured review annually might not be enough and should possibly occur bi-annually if it was not for time constraints within healthcare.

“Just combine the two. So, I wouldn’t do a medication review like a pharmacist would or like a doctor would. I look to see, as I say I tend to prioritise their asthma, COPD medication. That’s a mean feat in itself really, because usually they’re on too much treatment…”
N6, England, Female
“Yes, so I do go over their medication, so certainly their asthma medication I do, and I ask them if they’re on any new medication, but yes, so - we used to be bad...But we’ve moved that cohort of patients into a separate clinic now, which is run by our pharmacist, to make sure that we do all of that properly.”
S2, England, Male

It was viewed by GPs and asthma consultants that official structured medication reviews were the pharmacists’ job and in their role description. Even GPs mentioned that, while they did conduct structured medication reviews from time to time, they mainly conducted informal medication reviews where they perused the patients’ medication list when they visited the surgery rather than conducting a full review. If the patient had a more complex treatment regimen and the practice had an in-house pharmacist or a regularly visiting community pharmacist, the GPs would refer the patient to the pharmacist. In general, doctors considered medication reviews to be an informal process, which they performed as and when the patient came to the practice rather than strictly annually, and due to time constraints during COVID, a structured medication review was less likely to be implemented. Furthermore, it was apparent that patients did not always receive structured medication reviews annually, pre- or post- COVID. The consequences of this lack of structured medication review meant that patients had medications that could or should have been removed left on their repeat prescription list and could cause a prescribing cascade if any existing medications caused side effects.

“It’s usually a much more informal process. I mean, I think, particularly now with Covid, doing that sort of review is quite challenging.”
GP8, Scotland, Male

GPs and pharmacists in primary care delegated their patients’ asthma to nurses. Specialist nurses in asthma conducting asthma reviews deemed asthma as of the
utmost importance, however, generalists in primary care did not share this view. In primary care, they viewed their patients’ treatments as a whole and this caused their asthma to be put further down the importance list, particularly if these patients had, what was considered to the HCPs, more serious comorbidities. Due to this, the specialist nurses in asthma were perceived by pharmacists and doctors to be the ones to whom the patient would visit to discuss their asthma, and this was aided by nurses observing asthma as highly important.

“In polypharmacy, it is easier for the asthma to get overlooked because of all the other comorbidities. It’s sad really because you get some patients on 15 plus medications and then they’ve got the inhalers at the bottom, so, by the time you’ve discussed everything else, the inhalers can just be on the back burner. It’s making sure everybody has the annual asthma review, that is why I like to [refer to] the nurses because they’re specialists in this area and I don’t have time to fully discuss asthma like I want to in a proper medication review”
P1, England, Male

5.2.5 Deprescribing in asthma, shared decision making and its barriers for implementation
Deprescribing was unanimously regarded as the next step in patients with inappropriate polypharmacy. Two of the nurses said that they would regularly step-down treatment or would present an alternative treatment but that they felt not confident enough to fully deprescribe treatment or felt that it was more within the doctors’ or pharmacists’ role to deprescribe.

“I wouldn’t say de-prescribe, I would say that I’ll try an alternative and if it works then I’ll say, right we’ll get that one removed from the repeat prescription....”
N7, England, Male

“I think probably if I’m honest I think confidence is probably a barrier.”
N5, Scotland, Female
Furthermore, all the HCPs believed that they would only deprescribe or step-down medications if the patient was getting their symptoms under control from a lower dose. Furthermore, an issue that was viewed as prevalent in asthma was that asthma diagnoses are not always conclusive. Sometimes, patients were diagnosed with asthma and yet this was not the disease they suffered from. In some cases, their symptoms were not a disease type but a side effect from the other medications they were taking. This posed a unique issue in deprescribing in asthma as HCPs needed to confirm the diagnosis first and foremost and the inappropriate polypharmacy second. Subsequently, a cycle appeared when patients were over-prescribed medications that were not taken off repeat prescriptions.

"But that sort of concept of, first of all, is this asthma I’m dealing with, or is this hyper responsiveness from a short acting beta agonist, or is this breathlessness because of a raised BMI…is really important to still continue to assess, before you even start thinking about stepping up/stepping down… is the diagnosis right? Even if the diagnosis has been right are the symptoms still linked in with what I’m trying to treat?"

GP6, Scotland, Female

Once this confirmation of diagnosis and the symptom control complication was analysed by the HCP, deprescribing commenced. However, to effectively deprescribe treatments, it is best to include the patient where a shared decision-making discussion could be had, according to the pharmacists interviewed. All the HCPs shared this perspective that when they discovered a medication to deprescribe, they would communicate with the patient their thoughts on stepping down treatment and, possibly, its removal. The HCPs deemed educating their patients to make an informed decision on the removal of their medication to be paramount to the patients experience in a healthcare environment as HCPs wished their patients to be knowledgeable about their treatments and understand the rationale behind deprescribing. The HCPs viewed
that the final decision lay with the patient. Fundamentally, if the patient did not want the medication to be removed, the HCP could not deprescribe the treatment.

“So you explain why you would want to change it, and obviously it’s a shared decision, and ultimately patients have a right to choose or decline a treatment, but you would explain why and what is the rationale behind it, and some patients are accepting, and some patients are not, so you just have to accept that…”
GP4, Scotland, Male

There were situations where the patients did not want to have their treatments deprescribed. Common reasons cited by HCPs were that patients did not like change, were psychologically attached to their medications and could not envisage themselves not taking every single medication or were confused as to the reason the HCP would be suggesting such advice. These barriers were viewed by the HCPs to be solved by continuing their shared decision-making discussion to include educating the patients on the negative effects that taking too many medications can have on them.

“they can be very psychologically attached to their treatment, so it could be hard to remove them”
S7, England, Male

“Yes, I think because obviously they are worried that if things are going well why would you stop it, and reduce it down? For some of them that is I think, and then it’s a case of educating them around a balance between overtreatment and control”
P9, Scotland, Female

“we talk about understanding people’s beliefs and concerns about medicines, and making sure you get that balance right when you prescribe, but you almost need to do that when you deprescribe as well. So you address what their concerns are for deprescribing. So what is it they think might happen if we take this medicine away? What is their beliefs around what they think that medicine is doing for them? So you almost need to, I think, address that in the same way as you should do when you’re prescribing, to ensure that then the patient adheres to deprescribing, because otherwise what will happen is that a patient is likely to just restart it again.”
P9, Scotland, Female
Additionally, there were several HCPs, particularly GPs, who perceived that they had never encountered any barriers to the deprescribing of treatment and believed that patients, generally, wanted to take less medications. Patients, particularly those with a higher health literacy, were perceived by these HCPs who did not encounter barriers as willing to have their medications removed. Barriers to deprescribing medications were often noted by HCPs as patients being psychologically attached to their existing medications, the patient belief in having multiple medications for each symptom they possess and patients feeling abandoned by HCPs if treatments are removed, particularly if they did not consider anything to be wrong with their existing treatment. However, other patients were willing to have their medications removed and had no issues with removing medications. These patients preferred less medications.

“So, I very rarely find a barrier to stepping down, especially people, most people have a perception about inhaled corticosteroids; that they’re still bad things, so they’re only too happy to reduce a dose of steroids, which is usually what the stepping down is”

GP5, England, Male

Conversely, several of the HCPs attributed concerns in other HCPs not attempting to deprescribe. This opinion was mainly held by specialists and GPs where there was a misperception on the roles and responsibilities for doctors in deprescribing. Most specialists stated that GPs did not endeavour to remove treatments at all and this exacerbated the over-treatment of patients. They felt that every time they encountered patients’ additional medications had been added and that, to their knowledge, they could see no attempt to deprescribe medications. Usually, specialists encounter patients for specific ailments and so do not look at the patient in general terms, therefore, they feel it is not their job to deprescribe medications that are outside the scope of their specialisation. However, even within their specialisation, it is unclear if
they deprescribe medications within the grounds of their expertise. Similarly, GPs remarked that patients would attend the clinic in hospital and would return with supplementary medications. This confusion in roles and responsibilities was contributed to the lack of guidance and generalised processes for deprescribing in healthcare. These HCPs sought a specific set of guidelines or tools that would clarify who was responsible for deprescribing so they could effectively apply these rules in their daily surgeries. Deprescribing tools and guidelines exist but GPs and specialists perceived that they did not clarify their individual roles and responsibilities. The deprescribing tools that do exist the doctors did not mention them or seem to use them. One pharmacist and one nurse were aware of the presence of these tools but did not utilise them due to the perceived time it would take for them to use them. The PINCER tool which is aimed to reduce medication errors by improving medication safety by GP pharmacists and MedStopper, an electronic clinical decision support system for deprescribing were mentioned, respectively.

“What’s more nobody is going to take it away; the reality is there is no mechanism that is really effective at stopping. I don’t really know whose job that is, it’s definitely not the GP’s job because they don’t do it. They don’t cut, they only add in my experience they don’t cut and when you try to cut, when you cut, they add it back.”

S4, England, Male

“What from sort of deprescribing and stuff like that, I guess I don’t use any of the sort of pincer tools and things like that, but I have looked at sort of deprescribing tools and things like that, as part of, just out of interest”

P3, Scotland, Female

Some GPs recognised the implications on patient treatment due to lack of communication between primary and secondary care. The patient perception of the discontinuity of care, regardless of the truth, could be deeply damaging for future interactions with patients. If patients presenting with polypharmacy believed that the
HCPs that they encounter for each of their comorbidities were unaware of each other’s actions in terms of prescribing, this could cause barriers in future prescribing and polypharmacy management decisions as the patient may not view their HCPs as knowledgeable if they do not perceive the entire picture of their patients’ health. The HCPs all conceded that the communication between primary and secondary care would need to be improved to enhance patient treatment generally and, specifically, in deprescribing to prevent patients receiving conflicting information from different HCPs making it difficult for them to adhere to the changes in their medication lists.

“the problem is, I mean it must be so confusing because they see one doctor and the doctor slightly tinkered with the medication and then they come and see someone else and another doctor says something else, I think there is a sort of role where continuity of care is important”
GP5, England, Male

5.2.6 Interprofessional relationships across care settings in asthma

Within primary care, the GP surgeries mostly contained at least one pharmacist or a pharmacist who would visit the surgery regularly. In addition, all the surgeries had a nurse on site. Due to this close contact, discussions about patients would occur regularly in primary care. Primary care HCPs viewed that there was an open communication between HCPs and each individual HCP had their own valuable expertise to provide in clinical settings. Most GPs would ask advice from the nurse on asthma treatment as they viewed the nurse to be more experienced and, additionally, they would ask pharmacists information on more complex prescribing. Furthermore, the pharmacists and nurses would reciprocate and would ask the GP about any information that felt unsure about.

“Well I tend to go along with what the nurse has suggested, because they’re doing this asthma regulations on a regular basis. They are very very clued up on the latest guidance on the stepping up and stepping down of medications.”
GP8, Scotland, Male
The perceived existence of this open communication caused the HCPs to remark that there were no differences of opinion when talking about patients. Unanimously, amongst the HCPs in primary care, they perceived that they had no issues with communicating their thoughts to each other and this fostered a healthy working relationship. The GPs, pharmacists and nurses respected each other’s individual roles and responsibilities and would value their colleagues’ expertise in comparison to their own.

“No, I know that’s somewhat surprising but no, no I don’t really. We kind of chat things through and generally we come to a view quite quickly. It seems, yeah, there’s not really much in the way of, of disagreement.”

GP7, England, Male

The close bond that existed in the primary care dialogues were caused by proximity. In secondary care, communication and HCP relationships were cultivated by regular MDTs, in addition to proximity similarly found in primary care. This is due to hospitals contained higher volumes of staff and, in general, large teams that vary quite considerably across specialisations. Furthermore, there was a wider gap between higher and lower levels of staff in terms of communication. Therefore, differences of opinion would occur in MDTs, but a discussion would ensue to achieve a final agreement on the patients’ treatment. The differences in opinion were not regarded as a negative but, merely, as a fact of bringing people together from different job descriptions. It was considered a natural process to go through and that the discussions occurring to reach a final agreement fostered a better working environment within different healthcare teams. Furthermore, these conversations always placed the patient at the forefront of their treatment, the HCPs viewed their own individual roles as secondary. All the HCPs interviewed in secondary care were in at least one MDT, if not several.
“we are all in an MDT, we're all having a discussion together about the patient. So, like, my recommendations are if you like, acted on immediately because we have all agreed and made the decision.”
P3, Scotland, Female

“Sure, you do, don't you but then you – that’s the whole point of discussion, is to try and work out what works the best and it doesn’t mean that changing is always the right thing, and the individual clinician has autonomy with the patients, so if someone should say to me, “No, I think this is what we need to do” then that’s what we would do.”
S3, Scotland, Male

The main concern amongst revolved around communication between primary and secondary care. In Scotland, the existence of CHI numbers allowed for an easier transfer of information of patients' medication histories between care systems. However, this did not necessarily guarantee better communication between the two according to the HCPs. Yes, the HCPs could see what was changed in the medication list but the reasoning behind changes in prescribed treatments were less clear. In Scotland, EMIS was quite commonly used as the electronic health record of choice but the links to secondary care are less prevalent. English practices use EMIS as well and EMIS for secondary care exists which can be used to link both primary and secondary care but this is limited by which hospitals/GP practices use it. In England, NHS numbers exist which are similar to CHI numbers but individual countries have their own electronic systems for patients. Therefore, despite the existence of NHS numbers, the links between primary and secondary care can be difficult to deal with in terms of changes in treatment across counties/clinical commission groups (CCGs).

Some HCPs noted that they could only see basic information of patient drug histories, while others noted that they could not see what primary care was doing and vice versa. There was no electronic health record across primary and secondary care. Some secondary care HCPs could access GP records as in they could access their patients’
summary care record but, in primary care, HCPs in England relied on discharge summaries and clinical letters to inform them of their patients’ treatments in secondary care. Similarly, Scotland has an emergency care summary as a transfer of information between secondary and primary care. Among the English HCPs interviewed within primary care, they noted using either EMIS, SystmOne or Vision as the electronic health record used in their practices. Most HCPs in both Scotland and England would send a letter to the consultant or GP on changes in treatment or a smaller number of HCPs would send an email to inform the other care system. However, both sides were unsure how seriously these email or letters were taken or if they were even looked at all. One specialist mentioned sending the letter to the GP via the patient. A select few HCPs would opt for a phone call if they were friendly with the other HCP.

“we don’t have kind of open channels, we send letters if I need something done in primary care and I can look up the GP and send them an email, that usually goes to a receptionist- So it’s not kind of a really open communication”
N5, Scotland, Female

“I communicate back to the GPs by letters. I no longer write letters to GPs; I write them to the patients.”
S8, England, Male

“If I wanted somebody seen urgently as a result of worsening asthma, it would be an email or writing to the consultant to ask for an expedited appointment, but we have no other way of doing it.”
GP6, Scotland, Female

5.3 Discussion

To talk about polypharmacy in patients with asthma, the patients’ other comorbidities and the severity of the asthma that they possess must be taken into consideration. Despite some patients with asthma having polypharmacy due to their asthma alone, this is due to the more severe the asthma the patient has, the more medications they
take to treat their asthma. It was found that HCPs did try to consider their patients’ other medications and comorbidities. However, HCPs would not like to be perceived as neglecting their specified duties and so it would be unlikely that that they would be forthcoming about not taking their patients other medications and comorbidities into consideration. Furthermore, it was shown that the propensity for specialists, whether that be doctors, pharmacists or nurses, they were more likely to not disclose whether they considered patients additional comorbidities and/or other medication in addition to their asthma treatment. Therefore, it can be deduced that the narrower the scope of the HCP, the narrower their frame of reference when treating their patients but this finding could benefit from additional research to confirm this\textsuperscript{95,146}. Additionally, the possible correlation of asthma severity to multiple morbidities was viewed in a mixed manner\textsuperscript{224}. Some HCPs believed that there was a definite association that had not been considered before or that they had not reflected on an association but would ponder the connection in more depth after their interviews. The latter viewpoint was mainly thought of by pharmacists and nurses. There were a select few doctors who believed there was no correlation and to associate the two was incorrect. This corresponds with Wardzynska et al. and their work on comorbidities and elderly patients with asthma, they found that the higher prevalence of comorbidities did not correlate with worsened asthma control or severity\textsuperscript{225}. Whereas Schleich et al. showed that patients with severe asthma were associated with obesity (47\%), depression (19\%), rhinitis (49\%), GERD (36\%) and nasal polyps (19\%). Specialised HCPs do not fully admit that they do not take other patients’ treatments and discovering the exact context of how specialised HCPs factor in other comorbidities merits further investigation.
In relation to asthma severity, the long-term treatment of severe asthma with the use of irregular oral steroids, Prednisolone, was contentious. All HCPs believed that irregular oral steroids should not be on patient medication lists for a long period of time and should only be added for short courses, i.e., 7 days to one month. Biologics were considered a much better treatment for asthma exacerbations by the HCPs. Although, irregular oral steroids are still very commonly prescribed to patients with asthma for long periods of time despite the well-known side effects and withdrawal symptoms. HCPs knew that there was an issue with steroids being on repeat prescriptions. The HCPs would either respond that they would aim to prescribe biologics or only prescribe short ‘rescue’ courses of prednisolone. It would be unlikely that an HCP would admit that they themselves would forget a short course of prednisolone so it would find itself in the patients repeat prescriptions list. However, HCPs recognised that other previous HCPs had forgotten steroids.

Similarly, some of the HCPs, in one of the practices that did not have a repeat prescribing monitoring system in place, were quick to shift the responsibility onto another member of staff as they considered it another persons’ job. With the existence of online repeat prescription requests, these requests go through the reception desk and not the HCPs, therefore HCPs, when not included in this request system, view it as the practice’s responsibility and not their own. In practices where they had a monitoring or flagging system, these HCPs knew their own roles in the repeat prescription pipeline. Garth at al. highlighted a similar issue in Australia, that closer examination of the repeat prescription system was required both to allow a more streamlined approach to repeat prescriptions and in preventing over-use.
Currently, there is no universal system or guidelines for the monitoring of repeat prescriptions. There are guidelines for deprescribing and other monitoring systems such as medication reviews which can be linked to repeat prescriptions. Currently, the protocol for medication reviews is at least one medication review annually. However, this seems to be too infrequent particularly when polypharmacy is defined in six-month periods. Therefore, it could be proposed that medication reviews are conducted bi-annually at the very least. However, as much as conducting medication reviews more frequently could assist patients, the feasibility of such an intervention would be difficult to achieve as it would in all probability cause a heavier burden on NHS staff and their sizable workloads. Furthermore, this could also place more stress on patients, as they will be required to visit their HCP more frequently which could cause them to be more worried about their medical treatments and/or care. A study by O’Connell et al., investigating self-management support for patients with COPD or asthma found that patients stated they felt the management of their asthma would be more appropriate if their asthma reviews occurred bi-annually rather than annually. Also, patients felt that those with severe symptoms should have a review every three months. If an HCP conducted medication reviews regularly, this would influence their repeat prescriptions as the HCP would know exactly what the patient was prescribed and at what dose. However, this does not occur. Very few HCPs interviewed used prescribing or deprescribing guidelines. However, this study interviewed asthma HCPs and therefore, they did use asthma guidelines or other disease guidelines when dealing with their patients. Perhaps, asthma HCPs are more familiar with asthma guidelines and, therefore, are much more likely to use them. In addition, as this research was conducted with asthma HCPs there is a possibility of bias when using other guidelines. It would be expected that asthma HCPs would predominately use asthma guidelines,
particularly as they would be following existing asthma protocol. The widespread usage of prescribing or deprescribing guidelines for asthma HCPs might not be feasible if time constraints, staff roles and responsibilities and other workload commitments are added into the equation. A possible solution to this could be asthma protocol that features these issues with guideline usage, however, this could just add to HCPs workload rather than offering a better solution.

Although, prescribing and deprescribing guidelines are relatively new and are not as widespread in their utility. The Scottish Polypharmacy Guidance which contains an explicit 7 step process for deprescribing was rarely used by the asthma HCPs even in Scotland\textsuperscript{1}. This emphasises that work needs to be accomplished on creating the widespread usage of these guidelines. These prescribing/deprescribing guidelines do not require to be used verbatim but they may assist HCPs, such as nurses, in giving them the confidence to deprescribe more frequently. Furthermore, guideline usage is inversely related to HCP experience, the more experienced the HCP, the less likely they are to use it\textsuperscript{101}. Experienced doctors tended not to use the guidelines at all, whereas experienced nurses and pharmacists would use the guidelines as a prompt but would not follow the guidance religiously. The generalisation of guidelines was a deterrent for HCPs to use them.

In relation to roles and responsibilities of individual HCPs, medication reviews, although all the HCPs maintained that they would conduct them, were deemed to be the pharmacist’s role. GPs and specialists would state that their medication reviews were more informal in structure, especially in COVID-19 times, and that pharmacists were the HCP conducting structured medication reviews. Therefore, if patients did get
referred to the pharmacist with a complex medication regimen, or nurse, they did not necessarily receive their annual structured medication review. With patients with asthma, they would, if they attended their annual asthma review, receive a medication review simultaneously according to the nurses interviewed. This should mean that patients with asthma are more likely to receive a medication review due to the presence of the annual asthma review, in comparison to other disease types with no pre-planned annual assessment. There have been several studies conducted in the endeavour to improve asthma management by referral to pharmacists and nurses in the literature. Bereznicki et al. examined referring sub-optimally managed patients with asthma to community pharmacists and discovered that asthma symptom control was significantly improved after 6 months of the intervention\textsuperscript{229}. Furthermore, Armour et al. discovered that primary care pharmacists trained in conducting an asthma service over 6 months reported an improvement of around 40% in asthma knowledge, quality of life and perceived symptom control by patients\textsuperscript{230}.

Moreover, deprescribing medications was controversial in its imagined role for doctors. There was a disagreement over who bears the responsibility in healthcare to deprescribe. GPs believed that their patients would return with additional treatments and specialists held the same belief of their counterparts in primary care\textsuperscript{231}. However, it was found that most doctors were more likely to rely on their own expertise when treating patients rather than referring to guidelines. Furthermore, most nurses did not feel comfortable fully removing medications from a patients’ list, their inclination was to step down medications or suggest alternatives but not completely remove a medication. They would prefer that the doctor or pharmacist would remove medications due to lack of confidence or supposed expertise. Also, nurses may
believe that patients are more responsive to a gradual change in medication rather than an immediate change in treatment\textsuperscript{128}.

The benefit versus risk strategy in deprescribing applies to both stepping down and removing medications\textsuperscript{38,232}. However, reducing medication dosages are perceived to be less risky than removing medications according to nurses. Regardless of care type, doctors and pharmacists did not share this view. In general, the role of nurses in deprescribing is quite limited in the literature and this topic needs to be, further, discussed\textsuperscript{128}. Naughton & Hayes stated that nurses’ role in deprescribing and lifting medication burden needs to be carefully articulated and that nurses, themselves, need to acknowledge the importance of their role in this process\textsuperscript{233}. Therefore, nurses require augmented training to provide them with the additional confidence in their prescribing skills. This would remove a major portion of concerns that nurses may have over deprescribing. They would continue to follow protocol and/or guidelines and would, possibly, have less fear of changing another’s prescribing decision. Moreover, a carefully curated protocol or guideline could to be created with explicit information on the actors involved in the different aspects of deprescribing to remove uncertainties about roles and responsibilities of the deprescriber\textsuperscript{1,234}.

This absence of standardised roles and responsibilities for deprescribing across different roles and organisational positions could affect patient treatment\textsuperscript{171}. The possible patient perception of the discontinuity of care, regardless of harm, could be deeply damaging for future interactions with patients across multiple care systems\textsuperscript{235}. Communication is imperative for the understanding of reasons for deprescribing and this would be lost if patients’ do not trust their HCPs. If this discussion does not occur,
the patient could be missing out from structured medication reviews and, subsequently, optimal polypharmacy levels in their treatment lists. Therefore, to improve the dialogue between HCPs and patients, staff need to be trained in how to effectively deprescribe and communicate both with the patient in a shared decision manner and with other members of the healthcare team. Despite interactions, according to the HCPs, being perceived as respected between primary care staff alone and secondary care staff alone, the collaboration between primary and secondary care could be improved. The absence or limited level of contact between primary and secondary care needs to be addressed as the gulfs between actors create gaps in communication and, in turn, inhibit actioning changes in polypharmacy treatment. Adamson et al. created a four-step model in which HCPs could gain interprofessional empathy for one another which would improve social interactions\textsuperscript{236}. Both Dow et al. and Reeves et al. introduced another concept of viewing interprofessional practice across care systems as networking\textsuperscript{237,238}.

Therefore, medication reviews and, in turn, deprescribing assessments should be performed in a concordant manner. Deprescribing medications requires a delicate balance of discussing possible changes in medication, based on the previous evaluation of symptom control and benefit vs risk strategy of certain treatment(s), and educating the patient\textsuperscript{97,239}. However, even HCPs informing the patient on their thought processes on over-treatment and control, did not indicate that the patient would provide their consent to have medications deprescribed. HCPs perceived that many of the reasons that patients would not want their treatment removed were psychological. Primary care doctors have described deprescribing as ‘swimming against the tide’ of patient perception\textsuperscript{190}. If patients could understand the reasoning
behind their treatments being deprescribed, the patient could adhere better to their treatments in general, and would, also, continue to keep their removed medications deprescribed as they would be happier in the knowledge of comprehending their HCP and their HCP being understanding of their perspective\textsuperscript{240}. This improvement in the patient-HCP relationship is crucial to the success of deprescribing.

5.4.1 Strengths and Limitations

The main strength of this study was that it compared the viewpoints of HCPs in both primary and secondary care. Many studies into polypharmacy have focussed on primary care alone or secondary care alone. Moreover, this study examined polypharmacy in patients with asthma in both sets of care and this type of research is in its infancy. Polypharmacy in patients with asthma has not been greatly researched at present. Moreover, as much as it is well-known that steroids should be limited in their usage in patients with asthma, this study highlights that there is still much work to be done in reducing/removing the long-term usage of steroids in repeat prescriptions. Additionally, it was discovered that asthma HCPs do not frequently use prescribing or deprescribing guidelines. This emphasised a need for these guidelines to be better promoted amongst HCPs particularly in individual disease types.

Furthermore, this study features concerns that HCPs had regarding their roles and responsibilities in asthma treatment due to the absence of deprescribing guidelines. This presented a lack of clarity in certain roles, principally in deprescribing and repeat prescriptions, that could be targeted for future guidance. The examination of interprofessional relationships between primary and secondary care provided some interesting gaps and findings that could allow for the improvement of these rapports in future.
One limitation in this study was that the participants knew that this was a study on polypharmacy, and this may have caused the sample of interviewees to be more concerned about polypharmacy and would have been alerted to the topic through their introduction to the study via the email and PIS. This could be an indicator of the sample being not wholly representative of the general healthcare perspective. This was a small sample of HCPs and their perspectives; a larger study might be more transferrable for real world application. Additionally, there could be an element of interviewer bias, as much as reflexivity and unconscious bias was accounted for in the early stages of the study design, there will always be the possibility of interviewer bias particularly in negative cases. For example, it was a surprising outcome that the HCPs in primary care stated that they rarely had differences of opinion in interprofessional relationships. Furthermore, some HCPs acknowledged this finding was seemingly irregular.

An additional limitation was not acquiring the patient perspective on how they view their treatment. Of course, there is a place in research for ascertaining HCP observations on their treatments, but healthcare is a ‘two-way street’ with the HCP and the patient collaborating to provide the best standard of care. To understand the HCP perspective has significant merit, but future studies on polypharmacy in patients with asthma should consider examining patient perspectives, particularly in regards shared decision making. Furthermore, this study did not examine digital tools available for deprescribing and asthma HCPs in great depth and instead focussed on the use of guidelines in asthma and polypharmacy.
5.4.2 Future work

Future research would need to be conducted into improving the fragmentation of care, cultivating communication between HCPs across care types in other disease areas and in general within healthcare. Additionally, interventions to help improve nurses to gain the confidence to not only step-down medications but fully remove medications from patients list should be investigated. Also, this research only studied guidelines and did not focus on tools, therefore, examining which digital tools are used by asthma HCPs to assist their patients. Subsequently, the individualised roles for doctors, pharmacists and nurses in both primary and secondary care need to be fleshed out regarding patients with asthma with polypharmacy and considering additional co-morbidities and treatments. Exploring how best to standardise roles and, in turn, guidelines or general practice protocols for repeat prescription over-use and deprescribing could be beneficial to permit better handling of patients presenting with polypharmacy and the accidental long-term prescribing of oral steroids. In relation to patients, if we could improve HCPs roles and responsibilities, this could be used to guide a study where we could attempt to improve care for patient with asthma and polypharmacy.

5.5 Conclusion

In conclusion, asthma HCPs seemed to not take other medications and other diseases into consideration as much as they would like to. Annual asthma reviews allowed for medication reviews to occur in patients with asthma but, unfortunately, polypharmacy did not seem to be a primary focus of the review. Structured medication reviews in patients with asthma could benefit from being optimised beyond their current form and existing time constraints, workload issues and poor communication between primary
and secondary care seemed to be perpetuate the failings of these medication reviews. Targeting these issues in healthcare services plus clarifying the roles and responsibilities of individual HCPs when auditing repeat prescriptions and conducting deprescribing could improve future medication reviews and polypharmacy management.

5.6 Summary

Thirty-two doctors, nurses and pharmacists from primary and secondary care were interviewed on their perceptions of polypharmacy in patients with asthma which resulted in six themes; Polypharmacy in asthma and its relationship to comorbidities and asthma severity, repeat prescribing and treatment burden and the associated education of patients, the use of guidelines in asthma treatment, the feasibility of medication reviews and HCP responsibility, deprescribing in asthma and its barriers for implementation, and interprofessional relationships across care systems in asthma. Some practices had repeat prescription flags and audits, but the majority had no standardised procedure to monitor repeat prescription overuse. Asthma-specific or other disease guidelines were used by HCP but prescribing and/or deprescribing guidelines were rarely used. Medication reviews were more informal for doctors, conducted with the asthma annual review for nurses and a more structured medication review for pharmacists. Most nurses did not possess the confidence to deprescribe beyond reducing dosages and doctors in primary and secondary care were confused about deprescribing roles. Interprofessional relationships were deemed satisfactory within the same care type but, across care types, future work is required in communication between different care types and refining the fragmentation of care. Interventions are required to empower nurses to deprescribe, to strengthen repeat
Chapter 6

6.1 Introduction

The previous chapter discussed the qualitative analysis entailed in this research by way of interviewing HCPs on their views and experiences with polypharmacy in patients with asthma and how classic polypharmacy management techniques such as medication reviews and deprescribing are conducted. Gaining an understanding of how polypharmacy is displayed in real world data could be used to enhance and develop the findings from the qualitative research. It is known that older patients are susceptible to higher levels of polypharmacy which is demonstrated in existing guidelines for polypharmacy and the prescription of high-risk medications focusing on this at-risk group. However, our knowledge surrounding younger patients with polypharmacy, particularly those with an existing asthma diagnosis, requires more in-depth analysis and understanding. To identify the demographics of those who are
more susceptible to experiencing polypharmacy, stratifying populations with polypharmacy according to their age, gender and socioeconomic background can further improve our comprehension of polypharmacy in patients with asthma. Multimorbidity is heavily linked to polypharmacy and needs to be further investigated in patients with both asthma and other (or multiple) additional comorbidities. Other factors such as smoking and BMI will, also, be explored to further develop our understanding of asthma and polypharmacy. Therefore, this chapter endeavours to introduce the retrospective quantitative analysis of a prescribing data containing patients with asthma in Scotland over a seven year period, investigate the patterns in demographics of polypharmacy patients with asthma across various socioeconomic backgrounds, genders and ages and examining multimorbidity, smoking and BMI in relation to polypharmacy and asthma to expand our knowledge of polypharmacy in patients with asthma that can be utilised to improve polypharmacy management techniques in this particular group. The methodology, data analysis techniques, strengths and limitations and potential for future research are also discussed in this chapter.

6.2 Methodology

6.2.1 Data Cleaning
The analysis of the prescribing data was carried out in the eDRIS safe haven. Access to the eDRIS safe haven was secured by the addition of this study to an existing study being conducted by asthma UK via the submission of an application to the PBPP (Public Benefit and Privacy Panel for Health and Social Care). Prescribing data was loaded into R studio. The version of R studio used was 1.2.1335. The prescribing data contained primary care data regarding patients with asthma in Scotland alone. The prescribing data was formatted to allow for an easier and more uniform dataset. The
data was required to be more uniform to allow for easier combining of multiple datasets. As the prescribing data columns were not formatted, the columns were constructed to show the IDs correctly. These IDs were anonymised CHI numbers. Data cleaning was completed by checking if there was any missing data by corroborating the number of rows in the dataset, the IDs and any dates found in the dataset. Also, the dates were formatted to make sure they were in the correct format. The prescribing dates and dispensing dates were correctly formatted to show the full year-month-year throughout the dataset. Any missing dates in the dataset were checked at this stage where no missing dates were discovered. The minimum and maximum prescribing dates were 1999-01-01 and 2017-04-06, respectively. Furthermore, the ages of patients were formatted to confirm that they were in a numeric form in R. Again, the number of IDs prescribed any drug per year was checked for confirmation of any possible missing data.

Dose data was found in a separate file and was required to be connected to the prescribing data. Dose data was loaded into R studio and was combined with the prescribing data. Once this dose data was combined with the prescribing data, the dose data separate file was removed from R. To make sure that as the dose data was combined not missing data was found or introduced, the columns taken from the dose data now located in the prescribing data were checked. The “approved name” and the “prescribable item” name columns were combined as they were heavily duplicated, and a separate column called “drugname” was produced. Some drugs were accidentally deleted in this combining effort and the deleted items were re-coded back into the prescribing dataset by comparing to the original columns.
The drugs were classified by creating a separate dataset selecting the drug names, the dose, the brand name of the drug, the drug formulation and the BNF chapter code. These drugs were, then, counted, grouped by the BNF code, any duplicates removed and arranged in descending order to highlight individual prescribed drugs. This separate dataset was merged with the prescribing dataset with any duplicates in either dataset removed. The classified drug data was removed from the R console to limit the amount of data left in the R console. The prescribing and dispensing dates were reformed again to make sure there was no accidental changes to the date formats when the data had been merged with the existing prescribing data.

6.2.2 Merging Prescribing Dataset with the Demographics file
Most files in the safe haven were loaded into the system individually. Therefore, a separate file containing the demographics data was loaded into R to analyse the demographics of the patients in the prescribing data. As with all data loaded into R, the anonymised CHI numbers were formatted as IDs so they could be combined with the ID as the link to the prescribing dataset. To determine whether there were any missing data found in the demographics data, the sex column was used to see if any information was missing. No missing sex information was found. To make sure that all the ages of the patients in the demographic dataset were correct and not missing, a fake date of birth column was created by checking if there were any missing dates found in the column, named deduction date, which is the date the patient was added to the demographics file. Once any missing dates were removed from the deduction date column, the temporary date of 2018-03-31 was used as this was the final recruitment date for this data. The age provided for the patients was taken away from the temporary date and provided a fake DOB. For up-to-date socioeconomic analysis of the data, the SIMD column was formatted to include the most recent SIMD value by
formatting the SIMD columns, SIMD2012quintile and the SIMD2009quintile. as a character variable rather than a numeric variable. These two columns were then combined and if any missing values were still found, they were labelled as missing. Furthermore, the urban rurality column, UR6, was formatted to determine the location and socioeconomic background of patients, again, as a character variable and any missing values were labelled as such. A baseline record was created as a column to remove any duplicated patient values, by finding distinct values in the ID column and duplicates removed. The demographic file columns were filtered to include the ID, Sex, Age, DOB, Datazone, SIMD, UR6, UR6 description and Registration date (at GP).

To convert datazone codes noted in the data to location names in Scotland for easier legibility, a file that contained conversion information to alter the datazone to NUTS3 was loaded into the R console. The columns, Zonecode and NUT3_CODE columns were renamed to datazone and NUTS3 respectively, to allow merging of the conversion file and the demographics file. The demographics and conversion files were combined to allow the converted data to be reflected in the demographic dataset and both datazone and nuts3 columns were checked to indicate if there were any missing information. No missing data was found. The conversion file was removed from the R console. The cleaned prescribing and demographics datasets were combined by ID to allow for the prescribing data to contain demographics data that could be simultaneously analysed with the prescriptions and any missing SIMD, NUTS3 and UR6 description columns were labelled as the datasets are not the same. The final dataset contained the columns; ID, Prescribing Date, Patient Age at Paid Date, Dispensing Date, Drug name, Formulation, BNF Chapter Code, Dose, Item
The prescribing-demographics dataset was filtered to remove those over the age of 100 so as not to overly bias the data for older age and the data contained a small percentage of patients over 100, the year of each prescription date was extracted, and the data was grouped by the patient and the year of prescription date. Patterns in yearly prescriptions were discovered by adding a count to calculate how many prescriptions were given a year and all distinct values were highlighted (duplicates removed). The dataset was ungrouped to prevent any skewing of the data by R.

As polypharmacy is defined by how many medications are prescribed every six months, a frame was generated to allow a time interval of six months to be created within the data. The prescribing data alone was used for the frame to allow for quicker coding to occur and the likelihood of the safe haven to have fewer struggles with coding smaller chunks of data. The patient ID and associated prescribing dates were selected and the data was grouped by the patient ID. The minimum and maximum prescription dates per patient ID were fashioned into a new column, containing all prescription dates between those two dates. All distinct values for each patient ID were selected to remove any duplicates and the prescription dates were put into sequence. These sequenced rows of prescriptions were, subsequently, combined into two sets per year labelled “demi_year”. A new dataset was invented to create a new column to separate the prescribing data into six-month prescriptions and was also called “demi_year”. A flag was added if any prescriptions occurred into each six-month period. This flag was used to remove any patients who did not have polypharmacy in
the six-month timeframe. Individual prescriptions were counted by period and any possible skewed grouped data was removed. The time interval frame was joined onto this prescribing data via the “demi_year” column and any unflagged prescriptions, i.e did not have a prescription in a specific six-month period, were removed.

The calculation of the volume of drugs prescribed were coded by counting the number of specific drugs per patient per six-month period. This was achieved by adding the same “demi_year” column to the joined prescribing-demographic data, selecting all distinct patient IDs, drug name, any occurrence of a drug prescribed within any of the six-month periods and age at dispensing date. These distinct values of individual drugs prescribed were counted and labelled as “unique’. Any grouped data was removed, and the data was arranged by patient ID, “demi_year” (six-month period) and number of unique drugs. The six month filtered prescription data and the filtered six-month drug data was combined and all unflagged drugs in any six-month period were removed. This was for each analysis of both repeat prescriptions and the individual drugs prescribed in these prescriptions. The demographic data was, also, re-combined in case any demographic data had been lost.

As the definition of polypharmacy in this study was determined to be 5 medications or more per six-month period, the filtered six-month prescribing data was analysed by flagging any patients with the aforementioned number of medications per six-month period. Distinctive patient IDs, six-month period and the 5 or more medications flag were separated. These values were ungrouped and subsequently, the six-month period and flags were counted labelled “x”. The percentage proportion of patients taking 5 or more medications per six-month period were calculated by the count “x”
and the sum of patients per six-month period were divided and multiplied by 100. The percentage proportion was utilised rather than a simple count of the patients to provide a comparison between those having and not having polypharmacy in the data. All flags that did not have 5 or more medications were removed and the first six-month period of 2017 was removed as the dataset only contained the first 4 months of data for 2017 and therefore, an incomplete six-month period. A line graph was created with these values, the x axis as the six-month period and the y axis as the percentage proportion.

The examination of polypharmacy according to varied socioeconomic background, age ranges and sex was conducted by stratifying the six-month prescribing data by sex, SIMD and age alone and the number of unique drugs per person were split into more than 5, more than 10 and more than 15 medications. A combined filter was used when stratifying by age and SIMD and age and sex to define how age and socioeconomic background/gender can affect polypharmacy. The percentage proportion was calculated as the above paragraph, but the data was grouped by SIMD, sex or age, respectively, in this instance. This data was plotted into a graphs per number of drugs prescribed per six months.

6.2.3 Comorbidity and Primary Care Record Coding
Primary care records were added to the prescribing data to allow for analysis of multiple morbidities and asthma exacerbations. The primary care data was loaded into R studio and the patient ID column was formatted to provide a column to link the data later after data had been cleaned. The dates in the dataset where an event had occurred was correctly formatted to be consistent throughout the dataset. Once this formatting had occurred, the dates were checked for any missing dates, in which none were found. The read codes in the dataset were assessed for any missing codes, in
which 2 missing codes were found and 11765923 codes remained. All duplicates in the read code column were removed and the read codes were formatted correctly to be the length of 5 characters long. 10876479 records remained post data cleaning.

The primary care data was formatted to show comorbidities through the coding of the read codes. A separate file called comorbidity was created. Comorbidities were coded using the Charlson Comorbidity Index. As the Charlson Comorbidity Index groups morbidities into a single factor name, a read code dictionary was created to include all the comorbidities that was included all the different disease types included. This dictionary is located in appendix 3. The read codes were formatted to show diseases as AIDS, Cerebrovascular Disease, COPD, Congestive Heart Disease, Dementia, Diabetes, Diabetes with complications, Hemiplegia, Metastatic Tumour, Mild Liver Disease, Moderate Liver Disease, Myocardial Infarction, Peptic Ulcer Disease, Renal Disease, Rheumatological Disease and Cancer. As the Charlson Comorbidity Index codes for severity of disease types, these were also coded into the dataset. The first occurrence/diagnosis of each comorbidity was coded into the dataset to prevent duplication and the dataset was formatted so only the patient ID, date of diagnosis, comorbidity and severity of condition was kept.

Some disease types or indicators commonly associated with patients with asthma that were not coded into the dataset were added. Asthma attacks, asthma severity, nasal polyps, respiratory infections, anaphylaxis, rhinitis, anxiety/depression, eczema and GERD were coded via formatting read codes. The indicators that required a little more coding were smoking and BMI. Smoking was coded, generally, via read code and, subsequently, the read codes were formatted as “never” having smoked, “former”
smoker and “current” smoker. Patients with the read codes N/A were formatted as having never smoker based on previous analysis of missing regarding patients who were not smokers being similarly coded\textsuperscript{241,242}. Also, BMI was coded generally, and the numeric value connected with BMI was formatted. Furthermore, BMI was coded by category; “Underweight/Low BMI”, “Normal BMI”, “Overweight/High BMI” and “Obese”. For patients with a missing BMI value, height and weight was formatted in the dataset to be used to manually calculate BMI. All non-specified read codes and superfluous variables were removed from the dataset and any missing BMI, height, weight, smoking or any missing severity values were removed. The primary care records and the separated comorbidity file were combined. The combined GP-comorbidity dataset was also combined with the six-month prescribing data to analyse prescribing and comorbidities simultaneously.

Obesity and smoking greatly affect patients with asthma and so polypharmacy stratified by both those variables were conducted by using the filtered six-month prescribing data stratified by BMI and Smoker alone and the number of unique drugs per person were split into more than 5, more than 10 and more than 15 medications. A combined filter was used when stratifying by BMI and SIMD, BMI and sex, smoker and SIMD and Smoker and sex. The percentage proportion was calculated as the above paragraph, but the data was grouped by SIMD or sex in this instance. This data was plotted into graphs per number of drugs prescribed per six months.

The combined six-month prescribing data and comorbidities data was analysed for patterns of comorbidities in the dataset that were common with these patients with asthma. This was coded in the dataset by selecting unique patient ID’s and
comorbidities and then stratifying by a specific indicator; sex, SIMD, age category, age and SIMD joined, and age and sex combined. The comorbidities were, further, analysed by calculating the percentage proportion of patients prescribed 5 or more medications grouped by co-morbidity. The comorbidities were grouped into most common to least common comorbidity. As the Charlson comorbidity index is 24 conditions, the comorbidities were grouped into three groups of eight conditions. The grouping changed depending on the indicators being analysed. The most common comorbidities were split into those affecting socioeconomic background, age, and sex. This data was plotted into graph per six months.

The plots in which a smoothed average was calculated in R was based on Kernel Density Estimates (KDEs) calculated with Gaussian kernels for the polypharmacy and multimorbidity graphs described in this analysis. KDE aims to provide a smooth density estimate. For more information, please refer to Chapter 6 of Hastie et al.

6.3 Results

6.3.1 Demographics of the Patient Presenting with Polypharmacy
The number of patients (IDs) found in the prescribing data was 671,286 people and the percentage of men to women in the data was found to be 48.88% and 51.12% respectively. SIMD 3 has lower numbers in the prescribing dataset than the remainder of the SIMD levels. Over the seven-year period, the highest percentage of patients were prescribed 0-4 medications but that 47.5% of patients had polypharmacy with 22.8% prescribed excessive polypharmacy, defined as 10 or more medications.
Table 6.1 Demographics of the Prescribing Dataset

<table>
<thead>
<tr>
<th>Sex</th>
<th>(%)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>51.12</td>
<td>348868</td>
</tr>
<tr>
<td>Male</td>
<td>48.88</td>
<td>333526</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SIMD</th>
<th>(%)</th>
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<tbody>
<tr>
<td>1</td>
<td>14.95</td>
<td>100659</td>
</tr>
<tr>
<td>2</td>
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<tr>
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<td>13.45</td>
<td>90255</td>
</tr>
<tr>
<td>4</td>
<td>17.86</td>
<td>119891</td>
</tr>
<tr>
<td>5</td>
<td>15.62</td>
<td>104819</td>
</tr>
<tr>
<td>Missing</td>
<td>23.08</td>
<td>154955</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Category</th>
<th>(%)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>0.07</td>
<td>442</td>
</tr>
<tr>
<td>10-19</td>
<td>7.64</td>
<td>102237</td>
</tr>
<tr>
<td>20-29</td>
<td>13.7</td>
<td>91960</td>
</tr>
<tr>
<td>30-39</td>
<td>14.72</td>
<td>98819</td>
</tr>
<tr>
<td>40-49</td>
<td>14.46</td>
<td>97049</td>
</tr>
<tr>
<td>50-59</td>
<td>12.12</td>
<td>81379</td>
</tr>
<tr>
<td>60-69</td>
<td>9.83</td>
<td>65964</td>
</tr>
<tr>
<td>70-79</td>
<td>6.81</td>
<td>45747</td>
</tr>
<tr>
<td>80-89</td>
<td>4.34</td>
<td>29167</td>
</tr>
<tr>
<td>90-99</td>
<td>1.08</td>
<td>7237</td>
</tr>
</tbody>
</table>

Table 6.2 Percentage Distribution of Patients by Number of Medications

<table>
<thead>
<tr>
<th>Polypharmacy Levels</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>54.51</td>
</tr>
<tr>
<td>5-9</td>
<td>22.68</td>
</tr>
<tr>
<td>10-14</td>
<td>12.84</td>
</tr>
<tr>
<td>15+</td>
<td>9.98</td>
</tr>
</tbody>
</table>
Figure 6.1 shows the percentage of women and men by age in the Scottish population taken from the National Records of Scotland.
Figure 6.2 shows the percentage proportion of patients with asthma with polypharmacy every six months. The graph shows six-month periods from the year 2009 to 2016.
In fig. 6.2, the highest percentage proportion of patients were prescribed 5-9 medications, at around 15 to 12.5%, in a six-month period followed by 15+ medications, around 12.5 to 10%. The general proportionate levels of polypharmacy have decreased from 2009 to 2012 and plateaued between 2012 to 2014, with a slight rise from 2015 onwards.
Figure 6.3 shows the percentage proportion of patients on 5 or more medications every six months stratified by sex. The graph shows six-month periods from the year 2009 to 2016.
In fig. 6.3, women exhibited slightly higher levels of polypharmacy prescribing than men in the 5-9 medication category. Prescribing levels were similar in both sexes when prescribed over 10 medications. The graph shows a steady decrease in the proportion of patients with polypharmacy from 2009 to 2012. There seems to be a gradual increase in men prescribed 15+ medications from 2012 onwards in comparison to women and have a gradual increase in the proportion of patients with polypharmacy occur from the latter half of 2013 in all categories with the exception of 10-14 medications.
Figure 6.4 shows the percentage proportion of patients on 5 or more medications every six months stratified by Scottish Index of Multiple Deprivation (SIMD). The SIMD levels are indicated as 1 for the most deprived populations and 5 for the least deprived populations.
In fig. 6.4, SIMD 4 and 5 has the next highest proportion of patients taking 5-9 medications, however, SIMD 2 had the highest proportion of patients prescribed 15+ medications. SIMD 4 in all categories seemed to have the highest proportion of patients prescribed medications, however, this could be attributed to the higher number of patients in this study being found in SIMD 4. Furthermore, the levels of people taking 15+ medications are higher in SIMD 1 and 2 in comparison to SIMD 5. The difference between patients prescribed 15+ medications and 5-9 medications in SIMD 1 and 2 was quite small. This indicates that lower socioeconomic backgrounds are more likely to be prescribed more medication, particularly excessive polypharmacy. Therefore, the more socially affluent the area, the lower the number of medications prescribed. As in figs. 6.2 and 6.3, there is a general decrease in prescribing from 2009 to 2013 increasing gradually from 2014.
Figure 6.5 shows the proportion of patients with polypharmacy every six months based on their BMI. The BMI of 30 was selected due to it indicating obesity.
Figure 6.6 shows the proportion of patients with polypharmacy every six months based on their BMI stratified by Sex. F is female sex and M is male sex.
Figure 6.7 shows the proportion of patients with polypharmacy every six months based on their BMI stratified by SIMD.
Fig. 6.5 shows clearly that the prescription of 15+ medications is at its highest in patients with a high BMI. Whereas patients with lower BMIs have a higher proportion of patients with lower levels of polypharmacy (5-9 medications). Therefore, this indicates that higher BMIs and, subsequently, obesity is a factor in polypharmacy with excessive polypharmacy being more common in overweight and obese patients in comparison to those with BMI in the normal range. Moreover, in both categories, the proportion of patients taking 15+ medications have been increasing over time in both BMI categories. In contrast, patients taking 5-9 medications has very slightly lowered over time in both categories. Patients taking 10-14 medications seemed to have plateaued or only increased very slightly in both categories. Similarly, in fig. 6.6, as fig. 6.3, patients with a BMI of 30 and higher, women were more likely to have higher proportions of polypharmacy than men. However, since the latter half of 2011, women with a BMI lower than 30 have been had an increase in the proportion of people prescribed 15+ medication to the point where is it nearing the levels of 5-9 medications. This shows that obesity in relation to polypharmacy is linked to gender but is more obvious in men than in women as women have high levels of polypharmacy in both BMI categories.

In fig. 6.7, the proportion of patients prescribed 15+ medications has increased in all SIMDs and BMI categories. However, in SIMD 1 and 2 has increased over the seven-year period of this dataset to the point where it has surpassed the proportion of patients on 5-9 medications. The remaining levels of polypharmacy seem to have stayed fairly the same according to BMI. This indicates that lower socioeconomic background has more of an effect on polypharmacy than BMI and obesity.
Figure 6.8 shows the proportion of patients taking 5 or more medications every six months by smoking status. Patients in the missing category were considered as not smokers.
Figure 6.9 shows the proportion of patients taking 5 or more medications every six months by smoking status and sex.
Figure 6.10 shows the proportion of patients with polypharmacy every six months by smoking stratified by Scottish Index of Multiple Deprivation (SIMD).
Investigating smoking in relation to polypharmacy levels in patients with asthma (fig. 6.8), the proportion of patients taking 15+ medications were higher in former smokers. Current smokers have had a rise in the proportion of patients prescribed 15+ medications over time and from late 2011 have eclipsed patients prescribed 5-9 medications. This indicates that there is a link between high levels of polypharmacy, particularly excessive polypharmacy, and smoking. The proportion of patients presenting with polypharmacy stratified by smoking across all categories seemed to have stayed at consistent levels over the seven-year period with the exception of patients prescribed 15+ medications where in all smoking categories has increased. The lowest increase occurred in patients in the ‘never’ smoked category, further indicating that excessive polypharmacy is linked to smoking. However, in the missing category showed the highest increase in patient proportion which shows that excessive polypharmacy needs to be carefully focused on.

In fig. 6.9, similar to fig. 6.8, women show a higher proportion of patients taking 15+ medications, particularly in the current smoker category where in women it eclipses the proportion taking 5-9 medications from 2010 which was earlier as shown in fig. 6.8. Whereas men it surpasses the proportion of patients with 5-9 medications in 2016. This shows that women who were smokers are more predisposed to high levels of polypharmacy in comparison to men. The overall patterns of smoking in relation to polypharmacy are similar in both figs. 6.8 and 6.9.

Correspondingly, people from lower socioeconomic backgrounds who are current or former smokers are more likely to be prescribed 15 or more medications with the proportion of patients in SIMD 1 and 2 (fig. 6.10). In the missing category and SIMD 1
and 2, in 2016 the proportion of patients taking 15+ medications again surpassed patient prescribed 5-9 medications. This, further, reveals that lower socioeconomic backgrounds are linked to higher levels of polypharmacy that can be additionally exacerbated by smoking.
Figure 6.11 shows the proportion of patients with polypharmacy every six months by age category. The age categories were presented in 10-year chunks.
In fig. 6.11, higher proportions of polypharmacy begin from around the 30s and 40s age categories and consistently increase until 70-79 years of age. From age 60-69 onwards, there is a shift where the highest proportion of patients receive 15+ medications instead of 5-9 medications. Between 70-90, there is quite a significant gap in proportion of patients receiving 15+ medications and those receiving 5-9 medications. These proportions show that with increasing age, higher numbers of medications are prescribed to patients. As in fig. 6.2, the overall change in polypharmacy levels over time are a lowering from 2009 to 2012, plateaued and then gradually increased from 2014.
Figure 6.12 shows the smoothed average percentage proportion of patients on 5 or more medications every six months stratified by age and class. The age categories were stratified into 10-year periods.
As had been previously shown in figs. 6.11, increasing age is linked to increasing proportion of patients with polypharmacy. In fig. 6.12, SIMD 1 reaches a peak percentage proportion of patients taking 15+ medications earlier than the other categories at ages 50-59. SIMD 2 and 3 peak at 60-69 and SIMD 4 and 5 peak at 70-79. This clearly indicates that patients from lower socioeconomic backgrounds reach higher levels of polypharmacy significantly earlier than those in more affluent areas. Furthermore, the percentage proportion lowering significantly from 80 onwards could be attributed to higher mortality rates. The lower proportions from 80 and beyond in patients from lower socioeconomic backgrounds could be linked to patients having worsening health from an earlier as noted by the excessive polypharmacy prescribing occurring at an earlier age in this population and, therefore, dying at an earlier age.
Figure 6.13 shows the smoothed average percentage proportion of patients with polypharmacy every six months stratified by age and sex.
Unlike fig. 6.3 where women had higher levels of polypharmacy overall, when delving deeper by comparing sex and age, the shift of the highest proportion of patients being prescribed 15+ or more medications occurred earlier in men at 60-69, whereas this shift occurs in females at 70-79 (fig. 6.13). Therefore, this shows that despite females being prescribed slightly more medications throughout their lives, men reach polypharmacy levels at an earlier age than women. Like fig. 6.12, at 40-49, there is a sharp rise in the proportion of patients across all polypharmacy categories and this rise continues until 70-79. Also, at 80-99, the number of males with polypharmacy considerably lowers in comparison to females which tapers off more slowly, most likely due to women living longer than males.

6.3.2 Demographics of Co-morbid Patients Presenting with Polypharmacy
Figure 6.14 shows the percentage proportion of patients with one or more additional comorbidities in addition to Asthma stratified by Sex.
In fig. 6.14, it is indicated that for most conditions, females are more likely to proportionally suffer one or more comorbidity. The most common comorbidities seen in females are Anxiety/Depression, Dementia, Hemiplegia and Rheumatological disease. In contrast, the conditions seen less in females than males are AIDS, metastatic tumour, myocardial infarction, nasal polyps and peripheral vascular disease.
Figure 6.15 shows the proportion of patients on 5 or more medications every 6 months stratified by sex and grouped by most to least common morbidities in the prescribing dataset. The comorbidities are based on the Charlson Comorbidity Index. The comorbidities are noted in the legend in the graph. (F = female, M = male)
In fig. 6.15, a higher proportion of females are prescribed 5 or more medications every six months with at least one additional comorbidity. Generally in females, there seems to be a slight lowering of the proportion of patients taking 5 or more medications with two or more comorbidities in the most common comorbidity category. Whereas, in males, generally, there doesn’t seem to be a huge change in the patterns of prescribing in association with multiple comorbidities with the exception of lowering occurring in the female population in the most common comorbidities after the latter half of 2011 and a slight lowering seen in the male population after the first half of 2012.
Figure 6.16 shows the percentage proportion of patients with one or more comorbidities in addition to Asthma stratified by Scottish Index of Multiple Deprivation (SIMD).
In fig. 6.16, it is indicated that the lower socioeconomic level, the higher the proportion to suffer from an additional comorbidity. The exception is in SIMD 4 where higher proportions of patients having the comorbidities are perceived in comparison to SIMD 3. In SIMD 1 and 2, the most common comorbidity is Moderate Liver Disease. In SIMD 3, Hemiplegia has the highest percentage proportion of patients. In SIMD 4, Metastatic Tumour contains the highest proportion of patients. Nasal Polyps is the most common comorbidity seen in SIMD 5.
Figure 6.17 shows the proportion of patients on 5 or more medications every 6 months stratified by Scottish Index of Multiple Deprivation (SIMD) and grouped by most to least common morbidities for lower socioeconomic backgrounds. The comorbidities are noted in the legend in the graph.
The graphs in fig. 6.17 give a better representation of the correlation between lower socioeconomic background and higher levels of comorbidities and polypharmacy. The percentage proportion of patients taking five or more medications with two or more comorbidities is almost double in SIMD 1 in comparison to SIMD 5. Furthermore, there is a consistent lowering of the percentage proportion going down each SIMD level.
Figure 6.18 shows the proportion of patients on 5 or more medications every 6 months stratified by age and grouped by most to least common morbidities in older age groups. The morbidities are noted in the legend in the graph.
Fig. 6.18 shows that the percentage proportion of patients is higher in older age groups, particularly from the 50-59 age groups and above. Smaller numbers of the most common comorbidities are seen in the younger age groups. The 60-69 & 70-79 age range seems to have the highest numbers of comorbidities across the graph, with the peak being at 70-79.
Figure 6.19 shows the proportion of patients on 5 or more medications every 6 months with additional comorbidities by age category and sex. The comorbidities are noted in the graph. (F = female, M = male)
Prior to the age range 70-79, in fig. 6.19, the prescribing difference between men and women seems to be comparable with a very slight difference seen in males and females (women being the slightly higher proportion of the two). In the age range 80-89, the difference in prescribing with additional comorbidities in males and females are different. Females are in much higher proportion than males in the 80-89 age range.
Figure 6.20 shows the proportion of patients on 5 or more medications every 6 months stratified by age and SIMD and grouped by most to least common morbidities in older age groups. The comorbidities are noted in the legend of the graph.
In fig. 6.20 as with fig. 6.19, SIMD 1 had higher levels of polypharmacy and an additional co-morbidity than the remaining SIMD levels, SIMD 5 being the lowest. SIMD 4 had higher levels than SIMD 3. As young as people in the age range 40-49 are shown to suffer from multi-morbidity and polypharmacy.
Figure 6.21 shows the proportion of death rates of patients with polypharmacy per year stratified by age.
The death rates in patients with polypharmacy over the years has been decreasing in patients between the age of 60 and 89 (fig. 6.21). As expected, the highest proportion of death rates in all age categories was found in those prescribed 15 or more medications. To compare the death rates with polypharmacy levels found in figs. 6.2 and 6.11 shows that, despite patients having increased levels of prescriptions of 15 or medications over time, the death rates have been decreasing over time in all polypharmacy cohorts apart from 5-9 medications. Over time, there has been an increase in patient deaths between 90 and 99, probably due to patients living longer and not dying in the earlier age categories.

6.4 Discussion
Around 47% of patients with asthma in this dataset would be considered to meet the criteria for polypharmacy under the definition 5 or more medications prescribed every 6 months. Levels of polypharmacy have decreased very slightly between 2009 and 2016. The small reduction in polypharmacy in patients with multimorbidities after the year 2012 could be associated with several factors. The Scottish Polypharmacy Guidance was first published in 2012\(^1\)\(^{17}\) and, it could be speculated albeit not definitively, that changes to levels of polypharmacy in this data could be related to this. The most up-to-date Scottish Polypharmacy guidance shows a decrease in polypharmacy from 2012 onwards whereas the King's Fund Polypharmacy guidelines, the English version of the Scottish guidelines, showed steady increased levels of prescribing since 2011\(^2\)\(^{20}\). Another possible factor could be that, in relation to guidelines, the BTS/SIGN guidelines\(^{21}\) were changed to be updated biennially rather than annually after the year 2012, with the updates being implemented in the year
2011 related to pharmacological management and asthma monitoring. This could cause prescribers and doctors to be more hesitant to change their patients’ medication list or diagnosis of their asthma after 2012\cite{98,99,243}, with a rise in general polypharmacy occurring between 2014 to 2016. However, the levels of polypharmacy were not lower than those found in the year 2009 and, therefore, it could be the peak prescribing occurring in the 2011 in patients with multimorbidities is the anomaly rather the decrease of polypharmacy\cite{16}.

The graphs clearly show that the lower the socioeconomic background, the higher the levels of polypharmacy. Moreover, the levels of obesity and current/former smokers were greater in lower socioeconomic backgrounds, as indicated in the literature\cite{14,244,245}. However, people from lower socioeconomic backgrounds are more prone to smoke or previously be a smoker or have high obesity levels, nevertheless, obesity does affect all socioeconomic backgrounds and not just lower socioeconomic areas\cite{37,48}. SIMD 2 was seen to have higher levels of polypharmacy than SIMD 1 in most of the proportion graphs stratified by number of medications, which could account for the most socially deprived areas feeling disenfranchised and not ‘seen’ by HCPs\cite{67,85,246}.

To understand socioeconomic background better, stratifying by both age and socioeconomic background was analysed. Patients in more deprived areas were more likely to suffer from polypharmacy at a younger age (starting at ages 50-59 and peaking around the 60-80 age ranges) and people from more affluent areas reached a peak of polypharmacy levels at age ranges 70-90\cite{7,247}. This could indicate that as higher socioeconomic backgrounds have higher mortality rates, their levels of
polypharmacy do not lower significantly as the proportion of people are living longer and, therefore, requiring more medication to increase their quality of life. Therefore, levels of polypharmacy could be quite similar overall if you consider the differences in SIMD level and age as a factor changing the distribution of prescribing per patient. Consequently, in the analysis with age and sex stratified, men have higher levels of polypharmacy at a younger age than women. The data does indicate that women are prescribed more medications at a younger age which is consistent with the narrative that younger men are less likely to go to the doctor if there is something wrong with them. However, at the 40-49 age category, the proportion of men with polypharmacy sharply escalates which is consistent with men and then suddenly falls at from the 70-79 age category and beyond. This could be due to men quite commonly dying earlier than women hence why, despite the decrease in patients seen in women, the numbers are not as extreme as is shown in the men.

Contrastingly, this data differed from previous studies conducted on sex and polypharmacy where the numbers of women with polypharmacy was lower than men in all the medication level categories (~5-15 total medications per 6 months). This could be due to men being more likely to suffer from more high-risk comorbidities which could be the reason for the high levels of polypharmacy. Men are more likely to suffer from cardiovascular diseases, with hypertension and angina being the most common, which require multiple medications to target the diseases in question. As shown in fig. 6.2 and 6.3, the levels of polypharmacy declined in all categories up until the year 2013 and the level of polypharmacy subsequently increasing very slightly after 2015 in all categories. However, there was a continuous increase in patients being prescribed 15 or more medications. This could be due to more problematic
polypharmacy not being dealt with, worsening their health as it would be highly unlikely that a patient would require every single medication when their medication count is 15,20,251. Whereas a patient may require the 5 to 9 medications in their list and, therefore, the polypharmacy could be appropriate1,2,13. However, in the 5-9 medications category, the levels of polypharmacy did not lower and remained steady from 2013 to 2015 in men and lowered slightly in women in the same category. This could be due to men being more reluctant to change their medications or women being more likely to visit their health care provider on a more regular basis than men5,252. Men could be on these medications as a repeat prescription and have not had them taken off yet253.

Additionally, women were seen to be more likely to be obese, or have a high BMI, than men with polypharmacy. According to the Scottish Health Survey in 2016, it was found that 68% of men and 61% of women being either overweight or obese rising to 63% of women in 2018254,254. The levels of BMI increased both in men and in women. This is consistent with the literature as obesity levels have been consistently rising for several years14 rather than an indicator that polypharmacy is growing. Comparably, women were shown to be higher in the current or former smoker category with the levels of polypharmacy increasing over the 7-year time frame. BMI and smoking are commonly associated with aggravating both asthma symptoms and many other co-morbidities which could explain the rising levels of polypharmacy as the higher the number of co-morbidities, the greater the volume of medications patients are prescribed14,37.
Polypharmacy and multimorbidity quite commonly coexist. Frequently, polypharmacy has arisen due to patients being multimorbid\textsuperscript{12,16,255}. Therefore, to analyse polypharmacy, multimorbidity should be analysed to provide a broader picture of why patients are on multiple medications. In the comparison between sex and comorbidities, women were seen to be diagnosed with more multi-morbidities than men in general terms, though some disease types were specifically more common in men\textsuperscript{70,256,257} This is corroborated in previous studies conducted in sex differences in prescribing and could be due to the fact that women are more likely to visit their doctor once they feel that something is wrong with them\textsuperscript{29,54,67,247}. Similarly, women were seen to be associated with 5 or more medications every 6 months and multi-morbidities than men. There was a considerable decrease in women prescribed 5 or more medications with at least one comorbidity seen after the conclusion of 2011 and a smaller decrease seen in men in the same category in 2012 onwards which was, also, seen in the overall levels of polypharmacy graph. This indicates that women are the factor affecting the decrease in polypharmacy levels with multiple morbidities rather than men.

In relation to lower socioeconomic background and multimorbidity, as seen with the polypharmacy alone, higher levels were discovered in those from lower socioeconomic background. Patterns of prescribing with multi-morbidities can be, further, understood by analysing age and SIMD simultaneously. It was shown that the lower the socioeconomic background, the higher the number of patients with polypharmacy and an additional comorbidity at a younger age than more affluent areas\textsuperscript{36,48,82,85}. In age and sex stratified, women, as with the other stratified categories, are prescribed slightly more across the age ranges with co-morbidities as a factor.
After the age range 70-79, the difference in prescribing with additional comorbidities drastically changes with woman in much higher proportion than men between the ages 80-89. This could be due to the higher levels of mortality rates in women in comparison to men\cite{16,249}. Over the age of 80, patients exhibited lower levels of polypharmacy. Comparing these levels with death rates showed that the lower levels of polypharmacy do not seem to be entirely linked to mortality rates. Therefore, patients over the age of 80 may experience low levels of polypharmacy due to their increased visitation to healthcare services and, subsequent, increased opportunity to have medication reviews. Most of the literature surrounding age analysis and polypharmacy focuses on the elderly population from the ages of 75 and older, some studies will include 65-year-olds and older\cite{2,7,188,258}, but this study indicates that age analysis for polypharmacy should begin around 40+, or at the least 50+, years of age for those in lower socioeconomic backgrounds and in men who suffer from comorbidities at a younger age.

Additionally, the multi-morbidities that are seen as common comorbidities with asthma are different in this dataset to those seen in the literature. Asthma and COPD are quite often diagnosed in people together, however, in this dataset COPD is not found in the most common morbidities in any category\cite{48,258,259}. COPD was found in the least common category when stratifying by socioeconomic background and in the average category for the remaining graphs. This could be explained by the data showing people with multiple medications and perhaps those with COPD are higher in the people without polypharmacy. Also, it could be that those morbidities that are seen highly in the literature as being found in patients with asthma such as cerebrovascular disease, cardiovascular disease, diabetes and renal disease push COPD further down the list.
of most common. Correspondingly, rhinitis and eczema were in the least common category. Conditions associated with allergy are, similarly, commonly seen in patients with asthma, due to some forms of asthma being allergic in form\textsuperscript{92,260}. However, allergies are commonly found in patients from more affluent areas and stratifying by SIMD may have affected the results. According to SIMD levels, the multimorbidity seen commonly was Moderate Liver Disease in lower socioeconomic backgrounds, 1 and 2. This is commonly seen in the literature due to patients from lower socioeconomic backgrounds having a history of alcohol abuse\textsuperscript{14}.

Furthermore, the results that the association between women with asthma and rheumatological disease were shown in this data with a high proportion of women suffering from rheumatological disease\textsuperscript{258}. Furthermore, men being more prone to suffering from myocardial infarction and peripheral vascular disease is also corroborated in the literature. Dementia was seen less in men, possibly due to lower mortality in men\textsuperscript{13,204}. As mortality is higher in women there is a greater opportunity for dementia to occur in the elderly female population. Anxiety/depression was perceived highly in women, anxiety and depression are greatly associated with asthma in the literature\textsuperscript{54,252,261}.

6.4.1 Strengths and Limitations
The limitation in this dataset is that it only provides around 7 years of prescribing and dispensing data. An improved longitudinal study would have a longer time period to analyse. Unfortunately, the data shows a number of potentially significant shifts at the end of the survey period with several of the graphs illustrating plateauing or changes around 2015 onwards but the dataset only containing data up and until 2017 prevents further analysis or information to be mined from these graphs and hinder in depth
patterns to be correlated from the data. There are additional limitations regarding the variables contained in the dataset. The dataset does not contain care home residency information which could be used to analyse polypharmacy in a closed and controlled environment, therefore, these results only contain real world examples and eliminate a proportion of the elderly, frail and sick populations who may be in care homes.

In addition, this dataset only has patients who suffer from asthma and, hence, limits the amount of analysis on polypharmacy. This is due to patients with asthma not being fully representative of the polypharmacy population. However, this analysis does allow for detailed analysis of asthma prescribing and polypharmacy found in patients with asthma and, in turn, multi-morbidities found in patients with asthma. However, a clearer picture of polypharmacy generally would be more suited to find correlations and patterns that can be implemented in real life situations. Not limiting the analysis to patients with asthma could provide improved results that could be better applied in prospective guidelines and research into polypharmacy as a whole.

Moreover, grouping of the comorbidities does not allow for in depth analysis of each morbidity and only provides a general picture of polypharmacy and multimorbidity. Further analysis could explore links with specific medications to the multimorbidity data to provide a bigger picture on prescribing, polypharmacy, and its links to multi-morbidity. Another limitation is that there is possible confounding of the data with the age, sex, and SIMD analysis, therefore, these graphs will need to be adjusted for these potential confounders which could cause unintentional statistical bias in the results. Also, statistical analysis has not yet been conducted, consequently, confidence intervals and p values have not been discovered meaning that it is unclear if this data
is statistically significant. In addition, analysing data, in this fashion, runs the risk of over-stratifying.

6.4.2 Further Study
Analysis of repeat prescriptions could provide a little more in-depth analysis of asthma prescribing and, in turn, polypharmacy in patients with asthma. Repeat prescribing could, also, show more patterns in the dataset and could highlight issues that arise from prescribing cascades that are commonly associated with polypharmacy. Furthermore, the data analysed in this chapter was primary care records and, therefore, asthma attack read codes were taken from primary care. A clearer picture could be determined in regarding asthma attacks/exacerbations and, in turn, asthma severity from hospital records. In addition, dose information has been loaded into the dataset and has not been analysed yet. Dosage analysis will be conducted in situ with prescribing cascade analysis as the two go hand in hand as doses increases can, also, be a prescribing error or inappropriate polypharmacy if not removed or stepped down at the correct moment. Another key point to polypharmacy is discovering if patients have been stepped down or removed from medication list. Further analysis needs to be conducted in deprescribing in this data.

Additionally, the prescribing dataset contains dispensing data which can, also, be analysed to determine patterns of dispensing data in relation to prescribing data. Analysis of dispensing data could show the differences is how a patient is prescribed a specific set of drugs and whether the patient has gone to have the drugs dispensed. Despite drugs being dispensed does not equal the patient having taken the medication dispensed it can provide information on adherence to medications as we know that a patient cannot take the drug if they never had the drug dispensed.
6.5 Conclusion
To conclude, polypharmacy levels have been decreasing from 2009, with levels plateauing from 2013 onwards in conjunction with the introduction of the Scottish Polypharmacy Guidance in 2012. From 2015, polypharmacy levels have increased slightly but, generally, polypharmacy levels are still lower, overall. Men from lower socioeconomic backgrounds are more likely to experience polypharmacy from a younger age. Older patients displayed lower levels of polypharmacy, possibly because the increased interaction with health services gave greater opportunity to receive medication reviews with more ease than younger patients. Patients with asthma seemed to experience polypharmacy at a younger age, from their 40s onwards. The levels of polypharmacy in patients with excessive polypharmacy are still quite high and require the targeting of at-risk patients in this category for future polypharmacy management development.

6.6 Summary
Polypharmacy has been defined as patients prescribed 5 or more medications over a six-month period. When polypharmacy rises to 10 or more medications it becomes excessive polypharmacy. Therefore, to analyse polypharmacy in this research, 3 categories of polypharmacy levels were analysed, 5-9, 10-14 and 15+ medications per six months was used as the definition to stratify patients into patients presenting with polypharmacy and the removal of those patients who did not come under the umbrella of polypharmacy. To investigate polypharmacy, access was granted via the PBPP to prescribing data in patients with asthma from the years January 2009 to April 2017. This data was cleaned and combined with cleaned multimorbidity data, demographic data, and dose data to allow for analysis to be conducted. The combined data was
split into six-month time intervals and polypharmacy levels were analysed over the 7-year period. As polypharmacy has several contributing factors, these factors were analysed in this chapter. Hence, multimorbidity, age, sex and socioeconomic background were used as stratifying variables to quantify which factors contributed heavily to the increase of polypharmacy. Patients with asthma are affected by obesity and smoking levels, and these were used to highlight polypharmacy in asthma. It was found that 47.5% of patients with asthma have polypharmacy with levels decreasing slightly overall between 2009 and 2016, the peak decrease occurring between the years 2009 and 2013. Patients from lower socioeconomic backgrounds, older age, mainly peaking in the 70-79 age range, and women were more likely to have polypharmacy. Common co-morbidities seen in polypharmacy patients with asthma were moderate liver disease in men and rheumatological disease in women. Analysis into multimorbidities showed that overall polypharmacy decreased with a peak in 2012. This coincided with the introduction of the Scottish Polypharmacy Guidance. This study is limited in its analysis of polypharmacy per six-month period, further work in analysing repeat prescriptions over a much smaller time frame in these patients requires to be analysed to paint a wider picture of polypharmacy patterns in Scotland. Future work on indicators of whether these prescriptions are problematic or appropriate polypharmacy, also, needs to be investigated.
Chapter 7

7.1 Introduction

In the previous chapter, polypharmacy levels over time and their associations with multimorbidity were discussed. How these levels alter according to differences in various ages, socioeconomic background and gender were further examined. However, to obtain a better understanding of possible levels of inappropriate polypharmacy, hospital admissions caused by ADR requires investigation. This is due to the knowledge that the more medications that a person consumes, the higher the risk of ADRs. Hence, the ways in which this polypharmacy can be regulated needs to be examined. The reduction of patients' medications can be achieved by either stepping down or fully removing medications known as deprescribing. To effectively deprescribe, medications where the risks outweigh the benefits are discovered during a medication review and during a comprehensive drug history review. Currently, one
of the main aims of deprescribing is to prevent patients from hospitalisation due to ADRs and to subsequently improve an individual’s quality of life. Therefore, this chapter endeavours to longitudinally investigate adverse drug reaction hospital admissions and to examine long-term medication deprescribing levels in greater depth across various socioeconomic backgrounds, genders and ages.

7.2 Methodology

7.2.1 Hospital admissions
The inpatient hospital admissions data was loaded into R as per the previous chapter on quantitative research. The IDs and dates were correctly formatted for analysis. The inpatient data was analysed twice, once using all the inpatient data and the second was the hospital admissions stratified based on admissions caused by ADRs. All possible ADR found in the data were coded to be included in this research. Subsequently, both versions of the hospital admissions data were separately joined to the six-month stratified prescribing data mentioned in chapter 5. The general inpatient admissions and the ADR admissions were investigated by comparing the number of medications prescribed (five medications and above) and hospital admission. These hospital admissions were stratified by socioeconomic background, gender, age and the combination of age and gender and age and socioeconomic background and were put into graph form to be evaluated.

7.2.2 Deprescribing
To create the deprescribing dataset, the original prescribing dataset and the repeat prescription dataset were joined. Overlap between the two datasets were merged and any duplicates were removed in this combination. To determine that doses of medication had been stepped down, all distinct prescribed drugs and doses were
highlighted. The data was coded to identify the first dose of any specific drug that had been prescribed to the patient. Any patients with a dose change at any point after this initial first dose was selected. Only the doses that had been lowered or ceased completely were used and all doses that had been stepped up were removed. This filtered dose reduced dataset was combined with the demographic dataset for analysis. The number of medications per repeat prescriptions being over five medications and the number of patients with doses stepped down were compared. The repeat prescriptions were grouped into yearly analyses of deprescribing rather than graphs containing analysis every 84 days. These stepped down doses were stratified by socioeconomic background, sex, age and the combination of age and sex and age and socioeconomic background. The top ten drugs commonly dose reduced were noted and put into table form.

The analysis of patients having at least one medication completely removed from their medication list was accomplished by highlighting each individual drug prescription in each patient. The first date of each individual drug prescription was noted and was compared to the final prescription date of said drug. All drugs that were prescribed for less than six months were removed from the analysis as they were not long-term drugs being deprescribed. This was to eliminate any medication that was correctly removed at the correct time. Long term inappropriate polypharmacy was the aim for the reason for deprescribing hence why repeat prescriptions that were less than six months were removed. To determine that the drugs were deprescribed and not stopped due to the patients’ death or other external factors not linked to deprescribing, the overall final prescription date for the patient was calculated and compared to the final individual drug prescription date. If these dates matched, this indicated that the patient did not
have this drug deprescribed and these records were removed. Like the analysis for the drug dose deprescribed, a yearly analysis was carried out and stratified in the same manner and the results were produced in graph form.

7.2.3 Statistical Analysis
The primary form of analysis used was accomplished by Poisson regression. This form of statistical analysis was used as a measure the degree of association between the drug count in an individual and the outcome measures, which in this chapter was hospital admission, stepping down medication and removing medications. As Poisson regressions is used to analyse discrete variables such as the polypharmacy drug count, it was considered the best form of analysis to utilise\textsuperscript{262}. Initially, an unadjusted Poisson regression was executed and the P values, the incident rate ratios (IRRs) and the 95% confidence intervals were noted. The rate ratios were calculated by offsetting the variable of year to not overpredict a possible association between two possible measures, Subsequently, an adjusted regression analysis was performed to remove possible confounding. Therefore, the regression was adjusted for age, sex, socioeconomic background and multimorbidity. The same values as the unadjusted regression were recorded.

7.3 Results
7.3.1 Hospital Admissions

The number of patients with a hospital admission caused by an adverse drug reaction shows that patients taking 15 or more medications were more likely to have a hospital admission. This shows that the greater the number of medications, the more likely a person has a hospital admission caused by an adverse drug reaction. Patients taking 10-14 medications experienced the least percentage of hospitalisations followed by the 5-9 medication category (fig.7.1). Across time, there has been a steady decline in the number of hospitalisations in the 5-9 and 10-14 category. However, the number of hospitalisations for patients with 15 or more medications has remained largely
unchanged. This indicates that the higher the number of medications the more likely that ADRs from polypharmacy will occur leading to ADR hospitalisations, whereas patients being prescribed less medications have fewer opportunities for their drugs to interact causing less hospitalisations. Furthermore, the decline in patients with 5-14 medications could be linked to interventions lowering patient medications which could explain the decline being seen.
Figure 7.2 shows the percentage proportion of patients presenting with polypharmacy with an adverse drug reaction hospital admission stratified by age.
In ages 80-89 and 90-99, there has been an increase in the number of hospitalisations caused by ADRs over time in patients taking 15 or more medications (fig. 7.2). However, in the same polypharmacy category, there has been a very slight decline in 60–69-year-olds being hospitalised. This suggests that patients over the age of 80 are being hospitalised mainly due to their age and other multimorbidities in addition to the ADR causing their hospitalisation. Moreover, in the age ranges 60-69, 70-79 and 80-89, there has been a decrease in patients being hospitalised taking between 5-14 medications. In the 50-59 and 90-99 age ranges, similar patterns are displayed with an increase in hospitalisations in the 15+ category with the exception of the 10-14 age range showing a reduction from late 2014 onwards. Also, the increase in hospitalisation is much more gradual in the 50-59 age range in comparison to the 90-99 age range. In the 5-9 polypharmacy category in the 50-59 range showed declining of hospitalisations from 2009 to 2011 but a slight continuous increase in hospitalisations from 2012 onwards. Overall, fig. 7.2 indicates that the cohorts are similar with the exception of the 60–80-year-olds taking more than 15 medications.
Figure 7.3 shows the percentage proportion of patients with an adverse drug reaction hospital admission stratified by sex.
Figure 7.4 shows the percentage proportion of patients with an adverse drug reaction hospital admission stratified by age and sex.
In fig. 7.3 and 7.4, females were more likely than males to have a hospital admission caused by an adverse drug reaction, particularly in the 60-80 cohort. It is more likely that this increase in hospital admissions in females is linked to their increased levels of polypharmacy and more frequent visits to the GP in comparison to males. As with fig. 7.1, there was a drop in both sexes in the 10-14 and 5-9 polypharmacy categories in adverse drug reaction hospitalisations in fig. 7.2. In contrast, in males taking 15 or more medications there was a slight increase in hospitalisations, whereas females were starting to see a slight decline from the year 2015 onwards. In fig. 7.4, women in the 70-79 range showed the highest decline in hospital admissions when taking 15 or more medications. The highest levels of hospitalisations were seen in the 80-89, 70-79 and 60-69 ages in women, respectively, whereas the highest levels in men were seen at ages 70-79 followed by 60-69 and 80-89. However, there has been an escalation in hospitalisations in women between 90-99 years of age in the 15+ polypharmacy category which could show increased mortality over time. In the 5-9 and 10-14 category of polypharmacy, there has been a steady decline in hospitalisation across the ages in both men and women as seen in fig. 7.4.
Figure 7.5 shows the percentage proportion of patients presenting with polypharmacy with an adverse drug reaction hospital admission stratified by SIMD.
The highest number of patients presenting with polypharmacy taking 15 or more medications are located in SIMD 2 (fig. 7.5). The percentage of patients presenting with polypharmacy have been increasing in both SIMD 2 and 3 with SIMD 3 increasing more rapidly than SIMD 2. SIMD 5 is the only socioeconomic background with a very gradual decline in ADR hospital admissions in patients taking 15 or more medications which could be linked to enhanced GP services in these more affluent areas. SIMD 3 has the lowest number of hospitalisations but SIMD 3 has the smallest number of patients by sample size. SIMD 1 and 4 shows an inconsistent pattern of hospitalisations. SIMD 4 has a curve where hospitalisations decreased from 2009 to early 2012 and began to rise until 2014 where hospitalisations fell again. SIMD 2 has stayed consistent in the 15+ category but in 2012 to 2014, hospital admissions increased due to ADRs.
Figure 7.6 shows the percentage proportion of patients presenting with polypharmacy with a hospital admission caused by an adverse drug reaction stratified by SIMD.
As seen in fig. 7.2, there is decline in ADR hospitalisations in patients taking between 5 to 14 medications across the SIMD levels (fig. 7.5 & 7.6). In SIMD 1, the highest proportion of patients being hospitalised was in the 70-79 category where there has been a drastic decrease from late 2010 (fig. 7.6). This late 2010 decline in hospitalisations is seen in the same age range in SIMD 2 as well. This denotes improved monitoring of ADRs in the 15+ category of patients presenting with polypharmacy which is particularly seen in lower socioeconomic backgrounds but is seen to a lesser extent in more affluent areas. In SIMD levels 1-3, patients in the 90-99 age range have shown an upsurge in hospitalisation until around 2012 where it began to slowly taper off and decrease hospitalisations. This could imply either increased deaths or better polypharmacy management in this population. 50–59-year-olds in SIMD 1 have been showing a reduction in patient hospitalisations from the year 2012 connected to the knowledge that younger patients suffer from multimorbidity at a younger age in lower socioeconomic backgrounds and could be targeted for medication review to explain the reduction in ADR hospitalisations. SIMD 5 had the smallest number of hospitalisations across the ages as it is known that polypharmacy levels are lower in higher socioeconomic classes. In SIMD 2-5, the highest level of hospitalisations was in the 80-89 age range. Similar patterns are seen in SIMD 2-4 where there is a slight increase until around the year 2011 where hospitalisations began to decrease.
Figure 7.7 shows the yearly proportion of patients presenting with polypharmacy (who have had at least one medication deprescribed by repeat prescription. Repeat Prescription was defined as having a prescription once every 84 days.

The yearly proportion of asthma patients presenting with polypharmacy taking 5-9 drugs with at least one medication removed from their medication list per repeat prescription had the uppermost levels of deprescribing (fig. 7.7). The increase in medications being deprescribed in these patients plateaued around 2009 to 2011. From 2012 onwards, deprescribing proliferated at a faster rate. In patients taking more than 15 drugs, their deprescribing levels have remained the same over the 7-year time
frame and have the smallest levels of deprescribing across the categories. This result could indicate that in patients with extreme polypharmacy there is no opportunity for their long term medications being removed due to their medication being optimal or it could be suggested that the trigger of a medication review resulting in eventual deprescribing could be inadequate. Patients taking 10-14 medications have had a small gradual increase in medications being deprescribed from 2014 onwards.
Figure 7.8 shows the yearly smoothed average proportion of patients presenting with polypharmacy who have had at least one medication deprescribed by repeat prescription stratified by age. The age categories are in 10-year periods.
The levels of deprescribing in the age categories (Fig. 7.8) reached an all-time high in the 70-79 age range across all the polypharmacy categories. Deprescribing in the 60-69 age range was very similar to the 70-79 range. The levels of deprescribing in the 50-59 age range was like that of the 80-89 category with the change in deprescribing occurring from the year 2011. Across the age groups and polypharmacy categories, there seems to be a gradual increase in deprescribing throughout the years with the exception of the 70-79 age category taking 5-9 medications as there seems to be an active decrease from the 2009 to 2012 followed by a dramatic rise in deprescribing. Between the ages of 50-79, there seems to be a more obvious pattern in the changes of deprescribing. The 60-69 age ranges show that after 2011, there is an increase in patients receiving at least one medication deprescribed in the 5-9 and 10-14 medication categories, similar to that shown in fig. 7.7. There has been a sharp rise in the number of patients being deprescribed medications in the 80-89 and 90-99 age range taking 5-9 medications which could indicate that patients are living longer hence the levels of polypharmacy are higher for a longer period. Furthermore, the rise in deprescribing seen in 2012 occurs while the Scottish Government Polypharmacy Guidance was introduced. Therefore, the increase of deprescribing could be associated with medication reviews occurring in over 75s as per the medication review guideline suggesting that medical professionals pay more attention to these possible ‘frail’ patients due to being prompted by the guidance. However, this does not explain the low levels of deprescribing in the patients with extreme polypharmacy.
Figure 7.9 shows the smoothed yearly proportion of patients presenting with polypharmacy (5 or more medications every 6 months) who have had at least one medication deprescribed by repeat prescription stratified by SIMD level. The missing category was removed.
Figure 7.10 shows the smoothed yearly proportion of patients presenting with polypharmacy who have had at least one medication deprescribed by repeat prescription stratified by age and SIMD.
Deprescribing levels across the SIMD categories are consistent in SIMD 1,2 and 4, with SIMD 2 having slightly higher levels of deprescribing across the years (fig. 7.9). Staying consistent with fig. 7.7, the increase in deprescribing has been rising. Deprescribing is lower in SIMD 3 and 5. SIMD 5 has had consistent levels of deprescribing from 2009 to 2012, from 2012 onwards, deprescribing levels have been growing. SIMD 4 seems to have high levels of deprescribed medications like that of SIMD 2. SIMD 4 having elevated deprescribing points could be due in part to the advanced engagement of patients from higher social classes in their healthcare services. SIMD 1 has had the highest increase of deprescribing over time, particularly in the 5-9 medication category.

As shown in fig. 7.9, the highest level of deprescribing in fig. 7.10 is indicated in SIMD 4 in the age range of 70-79 in the medication category of 5-9. The highest levels of deprescribing occurred in the age range 70-79, followed by the 60-69 category in SIMD 4 and 5. Contrastingly, in SIMD 1 and 2 where the highest level of deprescribing occurs in the age range 60-69. The levels of deprescribing across both age and SIMD have only very gradually increased with the most change in deprescribing with time across the SIMD levels. Also, there was shown to be no deprescribing that occurred in the 20-29 age range in SIMD 4. Overall, the results show that the optimum deprescribing levels occur in different age groups for different classes. Lower socioeconomic backgrounds have higher levels of deprescribing at a younger age as they have polypharmacy at a younger age and have lower mortality rates.
Figure 7.11 shows the smoothed average yearly proportion of patients presenting with polypharmacy who have had at least one medication deprescribed by repeat prescription stratified by Sex (M indicates Male sex and F indicates Female sex).
Figure 7.12 shows the smoothed yearly proportion of patients presenting with polypharmacy (5 or more medications every 6 months) who have had at least one medication deprescribed by repeat prescription stratified by both age and sex.
Fig. 7.11 indicates that deprescribing levels have been increasing in both men and women but that women have considerably higher deprescribing levels than men do. Women having higher levels of polypharmacy, ADR hospital admissions and deprescribing levels has been noted throughout this research. Higher levels of polypharmacy allow for amplified deprescribing if the medication reviews are being completed which the elevated deprescribing in fig. 7.11 and 7.12 seem to suggest. When analysing age and sex combined, the levels of deprescribing seem consistent across the ages in men and women, with men having slightly lower levels across the ages (fig. 7.12). The rise of deprescribing shows a different form in men and women. Men in the 80-89 age range had a higher increase of deprescribing than women in the same range. The 70-79 age range in women shows more of a curve similar to that seen in fig. 7.7. This pattern is linked to lower mortality in men which translates to polypharmacy occurring at an earlier age in men.
Figure 7.13 shows the smoothed average of patients taking five or more drugs that had one or more doses of their medications stepped down by repeat prescription. Repeat prescription was defined as having a prescription at least once every 84 days.
Figure 7.14 shows the smoothed average of patients taking five or more drugs that had one or more doses of their medications stepped down by repeat prescription stratified by Sex.
Figure 7.15 shows the smoothed average of patients taking five or more drugs that had one or more doses of their medications stepped down by repeat prescription stratified by SIMD. The missing category was removed.
To further analyse deprescribing, stepping down medications were investigated. It was shown that the percentage proportion of patients presenting with polypharmacy having at least one dose of their medication stepped down has been accumulating across the polypharmacy categories with the highest growth found in the 5-9 category (fig. 7.13). The elevated stepping down in the 5-9 category and to a much lesser extent in the 10-14 medication category suggests that proper medicines management has been occurring in tandem. In keeping with the rest of the study, women with polypharmacy were more likely to have their medications stepped down than men (fig. 7.14). SIMD 2 and 4 had the peak number of patients with their medications stepped down increasing over time and SIMD 5 had the lowest proportions (fig. 7.15). Overall, the levels of stepping down medication (fig. 7.13) is greater than fully removing medications (fig. 7.7) which suggests that in medication reviews HCPs are more inclined to lower dosages that remove entirely. Lowering doses could be more appropriate in certain patient demographics or diseases rather than stopping altogether which could explain one of the reasons that stepping down was found to be more frequent than fully removing medications. Stepping down is highly preferable in the 10-14 category in comparison to ceasing medications completely with around double the proportion of patients being stepped down medications. Also, this pattern of stepping down being higher than that of removal is shown when stratifying by sex and socioeconomic background (figs. 7.8, 7.11, 7.14 and 7.15).
Figure 7.16 shows the smoothed average of patients taking five or more drugs that had one or more doses of their medications stepped down by repeat prescription stratified by Age Category. The age categories are shown in 10-year periods.
The age category with the greatest percentage proportion of patients presenting with polypharmacy with a medication stepped down was the 70-79 range followed by the 60-69 age range in patients (fig. 7.16). However, in the 5-9 polypharmacy category, the 80-89 age range showed the highest increase over time starting with similar levels of stepped down medication as the 50-59 age range and ending with stepped down medication levels like that of the 60-69 range. The 60-69 age range had a small increase of stepping down over time whereas the 40-49 category showed a decrease percentage proportion and 50-59 showed a steady level of patients with medication stepped down. Additionally, there has been a small steady increase in the percentage proportion in patients aged 90-99. Patients taking 10-14 medications saw the highest levels of stepping down proportions in ages 70-79, 60-69 and 80-89 respectively with less drastic changes over time like the 5-9 category. As noted in the patients receiving their medications fully removed, the changes occurring in age categories, 50-59, 60-69, 80-89 and 90-99 in 2012 could correspond with the Scottish Polypharmacy Guidance. The step-wise approach noted in the 2012 and the 2015 update could lend itself to improved dosage reductions rather than ceasing medications completely\textsuperscript{1,263}. The exponential growth seen in ages 70+ shows that stepping down as a form of polypharmacy management is occurring more frequently than removing medication over time (figs. 7.16 and 7.10).
Figure 7.17 shows the smoothed average of patients taking five or more drugs that had one or more doses of their medications stepped down by repeat prescription stratified by Age Category and SIMD.
In relation to fig. 7.16, the highest percentage proportion was shown in age category 70-79 in SIMD 4 (fig. 7.17). This proportion was slowly increasing. There was a higher percentage proportion of patients in SIMD 5 in the same age category with medications stepped down rather than medications fully deprescribed. The percentage proportion across all the SIMD levels were slightly lower in ages 60-69 in comparison to the highs of ages 70-79, followed by 80-89 like fig. 7.7-7.12. In SIMD 2 and 5, there seemed to be an increase in stepping down medications until the year 2013 for SIMD 2 and 2012 for SIMD 5 where stepping down began to plateau in ages 80-89. This plateau could be associated with compounded mortality rates in SIMD 5 occurring between 80-89 years of age. Comparing to fig. 7.10 where patients with medications removed were stratified by age and class, the peak ages where both types of deprescribing occurs is the same but the percentage proportion of the patients from these age categories and backgrounds is higher when stepping down.
Figure 7.18 shows the smoothed average of patients taking five or more drugs that had one or more doses of their medications stepped down by repeat prescription stratified by Age Category and Sex.
As in fig. 7.14, the proportion of men being stepped down medications is slightly lower than women and the highest levels seen in patients prescribed 5-14 medications and in ages 70-79, 60-69 and 80-89 respectively (fig. 7.18). In ages 70-79 and 80-89 and the 5-9 polypharmacy category, the percentage proportion of men starts off lower than the women in 2009 and, subsequently, increases to become similar in percentage proportion than that of women by 2016. In ages 70-79 and 80-89, the percentage proportion of men with medication stepped down is like that of women, again due to men having polypharmacy at a younger age. In the year 2009, the proportion of men is slightly lower than that of women but increased to slightly higher than women by 2013 onwards. The age differences in stepping down medication across sexes is not as stark as that seen in removing medications. The only difference seen is in older men (over 80s) caused by lower mortality. This lack of variation could be due to the lack of hesitation in HCPs of lowering dose rather than fully removing.

7.3.3 Drugs Frequently Deprescribed and Stepped Down

Tables 7.1 and 7.2 show the top 15 drugs with the prescribing dataset that were most deprescribed and stepped down in patients with asthma and presenting with polypharmacy.
In tables 7.1 and 7.2, there is a slight difference in the top 15 medications removed in comparison to those stepped down. Most of the medications in both lists are medications targeting the cardiovascular system. Bendroflumethiazide, bisoprolol fumarate, atenolol, amlodipine, lisinopril and ramipril are all cardiovascular drugs, though lisinopril and ramipril can be used in diabetes and kidney failure patients. Salbutamol is the only inhaler listed in both deprescribing lists. Crucially, prednisolone
makes the list of medications stepped down but not the list of top medications fully removed. In general, the removal of prednisolone is more essential than its dosage merely being reduced as prednisolone should really only be prescribed for very short periods of time as and when a patient has an asthma exacerbation and should be promptly removed.\textsuperscript{264} The anticoagulant warfarin sodium being located at the top of the dose reduction table is an expected finding as warfarin has a variable dose regimen and interacts with multiple other drugs causing warfarin to be heavily monitored by HCPs\textsuperscript{13,117}.

7.4 Discussion
Evaluating how hospital admissions affects polypharmacy prescribing gave some interesting results. The analysis indicates excessive polypharmacy creates an elevated risk of ADRs leading to hospital admissions. Furthermore, over the 7-year period, the proportion of patients taking 15 or more medications has been gradually increasing. Whereas patients taking between 5 to 14 medications were shown to have decreasing hospital admissions due to ADRs over time. This could be expected as the more medication a person consumes the more likely they are to have an adverse drug reaction\textsuperscript{21,117,265,266}. Additionally, these patterns were displayed in the socioeconomic, sex and age stratification analysis. As shown in the previous qualitative chapter, women displayed higher levels of polypharmacy in association with ADR hospital admissions. This could be due to women visiting their healthcare provider more frequently than men and being prescribed more medications as a result that could lead to these hospital admissions\textsuperscript{29,205,267–269}. Also, SIMD 2 had the highest levels of ADR hospital admissions caused by ADR linked by excessive polypharmacy. With the results described in Chapter 6, where patients located in SIMD 2 were shown to be more predisposed to polypharmacy than other socioeconomic backgrounds.
Furthermore, SIMD 5 had the lowest ADR hospital admissions of the 5 SIMD levels. This could be linked to patients from more affluent backgrounds being prescribed fewer medicines and, therefore, lowers their chances of having an adverse drug reaction\textsuperscript{257,270}. Patients from affluent socioeconomic backgrounds have higher levels of health literacy and better quality of medical services. Hospital admissions have been decreasing across all SIMDs and age categories except from ages 90-99 where patients have been shown to have increasing hospitalisations due to ADR until around 2013 where they have begun to decline. This could be due to people living longer and therefore, being monitored by their GPs for frailty and excessive polypharmacy and possibly being deprescribed medication\textsuperscript{271,272}.

In relation to deprescribing medication, the research showed that around 20-25% patients taking 5 to 9 medications had at least one long term medication removed from their repeat prescription, dropping to around 4% when prescribed 10 to 14 medications and 1% in patients with 15 or more medications. This shows that removal of medication in patients with excessive polypharmacy requires development to become more widespread in its use. This shows the real time utilisation of deprescribing and demonstrates in data form the reluctance exhibited from the participants in the qualitative interviews to deprescribe. The removal of medication over time stratified by age group was shown in graph form by parabola with overall decreases in deprescribing occurring from 2009 to 2011 and, subsequently, increasing from 2012 to 2016. The changes in deprescribing occurring in 2012 could be heavily linked to the introduction of the Scottish Polypharmacy Guidance if HCPs had been following the 7 steps to deprescribing medications and conducting medication reviews by shared decision making\textsuperscript{1}. 70–79-year-olds displayed the highest levels of medication
removal, particularly women in this age category. However, 60–69-year-old men were shown to have the highest levels of medication removal. Moreover, patients in SIMD levels 1 and 2 had the highest levels of medication removal in their 60-69-year-old patients. This could be due to men and patients from lower socioeconomic backgrounds having a higher mortality rate at a younger age than women and patients from higher socioeconomic backgrounds as indicated in chapter 6273. These younger men in their 50s and 60s from lower socioeconomic backgrounds will likely visit their GP more frequently once they notice multiple issues with their health as they reach polypharmacy and multimorbidity at an earlier age than people from affluent backgrounds273. Conversely, patients in SIMD 1 had the peak medication removal over time in patients taking 5 to 9 medications. This positive discovery could indicate that deprescribing is being taken seriously in lower socioeconomic background healthcare services274,275. Therefore, it could be suggested based on this research that there is an inverse distribution of medicine management by socioeconomic background. As patients in lower socioeconomic backgrounds are more likely to experience high polypharmacy levels, there is a greater opportunity for these patients to be targeted for medication reviews and subsequently have their medications deprescribed. Despite deprescribing guidelines paying particular attention to patients over 80 years old and frailty, 80–89-year-olds had similar levels of medication removal as patients in their 50s276,277. This could be linked to HCPs being wary of removing existing medication from a patients’ medication list especially in elderly patients where they might be psychological attached to their medications or may perceive their medications being removed as a sign that their healthcare providers are losing interest in them as a patient as was discovered in the qualitative analysis204. However, in all age groups, medications being removed have been increasing in patients taking
between 5 to 14 medications. It could be speculated that from 2017 onwards there are more patients having medications removed. Over time and across all socioeconomic backgrounds, sexes and polypharmacy categories except 15 or more medications, there has been a gradual increase in medication removal. Hence, this gradual escalation in deprescribing should be viewed in a positive light, despite the future effort required to improve the levels of removals occurring in patients taking between 10 or more medications, if their medication is inappropriate.

There are some key differences in stepping down medications versus fully ceasing medications. The main distinctions are linked to the action of stepping down medication in comparison to that of removing treatment. To deprescribe, HCPs conduct a medication review usually with work with patients to discuss the benefits they are gaining from the medications they are taking. Once the HCP considers the benefits versus the risks of this treatment and view the risks of the treatment to be greater, they have one of three options, stepping down, ceasing treatment or continuing treatment due to optimal management. In the qualitative chapters, it was discovered that some HCPs lack confidence to remove medications and when they reach this crossroads in their treatment management decision making, they choose to step down out of fear of the repercussions of ceasing medications particularly in frail, elderly and/or at risk patients\textsuperscript{101,243,278}. Over the 7-year period, stepping down medications occurred at a much higher rate than removing medications. Additionally, stepping down occurred slightly more often in the data than removing medications. Around 24 to 31% of patients taking 5-9 medications had a medication stepped down, dropping to 5-6% in patients prescribed 10-14 medications and 2% in 15 or more medications prescribed. When focusing on patients taking 5-9 medications and
stratifying by age, sex and socioeconomic background, the proportion of patients with medications stepped down is around 1.5 times higher than removal of medications. This further highlights the possible reluctance of HCPs to cease treatment.

Therefore, stepping down medications revealed similarities to that of removing medications. Women had elevated levels of stepping down medications than men with peak levels of stepping down occurring at ages 70-79 in women and 60-69 in men like that of the ceased medications. Moreover, SIMD 2 and 4 had the highest levels of stepping down medications and SIMD 1 and 2 had their maximum in ages 60-69 versus 70-79 for the remaining SIMD categories as was illustrated in the removed medications analysis. In stepping down medication, the highest levels in both men and women were noted in ages 70-79. However, men had significantly more medications stepped down between ages 60-69 whereas women had more medications stepped down between 80-89 years of age. Both age categories have had stepping down medications increase exponentially to the point that they are to the level of the peaks seen in the 70-79 category. Again, this could be linked to women having longer life expectancies than men\textsuperscript{279}. The similarities found in stepping down and removing medications could be limited by the population distribution of the dataset as overall there is no difference in the age, socioeconomic background and gender distribution in both forms of deprescribing however the growth of stepping down and deprescribing does show differences across the varying stratified populations over time. This shows a dichotomy that female sex, lower socioeconomic background and increasing age does not affect proportions of deprescribing and proposes that polypharmacy review is not disturbed by the factors that would be expected such as lower access to medical services in lower socioeconomic backgrounds.
The analysis of the top drugs deprescribed in the dataset highlighted some of the associated multimorbidities that may be linked to patients with asthma. The main drugs deprescribed were gastrointestinal, cardiovascular, cholesterol lowering and diabetes drugs. Cardiovascular medication, it could be suggested, is reduced and removed more than asthma medications possibly due to older patients requiring lower doses with age\textsuperscript{280}. Simvastatin, a cholesterol lowering drug, is featured in the top medications stepped down due to the existence of guidance from the MHRA in 2014 due to drug interactions occurring with frequently prescribing medicines for blood pressure, amlodipine and diltiazem, where doses were stepped down from 40mg to 20mg\textsuperscript{281}. It was most noticeable that in an asthma patient dataset, most asthma medications were curiously absent from the top deprescribed medications, with the exception of salbutamol and prednisolone. This could be because patients with asthma require their inhalers for the rest of their ongoing life\textsuperscript{37}. However, both salbutamol and prednisolone are featured in the top medications to be stepped down. In prednisolone’s case, both in the literature and noted by the HCPs in the interviews, prednisolone should be a short course prescription\textsuperscript{243}. With salbutamol, it insinuates that the controversial nature of salbutamol has been taken into consideration in patients with asthma and that their annual asthma reviews are targeting the correct removal of salbutamol\textsuperscript{282}.

Multimorbidity has a huge impact on polypharmacy and subsequently ADR hospital admission and deprescribing\textsuperscript{82}. Multimorbidity is one of the main hindrances to fully remove a medication from a patients’ medication list\textsuperscript{283,284}. It was discovered earlier that patients with extreme polypharmacy have extremely low levels of deprescribing
(both stepping down and ceasing completely). Multimorbidity affects this as HCPs are reluctant to remove medication that another colleague has prescribed as noted in the qualitative research\textsuperscript{101}. Furthermore, additional comorbidities could affect deprescribing as deprescribing affects the patient's medication list and possible ADRs but these comorbidities will continue to exist regardless of whether the patient has drugs deprescribed or not. Therefore, considering which comorbidities medication to target for deprescribing is a point of contention in healthcare services. Consequently, the reluctance to remove medication could lead to excessive polypharmacy which would heighten a patients' risk of an ADR which could lead to a hospital admission. This reluctance would need to be alleviated to advance deprescribing in patients presenting with polypharmacy. However, inappropriate deprescribing is also unsafe and can lead to ADRs and hospital admissions. Furthermore, ADRs can occur not just from drug interaction in excessive polypharmacy but if the wrong dose was prescribed or being prescribed the wrong medication for an extended period\textsuperscript{136}. Therefore, it is of great importance that safe and appropriate deprescribing is enhanced rather than deprescribing to fulfil potential quotas. In terms of person-centred care and patient education, the WHO emphasises the importance of encouraging patients to disclose all the medications that they are taking to their HCP including over the counter medications\textsuperscript{285}. Over-the-counter medications could not be monitored in this research which is a limitation. This could translate into potentially more medications that patients could be taking that might potentially be unsafe for them and might need to be de-escalated or stepped down. Therefore, there needs to be support for patients to be able to feel safe enough with to converse with their HCPs to safely remove, step down or add medications via medication review which could allow for a change in the percentage proportion of patients being deprescribed medication in future research\textsuperscript{114}. 
Furthermore, we need to take an understanding in an individual’s medical condition and management as a whole in order to endeavour to add or remove a patients’ medication from their list. Effective shared decision making and concordant approaches that facilitate opportunities for both the HCP and the patient to discuss how their treatment can be best improved is the goal for patients presenting with polypharmacy\textsuperscript{286}. This means that potentially harmful deprescribing is to be avoided at all costs and the aim in effective polypharmacy treatment is to discover the optimal medication regimen based on the individuals’ needs and preferences.

Comparing deprescribing and hospital admissions, hospital admissions occur more frequently in the 15+ category whereas the inverse of this is identified in the deprescribing analysis. Both stepping down and removing medication occurred more frequently in those patients prescribed between 5 to 14 medications which could account for the decline in hospital admissions observed. The Scottish Polypharmacy Guidance 7-step guide to medication reviews has ADRs mentioned in great importance as step 5 of the guideline\textsuperscript{1}. Also, there is a section highlighting certain drugs and their associated ADRs\textsuperscript{1}. Therefore, ADR hospital admissions and polypharmacy go hand in hand, therefore, if HCPs were to deprescribe regularly in patients with excessive polypharmacy this could prevent future hospital admissions caused by ADRs\textsuperscript{127,271,283}.

7.4.1 Comparison to existing literature

In Pirmohamed’s review of hospital admissions due to adverse drug reaction, it was shown that the prevalence of hospitalisations caused by ADRs was 6.5% with women being hospitalised more than men and older patients (between 65-83 years of age)
being more susceptible\textsuperscript{117}. These findings corroborate with the discoveries of this study where women have more hospital admissions due to ADRs and excessive polypharmacy. Additionally, older patients in the age range found in Pirmohamed’s trial matched the age outcomes in this research. A Japanese study on hospital admission in patients over the age of 85 discovered that after adjusting for confounding, polypharmacy was related to hospital admissions and adverse drug events\textsuperscript{287}. Moreover, a recent Scottish study on hospital readmission and polypharmacy showed that patients with polypharmacy had a 22% chance of an emergency hospital admission within one year of their previous admission and that each additional medication prescription increased this emergency readmission by 3\%\textsuperscript{288}. This gives a clear indication that lowering peoples’ medication lists has an advantageous effect on lower hospital readmission. The primary aim in secondary care is to prevent readmission. Correspondingly, this study confirmed the findings of the above research by observing polypharmacy and hospital readmission being associated with female sex, lower socioeconomic background and older age. Furthermore, there is an ongoing randomised multicentre European study investigating avoidable hospital admissions in multimorbid patients over the age 70 taking more than 5 medications\textsuperscript{289}. The results of this trial could provide valuable data on hospital admissions in older patients presenting with polypharmacy that could be linked to this research.

Many studies and guidelines focus very strongly upon hospital admissions and deprescribing occurring in patients over the age of 70\textsuperscript{1,199,202}. However, this research shows that patients over the age of 50 do have elevated levels of polypharmacy and multimorbidity, particularly men and people from lower socioeconomic backgrounds.
Therefore, wider research into polypharmacy and deprescribing should include ‘younger’ patients and this could prevent hospital admissions caused by ADRs in these patients in addition. In a Dutch study, GPs were asked about their views on deprescribing anti-hypertensive medications in patients over the age of 80. The study showed that GPs in Holland were reluctant to deprescribe medications and that GPs anticipated that the patients would disagree with the GPs judgement. The study indicated that the proportion of patients over the age of 80 had at least one medication deprescribed, corroborating the findings in this study. Moreover, it highlights that despite current research aiming at frail older adults, the actuality of deprescribing in healthcare involves many factors to consider before deprescribing and the data confirms these difficulties. Therefore, this research confirms that targeting older adults (>70 years of age) is still greatly beneficial but including younger patients presenting with polypharmacy in these trials could focus on added issues and concerns within the polypharmacy community.

7.4.2 Strengths and weaknesses
The longitudinal nature of this study provides information on deprescribing and hospital admission patterns over time. This is valuable knowledge as we can determine how deprescribing and hospital admissions caused by ADRs have altered over the 7-year period. Another strength is the ability to compare prescribing data with hospital admission data. These two datasets are separate and the ability to compare the two to make associations between polypharmacy prescribing and adverse drug reaction hospitalisations. Furthermore, as deprescribing is defined both as tapering medication doses and fully removing medication, having a comparison between doses stepped down and fully removing medications gives a wider analysis of analysing medication removal on its own. Equating the general deprescribing and hospital
admissions to the stratified socioeconomic, sex and age models allows for patterns in the data to emerge. In addition, many of the studies conducted in polypharmacy and hospital admissions are limited to those over the age of 70. This study included all age groups except for children to prevent this limitation of simply investigating only elderly patients as patients from lower socioeconomic backgrounds have polypharmacy earlier in life. The findings of this research showed that the differences in deprescribing and hospital admissions were at their overall peak between 70-79 years of age but increased polypharmacy can occur from a wide range of ages but is most noticeable between 60 and 80. Adding factors such as lower socioeconomic background and male gender can lower this peak to the 50s or 60s.

One weakness of this research is the short time frame analysed and the gap between 2017 and the present day. Seven years of analysis does not give a huge frame of data to work with, though it does allow for patterns to emerge and associations to be considered. Also, the levels of deprescribing and hospital admissions beyond 2017 are unknown in this research and could provide more valuable information to the levels of these variables in recent years. Furthermore, not having data from after 2017 also means that I am unable to definitively conclude there is a true decrease in prescribing as levels of prescribing could look very different in the present day. A further limitation of this research was the inability to capture individual comorbidities and evaluate polypharmacy prescribing on a more individual and personalised basis. The comorbidities investigated in this study were more generalised based on the population of the dataset. The Scottish Polypharmacy Guidance introduction in 2012 and its update in 2015 could have created a bias which, during those two separate years, allowed for its effects to be inferred in the data analysis. Another limitation is
the sample size and stratification with patients with asthma. These patterns of deprescribing and hospital admissions could be very different in a general subsection of the Scottish population. The levels of stepping down could be skewed since official asthma guidelines include the stepping up and stepping down of asthma medications depending on the severity and frequency of exacerbations.

7.4.3 Future Work

Continued research into deprescribing and hospital admissions in polypharmacy patients with asthma could be beneficial to understanding how polypharmacy interventions have been utilised in recent years. Tailoring polypharmacy interventions to specific groups of people and improving the real-world application of deprescribing techniques could allow for enhanced to polypharmacy asthma treatment. The inverse socioeconomic relationship between increased polypharmacy and deprescribing frequency requires further investigation. Rising levels of polypharmacy in patients in their 50s in lower socioeconomic backgrounds need to be acknowledged. Similarly, patients in their 80s do not get their medications deprescribed as regularly either. Focussing on these patients along with improved education of healthcare staff in deprescribing as mentioned in the qualitative research could improve deprescribing levels by enhancing medical care for patients. If patients received their medication reviews annually throughout their lifetime and not because of a healthcare trigger such as frailty or increased multimorbidity, polypharmacy levels could be naturally lower and levels of deprescribing would be higher. Also, another recommendation for future work could be a cohort study of Scottish patients whose records can be examined in the period before and after the introduction of the deprescribing outcomes investigating its impact on practice and on patient outcomes in relation to ADRs and
hospitalisation. Furthermore, more work could be achieved with GPs to discuss and assess different scenarios of de-prescribing would also be useful.

7.5 Conclusion

From this analysis, we can determine that deprescribing, both stepping down and removing medications, is increasing albeit very gradually and unevenly in distribution. The data revealed that patients prescribed 10 or more medications showed the lowest percentage proportion of deprescribing whilst patients prescribing 5-9 medications exhibited the highest. Hospital admissions have lowered in patients taking 5 to 14 medications but are rising in patients prescribed more than 15 medications. Determining the levels of deprescribing and hospital admissions in recent years could paint a wider picture of how they have changed over time. Future work in the patients’ groups targeted for deprescribing and education of HCP staff could alleviate hospital admissions caused by excessive polypharmacy and adverse reactions.

7.6 Summary

Hospital admissions caused by ADRs, stepping down and removing medications were evaluated between 2009 and 2017. Patients prescribed 15 or more medications were more likely to be hospitalised than patients prescribed 5 to 14 medications. It was shown that women had more hospital admissions and medications deprescribed than men and at an older age. Over the 7-year period, patients prescribed 5 to 14 medications saw a decline in hospital admissions whereas there was an increase found in patients with more than 15 medications. Patients from lower socioeconomic backgrounds were predisposed to higher levels of polypharmacy, hospital admissions and deprescribing. Deprescribing occurred more frequently in patients taking 5 to 9
medications per repeat prescription than patients taking more than 10 medications. Stepping down medication occurred more frequently in polypharmacy patients with asthma than fully removing medications. Despite the levels of deprescribing rising, particularly in those aged between 60 and 80, improving deprescribing in patients with excessive polypharmacy could prevent ADRs and, therefore, hospital admissions. Advancements to the removal of medications could be achieved by educating healthcare staff on a definitive way to deprescribe and to improve patient health literacy to allow them to feel confident enough to inform and discuss with HCP regarding their medications.

Chapter 8

8.1 Introduction

The aims of this PhD were to gain a deeper understanding of polypharmacy in patients with asthma and to discover how successful attempts to mitigate inappropriate pharmacy in patients with asthma have been. This was pursued via mixed methods research combining qualitative interviewing methods and quantitative analysis of prescribing data. This investigation sought to address the extent to which polypharmacy management techniques are adopted, how this varied between demographics and was linked to the analysis of experience and perceptions of stakeholders involved in polypharmacy mitigation in patients with asthma. This chapter presents the conclusions of this investigation, starting with a summary of the key findings, and then exploring how the findings contribute to the existing literature, the
clinical and research implications, strengths and limitations and recommendations for future work that can be derived from this study.

8.2 Summary of key findings

This study demonstrated that medications reviews could be further developed in cohorts of patients with excessive polypharmacy. Whilst HCPs do undertake medication reviews, there do appear to be shortcomings in relation to current guidelines. in terms of the insufficient frequency, consistency or level of detail. In most cases, GPs stated they resorted to, informally, inspecting patients’ medication list and only transferring patients to pharmacists for an in-depth structured medication review for complex cases. This observation, in combination with the high levels of hospital admissions in patients prescribed 10+ medications, suggests that patients most at-risk of inappropriate polypharmacy are possibly either not receiving adequate treatment or polypharmacy management from HCPs or their treatment regimen appears to be optimally managed. Thus, the cessation of problematic polypharmacy, which is achieved by fully removing the unnecessary medication in question, may need to be examined further by HCPs in future consultations with patients.

Asthma specialist nurses implemented annual asthma reviews providing the main form of medication review for these patients, in line with asthma treatment protocol, though polypharmacy was not an explicit focus. Nurses and pharmacists expressed a preference for reducing dosages rather than completely removing medications (for fear that their patients’ symptoms might return). The inclination of HCPs to step down medications rather than fully remove could be linked to existing asthma guidelines where inhalers and steroids are explicitly stated that they need to be gradually
deprescribed, therefore, nurses and pharmacists could be continuing this in their deprescribing of other medications. It was discovered that the top asthma treatments deprescribed contained the inhaler, salbutamol and steroid, prednisolone. However, other medications, particularly cardiovascular and cholesterol lowering drugs, were contained in this top deprescribed drug category and commonly preceded asthma medications in these lists. This suggested that asthma HCPs may be extending step down approaches to other clinical areas but are still generally resistant to total deprescribing.

The qualitative research found that HCPs perceived that some patients, particularly elderly patients and/or carers, still held the view of ‘a pill for every ill’ and felt abandoned by HCPs if deprescribing was suggested. This could further explain the low levels of deprescribing in the quantitative data. GPs and asthma specialists were more inclined to remove medications than specialist nurses in asthma and pharmacists but did have issues with altering a different member of staffs’ prescribing decision. The lack of clarity about roles and responsibilities noted by HCPs in relation to medications reviews, repeat prescription monitoring and deprescribing caused confusion as to who was required to conduct these tasks. This seemed to cause HCPs to be hesitant to take overall control/responsibility for potential deprescribing decisions.

This investigation observed that polypharmacy was decreasing and deprescribing increasing, gradually, since the introduction of the Scottish Polypharmacy Guidance in 2012, which offers detailed advice on conducting medication reviews and deprescribing. Polypharmacy increases significantly in people aged 50-59 years.
However, patients with asthma from lower socioeconomic backgrounds, particularly men, were found to experience polypharmacy at a younger age, beginning from the age of 40. These patients were prone to additional multimorbidities which contributed to polypharmacy. Early high levels of polypharmacy amongst this lower socioeconomic demographic which disappears as this cohort ages. This suggests that people in this group have less interaction with healthcare services and, thus, do not benefit from opportunities for a medication review that is available to other cohorts and, particularly, the frail over 75 cohort. In contrast, high levels of deprescribing were shown in patients taking 5-9 medications, particularly in those aged between 70-90 years of age. Generally, levels of deprescribing of medications over time in the 5-9 medication category were irrespective of their social class, age and/or gender. Thus, although patterns of prescribing levels broadly followed Tudor Hart’s inverse care law, where access to care by different social demographics is inversely proportional to need, this seemed to not apply in this older and arguably frailer cohort of patients who heavily interacts with healthcare services. This allowed frail over 75s to display decreasing polypharmacy over time, perhaps, because increasingly frequent engagement with health services created increased opportunities to have a medication review.

One implication is that targeting those demographics with less interaction with healthcare services could advance polypharmacy mitigation/management. Within primary care, HCPs viewed the communication was well-conducted with GPs finding the proximity easy to share ideas and concerns. In secondary care, the existence of multidisciplinary teams allowed for a variety of different HCP members of staff to discuss and evaluate patient treatment from different perspectives. However, interprofessional communication between primary and secondary care was limited,
particularly regarding patient medication changes. Beyond a letter or email from either party, there was very little connection between primary and secondary care.

8.3 Integration with the existing literature

8.3.1 Medication Reviews in Patients with Asthma

Despite the general levels of deprescribing increasing over time, high levels of hospital admissions, due to ADRs, between the ages of 50 and 70 and the relative low levels of deprescribing in patients prescribed 10 or more medications provides an indication that medication reviews appear to be insufficient. It was widely acknowledged by HCPs that medication reviews and monitoring of polypharmacy occurred less frequently than it should. Pharmacists were more likely to execute structured medication reviews with shared decision making than GPs and specialists who were inclined to conduct a more informal medication review and discussion during routine patient appointments rather than a specific set aside time for a medication review. However, within some of the literature, it was suggested that pharmacists in England do not consider structured medication reviews as a priority and placed corporate incentives as higher value. If structured medication reviews are not carried out, patient outcomes will suffer. Moreover, patients need to have their medications regularly reviewed to prevent prescribing cascades, where patients are prescribed additional medications to counteract the side effects caused by previously prescribed medications, which is a common occurrence in patients presenting with polypharmacy.

In England, structured medication reviews have been recently introduced due to the COVID-19 pandemic to replace the now defunct Medicine Use Reviews (MUR). So far, it has had limited success in viewing patients in a holistic manner but has been recently introduced and may improve as it becomes more established. This improvement is essential as this study has established the importance of patient social
factors were discovered to be of importance in the multimorbidities associated with asthma patients presenting with polypharmacy.

Our qualitative research found one factor underpinning the lack of medication reviews in primary and secondary care was the confusion surrounding which HCPs had the duty to conduct medication reviews, monitor repeat prescriptions and/or deprescribe treatments. GPs and asthma specialists in hospital expressed concern about the lack of clarity about the allocation of ‘responsibilities’ or lack thereof. Some studies note that roles and responsibilities of primary care staff in medication reviews require clarification which could allow for enhanced communication, which supports the findings of this research. In primary and secondary care medications reviews, effective interprofessional collaboration is fundamental and that the improvement of medication review outcomes can only come about from this effective communication. From 2018 in Scotland, there has been a shift in work from GPs to general practice pharmacists to deliver the General Medicinal Service, a three-tiered medication management service. This has allowed some reduction in workloads for GPs but now places additional pressure on pharmacists. This service demonstrates that in both Scotland and England, medication management interventions require better defined roles for HCPs and require further development to be fully effective. In Australia, the New South Wales guide for medication reviews contains specific examples in which multiple HCPs are mentioned to carry out specific functions. These examples seem to be missing from the main polypharmacy guidelines in the UK. A study with pharmacists in Belgium conducting medication use reviews found that, despite reducing medication burden, the service had no effect on patient self-management, adherence and preventing hospital admissions.
could indicate that regardless of how roles and responsibilities are defined, medication reviews themselves might not have the desired effect upon patients to improve their quality of life and how they interact with their medications.

Moreover, hospitals provide an optimal setting to complete medication reviews. A small integrated care pilot study conducted in London where a full structured medication review tool was created and implemented estimated that if put into wider use could remove on average three drugs per patients and the ADR burden almost halving, preventing a large chunk of avoidable ADR hospital admissions\textsuperscript{304}. However, most patients attend hospitals infrequently and intermittently. Medication reviews, therefore, need to be carried out as part of routine care in the community rather than by secondary care bodies – especially given the enduring concern to prevent unwanted hospital admissions in the long term\textsuperscript{115}. Better interprofessional collaborations, including improvements in the flow of medication rationale and knowledge between primary and secondary care regarding their patients could prevent future hospital admissions particularly ADR hospital admissions. Moreover, the introduction of detailed e-prescribing systems across primary and secondary care that display more information beyond the basic medication list could be beneficial\textsuperscript{128,170,305,306}. This is beginning to happen in Scotland as, since 2019, there has been a new collaboration with the Royal College of Physicians (RCGP) towards improving primary/secondary interprofessional relationships and systems by establishing a dedicated interface group named the Effective Interface Module\textsuperscript{307}. However, due to COVID, the effect of this interface group has yet to be determined. Additionally, the discoveries within this PhD could guide and assist the development
of effective ways to combine multimorbidity prescribing and management interventions in the NHS.

8.3.2 Polypharmacy Demographics in Patients with asthma

Amongst patients with asthma from lower socioeconomic backgrounds with multimorbidities, our quantitative research observed the onset of polypharmacy at a much younger age, over the age of 40. A recent survey in the northwest of England, the Household Health Survey evaluated age and socioeconomic factors associated with patients presenting with polypharmacy and medication management\textsuperscript{105}. Patients older than 55 years of age with multimorbidities frequently exhibited polypharmacy. In contrast in this study, patients with asthma seem to experience polypharmacy at a younger age than general patients presenting with polypharmacy. This may in part be because the onset of asthma most commonly occurs in childhood. As a result, these patients are likely to have multiple medications from a younger age. Also, this younger experience of polypharmacy was linked to the onset of additional multiple morbidities. This may in part indicate that patients with asthma have increased propensity for multimorbidities. However, other factors may be at play. Our quantitative analysis revealed high levels of polypharmacy amongst younger cohorts of patients with asthma from lower socioeconomic backgrounds. This suggests that lack of access to educational, informational and monetary resources may be key to developing multimorbidities and, consequently, polypharmacy. Again, it was discovered that polypharmacy is linked to increasing age and lower socioeconomic backgrounds. Multiple studies investigating asthma and associated comorbidities, asthma was frequently associated with other conditions; notably allergy, anxiety/depression and rhinitis\textsuperscript{48,52,184}. This was corroborated by the HCPs. However, our quantitative analysis
of multimorbidity found that the most prevalent multimorbidities amongst polypharmacy patients with asthma were cardiovascular disease, dementia and diabetes. Similar findings were found in a meta-analysis of eleven studies analysing the prevalence of comorbidities in both patients with and without asthma where more patients with asthma were associated with cardiovascular disease, gastrointestinal disease and diabetes than their non-asthma patient counterparts. These diseases are linked to older age/frailty, poor diet, social deprivation, lack of exercise and obesity. This suggest that polypharmacy is multifactorial in its causes and results from multimorbidity and wider social factors rather than one singular morbidity. These comorbidities are generally considered (in medical research as well as the perceptions of the HCPs we surveyed) to be more clinically severe than asthma. However, this study found a strong association between asthma, including young onset asthma and other comorbidities perceived as more severe than asthma. The association indicates that asthma could be a risk factor or an advance indicator of possible serious detrimental effects to peoples’ health. Better research and monitoring of this association should be called for. It is a paradox given that we determined from the interviews that patients with asthma suffer from other co-morbidities when it appeared that some of the asthma HCPs viewed that they could improve the way and/or frequency in which they consider additional morbidities and multiple medications in relation to a patients’ asthma. Asthma focused HCPs, most nurses, pharmacists and specialists admitted that they do not take their patients other comorbidities or medication into consideration outside of their asthma as much as they would hope. Hence, these findings highlight that it is imperative that asthma HCPs pay attention to their patients’ other co-morbidities and polypharmacy. The specialisation of asthma consultants perpetuates this singular morbidity focus.
Furthermore, specialist nurses in asthma and pharmacists, despite having time constraints, stated in the interviews preferring to focus on asthma protocol and guidelines. Current asthma guidelines rarely recommend guidance for other disease types\textsuperscript{309,310}.

Though we identified clear correlations, it is not possible to completely establish causes through this research. For example, another possible explanation is that as asthma is associated with younger patients and, generally in medical research, elderly patients are commonly misdiagnosed and undertreated for asthma\textsuperscript{311,312}. A sample of 369 patients over the age of 65 were examined for asthma symptoms from UK general practices and despite 70\% having the appropriate symptoms, only 7\% reported an asthma diagnosis\textsuperscript{313}. Therefore, the higher levels of polypharmacy and multimorbidities found in younger age groups in my quantitative analysis could be due to asthma being more commonly diagnosed at a younger age. In the demographics of the prescribing dataset, there were a lower number of patients over the age of 80 which could be due to patients not being correctly diagnosed with asthma and, consequently, not being recruited to be included in the prescribing dataset and are potentially missing from this analysis due to being undiagnosed\textsuperscript{218,314,315}. As previously mentioned, asthma is considered to be ‘less serious’ than other conditions in healthcare which could further exacerbate this underdiagnosis of asthma in elderly patients. Thus, the underdiagnosis of asthma needs to be taken into consideration for both our inferences in the analysis of asthma polypharmacy management in this particularly vulnerable group and, in future, in clinical settings with HCPs to ensure that elderly patients are correctly diagnosed with asthma.
The prescribing data showed the expected pattern with polypharmacy levels being associated with increasing age and lower socioeconomic background (as observed by Tudor Hart’s inverse care law). However, an important exception was discovered. This research showed that the excess of polypharmacy visible amongst younger patients from lower socioeconomic background disappeared as they became older. This appeared to be the result of older frail patients’ increased engagement with healthcare services allowing them to have greater opportunities for their medication to be reviewed (informally as well as through formal medication review) and increasing opportunities to deprescribe from their increased propensity to be admitted into hospital. Though socioeconomic inequalities in access to care may persist, these are countered by the increased access to use of health services amongst older cohorts – and especially frail patients over 75. As a result, the incidence of polypharmacy and deprescribing patterns, whether by stepping down or fully removing medications, counters the inverse care law. Multiple systematic reviews on implementing deprescribing highlighted the importance of frailty and age but not in relation to socioeconomic factors\textsuperscript{187,316–318}. A study in Northwest England on polypharmacy and medication management found that income deprivation was linked to increased medications in patients but they did not examine medication management linked to health inequalities\textsuperscript{105}. Since 1971, when Tudor Hart drew attention to the inverse care law, health inequalities have been an important part of health policy in the UK\textsuperscript{319}. In Scotland, in 2017, there was a collaboration between NHS Scotland and the Scottish Government to tackle these inequalities\textsuperscript{299}. In England, there have been policies to increase funding and close the healthcare disparity in general practices and a new healthcare inequalities manifesto introduce due to fears this gap would be widened as a result to COVID-19\textsuperscript{320}. However, there is limited evidence that these policies have a
great effect on people from lower socioeconomic backgrounds and sufficiently tackle the inverse care law\textsuperscript{84}. There have been very few situations in which the inverse care law no longer applies. More recently, health care inequalities were narrowed due to the widespread immunisation of people due to COVID-19, in which all backgrounds, ages and genders were included\textsuperscript{321}. Furthermore, anticipatory care planning policy in Scotland, where population modelling is used to identify those over 65 years of age with a high risk of readmission to hospital, has been shown to be effective in regards to the inverse care law and could ensure adequate polypharmacy management for at-risk patients\textsuperscript{235,322}. The observation of the inverse care law arises as a failure to address and mitigate long term existing health inequalities in current policies improving public health, therefore, developments to these policies and inequalities are important and require attention. A 24 year follow up study in social inequalities revealed that socioeconomic status affected the risk of multimorbidity, frailty and disability but did not affect the risk of mortality after these health conditions were displayed in patients. The authors suggested that we need to reduce social inequalities in mortality by way of targeting these aforementioned conditions\textsuperscript{323}. Studies which reveal factors that serve to counteract the uneven socioeconomic access to health care may be of particular importance for current policies which see to overcome (currently widening) health inequalities as well as targeting polypharmacy and multimorbidity. Furthermore, with the lack of evidence that is associated with policy intervention, this tackling of the inverse care law in deprescribing indicates that despite at low levels, the decreasing polypharmacy levels may suggest that the policy on health inequalities and polypharmacy in Scotland is having a positive effect albeit quite small\textsuperscript{295,301,324}. The literature suggests that deprescribing interventions have had a positive effect on patients. This study suggests that, though may be moving in the right direction, more
work is needed\textsuperscript{239}. This research has indicated some ways by which polypharmacy could be tackled by refining medicine management interventions, better access and availability to healthcare services, improved system alerts for deprescribing and medication review, widespread publicising of deprescribing tools for HCP to assist them in deprescribing and educating HCPs on effective ways to deprescribe to improve their confidence, clarifying the roles and responsibilities of those involved in deprescribing and enhancing interprofessional communication skills, particularly between primary and secondary care, without affecting their relationships with their colleagues. Further research would need to be carried out in terms of the effect polypharmacy policy has in practice in Scotland.

8.4 Strengths and Limitations

Utilising mixed methods is one of the strengths of this research. The results of the qualitative research informed the quantitative study by providing a wider and more systematic picture of distribution of polypharmacy amongst patients with asthma. A longitudinal analysis of asthma prescribing provided systematic data on polypharmacy levels, its confounders, age, gender and socioeconomic background, its links to multimorbidity, deprescribing and, also, to hospital admission data/ADR. Using only one methodology would limit my findings. Therefore, comparing the results of these two methodologies allows us to evaluate the experiences of HCPs from their responses in the qualitative interviews and discover insights in changes over time from the graphical findings in the quantitative data analysis. Furthermore, it improves our understanding of medicines management as the exploration of HCPs point of view enhances our awareness of what is happening behind the data. Interviewing HCPs to determine the social contexts in which polypharmacy is managed by HCPs creates a
rich picture of the processes giving rise to polypharmacy and the opportunities and barriers for better polypharmacy management.

However, a challenge presented by mixed methodology is the difficulty to which combine the findings of both the qualitative and the quantitative analyses for a deeper and more robust understanding of the research. Qualitative methods analyse processes but the findings are not always readily generalisable for wider usage beyond the scope of the research. Quantitative methods provide analysis with systematic data but its significance can be hard to establish as the findings are divorced from context. Therefore, when using mixed methodology, crosschecking between each methodology type provides the combined findings of the research. However, it sometimes occurs that the findings of the quantitative data cannot be explained through the qualitative data and vice versa. Due to correlation not equalling causation, occasionally patterns emerge in one part of the investigation that we cannot directly link to behaviours in the other and therefore, the two methodologies do not talk to each other. This was mitigated by attempting to always link the qualitative and quantitative analyses. Any result that could require a deeper explanation in one research method was cross-referenced with the analysis from the second method for clarification. Therefore, both methodologies guided the other in these situations. However, this weakness can be a positive as using mixed methods provides ways to reconcile divergences of findings from different areas of the research that would and could not be identified had only one method of analysis been used. Multiple methods exploring different forms and sources of evidence offers a richer picture (e.g. you can cross check processual understandings from interviews with data about cumulative outcomes from the data modelling) that offers a more intricate and arguably more
robust understanding than one or other approach on its own due to lack diversity of evidence and method\textsuperscript{325}. However, mixed methods utilise greater resources and skill requirements and require dividing effort between two kinds of enquiry and difficulties integrating findings from different kinds of research\textsuperscript{326}.

In this research, using a combination of qualitative and quantitative methods provides an insight into complicated processes and challenges that occur whilst implementing polypharmacy management albeit, at this stage, this study and the existing literature are only able partially to explain these processes. Mixed methods provide a more diverse body of evidence that allow exploration of different factors. However, using mixed methods can still be limited by bias. Initially, a possible bias occurs in sample bias. Convenience sampling was utilised in the qualitative study which can cause bias if the researcher selects a small sample of similar respondents. In this research, this was avoided by actively pursuing a diverse group of respondents from different areas and, therefore HCPs encountered different patient samples, and backgrounds. Additionally, the snowballing technique for recruitment for the qualitative interviews limits to people who consent to being interviewed and are known for having an existing interest in polypharmacy which could affect the research analysis. It could be possible that HCPs with no interest or detailed experience with polypharmacy might not consent to be interviewed. Perhaps, recruiting from an entire GP surgery or hospital department could provide a wider evaluation as this would include people who would not put themselves forward for interview. This could not be achieved in this study due to the difficulty obtaining consent from a GP surgery within the allocated study time frame to test out this hypothesis. Another bias that could influence the research is from the researcher who may unintentionally guide the study by what they think may occur
based on their conduct and interpretation of the research. This was attempted to be removed by way of reflexivity in the qualitative interviews and by using the qualitative analysis to guide the quantitative research continuing the reflexivity and attempting to remove bias in the quantitative analysis as well. Additionally, diverse evidence sources were identified to prevent the limitation of the researcher’s previous knowledge on the research area. This afforded a greater opportunity to identify confounding factors as well as wider supporting evidence.

Though initially adopted as an expedient to secure access to quantitative data, concentrating on asthma in relation to polypharmacy provided a specific focus that became a strength of this research. Asthma is a common comorbidity associated with polypharmacy but it is not well researched\textsuperscript{48}. According to HCPs, in research it is considered less important than other comorbidities such as cardiovascular and renal diseases but asthma provides an interesting narrative in relation to polypharmacy due to multiple inhalers and medications that can cause polypharmacy in its own right and its links to allergies\textsuperscript{36,92}. However, it was discovered that the most prevalent multimorbidities linked to asthma patients presenting with polypharmacy were, in fact, cardiovascular diseases determining that focusing on asthma granted exposure to other comorbidities that are wildly regarded as a more pressing polypharmacy issue\textsuperscript{327}. Moreover, adult-onset asthma affects patients who are more likely to suffer from polypharmacy such as older women and patients from lower socioeconomic backgrounds due, perhaps, to poor air pollution, underemployment leading to poor housing quality and poor diet, high stress levels and depression\textsuperscript{328–330}. These social factors could not be examined in this research but future work could factor these issues in relation to asthma polypharmacy. Therefore, focusing on a comorbidity that
has ties to similar characteristics found in polypharmacy can ameliorate our existing knowledge on asthma polypharmacy and management.

However, focusing on asthma could be seen as a limitation as it inhibits the knowledge gained in this study to be fully applicable to general polypharmacy. In this research, the existence of the interviews with staff having strong polypharmacy experience from a variety of different specialisations attempted to mitigate this limitation. However, the quantitative data had no comparison with general patients presenting with polypharmacy and asthma patients presenting with polypharmacy, therefore, limiting the conclusions to only patients with asthma. The findings in this research are pertinent to a biased sample of patients with asthma and may not be generalisable to patients presenting with polypharmacy with a selection of multiple morbidities that do not include asthma. The decision to focus on asthma polypharmacy data proved to be a beneficial and pragmatic decision but this focus is attributable to delays in data access acquisitions and directed the study to focus on a particular condition and not polypharmacy generally. This focus limits the generalisability of the research findings to all patients presenting with polypharmacy but did allow for generalisability in patients with asthma that could be linked to other comorbidity focused effects of polypharmacy. Moreover, this experience was welcome as the process of obtaining data access and making difficult research choices are vital learning experiences.

Beyond focusing on asthma, a further weakness of this research is being limited to a single geographical area within the quantitative analysis. The prescribing dataset contained just under 10% of the Scottish population to analyse. It is not a huge sample size, particularly as it only contained people with an asthma diagnosis, however, it
does contain a significant number of patients to analyse despite the limitations of not containing the whole Scottish population and the limitation of only patients diagnosed with asthma. Within the interviews, a small sample of HCPs from both Scotland and England were included in the study to allow for a comparison between both countries. However, the prescribing data only contained patients from Scotland. This causes a disconnect between the quantitative and qualitative arms of the study. As a comparison, the prescribing data in England cannot be analysed. The interviews were conducted to account for a wider geographical area to alleviate the issues in the prescribing data being limited to Scotland to understand the differences between Scotland and England in polypharmacy management practice. Also, regardless of whether the interviews allowed for a comparison between two countries, there is always a limited number of stakeholders being interviewed. Reaching saturation is a way in which the small number of opinions can alleviate some of the issues with smaller sample sizes. However, it does still affect the generalisability of the opinions and subsequent data analysis to the general HCP population to have such small numbers of HCPs to pool from.

In terms of the analysis and the literature utilised to back up said analyses, many of the studies referenced are not UK-based studies. This was both a strength and a weakness to the research. The strength in the inclusion of international studies provides a wider base of investigation to discover how polypharmacy presents itself and is monitored in different parts of the world. However, the limitation in including such international studies is that it fails to consider the economic differences in polypharmacy treatment worldwide. As the UK healthcare landscape is very different to other countries, given that it is free at the point of access and patients with asthma
receive their prescriptions for free in both Scotland and England, using international studies might not give a full detailed view of what is occurring in the UK.

Another limitation is linked to issues regarding the modelling of quantitative data. Due to the possibility of complex effects where association is not causation, the findings may reflect other factors at play. One example is the influence of mortality rates on levels of polypharmacy over time, particularly in older age categories. This study discovered that older patients (over 80) exhibited both lower and declining polypharmacy levels in comparison to younger age groups, particularly between 60-80. Earlier death rates amongst younger patients from lower socioeconomic backgrounds could skew the socioeconomic status distribution of polypharmacy particularly in older patients. However, as it was not possible to adjust for death rates as a confounder on this dataset, the rate of deaths was analysed over time and the levels of mortality per age range and socioeconomic background was calculated to ensure that these low levels of polypharmacy in the over 80s were occurring due to a decrease in polypharmacy and not because of the possible impact of mortality and, consequent changes in the socioeconomic distribution of patients over 80. This was to take into consideration the possibility of patient death altering the appearance of the results. The demographics of each of age range and SIMD category were calculated as a summary beforehand which allowed us to determine the size of each stratified population before conducting any polypharmacy analysis to further check for possible issues with death rates affecting the results. To account for death rates in the deprescribing analysis, any prescriptions that had stopped due to patient death were removed from analysis, eliminating patients who would possibly have died over the seven-year period analysed and skewed the analysis. The findings suggest that
mortality is not an artefact of attrition. However, these death rates do not provide a complete picture of mortality in the data. In future research, a population wide analysis of mortality rates and confounding in patients with asthma with polypharmacy could provide concrete findings and detailed explanations to the polypharmacy levels in relation to patient death which entails a different quantitative methodology that this research was unable to undertake.

Another possible confounding factor is determining if patients have been correctly diagnosed with asthma. Asthma is very commonly misdiagnosed according to the literature and, consequently, some of the patients in this study could have been misdiagnosed with asthma. To deal with this, the polypharmacy levels in the prescribing data were analysed by ‘asthma attack’ and ‘asthma encounter’ to confirm if there were differences in patterns in polypharmacy in patients with a confirmed asthma exacerbation. There were no great differences between the patterns with a more confirmed existence of asthma in patients. These graphs are located in appendix 2 (figs. 2.5 and 2.6). Attempting to analyse hospital admissions caused by asthma using the read codes in the asthma hospital admissions data resulted in small sample sizes when stratifying by polypharmacy level, this limited what conclusions could be drawn from this data. More detailed research is required to account for the misdiagnosis of asthma particularly in secondary care data.

8.5 Implications for policy and practice

The clinical implications of this research could influence polypharmacy policy and practice by revealing the way in which patients presenting with polypharmacy interact with healthcare services. As noted in the main findings, elderly frail patients have a
propensity to ill health linked to both their age and increased multimorbidity. Due to this, patients over the age of 75 with frailty engage with healthcare services more frequently. This may account for the lower levels of polypharmacy and higher levels of deprescribing found in this demographic. The picture that was revealed diverged from broader socio-economic patterns in the distribution of ill health. There was the expectation that higher levels of polypharmacy over time being displayed would coincide with increased disease incidence. This was not observed as multimorbidity levels were high with higher polypharmacy levels but stayed consistently higher as polypharmacy reduced over time and then, subsequently, lowered more than polypharmacy levels reduced. This could be due to changes to diagnoses and prescriptions taking time to be implemented by HCPs. Furthermore, higher levels of deprescribing were expected over time in patients with excessive polypharmacy when, in actuality, low levels were observed. Also, it was expected that higher levels of polypharmacy and multimorbidity occurred based on increasing age and lower socioeconomic background combined. However, the actual findings showed reduced polypharmacy and a slight increase in deprescribing over time in older patients from poorer backgrounds. This indicates that polypharmacy management techniques are developing albeit slowly, particularly in elderly patients but that management techniques need improving in younger multimorbid patients from lower socioeconomic backgrounds. Moreover, deprescribing incentives need to be developed further, particularly in those with more than 10 medications.

Currently, polypharmacy management procedures are codified in polypharmacy/deprescribing guidelines that point the reader in the direction to which these techniques are performed\textsuperscript{331–333}. However, these guidelines are few and far
between, maintain one-size-fits-all instructions, not well implemented, not standardised and/or are limited in focus to older people, usually over 65\(^{290}\). Generally, patients between the ages of 60 and 80 are at the highest risk of polypharmacy. However, this study showed that patients as young as 40 to 49 began experiencing polypharmacy. These younger patients, particularly those with multimorbidities and from lower socioeconomic backgrounds, who may not regularly encounter their healthcare provider and thereby may have less opportunity to receive adequate polypharmacy management. The evidence in this study found this younger and socially deprived cohort experiences a high incidence of polypharmacy, coupled with extremely low levels of deprescribing. These patients do not seem to receive an adequate medication review. This could arise from a range of factors, including inadequate healthcare services located in these socially deprived areas and patients in these areas feeling disenfranchised. In recent literature, opportunities related to medication reviews only speak of healthcare staff collaboration to improve polypharmacy management but there is no literature referring to the inability of patients to have a medication review due to lack of opportunity/access to health services\(^{212}\).

Furthermore, there is a fixation on the effectiveness of medication reviews to focus on reducing or identifying high risk medication rather than considering ‘how’ patients are able to receive these medication reviews. Therefore, there is a focus on how the HCP conducts the medication review rather than whether the patient has the opportunity to have one. Additionally, a lack of opportunity could exist, amongst patients who do not regularly visit their GP, get admitted to hospital or feel empowered by their HCPs, to receive medication reviews. Opportunities for medication reviews and, in turn, shared decision making is worthy of further research to determine why this possible lack of polypharmacy management opportunities are being perpetuated in healthcare
environments. Also, it would be beneficial to investigate how we can provide better opportunities for future patients to obtain structured medication reviews. Adherence to guidelines is generally low. Additionally, HCPs are not highly inclined to follow polypharmacy guidelines, especially GPs and asthma specialists, due to heavy workloads, time constraints, possible anxiety regarding changing prescriptions by another colleague and, perhaps, concerns about harming patients by deprescribing, particularly if these patients are keen to keep/have multiple medications. Therefore, despite the importance of old frail patients receiving better access to medical services, there is a need to also target groups with poor access to health information and to health services, mainly located in younger and lower socioeconomic groups. Equity in healthcare is an issue the Scottish Government is aware of in their 2022 report on primary care health inequalities\(^{334}\). Perhaps evaluating polypharmacy management strategies to provide a better ‘guide’ for HCPs to follow could improve techniques to reduce polypharmacy in patients outwith the current guideline limits. It might not be best to suggest enhancing current guidelines due to their contentious usage but altering guidelines could provide a steppingstone for polypharmacy management improvement. An issue with the introduction of guidelines or documentation in polypharmacy is HCP implementation. However, there is a policy-implementation gap often related to lack of resources indicating that the policy might be fine but fails because HCPs can’t find the resource to do the job or are unaware of the resources’ existence. Also, some HCPs may not feel they need to look at the guideline due to their knowledge already sufficient to review medications holistically with patients. Among the respondents, few HCPs made systematic use of polypharmacy guidelines, despite the quantitative research identifying changes in pattern that occurred in
parallel with the introduction of Scottish Polypharmacy Guidance in 2012. Therefore, these documents may not be utilised effectively throughout the NHS.

Continuing on the topic of guidelines and polypharmacy management techniques, this research suggests that polypharmacy policy and practice could develop specific deprescribing techniques. Proactive deprescribing can occur if regular medication reviews are conducted in tandem with the patient\textsuperscript{127,128}. This research discovered that medication reviews did not occur regularly as they potentially could do and the patient was not necessarily always involved in shared decision making. Polypharmacy medication reviews could be regulated to the same degree that annual asthma reviews are or existing asthma reviews could include a more in-depth polypharmacy component. However, regulating polypharmacy reviews would increase the workloads of both the regulatory bodies and the HCPs required to conduct these reviews. It would cause polypharmacy reviews to become a tick-box exercise for HCPs which would remove the patient-centred care element of medicines management. Furthermore, HCPs are already overworked and have restricted time to implement these reviews. This means that trade-offs would occur to make time in HCPs busy schedule to conduct these reviews. These reviews are viewed by HCPs as time-consuming and could take time away from other patients who urgently require their HCP. Possibly, incentives to conduct medication reviews similar to the now defunct QOF in Scottish healthcare could increase the implementation of medication reviews despite the time-consuming element perceived by HCPs.

Levels of deprescribing were found to be significantly lower in patients with excessive polypharmacy. But, because it is more likely that patients prescribed 10 or more
medication have inappropriate polypharmacy it seems that polypharmacy management techniques do not, this population undergo regular medication reviews. As well as targeting younger patients, there needs to be more effective ways for management to target and mitigate inappropriate polypharmacy. Moreover, the benefit vs risk strategy used in evaluating medications may be ineffective as it does not alleviate nurses’ and pharmacists’ concerns that removing medication might cause their patient harm. This explains why nurses and pharmacists are reluctant to remove medication and are more comfortable with reducing dosages than with completely deprescribing. As a result, we observe that fully deprescribing a medication is much less frequent than reductions in dose. Furthermore, it could be linked to the fact that HCPs have less experience removing medications than prescribing new medications\textsuperscript{127}. Henceforth, empowering HCPs to deprescribe could be achieved by teaching how to deprescribe medication effectively to HCPs who missed receiving deprescribing training at either medical school or before it was introduced into independent prescribing curriculums\textsuperscript{335}. If all nurses and pharmacists were trained to deprescribe effectively, this could assist GPs and hospital doctors with their workload and could arrange a balanced distribution of work. However, this would cause more pressure to be added to nurses’ and pharmacists’ already busy schedules and, therefore, might cause additional workload issues as well. Considering deprescribing like prescribing could alleviate issues with triggering medication reviews and identifying patients requiring deprescribed medications\textsuperscript{284}. Furthermore, HCPs noted that the role of the deprescriber was unclear which caused issues during medication reviews. None of the HCPs could agree on who had the final authority when deprescribing. The lack of clarity regarding roles and responsibilities when deprescribing was exacerbated by issues in poor communication between primary and
secondary care. Poor communication perpetuated this cycle of each care system considering the other responsible for deprescribing. Therefore, the function and roles associated with medication reviews across care systems need to be developed to enhance the discovery of inappropriate polypharmacy in patients, improve interprofessional communication between HCPs and prevent unnecessary drug related hospital admissions. However, though developing clear roles and responsibilities would be the solution in an ideal world, given the reality of healthcare with the existing time constraints and workload issues for HCPs, simply (re)defining roles may not be sufficient to fix issues with polypharmacy management.

If there were guidelines or detailed regulations/documentation in which HCPs have the final say on deprescribing with clearer roles when conducting medication reviews and deprescribing decisions could alleviate these concerns\textsuperscript{190,333}. Nonetheless, the issue of adherence to these documents still presents a major concern\textsuperscript{55}. This research did not focus on adherence to guidelines but merely explored how guidelines are utilised. Therefore, the existence of these documents may not improve adherence but having clear cut rules and regulations in place will prevent confusion with roles and responsibilities and put the responsibility on the HCP to be aware of these facts if they are realised in healthcare policy. Additionally, having such documentation could prevent any possible medico-legal issues that could arise when deprescribing. This could prevent disagreements in changes in medications that are accentuated with negative patient perception\textsuperscript{336}. However, a document of this nature might hinder clinical judgement and patient-centred care, so the creation of such regulation would need to be carefully worded and crafted in order to prevent this from occurring.
8.5.1 Implications for future research

This study discovered that patients prescribed 15 or more medications do not receive the levels of polypharmacy management that they require. It is unlikely that a patient would require 15 or more medications for all their comorbidities that they possess and that these medications would have no contraindications\textsuperscript{337}. Extreme polypharmacy is a clear indicator for multimorbidity. Thus, there is always a degree of risk involved when prescribing patients multiple medications due to multimorbidity\textsuperscript{338}. Furthermore, the levels of ADR hospital admissions are overwhelmingly high in excessive patients presenting with polypharmacy in comparison to the low levels of deprescribing, both in stepping down and removing. However, this study shows that patients with excessive polypharmacy require increased monitoring and attention regardless of their social factors. Moreover, the discovery of the predominant multimorbidities and drugs prescribed in patients with asthma with polypharmacy being related to cardiovascular diseases and not respiratory diseases such as COPD or other allergic conditions such as eczema. This discovery can place asthma as an important comorbidity to factor into polypharmacy research due to its substantial connection with other diseases that are considered more serious in nature. Likewise, the discovery that there is an inverse distribution of deprescribing in relation to age, gender and socioeconomic background in patients with asthma informs us that polypharmacy can be more influential on peoples’ health rather than the social features found in peoples’ lives. This positive breakthrough could be found in other comorbidities with polypharmacy and other general patients presenting with polypharmacy.

8.6 Future Work
This study can be developed and expanded to tackle a range of limitations. The study covers a limited timeframe and does not extend to current data. This limitation caused analysis over time to be restricted. Analysing data after 2017 allows a longer timeframe on processes that were changing over time in ways that could not be fully explored with pre-2017 data. This could explore interesting outcomes on polypharmacy levels in the last 4-5 years. Of particular interest would be changes after 2018 when the Scottish Government introduced an updated version of their Polypharmacy Guidance, particularly as the focus of the guidance shifted to ‘Realistic Medicine’ rather than lowering polypharmacy overall\textsuperscript{17}. Additionally, the qualitative research in this PhD touched on COVID-19 in relation to polypharmacy management and healthcare service provision. Analysing the prescribing data since 2020 could detect some novel findings beyond the lack of access and continued relying on repeat prescriptions which may not have been monitored during lockdown\textsuperscript{339}. Thus, researching the monitoring systems of repeat prescriptions in both primary and secondary care could point to more situations in which inappropriate polypharmacy and prescribing cascades occur.

Researching deprescribing tools in healthcare e-prescribing systems is, also, potentially interesting. This study investigated the links between primary and secondary care in relation to interprofessional communication and polypharmacy monitoring across care types and deprescribing guidelines were explored. However, evaluating whether HCPs use deprescribing tools or would consider utilising deprescribing tools in their future polypharmacy management techniques could ascertain views on deprescribing and create opportunities for shared decision making and improvements in the prescriber-patient relationship\textsuperscript{240}. These issues remain
unexplored. Furthermore, assessing the implementation of such tools and their possible long-term efficacy could be important to understand.

This study could be replicated in longitudinal data with patients presenting with polypharmacy not linked to a specific morbidity. This would provide outcomes that could be more universal to the polypharmacy population. Having a general understanding of polypharmacy in relation to how individual comorbidities affect patients could contribute to improving our knowledge of how polypharmacy is experienced on an individual basis. Furthermore, detailed research on polypharmacy demographics by way of different stratification factors could paint a more precise picture of patients presenting with polypharmacy. Over-stratification can become an issue in research but with the movement towards more personalised medicine, stratification is very important to discover possible associations in smaller or less researched groups of patients. Healthcare equity is a priority for the Scottish Government at present and a study on equity and its links to potential over-stratification of populations may be beneficial for future policy. Therefore, one of these factors is polypharmacy and ethnicity. As certain populations are pre-disposed to certain disease types this could be linked to certain polypharmacy patterns which could cause higher levels of polypharmacy in other parts of the world.

This study focuses on the HCP perspective on polypharmacy management but it seems imperative to gain patients perspectives on polypharmacy management with particular emphasis on medication reviews, shared decision making and deprescribing. Securing ethical access to interviewing patients is particularly difficult. Furthermore, as patients interact with health services sporadically, their views are
difficult to assess, particularly as they are not well equipped to observe changes in service due to technology or adoption of tools. Patients might be unaware of the introduction of these particular innovations. Literature examining patient perspectives on polypharmacy and deprescribing using qualitative methods mainly focuses on the older population with polypharmacy and not younger patients, particularly those from lower socioeconomic backgrounds\textsuperscript{341,342}. Furthermore, interviewing patients on their perspectives of the findings of this research regarding the inverse distribution of deprescribing by age, gender and socioeconomic backgrounds could deliver some interesting conclusions. Also, patient views regarding medication reviews could assist HCPs and future medication review guidelines in providing a better experience for both HCP and patient. Empowering patients through shared decision making should be the aim of future polypharmacy treatment as the patient should be at the centre of their care and viewed as a priority by their HCPs, particularly those from lower socioeconomic backgrounds and lower levels of health literacy who are less likely to challenge prescribing or deprescribing decision without a prompt from their HCP\textsuperscript{130,343,344}.

8.7 Conclusion

This study aimed to enhance our comprehension of polypharmacy and polypharmacy management in patients with asthma through a mixed method study of prescribing data and qualitative interviews with HCPs. Qualitative research provided a rich picture of the complex processes involved in asthma polypharmacy but did not offer the generalised applicability and outcomes of these processes that quantitative methods offer. Conversely, quantitative research provided key insights into the outcomes of asthma polypharmacy but not the processes. Undertaking both detailed qualitative
interviews and longitudinal quantitative studies presented challenges by way of increasing the scale of research methods and the range of tools and skills required. These challenges are, further, intensified by the difficulty in combining these differing forms of evidence. However, additional insights were mined from these mixed methods linking HCP perceptions regarding care processes with general data modelling of patient morbidity patterns and engagement with health services that were not necessarily apparent to the participants.

This study highlighted the importance of medication reviews and deprescribing in asthma patients presenting with polypharmacy. It was suggested that frail over 75s had more opportunity for medication reviews explaining their levels of polypharmacy decreasing in comparison to younger multimorbid patients who, seemingly, did not receive sufficient medication reviews due to their lack of interaction with health services. Younger patients did not exhibit a similar decline in their polypharmacy as their frail older counterpart. It was demonstrated that patients with asthma with multimorbidity at a younger age in lower socioeconomic backgrounds were inclined to experience polypharmacy. Low levels of deprescribing in patients with excessive polypharmacy indicated that medication reviews are insufficient in this at-risk population and/or HCPs face a series of barriers to deprescribe, mainly due to a lack of confidence in deprescribing or fears of backlash of medication removal from either patients or, if applicable, their involvement in another colleagues’ prescribing decision. The discovery of the lowering of polypharmacy and the increase of deprescribing over time suggests an association with the introduction of the Scottish Polypharmacy Guidance. Despite traditional access to care inequalities persisting in healthcare, deprescribing patterns were complex, despite existing social factors, suggesting that
common health inequalities as noted by Tudor Hart’s inverse care law may not exist with the confines of deprescribing in this study.

This research provided insight into the patterns of deprescribing in asthma patients presenting with polypharmacy and highlighted unique barriers in the implementation of polypharmacy management techniques by HCPs. The analysis of primary and secondary care treatment of asthma patients presenting with polypharmacy showed areas of polypharmacy management that require further development. In future, polypharmacy, and healthcare, policy might be usefully guided by detailed evidence about the operation of health services and their health outcomes in reducing polypharmacy and recommendations for the practice of effective medicine management.
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Appendices

Appendix 1

1.1 PIS and Informed Consent Form
Participant Information Sheet

Understanding and Managing Polypharmacy

You are invited to take part in a research study. To help you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Polypharmacy refers to patients on various medications, usually five or more, at any given time. In order to manage inappropriate polypharmacy, which is when one or more drugs prescribed to a patient are not required as they are, possibly, ineffective or harmful, a new system will need to be created to improve the care of multi-morbid patients while minimising the risks of adverse drug reactions. Some EU countries are developing polypharmacy guidelines to monitor inappropriate polypharmacy at primary levels.

The aim of my research is to identify the demographics of patients presenting with polypharmacy primarily by analysing prescribing data, focusing in the first instance on asthma. A further aim is to examine whether polypharmacy is considered an important factor for asthma healthcare professionals when prescribing medications and, if there are issues with the medical treatment of asthma patients. Also, another aim will be observing the use and effectiveness of medication reviews. To guide this, a qualitative study will be undertaken with stakeholders to characterise the context and social processes involved in prescribing in primary and secondary care.

Why have I been invited to take part?

You have been asked to take part as you are a healthcare professional that works with asthma patients in any capacity.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.
What will happen if I take part?

The research investigator, Maram Zahraa PhD student, will be responsible for the data collected in this study. Qualitative data will be collected in the form of interview questions and responses. Interviews will take around 20-60 minutes depending on the responses of the participant. All interviews will be recorded unless the participant does not wish to be recorded in which case their responses will be noted. These responses will, then, be de-identified, transcribed by a third party, anonymised and used towards a PhD project analysis. Data will be stored safely on a university laptop, transferred to an encrypted university server and will be deleted upon the student completion of PhD studies. This data will not be shared with any other organisations.

Is there anything I need to do or avoid?

Participants must avoid talking about specific patients or other health care professionals and speak in general terms.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the healthcare of patients in the future.

What are the possible disadvantages of taking part?

The possible disadvantages are that the interview may take up too much time for the participants.

You will receive no payment for your participation. The data will not be used by any member of the project team for commercial purposes. Therefore, you should not expect any royalties or payments from the research project in the future.

What if there are any problems?

If you have a concern about any aspect of this study please contact Maram Zahraa, maram.zahraa@ed.ac.uk who will do their best to answer your questions.

What will happen if I don’t want to carry on with the study?

Your participation is voluntary and, therefore, all participants will be able to withdraw their responses at any point, until publication of the findings.
What happens when the study is finished?

All data pertaining to this research will be kept for one year post completion of the researchers’ PhD studies and will subsequently be permanently deleted. The data analysis will, then, be published in an article format.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage.

How will we use information about you?
We will need to use information from you for this research project. This information will include your name, contact details and job description. The Researcher will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.
Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason, and all data that has been collected about you will be immediately deleted.

Where can you find out more about how your information is used?

You can find out more about how we use your information
By contacting the sponsor researchgovernance@ed.ac.uk,
by asking research investigator, Maram Zahraa
by sending an email to maram.zahraa@ed.ac.uk
by ringing us on 07758800622

What will happen to the results of the study?

This study will be written up as a publication and as part of a PhD thesis. You will not be identifiable from any published results.

The completed analysis will aim to be published. Once published, this will be sent to the participants as a pdf via email if they so wish.

Who is organising and funding the research?

This study has been organised by the University of Edinburgh and sponsored by ACCORD.

Who has reviewed the study?
The study proposal has been reviewed by Ethics Committee at the School of Social and Political Science and by the Edinburgh Medical School Research Ethics Committee, University of Edinburgh.

**Researcher Contact Details**

If you have any further questions about the study, please contact Maram Zahraa on 07758800622 or email on: maram.zahraa@ed.ac.uk

You can also contact Maram Zahraa’s supervisor:

Prof. Robin Williams  
Old Surgeon’s Hall  
High School Yards, Edinburgh  
EH1 1LZ  
Tel: 0131 650 6387  
Email:

**Complaints**

If you wish to make a complaint about the study please contact:

ACCORD  
The Queen’s Medical Research Institute  
47 Little France Crescent  
Edinburgh  
EH16 4TJ  
Tel: 0131 242 9261  
Email: researchgovernance@ed.ac.uk
CONSENT FORM
Understanding and Managing Polypharmacy

1. I confirm that I have read and understand the information sheet (16/02/2021 v4.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my legal rights being affected.

3. I understand that relevant sections of the data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), from regulatory authorities or from the NHS organisation where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.

4. I understand that data collected about me during the study will be converted to anonymised data.

5. I agree to my interview being audio recorded.

6. I agree to my audio recorded interview being transcribed by a University approved third-party contractor.

7. I agree to take part in the above study.

Name of Person Giving Consent ___________________________________________ Date ____________ Signature ______________________________

Name of Person Receiving Consent _________________________________________ Date ____________ Signature ______________________________

1x original – into Site File; 1x copy – to Participant;
### Appendix 2

**Table 2.1: Charlson Comorbidity Index Conditions and Weight**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Weights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial Infarction</td>
<td>1</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>1</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>1</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>1</td>
</tr>
<tr>
<td>Dementia</td>
<td>2</td>
</tr>
<tr>
<td>Paraplegia and Hemiplegia</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes with Complications</td>
<td>2</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>2</td>
</tr>
<tr>
<td>Mild Liver Disease</td>
<td>1</td>
</tr>
<tr>
<td>Moderate or Severe Liver Disease</td>
<td>3</td>
</tr>
<tr>
<td>Peptic Ulcers</td>
<td>1</td>
</tr>
<tr>
<td>Rheumatic Disease</td>
<td>1</td>
</tr>
<tr>
<td>Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS)</td>
<td>6</td>
</tr>
<tr>
<td>Cancer</td>
<td>2</td>
</tr>
<tr>
<td>Metastatic Solid Tumor</td>
<td>6</td>
</tr>
</tbody>
</table>

**Table 2.2 Average number of medications prescribed every 6 months**

<table>
<thead>
<tr>
<th>Number of Medication Prescribed every six months</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>4</td>
</tr>
<tr>
<td>Mean</td>
<td>5.19</td>
</tr>
<tr>
<td>3rd Quartile</td>
<td>7</td>
</tr>
<tr>
<td>Max</td>
<td>35</td>
</tr>
</tbody>
</table>

Table 2.3 shows a summary of the number of drugs that are prescribed to patients every six months within the dataset.

**Table 2.3 Percentages of the most prescribed drugs in the prescribing dataset**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>6.32</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>5.32</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>5.06</td>
</tr>
<tr>
<td>Aspirin</td>
<td>5.04</td>
</tr>
</tbody>
</table>
Table 2.3 shows the most prescribed drugs in the asthma dataset and the percentage of patients within the dataset with asthma that have been prescribed these drugs.

---

Figure 2.4 shows the number of days of since the last prescription and the percentages of patient who had repeat prescriptions in that time frame.
Figure 2.5 shows the percentage proportion of patients with polypharmacy every six months who have had an asthma attack.

Figure 2.6 shows the smoothed average proportion of patients stratified by asthma attack every 6 months. The levels of polypharmacy were stratified by 5-9, 10-14 and 15+ medications.

Table 2.7 Statistical Analysis of the Variables in the Prescribing Dataset
<table>
<thead>
<tr>
<th>Variable</th>
<th>Statistical Analysis &gt; 5 drugs</th>
<th>Age-adjusted for confounders</th>
<th>Statistical Analysis &gt; 10 drugs</th>
<th>Age-adjusted for confounders</th>
<th>Statistical Analysis &gt; 15 drugs</th>
<th>Age-adjusted for confounders</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIMD 1</td>
<td>0.001</td>
<td>0.995</td>
<td>0.995</td>
<td>0.985</td>
<td>&gt;0.001</td>
<td>0.995</td>
</tr>
<tr>
<td>SIMD 2</td>
<td>0.001</td>
<td>0.997</td>
<td>0.996</td>
<td>0.996</td>
<td>&gt;0.001</td>
<td>0.996</td>
</tr>
<tr>
<td>SIMD 3</td>
<td>0.001</td>
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<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>SIMD 4</td>
<td>0.001</td>
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<td>0.996</td>
<td>0.996</td>
<td>&gt;0.001</td>
<td>0.996</td>
</tr>
<tr>
<td>SIMD 5</td>
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<td>0.994</td>
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<tr>
<td>Sex - Male</td>
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<td>0.999</td>
<td>0.999</td>
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<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Age</td>
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<td>0.995</td>
<td>0.995</td>
<td>&gt;0.001</td>
<td>0.995</td>
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<tr>
<td>10-19 yrs</td>
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<td>0.999</td>
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<tr>
<td>20-29</td>
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<td>0.999</td>
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<tr>
<td>80-89</td>
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<td>0.999</td>
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<td>90-99</td>
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<td>0.999</td>
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<tr>
<td>BMI</td>
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<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
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</tr>
<tr>
<td>Smoking Current</td>
<td>0.001</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Current</td>
<td>0.001</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Never</td>
<td>0.001</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>0.001</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>AIDS</td>
<td>0.001</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>0.001</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
<tr>
<td>Anxiety &amp; Depression</td>
<td>0.001</td>
<td>0.999</td>
<td>0.999</td>
<td>0.999</td>
<td>&gt;0.001</td>
<td>0.999</td>
</tr>
</tbody>
</table>

318
<table>
<thead>
<tr>
<th>Condition</th>
<th>Probability</th>
<th>10-year Survival Rate</th>
<th>50-year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Attack</td>
<td>0.009 1.093 1.022-1.170</td>
<td>0.003 1.110 1.038-1.188</td>
<td>0.622 1.017 0.952-1.087</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.002 1.113 1.041-1.191</td>
<td>0.005 1.101 1.030-1.179</td>
<td>0.459 1.025 0.961-1.086</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>&gt;0.001 1.134 1.060-1.215</td>
<td>0.001 1.120 1.041-1.201</td>
<td>0.277 1.037 0.972-1.109</td>
</tr>
<tr>
<td>Congestive Heart Disease</td>
<td>&gt;0.001 1.132 1.057-1.214</td>
<td>0.001 1.017 1.043-1.199</td>
<td>0.270 1.038 0.971-1.110</td>
</tr>
<tr>
<td>COPD</td>
<td>0.011 1.082 1.021-1.169</td>
<td>0.005 1.012 1.031-1.180</td>
<td>0.51 1.023 0.959-1.093</td>
</tr>
<tr>
<td>Dementia</td>
<td>0.001 1.120 1.047-1.201</td>
<td>0.011 1.093 1.021-1.172</td>
<td>0.336 1.033 0.987-1.105</td>
</tr>
<tr>
<td>Diabetes</td>
<td>&gt;0.001 1.133 1.059-1.213</td>
<td>&gt;0.001 1.132 1.058-1.212</td>
<td>0.32 1.034 0.969-1.106</td>
</tr>
<tr>
<td>Diabetes with complications</td>
<td>&gt;0.001 1.145 1.070-1.226</td>
<td>&gt;0.001 1.144 1.070-1.226</td>
<td>0.32 1.034 0.969-1.106</td>
</tr>
<tr>
<td>Eczema</td>
<td>0.037 1.075 1.005-1.151</td>
<td>0.005 1.102 1.031-1.180</td>
<td>0.675 1.014 0.950-1.104</td>
</tr>
<tr>
<td>GERD</td>
<td>0.007 1.097 1.027-1.175</td>
<td>0.006 1.100 1.029-1.178</td>
<td>0.553 1.020 0.956-1.097</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>0.007 1.106 1.028-1.190</td>
<td>0.004 1.114 1.030-1.199</td>
<td>0.438 1.028 0.960-1.101</td>
</tr>
<tr>
<td>Metastatic Tumour</td>
<td>0.001 1.125 1.049-1.209</td>
<td>0.003 1.114 1.038-1.198</td>
<td>0.334 1.034 0.967-1.108</td>
</tr>
<tr>
<td>Mild Liver Disease</td>
<td>0.003 1.109 1.036-1.189</td>
<td>&gt;0.001 1.110 1.037-1.191</td>
<td>0.470 1.025 0.950-1.107</td>
</tr>
<tr>
<td>Moderate Liver Disease</td>
<td>&gt;0.001 1.140 1.061-1.227</td>
<td>&gt;0.001 1.143 1.063-1.230</td>
<td>0.756 1.011 0.945-1.103</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>&gt;0.001 1.145 1.075-1.227</td>
<td>&gt;0.001 1.132 1.058-1.213</td>
<td>0.194 1.045 0.978-1.118</td>
</tr>
<tr>
<td>Nasal Polyps</td>
<td>0.001 1.119 1.046-1.198</td>
<td>0.011 1.118 1.045-1.197</td>
<td>0.794 1.011 0.947-1.081</td>
</tr>
<tr>
<td>Peptic Ulcer Disease</td>
<td>&gt;0.001 1.135 1.061-1.217</td>
<td>&gt;0.001 1.132 1.058-1.213</td>
<td>0.444 1.026 0.961-1.099</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>&gt;0.001 1.138 1.062-1.220</td>
<td>&gt;0.001 1.124 1.049-1.205</td>
<td>0.235 1.041 0.975-1.114</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>&gt;0.001 1.136 1.062-1.216</td>
<td>0.003 1.118 1.046-1.186</td>
<td>0.316 1.035 0.969-1.106</td>
</tr>
<tr>
<td>Rheumatological Disease</td>
<td>&gt;0.001 1.117 1.094-1.197</td>
<td>0.003 1.110 1.032-1.199</td>
<td>0.492 1.024 0.998-1.095</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>0.348 1.075 1.066-1.151</td>
<td>0.007 1.098 1.027-1.176</td>
<td>0.777 1.010 0.946-1.080</td>
</tr>
<tr>
<td>RI</td>
<td>0.009 1.094 1.024-1.171</td>
<td>0.003 1.107 1.035-1.185</td>
<td>0.547 1.021 0.956-1.090</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition</th>
<th>Probability</th>
<th>10-year Survival Rate</th>
<th>50-year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Attack</td>
<td>&gt;0.001 1.004-1.106</td>
<td>&gt;0.001 1.004-1.106</td>
<td>0.379 1.004-1.106</td>
</tr>
</tbody>
</table>
Table 2.7 shows the statistical analysis carried out on the prescribing data. The statistical analysis shows the p values, rate ratios and 95% CI of the age categories, SIMD, comorbidities, gender, BMI and smoking with and without adjusting for confounders. The confounders were age, SIMD, gender and comorbidities. A statistically significant P value was deemed lower the 0.05.
Appendix 3

Table 3.1 Number of patients with a Prednisolone Prescription per year

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>855</td>
<td>479</td>
<td>376</td>
</tr>
<tr>
<td>2010</td>
<td>601</td>
<td>343</td>
<td>258</td>
</tr>
<tr>
<td>2011</td>
<td>357</td>
<td>182</td>
<td>175</td>
</tr>
<tr>
<td>2012</td>
<td>490</td>
<td>240</td>
<td>250</td>
</tr>
<tr>
<td>2013</td>
<td>624</td>
<td>332</td>
<td>292</td>
</tr>
<tr>
<td>2014</td>
<td>721</td>
<td>415</td>
<td>306</td>
</tr>
<tr>
<td>2015</td>
<td>1088</td>
<td>620</td>
<td>468</td>
</tr>
<tr>
<td>2016</td>
<td>876</td>
<td>466</td>
<td>410</td>
</tr>
</tbody>
</table>

Table 3.1 shows the number of patients who had a Prednisolone prescription per year noted in the asthma dataset. This shows if a patient had at least one prescription of Prednisolone. All of these patients have an asthma diagnosis.

![Number of patients with a Prednisolone prescription per year](image)

Figure 3.2 represents table 1 in graph form.

Table 3.3 Total Volume of Prednisolone Prescriptions by sex

<table>
<thead>
<tr>
<th>Year</th>
<th>Prednisolone Prescriptions in Men</th>
<th>Prednisolone Prescriptions in Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>7534</td>
<td>12522</td>
</tr>
<tr>
<td>2010</td>
<td>8910</td>
<td>14887</td>
</tr>
<tr>
<td>2011</td>
<td>8276</td>
<td>13807</td>
</tr>
<tr>
<td>2012</td>
<td>10704</td>
<td>17317</td>
</tr>
<tr>
<td>2013</td>
<td>11092</td>
<td>17476</td>
</tr>
<tr>
<td>2014</td>
<td>11332</td>
<td>18392</td>
</tr>
<tr>
<td>2015</td>
<td>11605</td>
<td>19249</td>
</tr>
<tr>
<td>2016</td>
<td>11704</td>
<td>19426</td>
</tr>
</tbody>
</table>

Table 3.3 shows the total volume of Prednisolone prescriptions each year filtered by gender. This shows any time an ID was prescribed Prednisolone.
Figure 3.4 shows table 2 in graph format.
Figure 4.1 shows a smoothed average of the number of annual prescriptions against the age of the patient at the time of dispensation.
Figure 4.2 shows a smoothed average of the percentage proportion of repeat prescriptions per patient per year.

Figure 4.3 shows the average number of repeat prescriptions per year between the years 2009 and 2016.
Appendix 5

Figure 5.1 shows the six-month proportion of patients with polypharmacy who had a hospital admission. The polypharmacy categories were 5-9 medications, 10-14 medications and 15+ medications.

Figure 5.2 shows the six-month proportion of patients with polypharmacy who had a hospital admission stratified by sex.
Figure 5.3 shows the six-month proportion of patients with polypharmacy (5 or more medications) who had a hospital admission stratified by age.
Figure 5.4 shows the six-month proportion of patients with polypharmacy (5 or more medications) who had a hospital admission stratified by age and sex.
Figure 5.5 shows the six-month proportion of patients with polypharmacy (5 or more medications) who had a hospital admission stratified by SIMD.
Figure 5.6 shows the six-month proportion of patients with polypharmacy (5 or more medications) who had a hospital admission stratified by SIMD and age.