

# Concurrent Use of Prescription Drugs and Herbal Medicinal Products Among Older Adults

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partial fulfilment of the requirements of the degree  
of PhD

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# Abstract

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**Background:** Polypharmacy is a recognised patient safety risk, with older adults at greater risk due to co-morbidities and reduced clearance of drugs due to ageing. However, very little is known about the concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults. There is no common understanding of what HMPs are and no UK based studies among older adults completed in the last 15 years were identified.

**Aim:** To understand the concurrent use of prescription drugs and HMPs among UK older adults.

**Research questions:** The different phases of the study were guided by the following questions.

## **Phase 1: Systematic Literature Review**

- What is the prevalence and pattern of concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults?
- What patient and clinical characteristics are associated with concurrent use of prescription drugs and HMPs?
- What are the range of prescription drugs and HMPs most concurrently used by older adults?
- What safety issues and other factors are associated with concurrent prescription drug and HMPs use in older adults?

## **Phase 2: Questionnaire Survey**

- What is the prevalence and patterns of concurrent prescription drugs and HMPs use among UK community dwelling older adults?
- What types of HMPs and prescription drugs are concurrently used?
- What is the potential herb-drug interactions from the HMPs, and prescription drugs reported?
- What patient and clinical characteristics are associated with concurrent HMPs and prescription drugs use?

## **Phase 3: In-depth exploration of older adults' experiences of using HMPs with prescribed medications**

- Why do older adults concurrently use prescription drugs, HMPs and dietary supplements (DS)?
- What is the experience of concurrent users?

**Methods:** Three phased mixed method sequential explanatory study. Phase1 was a systematic literature review to evaluate and summarise available evidence. Phase 2 estimated the prevalence of concurrent use and identified the pattern and range of medicines combined using questionnaire survey among community dwelling older adults from two GP surgeries in Essex and London. Phase 3 Interviews with older people to gain in-depth understanding of the older peoples' reasons for concurrently using HMPs with prescription medications, their experiences and views.

**Findings:** Both the review and survey demonstrated that concurrent prescription drugs and HMPs use among older adults is widespread, with potentially serious herb-drug interactions from certain combinations. Prevalence among older adults

varied widely between 5.3% and 88.3% among previous studies, while this study estimated it to be 33.5%. Dietary supplements (DS) are also concurrently used with prescribed medicines. The most commonly used HMPs were evening primrose oil, valerian, and Nytol Herbal<sup>®</sup> (a combination of hops, gentian, and passion flower) while cod liver oil, glucosamine, multivitamins and vitamin D were the dietary supplements most reported. The prescription drugs most commonly combined with HMPs are beta blockers, diuretics, antihyperlipidemic agents, anticoagulants, analgesics, antihistamines, antidiabetics, antihypertensive drugs, antidepressants, non-steroidal anti-inflammatory drugs (NSAIDs) and statins. Although most of the survey participants were not exposed to significant harm from concurrently using HMPs and DS with prescription medicines, the potential risk of herb-drug and supplement-drug interactions cannot be ignored.

The interviews revealed that older adults draw on different rationale and sources of information when making the decision to use HMPs or dietary supplements concurrently with prescription drugs. Six main themes captured the range of experience and underlying reasons for concurrent use. These were: older people's values and beliefs, the decision to use HMPs and DS, sources of information and advice, self-management and taking control, disclosure and non-disclosure, awareness of potential herb-drug interactions.

**Discussion:** This study has provided the first estimate of the prevalence of concurrent HMPs and prescription drug use among UK older adults and established the range of HMPs and dietary supplements that older adults most commonly combine with prescribed medicines. It has highlighted potential interactions from

certain combinations of prescription drugs, HMPs and dietary supplements which healthcare practitioners should routinely ask older adults about. As well as the need to systematically identify older people who may be at risk of potential herb-drug interactions, the range of reasons for concurrent use provided by this study adds to the literature on polypharmacy and interventions to support medicine management for older adults living at home with multiple health needs. Evidence from the study demonstrates the range of experience that reflects individual and system issues about accessing medical care and advice on medication. The findings highlight the difficulties that this population face in accessing the advice and support they need. It also indicates a need to revisit the responsibilities of clinicians and regulators with regards to the regulation and sale of HMPs. Likewise, accurate and key information regarding interactions with other products and possible adverse effects should be readily available. Future work could test what enables older consumers to make informed choices about the safe use of HMPs.

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# Declaration

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All the chapters in this thesis are entirely the product of my own work.

The systematic review reported in Chapter 4 was primarily undertaken by me, with contributions to the conduct of the literature search by Leila Watson, data extraction and second review by Barbara Wider, both of the Institute of Health Research (University of Exeter). My colleague, Sabina Khanom, who is a registered pharmacist double checked reported medicines for interactions on Stockley's Drug Interactions database.



# List of Abbreviations

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ADR	Adverse drug reaction
DS	Dietary supplements
BAME	Black, Asian and Minority Ethnic
CAM	Complementary and Alternative Medicine
CRIPACC	Centre for Research in Public Health and Community Care
CSM	Common-Sense Model
EPPI	The Evidence for Policy and Practice Information Co-ordinating Centre
HMPs	Herbal Medicinal Products
INR	International Normalised Ratio
JBI	Joanna Briggs Institute
IRAS	Integrated Research Application System
NSAIDs	Nonsteroidal Anti-inflammatory Drugs
PIS	Participant Information Sheet
PPI	Patient and Public Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	The International Prospective Register of Systematic Reviews
RCUK	Research Councils UK
SRM	Self-Regulatory Model
THR	Traditional Herbal Registration
WHO	World Health Organisation
MHRA	Medicines and Healthcare Products Regulatory Agency

# Glossary

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**Concurrent:** given or used at the same time as another.

**Dietary supplements:** a product taken orally that contains one or more ingredients (such as vitamins or amino acids) that are intended to supplement one's diet and are not considered food.

**Herbal medicinal products:** any medicinal product, exclusively containing as active ingredients one or more herbal substances, one or more herbal preparations, or a combination of the two.

**Herb-drug interaction:** Any pharmacological modification caused by herbal substances to another prescription medication (diagnostic, therapeutic or other action of a drug) in or on the body. An herb might increase or decrease the effects of co-administered drugs.

**Older adults:** The age of 60 or 65, roughly equivalent to retirement ages in most developed countries and is said to be the beginning of old age. In many parts of the developing world, chronological time has little or no importance in the meaning of old age.

**Prescription drugs:** A prescription drug (also prescription medication or prescription medicine) is a pharmaceutical drug that legally requires a medical prescription to be dispensed. In contrast, over-the-counter drugs can be obtained without a prescription.

**Polypharmacy:** Polypharmacy refers to the use of a large number of medications, commonly considered to be the use of five or more. Since polypharmacy is a

consequence of having several underlying medical conditions, it is much more common in elderly patients.

**Patient safety:** The simplest definition of patient safety is the prevention of errors and adverse effects to patients associated with health care.

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# Chapter 1: Introduction and Outline of Thesis

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## 1.1 Introduction to the Study

This thesis reports the findings from a study on the concurrent use of herbal medicinal products (HMPs) and prescription drugs among older adults. It examines the prevalence and potential interactions, as well as, the reasons why older adults concurrently use HMPs with prescribed medicines.

The aim of this research is to explore and better understand the concurrent use of prescription drugs and HMPs among UK older adults. The following sets out the study's objectives and research questions and describes how the different study phases systematically addressed the questions. It then summarises the content of the thesis chapters.

## 1.2 Objectives

- a. To collate, evaluate and summarise available evidence on concurrent use of prescription drugs and HMPs in older adults (**Phase 1: systematic literature review**).
- b. To identify the different types of HMPs and prescription drugs concurrently used by UK older adults. ( Phases 1 and 2: **review, survey** )
- c. To identify patient and clinical characteristics associated with concurrent use. (**Phases 1,2,& 3: review, survey and in-depth study**)
- d. To examine potential major herb-drug interactions from the concurrent HMPs and prescription drugs reported (**Phase 2: Questionnaire survey**).

- e. To explore any other factors and reasons for concurrent use of prescription drugs and HMPs (**Phase 3: In depth study**).

### 1.3 Research Questions

The different phases of the study were guided by the following questions:

#### Phase 1: Systematic Literature Review

- What is the prevalence and pattern of concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults?
- What patient and clinical characteristics are associated with concurrent use of prescription drugs and HMPs?
- What are the range of prescription drugs and HMPs most concurrently used by older adults?
- What safety issues and other factors are associated with concurrent prescription drug and HMPs use in older adults?

#### Phase 2: Questionnaire Survey

- What is the prevalence and patterns of concurrent prescription drugs and HMPs use among UK community dwelling older adults?
- What types of HMPs and prescription drugs are concurrently used?
- What are the potential herb-drug interactions from the HMPs, and prescription drugs reported?
- What patient and clinical characteristics are associated with concurrent HMPs and prescription drugs use?

### **Phase 3: In depth exploration of older adults' experiences of using HMPs with prescribed medications**

- Why do older adults concurrently use prescription drugs, HMPs and dietary supplements (DS)?
- What is the experience of concurrent users?

#### **1.4 Thesis Outline**

This thesis is formed of eight chapters. Chapter 1 begins with a brief introduction to the study; outline of the research aims and objectives and the research questions.

The chapter concludes with an outline of the chapters that make up the thesis.

Chapter 2 provides a background to the research, with an overview of polypharmacy and potential herb-drug interactions within the context of concurrent HMPs and prescription drugs use. It discusses the rationale for focusing on older people, recent and relevant research and why the concurrent use of HMPs and prescription drugs is an important topic to study.

Chapter 3 provides an account of the design and development of the three phases sequential mixed method used in the study and how it was applied. It also describes the data collection and analysis methods for all three phases. Patient and participant involvements and the process of developing, testing, and refining the mixed method study is explained. Some of the challenges faced during recruitment are also discussed. The data and findings from one phase provided the basis for subsequent phases (Mertens, 2014).

Chapter 4 sets out evidence from Phase 1; a systematic literature review which synthesised and critically appraised available studies to establish what is known on concurrent use of prescription drugs and HMPs among older adults. The review also explored possible explanations as to why this occurs and identified gaps in knowledge. No recent UK study on the topic was found but previous studies from other countries acknowledged there are potentials for interactions to occur between herbal and conventional medicines. Chapter 4 reports the findings and discussions from the literature review.

Findings from the systematic review were used to refine objectives for the phase 2 study. In this, a cross sectional survey was used to establish the prevalence of concurrent prescription medicines, HMPs and DS use among UK community dwelling older adults. Chapter 5 reports findings from the survey including demographics and the range of medicines that respondents combined. The potential interactions from these combinations were also explored and reported with a discussion of the findings and how it relates to existing research.

Phase 3 built on findings from the survey to explore the experiences of older people using HMPs and prescribed medications. Thirteen in depth qualitative interviews were conducted with concurrent users who responded to the phase two survey. Chapter 6 reports these interviews and findings about the reasons, motivations and experiences of older adults concurrently using prescription drugs with HMPs and/or DSs. The main themes from older adult's narratives in relation to decision making,



reasons and motivations for concurrently using HMPs and DS with prescription drugs are presented.

Chapter 7 draws together findings from the three phases to answer the study objectives. It also provides a discussion of all the findings by considering related literature and the study's contributions to knowledge around concurrent use of HMPs, DS and prescription drugs. The chapter ends with how this work has enhanced the understanding of the multiple personal, organisational and cultural factors that inform decisions about concurrent use of HMPs and prescribed medications.

Finally, Chapter 8 presents the conclusions of the study, implications of the findings for current and future work and recommendations for future research. Particular attention is also given to the implications of the findings for clinicians, service provision and patient safety.

# Chapter 2 Background to the Study

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## 2.1 Introduction to Chapter

This chapter explores polypharmacy among older adults, the use of HMPs and the patient safety issues that can arise. A brief overview of the policies and regulations regarding HMPs in Europe and the United Kingdom is also provided. For the purpose of this study, the WHO definition of 'elderly' as individuals over the age of 65 years in developed countries, and over 60 years in developing countries (World Health Organisation, 1984) have been adopted. Therefore, in this research, all participants were aged 65 years or older.

## 2.2 Polypharmacy and Older Adults

The world population is ageing and according to the World Health Organisation (WHO), by 2050 the population of people aged  $\geq 60$  years will double and around 400 million people will be  $\geq 80$  years (World Health Organisation, 2012). Around 18.2% of the UK population are aged over 65 years, by 2068 a quarter of UK residents will be aged 65 years or over (Office for National Statistics, 2018).

Before addressing the issue of concurrent use of HMPs with prescribed medications among this population, it is important to acknowledge two issues; polypharmacy, drug reactions and interactions and the impact this has on individual's health and health care organisations.

Older adults, especially those with multiple chronic conditions (Nyborg, Straand, & Brekke, 2012) and those with serious conditions such as cancer rely on medicines to

manage their conditions. Consequently, multiple drugs are used resulting in polypharmacy (Maggiore, Gross, & Hurria, 2010). There are inconsistencies in the definition of polypharmacy but it is often described as the use of multiple medications to treat health problems (Junius-Walker, Theile, & Hummers-Pradier, 2007). Polypharmacy is often clinically indicated and is beneficial in conditions such as diabetes and hypertension and among patients with multimorbidity. However, multiple use of medicines has been associated with drug-drug interactions, adverse drug events, hospitalisation and increased length of stay, as well as mortality (Guthrie, Makubate, Hernandez-Santiago, & Dreischulte, 2015; Maher, Hanlon, & Hajjar, 2014).

Polypharmacy is a recognised patient safety risk and older adults are a high risk group (Leiss et al., 2015). The chances of medication-related problems are higher in older people because of existing co-morbidities, metabolic changes and reduced clearance of pharmacologically active compounds (Mangoni & Jackson, 2004; Salmond, 2002; Vacas Rodilla et al., 2009). Moreover, the likelihood of an adverse drug event increases with the number of medications (Eichhorn, Greten, & Efferth, 2011; Heuberger, 2012). About 20% of people aged over 70 years take five or more prescribed medications (Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002; Rollason & Vogt, 2003). This is further complicated when older people use over-the-counter medicines, as well as DS; a situation that is prevalent among older adults (Qato, Wilder, Schumm, Gillet, & Alexander, 2016). Although herbal medicines and dietary supplements are generally not included in standard definitions of polypharmacy, it is known that they could increase the risk for drug interactions (Qato et al., 2016).

In addition to the harm to the individual, adverse drug reactions are major clinical and economic burden on healthcare systems, with increased hospitalisation and prolonged hospital stays raising costs (Sultana, Cutroneo, & Trifirò, 2013). About 1,105.8 million prescriptions were dispensed in England pharmacies in 2017 (HSCIC, 2018). NHS spending on medicines in England was estimated at a total of £17.4 billion in 2016/17, increased from £13 billion in 2010/11. This is an average growth of about 5% per year and substantially a faster rate of increase than the total NHS budget over the same period (Ewbank, Omojomolo, Sullivan, & McKenna, 2018). Prescription medicines dispensed for older people accounted for 52.6% of the net cost for exempted categories (HSCIC, 2018), this is more than half of the total prescription cost and a big pressure on the healthcare budget.

### **2.3 Herbal Medicinal Products (HMPs), Policies and Regulations**

Herbal medicinal products are medicinal products where the *active ingredients consists exclusively of herbal substances or herbal preparations* (Commission of the European Communities, 2003). Herbal medicinal products are covered by Directive 2001/83/EC on the Community code relating to medicinal products for human use "Directive on human medicinal products" (Commission of the European Communities, 2003). The World Health Organisation (WHO) has defined herbal medicines as finished labelled medicinal products that contain an active ingredient, aerial, or underground parts of the plant or other plant material or combination (World Health Organisation, 1991).

Herbal medicines include herbal supplements, herbs, herbal preparations and finished herbal products. The terms herbal product, herbal medicinal product and natural product are often used interchangeably but they are different. Herbal products could be food, medicine or cosmetic. In herbal medicinal products, the active ingredient consists exclusively of herbal substances or herbal preparations (e.g. parts of plant) or pharmaceutical preparations (e.g. essential oil, extracts)(Gupta, 2015). While natural products are medicinal products where the active ingredient is of natural origin and consists of an animal part, a bacterial culture, a mineral or a salt (Gupta, 2015). This distinction is important because the active ingredients differ and so does the manner in which they react when consumed with food and conventional medicines.

The Dietary Supplement Health and Education Act of 1994 classified herbal products as dietary supplements. A dietary supplement is defined as a non-food, non-drug product taken by mouth and containing at least one identified dietary ingredient such as a vitamin, mineral, herb or botanical, amino acid, enzyme, or metabolite (Office of Dietary Supplements, 1994). Herbal supplement is a type of dietary supplement made from plants.

Herbal medicine is one form of complementary and alternative medicine (CAM). Complementary and alternative medicine refers to any medical systems, practices, treatments or therapies that do not currently fall into accepted mainstream or conventional medicine (National Center for Complementary and Alternative Medicines (NCCAM), 2019). In addition to herbal medicine, CAM includes diverse therapies such as acupuncture, Ayurveda, homoeopathy, hypnotherapy,

naturopathy, osteopathy, reflexology, Reiki, traditional Chinese medicine (TCM) and yoga. Some of which do include herbal medicines as part of their treatment regimens e.g. Chinese medicine.

Many drugs are derived from plants, with up to 25% of conventional medicines directly or indirectly from medicinal plants (Robinson & Zhang, 2011). In some cultures, medicinal plants have been the main source of healthcare for thousands of years and continue to be (Halberstein, 2005). Populations in middle and low income countries continue to rely on herbal medicines as primary source of health care. Although, this is at a much lower number than the 75-80% reported in earlier literatures (Bodeker & Ong, 2005; Robinson & Zhang, 2011). In these countries, it is mainly the patients who cannot afford conventional drugs that rely on herbal medicines. In contrast however, higher social class patients are the top users in developed countries (Eichhorn et al., 2011).

Global consumption of herbal medicines is considerable although correct estimates are difficult to arrive at because it is uncoordinated and with variable regulations. Inconsistencies in what is and what is not herbal medicine also makes it extremely difficult to provide precise economic valuations (Robinson & Zhang, 2011). It is estimated however, that the herbal industry is worth about US\$100 billion worldwide, with trade in medicinal plants, herbal raw materials, and herbal drugs at annual growth rate of about 11% between 2017 and 2022 (Zion Market Research, 2017). The herbal market varies from region to region, with Europe accounting for the largest share of the market (Chapman 2012).

Historically, there have been efforts to regulate the production and use of HMPs. The Alma Ata declaration of 1978 by the WHO recognised the role of traditional, complementary and alternative medicine (CAM) in the healthcare of developing and developed nations. This was informed by a renewed focus on primary health care (WHO, 1978), highlighting the need to address those aspects of public health that were outside conventional and western health care. The declaration called for the inclusion of proven traditional remedies in national drug policies and regulatory measures (World Health Organisation, 1978) and strengthen the role of primary healthcare in access to medicines. The WHO also developed key documents (World Health Organisation, 2000, 2003, 2007; World Health Organisation & Zhang, 2004) to strengthen regulatory capacity and assist national authorities, scientific organisations and manufacturers in the monitoring of herbal medicines. These documents provide basic criteria for evaluating the safety, quality and efficacy of traditional medicines to assist regulatory authorities in dossier assessments for herbal products (Ajazuddin, 2012). Policies and frameworks of South Africa (Ngcobo, Nkala, Moodley, & Gqaleni, 2011), Australia and many others (Calixto, 2000) have all evolved from these documents. Nevertheless, the regulation of herbal medicines depends largely on the ethnological and historical background of each country.

As the demands for herbal products grew, regulations continue to present challenges to many countries including the UK. Consumer access to herbal medicines is not prescription controlled and whether or not access and use is included in medicines regulation vary widely from country to country (Girard & Vohra, 2011). The UK has a historical tradition of herbal medicine (Culpeper, 1653/1995), with remedies sold alongside other products in pharmacies as OTC products (Nissen, 2010), this is also

widespread and well established in some other European countries like Spain and Italy (Pieroni, Pardo-de-Santayana, Firenzuoli, & Quave, 2013; Williamson & Chan, 2015). One of the many reasons for the continued demand for herbal therapy in these developed countries is that it is perceived that the use of home remedies and over-the-counter drugs is consistent with consumer choice; taking control in maintaining ones health and wellbeing (Ekor, 2014). It is reasonable to predict that the herbal medicines market will continue to expand exponentially, representing a substantial proportion of the global drug market, especially as the number of older people living with multiple conditions that affect their quality of life in different ways grow (Barnett et al., 2012; Zion Market Research, 2017).

In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) regulates medicinal products for human use in accordance with the European Community's medicinal product directive (*Directive 201/83/EC*) and the UK law. For regulatory and legal reasons, many herbal products are considered food supplements even though most of them are medicines (Williamson, 2003). For example, Gingko (*Gingko biloba*) is sold as a food supplement in the UK and Netherlands, as registered OTC medicine in Germany and France but available in Ireland as prescription only (Gulati & Berry Ottaway, 2006). Due to these diverse classifications, HMPs are subject to multiple or concurrent levels of certification resulting in further complications in how they are regulated and who is responsible for their oversight (Coppens et al., 2007). Consequently, HMPs are manufactured, licensed, dispensed and sold differently all over the world. Moreover, HMPs and DS are easily sourced cheaply online. The availability of these products on the internet with little or no regulations emphasises the challenges of dealing with different



legislative frameworks between countries and information on quality and safety (World Health Organisation, 2015). Inadequate labelling, exaggerated reports of efficacy and minimal safety warnings (Owens, Baergen, & Puckett, 2014) are the main concerns about these products bought online. Around 83% of UK older adults in the 65 to 74 age group use the internet (Office for National Statistics, 2019), with up to 30% using the internet to look for health-related information (Age UK, 2018), including HMPs and DS.

Since April 2011, all HMPs sold in the UK market must have a Traditional Herbal Registration (THR) or a marketing authorisation (previously known as a product licence). Currently, there is no requirement under the THR scheme to provide scientific prove that a product works, but registration is restricted to HMPs requiring no medical personnel for administration or monitoring and oral medicines for external use or inhalation (Medicines and Healthcare products Regulatory Agency, 2012).

## **2.4 Older Adults and Herbal Medicinal Products**

Globally, the use of herbal medicines continue to grow particularly among older adults (Arcury et al., 2007; Canter & Ernst, 2004; Loya, Gonzalez-Stuart, & Rivera, 2009; Yoon, Horne, & Adams, 2004). In the last decade, about a quarter of UK adults (MHRA & Ipsos MORI, 2009) and up to 35% of adults in the United States frequently use herbal products (Rashrash, Schommer, & Brown, 2017). Some of the reasons cited for the use of herbal medicines include dissatisfaction with effectiveness of conventional drugs, poor therapeutic outcomes (Astin, 1998; Chan, 2003) and the perception that herbal medicines are safe (Delgoda et al., 2004; Delgoda, Younger, Barrett, Braithwaite, & Davis, 2010). Moreover, cultural and

personal beliefs, and in some cases better experiences with herbal medicine practitioners compared to conventional healthcare professionals may explain preferences for herbal medicines (Ernst & White, 2000).

Compared to other forms of CAM, herbal therapy is the most popular across different ethnic and age groups (González-Stuart, 2011; Posadzki, Watson, Alotaibi, & Ernst, 2013). Herbal medicines are used to maintain health, treat chronic illnesses (Albert et al., 2009; Marinac et al., 2007), for cardiovascular problems (Elmer, Lafferty, Tyree, & Lind, 2007; Farina, Austin, & Lieberman, 2014; Izzo, Di Carlo, Borrelli, & Ernst, 2005; Tachjian, Maria, & Jahangir, 2010) and pain management (Artus, Croft, & Lewis, 2007; Wilkinson & Jelinek, 2009). Likewise, they are also used for the management of anxiety (Parslow & Jorm, 2004) and depression (Hsu et al., 2009; Parslow & Jorm, 2004).

The use of herbs and HMPs by older adults may not be disclosed to health care professionals (Barnes, Mills, Abbot, Willoughby, & Ernst, 1998; Walji et al., 2011). Only 55% of those who concurrently used herbal medicines with prescriptions reported that their doctors knew about their co-use, 73% of these co-users voluntarily informed their doctors (Delgoda et al., 2010). Considering that almost one in four adults co-use prescription medications with HMPs (Gardiner, Graham, Legedza, Eisenberg, & Phillips, 2006; Loya et al., 2009), the potential risk for adverse reactions may be under-estimated or not considered.

## 2.5 Rationale for the study

Although there is some awareness that older adults concurrently use prescription drugs and HMPs (Arcury, Bell, et al., 2006; Dergal et al., 2002; Elmer et al., 2007; Gonzalez-Stuart, 2011; Loya et al., 2009; Qato et al., 2008; Yoon & Schaffer, 2006), very little has been done to find out what is happening and why. The majority of studies that have explored the concurrent use of prescribed medications with HMPs among older adults were conducted in the United States (Dergal et al., 2002; Elmer et al., 2007; Nahin et al., 2009; Qato et al., 2016). Only one study on this issue among this age group within the context of the NHS has been reported from the UK (Canter & Ernst, 2004).

There is evidence that some HMPs are clinically effective for particular conditions and patient groups (Izzo, Hoon-Kim, Radhakrishnan, & Williamson, 2016). However, there is potential for adverse drug reactions (ADRs) to occur between conventional drugs and HMPs, some of which may have serious consequences (Fugh-Berman, 2000; Izzo & Ernst, 2001; Williamson, 2001; Williamson, Driver, & Baxter, 2013). For example, Ginkgo (*Ginkgo biloba*) when combined with anticoagulants could interfere with platelet functions (Fugh-Berman, 2000). Although many reported interactions between herbal products such as Echinacea or valerian and conventional medicines are of minor risks, with limited clinical significance. However, HMPs such as St. John's wort may cause serious and life-threatening interactions with certain antidepressants (Izzo, 2012; Izzo et al., 2016; Williamson, 2003).

Considering that the half-life of most drugs is 72 hours, polypharmacy combined with the use of HMPs raises the risk of interactions significantly. Interactions could occur

during the absorption, distribution, metabolism and excretion of drugs (Holford, 2009). For this reason, it is important that healthcare professionals consider potential interactions between herbal medicines and prescribed drugs, especially drugs with a narrow therapeutic index (Izzo, 2012). Most drug-drug interactions are due to concurrent use of drugs, many of which are well-known and preventable. For example, Warfarin and acetaminophen could increase bleeding or increase the international normalised ratio (INR); it is recommended that this is managed by using the lowest possible acetaminophen dosage and monitoring the INR (Hughes, Patel, & Saxena, 2011; Lopes, Horowitz, Garcia, Crowther, & Hylek, 2011). Nevertheless, the interactions between most HMPs and prescription drugs remain unknown.

The quality and safety of herbal medicines has been subjected to more scrutiny in the last decade (Ekor, 2014), with research on specific health conditions such as cancer (Molassiotis & Xu, 2004) and irritable bowel syndrome (Bahrami, Hamedi, Salari, & Noras, 2016). Nevertheless, the incidence of herbal interactions is still unknown and there is no reliable up-to-date evidence on which to assess the scale of the problem or predict possible clinical outcomes. Of the few studies that have researched concurrent use of HMPs and prescription drugs in the UK (Alsanad, Howard, & Williamson, 2016; McLay et al., 2017; Steyn et al., 2018; Williamson et al., 2013), only one was conducted with older adults as participants (Canter & Ernst, 2004). Although these studies share a common methodological approach i.e. cross-sectional surveys, participants had conditions e.g. cancer and diabetics or were of all ages and not just older people. For the only study among older adults (Canter & Ernst, 2004), there was an implicit assumption that all older people are similar, and their identification and inclusion may have relied on self-selection.

The risks from concurrent use of HMPs and prescription drugs among older adults has been investigated (Bush et al., 2007; Elmer et al., 2007; González-Stuart, 2011; Kaufman et al., 2002; Nahin et al., 2009; Qato et al., 2008; Zyoud et al., 2014). Many herb-drug interactions were identified, with a risk of interaction reported in 5.8% of herbal products concurrently used with conventional medicines(Elmer et al., 2007). However, very little research has been done to investigate the incidence and severity of these herb-drug interactions and if certain patient groups are more susceptible than others (Williamson et al., 2013).

Although older people are the main users of the NHS, old age is not synonymous with ill health; the markers for being frail or vulnerable are not the same. Adverse drug reactions increase the risk of hospitalisation and can prolong hospital stay thus raising costs and putting pressure on the NHS. The prevalence of nearly all major chronic and long-term conditions increase significantly with age (Age UK, 2015). The majority of people aged 75 and over have one or more health conditions (Melzer et al., 2015). While having a health condition may not necessarily impact on daily life, having more chronic conditions could have limitations on daily living and the likelihood for health and social care needs. The rise in demand for health and care services is driven by the increasing complexity of health needs. As people age, they acquire multiple long-term conditions and disabilities or become frail (Mortimer & Green, 2015). Frailty affects around 10% of people aged 65 and over, rising to 25-50% of those aged 85 and over (Collard, Boter, Schoevers, & Oude Voshaar, 2012). Frailty is a distinctive health state relating to the ageing process whereby multiple body systems gradually lose their in-built reserves (Clegg, Young, Iliffe, Rikkert, &

Rockwood, 2013). Older people living with frailty are at risk of adverse health events such as a fall or infection, with dramatic changes in physical and mental wellbeing even after minor incidents (Mortimer & Green, 2015). Individuals' experience of ill health as they age is also affected by their socio-economic status and access to formal and informal networks of support (Centre for Ageing Better, 2017). These variables are of clinical and public health relevance, and key to understanding if there are certain groups of older people who are more or less likely to use HMPs concurrently with prescribed medications and why.

## **2.6 Significance of the study**

Failure to review and manage concurrent use of prescription drugs and herbal medicines in older adults is a patient safety risk. Excessive and inappropriate medicine use is a common problem among older adults (O'Mahony & Gallagher, 2008; Pérez-Jover et al., 2018) and concurrent use with HMPs further complicates the issue. It is important to have a better understanding of the way older adults co-use medications, if there are specific health conditions where HMPs are used alongside prescribed medication and how they are used. For example, if they are used for the relief of symptoms as part of ongoing health management regimen or used intermittently. There is considerable heterogeneity within the older population (Looman et al., 2018). Therefore, it is unclear how people with more or less functional ability, those who come from particular cultural backgrounds or have different levels of health literacy and knowledge (Jill Roberts, 2015) engage with the use of HMPs and when.

From the perspective of the health service and practitioners, knowing why older adults concurrently use HMPs and DS with prescribed medications has the potential to reduce adverse drug events and uncover symptoms not previously disclosed in clinical encounters. This awareness and improved understanding will equip health care professionals to identify older adults at risks of potential herb-drug interactions, the reasons for medication non-adherence and how best to discuss treatments and target interventions.

This study updates and builds on evidence from the UK on this issue. Previous related study (Canter & Ernst, 2004) was published 15 years ago and investigated only prevalence but not the reasons and factors associated with concurrent use of prescription drugs and HMPs. By focusing on community dwelling older adults, this study considers the breadth of use of HMPs and explored in-depth, the reasons and factors associated with concurrent use through individual qualitative interviews. Importantly, this study provides some answers to why older adults concurrently use their prescriptions drugs alongside HMPs; an area that is still under-researched.

## **2.7 Chapter Summary**

Chapter 2 sets the scene for the study presenting a case for the research in the context of polypharmacy and herb-drug interactions and establishing the rationale for a better understanding of concurrent HMPs and prescription drug use among older adults. A discussion of challenges with the regulation of HMPs and DS due to differences in national policies is also presented.

Chapter 3 now reports on the three phases mixed method research design selected as suitable to meet the aims of this research. The strength and limitations of this research design, as well as details of the individual phases are discussed.



# Chapter 3: Methods

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## 3.1 Introduction to Chapter

This chapter outlines the research design, data collection and analytic methods employed to investigate the concurrent use of prescription medicines and herbal medicinal products (HMPs) among UK older adults. The rationales for adopting a mixed method sequential explanatory design to address the research questions are articulated. The advantages and challenges of the approaches adopted are also discussed. Ethical considerations and the involvement of public and participants throughout the study are considered. In addition, the chapter provides detailed accounts of how validity and reliability were ensured throughout the study and how data from the three phases were analysed and drawn together. The chapter concludes with a critical reflection of the chosen method and approaches.

## 3.2 Research Paradigm: Pragmatism

All research has a foundation. Whether explicit or not, this foundation is found in the 'worldview' or theoretical framework adopted by the researcher (Creswell & Clark, 2011). The overarching aim of this study was to explore the concurrent use of prescription medicines and HMPs among older adults in the UK. As the researcher in pursuit of the 'realities' for this social issue, I bring along my beliefs and assumptions about herbal medicines. In addition, my previous knowledge about concurrent use and the safe use of medicines, all of which may have influenced my approach to this research. It is important that I understand and acknowledge this at the outset.

The assumption underlying the research questions are; that the use of herbal medicinal products (HMPs) is common among older adults. Herbal medicinal products are frequently bought over the counter, consumed concurrently with prescription drugs and not disclosed to health care professionals. An important patient safety concern for the concurrent use of herbal and prescription medicines is potential herb-drug interactions.

Older adults are a growing percentage of the UK population (Office for National Statistics, 2013) and the risk for adverse drug reactions (ADRs) increases with age (Davies et al., 2009). The chances of medication-related problems are higher among older people because of co-morbidities, metabolic changes and reduced clearance of pharmacologically active compounds (Mangoni & Jackson, 2004; Salmond, 2002; Vacas Rodilla et al., 2009). Also, the number of medications increases the risk of an ADR (Eichhorn et al., 2011; Heuberger, 2012). Considering that up to 20% of over 70s take five or more prescribed medications (Kaufman et al., 2002; Rollason & Vogt, 2003), the clinical and economic implications of ADRs on healthcare systems are huge (Sultana et al., 2013).

Despite these concerns, little is known about concurrent use of prescriptions and HMPs by older adults and possible interactions. Therefore, the focus of this study is patient safety. And this is threaded all through the different stages of the research.

This study is grounded in pragmatism, a claim on knowledge based on the assumption that collecting different types of data provides better understanding of a research problem (Creswell, 2013). Pragmatism is a philosophical theory seen as a

bridge between the conflicting inductive-subjective-contextual approach (qualitative) and the deductive-objective-generalising approach (quantitative) (Morgan, 2007). According to Tashakkori and Teddlie (2003), pragmatism debunks concepts such as 'truth and reality' and rather focusses on 'what works' as the truth regarding the research question under investigation. Proponents of pragmatism view it as a philosophy of common sense with purposeful inquiry as its focal point (Shields, 1998).

The research questions have informed the choice of methods and approaches. A mixed method approach that draws on quantitative and qualitative approaches and data ensures that the study questions can test what is effective (systematic review), establish how many people use HMPs with prescribed medication (systematic review and survey) and explore the reasons that have informed these choices (survey and interviews).

### **3.3 Research Design: A mixed method sequential explanatory study**

There is no consensus about what mixed methods design should or should not include or the kind of research questions that it is most suited to as an approach (Creswell & Clark, 2011; Morse & Niehaus, 2009; Tashakkori & Teddlie, 2003). However, there is a general understanding that combined methods can provide different perspectives and richer insights that challenge or enlighten a particular world view of what the problem or issues are (Creswell & Clark, 2007; Johnson, Onwuegbuzie, & Turner, 2007; Tashakkori & Teddlie, 2003).

For mixed method designs, both quantitative and qualitative data are collected and analysed using suitable approaches and techniques, both data sets are then synthesised at the point of interpretation (Creswell & Clark, 2011; Creswell, Plano Clark, Gutmann, & Hanson, 2003).

Quantitative and qualitative methods can complement each other (Greene, Caracelli, & Graham, 1989; Plano Clark & Creswell, 2011; Tashakkori & Teddlie, 1998). It builds an account based on the data to answer the research question. In this study, using mixed method design where each stage established what was known and each stage informed the next. The systematic review tested possible explanations as to why older people use HMPs concurrently with prescribed medications and then explored in depth key issues of interest in a survey with a small group of concurrent users (interviews). This contrasts with multiple methods studies which involves the simultaneous collection of either multiple qualitative or quantitative data to maximise understanding of how research questions are understood and answered within one study (Morse, 2003). For example, a study on prescribing that includes secondary data analysis of prescribing practice, and in-depth exploration of how supplementary prescribing has worked from the perspective of patients, pharmacists, and nurses provides multiple perspectives on the same issue (Bissell et al., 2008).

However, combining methods that are usually associated with a paradigm requires that the researcher is explicit about how data are synthesised and interpreted. There are a number of ways in which qualitative and quantitative methods can be combined within mixed methods design (Greene et al., 1989). A typology by Green

*et al* provides an overview of different types of mixed method approaches and their supporting rationale. Table 3.1 provides a summary.

**Table 3.1:** Purposes of mixing methods in a research study and appropriate mixed method design

Purpose	Description	Mixed method design
<i>Triangulation</i>	Using two or more methods to measure the same phenomenon, such that convergence or corroboration gives weight to the interpretation or make it more reliable.	Convergent parallel
<i>Complementarity</i>	Using results of one research method to clarify, elaborate or illustrate results of another method, to achieve a more comprehensive understanding of the phenomenon	Sequential Exploratory Sequential Explanatory
<i>Development</i>	Results from one method help to develop, to inform or refine the second method	Sequential Exploratory
<i>Expansion</i>	Seeking to analyse and to explore different facets of a phenomenon, to get a richer and more detailed understanding e.g. Explaining quantitative results with qualitative data	Sequential Explanatory
Initiation	Discovering paradoxes or seeking contradictions which lead to the reframing of research questions. Different methods are used to assess various dimensions of the phenomena of interest to arrive at new insights and understanding	Concurrent nested  Concurrent transformative

To address the different objectives of this study, a mixed method approach using a sequential design was chosen, the decision to use qualitative and quantitative methods was planned before the start of data collection. This contrasts with emergent mixed method design where the decision to use a second approach arises

due to issues during the conduct of the research for example, unexpected findings or gaps in understanding (Morse & Niehaus, 2009).

The mixed method design was adaptable to reflect the research experience. For example, an interview was used to inform the survey design when it became apparent that people were unwilling to participate in focus groups. Therefore, using a mixed method approach provided flexibility and maximised the opportunities to provide a comprehensive approach when addressing the research question within the resources available (Onwuegbuzie & Leech, 2006). The different sources of evidence also had the potential to achieve a more nuanced account of the issue under study. The sequential mixed method study was organised in three phases (Fig 3.1), with data from each phase answering the research questions and providing basis for further refinement of the questions for the next phase (Mertens, 2014).

Findings from the systematic review informed development of the survey, its focus, structure and content. The survey established prevalence of concurrent use; the range of medicines combined and identified a sample of concurrent users. The interviews with a sub- sample of concurrent users explored experiences, reasons for concurrent use, understanding of risks and therapeutic benefits of taking HMPs concurrently with prescribed medication for linked or different conditions. The design did not assume a hierarchy of evidence but used the findings from one phase to inform the next, with the different methods linked in their common focus on this issue.

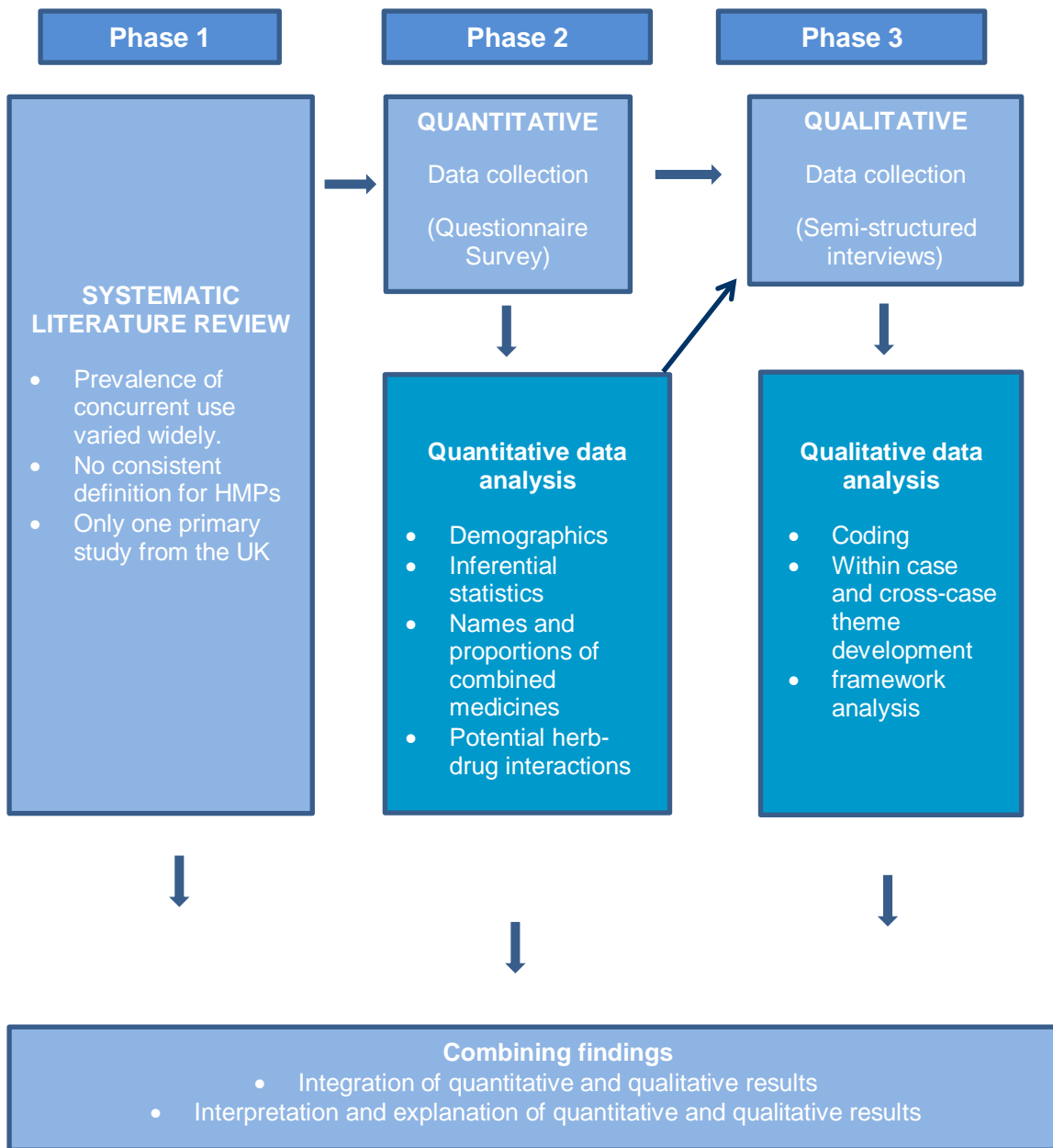


Figure 3.1: Sequential mixed method design (Adapted from Cameron (2009))

### 3.4 Strengths and Limitations of Mixed Method Design

The strength of mixed methods design is that it supports the use of a range of data collection tools, to study the problem of interest from a range of perspectives (Lewin, Glenton, & Oxman, 2009). It enables the researcher to test different explanations of why what is observed has occurred. Using both qualitative and quantitative data allows for a fuller understanding of the research problem (complementarity). Mixed methods often combine approaches to serve the dual purpose of gaining overview of issues from a larger sample, as well as gaining in-depth understanding through detailed study of a smaller sample (Bazeley, 2004). For example, Fox et al.,(2013) used semi-structured interviews to ascertain the views of oncology professionals and CAM practitioners regarding the role of CAM in patients with cancer. In Phase 2, a survey of women with breast cancer determined the rate and type of CAM, reasons for use, and perceptions regarding the utility of CAM. Lastly, individual interviews with a sub-set of the survey sample elucidated in greater detail the reasons for CAM use and patients' experience of CAM.

However, using mixed methods approach is not without limitations. A common criticism is that full integration of findings from the multiple approaches is difficult, and there is tendency to privilege one source of evidence or set of theoretical assumptions (Bazeley, 2004). Greater resources and time are also often required for data collection, analysis and interpretation than might be the case for single method studies.

To summarise, the rationale for the study was that concurrent use of prescription drugs with HMPs is a patient safety issue. The sequential mixed method design



involving quantitative and qualitative data provided an in-depth understanding of the issues in ways that would capture both the scale of the problem, patient perspectives of the benefits and risks of using HMPs alongside prescribed medication and the implications for patient safety (Plano Clark & Creswell, 2011). The combination of quantitative and qualitative methods was both complementary and developmental (O'Cathain, Murphy, & Nicholl, 2007).

### 3.5 Ethical Considerations and Approvals

Permission to conduct the study was sought from the University of Hertfordshire, the NHS Research Ethics Committee (REC) and Research & Development (R&D) office for the two study sites. Application forms and study proposal were submitted to the University of Hertfordshire Ethics Committee for Studies Involving the Use of Human Participants for ethical scrutiny and approval (EC1). The study was examined, approved and granted research indemnity by the University of Hertfordshire Ethics Committee. **Reference no: HSK/PG/NHS/00336 (Appendix A).**

Since the study involved NHS participants, an online application was made to the REC on the Integrated Research Application System (IRAS). The study had a proportionate review because patient records were not accessed, and the research did not involve sensitive issues. Permission to contact and interview interested participants in the next phase of the research was sought as part of this application. The study was granted a full REC approval, **Reference no: 15/LO/1870 (Appendix B).**

Permission was also required from the local R&D office to conduct the study at identified general practices. This process took 7 months, from May to December 2015. The delay was in identifying the responsible R&D offices. Due to the reorganisation of primary care in England in 2012, R&D offices were either merged or non-existent. This further complicated research management and governance (RM&G) within primary care, making it harder to navigate the application process.

Protecting participant's rights to confidentiality and anonymity are some of the ethical principles of research upheld throughout the conduct of this study. Key obligations included privacy, minimising distress, intrusion, and protecting participants from harm if possible adverse interactions from concurrent use of HMPs were identified based on their responses.

### **3.5.1 Ethical considerations for conducting research with older adults**

Research involving older adults can present challenges resulting from the physiological and psychological factors such as decline in physical and cognitive functions associated with ageing (Quinn, 2010). Nonetheless, age and vulnerability should not be used as reasons for exclusion in research (Diener et al., 2013).

Therefore, special measures should be taken in designing research involving older adults, to support their inclusion and participation.

In this study, some of the ethical issues were treating personal data confidentially and storing them securely. To maintain privacy and anonymity for the survey, individual questionnaires were coded using letters and digits written on the front

page. To protect participant's personal information, section 5 of the questionnaire where those interested in being interviewed provided names and addresses were detached from the questionnaire after the participant's ID was copied onto it (Appendix C). All questionnaires were stored securely in a locked cabinet. Access to the research data was restricted to me, and my two supervisors. In accordance with the ethics approval obtained for the study, digital records are destroyed after transcription and data will be stored for five years and then destroyed.

Study Information was written in plain language and the choice to participate or pull out of the study without providing any reason to do so was explained. It was also made clear on the participant information sheet (PIS) (Appendix D) that their GPs will be contacted, if potentially dangerous herb-drug interaction was suspected from the information they provide.

While every effort was made to ensure that enough participants were recruited for this study, there was a risk that participants would feel pressurised to take part in the study. To minimise the likelihood of this occurring, it was explained in the PIS, that those who do not wish to participate could send uncompleted questionnaire back in the reply-paid envelopes.

The principles outlined by the UK Framework for Health and Social Care Research (Health Research Authority, 2017) for the conduct of human research such as right to privacy, respect and autonomy, benefit and risks were adhered to throughout the study. Interviews were always conducted in the place of the participants' choice and

attention was paid to privacy and their right to withdraw at any point. All data was anonymised so individuals would not be recognised.

### **3.6 Patient and Public Involvement (PPI)**

Patient and public involvement (PPI) is a process whereby patients, service users and members of the public are actively involved in the planning, prioritisation, commissioning, conduct and communication of research (INVOLVE, 2012), as opposed to just being the 'researched'. Patient and public involvement is a statutory part of the UK policy framework for health and social care research (Health Research Authority, 2017), and a key requirement by major funding bodies (Staniszewska & Denegri, 2013). The responsibilities and expectations of research funders with regards to public engagement is also well described in the Concordat for Engaging the Public with Research (Research Councils UK (RCUK), 2010). The aims of PPI are to improve dialogue and trust between researchers and the public, and to enhance the quality and impact of research for the benefit of the society and economy. In this study, PPI was particularly important to ensure that the research design and researcher approach would be acceptable to participants and the needs for the research (how the questions were framed) were credible to older people.

The transparency and accountability inherent in the PPI process, helps to create trust between researchers and the public. Involving PPI at all stages of the research activity leads to a higher quality research. This is due to the unique perspectives that patients and member of the public bring to the process (Brett et al., 2014; Brett et al., 2010; Staley, 2009). When there is a lack of shared understanding on the moral and

methodological purpose of PPI between researchers and the public, this has been reported as a major barrier to effective PPI (Wilson et al., 2015).

Throughout this study, I ensured that PPI representatives were part of the research process. Community dwelling older adults in Broxbourne, Hoddesdon and Cheshunt, members of a public involvement and research group (PIRg), were involved in providing advice and helping to improve the study. They highlighted the confusion around what is and what is not an HMP as an issue to address. At the planning stages, in addition to formal conversations with PPI representatives, there were discussions with older family members, colleagues and friends who helped to clarify key questions and challenged my assumptions.

The PIRg members made suggestions on the survey protocol, reviewed early versions of the PIS, the questionnaire and interview guide. They suggested sending an invitation to participate in the study personally addressed to prospective participants, along with the PIS and questionnaires. This is because older adults were more likely to agree to participate in the study, if they get a letter in their name and not a general invitation. The PIRg group also suggested including examples of HMPs on the PIS and questionnaire, so that participants know the types of medicines that are of interest to the study. Also, they suggested reducing the length of the PIS, helped to reframe survey questions and write the instructions in plain language.

## 3.7 Overview of Study Methods

### 3.7.1 Phase 1- Systematic Review

Systematic reviews are summaries of the best available evidence addressing sharply defined questions (Sackett, Rosenberg, Gray, Haynes, & Richardson, 1996). To limit bias and random error, pre-planned strategies are used during literature search.

Critical appraisal and synthesis of relevant data is also important, with clear documentation of the process (Chalmers, Altman, & Gotzsche, 1995; Cook, Sackett, & Spitzer, 1995) .

Systematic reviews differ from other types of literature reviews such as scoping and narrative reviews as they are designed to answer specific, often narrow questions in depth (Richardson, Wilson, Nishikawa, & Hayward, 1995). Questions for systematic reviews are often formulated according to four variables; patient, problem or population (P), intervention (I), comparison, control or comparator (C ) and outcome (O) (Guyatt, Rennie, Meade, & Cook, 2002). In addition, the sources of and the searches for evidence in systematic reviews are comprehensive and explicit, for narrative review this is often not specified (Cook, Mulrow, & Haynes, 1997). Rigorous critical appraisal is also a key stage in the conduct of systematic reviews.

Systematic reviews are considered important tools for policy makers because they are scientifically rigorous and informs decision making based on the totality of evidence rather than a single study (Sheldon, 2005).

The systematic review addressed the following questions:

- a. What is the prevalence and pattern of concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults?
- b. What patient and clinical characteristics are associated with concurrent use of prescription drugs and HMPs?
- c. What are the range of prescription drugs and HMPs most concurrently used by older adults?
- d. What safety issues and other factors are associated with concurrent prescription drug and HMPs use in older adults?

#### **a. Data Sources**

The Medline, PsychInfo, Embase, CINAHL, AMED, Web of Science and Cochrane electronic databases were searched systematically from inception until May 2017, for studies reporting concurrent use of prescription medicines with HMPs among older adults ( $\geq 65$  years) (Appendix E). Also, lateral searching via related citation (PubMed) and reference lists of identified studies. Two reviewers independently screened studies, extracted data and appraised methodological quality using the Joanna Briggs Institute (JBI) checklists for appraising studies reporting prevalence data (Munn, Moola, Lisy, Riitano, & Tufanaru, 2015) and for case reports (The Joanna Briggs Institute, 2016). Qualitative and quantitative studies from all settings were included. Non empirical papers, experiments and animal studies were excluded. Primary outcomes were prevalence and patterns of concurrent use, number and types of prescription and HMPs, and adverse reactions reported. Secondary outcomes included disclosure of HMP use to health care professionals and cost of HMPs. A narrative synthesis of included studies was done to summarise the

evidence. More detailed account of the systematic review method is provided in Chapter 4.

The systematic review identified what was known and not known about concurrent use of prescription drugs and HMPs among older adults, and other issues that needed further exploration. These findings informed the next stages of the study.

### **3.7.2 Phase 2- Quantitative Study (Cross-sectional Survey)**

Cross-sectional studies such as surveys are used to establish prevalence or incidence of particular conditions, and to collect information on attitudes and behaviour about a population of interest (Lavrakas, 2008; Sapsford, 2006). They are particularly useful in providing a snapshot of a population, at a given time (Olsen, Christensen, Murray, & Ekbom, 2010). Cross-sectional, cohort and case control studies are referred to as observational studies, because no intervention is required and the investigator simply observes (Mann, 2003). Moreover, there is no need to allocate participants into different groups, data are collected only once and multiple outcomes can be studied (Mann, 2003).

Surveys have several advantages. They are flexible and a cost-effective way of gathering information from widely dispersed participants (Gillham, 2008). In fact, the majority of studies investigating medication use among older adults have used cross-sectional surveys (Canter & Ernst, 2004; Kaufman et al., 2002; Peklar, Henman, Kos, Richardson, & Kenny, 2014; Qato et al., 2008; Turkmenoglu, Kutsal, Dolgun, Diker, & Baydar, 2016). Questionnaires are the commonly used tool in surveys and data can be collected with standardised measures (Bulmer, 2004).



Previous research suggests that sensitive behaviours are reported more in self-completed questionnaires than in face- to -face interviews (Beebe, McRae, Harrison, Davern, & Quinlan, 2005; Bowling, 2005; Tipping et al., 2010; Tourangeau & Smith, 1996). Therefore, for a descriptive study such as this one, which seeks to describe reality (Creswell, 2013), a cross-sectional survey, using self-completed questionnaire was chosen. A major strength of this approach is that it allowed for populations of older adults from different backgrounds and social groups, representative of those who may take HMPs with prescribed medications to be surveyed, expanding on the findings from the systematic review.

The self-completed questionnaire survey was designed to address the following objectives:

- Establish the prevalence of concurrent prescription drugs and HMPs use among UK community dwelling older adults.
- Identify the pattern of concurrent use and the range of medicines combined.
- Examine potential herb-drug interactions from such combinations.

#### **a. Exploratory and Pilot Work (March – November 2015)**

I attended five coffee mornings with residents of retirement settlement schemes at Cheshunt, Broxbourne and Hoddesdon between March and June 2015 to discuss my research and solicit participation in focus groups. Only 8 of the 45 older adults (38 residents and 7 staffs) at the coffee mornings had any experience of using HMPs (two in the past and six currently using HMPs). An interesting finding from these meetings was that older adults were unwilling to talk about their herbal medicine use

in a group but were happy to speak to me one-to-one. Therefore, initial plans to develop the questionnaire out of findings from focus groups was abandoned and replaced with individual interviews and findings from the systematic review.

The questionnaire and participant information sheet (PIS) were tested in a pilot of 15 older adults identified from records of the two GP practices ( $n= 10$ ), family and friends ( $n= 5$ ). The purpose of the pilot was to find out if the questions were understood and if they elicit responses that related to the research objectives.

Responses from the pilot work prompted some minor amendments to the PIS and the questionnaire. The PIS was changed to make it clear that the survey can be completed, even if participants do not currently use HMPs. And because it was evident from the systematic review that no consistent term exists for HMPs, different terms are used in different countries and HMPs mean different things to different people (Agbabiaka, Wider, Watson, & Goodman, 2017). It was therefore important to rephrase section three of the questionnaire, and to include some examples of common HMPs to show participants the possible breadth of responses.

Also, changes were required to ensure that detailed responses regarding prescription medicines were captured, especially from participants who may use many prescribed medicines. Question 2.1 was amended to include an option of attaching a copy of the repeat prescription sheet they got from their GP.

Furthermore, two questions with duplicated information on participant's level of educational were re-phrased and merged into one, thus reducing the length of the questionnaire. Initially, Question 1.1 asked participants to write their age. However,

to make the question less personal, so that respondents were more willing to provide a response, it was amended so they could select which age group they belong.

Question 3.2 was also expanded to seek information on the appearance of HMPs and how often it was taken.

## **b. Setting and Participants**

The study was limited to a sample from a purposive sampling frame of older adults aged 65 years or more and on at least one prescription medication registered at two general practices.

- i. **Practice A (NZ):** a small practice in an Essex village of Epping Forest with predominantly white population. About 19.5% of the population was aged 65 years or older.
- ii. **Practice B (SG):** a large urban practice in North London with a sizeable British, Black, Asian and minority ethnic (BAME) population. The percentage of older people living within the catchment area was 9% and there are small pockets of social deprivation.

It is assumed that people from BAME groups use more HMPs than people who are white (Gardiner et al., 2013). There is however very little research on concurrent use with prescription drugs among these groups. The systematic literature review (Agbabiaka et al., 2017) found only one study that assessed concurrent use between different ethnic groups (Elmer et al., 2007). Therefore, including Practice B (SG), which has a sizeable BAME population in the sampling frame will provide some information on BAME population.

Table 3.2 compared the demographic profile of older adults in England with the two local authorities for the GP practices where older adults were recruited for this study.

Table 3.2: Demographic profile of study sites A and B

<b>% (Year)</b>	<b>England</b>	<b>Epping Forest</b>	<b>Haringey</b>
<b>Population aged 65+ (2016)</b>	17.9	19.5	9.3
<b>Life expectancy at 65+ (male) 2013-15</b>	18.7	19.2	19.2
<b>Life expectancy at 65+ (female) 2013-15</b>	21.1	21.2	22.4
<b>Index of multiple deprivation IMD (2015)</b>	21.8	15.3	31.0
<b>Deaths in usual place of residence among people aged 65 years and over (2016)</b>	47.2	41.4	33.4
<b>Population from Black and Minority Ethnic (BME) groups (2011)</b>	14.6	9.5	39.5

Source: Public Health England (2016)

The two general practises randomly selected from their records 400 patients (200 each) who met the following inclusion criteria:

- 65 years and older
- using at least one prescription medication
- able to consent

Patients were excluded from the sample based on the following criteria:

- terminally ill
- have dementia or
- assessed as lacking capacity to consent.

### c. Sample size

To ensure that the proposed number of participants to be recruited for the study is enough to meet the research objectives, such that resulting estimates of means or proportions can be reported with a satisfactory degree of accuracy, a sample size calculation was necessary. Sample size is a function of three factors - significance level, power and magnitude of the difference (effect size) (Devane, Begley, & Clarke, 2004; McCrum-Gardner, 2010). Two main approaches are adopted in calculating sample size; one is based on the precision of the estimates i.e. the sampling error deemed acceptable. The other approach is based on the power of a study, this is the ability to detect a significant change in the true magnitude of the effect anticipated (Barlett, Kotrlik, & Higgins, 2001). For example, a hypothesis test is conducted, and power calculation is done to ensure that the sample is large enough for the test to have enough power.

For this study, the focus was on estimating prevalence of concurrent use in the population of older adults and not the statistically significant change of an intervention. The primary outcome measure was the proportion of older adults who take HMPs alongside prescription medicines. Therefore, the sample size calculation was based on the following:

- Previous research that up to 50% of older adults use HMPs (Farina et al., 2014; Schnabel, Binting, Witt, & Teut, 2014; Yoon et al., 2004)
- achieving a confidence interval (CI) of 95%
- with  $\pm 7.5\%$  accuracy

So, using normal distribution to approximate the binomial distribution gave the sample size required as 171 respondents (the worst-case scenario of the actual proportion being 50%).

In addition, to conduct *t* tests for differences in normally distributed variables between the two groups (i.e. those concurrently using HMPs and prescription drugs and those who do not), a power calculation showed that a sample of 128 (64 in each group) would be sufficient (and hence the above 171 would be sufficient). This was based on having 80% power, a medium standardised effect size of 0.5 for each of the dependent variables, and a significance level of 5% for a two-tailed test. For differences in proportions between the two groups, the above sample size of 171 would be sufficient to be detecting differences of about 21 percentage points between the groups (assuming the sample to be equally split between the groups and again using 80% power, two sided tests and the 5% level of significance). Although this is a relatively large difference in percentage points, the sample sizes required for any substantially smaller difference were infeasible (e.g. 776 responses required to detect a difference of 10 percentage points). These calculations have been carried out using G\*Power version 3.1.9.2.

#### **d. Response rate**

Low response rates are common with mailed questionnaires (Blair, Czaja, & Blair, 2013; Edwards et al., 2009; McColl et al., 2001) and studies are often abandoned or the statistical power reduced due to poor recruitment (Bryman, 2012; Mangione, 1995). Expected response rates for surveys reported in the literature ranged from 20%-60% (Fincham, 2008). Therefore, oversampling by up to 40-50% is necessary

and often recommended for mailed surveys (Fink, 2003; Salkind, 2012). Although oversampling adds to the cost of research, it accounts for lost mails or non-response.

So, using the most conservative response rate of 50% obtained in similar previous studies (Ly, Percy, & Dhanani, 2002), it was necessary to invite more than double the required number of participants (McCrum-Gardner, 2010) hence, a total of 400 older adults were invited to participate in this survey.

#### **e. Questionnaire Design**

Self-completion questionnaires are like structured interviews but with the obvious difference that the interviewer asks questions and records responses in the latter.

Although face-to-face is considered a gold standard for surveys (De Leeuw & Dillman, 2008; Groves et al., 2011), self-completion questionnaires are cheaper and more convenient with regards to travel time and costs (Bryman, 2012).

The questionnaire consisted of 18 questions divided into five sections to cover demographics, prescription use, HMPs use, side effects and benefits. Closed-ended questions were used where possible responses could be predicted in advance (e.g. demographics) and respondents could choose a category from a selection provided. Using closed-ended questions means that the responses were easily coded, and the statistical analyses were done in a more structured and meaningful manner.

Moreover, answers from different respondents or groups of respondents could be compared (Bulmer, 2004).

On the other hand, open ended questions were more appropriate for obtaining information on the different prescription drugs and HMPs the participants used. Although more time consuming to administer and more difficult to analyse than closed questions, open questions are more suited for questions where responses are unknown or too numerous to pre-code (Bryman, 2012; Kelley, Clark, Brown, & Sitzia, 2003). Other considerations include, avoiding complex questions by ensuring that all questions were simply worded. The PIS explained what the research was about, the aims of the study, why and how they were selected, and the time required for completing questionnaire and the interviews.

Participants were asked to provide the names of medications, what they are used for and how often. They also had to provide any information on benefits, side effects and reactions experienced from taking the HMPs they have reported. Those who indicated use of HMPs were asked to provide contact details, if happy to participate in the next phase of the study. The questionnaire took an average of twenty to thirty minutes to complete.

#### **e. Main study (January to April 2016)**

A total of four hundred questionnaires were sent out to older adults from Practices A and B (two hundred from each practice). Eligible participants were sent a study pack by post containing:

- Letter of invitation
- Participant Information Sheet (PIS)



- Questionnaire (Appendix C) and reply-paid envelope addressed to the research team
- Request for permission to be contacted for an interview, if they meet the criteria for the next phase of the study.

Each of the 400 questionnaires and pre-paid return envelope were coded with study ID for the GP site (i.e. SG 001-200 and NZ001 – 200). Participants were asked to return completed questionnaire to me at the University address (i.e. Centre for Research in Primary and Community Care (CRIPACC), in the pre-paid envelope provided. Completing and returning the questionnaire implied consent to participate in the study. This was further explained in the PIS that were sent with the questionnaire. My contact details and that of the University Secretary and Registrar were provided on the PIS, if participants had any queries or concerns about the research.

An administrator received responses in the post, recorded codes from the envelopes on a spreadsheet and stored the envelopes safely in a locked cabinet. I contacted the administrator weekly to ascertain how many responses were received. And those who did not return the questionnaire after two weeks were sent a reminder letter, asking them to please complete and return the questionnaire (Figure 3.2). If no response had been received after two weeks, another copy of the questionnaire was sent to participants along with the PIS. Participants were not followed up again after this third contact.

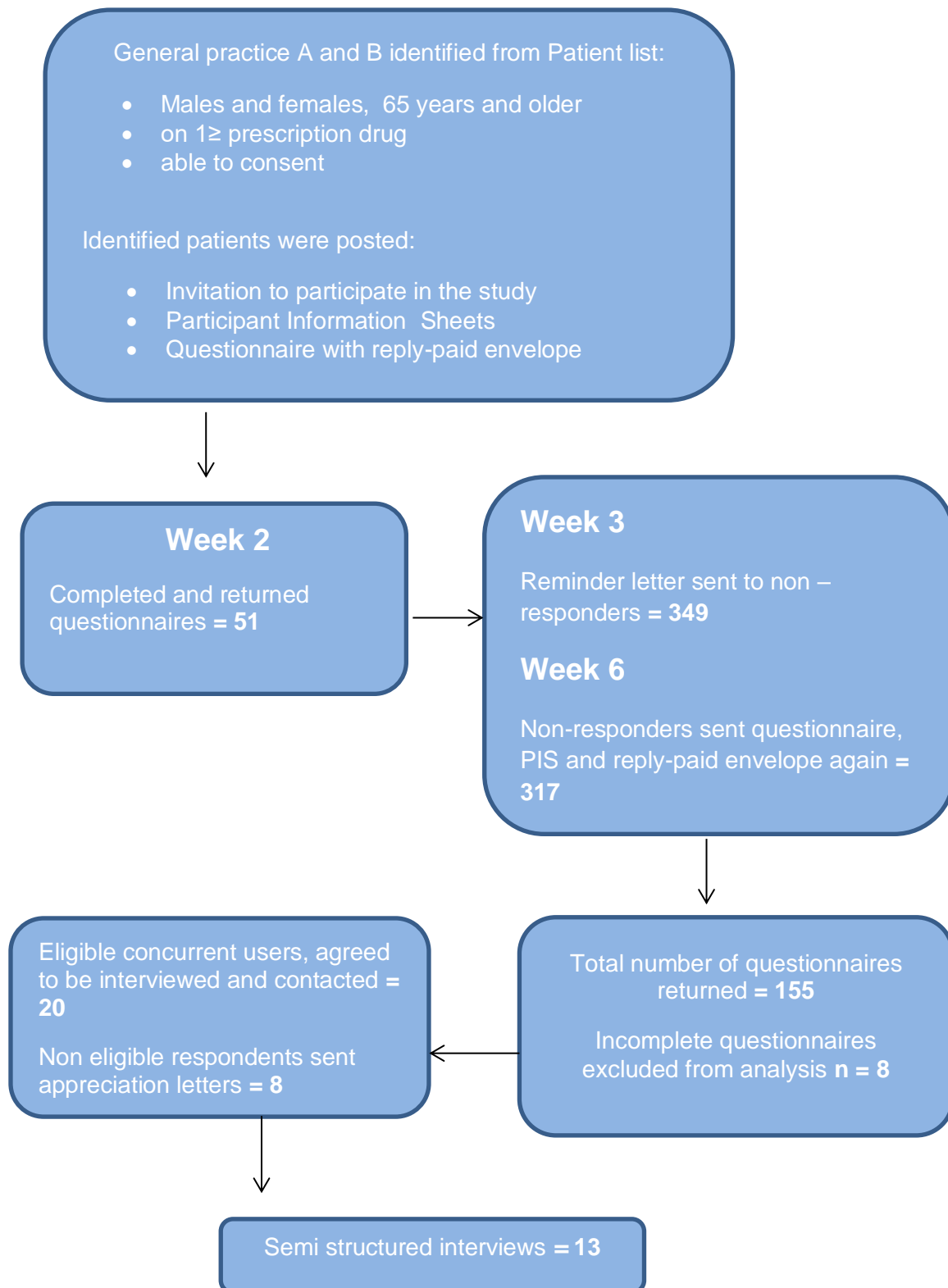


Figure 3.2 Survey Flowchart

### 3.7.3 Phase 3- Qualitative Study (Semi-structured Interviews)

The survey provided an overview of the HMPs used by older adults concurrently with prescribed medications and the possible interactions from such combinations (Agbabiaka, Spencer, Khanom, & Goodman, 2018). However, it did not provide an in-depth understanding of the reasons why older adults concurrently use medications neither did it examine their views and experiences.

Interview is the most frequently employed method in qualitative research. The strength lies in gaining information on the perspectives, understanding and meanings constructed by others regarding events and experiences (Patton, 1990). Interviews can be unstructured, semi-structured or structured. Semi structured interview are series of open-ended questions based on the topic under investigation (Bryman, 2012). An open and more relaxed approach to interviewing is achieved with the semi-structured approach because it is focused, yet less directive and less intimidating than structured interviews (Louise Barriball & While, 1994; Tashakkori & Teddlie, 2003). It also allows the participant to identify what is important to them about the topic being discussed.

The dynamics between interviewer and interviewee in semi-structured interviews provide opportunities to change the words but not the meaning of the questions to suit different participants when conducting the interview (Holloway & Galvin, 2016). For example, herbal medicinal product does not mean the same thing to every participant. Therefore, examples of herbal medicines, or the words 'herbal medicine', 'herbs' or 'herbals' were used at different occasions based on the participant's

understanding. More importantly, the interviews allowed for interrogation of new ideas or explanations as they emerge, while at the same time exploring and clarifying inconsistencies in the participant's account (Barriball & While, 1994; Hutchinson & Wilson, 1992).

A disadvantage of interviews is that it can be time-consuming and expensive to conduct. Also, the volume of data generated from interviews are more difficult and time-consuming to analyse or generalise (Moore, 2000; Potter & Hepburn, 2005). The quality of the interview depends heavily on the skills and how the personal biases of the interviewer are addressed.

In this study, the priority was adopting approaches that best answer the research aims and objectives, considering that collecting diverse types of data is key to better understanding a research problem (Plano Clark & Creswell, 2011). The exploratory nature of the semi-structured interviews provided additional depth to the issue of concurrent prescription and HMP use, and explained further the quantitative data collected from the survey providing detailed exploration of the problem (Creswell & Clark, 2011).

#### **a. Participant- Researcher Relationships**

Previous works have recognised the complex dynamics between researcher and the interviewee. According to Robertson (2011), the communication is different from that of a health interview survey and therefore a change in perspective is important.

While some authors perceived the power dynamics as fluid (Tang, 2002), dialogic (Russell, 2000) or egalitarian (Beale, Cole, Hillege, McMaster, & Nagy, 2004), other authors have questioned the asymmetries of power in interviews and considered the

interviewer as having control over what is said, how it is said and disseminated (Briggs, 2003; Kvale, 2006; Scheurich, 1995). However, as Reed (2000) pointed out, the hierarchy between participants and the researcher during interviews is fluid; moving from the researcher being dominant at particular times and respondents being dominant at others. For example, there were times during the interviews where I was perceived to be a 'Doctor', while at other times I was the 'researcher' or the 'herbal medicine expert' and asked for advice on herbal medicines. At other points it was the older person who was the expert controlling what information they would or would not disclose. This reinforces "the contextual location of knowledge and the production of knowledge through dialogue which makes room for a plurality of voice (Reed, 2000).

As argued by feminist scholars, possessing similar characteristics such as race, ethnicity, gender and socio economic status with participants may potentially benefit research relationships (Tang, 2002) but impacts on the power relationships (Bhopal, 2001; Finch, 1984; Hesse-Biber, 2007; Oakley, 1998). This can result in difficulties with gaining access, establishing trust and rapport, and developing non-hierarchical relationships (Riessman, 1987; Zubair, Martin, & Victor, 2012). Therefore, understanding that these multiple factors shape the quality and content of the information generated, is important to interpreting the research (Manderson, Bennett, & Andajani-Sutjahjo, 2006).

The two sites for this study were Practice A (NZ), a large agricultural village, predominantly White and middle class, but representing a range of socioeconomic status. Practice B (SG) is urban, deprived and multicultural inner- city area.

Participants on both sites were retired older adults receiving pensions, some living on council estates, retirement schemes or in large semi-rural properties. In contrast, I am Black, middle class, educated, middle aged, Muslim and hijab (Muslim head cover) wearing woman. Although I was dressed casually for the interviews, my style of dress and outlook was very different from many of the participants. This may have affected the way I was viewed by participants and subsequently the flow of the interviews.

It is probable that the interactions, rapport and disclosure between me and interviewees were determined predominantly by gender and ethnicity (McNay, 2003) rather than differences in age. This is because the interviews with female participants were longer, richer and more revealing, compared to those with the men. However, the notion that women's account of experiences, illnesses, and social worlds are expansive than those of men (Finch, 1984; Finlay, 2002), might explain this. Although this does not suggest that men place no emphasis on health or interaction with others.

It is not possible to know if different information would have come from the interviews if a white researcher was conducting them. Although the PPI input and the pilot interviews did not suggest this was a significant issue. Either way, this does not render such accounts invalid, but emphasises the complexity and the significance of social interactions in collecting and interpreting research data (Manderson et al., 2006).

## **b. Validity and Reliability**

A common criticism of qualitative research relates to the issues of validity and reliability. While credibility in quantitative research depends on construction of the instrument in qualitative research, “the researcher is the instrument” (Patton, 1990). Therefore, the credibility of a qualitative research depends on the ability and effort of the researcher to ensure credible and trustworthy findings by minimising biases. There are varied opinions regarding the suitability of extending rigour, validity and reliability as employed in quantitative research to qualitative research (Koch, 2006; Morse, Barrett, Mayan, Olson, & Spiers, 2002; Sandelowski, 1986). Considering that qualitative research methods does not lend itself to statistical or empirical calculations of validity, different ways to enhance the truthfulness or validity of qualitative findings must be employed (Golafshani, 2003). Terms such as credibility, trustworthiness, truth, value, applicability, consistency and confirmability are often used when referring to criteria for evaluating the merit of qualitative research (Golafshani, 2003). Although some authors believe that irrespective of the research tradition, validity and reliability have the same meaning, therefore nothing is gained by changing labels (Long & Johnson, 2000).

**i. Credibility and trustworthiness:** Bias in qualitative research may occur in many ways. Firstly, the researcher’s personal beliefs, pre-existing views on the topic, professional or cultural views can influence data collection, analysis and interpretation of findings either intentionally or otherwise (Brink, 1993; Patton, 1990). My personal biography as a Black, Muslim, middle class woman, inevitably shapes my perception and outlook of issues. Also, the influence of my African background and culture, where herbal medicines are commonly used to treat diseases, maintain

health and well-being cannot be overstressed. In addition, my training and experience in patient safety is also to be considered. All these are likely to influence my views and subsequently my interpretation of the findings. However, a first step towards reducing the risk of bias is an awareness of the possible ways that bias may be introduced throughout the research process (Brink, 1993). I have maintained reflexivity and thorough analyses of findings throughout the research process, some of which are outlined in a reflection on the strength and limitations of chosen methodology and methods in section 7.6 and 7.7. The research methods and data analyses were also regularly shared with and checked by my supervisors, to discuss and compare interpretations.

Another source of bias relates to participants behaving differently, portraying themselves in the best possible way to the researcher, withholding or distorting information (Goffman, 2006). To minimise this bias, a friendly and open rapport was developed with participants, through non-judgement of their narratives and interrupting them as little as possible. Also, the responses provided in questionnaires were verified during interviews and any discrepancies were noted.

Other forms of biases which threatens the credibility and trustworthiness of research are procedural, sampling and systemic bias (Coggon, Barker, & Rose, 2009). Asking leading questions or closed questions restrict participant's response, discouraging open accounts of their views and experiences. To minimise procedural bias, an interview guide was developed and used to shape the interviews, and efforts were made to use open-ended questions and allow participants tell their 'story'.



Sampling and systematic biases were minimised through purposive sampling, and a consistent approach to coding interviews. Also, all methods and findings have been reported transparently throughout this thesis.

**ii. Dependability:** In quantitative research, reliability and validity depends on the potential for subsequent research to reconstruct data collection and analysis to yield the same result. This is a problem for qualitative research; therefore, the alternative employed is dependability. Dependability is similar to accountability, and it is judged by clear explanation and presentation of the methods; with precise and thorough description of data analysis and strategies, to enable fellow researchers form valid judgement (Brink, 1993; Lincoln & Guba, 1985; Sandelowski, 1986).

The protocol for this study demonstrates a clear trend of the study and the rationales, with initial assumptions declared right from the onset (Lincoln & Guba, 1985). The systematic literature review (Chapter 4) highlighted existing gaps in the literature, from which decisions on the research questions, study objectives and research design were made. Also, dependability was strengthened by reporting the challenges encountered during the study and the decisions taken to overcome them.

**iii. Transferability:** this refers to the extent that the study findings can be transferred to another setting or group (Polit & Beck, 2004). Although no study is universally transferable, irrespective of the methods used. In qualitative research, transferability is synonymous with external validity or generalisability in quantitative research. This also relates to providing the reader with evidence that findings are applicable to other contexts.

To facilitate transferability, it was valuable to give a clear and distinct description of culture and context, selection and characteristics of participants, data collection and process of analysis (Graneheim & Lundman, 2004; Lincoln & Guba, 1985), all of which have been provided in this chapter. Where appropriate, the findings have been presented together with verbatim quotations from participants in Chapter 6 (semi-structured interviews). This information will enable others to determine the extent of transferability of the findings to another context (Fain, 2017).

### **c. Objectives**

Semi-structured interviews were conducted to:

- a. Further explain and interpret results obtained in the quantitative phase, using selected participants who can best provide these details.
- b. Gain a better understanding of why older adults combine HMPs with prescription medications, their views and experiences.

#### **d. Pilot Study (November 2015)**

The survey data informed how participants were identified for the semi-structured interviews as it ensured that those recruited were willing to participate and were taking HMPs concurrently with prescribed medications typical of this population. The main objective of the interviews was to provide a better understanding of why older adults combine HMPs with prescription medications. The findings from the systematic review and the survey informed areas that were explored in these qualitative interviews. For example, people use HMPs for different reasons and at different times, and this relates to how they believe they work, the length of time that they have used HMPs and whether they think the prescribed medication is complementary to the HMPs or vice versa. A focus of the interviews was to understand if participants are aware of possible interactions from combining HMPs with prescription medicines, and if they discussed using HMPs with healthcare professionals.

An interview guide with prompts (Appendix F) was developed to focus the conversation, but at the same time allow the flexibility to probe emerging issues and lines of thought identified from the survey and from earlier interviews (Corbetta, 2003). The content of the interview guide was informed directly from the survey and covered themes relating to concurrent use, attitude to HMPs, awareness of potential herb-drug interactions and disclosure to health practitioners. It asked participants about the different types of HMPs they used, their reasons and experience of combining them with prescription drugs.

The guide was tested on one older participant in a pilot interview in order to check if the questions were clear and likely to elicit responses specific to the concurrent use of HMPs and prescribed medications. It was also a practise exercise to develop my interviewing skills and gain some confidence.

The pilot interview lasted for 32 minutes. The questions were understood, and I was able to gather the information required. However, I interrupted the participant many times, sometimes completing the participant's sentences. The pilot helped me to address this and to consider structuring the interview so as to allow the older person to talk, but to also include points of clarification as part of the interview process.

## **i. Sampling**

Sampling was purposeful so as to include 'information-rich cases' to be studied in-depth (Patton, 1990). Initially, a total of 32 interviews were planned for this phase (i.e. at least two participants from the five age groups, single users and multiple users) in order to capture age and gender differences, ethnicity, as well as multiple uses (Table 3.3). However, only 20 of the 49 respondents who reported using HMPs in the survey wanted to be interviewed and provided contact details on the questionnaire.

Table 3.3: Selection of participants for semi-structured interviews

Group	Sub-groups	Age group (years) and number of participants			
		65-74	75 - 84	85 - 94	≥95
Gender	Male	2	2	2	2
	Female	2	2	2	2
Number of HMPs	Using 1HMP	2	2	2	2
	Using more than 1 HMP	2	2	2	2
<b>Total</b>		8	8	8	8

## ii. Recruitment

Participant information sheets (Appendix D) and consent forms (Appendix G) were posted to the 20 participants. Participants were contacted a few days later to arrange interview date and venue over the phone. Interviews were only confirmed, if participant understood the PIS and were still happy to proceed with interview.

## iii. Data Collection

All participants were over 65 years old and had a range of physical and mental capabilities. When preparing for the interviews, care was taken to ensure there was sufficient time to introduce the study and for discussion afterwards (Wenger, 2002). Before each interview, the choice to participate or not and to stop interview at any time without providing any reason for doing so was explained to participants. Their

consent was also sought to inform them and their GP, if potentially dangerous herb-drug interaction was suspected from the information they have provided.

Twelve interviews were held with thirteen participants (one interview with a couple) between April and August 2016. The focus of the interviews were participant's reasons, views and experiences of concurrently using HMPs with prescribed medications. Participants were given the opportunity to have the interview in their homes, as it was important to have the conversations in a setting most relaxing for participant.

### **3.8 Data Analyses**

Analysis involves the persistent interrogation of data in a critical, reflexive and iterative fashion that cycles between data and overarching frameworks (O'Leary, 2017). For mixed methods research, this includes data preparation, exploration, analysis, representation and validation (Creswell & Clark, 2011). Since a sequential explanatory design was used in this study, data was collected, analysed sequentially and integrated in the final stage (Creswell & Clark, 2011). See Figure 3.3

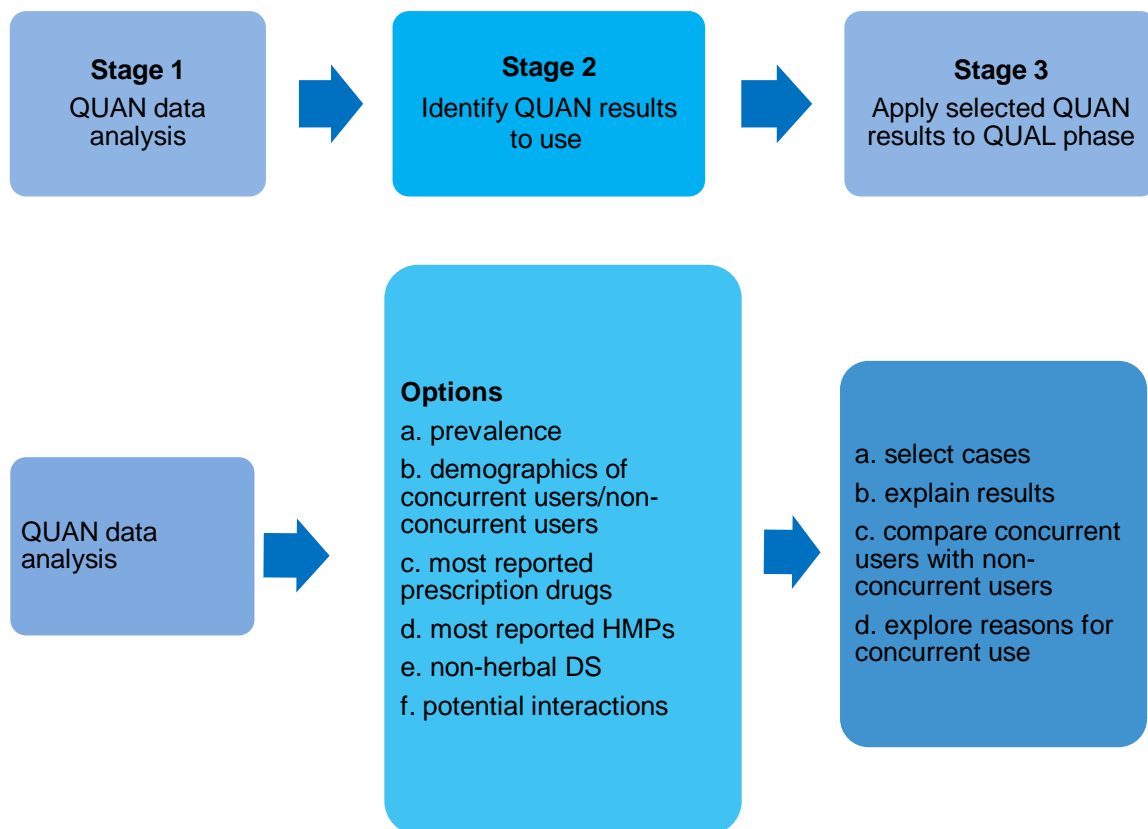


Figure 3.3 Sequential explanatory data analysis

### 3.8.1 Quantitative Data Analysis

Quantitative data analysis was done during and immediately after the survey. Data were recorded and analysed using SPSS version 23.0. Anonymised data were double-checked and discrepancies corrected. Descriptive statistics were calculated to summarise the sample. Names and number of HMPs and prescription drugs reported by participants were entered on a spreadsheet and the 10 most commonly reported prescription and HMPs identified.

Statistical significance was measured at  $p \leq 0.05$  level. Statistical significance is a measure that assesses actual probability that the results are more than coincidental

(O'Leary, 2017). However, statistical significance does not necessarily mean that the results have clinical or social significance. The observations recorded were number and names of prescription medications, HMPs and DS per participants.

#### **a. Descriptive data**

Prevalence was calculated as the number of those reporting concurrent HMPs and prescription medications intake over the total number of study subjects. Proportions were calculated to describe the frequency of use in prescription drug classes and HMP categories. Data were summarised as mean  $\pm$  standard deviation (S.D.) for continuous variables (e.g. age, number of herbal medicines used), and as frequency and percentages for categorical variables (e.g. sex of respondents, educational qualification, living arrangements and ethnicity).

#### **b. Demographic Analyses**

Using the chi-square test for independence, comparisons were undertaken to see whether concurrent use was affected by demographic factors such as gender, ethnicity, educational qualifications and living arrangements.

To conduct analysis for educational level and see if educational level was associated with concurrent use of HMPs, it was necessary to split data into two i.e. those with further education and with no further education. The further education group consisted of participants with some education or training after secondary school. While those without further education were those with no education or training beyond secondary school.



Considering that only 21 responses were received from non-white participants, compared to 126 responses from white participants, it was not possible to test for differences between individual ethnic groups. There were three responses from participants of multiple or mixed background (i.e. white and black Caribbean, white and black African and other multiple ethnic background), 15 from Black or Black British, two from other ethnic groups and only one of Asian or British Asian background.

On account of the small sizes in each of the ethnic groups, Fisher's exact test of independence was more appropriate to determine whether the proportion of one variable was different depending on the value of another variable. Statistical advice and support were provided by my second supervisor Dr Neil Spencer, a statistician and head of the Statistical Services & Consultancy Unit, University of Hertfordshire.

### **3.8.2 Assessing potential interactions between prescription drugs, herbal medicinal products and dietary supplements**

Participants were categorised as concurrent user if they reported current use or have used HMPs or DS in the last 12 months. Potential interactions between prescription drugs, HMPs and DS were assessed only among concurrent users. All medicines reported by participants were listed in a spreadsheet. Combinations of HMPs, DS and prescription medicines were assessed using an online interaction database, *Stockley's Herbal Medicines Interactions* (available on Medicines Complete at <https://www.medicinescomplete.com/mc/shmi/current/>). *Stockley's Herbal Medicines Interactions* is a comprehensive evidence database and the digital version of the

textbook (Williamson et al., 2013). Information regarding potential interactions between herbal medicines (including nutritional supplements and some food) and conventional medicines are expertly assessed with practical advice provided. This database was selected because it is comprehensive, rigorous and a critical evaluation of available evidence provided in easy-to-read format and regularly updated.

The Stockley's database rates herbal medicine interactions using three different categories i.e. action, severity and evidence.

#### **a. Action**

This describes whether an action needs to be taken to address the interaction or not.

And this could be one of the following five actions:

- No action: for drug pairs where no interaction occurs, therefore no action is required.
- Informative: for drug pairs where probability of interaction is low, and close follow up or monitoring is not required but more information is given in case there is a problem.
- Monitor: for interactions where biochemical or therapeutic drug monitoring is recommended since further action may be required based on the outcome.
- Adjust: for drug pairs where the interaction can be accommodated but recommended that either one of the drugs is changed, or the dose altered.
- Avoid: for contraindicated drug pairs, where the drug combination is best avoided.

- b. Severity:** This describes the severity of the interaction and the likely effect on a patient if interaction is unmanaged. Severity ranges from 'severe' to 'nothing expected'.
- c. Evidence:** This describes the weight of available evidence (both clinical and experimental) regarding the interaction. Much of the available data on interactions with herbal medicines comes from animal and *in vitro* studies. Even though these data do not always extrapolate to clinical situations, it provides some idea of the likelihood and potential severity of interactions. This category ranges from 'extensive' to 'theoretical weak'.

Based on these three categories (i.e. action, severity and available evidence), one of five symbols are used to describe the combination. And this ranges from 'life threatening outcome', 'significant hazard', 'potentially hazardous outcome', 'doubt about outcome of use' and 'no interaction'. The combinations are represented by the following symbols:



**Life- threatening outcome:** interaction is life threatening, concurrent use is best avoided.



**Significant hazard:** concurrent use may result in significant hazard, dosage adjustment or close monitoring required.



**Potentially hazardous outcomes:** interactions may have potential hazardous outcome, but data is poor or sparse. Therefore, it is difficult to draw conclusions regarding interaction.



**Doubt about outcome of use:** where there is doubt about outcome of concurrent use, but necessary to give patients advice/guidance about possible side effects and/or consider monitoring.



**No interaction:** no interaction occurs, or interactions are of no clinical significance.

In the Stockley's database:

- For each concurrent user, all the medications reported were entered in the search box as word or words separated by spaces, in "double quotes".
- Predictive text provided suggestions of drug names or herbal medicines, therefore helping with misspelt entries.
- Terms recognised as drug names or drug groups are checked by the database for specific interactions between any of the two terms entered.
- The default search is 'interactions' tab. When no result is displayed (i.e. no available information on interactions between the drugs entered), the 'Full Text' tab provides general information on the herbal medicine.
- One name is consistently used for each herbal medicine throughout the monograph, and across the database. However, a synonyms field is available to aid users who know the plant by different names to match the correct one.

Participants were categorised as having a potential for interaction if using an HMP or DS in combination with prescription drug for which there is documentation of an interaction in *Stockley's Herbal Medicines Interactions*. All recorded potential interactions were independently validated by a second reviewer (a colleague and qualified pharmacist) also using the Stockley's database. Any disagreements were resolved through discussions with the second reviewer.

### **3.8.3 Qualitative Data Analysis**

#### **a. Transcription and data management**

All thirteen interviews were audio recorded and transcribed verbatim, three by me and the remaining ten by a professional transcriber. All personal details were removed from the transcript in line with the rules of anonymity and confidentiality. All transcripts were saved on a secured NHS computer, with password protection only accessible to me.

Anonymised transcripts were imported into the computer-based programme Nvivo11 (QSR International) to organise the data and support analysis. Transcripts were read repeatedly to get immersed in the data, read line by line, and then word by word to derive codes. The process of re-reading, familiarisation and categorisation was to map the scope of the content and the range of responses. This was a descriptive process, a systematic sorting of the data.

The process of identifying and coding statements was to develop categories that were as close as possible to the individual participant accounts. The analysis followed the way that the interviews had been structured i.e. questions that addressed the gaps from the systematic review and the survey. Narratives to the questions were analysed one after the other.

#### **b. Framework analysis**

The primary method used for analysing qualitative data in this study was framework analysis, drawing on the approach by Ritchie and Spencer (2002). Framework analysis belongs to the broad family of thematic or content analytic methods,

characterised by identifying differences and similarities within data, seeking relationships and then drawing conclusions on the themes or patterns (Braun & Clarke, 2006; Gale, Heath, Cameron, Rashid, & Redwood, 2013).

The choice of framework analysis lies in its clarity and flexibility (Srivastava & Thomson, 2009). The method is open to change, addition and amendment throughout the analytic process. Analysis can be done during data collection or after all data has been collected. Following the clear steps to analysis generates highly structured outputs of summarised data (Gale et al., 2013). Although analysis is based on and largely driven by original accounts from participants (Ritchie & Spencer, 2002), thus making it quite similar to grounded theory. However, it differs in the sense that, it is better suited to research that has specific questions, a pre-designed sample and a priori issues that need to be dealt with. In this case, older adults' reasons and experiences of concurrently using HMPs with prescription drugs. Framework analysis involves systematic processes of sifting, charting and sorting transcript material according to key issues and themes. It allows analysis of cases (i.e. individual interviews) within the whole content, thus conferring accuracy and intricacies to the interpretation (Ritchie & Spencer, 2002). Theories may be generated through framework analysis, but the main task is to describe and interpret what is happening in a setting (Ritchie & Spencer, 2002).

Framework analysis involves a five-step process; familiarisation, identifying a thematic framework, indexing, charting and finally mapping and interpretation (Ritchie & Spencer, 2002). Although more recently expanded to seven stages (Gale et al., 2013), the main steps are still covered in the five steps by the pioneers.

## **i. Familiarisation**

The process of familiarisation is already explained (Ritchie & Spencer, 2002; Srivastava & Thomson, 2009). All the 13 transcripts and the field notes written during the interviews were read repeatedly to get familiar with details of each transcript and understand the context in which things were said. Reading a few times allowed for a full picture and for connections to be made between different aspects of participants' accounts. To organise the data, each interview was entered in NVivo Pro Version 11 (QSR International, UK) and initially treated as a unit of analysis.

## **ii. Developing the analytic framework**

This was done by identifying recurrent and important themes based around key areas of interest in the interview (Appendix H). Labels (or nodes as called in NVivo) were generated for codes inductively from the data using words and phrases that captured key thoughts and/or concepts. Highlighting and coding was undertaken in each transcript with attention to identifying the reasons, views and experiences of concurrent use. As a summary for each of the individual codes, analytic memos were written to capture what comes to mind about the data and early interpretations (Gale et al., 2013). For example, what were HMPs used for and why, the values and beliefs about HMPs, experiences and benefits of using HMPs, knowledge or experiences of herb-drug interactions. This was piloted on 2 transcripts and what was clear from the data was that participants were exhibiting or adopting different behaviours to concurrently use HMPs and DS with prescription drug but not abandoning their prescription drugs. Initially, it was not clear where to code data regarding how participants did not ditch their prescriptions but continue to use them with HMPs and DS. So, this draft framework was refined to fit with emerging data.



Highlighted sections of the transcripts were split into smaller segments or themes, thus establishing the first set of themes from the data (Alhojailan, 2012). Quotes from relevant transcripts were used to illustrate the memos and participants different from the themes emerging from the majority were noted. Using this approach allowed for similarities and differences between the different narratives to be identified. It also showed any links and connections between the categories (Leech & Onwuegbuzie, 2011). For example, participants' reasons for concurrently using HMPs with prescription drugs were often prompted by a specific focus on dissatisfaction with the healthcare system or alleviating pains and avoiding the side effects associated with conventional medicines.

There were regular discussions on codes and initial thoughts on the analysis with my principal supervisor. This process helped to enhance rigour and reliability in the coding (Bryman, 2012; Gale et al., 2013; Miles, Huberman, & Saldana, 1984). The codes were grouped into categories and the study questions were reviewed to identify information that relates to similar concepts. All data that related to each interview question were organised together and presented in that order. The key issues, concepts and themes formed the basis of the analytic framework (Table 6.2).

### **iii. Indexing**

The 59 codes were then organised into framework categories. This framework was then systematically applied to individual transcript. This process of charting and indexing was done in NVIVO by working through individual transcript, highlighting a chunk of text, deciding which category or categories (or node as it is known in

(NIVIVO) from the framework to assign it to and dropping it into the relevant category.

#### **iv. Charting or summarising data in the analytical framework**

At this stage, the data was summarised and organised into manageable format to facilitate analysis in the next stage. Using the auto summarise function in NIVO made this relatively easy, as it automatically populates relevant cells in the framework with indexed data for each category. With the data presented in this format, it was possible to do within-cases and between-cases analyses, by reading across for the former and downwards for the latter. I worked through each framework category and summarised all the data indexed to that category for each participant.

#### **v. Mapping and interpretation**

By mapping and summarising the data as described above, I was able to identify cross cutting links and patterns of responses. I was also able to develop concepts and themes around the concurrent use of HMPs, DS with prescription drugs which could be seen to resonate with some of the existing wider literature on self – management. For example, a dominant cross cutting theme identified from the interviews was maintaining health. Within that are concerns with managing pain and not wanting to bother their GPs, not getting appointments or enough time with the GP to explain their conditions. This was also linked to a perception that these issues were minor complains and the importance of being left to ‘deal with it’ themselves.

### **c. Analytic Framework**

A descriptive and interpretative analytic approach as described by (Elliott & Timulak, 2005) was undertaken with each transcript. A set of 59 preliminary codes (or nodes as they are known in NVivo) were developed from the data, informed by the interview prompts (Appendix F) and emergent issues relating to participant's beliefs and values, cultural or family history of using herbal medicines, sources of information, experiences of using HMPs and the benefits derived. Subsequently, numerous codes were grouped together to form categories. This was an iterative process where making sense of the data was facilitated by previous understanding of the herbal medicine use literature. For example, codes for specific ailments such as joints related pain and where participants described HMP use as being for minor health related problems were grouped together as a category - used for less serious conditions. Codes were frequently compared to each other until all interview data were mapped and captured. The interpretation of the categories and the development of themes were derived from the identification of recurring issues and explanations in the data of how HMPs and DS were used, and these were further discussed with the supervisory team.

### 3.9 Data Integration

This study began with an emphasis on patient safety and an assumption that there were right and wrong uses of HMPs. The survey and interviews not only addressed this, but they also provided the opportunity for alternative explanations and insights as to how medication is used and understood. The key assumption was that people take their prescribed medications and that there is a risk if they are taking HMPs concurrently. It is also possible that they are not taking the prescribed medications at all, which raises a different set of questions for non-adherence.

The data generated in phases 1, 2 and 3 were analysed and interpreted separately to address the research questions but combined at the point of interpretation (Moran-Ellis et al., 2006). Data synthesis in this study was a logical accumulation and corroboration of findings from the different phases, therefore more of an aggregation than integration. The data was merged in a side-by-side process as outlined by Creswell and Plano Clark (Creswell & Clark, 2011) and compared to the self-management theory. This side-by-side comparison allows for the presentation of results that can be drawn upon to describe the study findings. A further synthesis of data was conducted to generate a smaller number of overarching themes representing key reasons why older adults concurrently use HMPs and prescription medicines.

### 3.10 Chapter summary

This chapter has justified the methods applied to this study which explores the concurrent use of prescription drugs and HMPs among older adults. Evidence shows no recent UK study exists on the topic and there is limited research exploring the reasons for concurrent use and the experiences of concurrent users. To meet the aims of this research, a mixed method sequential explanatory design was considered most suitable to answer the research questions. Self-completed questionnaire survey was employed to gather information on concurrent use among UK community dwelling older adults. Using a purely quantitative approach would not provide adequate understanding of the reasons why older adults combine their prescriptions medicines with HMPs or their experience of doing so. Therefore, semi-structured interviews were used to explore reasons, views and experiences of older adults concurrently using prescriptions with herbal medicines. Results from the survey identified participants for the in-depth interviews and informed areas to further explore.

The Chapter also provided details of the systematic review, the cross-sectional study design and the semi-structured interviews. This included information on ethical issues, setting, access and data collection, questionnaire design, sample size and statistical analysis. Details of the thematic analysis processes have been provided including how themes were developed from the initial stages using the computer software package NVivo. The next chapter presents the findings from Phase 1 of the study i.e. a systematic literature review to critically assess available evidence on the concurrent use of prescriptions drugs and HMPs among older adults.

# Chapter 4: Concurrent use of Prescription Drugs and Herbal Medicinal Products in Older Adults: A Systematic Review

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*A paper based on the work presented in this chapter has been published as: Agbabiaka, T. B., Wider, B., Watson, L. K., & Goodman, C. (2017). Concurrent use of prescription drugs and herbal medicinal products in older adults: a systematic review. Drugs & Aging, 34(12), 891-905.*

## 4.1 Introduction to Chapter

This chapter will present the findings from a systematic review which evaluated the prevalence, patterns, potential interactions and factors associated with the concurrent use of prescription drugs and HMPs among older adults. The Chapter provides the methods for the review including criteria for literature searches, selection of studies, data extraction and synthesis. The findings were summarised as a narrative account addressing each of the review questions. A detailed discussion of the limitations of included studies and implications of the findings were also provided.

## 4.2 Background

The world population is ageing and according to the World Health Organisation (WHO), the population of people aged  $\geq 60$  years will double and around 400 million people will be  $\geq 80$  years by 2050 (World Health Organisation, 2012). By 2040, nearly one in four people (24.2%) in the UK will be aged 65 years or older (Office for National Statistics, 2015). Pharmacotherapy is facilitating an ageing population

(Cherubini, Corsonello, & Lattanzio, 2012) and older people rely on complex polypharmacy in managing chronic health conditions (Nyborg et al., 2012).

Older adults are the biggest consumers of prescriptions and over-the-counter (OTC) medicines (National Council on Patient Information and Education, 2010; Qato et al., 2008; Qato et al., 2016). Self-medication (Jerez-Roig et al., 2014; Vacas Rodilla et al., 2009), consumption of non-prescription medicines, particularly herbal and other DS is also widespread among older adults (Bruno & Ellis, 2005; de Souza Silva et al., 2014; Gonzalez-Stuart, 2011; Izzo & Ernst, 2001; Izzo & Ernst, 2009; Marinac et al., 2007; Raji, Kuo, Al Snih, Sharaf, & Loera, 2005).

In 2014, prescriptions dispensed for those aged over 60 years in the UK accounted for about 51% of the total net cost for all prescriptions (Health and Social Care Information Centre, 2015). Also, up to a quarter of UK adults use HMPs (Lynch & Berry, 2007; MHRA & Ipsos MORI, 2009; Qato et al., 2016), mostly bought over the counter, by self-prescription and generally not disclosed to healthcare practitioners (Lynch & Berry, 2007; MHRA & Ipsos MORI, 2009; Qato et al., 2016). Adverse drug reactions (ADRs) could occur due to interactions between conventional drugs and HMPs, some of which may have serious consequences (Fugh-Berman, 2000; Izzo & Ernst, 2001; Williamson, 2001; Williamson et al., 2013). For example, St. John's wort (*Hypericum perforatum*) taken with serotonin-reuptake inhibitors increases the risk of serotonin syndrome in older adults (Fugh-Berman, 2000).

Currently, there are many studies on the use of herbal medicines and DS by older people (Bruno & Ellis, 2005; de Souza Silva et al., 2014; Gonzalez-Stuart, 2011; Izzo & Ernst, 2001; Izzo & Ernst, 2009; Marinac et al., 2007; Raji et al., 2005). However, less is known about the potentially more troubling practice of concurrently using herbal medicines with prescription drugs.

The aim of this systematic review was therefore to evaluate the literature on concurrent use of prescription drugs and HMPs among older adults to identify the prevalence, patterns, potential interactions and other factors associated. The systematic review was registered on PROSPERO (registration number: CRD42014009091) (Agbabiaka, Wider, Goodman, & Watson, 2014).

### **4.3 Review questions**

The review will seek to answer the following questions:

- a. What is the prevalence and pattern of concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults?
- b. What patient and clinical characteristics are associated with the concurrent use of prescription drugs and HMPs?
- c. What are the range of prescription drugs and HMPs most concurrently used by older adults?
- d. What safety issues and other factors are associated with concurrent prescription drug and HMPs use in older adults?



The review was conducted according to the principles of systematic review (The Cochrane Collaboration, 2011) and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Shamseer et al., 2015). The methods are fully described in this chapter and in a previously published review protocol (Agbabiaka, Wider, Watson, & Goodman, 2016).

## **4.4 Eligibility criteria**

### **a. Types of studies**

All cross-sectional studies, case reports and case series reporting prevalence, patterns and interactions from concurrent HMPs or herbal DS used with prescription medicines were considered. PhD theses, editorials, commentaries, *in-vitro* experiments and animal studies were excluded.

### **b. Types of participants**

The WHO defined 'elderly' as individuals over the age of 65 years in developed countries, and over 60 years in developing countries. For the purpose of this review, the minimum age of 65 years was adopted since most studies identified from literature searches were conducted in developed countries. Therefore, studies with participants aged 65 years or older, studies with mean participant age  $\geq 65$  years or studies from which data for participants aged  $\geq 65$  years could be extracted were included in this review.

### **c. Types of interventions**

The review included studies where any type of HMPs was used concurrently with prescribed medicines. Herbal medicinal products are medicinal products where the active ingredients consists exclusively of herbal substances or herbal preparations (Commission of the European Communities, 2003). Excluded were studies assessing herbal medicine as part of a therapeutic system or system of medicine such as traditional Chinese medicine, Ayurveda, Kampo, Siddha, Unani. Homeopathic herbal remedies were also excluded. Studies assessing concurrent use of vitamins, minerals and non-herbal DS or combination products containing herbal and non-herbal substances with prescription medicines were also excluded from the review.

### **d. Primary and secondary outcomes**

The primary outcomes of interest include prevalence and pattern of concurrent use, names and number of concurrently used medicines, adverse reactions or potential herb-drug interactions reported.

Secondary outcomes of interests were disclosure of HMPs use to healthcare professionals, satisfaction with HMPs and cost of HMPs, where reported.

#### **4.4.1 Identification and selection of relevant studies**

##### **a. Databases**

The following databases were searched from inception until November 2015:

Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO, Cochrane Library, Excerpta Medica database (EMBASE) via OVID, MEDLINE via OVID, the Allied and Complementary Medicine Database (AMED) via EBSCO, PsycINFO via OVID and Web of Science.

The search was updated in May 2017 to include new relevant studies before the review was submitted for publication. To keep up to date with the evidence on this topic, a third search was conducted in February 2019.

##### **b. Search terms**

Medical subject headings (MeSH) and text words related to ‘herbal medicine’, ‘prescription drugs’ and ‘aged’. The scientific names, common names of herbs most documented for concurrent use were applied to ensure a broad search strategy. See Appendix E for full search strategy.

No restrictions were placed on language of publication. Reference lists of all identified studies were checked for relevant studies not identified by the electronic searches. Lateral searches were also conducted using the related citation function in PubMed and cited by function in Google scholar to capture all relevant articles.

### **c. Study selection**

All references retrieved from all the databases were downloaded into Endnote files and merged. Duplicate studies were recorded before discarding. Two reviewers, I (TA) and a colleague (BW) individually scanned all titles and abstracts for potential relevance. Any article for which there was uncertainty about relevance was retained and the full text assessed. Using a pre-designed eligibility checklist, two reviewers (TA and BW) independently assessed full text articles against the eligibility criteria and recorded an eligibility code. Studies that did not meet inclusion criteria were excluded and the reasons recorded. Disagreements on eligibility were resolved through discussions between the two reviewers (TA and BW), the third reviewer and my principal supervisor (CG) was consulted if no consensus was reached. Full texts of all articles which met the eligibility criteria were obtained and downloaded into Endnote.

### **d. Data extraction**

A data extraction form was designed for the review, piloted and amended to ensure that all the required information can be extracted. Data from individual studies were extracted by the first reviewer (TA) using this form and validated by the second reviewer (BW). Key information extracted included:

- Publication details: Authors, year of publication, country in which study was conducted.
- Study design: study type, recruitment and data collection method.
- Participants: demographic and socio-economic characteristics, sampling and sample size, previous medical diagnosis etc.

- Primary outcomes: prevalence of concurrent use, name and number of HMPs and prescription drugs, pattern of use, number and types of adverse reactions or potential interactions.
- Secondary outcomes: Disclosure, satisfaction or dissatisfaction and cost expended on HMPs.
- Study limitations: response bias, selection bias, representativeness of sample etc.

#### **e. Quality assessment of included studies**

The Joanna Briggs Institute (JBI) checklists for appraising studies reporting prevalence data (Munn et al., 2015) and for case reports (The Joanna Briggs Institute, 2016) were used to screen selected studies prior to inclusion in the review. Two reviewers (TA & BW) independently assessed each of the included studies against the criteria on the JBI checklist to minimise bias and establish methodological validity. The JBI checklist for prevalence studies was the preferred assessment tool because it can be used across different study designs reporting prevalence. The checklist also addresses issues of internal and external validity critical to prevalence data. Disagreements between reviewers were resolved through discussion.

#### **f. Data synthesis**

The Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) three stage approach to mixed method research to synthesise data (Kavanagh, 2011) was used. A first synthesis was done to address prevalence, pattern of use and patient characteristics associated with concurrent use of HMPs and prescription medicines. The second synthesis focused on the safety issues and

other factors associated with concurrent use i.e. disclosure, satisfaction and cost/resources. Finally, using thematic synthesis, key themes and commonalities were identified.

## 4.5 Results

The literature searches identified 20,837 titles and abstracts. Initial screening of titles and abstracts identified 2,199 potentially relevant articles. A total of 2,106 articles were excluded for not satisfying all inclusion criteria. Full texts of the remaining 93 articles were obtained to assess for eligibility. At the end of the eligibility process, 71 articles were excluded for the following reasons: type of intervention (e.g. non-herbal combinations, non-oral) = 9; age = 24; study type = 19; no concomitant use = 19. Twenty-two studies met the inclusion criteria and were included in this systematic review (Figure 4.1).

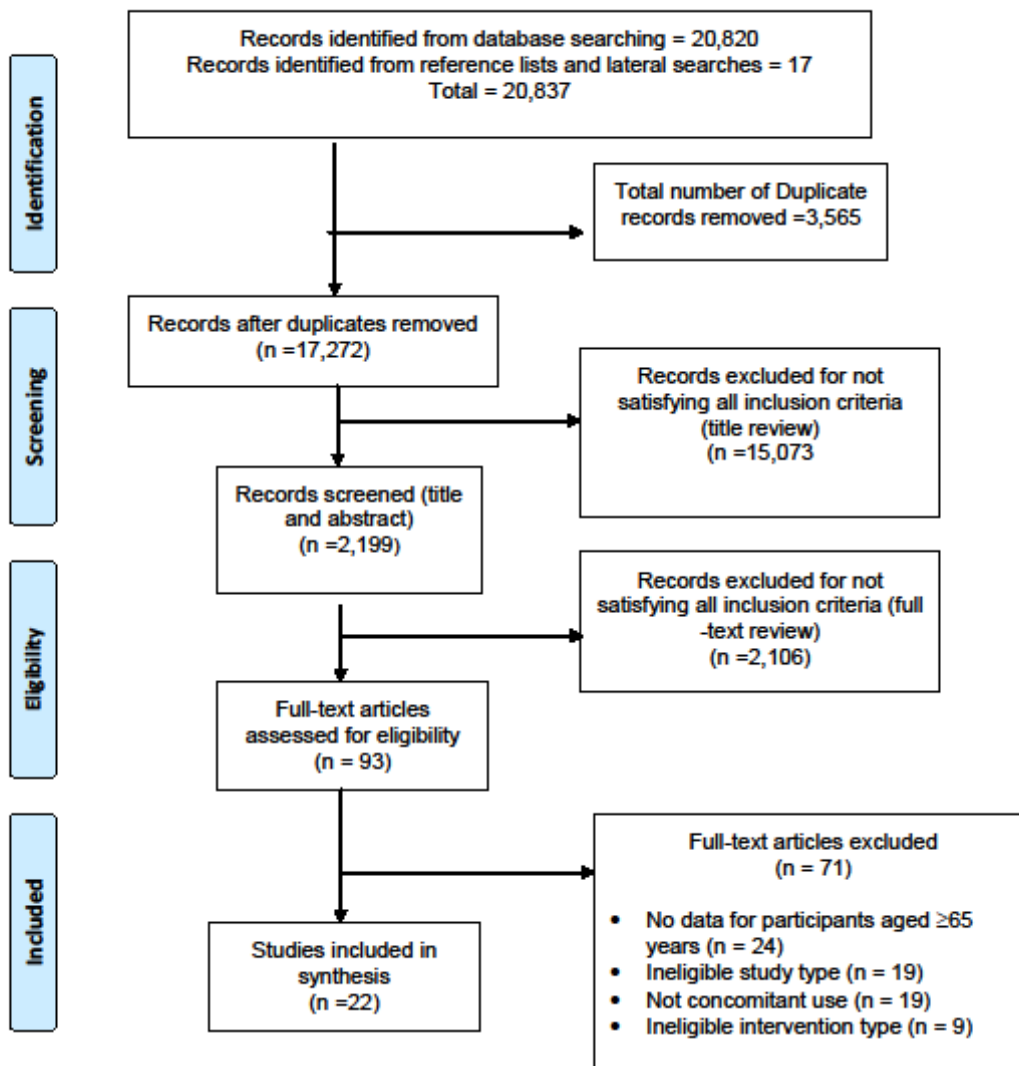


Figure 4.1: Flow chart of study selection process

### 4.5.1 Characteristics of included studies

All but one of the studies included in the review were published in English language, one study published in Spanish (Batanero-Hernán, Guinea-López, García-Jiménez, & Rodríguez-Chamorro, 2017). Thirteen studies were conducted in the USA (Blalock et al., 2009; Kaufman et al., 2002; Lantz, Buchalter, & Giambanco, 1999; Loya et al., 2009; Ly et al., 2002; Nahin et al., 2009; Parkman, 2001; Peng, Glassman, Trilli, Hayes-Hunter, & Good, 2004; Qato et al., 2008; Shane-McWhorter & Geil, 2002; Yoon & Horne, 2001; Yoon & Schaffer, 2006), two in Canada (Dergal et al., 2002; Singh & Levine, 2007). Two studies conducted in the UK (Canter & Ernst, 2004; Izzo & Ernst, 2009). Only one study each was conducted in Ireland (Peklar et al., 2014), Norway (Djuv, Nilsen, & Steinsbekk, 2013), Turkey (Turkmenoglu et al., 2016), Spain (Batanero-Hernán et al., 2017) and Jamaica (Delgoda et al., 2010).

The majority of studies (n=16) were described as cross-sectional (Batanero-Hernán et al., 2017; Blalock et al., 2009; Canter & Ernst, 2004; Delgoda et al., 2010; Dergal et al., 2002; Djuv et al., 2013; Kaufman et al., 2002; Loya et al., 2009; Ly et al., 2002; Nahin et al., 2009; Peklar et al., 2014; Peng et al., 2004; Qato et al., 2008; Singh & Levine, 2007; Turkmenoglu et al., 2016; Yoon & Horne, 2001). Eight of them identified concurrent use of prescriptions with other medications using semi-structured interviews (Batanero-Hernán et al., 2017; Delgoda et al., 2010; Kaufman et al., 2002; Loya et al., 2009; Singh & Levine, 2007; Turkmenoglu et al., 2016; Yoon & Horne, 2001); others interviewed older people, and then checked and recorded their medications (Dergal et al., 2002; Elmer et al., 2007; Kaufman et al., 2002; Nahin et al., 2009; Peklar et al., 2014; Qato et al., 2008). Self-completed questionnaires were adopted in five studies (Canter & Ernst, 2004; Djuv et al., 2013;



Ly et al., 2002; Nahin et al., 2009; Peng et al., 2004) with participants self-reporting all the medicines they were taking on the questionnaire. Three studies (Elmer et al., 2007; Izzo & Ernst, 2009; Yoon & Schaffer, 2006) were secondary analyses of data from previous research and three were case reports (Lantz et al., 1999; Parkman, 2001; Shane-McWhorter & Geil, 2002) of possible interactions between herbal, dietary supplements and prescription medicines.

Only four studies have been published in the last five years (Batanero-Hernán et al., 2017; Djuv et al., 2013; Peklar et al., 2014; Turkmenoglu et al., 2016). Seventeen studies were published between 2000 and 2010, and one case report in 1999 (Lantz et al., 1999).

The twenty-two studies included in this review had a total of 18,399 participants aged 65 years or over. The average age of participants ranged from 63 to 78 years; number of participants ranged from one (case report) to 5,052. Only in ten studies was the focus on those aged 65 years or older, the other studies were conducted among the general population aged  $\geq 18$  years, but data for participants aged  $\geq 65$  could be extracted.

Participants were predominantly females in 12 studies, varying between 51% (Kaufman et al., 2002) and 100% (Yoon, 2001; Yoon & Schaffer, 2006). Male participants were the majority in five studies (Izzo & Ernst, 2009; Ly et al., 2002; Nahin et al., 2009; Parkman, 2001; Peng et al., 2004). The number of males and

females in the different age categories were not specified in four studies (Blalock et al., 2009; Delgoda et al., 2010; Djuv et al., 2013; Singh & Levine, 2007). One study each was conducted among older adults in hospital (Turkmenoglu et al., 2016) and nursing homes (Batanero-Hernán et al., 2017). The remaining studies were conducted among general populations (i.e. community-dwelling older adults) (Blalock et al., 2009; Canter & Ernst, 2004; Delgoda et al., 2010; Djuv et al., 2013; Izzo & Ernst, 2009; Kaufman et al., 2002; Lantz et al., 1999; Loya et al., 2009; Ly et al., 2002; Peklar et al., 2014; Qato et al., 2008; Shane-McWhorter & Geil, 2002; Singh & Levine, 2007; Yoon, 2001; Yoon & Schaffer, 2006), outpatients of memory clinics (Dergal et al., 2002; Nahin et al., 2009), emergency department (Parkman, 2001) and veteran centre (Peng et al., 2004).

By looking at the definition where provided and the herbal medications reported, it was ensured that only studies which evaluated HMPs were included. However, no consistent term exists for HMPs and different terms are used in different countries. For example in Canada, HMPs are referred to as natural health products (NHPs), i.e. “Substances or combination of substances consisting of molecules and elements found in nature and homeopathic preparations sold in dosage forms for the purpose of maintaining or improving health, and treating or preventing diseases/conditions’, and includes herbal medicines, vitamins and minerals” (Health Canada, 2003; Page 2). Both Canadian studies included in this review (Dergal et al., 2002; Singh & Levine, 2007) used the term ‘natural health products’. Only one study from the US (Blalock et al., 2009) used ‘herbs/natural products’ but excluded vitamins and minerals.

Elmer (Elmer et al., 2007) used the term CAM products, defined as “products such as herbal (botanical) products or non-botanical DS (e.g. glucosamine) excluding vitamins and minerals”. Five studies (Kaufman et al., 2002; Lantz et al., 1999; Nahin et al., 2009; Peklar et al., 2014; Peng et al., 2004) used the definition of DS according to Directive 2002/46/EC of the European Parliament and of the Council, 2002 (Commission of the European Communities, 2003) i.e. “potentially any product intended for ingestion as a supplement to regular diet, including vitamins or minerals (at any dose level), herbal products, and nutraceuticals”. Twelve studies (Canter & Ernst, 2004; Delgoda et al., 2010; Djuv et al., 2013; Izzo & Ernst, 2009; Loya et al., 2009; Ly et al., 2002; Parkman, 2001; Qato et al., 2008; Shane-McWhorter & Geil, 2002; Turkmenoglu et al., 2016; Yoon, 2001; Yoon & Schaffer, 2006) provided no definition or an explanation of HMP. All potentially eligible studies were therefore individually screened to ensure they met this inclusion criterion independent of the definition used.

Table 4.1 is a summary of included studies, providing information on study setting, sample characteristics, prevalence of concurrent use, most reported prescription medicines and HMPs, as well as interactions or potential interactions reported from such combinations.

Table 4.1: Summary characteristics of included studies (n= 22)

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Batanero-Hernán et al. (Batanero-Hernán et al., 2017) Spain	Cross-sectional survey/ semi-structured interview	384, ≥65y M = 129 F = 255 mean age or range NS	NS	88.3	Chamomile, anise, lime blossom tea, squaw mint or mosquito plant, red tea, valerian, plantago, Senna, alder buckthorn, balm mint	Paracetamol, omeprazole, benzodiazepines, lactulose, antacids, statins, NSAIDs Ventolin, antipsychotics, Alzheimer drugs	22; potential risk of hemorrhage from valerian with drugs metabolised by CYP3A4; plantago interferes with the absorption of statin, acenocoumarol, digoxin, paracetamol and metformin, Senna with digoxin

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Blalock. (Blalock et al., 2009) USA	Population-based epidemiological study/ face-to-face interviews	1423, ≥65y mean age 63y	Herbs/natural products, excluding vitamins and minerals	19.9	Garlic, <i>Aloe vera</i> , <i>Ginkgo biloba</i> , Echinacea, ginseng, St John's wort, ginger, saw palmetto	Metoprolol, atenolol atorvastatin, simvastatin conjugated oestrogens omeprazole, lansoprazole hydrochlorothiazide, lisinopril, enalapril	168; inhibition of cytochrome P450 3A4 substrates (e.g. atorvastatin, simvastatin) by garlic, <i>Ginkgo biloba</i> , Echinacea, St John's wort
Canter and Ernst, (Canter & Ernst, 2004) UK	Cross-sectional/ self-completed questionnaire	271, ≥50y 137, ≥65y F = 84 M = 53 mean age or range NS	NS	NS	Garlic, <i>Ginkgo biloba</i> , Echinacea, evening primrose oil, St John's wort, ginseng, <i>Aloe barbadensis</i> , devils' claw, cranberry, saw palmetto	Aspirin, Bendroflumethiazide, β-Adrenoceptor antagonist, HMG-CoA reductase inhibitors, ACE inhibitor, levothyroxine sodium, calcium channel antagonist, proton-pump inhibitor	Not possible to extract data for ≥ 65y

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Delgoda et al.(Delgoda et al., 2010) Jamaica	Cross-sectional survey/ semi-structured interview	365 32, ≥70y mean age or range NS	NS	NS	Different types of mints cerasee, garlic and ginger	Atenolol, metformin, Ventolin, nifedipine, enalapril, Glucophage, hydrochlorothiazide, ranitidine, Voltaren, NatriliX	NS
Dergal et al.(Dergal et al., 2002) Canada	Cross-sectional survey/ semi-structured interview	195, ≥65y M = 84 F = 111 mean age 73y	Natural health products	17	<i>Ginkgo biloba</i> , garlic and Echinacea	Aspirin, trazodone, amlodipine, lorazepam	n = 11 in 9 patients increased risk of bleeding (8), increased risk of coma, enhanced sedative effects of benzodiazepines, and blood pressure medication

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Djuv et al.(Djuv et al., 2013) Norway	Cross-sectional, survey/ self-completed questionnaire	381, ≥18y 32, ≥70y mean age 54.5y	NS	40	Bilberry, green tea, <i>Aloe vera</i> , Echinacea, garlic, ginger, <i>Ginkgo biloba</i> , cranberry	Antihypertensive and diuretics, antihyperlipidemic agents, anticoagulants, analgesics, antihistamines, antidiabetics, antidepressants	Not possible to extract data for ≥ 65y
Elmer et al.(Elmer et al., 2007) USA	Secondary data analysis / Population based analysis from a cohort study	5,052, ≥65y M = 2,009 F = 3,043; mean age 75y	CAM products	9.5	Garlic, <i>Ginkgo biloba</i> , ginseng, alfalfa, saw palmetto, Echinacea, <i>Aloe vera</i> , St. John's wort, bilberry	NSAID, warfarin, antihypertensive, statins, omeprazole, nifedipine, furosemide, oral hypoglycaemics	n = 294; elevated drug effect, decreased drug effect, risk of bleeding, affects blood coagulation

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Izzo and Ernst (Izzo & Ernst, 2009) UK	Secondary data analysis / systematic review	90, ≥65y M = 51 F = 39 mean age 68y	NS	NS	St. John's wort, ginseng, garlic, <i>Ginkgo biloba</i> and kava	Warfarin, sertraline, aspirin, caffeine, chlorzoxazone, debrisoquine, midazolam	n = 47; decreased INR, Abnormal bleeding, fatal intracerebral haemorrhage, Nausea, anxiety, restlessness, irritability
Kaufman (Kaufman et al., 2002) USA	Cross-sectional, survey / telephone interview	2590, ≥18y 494, ≥65y M = 243 F = 251 mean age or range NS	DS	16	Ginseng, <i>Ginkgo biloba</i> , garlic, St. John's wort, Echinacea, saw palmetto	Acetaminophen, ibuprofen, aspirin, conjugated oestrogens, lisinopril, atenolol, levothyroxine sodium, hydrochlorothiazide, furosemide, atorvastatin, calcium	Not assessed
Lantz et al. (Lantz et al., 1999)	Case reports	5, ≥65y F = 2 M = 3 mean age 77.4y	DS	NS	St. John's wort	Sertraline, calcium carbonate, conjugated oestrogens aspirin, multivitamin, cyproheptadine, nefazodone	n = 5; central serotonergic syndrome



Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Loya et al.(Loya et al., 2009)	Cross-sectional survey/ semi-structured interviews	130, ≥65y M = 30 F = 100 mean age 71.4y	NS	34.6	Chamomile tea, garlic, flaxseed, artemisia tea (wormwood), <i>Ginkgo biloba</i>	Aspirin, metformin, paracetamol, atorvastatin, levothyroxine sodium, hydrochlorothiazide, alendronic acid, metoprolol, Lisinopril, losartan	n = 220; the majority had potential to result in alterations in either blood glucose or blood pressure
Ly et al.(Ly et al., 2002) USA	Cross-sectional survey/ self-completed questionnaire	123, ≥65y M = 98 F = 25 mean age 78y	NS	22.8	Garlic, <i>Ginkgo biloba</i> , saw palmetto, Echinacea, ginseng	Antihypertensives, antidiabetic drugs, aspirin or another NSAID, corticosteroids	n = 5; Four involved <i>Ginkgo biloba</i> and aspirin, one involved garlic and warfarin. All can increase the risk of bleeding.
Nahin et al.(Nahin et al., 2009) USA	Cross-sectional survey/ self-completed questionnaire	3,072, ≥75y M = 1,653 F = 1,419 mean age or range NS	DS	83	Garlic, <i>Ginkgo biloba</i> , saw palmetto, Echinacea,	Aspirin, statin, beta-blocker, ACE-inhibitors, NSAIDs, thyroid agents, oestrogen, cyclooxygenase-2 inhibitor, thiazide diuretics, vasodilators	NS

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Parkman, (Parkman, 2001) USA	Case report	M =1, 68y	NS		Ginseng, <i>Ginkgo biloba</i> , valerian	Coumadin (Warfarin)	n = 3; nosebleeds, bruises on shins and forearms, and serious headache
Peklar et al.(Peklar et al., 2014) Ireland	Cross-sectional survey/ face-to-face-interviews	8081, ≥50y  3,446, ≥65y M = 3,706 F = 4,375 mean age 63.8y	DS	14	Evening primrose oil, garlic, ginseng	Bisphosphonates, antineoplastic drugs, other analgesics, antiarrhythmic, opioid analgesics	n = 5; increased risk of bleeding from evening primrose, garlic and ginseng combined with antithrombotic
Peng et al.(Peng et al., 2004) USA	Cross-sectional survey/self-completed questionnaire	458 260, ≥65y M = 244 F = 16  mean age or range NS	DS	38	Garlic, <i>Ginkgo biloba</i> , saw palmetto, ginseng, St. John's wort, DHEA supplements (soy, wild yam), Echinacea,	Ibuprofen, fluoroquinolone, Levofloxacin, warfarin, Hydrochlorothiazide, Digoxin, fosinopril sodium, lisinopril, paroxetine	n = 48; increased risk of bleeding due to lowered platelet aggregation, effectiveness of diuretic lowered, lowered anticoagulant effect, increased serotonin levels

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Qato et al.(Qato et al., 2008) USA	Cross-sectional survey/ interviews	2976, ≥57y  1960, ≥65y M = 920 F = 1040; mean age or range NS	NS	52	Saw palmetto, flax, garlic, <i>Ginkgo biloba</i>	Aspirin, hydrochlorothiazide, atorvastatin, levothyroxine, lisinopril, metoprolol, simvastatin, atenolol, amlodipine, metformin	n = 12; increased risk of bleeding
Shane-McWorter and Geli (Shane-McWhorter & Geil, 2002) USA	Case reports	2, ≥52y  M = 1,72y	NS		St. John's wort, Asian ginseng	Metformin, nateglinide, rosiglitazone, losartan, warfarin, digoxin, atorvastatin, paroxetine, acetaminophen	n = 3; reduced blood pressure–lowering effect, decreased INR, decreased Digoxin effect

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Singh and Levine (Singh & Levine, 2007) Canada	Cross-sectional survey/telephone interviews	11, 424, ≥18y mean age or range NS	Natural health product	5.3	Echinacea, garlic, evening primrose oil, <i>Ginkgo biloba</i> , ginseng, flax seed oil, St John's wort, apple cider vinegar	ASA, statin, NSAIDs, calcium channel blockers	n = 124; increased bleeding risk, increased blood pressure reduction, reduced drug level, reduced glucose control
Turkmenoglu et al.(Turkmenoglu et al., 2016) Turkey	Cross-sectional survey / semi-structured interview	1418, ≥65y M = 462 F = 956 mean age or range NS	NS	63.3	Lime, nettle, sage, mint, thyme, flaxseed, linseed, Senna, green tea, rosehip, chamomile	Cardiovascular, digestive and metabolism drugs, musculoskeletal, nervous system drugs, haematopoietic, systemic hormonal drugs, respiratory system drugs	Not assessed
Yoon and Horne (Yoon & Horne, 2001) USA	Cross-sectional survey / semi-structured interview	F = 86, ≥65y mean age 74.9y	NS	45.3	<i>Ginkgo biloba</i> or combinations, garlic and cloves	Multivitamin, calcium, Vitamin E, Vitamin C, aspirin	Not assessed

Study, Country	Study Design/ Data Collection Method	Sample size, Age	Definition or description of HMP	Prevalence of concurrent use (%)	Most reported HMPs	Most reported prescription medicines <sup>a</sup>	Number of potential herb-drug interactions; details
Yoon and Shaffer (Yoon & Schaffer, 2006) USA	Secondary analysis of data	F = 58, ≥65y mean age 75.6y	NS	NS	Garlic, <i>Ginkgo biloba</i> , ginseng, St. John's wort	Ibuprofen, ASA, nabumetone, oestrogen, progesterone, amlodipine, fentanyl, albuterol, warfarin, ticlopidine	n = 43; increased risk of GI bleeding, metabolism of calcium inhibited, antidiabetic activity, decreased contraceptive or hormone replacement efficacy

<sup>a</sup> 10 most commonly reported; **ASA**: acetylsalicylic acid; **NSAIDs**: Non-steroidal anti-inflammatory drugs; **ACE**: Angiotensin-converting enzyme; **HMG-CoA**: 3-hydroxy-3-methyl-glutaryl-coenzyme A; **CAM**: complementary and alternative medicine; **INR**: international normalised ratio; **GI**: gastro-intestinal; **M**: Male; **F**: Female; **NS**: not stated; **HMP**: herbal medicinal product; **DHEA**: dehydroepiandrosterone; CYP: cytochrome P450

#### **4.5.2 Risk of bias in included studies**

Considering the paucity of research in this area, a cut off score of 4 was accepted for each JBI checklist, to ensure there were enough studies to review while maintaining the strength of methodological quality. Typically, research in this area is not randomised. Therefore, a score of 7 and above indicated high quality, while 4 to 6 is moderate quality. All twenty-two studies were of enough quality and were included in the review.

#### **4.5.3 Prevalence of concurrent prescription drugs and HMPs among older adults**

Fifteen studies reported prevalence of concurrent use, while no such information was provided in four articles (Canter & Ernst, 2004; Delgoda et al., 2010; Izzo & Ernst, 2009; Yoon & Schaffer, 2006), and three were case reports where prevalence cannot be calculated (Lantz et al., 1999; Parkman, 2001; Shane-McWhorter & Geil, 2002). Prevalence of concurrent use varied widely between 5.3% (Singh & Levine, 2007) and 88.3% (Nahin et al., 2009).

Table 4.1 shows that the most concurrently combined prescription medicines and HMPs from the included studies. The common groups of prescription medicines concurrently combined with HMPs were antihypertensive drugs, beta blockers, diuretics, antihyperlipidemic agents, anticoagulants, analgesics, antihistamines, antidiabetics, antidepressants and statins.

The most commonly used HMPs as reported in the included studies were: Ginkgo (*Ginkgo biloba*), garlic (*Allium sativum*), Ginseng (*Panax ginseng*), St John's wort (*Hypericum perforatum*), Echinacea (*Echinacea purpurea*), Saw palmetto (*Serenoa repens*), evening primrose oil (*Oenothera biennis*) and ginger (*Zingiber officinale*).

In some studies, non-herbal dietary or nutritional supplements (Canter & Ernst, 2004; Ly et al., 2002; Nahin et al., 2009; Peklar et al., 2014; Shane-McWhorter & Geil, 2002; Singh & Levine, 2007), vitamins and minerals (Kaufman et al., 2002; Nahin et al., 2009; Peklar et al., 2014; Peng et al., 2004) and over-the-counter (OTC) conventional medicines (Delgoda et al., 2010; Dergal et al., 2002; Elmer et al., 2007; Loya et al., 2009) were also concurrently used by participants in addition to prescription drugs and HMPs. In one study (Nahin et al., 2009), 82.5% of participants on prescription medicines also used at least one non-herbal DS, and 54.5% used three or more.

#### **4.5.4 Potential interactions and safety issues**

Potential interactions from reported combinations of prescription drugs and HMPs were evaluated using different methods. Some studies used a combination of two or more of the following methods: review of possible interactions from previously published clinical data, case reports and textbooks (Djuv et al., 2013; Elmer et al., 2007; Izzo & Ernst, 2009; Ly et al., 2002; Nahin et al., 2009; Singh & Levine, 2007).

Others used comprehensive online databases such as Micromedex

(<https://www.micromedexsolutions.com>), Natural Medicines

(<https://naturalmedicines.therapeuticresearch.com/>, formerly Natural Standard),

## Stockley's Drug Interactions

([http://www.pharmpress.com/product/MC\\_STOCK/stockleys-drug-interactions](http://www.pharmpress.com/product/MC_STOCK/stockleys-drug-interactions)) (Loya et al., 2009; Nahin et al., 2009; Peklar et al., 2014; Peng et al., 2004; Qato et al., 2008; Yoon & Schaffer, 2006).

Due to how data were presented in two studies (Canter & Ernst, 2004; Djuv et al., 2013), it was not possible to extract potential interactions for participants aged  $\geq 65$  years. No evaluation of potential interactions was done in five studies (Delgoda et al., 2010; Kaufman et al., 2002; Nahin et al., 2009; Turkmenoglu et al., 2016; Yoon & Horne, 2001). A total of 1,010 individual interactions or potential interactions were reported in 15 studies.

Potential risks of bleeding due to use of *Ginkgo biloba*, garlic or ginseng with aspirin and warfarin were the most reported (Batanero-Hernán et al., 2017; Dergal et al., 2002; Elmer et al., 2007; Ly et al., 2002; Parkman, 2001; Peklar et al., 2014; Peng et al., 2004; Qato et al., 2008; Shane-McWhorter & Geil, 2002; Yoon & Schaffer, 2006) or other antithrombotic drugs (Peklar et al., 2014). Other interactions reported included risk of decreased international normalised ratio (INR) (Izzo & Ernst, 2009; Shane-McWhorter & Geil, 2002), alterations in either blood glucose or blood pressure (Loya et al., 2009), nausea and dizziness (Lantz et al., 1999), anxiety (Izzo & Ernst, 2009), headaches (Lantz et al., 1999; Parkman, 2001), restlessness and irritability (Izzo & Ernst, 2009). An important and risky mode of herb-drug interaction is the inhibition of cytochrome P450 3A4 substrates (e.g. atorvastatin, simvastatin, amlodipine, verapamil) by garlic, *Ginkgo biloba*, Echinacea and St John's wort



(Blalock et al., 2009). For example, St John's wort could reduce the blood pressure lowering effect of losartan or decrease the effects of digoxin (Shane-McWhorter & Geil, 2002).

Interactions were rated by the authors as 'major or high risk', 'moderate' or 'minor'. The majority of potential interactions reported in included studies were minor, of unknown clinical significance or uncertain risk for an adverse interaction (Elmer et al., 2007; Izzo & Ernst, 2009). These interactions were cited in the literature only based on theoretical evidence (Singh & Levine, 2007).

Potential major herb-drug interactions reported were between non-steroidal anti-inflammatory drugs (NSAIDs) and *Ginkgo biloba*, resulting in increased risk of gastrointestinal bleeds due to decreased platelet aggregation (Yoon & Schaffer, 2006). Other major interactions occurred between drug and non-herbal supplement (Peklar et al., 2014) or involved the use of non-prescription drugs (Qato et al., 2008).

#### **4.5.5 Concurrent use and associated factors**

Many studies included in this review did not assess concurrent use with demographic or clinical variables. For the eleven studies that assessed demographic or clinical factors (Blalock et al., 2009; Canter & Ernst, 2004; Delgoda et al., 2010; Djuv et al., 2013; Elmer et al., 2007; Kaufman et al., 2002; Peklar et al., 2014; Qato et al., 2008; Singh & Levine, 2007; Turkmenoglu et al., 2016; Yoon & Horne, 2001), the following can be summarised:

### a. Ethnicity

Only one study assessed the differences in concurrent use between different ethnic groups. African-Americans used significantly more garlic ( $p = .003$ ), although no significant difference was observed in the use of ginseng or *Ginkgo biloba* between African- Americans and white participants(Elmer et al., 2007).

### b. Gender and Age

An important difference in gender in relation to medication use was observed in seven studies (Blalock et al., 2009; Canter & Ernst, 2004; Djuv et al., 2013; Kaufman et al., 2002; Peklar et al., 2014; Qato et al., 2008; Singh & Levine, 2007). Women used more herbal supplements than men (Canter & Ernst, 2004; Qato et al., 2008). A significantly higher prevalence of use of 5 or more prescription medications among women aged 57 through 64 years was reported in two studies (Kaufman et al., 2002; Qato et al., 2008). Consequently, more women than men concurrently use HMPs with prescription medicines (Blalock et al., 2009; Djuv et al., 2013; Peklar et al., 2014; Qato et al., 2008). Qato et al. (Qato et al., 2008) found up to 60% of women in the oldest age groups used prescription medications in combination with herbal DS. Increased odds for a co-user to be female (34% vs 18%,  $p = 0.001$ ) and older (more than one in every three older than 50 years) was also confirmed by Djuv et al (Djuv et al., 2013).

Two studies (Peklar et al., 2014; Yoon & Horne, 2001) found no association between age and concurrent use. Singh and Levine (Singh & Levine, 2007) reported that

older users combining prescriptions with natural health products and females were more likely to have potential interactions than males combining prescriptions with NHPs (63% vs 48%).

### **c. Disease state or clinical condition**

Five studies (Delgoda et al., 2010; Djuv et al., 2013; Peklar et al., 2014; Singh & Levine, 2007; Turkmenoglu et al., 2016) compared concurrent use with disease state or clinical conditions. Herbal product use was slightly higher among participants who suffered ongoing health problems (31.1%) than healthy older adults (24.9%), although the difference was not significant. Consequently, herbal product use was significantly higher among participants who reported continuous drug use compared to those who did not use any drugs (Turkmenoglu et al., 2016).

Increased levels of co-use was associated with use of analgesics or a dermatological drug (Djuv et al., 2013). Chronic diseases were associated with an increased likelihood of concurrent prescription and supplement use (Peklar et al., 2014). High blood pressure and diabetes were also strongly associated with potential interaction (Singh & Levine, 2007). However, Delgoda *et al.* (Delgoda et al., 2010) found no significant association between concurrent herb-drug use and participant's disease.

#### **d. Education and household income**

Only four studies (Delgoda et al., 2010; Peklar et al., 2014; Singh & Levine, 2007; Turkmenoglu et al., 2016) assessed educational level or household income of participants with concurrent use. Concurrent herb-drug use was greater amongst individuals who had education no higher than secondary level (Delgoda et al., 2010; Peklar et al., 2014). Higher education was associated with a lower probability of potential interaction (Singh & Levine, 2007). Therefore, compared to post-secondary graduates, participants with less than a high school education were 70% more likely to exhibit at least one potential interaction (Singh & Levine, 2007).

The prevalence of concurrent herb-drug use was also greater amongst individuals from households with lower household income or with no form of health insurance (Delgoda et al., 2010). Having private medical insurance was associated with an increased likelihood of using HMPs (Peklar et al., 2014). However, Turkmenoglu *et al.* (Turkmenoglu et al., 2016) found no significant associations between HMP use and income.

#### **e. Disclosure of HMPs use to healthcare professionals**

Only six studies asked participants if use of HMPs was disclosed to their doctors or other healthcare professionals (Delgoda et al., 2010; Djuv et al., 2013; Ly et al., 2002; Peng et al., 2004; Turkmenoglu et al., 2016; Yoon & Horne, 2001). No distinct trend was observed among the six studies and disclosure varied widely between 12% (Turkmenoglu et al., 2016) and 78% (Peng et al., 2004). A study of 1,418 older adults (Turkmenoglu et al., 2016) reported that 42.2% ( $n= 180$ ) of concurrent users believed herbal products were not harmful and so did not need to discuss these with

their healthcare providers. Although 51 participants (12%) always reported herbal use to their physician, 40% ( $n= 169$ ) would only disclose herbal product use to healthcare providers if asked and 2.8% ( $n=12$ ) only if they had a problem. In another study (Peng et al., 2004), 78% of participants reported HMP use, although 58 of the 99 concurrent users said they were not asked by healthcare practitioners. About 64% of co-users ( $n= 18$ ) of HMPs and prescription drugs disclosed use in one study (Ly et al., 2002). Almost 80% of users of HMPs did not disclose use in another study (Djuv et al., 2013).

#### **f. Expenditure on HMPs and satisfaction**

Only two studies (Ly et al., 2002; Peng et al., 2004) considered the cost or resources spent on HMPs by older adults. Both studies were conducted in the USA in 2002 and 2004 respectively. Most concurrent users (64% and 83%) spent \$25 or less on HMPs monthly. About 15% spent between \$25 and \$50 monthly (Peng et al., 2004), only 3 out of 28 (11%) (Ly et al., 2002) and 1 of 99 (1%) (Peng et al., 2004) concurrent users spent more than \$100 per month on HMPs.

## 4.6 Discussion

This systematic review included a total of 22 studies that investigated concurrent use of prescription medicines with HMPs. Most studies were conducted in the USA and only four of the studies were conducted in the last 5 years. It can be concluded from the results presented that the prevalence of concurrent prescription and herbal medicinal products (HMPs) use among older adults is substantial. The most commonly combined prescription drugs by older adults are antihypertensive drugs, beta blockers, diuretics, antihyperlipidemic agents, anticoagulants, analgesics, antihistamines, antidiabetics, antidepressants and statins. The HMPs most commonly combined include *Ginkgo biloba*, garlic, ginseng, St John's wort, Echinacea, saw palmetto, evening primrose and ginger. There are demographic and clinical factors associated with concurrent prescription and HMP use. Women, individuals in the oldest age groups, with chronic conditions, less than a high school education and on low income are more likely to be concurrent users. The most common potential interaction was the risk of bleeding from combinations of *Ginkgo biloba*, garlic or ginseng with aspirin and warfarin, all of which are frequently used by older adults.

The included studies varied greatly in terms of participants, products and outcome measures. Generic terms such as 'elderly' or 'older persons' are commonly used (Singh & Bajorek, 2014) but there is no concrete definition of these terms, While ageing is an inevitable process measured by chronological age, its impact varies across populations (Levine, 2013). Therefore, different definitions and chronological age are adopted in clinical studies. While some authors regarded 'older adults' or 'elderly' as those aged 65 years and older, others used the cut-off point of 60 years

or even 75 years. This affected how participants were grouped and the synthesis of data. Furthermore, many studies looked at adult populations including “older adults” or “elderly” but did not or only partially report results separately for this age group. In the latter case, only results that were clearly reported for adults aged 65 and older were included in our analysis. We therefore had to exclude several potentially relevant articles due to either a lack of definition or separate reporting.

The heterogeneity in definitions adopted for HMPs and the inconsistencies on what is included as HMPs demonstrates the lack of precision around what may or may not be herbal medicinal products. While a study (Elmer et al., 2007) adopted the term complementary and alternative medicine excluding vitamins and minerals other studies adopted the terms natural health product and DS including both vitamins and minerals. Moreover, many did not differentiate between HMPs and DS, rather included all types of medications including vitamins, minerals, herbal and non-herbal dietary supplements. Only studies of HMPs that were explicitly named in the results section are included. This variation did not allow for comparisons across studies to be conducted. It also blurred what might be nutritional interventions to improve overall health and those that are used explicitly for medicinal purposes to address specific medical conditions.

The prevalence of concurrent prescriptions and HMPs use among adults aged 65 years and older ranged from 5.3 to 88.3%. Several factors might explain the discrepancies in prevalence of concurrent use reported in studies included in this review. Firstly, the variation in the range of prevalence reflected the different definitions, types of HMPs assessed and participants. Secondly, many of the studies

relied on patient recall of the prescription and herbal medicines they use, possibly resulting in recall bias. In some studies (Dergal et al., 2002; Elmer et al., 2007; Kaufman et al., 2002; Nahin et al., 2009; Peklar et al., 2014; Qato et al., 2008), participants took bottles and containers of medicines they were taking along to interviews for documentation by the research teams.

One of the outliers, an analysis of the 2000-2001 Canadian National Population Health Survey reported only 5.3% concurrent use of NHPs with prescription medications (Singh & Levine, 2007). This difference in prevalence may be explained by underreporting or recall bias due to how data were collected. Participants were asked of medications and NHPs used in the previous 24 hours. This is unusual compared to other surveys on this topic where current and previous use of two weeks (Nahin et al., 2009) and up to 12 months was requested (Blalock et al., 2009; Canter & Ernst, 2004; Ly et al., 2002). Therefore, the data may have revealed only a percentage of respondents exposed to a NHP during a limited time period. In addition, herbs and other NHPs are widely used in a variety of foods, beverages, and multivitamin supplements but because these were not specifically asked in the survey, it is possible that their use was not reported. Therefore, the true prevalence of concurrent prescription-NHP interaction in the study population may be higher than reported.

The other outlier is a Spanish study which reported prevalence of concurrent use of 88.3%. The study assessed both commercially prepared HMPs and home remedies concurrently used with prescription medicines among community dwelling older adults and those resident in care homes. All medicinal plants including teas and



spices widely consumed in Spain were included in the analysis. This may have contributed to the high prevalence recorded in this study.

Three (Nahin et al., 2009; Qato et al., 2008; Yoon & Horne, 2001) of the five studies (Batanero-Hernán et al., 2017; Nahin et al., 2009; Qato et al., 2008; Turkmenoglu et al., 2016; Yoon & Horne, 2001) with highest prevalence rates were conducted in the USA, ranging between 45.3% and 83%. The high prevalence rates could be due to the health care system or the sociocultural characteristics of the location where research was conducted. For the American studies, patients potentially used HMPs and non-prescription drugs for prevention or self-treatment (Yoon & Horne, 2001) as alternatives to expensive medical consultations and prescription drugs. Secondly, only one (Nahin et al., 2009) of the five studies provided a definition or what is regarded as a HMP. Considering the inconsistencies in what HMPs includes, it is possible that other non-herbal dietary products were considered.

Demographic characteristics as well as health status have been associated with use of herbal medicines and natural products. Sex, age, ethnicity and health status may result in greater use of herbs and natural products (Blalock et al., 2009). Although only 50% of the studies included in this review compared demographic characteristics and health status with concurrent use, the results confirms earlier findings (Raji et al., 2005) that the use of herbal medicines varies widely between countries and ethnic groups. For example, the two Canadian studies (Dergal et al., 2002; Singh & Levine, 2007) reported lower rates compared to studies from the United States. In addition, the rate of combining prescription medications and DS was higher among women than men across all age groups (Kaufman et al., 2002;

Qato et al., 2008). This trends were also reported in earlier studies (Gardiner et al., 2006; Radimer et al., 2004).

The differences observed in the sexes of older adult concurrent users may be explained by the higher prevalence of chronic conditions among women compared to men (Tsang et al., 2008). Concurrent use was greater amongst older adults from households with lower household income, no health insurance and no post-secondary education. This may be due to the kind of health care system i.e. paid for or free at the point of delivery. It is therefore reasonable to assume that in such countries; participants may rely more on HMPs or use them as alternatives to expensive medical consultations.

There is increased awareness of interactions between conventional drugs and HMPs. However, the lack of agreement on how to identify HMPs or rigorous clinical evidence hinders researchers, clinicians and consumers in making informed decisions about safe combinations of conventional drugs and HMPs (Zhang, Chen, Zhu, & Zhou, 2017). Most of the evidence on herb-drug interactions is from case reports. Arguably the scarcity and poor quality of primary research, may mean that interactions of serious consequences associated with concurrent use of HMPs are unknown and unrecognised (Posadzki, Watson, & Ernst, 2013). The evidence from this review would suggest that there is potential for harm.

There is potentially high rate of unreported use of HMPs among older adults. Only 28% of included studies asked participants if use of HMPs was disclosed to healthcare professionals. Our findings confirm previous research (Kennedy, Wang, &

Wu, 2008; Mehta, Gardiner, Phillips, & McCarthy, 2008; Robinson & McGrail, 2004) that only about one-third of HMP users disclose use to healthcare professionals. Disclosure of herbal medicine use is crucial to avoiding herb-drug interactions and non-adherence to prescription medications. Reasons for non-disclosure of HMP use as reported in this review and confirmed by other studies includes: perceived negative attitude of clinicians to complementary medicine use (Robinson & McGrail, 2004; Samuels et al., 2012), clinicians do not ask (Howell et al., 2006; Robinson & McGrail, 2004; Vickers, Jolly, & Greenfield, 2006) and the notion that HMPs are 'harmless' (Vickers et al., 2006) .

#### **4.7 Limitations of this Review**

The main limitation of this review is the heterogeneity or no definition of herbal medicinal product in available studies which prevented a meta-analysis. Secondly, we had to exclude many studies because either the use of HMPs was unclear or results reported were not age-specific to enable us extract data for  $\geq 65$  years. Finally, only four of the included studies were published in the last five years (Batanero-Hernán et al., 2017; Djuv et al., 2013; Peklar et al., 2014; Turkmenoglu et al., 2016), seventeen between 2000 and 2010, and one case report in 1999 (Lantz et al., 1999). The increasing use of HMPs worldwide could mean that the review underestimates the range and scale of the issues.

## 4.8 Conclusion

The prevalence of concurrent use of prescription drugs and HMPs by older adults is generally substantial, although variations in the extent of use are reported. These variations can be explained by methodological factors including definition of HMPs, participant selection, sociodemographic factors and differences in health care systems. Concurrent use of prescription drugs and HMPs is associated with risks, some with potentially serious consequences. The most reported interactions in older adults were risk of bleeding due to use of *Ginkgo biloba*, garlic or ginseng in combination with aspirin and warfarin, or other antithrombotic drugs. Under reporting is substantial and adds to the problem, considering that in most countries there are no appropriate safeguards to minimise the potential harm. By identifying the most commonly used combinations, healthcare professionals including pharmacists can be informed on how to identify and manage patients at risks appropriately. It also highlights the need for targeted patient information provided by health care professionals and pharmacists as part of routine consultations. Further research is needed to explore why older people use HMPs alongside their prescribed medication and how their decisions about preferred treatments can be documented and discussed by prescribing clinicians, in order to identify and manage potential risk of herb-drug interactions.

## 4.9 Chapter Summary

Chapter 4 presented the findings from a systematic literature review evaluating the prevalence, patterns, potential interactions and factors associated with the concurrent use of HMPs and prescription drugs among older adults. The chapter began with a rationale for exploring these issues, gave a summary of the methods used for the review before presenting the study findings. The findings have been presented as characteristics of the included studies and a description of the prevalence, patterns and potential interactions from the data synthesis. A discussion of the findings is provided including the strength and limitations of the review. The implications of the findings to clinical practice were also considered.

The next chapter will present the findings from the quantitative study which examined the prevalence and patterns of concurrent prescription drugs, herbal medicinal products and DS among UK community dwelling older adults.

# Chapter 5: Prevalence, Pattern and Potential Interactions among UK Community Dwelling Older Adults

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*A paper based on the work presented in this chapter has been published as Agbabiaka, T. B., Spencer, N. H., Khanom, S., & Goodman, C. (2018). Prevalence of drug–herb and drug–supplement interactions in older adults: a cross-sectional survey. The British Journal of General Practice, 68(675), e711.-717*

## 5.1 Introduction to Chapter

This chapter presents background and findings from the survey phase of the study. The aim of this phase was to build on the review findings (Chapter 4) and establish prevalence, patterns and potential interactions from the concurrent use of medicines among community dwelling older adults in the UK. Results from the cross-sectional study are presented. The demographic variations among the study population are identified and the prevalence of concurrent use is reported. Factors associated with concurrent use of prescription drugs, herbal medicinal products (HMPs) and dietary supplements were explored and reported. Demographic variation between concurrent users and non-concurrent users were also explored and reported. A discussion of the survey findings, the strengths and limitations of the approach is presented. The implications of the study findings for practice and policy conclude the chapter.

## 5.2 Background

The systematic review established that concurrent use is substantial among older adults, identified the range of HMPs and prescriptions frequently combined, for which conditions and potential herb-drug interactions from such combinations. The review also identified some limitations in current knowledge. Specifically, it identified that no recent UK study exists on the topic; the only UK study (Canter & Ernst, 2004) was over a decade old. Most importantly, while previous researches acknowledged potential interactions between herbal and conventional medicines due to concurrent use, much of this work was atheoretical or based on drug pharmacodynamics. Very little has been done to explore and explain the reasons for concurrent use and the experiences of concurrent users, to inform a theoretical understanding of why some groups are more likely to use HMPs alongside prescribed medications. These findings refine the study objectives and provided basis for survey of older people's concurrent use of prescription drugs and HMPs.

The working definition of herbal medicinal products for the survey (*Commission of the European Communities, 2003*) was “*any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations.*”

### 5.3 Study Objectives

The objectives of the survey were to:

- i Establish the prevalence of concurrent prescription drugs and HMPs use among UK community dwelling older adults.
- ii Identify the pattern of concurrent use and the range of medicines combined.
- iii Examine potential herb-drug interactions from such combinations.

### 5.4 Questionnaire Development and Pilot study

Only 9 of the 15 older adults invited to participate in the pilot study responded; 6 from the two GP practices and 3 family and friends. One questionnaire was not completed because the individual misunderstood the purpose of the survey and did not understand that it should be completed even if not currently using herbal medicines.

The patient information leaflets were changed to make this clear.

The remaining 8 respondents completed all questions. Areas where there was a need for clarification were around food and supplementary products. For example, garlic and ginger were regarded as food and not as medicines and some respondents could not differentiate HMPs from DS. This section of the survey was consequently reworded to capture all the HMPs used by participants. Some examples of common HMPs were also provided to demonstrate the possible breadth of responses (Appendix C).

One participant listed five prescription medicines and then wrote etcetera, which suggested there were more medications but not listed. So, the question on prescription medicines included an option to attach a copy of repeat prescription if



participants did not want to list all their prescribed medications. Other minor amendments made to the questionnaire included; merging and re-phrasing a couple of questions that duplicated information on medicine use and this reduced the length of the questionnaire. The question on age was changed to appear as multiple choices for respondents to select age group. Question 3.2 was also modified to include what 'does the HMPs looks like', how often it is used and what it was used for. Overall feedback indicated that the questions were clear and easy to answer. The questionnaire took an average of twenty to thirty minutes to complete.

## **5.5 Recruitment challenges**

Evidence suggests that non-participation in research increases with age (Christensen, Moye, Armson, & Kern, 1992; Grotzinger, Stuart, & Ahern, 1994). Non-responders to research tend to be male (Christensen et al., 1992), from ethnic minorities (Hussain-Gambles, Atkin, & Leese, 2006; Redwood & Gill, 2013), less educated (Christensen et al., 1992), in poorer health than responders (Grotzinger et al., 1994) and in most cases community dwellers (Dibartolo & McCrone, 2003) as opposed to in-patients. It is known that recruiting and retaining older participants is difficult, especially for research undertaken in the community (Provencher, Mortenson, Tanguay-Garneau, Belanger, & Dagenais, 2014; Warren-Findlow, Prohaska, & Freedman, 2003).

With this in mind, reported barriers to patient participation and retention (Bower et al., 2009; Herrera et al., 2010; NIHR, 2010) were mitigated by recruiting through general practice because older adults will participate in research, if recommended by

their doctors (Jenkins & Fallowfield, 2000) or by someone they know (Edelman, Yang, Guymon, & Olson, 2013).

Practice Managers of the two GP practices were key in the research. They acted as gatekeepers, identified participants and signed letters inviting participants to the study. The letter introduced me as the researcher, outlined the study and sought their participation in the study (Forster et al., 2010) (Appendix I).

## 5.6 Results

### 5.6.1 Response Rate

Of the 400 questionnaires sent to participants, 155 were returned (response rate of 39%). Six questionnaires were excluded from the final analysis for not providing information on medications. At the end of round 1 of mailing questionnaires, 69 responses were received. Response from site SG was particularly low, only 15 questionnaires were returned. Reminder letters sent to all 331 non –responders in round 2 (i.e. Week 4) generated only 28 more responses. The offer to win one of five £10 vouchers in the third round increased the number of responses. About one-third of the total responses (n=58) were received in the third round (Table 5.1).

Table 5.1: Weekly record of response to survey

<b>Weekly mailing</b>	<b>No of responses Site NZ</b>	<b>No of responses Site SG</b>
<b>First mail out</b>		
Week 1	10	7
Week 2	27	6
Week 3	17	2
<b>Week 4 (<i>Reminder letters posted</i>)</b>	5	4
Week 5	3	3
Week 6	8	5
<b>Week 7 (<i>New study pack posted with the offer of winning a voucher</i>)</b>	2	2
Week 8	11	22
Week 9	19	2
<b>Total</b>	<b>102</b>	<b>53</b>

## 5.6.2 Participants' Characteristics

Fifty-one percent (n= 76) of respondents were females and 47.7% (n= 71) males, two participants did not indicate gender. The majority (106; 71.1%) belonged to the youngest age group of 65-74years. No respondent was 95 years or older. About half of the participants (73; 49.6%) lived with a partner or spouse while 31.3% lived alone. Most respondents identified as White (126; 85.7%); about 10% were of Black or Black British origin and only 1% Asian or Asian British (Table 5.2).

There was almost an even split in educational level between responders: 70 (46.9%) had some form of further education after secondary school. The majority had been to a technical college (42; 60%), university (18; 12.1%), distance learning or a correspondence course (2; 1.3%). Eight participants (5.4%) had other forms of further education i.e. professional qualifications in teaching, accountancy and nursing. Two participants did not specify their level of education. The remaining 77 respondents (51.2%) had no further education or training after secondary school.

Table 5.2: Demographics of all participants (n=149)

Characteristics		Total (%)
<b>Age group</b>	65-74	106 (71.1)
	75-84	33 (22.1)
	85-94	10 (10.0)
	>94	0
<b>Sex</b>	Male	71 (47.6)
	Female	76 (51.0)
	Not specified	2 (1.3)
<b>Ethnic background</b>	White	126 (84.5)
	Asian or Asian British	1 (0.7)
	Black or Black British	15 (10.0)
	Mixed/Multiple background	3 (2.0)
	Other Ethnic Group	2 (1.3)
	Not specified	2 (1.3)
<b>Education</b>	Tech College	42 (60.0)
	University	18 (12.1)
	Distance learning /Correspondence	2 (1.3)
	Others	8 (5.4)
	No further education	77 (51.2)
	Not specified	2 (1.3)
<b>Living arrangement</b>	Alone	46 (30.9)
	With partner/ spouse	73 (49.0)
	With partner/ spouse and children	15 (10.1)
	With children	7 (4.7)
	Other	5 (3.3)
	Not specified	3 (2.0)

## 5.7 Prevalence and Patterns of Concurrent Use among UK Community Dwelling Older Adults

Six participants did not provide any information on medications used and were excluded from the final analysis. Of the 149 participants included in the study, fifty (33.6%) or about one in three respondents reported the use of other medicines aside those prescribed by a healthcare practitioner in the last 12 months.

Females were more likely than males to be concurrent users (43.4% versus 22.5%,  $P= 0.009$ ) (Table 5.3). There is little difference between groups that had or had no further education with each having about a third reporting concurrent use. Similarly, there were little differences between the categories of living arrangements. Those living with children reported somewhat lower levels of concurrent use, but this was not statistically significant.

### a. Concurrent Use

Table 5.4 shows the number of non-prescribed medicines used by the participants, ranging from 1 to 8, with a mean value of 3 (standard deviation =1.65, median=1). Concurrent users ( $n=50$ ) reported 55 herb-drug and supplement-drug combinations. Most concurrent users (39; 79.6%) used both HMPs and DS (including vitamins and minerals) with prescription drugs.

Table 5.3: Demographic of concurrent users and non-concurrent users ( $n = 149$ )

Characteristics		Concurrent users n = 50 (%)	Non-Concurrent users n = 99 (%)	Total	P value <sup>a</sup>
Age group	65-74	37 (34.9)	69 (65.1)	106 (100)	p = 0.729
	75-84	11 (33.3)	22 (66.7)	33 (100)	
	85-94	2 (20.0)	8 (80.0)	10 (100)	
Sex	Male	16 (22.5)	55 (77.5)	71 (100)	p = 0.009 <sup>b</sup>
	Female	33 (43.4)	43 (56.6)	76 (100)	
	Not specified	1 (50.0)	1((50.0)	2 (100)	
Ethnic background	White	40 (31.7)	86 (68.3)	126 (100)	p = 0.184
	Asian or Asian British	1 (100.0)	0 (0.0)	1 (100)	
	Black or Black British	5 (33.3)	10 (66.7)	15 (100)	
	Mixed/Multiple background	1 (33.3)	2 (66.7)	3 (100)	
	Other Ethnic Group	2 (100.0)	0 (0.0)	2 (100)	
	Not specified	1(50.0)	1(50.0)	2(100)	
Further education	Yes	24 (34.3)	46 (65.7)	70 (100)	p = 0.862
	No	25 (32.5)	52 (67.5)	77 (100)	
	Not specified	1(50.0)		2(100)	
Living arrangement	Alone	17 (37.0)	29 (63.0)	46 (100)	p = 0.929
	With partner/spouse	26 (35.6)	47 (64.4)	73 (100)	
	With partner/spouse and children	4 (26.7)	11 (73.3)	15 (100)	
	With children	2 (28.6)	5 (71.4)	7 (100)	
	Other <sup>c</sup>	1 (20.0)	4 (80.0)	5 (100)	
	Not specified	0	3 (100)	3(100)	

<sup>a</sup>Fisher's Exact test, <sup>b</sup>Statistically significant result ( $p < 0.05$ ), <sup>c</sup>Such as living with friends or relatives

## b. Prescription Drugs

All the 149 participants were taking one or more prescription drugs regularly, ranging from 1 to 18 (Median =3) (Table 5.4). A total of 180 different types of prescription drugs were reported (mean = 3.96, standard deviation = 2.52). Table 5.5 shows the most reported drug classes as statins (69; 46.3% of respondents), beta blockers (26; 17.4%), calcium channel blockers (23; 15.4%), non-steroidal anti-inflammatory drugs (NSAIDs) (19; 12.7%), biguanides (18; 12.1%), angiotensin-converting enzyme (ACE) inhibitors (18; 12.1%) and proton pump inhibitors (18; 12.1%).

Table 5.4. Number and frequency of prescription medicines reported by participants

No of prescription medications	Frequency	Percentage
1	18	12.1
2	28	18.8
3	25	16.8
4	20	13.4
5	18	12.1
6	11	7.4
7	12	8.0
8	3	2.0
9	1	0.7
10	3	2.0
11	1	0.7
18	1	0.7
information not provided	8	5.4
Total	149	100.0



Table 5.5 Range of prescription drugs reported by participants

Drug class by BNF sections (Joint Formulary Committee, 2016)	Prescription Drugs	N	%
<b>2.5 Hypertension &amp; Heart Failure</b>			
<b>Renin-Angiotensin System Drugs</b>	Ramipril Lisinopril	18 11	12.1 7.4
<b>Alpha-Adrenoceptor Blocking</b>	Tamsulosin Doxazosin	8 11	5.3 7.4
<b>2.8 Anticoagulants and Protamine</b>	Warfarin	10	6.7
<b>2.4 Beta-Adrenoceptor Blocking Drugs</b>			
<b>Beta blocker</b>	Atenolol, Bisoprolol	26	17.4
<b>6.1 Drugs used in Diabetes</b>			
<b>Biguanides</b>	Metformin	18	12.1
<b>3.1 Bronchodilators</b>	Salbutamol (Ventolin) inhaler	11	7.4
<b>9.5 Minerals</b>			
<b>Calcium</b>	Adcal- D3	5	3.3
<b>2.6 Nitrates, Calcium Channel Blockers &amp; Other Antianginal Drugs</b>			
<b>Calcium channel blockers</b>	Amlodipine	23	5.4
<b>2.2 Diuretics</b>			
<b>Loop Diuretic</b>	Furosemide	8	5.3
<b>Thiazide diuretic</b>	Bendroflumethiazide	9	6.0
<b>6.2 Thyroid and Antithyroid Drugs</b>			
<b>Thyroid hormones</b>	Levothyroxine	13	8.7
<b>4.7 Analgesics</b>			
<b>Opioid analgesics</b>	Aspirin Co-codamol	19 7	12.7 4.7
<b>1.3 Antisecretory Drugs and Mucosal Protectants</b>			
<b>Proton pump inhibitor</b>	Lansoprazole, Omeprazole,	18	12.1
<b>2.12 Lipid-Regulating Drugs</b>			
<b>Statins</b>	Simvastatin, Atorvastatin	69	46.3

\*only prescription drugs reported by 5 or more participants are listed on the table.

### c. Herbal Medicinal Products (HMPs)

Thirty-six different herbs (used either singly or as a combination product) were reported (Table 5.6). Figure 5.1 shows the most commonly used HMPs as evening primrose oil (*Oenothera biennis*) used by 10.2 %, a combination of hops (*Humulus lupulus*), valerian (*Valeriana officinalis*), gentian (Gentian) and passion flower (*Passiflora*) found in commercial products such as KALMS<sup>®</sup> and Nytol<sup>®</sup> used by 8.2 %, garlic (*Allium sativum* , 6.1%), cinnamon (Cinnamomum zeylanicum, 4.1%), Lutein and Zeaxanthin (4.1%) which are naturally occurring carotenoids and Echinacea (*Echinacea purpurea*, 4.1%). Ten concurrent users (20%) used only HMPs with prescriptions.

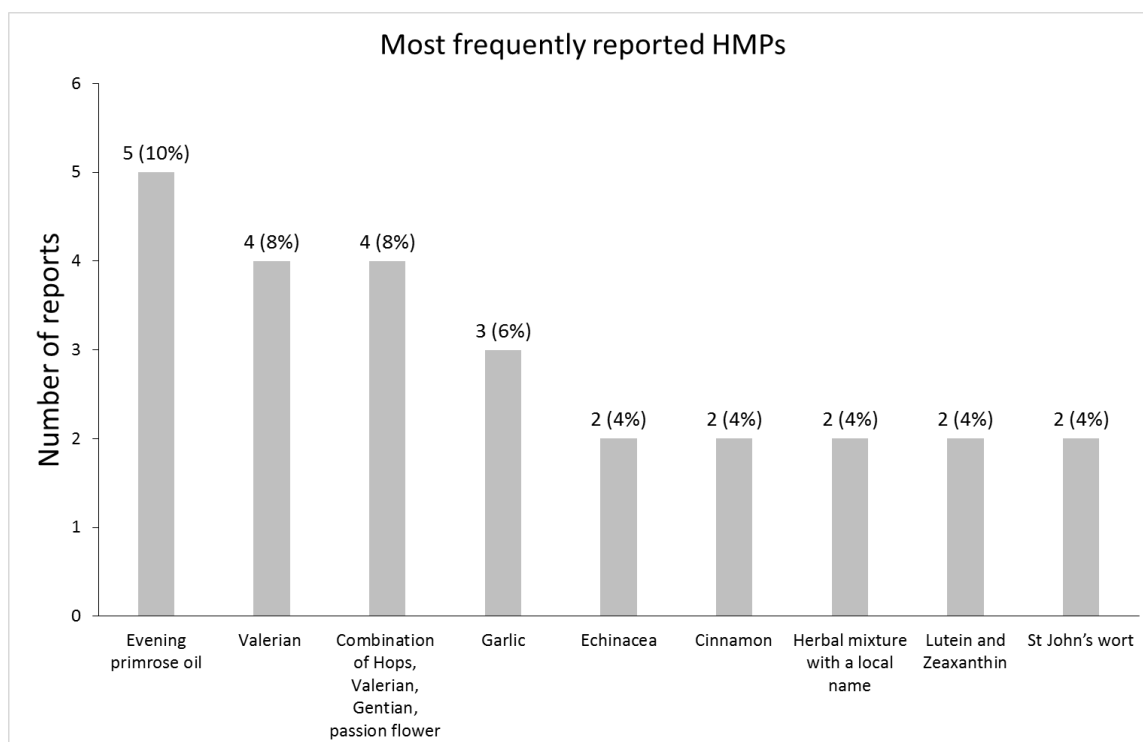


Figure 5.1: HMPs most frequently used concurrently with prescription drugs among UK older adults

Table 5.6 Range of herbal medicinal products reported by concurrent users (n= 49)

Herbal medicinal product	No of Users*	Herbal medicinal product	No of Users*
Arnica	1	Hawthorne	1
Arthrella	1	Herbal mixture remedy with local name	2
Artichoke	1	Lutein and Zeaxanthin (Retinex®, Visionace)	2
Bromelain	1	Mahanarayan oil	1
brown linseeds	1	mint green tea	1
Burdock	1	organic hemp oil	1
Cerassie (bitter melon)	1	Ortis cubes (Figs, Senna Leaves, lactose, tamarind pulp, natural orange extract)	1
Cinnamon	2	Peppermint	1
Combination of Hops, Valerian, Gentian, passionflower (KALMS®, herbal Nytol®)	4	Rosehip	1
cranberry tea	1	Sage	1
Echinacea	2	Senna	1
evening primrose oil	5	Stemflo (herbal supplement from extracts of Gotu kola, Indian gooseberry, Turmeric etc.)	1
flaxseed	1	St John's wort	2
Garlic (garlic oil, Black garlic)	3	Tamarind	1
Gingko + Ginseng (Sanatogen)	1	Turmeric	1
Green tea	1	Valerian	4

\*Total number of users more than 49 as some individuals reported more than one HMPs

#### d. Dietary Supplements

Most concurrent users (n=39; 79.6%) were using DS, including vitamins and minerals (Table 5.7). Dietary supplements are concentrated source of a vitamin, mineral or other substance with a nutritional or physiological effect, alone, or in combination, sold in dose form.

The most combined DS were cod liver oil, glucosamine, multivitamins and Vitamin D (Figure 5.2). Of the 50 concurrent users; 13 (26.5%) reported using both HMPs and DS concurrently with prescription drugs. 38.8% of concurrent users used three or more HMPs or DS concurrently with prescription drugs.

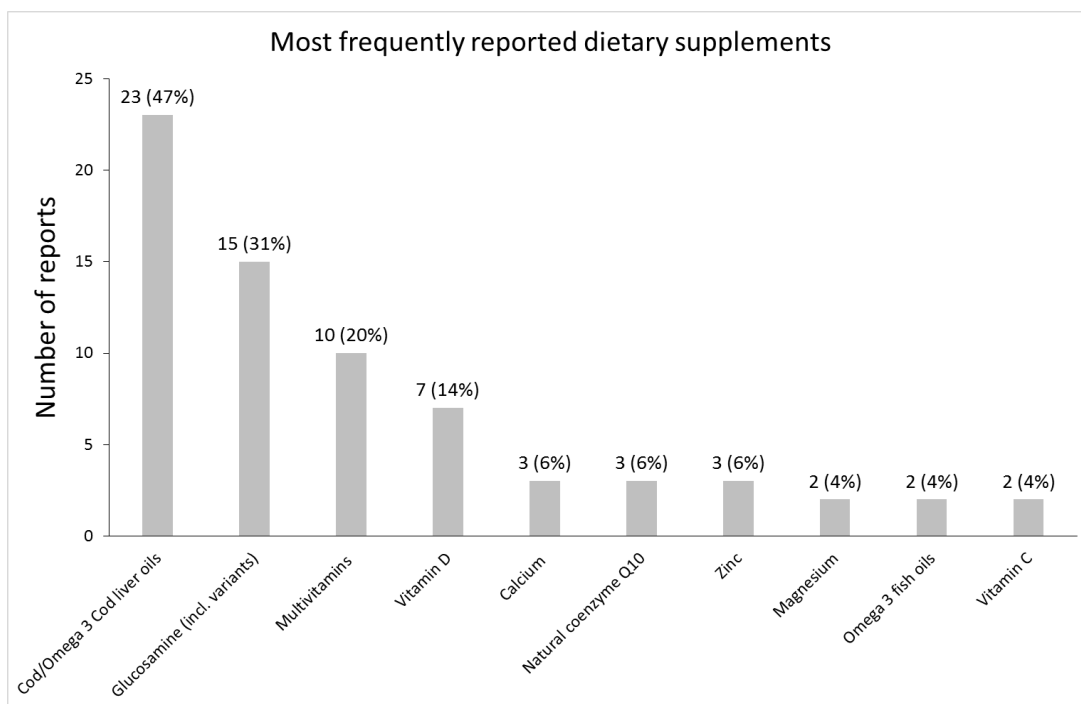


Figure 5.2: Supplements most frequently used concurrently with prescription drugs among UK older adults

\*Percentages sum to more than 100% as individuals could report more than one HMP

Table 5.7 Range of DS combined with HMPs and prescription drugs

<b>Dietary supplements</b>	<b>Number of participants taking named dietary supplement *</b>	<b>As % of concurrent users (n= 49)</b>
Cod / Omega 3 Cod liver oils	23	46.9
Glucosamine (i.e. glucosamine Hcl, Glucosamine + Chondroitin, Glucosamine + Chondroitin + MSM, Glucosamine sulphate)	15	30.6
Multivitamins (i.e. Wellwoman®, Berocca®, centrum advance 50+®)	10	20.4
Vitamin D	7	14.3
Calcium	3	6.1
Natural coenzyme Q10	3	6.1
Zinc	3	6.1
Magnesium	2	4.1
Omega 3 fish oils	2	4.1
Vitamin C	2	4.1
MSM (methylsulfonylmethane)	1	2.0
B-complex	1	2.0
Epsom salts	1	2.0
Vitamin A	1	2.0
Vitamin E	1	2.0
Iodine	1	2.0

\* Total number of participants more than 49 as some individuals reported more than one dietary supplements

## 5.8 Associations between Demographic Factors

Table 5.3 shows results of Fisher's exact tests of the relationships between some demographic characteristics and the concurrent use of prescription drugs with HMPs. Most concurrent users were in the age group 65-74 years (n=37, 35%). However, no statistically significant association exist between age group and concurrent use of prescription drug and HMPs ( $p= 0.729$ ). There was a statistically significant association between gender and concurrent use of prescription drugs and HMPs ( $p= 0.009$ ). There were more female concurrent users compared to men (65.3% vs. 32.6%). And women were using more medications than men, 73.3% of those using 3 or more HMPs and DS were women (Table 5.3).

There was limited response from people of BAME background and only five people who were Black or Black British (33.3%), and one participant each of Asian and mixed background reported concurrent drug use. Consistent with the overall sample, half of concurrent users had no further education after secondary school (n= 25, 32.5%). The remaining concurrent users (24; 34.3%); 18 had further education from technical colleges and 6 were university graduates. There was no significant association between completing further education and concurrent use of prescription drugs and HMPs ( $p= 0.862$ ).

There was nothing distinctive to concurrent users when compared with non-concurrent users with regards to living arrangements, although most concurrent users (26; 35.6%) lived with a partner or spouse.

## 5.9 Potential Interactions between HMPs/ Dietary Supplements and Prescription Drugs

Just over half of the 55 herb-drug and supplement –drug combinations (n=28, 50.9%) were assessed as ‘no interaction’ or ‘no interaction of clinical significance’. Nevertheless, 21 combinations were interactions with ‘doubts about the outcome of concurrent use’, 3 combinations categorised as ‘potentially hazardous outcome’ and another three of ‘significant hazard’ (Table 5.8).

The herb-drug interaction assessments showed that 10 HMPs were involved in some risk of interaction. The HMPs implicated in the potential risk for interaction include:

- flaxseed
- evening primrose oil
- St John’s wort
- peppermint,
- Senna
- Echinacea
- Hawthorne
- Ginkgo.
- Green tea

The five dietary supplements implicated in potential interaction are:

- glucosamine
- cod liver oil
- omega 3 fish oil
- calcium carbonate
- a multivitamin.



The following 21 prescription drugs were involved with a risk of interaction;  
Levothyroxine, Ramipril, Gangfort, Lansoprazole, Metformin, Amlodipine, aspirin,  
Bisoprolol, Propranolol, Rivaroxaban, Lisinopril, Indapamide, Co-codamol,  
Paracetamol, Furosemide, Bendroflumethiazide, Simvastatin, Nifedipine,  
Trimipramine, Rabeprazole, Simvastatin.


Most identified interactions involved potential alterations in the concentration or effect of the prescription medications, which included calcium channel blockers, HMG-CoA reductase inhibitors (statins) and aspirin.

Of all the potential herb-drug and supplement –drug interactions, only seven were hazardous (Table 5.8). These relates to increase in blood-glucose concentrations, risk of bleeding and reduced efficacy or bioavailability of the prescription drug.



Table 5.8 Evaluation of HMPs/ Dietary Supplement - Prescription medicine Potential Interactions

HMPs/ Dietary Supplement	Prescription medicine [no of patients <sup>a</sup> ]	Possible interactions *
<b>HDI Interaction category:</b>  <b>significant hazard, Dosage adjustment or close monitoring is needed</b>		
Bonecal	Levothyroxine	Case reports describe reduced levothyroxine effects in patients given antacids containing magnesium, aluminium, or a combination of both.
Peppermint	Lansoprazole	Antacids may compromise the enteric coating of some commercially available peppermint oil capsules. H <sub>2</sub> -receptor antagonists and proton pump inhibitors may interact similarly.
St John's wort	Amlodipine	St John's wort significantly reduces the bioavailability of nifedipine and verapamil. Other calcium-channel blockers would be expected to interact similarly.
<b>HDI Interaction category:</b>  <b>A potentially hazardous combination</b>		
Glucosamine	Metformin	In a controlled study, glucosamine supplements with chondroitin had no effect on glycaemic control in patients taking oral antidiabetic drugs but increases in blood-glucose concentrations have occurred in patients with treated and untreated diabetes.

Omega 3 fish oil	Bisoprolol [2]	The hypotensive effect of propranolol might be enhanced by fish oils.
Ginkgo	Rabeprazole	Ginkgo induces the metabolism of omeprazole. Most other proton pump inhibitors are likely to be similarly affected.
<b>HDI Interaction category:</b>  <b>Doubt about outcome of concurrent use <sup>b</sup></b>		
Omega 3 fish oil	Aspirin [2]	The concurrent use of aspirin and fish oils caused at least additive effects on bleeding time in healthy subjects, but clinical studies in patients taking aspirin alone and with clopidogrel have found no evidence of an increase in incidence of bleeding episodes.
Cod liver oil	Aspirin [2]	The concurrent use of aspirin and fish oils caused at least additive effects on bleeding time in healthy subjects, but clinical studies in patients taking aspirin alone and with clopidogrel have found no evidence of an increase in incidence of bleeding episodes.
Cod liver oil	Bisoprolol Propranolol	The hypotensive effect of propranolol might be enhanced by fish oils.
Flaxseed	Rivaroxaban	Limited evidence suggests that flaxseed oil may have some antiplatelet effects, which could be additive with those of conventional antiplatelet drugs and increase the risk of bleeding with anticoagulants.
Green tea	Lisinopril	Both black and green tea might cause a modest increase in blood pressure, which might be detrimental to the treatment of hypertension. Green tea reduced the effects of nadolol on blood pressure in healthy subjects.
Senna pods	Indapamide	Theoretically, patients taking potassium-depleting diuretics could experience excessive potassium loss if they also regularly use, or abuse, anthraquinone-containing substances such as <i>Senna</i> .
Glucosamine	Co-codamol Paracetamol	Limited evidence suggests that glucosamine might reduce the efficacy of paracetamol (acetaminophen).

Glucosamine	Furosemide Bendroflumethiazide [2]	Limited evidence from a large open study suggests that unnamed diuretics might slightly reduce the efficacy of glucosamine to some extent.
Echinacea	Midazolam	Echinacea does not appear to alter the AUC and clearance of oral midazolam, although the bioavailability may be increased. Clearance of intravenous midazolam may be modestly increased in patients taking <i>Echinacea</i> .
Hawthorne	Nifedipine	Limited evidence suggests that there may be additive blood pressure-lowering effects if hawthorn is taken with conventional antihypertensives, but the effects are small.
Visionace® (lutein, carotenoids, myrtillus, flavonoid compounds)	Lansoprazole	The desired effect of beta carotene supplementation may be reduced in those taking proton pump inhibitors.
Evening primrose oil	Aspirin	Evening primrose oil can inhibit platelet aggregation and increase bleeding time. It has therefore been suggested that it may have additive effects with other antiplatelet drugs, but evidence of this is generally lacking.

\* Potential interaction reports from Stockley's Herbal Medicine Interaction.

<sup>a</sup> The number of patients exposed to the particular combination of HMPs /DS and prescription drug

<sup>b</sup>Guidance about possible adverse effects, and/or some monitoring may be needed

AUC- area under the plasma drug concentration-time curve

## 5.10 Benefits and Side Effects from the Concurrent Use of Prescription Drugs and HMPs

In response to the question on the perceived benefits from using herbs and HMPs, many concurrent users (n= 17, 34.7%) reported that it helps to maintain bone health. Participants also reported that HMPs treat arthritis and help mobility (35.9%), prevent health problems (30.6%), ease pain (22.4%), useful when feeling unwell (16.3%), improves digestions (8.2%) and gives strength (6.1%). Only one participant thinks HMPs help other medications work better. Interestingly, nineteen (38.7%) concurrent users reported that HMPs or DS were recommended to them by a healthcare professional.

Forty-four of the 49 concurrent users answered the questions on side effects from taking HMPs. However, only two male participants had experienced a side effect. One participant reported stomach upset and frequent toilet visits after taking a liquid herbal remedy used for the treatment of haemorrhoids and impotency. The name of the remedy was provided in local dialect by one participant and the other participant wrote 'local remedy' on the questionnaire. Another participant taking StemFlo<sup>®</sup> (a blend of antioxidants and enzymes that supports optimal blood circulation) and Stem Release3<sup>®</sup> (supports natural release of stem cells) once daily, reported high blood pressure as a side effect from taking these supplements. Both supplements were discontinued by the second participant on the advice of his GP.

## 5.11 Places of Purchase of HMPs and DS

Herbal medicinal products and DS used by the participants were mainly purchased from health food shops (29%) and supermarkets (24.6%). Only 9.2% purchased HMPs from herbalists (Table 5.10). Other sources of HMPs and DS were over the internet (13.8%), through mail order and catalogues (9.2%). Most concurrent users bought commercially produced HMPs and DS over the counter in form of capsules, tablets and syrup. And only three participants (4.6%) had HMPs prepared by or purchased from herbalists.

Table 5.9 Places of purchase of HMPs and DS

Place of purchase	Concurrent users with fewer than 3 HMPs	Concurrent users with 3 or more HMPs	Total (% of total)
Pharmacy	7	5	12 (18.5)
Health food shop	10	9	19 (29.2)
Online	5	4	9 (13.8)
Supermarket	7	9	16 (24.6)
Herbalist	1	2	3 (4.6)
Others	3	3	6 (9.2)
<b>Total</b>	<b>33</b>	<b>32</b>	<b>65 (100)</b>

## 5.12 Discussion

Almost one-third of older adults in this sample were currently using some form of HMPs or DS concurrently with prescription drugs. Among concurrent users, about 33% were at risk for a potential interaction. The most commonly used HMPs were *evening primrose oil (Oenothera biennis)* a combination of hops (*Humulus lupulus*), valerian (*Valeriana officinalis*), gentian (Gentian) and passion flower (*Passiflora*) found in commercial products such as KALMS<sup>®</sup> and Nytol<sup>®</sup> garlic (*Allium sativum*), cinnamon (*Cinnamomum zeylanicum*), Lutein and Zeaxanthin and Echinacea (*Echinacea purpurea*). The most combined DS were cod liver oil, glucosamine, multivitamins and Vitamin D. And simvastatin, atorvastatin, amlodipine, aspirin, bisoprolol and metformin were the most frequently used prescription medications. And the most commonly combined prescription drugs by older adults were statins, antihypertensive drugs, beta blockers, diuretics, antihyperlipidemic agents, anticoagulants, analgesics, antihistamines, antidiabetics and antidepressants. These are similar to the range of prescription medications reported by older adults in previous studies (Qato et al., 2016). The number of prescription drugs each participant took ranged from 1 to 18, and 35 % were taking 5 or more prescription medications. This figure is consistent with a recent study of the US population which reported more than 1 in 3 older adults use 5 or more prescription medications concurrently (Kantor, Rehm, Haas, Chan, & Giovannucci, 2015). The number of HMPs and DS used by concurrent user ranged from 1 to 8, with almost half of concurrent users using three or more HMPs and DS with prescription drugs.

Previous studies reported prevalence of concurrent prescription drugs, herbal medicines and DS use among older adults varying widely from 9% to 88.3%

(Batanero-Hernán et al., 2017; Blalock et al., 2009; Dergal et al., 2002; Elmer et al., 2007; Loya et al., 2009; Ly et al., 2002; Nahin et al., 2009; Peklar et al., 2014; Peng et al., 2004; Yoon & Horne, 2001; Yoon & Schaffer, 2006). The prevalence of concurrent use in this study (33% ) is similar to that from a descriptive questionnaire-based study among community dwelling older adults on the US- Mexico border, 34.6% of participants reported use of at least one herbal product (Loya et al., 2009). It is also in the range of another US study with 38% prevalence rate, conducted among primary care older adults (Peng et al., 2004). However, two studies from the United States reported lower prevalence rates of 15% (Elmer et al., 2007) and 22.8% (Ly et al., 2002). The study by Elmer and colleagues was secondary analysis of data from a large sample of 5,052 older adults. While the study by Ly and colleagues had a smaller sample size of 285 primary care patients aged 65 years and older.

The reported prevalence of concurrent prescription drug and HMPs use among older adults vary widely. This is often due to the different definitions adopted for HMPs, the types of HMPs assessed and demographic characteristics of participants. There are inconsistencies on what may or may not be included as HMPs. Some studies exclude vitamins and minerals (Blalock et al., 2009; Elmer et al., 2007), other studies included DS, vitamins and minerals (Dergal et al., 2002; Kaufman et al., 2002; Nahin et al., 2009; Peklar et al., 2014; Singh & Levine, 2007). A current systematic review concluded that although the prevalence of concurrent prescription and HMPs use among older adults varies widely between different countries, it is however substantial (Agbabiaka et al., 2017).

Certain demographic and clinical characteristics are associated with concurrent medicine use. Women (Canter & Ernst, 2004; Qato et al., 2008), oldest age groups (Kaufman et al., 2002), people with chronic conditions *such as diabetes and high blood pressure* (Peklar et al., 2014; Singh & Levine, 2007), those with less than a high school education (Delgoda et al., 2010; Peklar et al., 2014) and those on low income (Delgoda et al., 2010) were more likely to be concurrent users. The majority of concurrent users in the current study were women ( $n=33$ ; 66.7%), confirming previous findings that women tend to use more herbals and DS than men (Canter & Ernst, 2004; Farina et al., 2014; Qato et al., 2008). In fact, up to 60% of women in the oldest age groups use prescription medications in combination with herbal DS (Qato et al., 2008). Increased odds for a co-user to be female (34% vs 18%,  $p=0.001$ ) has also been confirmed (Djuv et al., 2013). Higher herbal medicine use among women is likely to be for many reasons. Generally, women tend to live longer than men, they are main carers for children and older people; also responsible for buying medicines and remedies for the home and tend to use weight loss products than men. Although concurrent use was highest in the age group 65-74 years (24.1%) but declined among those 75 years and older. A similar trend was reported in the use of herbal medicines by Arcury and colleagues (2007).

The varying prevalence of concurrent prescription drugs and HMPs use among older adults from different countries suggests that the use of herbal medicines differs between countries and ethnic groups (Arcury, Suerken, et al., 2006; Cherniack & Pan, 2004; Raji et al., 2005). The 2007 USA National Health Interview Survey reported nearly 20% herbal use in the general population (Barnes, Bloom, & Nahin,



2008) . While the Czech (Schoen et al., 2007) and Saudi-Arabian (Elolimy & Albedah, 2012) population studies reported higher herbal use (50-57%) compared to the USA population. As ethnic groups favour certain herbal medicines over others (Cherniack et al., 2008), differences were observed in the HMPs and DS used by the different ethnic groups reported by Elmer and colleagues(Elmer et al., 2007). African Americans used significantly more garlic ( $p = .003$ ) and cod liver oil/fish oil ( $p < .001$ ) and less glucosamine and lecithin ( $p \leq .001$  for both). However, no significant differences were found in the use of ginseng, ginkgo, or CoQ10 between African-Americans and White participants. Due to low response of non- white participants in this study, it was not possible to assess differences in the use of HMPs among ethnic groups.

A total of 20 potential interactions affecting 7 older adults were identified, predominantly classified as doubts about the outcome of concurrent use, and three combinations potentially hazardous and another three as significant hazard. This suggests that 1 in 7 of all concurrent users were at risk of a potential interaction. While the potential for herb-drug interactions and supplement –drug interaction has been reported in studies from the USA (Elmer et al., 2007; Loya et al., 2009; Ly et al., 2002; Peng et al., 2004; Sultan, Viqar, Ali, Tajik, & Jahangir, 2015) , no previous study has reported the prevalence and severity of these interactions among UK older adults.

In this study, concurrent use of prescription drugs and HMPs was similar across educational levels. The number of concurrent users with further education was like those without further education. Although available evidence suggests that

concurrent herb-drug use was greater amongst individuals with education no higher than secondary level (Delgoda et al., 2010; Peklar et al., 2014). And higher education was associated with a lower probability of potential interaction and those with less than a high school education 70% more likely to exhibit at least one potential interaction (Singh & Levine, 2007).

Supermarkets and health food stores were the most common places to purchase HMPs and DS in this study. Previous studies have reported sources of information on HMPs as recommendation by friends and family, internet, magazine, physician, CAM practitioner (Molassiotis et al., 2005; Vickers et al., 2006). However, very little is available in the literature regarding where HMP is purchased or sourced.

### **5.13 Strengths and Limitations of the Survey**

This study has investigated concurrent prescription and HMPs use among older adults, whereas previous studies have looked at any conventional medicines, including over-the-counter medicines. This study is unique in that participants were community dwelling older adults recruited from general practices, whereas previous studies have researched patients with specific conditions. Also, this is the only UK study on concurrent herbal and prescriptions medicines use among older adults in over ten years.

The survey provided important information about participant's demographics, the types of herbal and prescription medicines, how they are combined and potential interactions. It also allowed for demographic characteristics such as age group gender and education between concurrent user and non-concurrent users to be examined and explored.

Response rate to postal questionnaires are often poor, and could be as low as 20% (Kelley et al., 2003). Low response rates increase the potential for bias and threaten study validity (Cook, Dickinson, & Eccles, 2009). For these reasons, a larger sample size is required to ensure respondents reflect demographic profile of the survey population and there is enough data for reliable analyses. The response rate of 39% for this study was substantial and enough to provide credible findings. Post hoc power calculations showed that the 155 responses achieved rather than the intended minimum of 171 still provides almost as much power as the 171 would have done. Every effort was made to increase responses; contact was made with participants three times even though some authors suggested two contacts (Bryman, 2012; Edwards et al., 2002; Edwards et al., 2009). Although there is limited evidence for health care research on how to improve response to postal questionnaires in patient populations (Nakash, Hutton, Jørstad-Stein, Gates, & Lamb, 2006), follow-up strategies such as reminder letters, postcards, repeat mailing or telephone contact are good ways to increase responses (Edwards et al., 2009; Salim Silva, Smith, & Bammer, 2002). However, the ethics of repeated patient contact and whether this is acceptable and would not cause distress to patients must be properly considered.

The survey also confirmed findings from the literature review that there was no consensus regarding the terms used for herbal medicines or herbal medicinal products. And although every effort was made to explain what was meant by HMPs and examples were provided. It was clear that some participants did not consider products such as garlic or ginger as HMPs and did not report them in the questionnaire. Therefore, the use of these HMPs also commonly used as foods may not have been well reported. It was also clear from responses that participants did not differentiate HMPs from dietary supplement, so non-herbal DS were reported. Therefore, it was decided to analyse and report non-herbal DS as well, even though the focus of the study was HMPs including herbal DS.

Questionnaire surveys are not without limitations. Although efforts were made to include participants from all ethnic backgrounds, respondents were largely from white background. And so, the sample may not be representative of the UK mixed population. Also, using postal questionnaires was an expensive approach to data collection. Online or telephone survey would probably have been less expensive, but the study population was 65 years and older, and are more likely to respond to postal questionnaires, so this was the preferred option.

Although the survey provided an overview of the HMPs and supplements used by older adults alongside prescribed drugs and the potential interactions. However, it did not provide an understanding of the reasons why older adults concurrently use medications, their views and experiences. Also, it provided limited data about

whether HMPs were regarded as preventive, curative or palliative (i.e. for symptom management). This was explored in the next phase of the study using semi-structured interviews. The survey data informed how participants were identified for in-depth interviews as it ensured that those recruited were willing to participate, were taking HMPs alongside prescribed medication and were typical of this population. Findings from the survey also informed areas to further explore within the qualitative interviews and informed development of the interview guide (Appendix F). Specifically, it was necessary to explore during the interviews if participants are aware of possible interactions from combining HMPs with prescription medicines, and if they discuss using HMPs with healthcare professionals.

## **5.14 Chapter Summary**

This chapter presented results from the cross-sectional survey, providing demographic characteristics of the participants, the prevalence of concurrent use of HMPs, DS and prescription drugs among a sample of UK community dwelling older adults. The names and the types of HMPs, DS and prescription drugs combined were provided. An assessment of potential interactions between the medicines reported revealed some potential risks of adverse herb-drug interactions.

The results from this quantitative study provide an insight into the prevalence and pattern of concurrent prescription drugs and herbal medicinal products (HMPs) use among community dwelling older adults in the UK. The findings demonstrate that certain combinations of prescription drugs and HMPs can have serious

consequences and contributes to the growing literature supporting evidence that concurrent drugs use among older adults is substantial.

Findings from a qualitative study to understand why older adults concurrently use HMPs, DS and prescription drugs will now be explored in Chapter 6. The Chapter will provide detailed accounts of the main themes from the interview data. This relates to the decisions and motivations to concurrently use HMPs and DS with prescribed medicines.

# Chapter 6: Understanding Concurrent use of HMPs and Dietary Supplements with Prescription Drugs among Older Adults

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## 6.1 Introduction to Chapter

The previous two chapters (systematic review and questionnaire survey) focused on answering questions on prevalence of concurrent use, what medications older adults combined with prescription drugs and possible interactions from such combinations. The systematic literature review (Agbabiaka et al., 2017) and cross-sectional survey (Agbabiaka et al., 2018) confirmed that concurrent use of herbal medicinal products (HMPs) and dietary supplements (DS) with prescription drugs is substantial among older adults. However, there is limited information about the reasons for concurrent use. Therefore, it is necessary to explore why older adults concurrently use HMPs or dietary supplements alongside prescribed medicines and understand the experiences of concurrent users.

The aims of the qualitative study reported in this chapter were:

- To explore reasons why older adults concurrently use HMPs and DS with prescription drugs
- To understand their experiences of concurrently using HMPs and DS with prescription drugs.

This qualitative phase of the study builds on the quantitative findings described in Chapter 5 to explore what drives concurrent HMPs, DS and prescription medicine use among older adults.

The chapter begins with an overview of the interview participants; including their characteristics and the HMPs and DS they were taking. The chapter provides an overview of the main themes and sub-themes in relation to what contributes to the decision by older adults to concurrently use HMPs and DS with prescription drugs.

## **6.2 Description of Interview Participants**

Of the 149 survey participants 19 indicated in their response that they were happy to be interviewed for Phase 2 of the study. By the time of the interviews, two participants had moved away from the area. Four people subsequently changed their mind and declined to be interviewed; two declined due to ill health. A total of 13 older adults, were interviewed between 30 November 2015 and 16 August 2016. Most of the participants belonged to the age group 65-74 years; eight women and five men. They have been identified with a code, made up of the study centre (NZ= Practice A; SG= Practice B) and a number. For example, SG 070 denotes Participant number 70 from Practice B. Table 6.1 provides an overview of interview participants.

All the 13 participants have been using HMPs and/or DS for a period ranging between 5 and 20 years. Consistent with the overall survey sample, most interview participants (i.e. 8 out of 13) were in the age group 65-74 years. Ten were White British, two self-identified as Black, first generation immigrants (one African and the



other Caribbean) and one from mixed/multiple background (i.e. white and black African). The majority lived with their spouse or partner (n=8). Only two participants were university graduates, but all had pursued other forms of training after secondary school. All the interviews but one was conducted individually, a couple (NZ 068 and NZ 069) was interviewed together at their request. Interviews lasted between 25 and 45 minutes and were conducted in English.

Table 6.1: Characteristics of interview participants including participant's demographics, names and number of medicines reported.

Code	Sex	Age group	Ethnicity	Education	Living arrangement	Prescription drugs (total)	HMPs/dietary supplements (total)
<b>SG 003</b>	M	65-74	Black	Further education/ Tech college	Living alone	Metformin (1)	combination of herbs
<b>SG 070</b>	M	75-84	Black	Further education/ Tech college	With partner/ spouse	Insulin (1)	Garlic, golden seal, Red clover, Dandelion roots, oleander (5)
<b>SG 072</b>	M	65-74	White	University	Living alone	Methamphetamine (1)	cod liver oil (1)
<b>SG 181</b>	F	65-74	Mixed	Further education/ Tech college	With partner/ Spouse/ children	Amlodipine, Atorvastatin (2)	multivitamins & minerals, Vitamin D3, Iodine calcium magnesium with Vitamin D3, Joint care (Glucosamine, chondroitin & MSM, Omega 3, Mahanarayan oil, Arthrella (8)
<b>NZ 001</b>	F	85-94	White	Other forms of further education	Living alone	Atenolol, Bendroflumethiazide, Macushield, Adcal-D3 (4)	herbal tincture containing celery seed, Bog bean, Artichoke, Black cohosh etc. for arthritis

Code	Sex	Age group	Ethnicity	Education	Living arrangement	Prescription drugs (total)	HMPs/dietary supplements (total)
<b>NZ 045</b>	M	75-84	White	Further education/ Tech college	With partner/ Spouse/ children	Metformin, Tamsulosin, Lamotrigine, Omeprazole, Allopurinol, Losartan, Aspirin (7)	Vitamin D3 (1)
<b>NZ 068</b>	M	65-74	White	Further education/ Tech college	With partner/ spouse	Ramipril, Bendroflumethiazide, Doxazosin, Tamsulosin (4)	Glucosamine sulphate (1)
<b>NZ 069</b>	F	65-74	White	Further education/ Tech college	With partner/ spouse	Bendroflumethiazide, Lisinopril, Lansoprazole, Ventolin inhaler, Clenil modulite inhaler (5)	Glucosamine, Visionace Plus (2)
<b>NZ 070</b>	F	75-84	White	No further education	Living alone	Alendronic acid, Calcichew D3 Forte, Aspirin, Bisoprolol, Losartan, iron magnesium hydroxy carbonate Lansoprazole (7)	cod liver oil, Vitamin A, Vitamin D, KALMS (Hops, Valerian, Gentian) (4)
<b>NZ 084</b>	F	65-74	White	Further education/ Tech college	With partner/ spouse	Ramipril, Amlodipine, Levothyroxine, Calcium (4)	Cod liver oil, evening primrose oil  2

Code	Sex	Age group	Ethnicity	Education	Living arrangement	Prescription drugs (total)	HMPs/dietary supplements (total)
<b>NZ 142</b>	F	75-84	White	No further education	Living Alone	Cetirizine, Estradiol patches (3)	Opti-omega3, Glucosamine + Chondroitin, Cod liver oil, St John's wort (4)
<b>NZ 146</b>	F	65-74	White	University	With partner/ Spouse	Simvastatin, Lisinopril, Lansoprazole (3)	Glucosamine + Chondroitin + MSM, Green lipped muscle, CoEnzymeQ10 (5)
<b>NZ 199</b>	F	65-74	White	No further education	With partner/ Spouse	Tramadol, Amlodipine, Paracetamol (3)	Turmeric, Cinnamon, KALMS (Hops, Valerian, Gentian) (3)

### 6.3 Why Older Adults Concurrently Use HMPs and DS with Prescription Drugs

How the participants engaged with the interview was revealing about how they understood the use and place of HMPs as an adjunct to their medication. All thirteen participants were happy to talk to me. Some of the participants had assumed that I was a doctor and were puzzled as to why a doctor was so interested in their use of herbal medicines. They were interested in knowing more about the study; particularly why I thought it was an important issue to research. This was explained as being because their previous experiences with GPs and some other healthcare practitioners have been that of little or no interest with regards to herbal medicines, abrupt or judgemental discussions. When they realised that I was neither a GP nor a healthcare practitioner, this changed the dynamic of the interview and participants appeared more open about their medication use. For example, NZ146 offered me a drink, became more expansive in her answers and voluntarily showed me containers of her HMPs and supplements. It may also have been an early indicator, subsequently demonstrated (see below), that participants did not perceive there was a connection between HMPs and prescribed medication.

Many of the participants stated that they did not consider HMPs or DS to be medicines. Rather, they were regarded as remedies or the 'help yourself' products to be used as and when required. They did not see that decisions about taking HMPs needed discussion with anyone. The suggestion that combining their prescriptions with HMPs and DS could be unsafe had not been considered. In fact, only two participants demonstrated an awareness of potential interactions and described how they considered the implications of concurrently using HMPs or supplements with

their prescribed medicines. One was a retired nurse, who suffers from arthritis, and will only consult and buy her remedies from a registered herbal medical practitioner. The other participant was a retired schoolteacher who also suffers from arthritis; she described how she checked online for information on HMPs and supplements and participates in online forums of complementary medicine users.

*I belong to a sort of blog site online for arthritis and so all these people, you know, they come up with these different things that you've probably never heard of. And they've tried it, they swear by it and all the rest of it, and it was like the MSM (Methylsulfonylmethane) which I started using about two years ago. I suddenly read this and there was a little string of information, I don't know, from people that had used it or were using it and I thought "do you know what? I'll give that a try. Where on earth do, I get it from?" Anyway, I sourced it from Holland & Barrett, they actually do it in a capsule with the Chondroitin and the other things, and I started taking it...*

(NZ199, Female, 75-84 years, White)

There were recurring and overlapping themes that explained why the participants choose to concurrently use HMPs and DS with prescription drugs (Figure 6.1). The cross-cutting narrative however was one that participants perceived HMPs as helpful, easing and improving health problems but low impact and not essential and by association safe and harmless. There was no expectation that HMPs were curative.

Six themes that captured the recurring patterns in the interview data explained the range of experiences and underlying reasoning as summarised in Table 6.2, with full codes (nodes) listed in Appendix H. The six main themes are: values and beliefs,

decision to use HMPs and DS, sources of information and advice, self-management and taking control, disclosure and non-disclosure, potential herb-drug interactions.

Table 6.2 Codes and categories from the analytic framework

Themes	Values and Beliefs	Decision to use HMPs or DS	Sources of information and advice	Self- management and taking control	Disclosure and Non-disclosure	Potential herb-drug interactions
Codes	<p>Length of use</p> <p>They work but don't know how they work</p> <p>herbal medicines are natural and safe</p>	<p>Convenience and access to conventional medicine</p> <p>Previous negative experience of using conventional medicines</p>	<p>Family and friends</p> <p>Online sources</p> <p>Healthcare professionals</p> <p>Herbalists and other CAM practitioners</p>	<p>HMPs and supplements for less serious conditions</p> <p>Maintaining and improving health and day to day ailments</p> <p>Trial and error</p>	<p>Disclosure and Non-disclosure</p>	<p>Knowledge of herb-drug interactions</p> <p>Experience of herb-drug interactions</p>



## 6.4 Values and Beliefs

There was an underlying assumption at the start of the study that traditional beliefs, custom and practice within families and ethnicities play an important part in the decision to use herbal medicine, and the HMPs that they decide to use. However, most participants in this study were of White British background. There was very little in the data to suggest that using herbal medicine was due to family traditions, ethnic or cultural beliefs, but there was evidence of family members influencing decisions to try HMPs or not. For many, the conviction to use HMPs arose from personal experience of using them over many years, testimonies from friends, wanting to avoid problems that others had experienced and from internet searches. For some participants, the use of HMPs and supplements could be linked to key events or people in their lives. As the quote below demonstrates, HMPs were taken on the recommendation of a family member or online discussions with peers. These were seen as having a positive effect, but participants were cautious in claiming it had cured the condition. The assumption was they were not doing any harm, NZ 199's daughter-in-law told her about turmeric tablets and bought her the first pack when her arthritis became problematic.

*Every morning I take two Tramadol and one blood pressure pill and, yeah, turmeric. I reckon they're good. My daughter-in-law, well, one of them anyway, got me onto these (turmeric tablets). I think they're really good, really good. I'm gonna say that. I mean, at the moment my arthritis is terrible, but my hair has got thicker, I don't know if it's anything to do with them.*

(NZ199, Female, 75-84 years, White)

NZ 070's account was different. For her, it was something her mother had done and now she was continuing its use, hoping it slows down the progression of her arthritis, even though she did not know if it was effective.

*Well because I understood it was good for joints and my mother had arthritis quite badly and I had a hip replacement now, but prior to that it had been troublesome for years really, gradually getting worse. And my thumbs [laughs] very ugly now, but I don't know if that [cod-liver oil] helps or not because I take it and I have taken it probably for 20 years. I sort of like to think that I'd be worse if I didn't take it, but I don't exactly know too much about the action of it on the body.*

*(NZ 070, Female, 75-84 years, White)*

For another participant, the decision to use HMPs was influenced by the information and experiences of other people that she read on blogs and online chat groups.

*I belong to a sort of blog site on there for arthritis and so all these people, you know, they come up with these different things that you've probably never heard of that they have tried. And they've tried it, they swear by it and all the rest of it, and it was like the MSM which I started using about two years ago, I suddenly read this and there was a little string of information, I don't know, from people that had used it or was using it and I thought "do you know what, I'll give that a try..."*

*(NZ146, Female, 65-74 years, White)*

The two participants that identified with a family history or cultural background of using herbal medicines were African and Afro-Caribbean. As the quote below demonstrates, the use of HMPs was rooted in having limited access to formal health care, possibly due to cost as well as a community knowledge of which HMPs could be used for different conditions.

*... I am Jamaican, well we believe in...., we don't call it herbal. But as far as we are concerned that is what we know about, what is available to use. It's our natural and traditional. Traditional... that is our belief. That is our system, we don't see a doctor. Well, you see my mother had 12 kids, we never see a doctor. So, you grew up with this knowledge of what is available. What to do and what to take and that's why ...*

*(SG 070, Male, 75-84 years, Black- Caribbean)*

The African participant has a similar narrative although with emphasis on the belief and understanding that herbal medicine works.

*... In Africa it's common, because most of the time you can't even afford to go to the hospital. You know yourself [referring to me], so most of them rely on the... you know herbal medicine, which is effective, most of them are very good. Because, well, I mean, I know a lot of them (herbs). You see, when we were young, our parents, they used to heal us with those (herbs). There was a tree in the farm, they'd go for the bark of it, put it in a pot, put pepper and everything, boil it. Every morning you have to drink it before you go to school. You see, and it kept us very, very strong. So, I think, to me, [laughs] I prefer that.*

*(SG 003, Male, 65-74 years, Black-African)*

#### **a. Length of use**

The systematic review and survey findings were unclear about how people used HMPs and DS or if there were different patterns of use. For example, if they were used when there was an exacerbation of ill health, or if HMPs were seen more as prophylactics.

All those interviewed were long term users, with length of use ranging from 5 years to over 20 years. It was difficult for some participants to recount or explain why they

started using HMPs, but after using them for such a long time, they see no reason to stop. They believe it had helped in treating their symptoms or promoted good health and some had evidence of what happened when they stopped taking the HMP.

*Yeah. I did stop taking 'em [glucosamine] last Christmas I think it was, and I thought perhaps I don't need 'em, but after about three months my knees and my hip ached and I started taking 'em again, and it gradually got better, so I, it's quite good at them now...*  
(NZ 069, Female, 65-74 years, White)

And for NZ 199:

*I don't take it all the time that actually. I take it, um, I mean I think, there are certain things that I take all the time because if I stop taking them my arthritis gets worse again within sort of two or three weeks of stopping taking them. So, I tend to take them all the time. But I stay on the lowest doses possible that they recommend.*  
(NZ199, Female, 65-74 years, White)

#### **b. 'They work but don't know how they work'**

Participants were often unsure of how the HMPs or DS worked for their conditions but continued to buy and use them. Interestingly, some of them also talked about their prescription medications in a similar manner. For example, NZ 070 was told by a friend that KALMS Lavender<sup>®</sup> tablets helps with anxiety. She (NZ 070) bought some over the counter to relieve her anxiety during a long journey with another older driver to Blackpool. She was calmer during the journey but uncertain if it was due to the tablets or not.

*Whether they worked or not, I don't really know, but I made the journey without having a heart attack [laughs]... And I took some again; I had a journey at the weekend which was an even longer one to Blackpool with an elderly driver aged 94*  
(NZ 070, Female, 75-84 years, White)

In the case of NZ 068, she wanted to avoid or delay the need for what she saw would be the unpleasant procedures associated with managing the macular degeneration in her eyes. So, she sought less invasive and less painful alternative. A supplement was suggested by her doctor. Although she could not say that it was certainly due to the supplement, she attributed the stabilising of her condition to the HMP.

*It could be coincidence, we don't know, but I will take them (supplement) 'cos I don't have to have an injection in my eye, 'cos they inject right into the eye. And I said to them (Doctor), 'is there any supplement I can take' and they said 'anything with Lutein in' which this has [referring to the supplement], and I haven't had the injection now for about eighteen months.*

(NZ 068, Male, 65-74 years, White)

And NZ 084 said although Evening Primrose oil helped her through menopause, but she has no idea how.

*... When I was going through the menopause, I decided to take Evening Primrose Oil and I mean, I just sailed through the menopause. Yes, like hot flushes and those sorts of things and I just found that I just felt better because I was taking it, whether it's a psychological thing, I don't know but I always take it ...*

(NZ084, Female, 65-74 years, White)

### c. Herbal medicines are natural and safe

The intrinsic safety of HMPs was a recurring theme. The overarching narrative was one that saw HMPs and supplements as helpful, easing and improving chronic conditions, but low impact and natural. This was integral to discussions about other issues such as non-disclosure to GPs, because HMPs were not perceived to be worth talking about. They were being used to supplement, or possibly augment the main action of the prescribed medication.

The perception of products as natural and are therefore safer than conventional medicines was linked to their perceived provenance. Herbal medicines were described as from plants; organic and thus synonymous with being natural and therefore free from the side effects or adverse reactions associated with conventional medicines.

According to NZ 069,

*You don't know if they're doing any good but they're definitely doing no harm, so...*

*(NZ 069, Female, 65-74 years, White)*

This extended to how they were made as well as the ingredients used, not only were they safe, they were not as strong or potent. For example, one participant compared the safety and effectiveness of HMPs with prescription medications;

*Um, they're produced more naturally [i.e. herbal medicines] whereas prescription medication things are added, it's from plants alright but things are added to them to be effective or maybe even more effective. But when you get something like the*

*Arthrella, it's produced naturally too but the extra things added to make them more effective are not there so it's safe...*

*(SG181, Female, 75-84 years, mixed/multiple background)*

This contrasted with the perceived danger of some prescription medicines, where HMPs were represented as safer alternatives. NZ146 was wary of taking more prescription medicines and the side effects associated with them.

***Interviewer:*** *Before you tried these supplements and herbal medicine did you try any prescription medicine for these aches and pains?*

***NZ146:*** *Well they just said take Ibuprofen. Really? I mean they said, "if it gets much worse, we can put you on these", I don't know what they were called to be honest with you but they're really strong drugs with quite a side-effect. I don't know whether they're steroids or something, I'm not really sure what they are. But I really didn't fancy taking them, I've got to be honest with you. And so, I was quite seriously looking round for some sort of herbal thing that I could use that wasn't going to have those awful side-effects from the sort of manufactured drugs. Because I do, I do feel that the drugs that we get are actually only there for us because they're there to make the drug companies a lot of money and they're not necessarily the best things for you.*

*(NZ146, Female, 65-74 years, White)*

## 6.5 Decision to use HMPs or dietary supplements

In addition to the participant's values and beliefs regarding HMPs and DS (Section 6.4) the interviews explored how other factors influencing the decision to use HMPs and DS with prescription drugs. The responses focused on two main areas:

convenience and access to conventional medicine and their previous negative experiences with conventional medicine.

### a. Convenience and access to conventional medicine

Primary care is usually the patient's first route to diagnosis and treatment. In the UK, the GP and their teams are the most commonly used access point to the NHS.

Participants explained the popularity of HMPs and DS particularly among older adults as being partly due to the inconveniences they experienced in accessing the GPs. This led to their taking control of their situations and seeking alternative more readily available options like HMPs and supplements to treat their symptoms. The problems with access to a GP was a recurring theme in the interviews and participants spoke about difficulties in booking appointments with the GP, insufficient time to discuss their symptoms, compounded by waiting times of up to two weeks or more. This woman described the encounter with GPs as impersonal,

*Yeah, they don't have time, 10 minutes is ridiculous, isn't it? Before when you go to the doctors, they go, "How's your mum? How's that?" But nowadays you're just in and out. They know my husband; they know because we've been going ever since we lived here. But no, they don't go, "How's your husband?" The girls on the reception do, they know us really well but once you go into the doctors, no, they*



*don't. I find that they're very impersonal... as you're talking to her; she's writing you a prescription. That's not family doctors, well, they're not...*

*(NZ 199, Female, 65-74 years, White)*

For some, avoiding the effort of getting to the GP outweighed the cost of using an HMP.

*I suppose, to be honest, because I don't like going to the doctor very often. I haven't got a fear of the doctor or anything but I just, I suppose, can't be bothered and as you say, it is, these things, over the counter medicine, is expensive but hmm...*

*(NZ 070 Female, 75-84 years, White)*

All participants were 65 years or older and eligible for free prescriptions. They were however willing to spend between £5 and £50 monthly on HMPs or DS. The cost of complementary medicines was discounted against the perceived benefits especially if the prescribed medication was not alleviating symptoms or problems e.g. Pure Cod Liver Oil with Evening primrose for healthy bones and muscles.

*Because I don't feel I could get these on prescription and I just feel that they are beneficial to me because I've been taking them for many years and I just feel, you know, it's not about the cost now but the benefit you get from it.*

*No, that's right. The cost is not important, no. I mean I would shop around and get them cheaper, but I did get those, it was buy three for two or something.*

*(NZ 084, Female, 65-74 years, White)*

Participants described a range of routes to sourcing HMPs and supplements. These were supermarkets, health shops, mail order catalogues and the internet. The majority (n=8) of these purchases were impersonal and did not involve advice seeking or discussion about options.

*Well I mostly source it on the Internet first and if I think Holland & Barrett do it then I will get it from there probably. Like the MSM and the Chondroitin and that sort of thing, they do that, so I've just stuck with them. Although I think there are other places on the Internet that I can, where I can get it. I think Health Nature or something, they do it and, but I just find it easier to get to the Holland & Barrett, mainly because they're just around more. And they have their penny sales so it's always a little bit more...*

*(NZ146, Female, 65-74 years, White)*

A few participants bought from popular health shops, with regular discounts and buy one get one free offers attracting them to buy more.

*Yes, I always buy it from Holland & Barrett, you get three for two. And I pay, I think, I just bought some actually; I think it's £27 for three.*

*(NZ 069, Female, 65-74 years, White)*

Three participants (NZ 001, SG 181 and SG 003) had consulted herbal medicine practitioners and purchase their supplies from them. SG 070 is himself a natural medicine practitioner.

*And it was while I was on the south coast; the manufacturers of Vegitex gave up, sold up. And so, it was then, that I thought have to go to an herbalist, which of*

*course is a lot more money. And it was the herbalist that picked up my erratic blood pressure...*

*(NZ 001, Female, 85-94 years, White)*

#### **b. Previous negative experience of using conventional medicines**

The side effects or adverse reactions from conventional medicines and procedures are why some participants turned to HMPs and DS. Some of them described their experiences as unpleasant, uncomfortable or very painful.

*I was getting quite a lot of discomfort here [she points to the side of her face] and I didn't want an eardrum washout. You know what they are? Is where they flush it and the gook comes out, but it doesn't cure it. All it does is that it flushes out your sinuses, but it flares up again. So, I have garlic ever since and it controls that [the sinuses] I would have had sinus trouble. So yes, I have proved medically it helped.*

*(NZ 001, Female, 85-94 years, White)*

So, they would rather actively seek and take alternative medicines which they believe treat their symptoms and have minimal side effects.

*Some years back, because a medicine like Co-codamol, I took it and it nearly killed me. So, from then, I say these tablets, no more. My stomach, I had a stomach upset, I tried to vomit, I couldn't, and I became sort of, you know, I was, I was very uncomfortable, so I have [laughs], I have sworn not to take Co-codamol again.*

*(SG 003, Male, 65-74 years, Black-African)*

There is awareness that as they are getting older, they were being prescribed more medications, and with that came additional risk which informed why some participants used HMPs. Paradoxically, it was an awareness of the problems and interactions associated with polypharmacy that could trigger considering HMPs as an alternative for the increasing number of health problems experienced.

*Yeah. As you get older, you're sort of looking for things, aren't you? Because you do develop things and you just think "oh do I have to put up with this? Can I go on this medicine or that medicine and what are the consequences of that? And I'm sure there are things that help arthritis a lot but unless I have to take them, I'm not going to, if you see what I mean? I mean I will go along while I can use just the herbal medicines because I don't like the look of the drugs that they're using. And I'm pretty sure that the drug, the drugs that are available, all, for everything virtually are only available there because somebody's making a lot of money and we all know who that is. [Laughs]*

*(NZ146, Female, 65-74 years, White)*

## **6.6 Sources of information and advice**

### **a. Family and friends**

The interviews demonstrated that participants drew on a wide range of information and advice. These included family, relatives and friends, online sources, health care professionals and herbalists. Of these the most favoured were family and friends. For a few, family members were the main source of information and recommended HMPs or DS.

*...Well, my daughter-in-law told me that it's good for arthritis. I don't know, that's what she told me, and to take it. ... yeah, I take them for arthritis ...*

*(NZ 199, Female, 65-74 years, White)*

#### **b. Online sources**

Online sources were not extensively used. Of those interviewed, two described actively searching online for guidance and as this quote shows it was not a systematic process.

*I had problem with my knees as well, they were very painful, so I was sort of hobbling around really and my lower back is quite painful as well. So, I was in a bit of a state really and I didn't really know whether to, what to do about it really. And in the end, I went onto the Internet and looked to see for these various things, and I found these blog sites and things. And they just come up with these things and I tried them and that was the thing (Green Lipped Mussel) that really worked for me. I mean I suddenly felt that the pain had gone, I didn't get that aching at night, nothing was waking me up, and my knees got much better and it was just such a relief.*

*(NZ146, Female, 65-74 years, White)*

#### **c. Healthcare professionals**

For two participants, and as counter to accounts that they were using HMPs to compensate for deficiencies in conventional medicine, it was the doctor, nurse or pharmacist who recommended HMPs or DS to them. These participants appeared to trust the recommendations of healthcare professionals over family and friends. So, when the recommendation to use HMPs or DS is from a healthcare practitioner, it is more likely to be taken more seriously.

*... It was recommended by... I think he was just a pharmacist... the Cod Liver Oil. I just feel is good for helping bones, you know, osteoporosis, all those sorts of things that people get as they age. I'm okay, at the moment.*

*(NZ084, Female, 65-74 years, White)*

For another participant it was a doctor who suggested trying supplements and this validated the use of an HMP. The participant expected that the doctor would know, if there were potential interactions with the patient's prescribed medication, or would have checked there is none before making the suggestion.

*I think it was the doctor there that suggested taking them (cod liver oil). He said, "Have you ever taken, other than prescription medicine?" and I said, "No." So he said, "Well I advise you to take that." And my husband did as well, so I've just kept on with them. You know, my doctor knew that I was taking them so I thought well, if he thought that I shouldn't be taking them, they would say so, you know, but...*

*(NZ 142, Female, 75-84 years, White)*

#### **d. Herbalist and other CAM practitioners**

Four of the thirteen participants had consulted a professional medical herbalist for their conditions. In the case of NZ 001; a retired nurse, she was seeking relief from arthritic pains and did not want to be dependent on conventional pain reliefs because of the side effects. Her clinical and nursing background may be why she sought help from a qualified practitioner and not from the internet or other sources.

*In 2008, I consulted a medical herbalist who has a BSc in this subject. Before then, I discovered through trial and error a selection of mixed herbal combinations, sold as*

*tablets in the health store. I discovered one that worked. Before I was woken up with pain where I had former fractures as a result of two car crashes, I was not the driver. This type of arthritis, in my experience, responds to herbal treatment and I was reluctant to seek Ibuprofen, Voltarol etc. I found it was the right mixture when I slept through the night and didn't need to take de-acidified aspirin. When the manufacturer (Lane's) stopped manufacture, I then consulted the medical herbalist in Brighton. She is a young mother with school age children and as I need more of her mixture (in an alcohol base), so she posts them 2 litres at a time, which helps me a lot.*

*(NZ001, Female, 85-95 years, White)*

Interestingly, SG 003 (Black African male) also consulted an herbalist while he was on holidays back home in Africa. According to him, herbalists are still very relevant in modern day healthcare in Africa. He too recognised their qualifications as educated practitioners combining traditional approaches with modern techniques and equipment for diagnosis and treatment.

## **6.7 Self-management and Taking Control**

Medication taking is a complex behaviour that involves multiple steps and decisions on the part of the patient. What was apparent from the older adults' narratives were the desire to be in control and care for their health based on what worked for them and the differentiation between serious health problems that needed prescribed medication and minor conditions that could benefit from HMPs, Figure 6.1.

The use of HMPs was expressed in terms of how they managed troubling symptoms, maintained existing health or dealt with problems where conventional medicine had

failed. This was seen as different to the activity of taking prescribed medication for specific health problems.

**a. HMPs and supplements used for less serious conditions**

Approaches to self-care included supplementing their prescribed medications with HMPs and/or DS, varying the dose of the prescribed medications to reduce the side effects, or using HMPs as supplement for what were perceived as less serious problems. A recurring narrative within this theme was the value of using HMPs in relieving symptoms as opposed to treating the underlying cause. These herbal medicines include evening primrose oil for menopausal symptoms, valerian for insomnia, Echinacea for colds and DS such as cod-liver oil and glucosamine for arthritis.

Participants said they disliked conventional medicines and would not use them unless necessary, but this did not apply to those that were seen as curative and lifesaving. For example, conditions such as cancer, asthma and heart problems. The participants' expectations of what HMPs could achieve for them were lower than for their prescribed medication.

One participant reaffirmed her reliance on herbal medicines and supplements but said she would seek help from conventional doctors and rely entirely on prescription drugs, if she were to be diagnosed with cancer. In fact, she has maintained her yearly appointments with the heart specialist for the heart murmurs she was diagnosed with as a little girl. As this quote demonstrates the woman placed herbal



remedies as only to be used for minor symptoms and health problems, not ones that were life threatening.

*...you know, you might as well just persist with it until it stops working. If at some point it doesn't work or if, I mean if I was to get something really serious like, you know, cancer or something like that, I wouldn't be looking at the herbal side of things. I mean obviously I'd go straight to the medical profession and anything that was serious wrong with me obviously then I would do that. But I think if you're looking at things where you've just got to live along with those conditions.*

*(NZ146, Female, 65-74 years, White)*

Another participant puts it differently; she relied on HMPs and DS for managing stress and anxiety but would seek help from the doctors if she were to get seriously ill or debilitated from any of these conditions.

*Well I wouldn't go to the doctor and ask for something to calm me down unless I very seriously felt that I was ill, and I don't feel I'm ill. When I am taking something because I'm a little bit stressed or because I'm going for a drive. So, I wouldn't ask the doctor for treatment then. Possibly the same with cod liver oil because they'd probably say, well, you know, "You don't really need it" [Laughs].*

*(NZ 070 Female, 75-84 years, White)*

## **b. Maintaining and improving health and day to day ailments**

Many participants used DS mainly to maintain or improve their health. This desire to keep the body strong, to continue leisure activities and daily chores was strongly expressed by many participants. Therefore, HMPs and supplements are used as a boost to keep on top of day to day living and coping with ageing.

Two participants reported using HMPs and DS to improve their appetite and digestion. Participant SG 003 was convinced that the improvement he experienced with his appetite was due to a mixture of herbs he got from an herbalist while he was on holidays in Ghana.

*It helped me in eating well [referring to the herbal mixture], you know, because there are some foods that I like a lot, but when I eat it, it gave me some problems. But not when I had this medicine...*

(SG 003, male, 65-74 years, Black)

The majority reported more general benefits, in order to maintain health and keep well.

*Um, well, um, I shall be 77 next month and I just, I'm on the go the whole day, I very rarely sit down. Yes, I do get tired and I nod off perhaps when I've got the television on in the evening, but I feel fit. Cos I'm very active and, I don't know if I told you on the phone, but I'm caring at the moment for a neighbour, so my energy levels have got to be..., I've got to keep going [laughs].*

(NZ 142, Female, 75-84 years, White)

*No, no, no, no. Just to keep me as I am, hopefully [laughs] for a few years anyway. But yes, I know some people are real pill pushers, aren't they, sort of thing? They just go on and go on and they can read something and think oh yes, I'll try that, irrespective of whether it is doing them any good...*

*(NZ 142, Female, 75-84 years, White)*

### **c. Trial and error**

The data had shown that there were a wide range of influences and information sources used by participants. How often and how much they used HMPs and supplements appeared to be driven by trial and error, and how long they were prepared to persevere

*...is it worth carrying on with this and just seeing, you know, a little bit longer?" And over the next week the symptoms, the gastric symptoms all went and then over the next two or three weeks I slowly upped the dose to two teaspoons. They recommend three flat teaspoons a day and I take two and that's what I've stuck with because it does work for me.*

*(NZ146, Female, 65-74 years, White)*

And for NZ 001:

*In 2008, I consulted a medical herbalist who has a BSc in this subject. Before then, I discovered through trial and error a selection of mixed herbal combinations, sold as tablets in the health store. I discovered one that worked.*

*(NZ 001, Female, 85-94 years, White)*

For many of the participants, nothing from the interviews suggests that they stopped taking their prescription medications altogether. Rather, the HMPs or DS were used concurrently or alongside the prescribed medicines. Therefore, suggesting that for

participants, the issue was not symptomatic of non-adherence or seeking alternatives to prescribed medications.

In many of the accounts, the use of HMPs was for conditions or complaints were different from those that they were using prescribed medicines for. The condition or symptoms for which they were using HMPs or DS were not diagnosed by a doctor. One female participant spoke of the pain she was experiencing and her assumption that nothing could be done with conventional medicine.

*... I've got to be honest with you I've never really gone to the doctors to have my arthritis confirmed but I've had it for years now and it's progressively got slightly worse... I would say over the last sort of seven or eight years. And I just think it is osteoarthritis. It's just wear and tear and I don't honestly think if I went to the doctors about it, they could really do anything much. I mean if I was so crippled that I couldn't walk then I would but what I do seems to make a lot of difference to me and so I'm happy to stick with that because I can lead an active and much more normal life just using those herbal supplements...*

*(NZ146, Female, 65-74 years, White)*

Medication sharing is one form of self-medication often seen among older adults. And often it involves lending and borrowing of prescription medications between family members, friends and acquaintances. The interviews showed that not only were prescription medications shared, but so were HMPs and DS. Three participants told me that they share or swap with family and friend's herbal product or supplement that has resolved a condition or symptom for them, to try them out before deciding to buy. Or in some cases, it was simply because they ran out of

supply and would borrow a few tablets until they can get to the shops to buy or before their online or mail orders were delivered

*Yes, that's in a different box because the gentleman that I'm caring for, he's had, he has cod liver oil and Chon, Chon, Chondroitin. I don't know whether it's the same as that, but he has them from this firm and he's had them for years and he ran out and I gave him one of my packs. Of course, when he got his next lot, he gave me a pack back but that's why it's a different manufacturer...*

*(NZ142, Female, 75-84 years, White)*

## **6.8 Disclosure and Non-disclosure**

Most of the participants in this study did not consult their doctors, pharmacists or other healthcare practitioners before starting HMPs or DS. Eight of the 13 participants were using HMPs and supplements without the knowledge of their doctors or other healthcare practitioners. The participants did not think there was need to inform the doctor since they did not ask. Some of the participants may have provided this information if they were asked by the GPs or other healthcare practitioners.

*No. No, they haven't, no. I mean, they never ask me what I'm on. They just look and see what I'm taking from them.*

*(NZ146, Female, 65-74 years, White)*

In some cases, the participants too did not think it was important to let them know of the other medicines they were taking

*Um, probably because they didn't ask. It didn't occur to me that it would be important, no. They've never asked me, in fact, you saying about they could have a counter-effect, yeah, I'm not aware of that.*

*(NZ 084, Female, 65-74 years, White)*

Participant NZ 199 thinks that the GPs are non-empathic to her condition. Therefore, she did not see reason to share her use of HMPs with them. In this case, she found Turmeric tablets helpful in relieving her arthritic pains, but the GP was dismissive. So, she never talked about her use of HMPs with healthcare practitioners. She was reluctant to talk to me about her non-disclosure of HMPs to healthcare practitioners and changed the subject when asked.

## 6.9 Potential Herb-Drug Interactions

### a. Awareness of herb-drug interactions

The awareness of possible herb-drug interactions from the co-use of prescriptions with HMPs or DS varied among the older adults. For many participants, HMPs and DS were believed to be safe.

A few participants have considerable knowledge of potential risks from combining prescription drugs with herbal medicines and supplements. And these participants either sought advice from a healthcare practitioner or searched the internet for information about the HMPs or DS and any potential side effects before using them. Those participants with an awareness of herb-drug interactions had a clinical background, went to University or technical college.

*Not without asking the pharmacist because, because if, if I didn't take anything, I might, you know, if I was 50 and on no medication, I probably would try it without discussing it with the pharmacist. But as I'm on all this medication I wouldn't take anything without discussing it.*

*(NZ 070, Female, 75-84 years, White)*

For SG 181, she was aware and concerned about side effects from conventional medicines. Although the conventional medicine may be working to treat her condition, it may have unwanted side effects or cause long term harm. So, the need to either not use it all the time or use a lower dose and look up to HMPs to act as important supplements. Like many older adults in this study, she had not considered that the HMPs could interact with her prescription drugs and cause side effects, which may be serious.

*Um, the prescription medication is something like Panadol, from which I will get the relief. But what I'm saying is that the daily use of it is not what I feel is not right...*

*(SG 181, Female, 65-74 years, mixed/multiple background)*

#### **b. Experience of herb-drug interactions**

One participant reported experiencing side effects from a DS. According to her, she was visiting the toilet frequently and unable to leave the house. However, she did not stop taking the supplement until the reaction stopped because it helped with the pains in her hips and knees and therefore it was worth it.

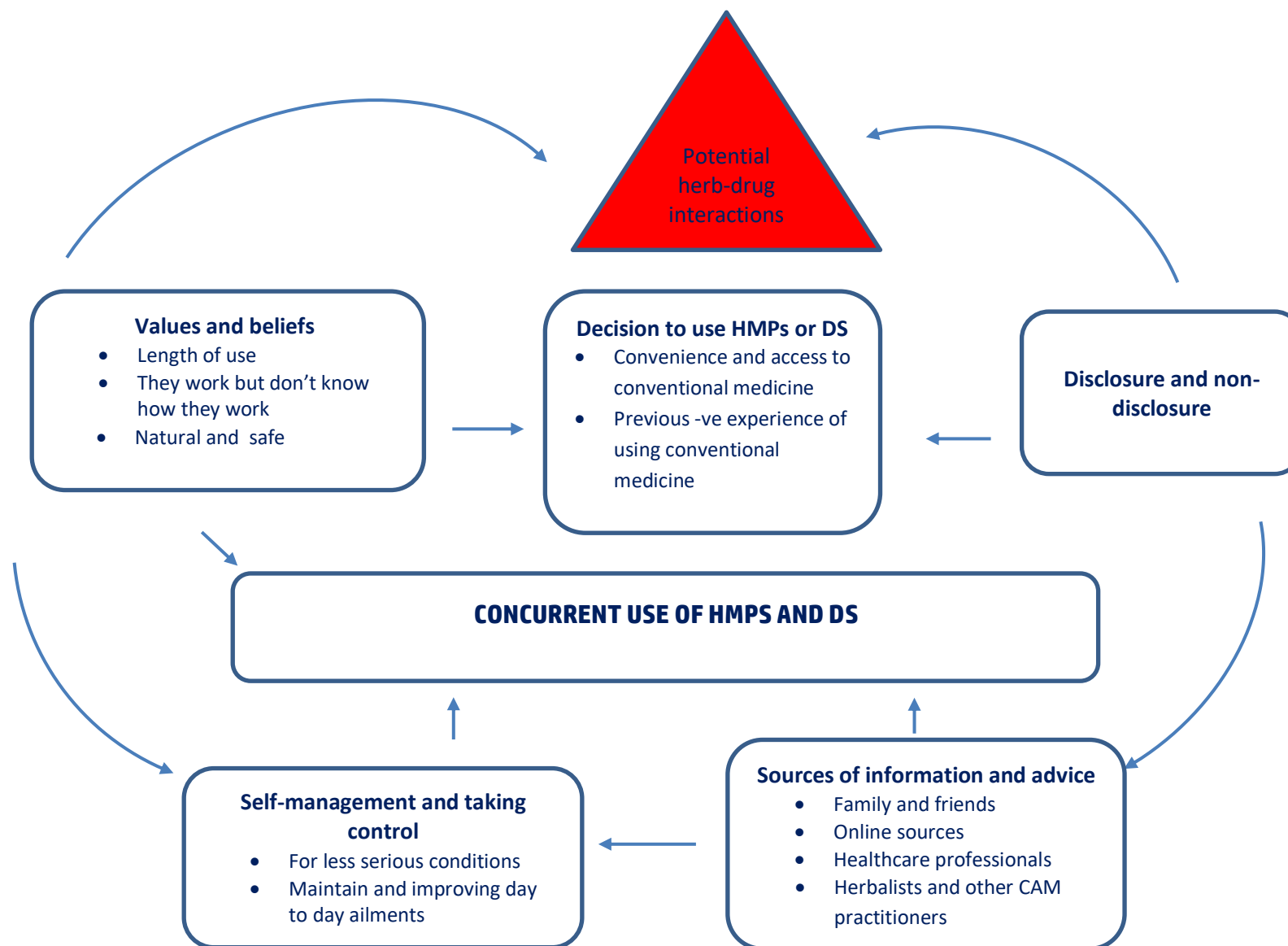
*... Anyway I sourced it from Holland & Barrett, they actually do it in a capsule with the Chondroitin and the other thing, and I started taking it because there are all these warnings about, you know, it might give you gastric upsets and all the rest of it . And I thought "well I'll try it". And I tried it and I did have a few problems for the first sort of week or so but, although I only took a very small dose, but then at the end of the week I thought "oh do you know what, I don't know if I can take this" because I couldn't really go out anywhere, you know, I had to keep going to the loo basically. I had to keep going to the loo basically. And [laughs], and then I thought "but just a minute, your hip doesn't ache anymore in bed and your knees are not hurting and your fingers are fine"!*

*(NZ146, Female, 65-74 years, White)*



Regardless, it could not be assumed that people will not seek help from the GP if there were adverse events. Two male participants also experienced some side effects. One of them reported stomach upset and frequent toilet visits after taking a liquid herbal remedy used for the treatment of haemorrhoids and impotency. The name of remedy was provided in local dialect by the participant who wrote 'local remedy' on the questionnaire. Another participant taking StemFlo<sup>®</sup> (a blend of antioxidants and enzymes that supports optimal blood circulation) and Stem Release3<sup>®</sup> (supports natural release of stem cells) once daily, reported high blood pressure as a side effect from taking these supplements. Both supplements were discontinued by the second participant on the advice of his GP.

Figure 6. 1: Concurrent use of HMPs and dietary supplement with prescriptions drugs among older adults



## 6.10 Strengths and Limitations of the In-depth Study

A major strength of this qualitative study is that it explored in-depth the reasons why older adults concurrently use HMPs, dietary supplements and prescription medicines and explained the factors that may influence this behaviour. I was reflexive throughout the study with regards to how my own social, academic and personal backgrounds may potentially compromise the way in which I interpreted participant's narratives

This study is limited by the fact that the sample of participants were self-selecting older adults (n=13), all of whom had been taking HMPs for a sustained period of time. The interviews did not capture older people who had tried HMPs and then discontinued using them. Moreover, most participants were White and primarily British. Therefore, the findings are not necessarily inclusive of the views of older adults from other cultures and ethnic backgrounds. The findings from the two participants with BAME background did suggest that they drew on traditional remedies and beliefs. Nevertheless, participants revealed a wide range of reasons for taking HMPs concurrently with prescribed medications, sources of information used and recurring issues around ease of access, wanting to delay the effects of ageing, and differentiating between minor and serious problems. All of which suggests that a range of experience of using HMPs concurrently with prescribed medication was captured.

In addition, only participants who were long term users of HMPs and DS are represented in this study, those who had tried HMPs or DS and then stopped were not captured. Therefore, further research is needed to understand these different

groups i.e. those who are regular users, those who try and give up and those who try it every now and again.

## **6.11 Conclusion**

This qualitative element of the study explored further the review and survey findings to provide in-depth understanding of the reasons why older adults concurrently use HMPs and dietary supplement with prescription drugs. The interviews demonstrate the wide range of motivations and sources of information that older adults draw on in making the decision to concurrently use HMPs or dietary supplements with prescription drugs.

Older adults were pragmatic in the use of HMPs and dietary supplements in the hope that they work and would continue to use them unless proven otherwise. The possibility of interactions by combining them with their prescribed medications was not recognised and participants were willing to experiment and sample a range of products until they found one that suited them. Many did not think of them as medicines per se and might partly explain why they did not see them as harmful, and worth trying. For many participants, the purpose was to delay the effects of ageing, keep well and deal with minor complaints. Disclosure of HMPs and supplement use to GPs were infrequent. The only examples being when there was an adverse event, there were low expectations that the GPs would be interested.

## 6.12 Chapter Summary

This chapter presented an overview of the main themes arising from the semi – structured interviews with 13 participants in relation to why older adults concurrently use HMPs and dietary supplements with prescription drugs. The motivations and decision to concurrently use prescribed medications with HMPs and DS is captured through the accounts of community dwelling older adults. It goes on to explain what influences these decisions and how it manifests into some self-management behaviours or strategies.

# Chapter 7: Discussion of Findings

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## 7.1 Introduction to Chapter

This chapter draws together findings from the three phases of the study to answer the study objectives and research questions regarding the concurrent use of prescription drugs and herbal medicinal products (HMPs) among UK older adults.

To demonstrate how this work contributes to new knowledge concerning the concurrent use of prescriptions drugs and HMPs among older adults, the discussion addresses the key findings from all phases of the work in relation to the research questions and the existing evidence. In this Chapter, particular attention will be given to how little empirical work has previously been completed in this area, the methodological challenges in this study and whether the findings about perceptions of safety and the challenges of accessing health care are specific to the experience of older people.

The aim of the mixed method explanatory study is to understand the concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults.

Specific objectives and research questions for the individual phases were:

### Phase 1: Systematic literature review

- What is known about the concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults?
- What patient and clinical characteristics are associated with concurrent use of prescription drugs and HMPs?
- What are the risks of concurrent prescription drug and HMPs use in older adults?

## Phase 2: Questionnaire survey

- What is the prevalence and patterns of concurrent prescription drugs and HMPs use among UK community dwelling older adults?
- What types of HMPs and prescription drugs are concurrently used?
- What is the potential herb-drug interactions from the HMPs, and prescription drugs reported?
- What patient and clinical characteristics are associated with concurrent HMPs and prescription drugs use?

## Phase 3: In depth exploration of older adults' experiences of using HMPs with prescribed medications

- Why do older adults concurrently use prescription drugs, HMPs and dietary supplements (DS)?
- What is the experience of concurrent users?

## 7.2 What is known about the concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults?

### a. Literature Evidence

The review and survey addressed this question and demonstrated that concurrent prescription drugs and HMPs use among older adults is widespread, with potentially serious herb-drug interactions from certain combinations. Whilst Previous studies have examined the use of herbal medicines among older adults (Bruno & Ellis, 2005; de Souza Silva et al., 2014; Gonzalez-Stuart, 2011) and potential interactions with conventional medicines (Dergal et al., 2002; Loya et al., 2009). The new learning is

about concurrent use of HMPs and DS with prescription drugs among older adults. Specifically, there has been no research on this issue conducted in the UK on older adults for over a decade. The findings demonstrated the existence of an elastic understanding of what is meant by old age and very little systematic work around the use of HMPs for conditions and medications common in old age.

#### **b. Prevalence and Patterns of Concurrent Prescription Drugs and HMPs Use**

Among 15 of the studies included in the review, the prevalence of concurrent prescription and HMP use varied widely between 5.3% and 88.3%, while this study estimated it to be 33.5%. An accurate estimate of the prevalence of concurrent HMPs use with prescription medicine is difficult, because of the array of definitions adopted for HMPs, what is considered an HMP or not, non-disclosure, as well as the way information about concurrent use was collected. Therefore, it is reasonable to assume that the review and survey have identified an important and under-researched issue. However, the true prevalence of concurrent prescription drug and HMPs among older adults is likely to be higher. Effort was made in this study to explain what was meant by HMPs with examples provided, because some participants may not consider products containing garlic and ginger as HMPs. Future studies may need to consider the most common phrases and terms to describe HMPs and always include these in questions and study materials. Providing some examples of the products being researched could also help participants in providing relevant responses.



The introduction of this thesis noted the previous attempts at definition and regulation. The findings from this study would suggest that this is important; not having a shared understanding of what HMPs are is a barrier to public understanding, professional guidance and future research.

### **c. Most Frequently Combined Prescription Drugs**

According to review evidence, the prescription drugs most commonly combined with HMPs are beta blockers, diuretics, antihyperlipidemic agents, anticoagulants, analgesics, antihistamines, antidiabetics, antihypertensive drugs, antidepressants, non-steroidal anti-inflammatory drugs (NSAIDs) and statins (Batanero-Hernán et al., 2017; Djuv et al., 2013; Nahin et al., 2009). Unsurprisingly the same classes of drugs were reported by participants in the Phase 2 survey of this research, confirming the findings of previous studies. This suggests that the participants were typical for their age group.

The study findings demonstrate the importance of focusing on this population as being potentially more at risk of adverse drug reactions secondary to use of HMPs with prescribed medication. Medication use increases with ageing (Gao et al., 2017; Health and Social Care Information Centre, 2015; Qato et al., 2016) and the average person over 65 years will be on five or more prescription drugs (Franchi et al., 2014; Guthrie et al., 2015). Participants in this study however described the difficulties of access and a belief that their health issues were not of interest to clinicians. Whilst it is not possible to prove that HMP use was a response to lack of access and increasing difficulty in managing health problems. There were multiple examples of where this was a preferable option to seeing a GP. Other studies have highlighted

the difficulties older people experience in continually accessing health care services (Allin, Masseria, & Mossialos, 2011; Mohan, Nolan, & Lyons, 2019; Reeves et al., 2018). Social exclusion and isolation can compound this experience (Ford, Wong, Jones, & Steel, 2016). The findings of this study are an expression of what is known about the difficulties this population face in accessing the advice and support they need and how proximity to a GP will affect access to services.

#### **d. Most Frequently Combined HMPs**

The survey further confirmed what was already reported in the literature regarding the most frequently combined HMPs with prescribed medicines. Evening primrose oil (Peklar et al., 2014), *Ginkgo biloba* (Elmer et al., 2007; Ly et al., 2002), garlic (Dergal et al., 2002; Loya et al., 2009) and Echinacea (Nahin et al., 2009) were the most used HMPs by survey participants. Other HMPs reported in the literature include ginseng, St John's wort (Yoon & Schaffer, 2006), Saw palmetto (Peng et al., 2004), and ginger (Delgoda et al., 2010).

Survey participants in this study also reported Valerian, Nytol herbal<sup>®</sup> (a commercial combination of hops, valerian, gentian and passionflower), and cinnamon. These HMPs were not frequently cited in the literature. The differences in the types of HMPs used by older adults in this study and those reported in previous ones may indicate a changing and expanding herbal medicines market. Europe is the second largest market for natural therapies and remedies due to large disposable income (Grand View Research, 2019). Another explanation for this difference is increased awareness of healthy lifestyle, which is raising demands for food supplements for healthy aging (CBI, 2018). More people are experimenting and trying out new or

foreign health foods, natural cosmetics and natural hygiene products (Nirmal SA, 2013).

The range of HMPs taken by older adults are used to manage degenerative or age-related conditions (Williamson et al., 2013) such as insomnia and other sleep related problems (Espiritu, 2008; Tel, 2013). Valerian is a common component of herbal sleeping pills and relaxation products (Alsanad et al., 2016; Bent, Padula, Moore, Patterson, & Mehling, 2006), Ginger and turmeric may be effective for the treatment of symptoms associated with osteoarthritis, especially pain (Ernst, Soeken, & Long, 2001). Garlic and Echinacea are used to treat upper respiratory infections such as cold, flu, and chronic bronchitis, nasal and throat catarrh (Kaufman et al., 2002; Kelly et al., 2005). Women use evening primrose oil to manage menopausal symptoms (Farzaneh, Fatehi, Sohrabi, & Alizadeh, 2013), while saw palmetto is mainly used by men to treat symptoms of benign prostatic hyperplasia (Marks et al., 2000).

While aging by itself is not a disease, many conditions worsen with age and the medicalisation of aging may lead to more harm than benefit for older adults (Birrer & Tokuda, 2017). Many older adults who participated in this study integrate non-prescribed medicines such as HMPs or DS into their self-management of daily symptoms. The focus on HMPs and DS provides some insight about health beliefs, and this links to the interview findings on safety and the perception that the use of HMPs was of little or no interest to GPs. Moreover, what we do not know is whether HMPs and prescribed drugs are equally valued or one is preferred over another (Arcury et al., 2012). Although the findings from the interviews suggested that older people differentiated between the curative function of prescribed medications, and

the augmentation or supplementary function of HMPs. A perception that prescribed drugs were no longer working or a possible dissatisfaction with the medical profession as a source of expertise for some conditions encourages the growing consensus among patients towards a more eclectic view of health, resulting in herbal and dietary supplement medicalisation.

#### **e. Dietary Supplements also combined with Prescription Drugs**

The review found that in addition to herbal remedies, dietary supplements (Loya et al., 2009; Shane-McWhorter & Geil, 2002) as well as vitamins and minerals (Kaufman et al., 2002; Peng et al., 2004) were also concurrently used with prescription drugs. The dietary supplements most combined with prescription drugs were cod liver oil, glucosamine, multivitamins and Vitamin D. Although cod liver oil and glucosamine are technically dietary supplements, they are advertised as ‘cures’ for various conditions including joint pain and arthritis, hence the blurring with HMPs. The lack of a common understanding or operational definitions of what is and what is not an HMP highlights the clinical and methodological challenges of tracking HMP use in the older population.

The use of dietary supplements among older adults continues to be high; 70% of US adults reported using  $\geq 1$  dietary supplements regularly (Gahche, Bailey, Potischman, & Dwyer, 2017) and about 79% of participants in this study. The findings from all three phases of the study provides further evidence that despite an increasing market in HMPs and dietary supplements, their use with prescribed medications is not seriously considered with regards to potential herb-drug interactions. The majority of concurrent use is not discussed or disclosed to healthcare practitioners

(Foley, Steel, Cramer, Wardle, & Adams, 2019; Jou & Johnson, 2016; Kennedy et al., 2008), some of which could have serious implications. Therefore, non-disclosure and not asking patients for information, poses a major concern from a safety-risk perspective. There is a dissonance between the level of use of HMPs and supplements and clinicians asking or documenting (Ben-Arye, Halabi, Attias, Goldstein, & Schiff, 2014; Pinto et al., 2012).

An up-to date national representative data on HMPs and dietary supplement use among UK older adult is long overdue, to provide reference data and information for public health policies including nutrition and health monitoring, and prevention initiatives. There is a vital role for healthcare practitioners in facilitating disclosure of CAM use by enquiring from patients. However, it appears that discussions about CAM use are more commonly patient rather than provider initiated (Roberts et al., 2006; Roter et al., 2016).

Healthcare practitioners initiating such discussions may be an avenue for improving disclosure and this may be achieved by including a use CAM inquiry as standard in case-taking. Including specific questions related to dietary supplements in case-taking doubled the rate of supplement use disclosure among patients (Ben-Arye et al., 2014). Encouraging shared responsibility for the communication and subsequent discussion of CAM use is also argued to be key to achieving optimum disclosure (Ben-Arye et al., 2014). This may be facilitated through person-centred approaches to clinical care, which encompass patient involvement in shared decision-making, face to face interactions, provider empathy and recognition of patients' values (Bunn et al., 2018; Pinto et al., 2012). However, the findings from this study suggest that

this would require structural changes to how clinical appointments are organised both in terms of access, how consultations are structured and length of time for discussing what is important to the older person. As the study also found that some older people were using online resources, there may be scope for investment in advice and interactive guidance that can be accessed online (Washington, Meadows, Elliott, & Koopman, 2011; Yardley, Morrison, Bradbury, & Muller, 2015). Although evidence to date suggests there are significant barriers to overcome (Yusif, Soar, & Hafeez-Baig, 2016; Ziebland & Wyke, 2012).

### **7.3 Factors Associated with the Concurrent Use of Prescription Drugs and HMPs**

It is known that demographic and clinical characteristics are associated with the use of herbal medicines, and this was explored as part of the study objectives. Being female, older than 70 years, using prescription medicines, having higher than high school education and a chronic condition, are some of the documented factors associated with herbal medicine use (Peklar et al., 2014; Rashrash et al., 2017).

Whilst, as in previous studies (Canter & Ernst, 2004; Farina et al., 2014; Qato et al., 2008) females more than males were likely to be concurrent users (43.4% versus 22.5%). The analysis of concurrent users in this study did not show consistent patterns for these characteristics known for HMPs and DS use. They were not easy to group into likely and unlikely users of HMPs, challenging narratives that a health condition, cultural beliefs or being an identifiable population or group will predispose people to use certain HMPs with prescription drugs. It is possible that this group are very different to those who are choosing herbal products as a conscious and

deliberate rejection of conventional medicine. This was not explored in the evidence reviewed; also the survey and interviews did not suggest that participants were suspicious of their medications. They supplemented or augmented prescription drugs with HMPs or DS which were self-prescribed, recommended by friends and relatives, or purchased from supermarkets, health shops or over the internet. There was no evidence of older adult adults substituting their prescribed medicines with HMPs or DS.

Previous work has found that older age groups are not significantly associated with concurrent use (Peklar et al., 2014; Yoon & Horne, 2001). When looking at within group characteristics, the survey found little or no differences in the education and living arrangements of concurrent and non-concurrent users. A third of participants with and without further education had reported concurrent use. The findings underline the importance of individualised care. There was little to suggest from the review, survey or interviews that there would be a particular “at risk” group, what was more striking was the cross generational assumption that this was a safe option.

#### **7.4 Potential Risks from the Concurrent Use of Prescription Drugs and HMPs**

This study identified specific risks associated with herb- drug interactions. Medication prescribing for older adults is complex, treating for more than one chronic illness increases drug burden and the risk of ADRs (Hajjar, Cafiero, & Hanlon, 2007; Nisly, Gryzlak, Zimmerman, & Wallace, 2010). Polypharmacy is a recognised patient safety risk and consistently associated with interactions and ADE (Guthrie et al., 2015). An average older adult is on 5 or more prescribed medications (Kim & Parish, 2017).

Considering that about one in four use prescribed medicines concomitantly with HMPs or supplements (Gardiner et al., 2006), the potential risk for drug interactions may be further increased.

The risk of bleeding due to concurrent use of Ginkgo *biloba*, garlic or ginseng with aspirin and warfarin are the most frequently reported potential herb-drug interactions amongst older adults (Elmer et al., 2007; Peklar et al., 2014; Shane-McWhorter & Geil, 2002). The potential interactions identified in many studies were either minor, of unknown clinical significance or of uncertain risk for an adverse interaction. A similar trend was recorded in phase 2 survey for this study. Over half of the herb-drug and supplement–drug combinations were assessed as ‘no interaction’ or ‘no interaction of clinical significance’. However, seven of the 55 combinations were assessed as potentially serious. These relates to increased blood-glucose concentrations, risk of bleeding and reduced efficacy or bioavailability of the prescription drug.

Despite this cumulative evidence, assessing the safety of HMPs remains complicated for many reasons, including poor and minimal data on herb-drug interactions (Izzo et al., 2016; Williamson, 2003) and no clear definition of what HMPs are. In fact, most of the available evidence on herb-drug interactions is from pre-clinical studies, uncontrolled clinical trials and case reports which are limited by the quality and quantity of information available on the herbal products and the adverse reaction, making them inconclusive and inconsistent. For example, the survey found that the 149 participants were prescribed 180 different types of drugs including a range of statins and beta blockers. Although herbal medicines are plant-derived, they are chemically complex mixtures of pharmacologically active



phytochemicals, with multiple potential targets and mechanisms (Jordan, Cunningham, & Marles, 2010; Pelkonen, Xu, & Fan, 2014). This complexity increases the risk of clinical drug interactions. However, most studies focus on single HMP and or their interactions with a drug (Barone, Gurley, Ketel, Lightfoot, & Abul-Ezz, 2000; Blonk, Colbers, Poirters, Schouwenberg, & Burger, 2012; Bressler, 2005). Therefore, the findings from this study suggest that evaluating the interactions of two products is over-simplistic and reductionist. It will only ever achieve a partial account because in real life situations, several prescribed drugs, HMPs and DS are used simultaneously.

The evidence on herb-drug interactions continues to grow and it is compelling (Alsanad, Williamson, & Howard, 2014; Awortwe, Bruckmueller, & Cascorbi, 2019; Henderson, Yue, Bergquist, Gerden, & Arlett, 2002; Izzo & Ernst, 2009; Kennedy & Seely, 2010; Posadzki, Watson, & Ernst, 2013; Ulbricht et al., 2008), even when many of the studies are limited by poor methodological quality and risk of bias. This would suggest that there is a growing awareness of the issues but is yet to affect public and lay perceptions of risk. In the survey and interviews, participants did not think there was a risk of harm or that it was worth mentioning to clinicians what other medicines they were taking. This must be considered against the survey findings that the majority of herb-drug combinations were unlikely to cause clinically significant interactions and appropriate herb-drug combination could benefit patients. To guide the practical application of this combined therapy in a manner that benefits consumers while minimising the risk of interactions, high-quality studies are required to evaluate the impact of specific herb-drug and supplement-drug combinations among different cohorts, in multiple settings and with larger sample sizes,

This study's findings would suggest that a general look at the use of HMPs is too broad. Therefore, there is a need to build on this and focus on specific HMPs and prescribed medicines that are known to have high risk of interactions and adverse outcomes. The consistent findings about certain prescription drugs that are most commonly combined with HMPs and supplements as provided by this study is a basis for more focused work, particularly among older adults.

## **7.5 Understanding Why Older Adults Concurrently Use Prescriptions Drugs with HMPs and DS**

One of the objectives of this research was to explore in depth older adults' reasons and decision making regarding the concurrent use of prescription drugs with HMPs and dietary supplements. Chapter 6 identified recurring themes from the interview data about why and how they used HMPs alongside their medications. Studies (Dergal et al., 2002; Elmer et al., 2007; Peng et al., 2004) have reported the potential but untested interactions between some of the prescription medicines and HMPs that older adults often combine. What this study adds is an in-depth exploration of why older adults combine HMPs with prescribed medicines. Although there are theories of how health beliefs affect interactions and discussions with medical services (Leventhal & Cameron, 1987; Munro, Lewin, Swart, & Volmink, 2007), understanding how health beliefs about HMPs are reconciled with using prescribed medication has received less attention. For younger populations, there is a divide between what is seen as medical need and activities and HMPs that support personal health. This was partly supported by some of the participants' accounts of what they did to keep

well. There were however multiple reasons why individuals choose to combine prescription medicines with herbal products.

The wide range of motivations and sources of information identified from a relatively small sample that older adults draw on in making their decisions about using HMP with prescribed medicines were striking. These motivations as discussed in Chapter 6 ranges from dissatisfaction with conventional medicine, perceptions that HMPs are safe and convenient, to the desire to take control over their own health and minimise the inconvenience and difficulty of accessing conventional medical support. These resonate with the findings from previous research on why people use CAM and herbal medicine (Bishop & Lewith, 2010; Cheung, Geisler, & Sunneberg, 2014; Welz, Emberger-Klein, & Menrad, 2018). It is an important finding that the reasons were so diverse and not always influenced by the experience of deteriorating health associated with ageing.

It could not be assumed from the survey findings that the people who are concurrently using prescription drugs with HMPs conform to any easy categorisation about who they are and why they are using HMPs. This is now discussed in more depth in relation to the themes and sub-themes from the interview findings.

### **7.5.1 Tried and Tested or Learnt from Personal and Others' Experience**

#### **a. Herbal Medicines are Natural and Safe**

Many participants did not consider HMPs or dietary supplements to be medicines. They were represented as remedies or 'help yourself' products to be used when

required. This affected how they made judgements about whether to mention it to the GP or not. There is an interesting paradox that whilst participants did not think HMPs were harmful, they had plenty of examples of where they thought prescribed medication and treatment were life threatening or likely to trigger additional health problems. The possibility of interactions from combining HMPs and DS with prescription medications was not considered and the interviews revealed a willingness to sample a range of products until they find one that suited them. These findings raise questions about the health literacy of the population studied (Mayor, 2012) and how clinicians manage and support people to make informed choices about their health.

Health literacy is considered to be the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions (Ratzan, Parker, Selden, & Zorn, 2000). Health literacy is therefore relevant here in this context. What emerges from this study is that we do not know if people knew what their prescribed medications did, or if they were clear what the HMPs achieved or not. Although the study highlighted beliefs about their purpose and how this was different from prescribed medication. Limited health literacy is associated with poor use of preventive health services (Kobayashi, Wardle, & von Wagner, 2014), lower ability to self-manage health conditions, poorer health outcomes (Berkman, Sheridan, Donahue, Halpern, & Crotty, 2011) and mortality (Bostock & Steptoe, 2012). Difficulties with reading and understanding medical information, making and keeping appointments and following medication instructions (Sørensen et al., 2012), as well as social stigma creates barrier to gaining social support and advice (Easton, Entwistle, & Williams, 2013; Parikh,

Parker, Nurss, Baker, & Williams, 1996). Although this study did not identify resistance or inability to read instructions in the findings, it reinforces a lack of understanding about the importance of sharing information and the significance of exploring different decisions. Participants did not really understand how HMPs or prescribed medications work. This possibly explained why and how they sourced their information, which came from such a wide range of informants including family, friends and the internet.

#### **b. 'They Work But Don't Know How They Work'**

Some participants were sceptical of how the HMPs or DS worked for their conditions but continued to buy and use them. Interestingly, some of them also talked about their prescription medications in a similar manner. A possible explanation for this might be that older adults are practising self-care maintenance, which are behaviours performed to improve well-being, maintain physical and emotional stability (Riegel, Jaarsma, & Strömberg, 2012). For people living with chronic illness, self-care behaviours often mirror recommendations from healthcare providers. For example, they proactively take non-prescribed medications to control persistent or minor symptoms that the prescription medicines did not resolve. Consequently, higher use of herbal medicines and nutritional supplements is reported among older adults with chronic diseases compared to the general population (Gonzalez-Stuart, 2011; Rashrash et al., 2017; Tulunay, Aypak, Yikilkan, & Gorpelioglu, 2015).

### **7.5.2 Decision to Use HMPs or Dietary Supplements**

This study looked at a specific group of older people who took both prescribed medication and HMPs. There was overlap in the findings from studies that consider

older people's use of CAM that report they are pragmatic and eclectic (Heller, Lee-Treweek, Katz, Stone, & Spurr, 2005; Sharma, 1992; Sharp et al., 2018), often interested in whether a therapy might work for them rather than the theory behind the practice. As reported in this study, older adults will try any treatment that seems to work or has worked for people they know. Reports (Bishop, Yardley, & Lewith, 2008; Family, Jordan, Blaxall, & Sengupta, 2018) show that consultations with CAM practitioners are reported as providing more satisfactory meanings and interpretations of their symptoms than orthodox practitioners. In this study however, CAM practitioners were rarely consulted and were not seen as preferable or more knowledgeable, the two world views of how medicine works were held in tension.

Evidence suggests that ethnicity and culture are important determinants in how a person implements health self-management (Greenhalgh, Helman, & Chowdhury, 1998; Shaw, Armin, Torres, Orzech, & Vivian, 2012), particularly how complementary and alternative health care such as herbs are incorporated into a self-management regimen (Arcury et al., 2007). Self-management is discussed further in Section 7.5.4. For many older adults in this study, the belief in or the conviction to use HMPs arose from using them over many years, testimonies from friends, desire to avoid problems that others had experienced and information from internet searches. The findings demonstrated these different influences on participants' decision making but none emerged as particularly dominant.

The modest data available about BAME from this study, would seem to suggest that it is learnt efficacy either from personal experience or peer recommendations that shapes decisions to use HMPs rather than cultural. The self-regulatory model (SRM)

framework (Cameron & Leventhal, 2012) argues that shared beliefs (culture) about what is right or possible to do for health, often dictates health behaviours. Members of an ethnic group share beliefs and common experiences that affect their willingness to use different forms of health care. Often, the use of herbs for the prevention and treatment of ill health has its roots in the traditional and contemporary cultures, including European, Asian, African, Latino, and Native American heritage (Arcury, Suerken, et al., 2006; Barnes et al., 2004; Raji et al., 2005). However, this study had limited evidence that the use of herbal medicine was due to family history, ethnic or cultural beliefs passed onto them by their parents or grandparents. Cost and access to health care were dominant reasons for herbal medicine use, and a pragmatic response to the difficulties of accessing mainstream care. The difficulties experienced by people from BAME backgrounds were likely to reflect deeper and more pervasive inequalities in lack of income and education.

#### **a. Convenience and Access to Healthcare**

Older people increasingly find life challenging and appreciate options that make their life less complicated and with “less hassle”. It is a recurring finding in the research literature that the impact of living with a long term condition and the endless visits to health care practitioners over time are exhausting (Goodwin, Curry, Naylor, Ross, & Duldig, 2010; Hill, Sutton, & Cox, 2009). For some participants, avoiding the effort of getting to the GP outweighed the cost of HMPs. It is also worth reflecting whether the findings were indicative of older people maintaining choice and retaining control, as more and more decision making about how and where they live is shaped by their functional ability and those who support them. There were several examples of older people resenting that they had to fit in with the systems of health care, specifically

experiencing a lack of choice about when and for how long they see clinicians. Decisions to use HMPs were an expression of patient choice only in as much there was a decision not to “battle” a system. It was not a positive action. The decisions were pragmatic responses to the difficulties they encounter in discussing and debating options for care (Bunn et al., 2018). The study by Hansen and colleagues (2014) found that where there was evidence of continuity of care, patients were less likely to seek out complementary and alternative medical practitioners. They suggested this may be due to mutual trust in the GP-patient relationship, quality of care they receive, good communication, mutual knowledge and understanding.

#### **b. Previous Negative Experience of Using Conventional Medications**

There is an interesting paradox that whilst participants did not think HMPs were harmful they had plenty of examples of where they were disappointed or frustrated with prescribed or conventional medication and treatment. They thought prescribed medicine was not working, too many side effects or were likely to trigger additional health problems. So, they would rather actively seek and take alternative medicines, which they believe treat their symptoms and were thought to have minimal side effects. Research on medication concordance and compliance in older populations highlights that many either do not take the medication or reject the medication because of limited opportunities to discuss its impact or unpleasant side effects (Holt, Rung, Leon, Firestein, & Krousel-Wood, 2014; Salter, 2010; Yap, Thirumoorthy, & Kwan, 2016). Communication with healthcare providers as a positive factor to medication concordance is a recurring theme in these studies. There were few examples from the interviews that identified positive encounters with



health care professionals although there was one example of a GP recommending an HMP and the advice seen as trustworthy because of their role.

The dissatisfaction and negative experience of prescribed medicine or treatments ('push' factor) and the positive beliefs or experiences of herbal medicine ('pull' factors) (Bishop, Yardley, & Lewith, 2010; Sirois, 2008; Welz et al., 2018) are thought to be closely associated with the decision to use HMPs and the motivation to continue using them and eventually using them with prescribed medications. This raises questions about whether future interventions to reduce the risk of adverse reactions should consider how much time and opportunity clinical consultations offer for discussion, review and continuity of care.

### **c. Disclosure and Non-disclosure of HMP Use to Healthcare Practitioners**

The findings from this research reinforced the literature about non-disclosure of HMPs to healthcare professional (Foley et al., 2019; Robinson & McGrail, 2004). It identified that many older adults do not disclose HMPs or supplement use either because healthcare practitioners do not ask, they believe that herbal products are 'natural' and therefore 'safe', they fear being judged, as well as practitioners lacking time or knowledge of HMPs.

There was evidence from the interviews that some older people would welcome the opportunity to discuss their medications but had low expectations that healthcare practitioners would be interested. They were interested in knowing more about the study; particularly why I thought it was an important issue to research. Given this knowledge, it is important that future research explores targeted questioning of

patients about the use of alternative medicines or supplements to initiate wider conversation about HMPs and possible interactions.

As widely shown in the literature (Brennan et al., 2012; Milosavljevic, Aspden, & Harrison, 2018; Van Wijk, Klungel, Heerdink, & de Boer, 2005), public conversations and debates can be used to enforce and improve medication adherence. Healthcare practitioners, particularly the community pharmacists could educate patients by explaining the potential risks of taking HMPs with their prescribed medicines and discussing with patients their beliefs and knowledge about their health and associated treatments. Good patient and doctor rapport, an understanding of the illness in the patient's terms and reaching a shared understanding and agreement about proposed treatment and alternative choices is likely to enhance concordance (Ng et al., 2018; Wahl et al., 2005).

This research becomes more relevant as cannabis is increasingly used medically (Hamilton, Brands, Ialomiteanu, & Mann, 2017; Park & Wu, 2017), particularly among the elderly (Abuhasira, Schleider, Mechoulam, & Novack, 2018; van den Elsen et al., 2014). This is an example of how an HMP, although mainly used for recreational purposes is becoming mainstream. The interaction between cannabis and other drugs is largely unknown but the metabolism of the cannabinoids may be altered when used concurrently with drugs which influence the cytochrome P450 (CYP) enzymes. For example, concomitant administration of cannabidiol (CBD) significantly changed serum levels of topiramate, clobazam, and zonisamide (Gaston et al., 2017), while rifampin reduced CBD levels by 50% to 60% (Jiang, Yamaori, Takeda, Yamamoto, & Watanabe, 2011). Although none of the participants in this

study acknowledged using cannabis not least because they are HMPs, but it is okay to declare some and not others.

### **7.5.3 Sources of Information and Advice**

Older adults are the fastest growing population of online users (Choudrie, Pheeraphuttharangkoon, Zamani, & Giaglis, 2014; Olson, O'Brien, Rogers, & Charness, 2011). The interview findings demonstrated that the internet is a major source of information on HMPs and dietary supplements among older adults.

Ordering of HMPs and supplements from around the world has also become a much easier process. For some participants, the decision to use HMPs was influenced by information and experiences of other people gathered from blogs and online chat groups. This represents a different source of peer to peer learning for different groups which may promote products but may not have standard information about adverse effects. None of the participants in the study mentioned receiving advice or warnings about side effects or potential interactions from family and friends or online chat groups where they had originally received information or the suggestions to try HMPs.

Users of health services are also more likely to use the internet for health information (Choi, 2011). On the other hand, many economically disadvantaged or under-represented groups still lack access to basic digital resources and the skills to use them effectively (Robinson et al., 2015). Hence, the lower rates of use recorded among the poor, disabled, home-bound or those from BAME backgrounds (Choi & Dinitto, 2013).

In this study and many others, advice on HMPs was rarely sought from doctors and pharmacists, although some studies reported other healthcare practitioners, especially pharmacists as major sources of information on HMPs (Anonymous, 2010; Cheung et al., 2014; Knotek, Verner, Chaloupkova, & Kokoska, 2012). This may be due to the way health care systems are organised or limited access to the literature and the internet. In the UK, there is a general lack of knowledge about herbal medicine among doctors and pharmacists (Anonymous, 2010; Cramer, Shaw, Wye, & Weiss, 2010); in particular many do not have standard sources or references for information about HMPs. Therefore, they may feel less confident and competent to discuss the use of HMPs or provide evidence-based advice regarding potential interactions (Williamson et al., 2013).

#### **7.5.4 Self-management and Taking Control**

The use of herbal medicines is a self- management activity (Arcury, Bell, et al., 2006) and a key argument of health self-management is that adults are actively involved in monitoring and making decisions about their health (Arcury, Bell, et al., 2006; Corbin & Strauss, 1985; Schulman-Green et al., 2012). What many of the participants in this study described were different behaviours or strategies to supplement their prescribed medications with HMPs or DS. This included using prescribed medicines for only serious conditions while relying on HMPs or supplements for less serious ones, using HMPs to prevent the onset of new disease, to treat symptoms of chronic conditions and not disclosing use to healthcare practitioners. All these behaviours represent self-management strategies in relation to the use of medicines, to exercise control over their health and maintain their quality of life. This resonates with existing

literature on the common-sense model (CSM) of illness behaviour (Diefenbach & Leventhal, 1996) and self-management (Arcury et al., 2012; Bandura, 1997; Bodenheimer, Lorig, Holman, & Grumbach, 2002; Cameron & Leventhal, 2012; Corbin & Strauss, 1988).

The Leventhal's self-regulatory model provides a theoretical framework for understanding specific health self-management behaviours that older adult exhibit (Cameron & Leventhal, 2012; Leventhal, Halm, Horowitz, Leventhal, & Ozakinci, 2004) and argues that individuals will select a self-management behaviour based on:

- their beliefs of a symptom or illness
- their perceptions and understanding of their health
- their knowledge of treatments, personal resources and structural factors that affect access to a therapy.

This theory also considers individual characteristics since it may differentiate their health seeking behaviours, hence the use of herbal medicines. For example, women tend to have more health knowledge and are better at seeking healthcare than men (Smith, Braunack-Mayer, & Wittert, 2006; Thompson et al., 2016). Moreover, women tend to use more HMPs than men (Farina et al., 2014; Qato et al., 2008) and the use of HMPs and dietary supplements also increases with age (Arcury, Bell, et al., 2006; Zeilmann et al., 2003) and among certain ethnic groups (Graham et al., 2005; Upchurch & Wexler Rainisch, 2012). It is beyond the scope of the survey and interview findings to know if this applies to the participants. However, the findings did suggest that the reasons were more nuanced than the difference between the sexes that this research highlights.

Medical pluralism is another manifestation of self-management and occurs when patients use more than one medical system or use both conventional and complementary and alternative medicine (CAM) for health and illness (Baer, 2004; Wade, Chao, Kronenberg, Cushman, & Kalmuss, 2008). This affects how clinicians engage with patients and vice versa. Kleinman (Kleinman, 1980) argued that all health care systems are composed of three overlapping parts i.e. the popular (lay, non-professional, non-specialist), the professional and the folk sector (complementary and alternative medicines). Patients make choices between these three sectors and make judgement about the advice they are given, and what they believe makes sense to follow. The evidence suggests that actively involving patients in their own care, treatment and support can improve outcomes and experience for patients, and potentially yield efficiency savings for the NHS and support people to stay well and manage their own conditions better (Lorig et al., 1999; Vassilev et al., 2015; Zwerink et al., 2016) .

Despite the availability of a range of treatment options including the NHS 111 telephone helplines and policy changes (NHS England, 2010) advocating greater use of self-treatment, patients are uncomfortable discussing their use of self-treatments (Stevenson, Britten, Barry, Bradley, & Barber, 2003) and the findings from this research also supports this (Section 6.8). Only a few GPs in the study by Stevenson and colleagues (2003) initiated conversations about self-treatment but some patients did not disclose this to avoid conflict during the GP consultations. The evidence from the interviews in this study however suggested that it was not avoidance of conflict that was the reason for non-disclosure but an assumption the

GP would not be interested. Opportunities should be created for older people to engage with clinicians in discussing what would be best for long term conditions and this could possibly influence their decision to use or not to use HMPs.

### **7.5.5 Awareness and Experiences of Herb-Drug Interactions**

The review, survey and interviews all demonstrated that the potential risks of herb-drug interaction among older adults were underreported and not widely recognised. The notion that herbal medicines are natural therefore safe encourages self-prescription (Lynch & Berry, 2007; Walji et al., 2011) and non-disclosure of usage to health care professionals. Moreover, in most cases health professionals do not routinely ask about herbal medicine use (Lisk, 2012). Only three participants (NZ 001, SG181 and SG003) had consulted herbal medicine practitioners and purchased their supplies from them. For NZ 001, this suggests a lack of safeguards with regards to the monitoring and use of HMPs.

Concurrent use, medication sharing, lending and borrowing of prescription medication are well recognised behaviours among older adults (Beyene, Sheridan, & Aspden, 2014; Markotic, Vrdoljak, Puljiz, & Puljak, 2017). However, there is not a great deal of awareness regarding the potential risks from concurrent medication use.

As people get older and are prescribed more medications, there are additional risks which they may try to mitigate by using HMPs for conditions they consider as less serious while relying on prescribed medications for more serious ones. However, they do not equate using HMPs with prescription drugs as carrying similar risks and

negative outcomes as polypharmacy. This is a further evidence of the dissonance between how using conventional medicine with HMPs is understood, and the illusion that they are separate and do not interact. Older adults did not recognise the possibility of HMPs interacting with prescribed medicines or see them as unsafe. The survey findings suggest that the perception of risk by older adults was not a misplaced view but there were key interactions that were of concern. For example, HMPs like kava, valerian and St John's wort have been found to interfere with anaesthetic agents and many other drugs administered at the pre-operative periods (Ang-Lee, Moss, & Yuan, 2001; Bajwa & Panda, 2012; Borrelli & Izzo, 2009; Wong & Townley, 2010). Therefore, a different approach is needed to highlight specific drugs that are most likely implicated and how this should be routinely reported rather than just talk about the concurrent use of HMPs with prescriptions.

## **7.6 Strengths and Limitations of the Study**

The key strength of this study is that it has demonstrated what is known about how many older people use HMPs concurrently with prescribed medication and explored some of the underlying reasons. The use of a mixed method approach allowed a progressive focusing on what is known, how extensive the practice of using HMPs with prescribed medication is and what influences people's decisions provided a comprehensive account of an under researched topic.

By recruiting older people through GP practices serving different populations, it showed that it was possible to identify older people systematically. Previous studies have relied on self-selected samples and people with a known interest in HMP use. The response rate of 39% for the survey and 13 participants for the qualitative phase



is small, but enough to provide credible findings. Moreover, the richness of the data demonstrated the multiple influences and reasons for older community dwelling people taking HMPs.

Methodologically, there is also learning about which approaches work best for this population. In the early stages of developing this research, I tried recruiting some older adults into pilot focus groups to inform and develop questions for the survey, but many of them declined to participate. Further interrogation revealed that many were not comfortable talking about their use of 'other' medicines in a group. This level of disclosure about personal health issues and being open to possible censure were significant barriers to participation. In individual interviews, participants in this study spoke freely about other medicines they were taking and what they use them for, when they realised that I was neither a GP nor a healthcare practitioner. On reflection, it is possible that some of the older adults surveyed did not disclose or underreported their use of HMPs and dietary supplements. Therefore, the true prevalence of concurrent use of HMPs and supplement with prescription drugs may be higher than shown by the survey.

## **7.7 Reflections on Chosen Methodology and Methods**

### **a. Resources**

Mixed method studies are challenging to plan and conduct. Careful planning and considerations were required for all aspects of each phase of this research. With the sample sizes for both the quantitative and qualitative phases carefully estimated, taking into consideration what was already known about the population. The quantitative phase had to be analysed very quickly after the survey ended, to identify

respondents that were eligible and willing to be interviewed for the next qualitative phase. It was also important to contact participants immediately to schedule interviews, since they may forget about the study after some time or change their mind about participating.

Good qualitative and quantitative research skills are essential to undertaking a mixed method study, often involving on a multi-disciplinary team of researchers. My background is within qualitative methods and this positivist sense of the world has been the driving force in this PhD research. My initial idea was to conduct a purely quantitative study, to assess the concurrent use of HMPs and prescription medicines among UK older adults, and the potential interactions from such combinations. Although previous studies have also used quantitative approaches to study this issue, but there were no recent studies from the UK. The systematic review identified an important knowledge gap in this area; the lack of evidence as to why older adults concurrently use medicines. It became increasingly clear that using purely quantitative approaches would limit not only the understanding but would also not answer the question 'why do UK older adults concurrently use prescription medicine and HMPs?' Therefore, a mixed method approach provided a pragmatic way of addressing both the 'what' and 'why' elements of the research question.

Mixed method studies are labour intensive and often require additional resources than single method study. Using postal questionnaires was an expensive approach to data collection. Online or telephone survey would probably have been less expensive. However, because the study population is  $\geq 65$  years, and more likely to respond to postal questionnaires, this was the preferred option.

## **b. Approaches**

Focus groups were planned for initial phase of this research, to test assumptions of the research objectives and inform focus for subsequent phases of the study.

However, recruiting for the focus groups proved difficult. As argued by some authors (Erzberger & Kelle, 2003), the outcomes of multi-strategy research is unpredictable.

There may be the need to combine strategy either because of unexpected results or non-realisation of potentials after data collection, even though advanced decisions about design were made pre-data generation. With this in mind, I was open to a change in the study design that may arise due to unexpected results. Therefore, Individual interview was adopted to inform the survey phase in place of focus groups, as enough participants could not be recruited.

Similar surveys that used interviewers achieved better response rate. For example, Of the 399 eligible persons invited to participate in a survey by Delgoda et al (2010), 365 agreed, yielding a 91.5% response rate.

## **c. Low Response Rate**

Although the response rate of 39% achieve is relatively low, but it is consistent with other studies on this topic and provides credible findings. Non-response is a known problem for questionnaire surveys. A lot of efforts were made to increase the response to this study by contacting participants three times, even though two contacts are suggested (Bryman, 2012; Edwards et al., 2002). In addition, an incentive of £10 voucher was offered during the third contact, and this might explain the increased responses of 58 for this round.

## 7.8 Chapter summary

This Chapter has presented an overview of the main findings from the research and this was discussed in relation to the research questions asked in each phase. It has discussed how the findings have reinforced and added to existing literature around the concurrent use of HMPs and dietary supplements with prescribed drugs. Older adults did not recognise the possibility of HMPs interacting with prescribed medicines or see them as unsafe.

# 8 Conclusions

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## 8.1 Introduction to Chapter

This thesis has addressed the concurrent use of prescription drugs and herbal medicinal products (HMPs) among older adults. It has provided a rationale for answering the research questions using a sequential mixed method design. It included a systematic literature review which suggests that the concurrent use of prescription drugs and HMPs among older adults is substantial. The quantitative phase examined the prevalence of concurrent prescription drugs and HMPs among UK community dwelling older adults and one-third of participants reported concurrent use in the last 12 months. Most concurrent users used dietary supplements with prescription drugs. Most commonly reported dietary supplements were cod liver oil, glucosamine, multivitamins and Vitamin D. HMPs most concurrently used with prescriptions were evening primrose oil, valerian and Nytol Herbal<sup>®</sup>.

The qualitative phase explored the reasons for concurrent use of prescriptions drugs, HMPs and DS. These interviews uncovered the influences their decisions to concurrently use HMPs and supplements with prescriptions and how this manifest into some self-management behaviours or strategies.

## 8.2 Contributions to Knowledge

There is a growing problem of polypharmacy with conventional medicines among older adults. The concurrent use of HMPs and DS increases the risks of drug interactions. Findings from this study have established the range of prescribed drugs, HMPs and DS that older adults most commonly combine. It also demonstrated the reasoning and system challenges that inform the decision to use HMPs in this way.

The study has provided the first estimate of the prevalence of concurrent HMPs and prescription drug use among UK older adults. It has also highlighted potential interactions from certain combinations of prescription drugs, HMPs and dietary supplements which healthcare practitioners could routinely ask older adults about.

The qualitative phase of this study addressed why older adults concurrently use their prescriptions drugs with HMPs and DS. Findings from this study provide a platform for health care professionals to review their own practice and knowledge. Also, it has demonstrated the need to systematically identify older people who may be at risk of potential herb-drug interactions.

The range of reasons for concurrently using HMPs and/or dietary supplements with prescriptions drugs provided by this study provides an added perspective to the literature on polypharmacy and interventions to support medicine management for older adults living at home with multiple health needs.

### 8.3 Implications for Practice and Recommendations

This is the first study exploring why community dwelling older adults concurrently use prescription drugs with HMPs and dietary supplements and there is scope for further work. Evidence from the systematic review indicates that many older adults concurrently use prescription drugs with HMPs and DS. It also showed the combinations of prescription drugs and HMPs concurrently used and the potential interactions from these combinations. In addition, the survey provided an overview of the HMPs and DS used by UK community dwelling older adults alongside prescribed medications and the possible interactions from such combinations. Therefore, this study provides healthcare practitioners with a 'snapshot' of some combinations commonly used by older adults to look out for during drug reviews and consultations.

Considering that the prevalence of concurrent use among UK older adults is substantial and the associated risks, healthcare professionals should regularly ask their patients questions regarding use of other medications. Moreover, a good understanding of the extent and the manner which older adults combine prescription drugs, DS and HMPs in their health regimens is important knowledge for healthcare practitioners. Based on the findings from this study, there is a need to revisit how responsibilities and conversations are negotiated with all the different people involved- from manufacturers to clinicians and regulators. With regards to regulation and sale of HMPs, accurate and key information regarding precautions for those with pre-existing conditions, interactions with other products and possible adverse effects should be provided. This will enable consumers make informed choices about the safe use of HMPs.

The evidence in this study suggested that quite a large number of older adults use HMPs and DS with their prescribed medicines. The implications of this for regulation and monitoring how these products are marketed include:

- Public education as the next step to inform and encourage patients to tell healthcare providers about their use of HMPs and DS.
- Healthcare practitioners routinely initiating discussions about HMPs and DS during consultations and treatment.
- Government, regulators and manufacturers to increase publicity for patient reporting by targeting advertising campaigns at the public.
- Regulators (e.g. MHRA) making reporting of suspected side effects or adverse reactions from HMPs and DS much more easier for patients and healthcare professionals, particularly through the Yellow Card Scheme (Medicines and Healthcare products Regulatory Agency, 2013). The Yellow Card Scheme helps the MHRA monitor the safety of all healthcare products in the UK and is available online at <https://yellowcard.mhra.gov.uk/yellowcards/tobaccoreportmediator/>
- This study highlighted that the responsibility for finding out and alerting people to possible interactions and adverse events is unclear. Therefore, the public should be helped and encouraged to check the quality of herbal products and where to find accurate information.
- Proactive efforts by healthcare practitioners particularly in community pharmacy and general practice could publicise and promote patient reporting of adverse interactions.
- Patients could be educated about the THR logo on the label of HMPs and encouraged to have raised expectations about the quality of HMPs (See



Section 2.3). The THR certification mark shows that the herbal medicine has been registered with the MHRA and meets standards of quality, safety, and patient information (Medicines and Healthcare products Regulatory Agency, 2012). A list of registered HMPs is available online and updated regularly at: <https://www.gov.uk/government/publications/herbal-medicines-granted-a-traditional-herbal-registration-thr/herbal-medicines-granted-a-traditional-herbal-registration>.

- Key drugs should routinely highlight potential interactions with HMPs and DS. For example, St. John's wort and cyclosporine, Coumadin, digoxin, and benzodiazepines, among others, and this should be linked to community pharmacist guidance.

#### **8.4 Implications for Pharmacy- led Research**

Clinical pharmacists increasingly work as part of general practice teams, to carry out structured medication reviews for patients with ongoing health problems. They support patients to get the most from their medicines and attend to some of the many self-limiting minor ailment consultations. Patients are also more likely to disclose use of HMPs and DS to pharmacists. Therefore, Pharmacists could

- Enquire and document the use of HMPs and DS as part of medication reviews, to capture the range of medicines used concurrently and provide advice where necessary.
- Commissioners could explore the opportunities for consultations and education of this group as health care professionals who have recurring contact with older people.

## 8.5 Implications for future research

These findings have implications for further research and implementation of risk reduction policies and strategies. They demonstrate the complexity behind the 'simple' decision to use HMPs concurrently with prescribed medications. Based on the conclusions from this study, future research on this issue should consider:

- Only participants who were long term users of HMPs and DS are represented in this study and not those who tried HMPs and DS then stopped.
- Future research should consider a larger study involving people with a wide range of experiences of using HMPs and DS with prescription drugs.
- Although health care professionals' knowledge of HMPs and DS was not explored in this study, the literature suggests it is underdeveloped. There is limited knowledge on and lack of access to information on herbal medicines (Kemper et al., 2003; Robinson & Lorenc, 2011; Shorofi & Arbon, 2017). This stops healthcare practitioners initiating discussions about herbal medicine use with patients. Pharmacists, especially community pharmacists are well positioned within the NHS to provide medicines advice and support. Educational opportunities for healthcare practitioners should be enhanced to provide them with up-to-date knowledge of complementary and alternative medicines, particularly HMPs and potential interactions. This will in turn empower them to assist patients in making informed decisions regarding alternative medicines. Future studies should explore the knowledge, attitude and experiences of healthcare practitioners to HMPs and DS, particularly GPs and pharmacists.
- The internet is a major source for information and advice and for the purchase of HMPs and dietary supplements. This study found that older adults were

using the internet for health information. Further research should explore the influence of online information on older adult's choices and health seeking behaviours.

- The volume and quality of patient reports to the Yellow card scheme is very poor. Providing links and advice on reporting adverse reactions to the Yellow Card Scheme will also improve pharmacovigilance of HMPs and DS. Future research should investigate the barriers and facilitators to patient reporting herb-drug, supplement-drug reactions.
- There is value in future research focussing on specific health conditions such cancer, diabetes, arthritis etc. for which prescribed medications and HMPs are most concurrently used. This has been done with cancer patients (Alsanad et al., 2016; Berretta et al., 2017; Farooqui et al., 2016; Yates et al., 2005) but further work is needed to address the long term conditions identified in this study such as diabetes and arthritis.

## **8.6 Impact and Dissemination of Research Findings**

Findings from research will only affect policy and improvement if they are effectively disseminated and to the right audience. There is a huge literature on dissemination and implementation science (Brownson, Colditz, & Proctor, 2018; Sandström, Borglin, Nilsson, & Willman, 2011; Wandersman et al., 2008) which shows that just communicating research findings may bring about little or no changes. I have made use of available opportunities throughout the PhD to network with other researchers, GPs and patients to discuss my research methodology, and present the findings as they emerged.

There is a high level of interest in HMPs and dietary supplement. Therefore, findings from this research will appeal to the public, media, the NHS, as well as regulatory authorities such as the MHRA. The systematic review and survey were published in reputable Open Access journals to make them accessible to all. The survey findings were shared widely in national newspapers and Radio stations, stimulated discussions and actions from the National Institute of Medical Herbalists (NIMH) and a leading herbal pharmaceutical company, Dr Willmar Schwabe Germany (Appendix K).

## **8.7 Chapter Summary**

This chapter concludes the thesis and presented the strengths and limitations of the study, significance of the research and implications of the findings to evidence, research and healthcare professionals.

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# Appendices

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## Appendix A: Ethics Approval University of Hertfordshire



Professor Claire Goodman &  
Mrs Taofikat B. Agbabiaka  
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4 June 2015

Dear Claire and Taofikat

**Re: UNIVERSITY OF HERTFORDSHIRE SPONSORSHIP IN PRINCIPLE for the following:**  
**RESEARCH STUDY TITLE:** Concurrent use of prescription drugs and herbal medicinal products among older adults  
**NAME OF CHIEF INVESTIGATOR (Supervisor):** Professor Claire Goodman  
**NAME OF INVESTIGATOR (Student):** Mrs Taofikat B. Agbabiaka  
**UNIVERSITY OF HERTFORDSHIRE ETHICS PROTOCOL NUMBER:** HSK/PG/NHS/00336

This letter is to confirm your research study detailed above has been reviewed and accepted, and I agree to give University of Hertfordshire sponsorship in principle.

Before you commence your research you must be in full compliance with all NHS Governance requirements. You must also secure full University of Hertfordshire sponsorship, for which you will need to have supplied the following documentation:

- Final version of the submitted IRAS form (pdf)
- Approval from the relevant NRES (NHS) Research Ethics Committee (REC) as well as confirmation of favourable opinion of any amendments
- Evidence of relevant NHS Permissions (eg Research Passport) and NHS Trust Management Permissions (previously known as R&D Approval) as they are received
- The final version of the protocol
- The final versions of the patient information leaflet and informed consent form
- One page summary CV for the Chief Investigator (CI) as submitted with the IRAS form
- Any other regulatory permissions required for your research, eg from the National Information Governance Board (NIGB), under the Human Tissue Act or the Ionising Radiation (Medical Exposure) Regulations
- If applicable, copies of any contracts/agreements with external organisations (eg funders, collaborators, co-sponsors) involved in your research study

As a condition of receiving full sponsorship, it is the responsibility of the Chief Investigator to inform the Sponsor of any changes to the duration or funding of the project, changes of investigators, changes to the protocol and any future amendments or deviations from the protocol, which may require re-evaluation of the sponsorship arrangements. It is also the responsibility of the Chief Investigator to inform the funder, the NRES (NHS) Research Ethics Committee (REC) and the relevant University of Hertfordshire Ethics Committee with Delegated Authority (ECDA) and any other relevant authority of any of these changes.

I look forward to receiving the above documents before you commence your research. Please email these to [research-sponsorship@herts.ac.uk](mailto:research-sponsorship@herts.ac.uk) so the University can confirm sponsorship. In the meantime, we wish you well in pursuing this interesting research study.

Yours sincerely,

Professor J M Senior  
Pro Vice-Chancellor (Research and International)

*Encl: Insurance certificate*



A Charity Exempt from Regulation under the  
Second Schedule of the Charities Act 1993

## Appendix B- NHS Research Ethics Committee Approval



### Health Research Authority

#### Research Ethics Service

#### London - Hampstead Research Ethics Committee

Barlow House  
3rd Floor  
4 Minshull Street  
Manchester  
M1 3DZ

Telephone: 0207 104 8002

10 November 2015

Professor Claire Goodman  
Centre for Research in Primary and Community Care (CRIPACC)  
University of Hertfordshire  
Hatfield  
AL10 9AB

Dear Professor Goodman

**Study title:** Concurrent use of prescription drugs and herbal medicinal products among older adults  
**REC reference:** 15/LO/1870  
**Protocol number:** HSK/PG/NHS/00336  
**IRAS project ID:** 138718

Thank you for your letter of 02 November 2015, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Assistant Miss Amber Ecclestone, [nrescommittee.london-hampstead@nhs.net](mailto:nrescommittee.london-hampstead@nhs.net). Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

#### Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

#### Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

**Management permission or approval must be obtained from each host organisation prior to**

A Research Ethics Committee established by the Health Research Authority

## Appendix C- Copy of Questionnaire



### Co-use of prescription drugs and herbal medicinal products among older adults

#### Questionnaire (Please return within two weeks)

Please complete the following questions

#### Section 1: Background information about you:

Please tick one correct answer

##### 1.1 Which age group do you fall into?

- Under 65 years
- 65-74 years
- 75-84 years
- 85- 94 years
- 95 years and over

##### 1.2 Are you?

- a. Male
- b. Female

##### 1.3 How old were you when you left school? .....

##### 1.4 Did you have further education or training after school?

- Yes  No

##### 1.5 If yes please tick all of the following that apply

- a. Further Education/ Technical College
- b. University
- c. Distance learning/correspondence course
- d. Other

**1.6 Do you live?**

- Alone
- With my partner/spouse
- With partner/spouse and children
- With my children
- With grandchildren
- Other please explain

**1.7 Please tick one only to indicate your ethnic background.**

- a. White(*British, Irish, Gypsy/Roma, Turkish, Italian, any other White background*)
  - b. Asian or Asian British (*Pakistani, Indian, Chinese, Bangladeshi, other Asian background*)
  - c. Black or Black British (*Caribbean, African any other Black background*)
  - d. Mixed/Multiple background (*white and black Caribbean, white and black African, other multiple ethnic background*)
  - e. Other Ethnic Group
- Please state.....

**1.8 Do you take medication prescribed by your GP, hospital doctor, nurse or pharmacist that you take every day or at least once a month (e.g. Tablets, syrup, ointments, patches, etc.)?**

- 1. Yes
- 2. No

**Section 2: Questions about prescription medicines**

2.1 If you answered YES to question 1.5 above, please list all the medicines currently prescribed for you by your GP or other healthcare professional. (You can attach your repeat prescription request form if you wish).

	What is the name of the prescription medicine you are taking?	How many times do you take this medicine each day?	What are you taking this medicine for?
1.			
2.			
3.			
4.			
5.			
6.			
7.			

8				
9				
10.				

**Section 3: Information about herbal and nutritional medicines you take that are NOT prescribed by the NHS, these are often described as dietary supplements.**

*These medicines are available to buy from pharmacies, health-food stores, and supermarkets and over the Internet. Some examples of are: fish oils, glucosamine, and Echinacea, Ginkgo, ginseng, saw palmetto, and St. John's wort).*

**3.1 Do you currently use or have you used any type of herbal medicine or dietary supplement in the 12 months?**

Yes  No  Unsure

If **YES**, please **continue with Question 3.2**

If **NO**, thank you for completing this questionnaire. Even though you do not take any other medications apart from those prescribed, it is very important for us to know that.

Please return your completed questionnaire in Taofikat Agbabiaka in the enclosed reply paid printed envelope

**Taofikat Agbabiaka  
C/o Kim Haynes  
Centre for Research in Primary & Community Care (CRIPACC)  
University of Hertfordshire  
College Lane, Hatfield  
AL10 9AB**



If you answered YES to question 3.1, please tell us which herbal or nutritional medicines you have used in the last 12 months.

3.2 Please list all those you have taken in the last 6-12 months and why you use them?

What is the name of the natural medicine you are taking?	What does your medicine look like? (Tablet, syrup, powder, herb)	How often do you take it? (please circle)	What are you taking this medicine for?
1		More than once a day Once a day Weekly Monthly Every now and again Other	
2		More than once a day Once a day Weekly Monthly Every now and again Other	
3		More than once a day Once a day Weekly	

4	.		Monthly Every now and again Other More than once a day Once a day Weekly Monthly Every now and again Other	
5	.		More than once a day Once a day Weekly Monthly Every now and again Other	
7	.		More than once a day Once a day Weekly Monthly Every now and again Other	

7

**3.3. Where do you get your herbs or herbal and nutritional medicines from?  
(Please tick all that apply)**

- 1. Pharmacy
  - 2. Health food shop
  - 3. Online
  - 4. Supermarket
  - 5. Herbalist
  - 6. Other
- (Please specify) .....

**3.4 What do you feel are the benefits from using herbs or herbal medicines  
in general? (Please tick all that apply)**

- They are recommended by a health professional
- They prevent health problems
- They are useful when I am feeling unwell
- They give me strength
- They ease my pain
- They improve my mobility
- They improve my digestion
- They treat my depression
- They treat my cancer
- They treat my arthritis
- They maintain my bone health
- They help my other medications to work better
- I am not sure
- Other, please state

.....  
.....  
.....  
.....

**Section 4: Information about side effects or reactions to taking herbal medicines**

**4.1 Have you experienced any problems whilst using the herbal medicines that you take now?**

Yes

No

**4.2 If Yes, Can you explain which one had that effect and what it was (for example, stomach upset, felt unwell, felt dizzy, just did not feel right)**

**4.3 Have you ever stopped taking a herbal medicine because of a bad reaction or unwanted side effect?**

Yes

No

**4.4 If yes what was the medicine and can you say why you stopped taking it (including if it did not work)**

**5. PERMISSION TO BE CONTACTED FOR NEXT PHASE OF THE STUDY**

**5.1 Would you be interested in talking to us in more detail about your use of herbal medicines?**

Yes

No

**If yes, please supply your contact details below and one of our researchers will contact you to discuss and arrange a meeting.**

**Name:**

**Address:**

**Telephone number:**

**Email address:**

**If you supply your details, this does not mean that you have to participate in the study. You can withdraw from the study at any time.**

**THANK YOU FOR TAKING THE TIME TO COMPLETE THIS QUESTIONNAIRE.**

Please return in the enclosed reply paid envelope to:

Taofikat Agbabiaka

C/o Kim Haynes

Centre for Research in Primary & Community Care (CRIPACC)

University of Hertfordshire,

College Lane, Hatfield

AL10 9AB

## Appendix D: Participant Information sheets



### **PARTICIPANT INFORMATION SHEET**

#### **Co- use of prescription medications and herbal medicinal products among older adults**

Thank you for considering taking part in my research study. Please take time to read the following information carefully and talk to others if you wish. Please contact me if you need more information or if there is anything you do not understand.

#### **What is the study about?**

About a quarter of UK adults use herbal remedies/ medicines such as Echinacea, ginkgo and ginseng in the management of their health. Research suggests that some herbal medicines may interact with prescription medicines when taken together. As we get older, some of us need to use more prescription medicines, and for this reason, we might be more at risk of herbal and prescription medications interacting. At the moment very little is known about the range of products older people take alongside their prescription medication, or the reasons why. For example, some people may have always taken herbal supplements for arthritic pain, whereas someone else might be taking them because their prescription medication is not as effective as it used to be.

We would like to gain a better understanding of the reasons, experiences and views of older adults using herbal and prescription medicines. This study will form the basis of the researcher's (Taofikat Agbabiaka) doctorate

in Health Research. The results will be used to develop a better understanding of the choices people make and why, and the range of drugs that they use.

**What do we mean by herbal medicines?**

Herbal medicines or herbal remedies are made from leaves, stem, bark, seeds or flowers of plants and sometimes fungi. Herbal medicines and supplements are available to buy from pharmacies, herbal stores and supermarkets without a prescription. Some examples of herbal medicines are: Echinacea, ginkgo, ginseng, saw palmetto, and St. John's wort.

**Why have I been chosen?**

The staff at Nazeing Valley Health Centre have sent information about this study to all 65 years and older on prescription medicine and registered at the surgery. We are hoping to contact up to 400 older adults in Essex and Haringey.

**Do I have to take part?**

It is completely up to you to decide whether or not to take part. If you decide to take part, you are still free to withdraw at any time and without giving a reason. This will not affect the type or standard of care that you receive from your GP.

**What will I be asked to do if I take part?**

If you decide to take part, we will ask you to complete and return the enclosed questionnaire which asks you about the medicines that you currently take, whether you have taken any herbal medicine in the last 12 months and your experiences of taking herbal medicine.

**Please complete and return the questionnaire even if you do not take any herbal medicine.**

If you are willing to talk to our researcher, please supply your contact details in the space provided at the end of the questionnaire. Please note that the Researcher is not clinically qualified, and will not be able to advise on your medication and symptoms.

**Will my data be kept confidential?**

The information you provide is completely confidential. Personal information such as names and addresses will be removed by the research team. For analysis, all data is anonymised and contain numbers only. Data collected for this study will be stored securely on a password protected NHS computer accessible only to the research team. Completed questionnaires will be kept securely locked in a cabinet for 5 years, and destroyed at the end of this period.

There are some limits to confidentiality. If you give any response which makes me think that you or someone else is at significant medical or psychological risk or harm, I will have to break confidentiality and speak to a member of staff about this. If possible, I will tell you if I have to do this.

**What will happen to the results of the study?**

The results of this study will form the basis of my doctorate and reported in a dissertation. Findings will be presented at research conferences and published in academic journals.



**Are there any benefits of taking part?**

We cannot promise the study will benefit you personally in any specific way. However, it is hoped that findings from this study will provide health care with information to better detect and manage older adults at risk of herb-drug interactions.

**Who has reviewed the study?**

All research in the NHS is looked at by independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the London Hampstead Research Ethics Committee.

**Where can I obtain further information about the study if I need it?**

If you have any questions, please contact the main researcher:

Taofikat Agbabiaka  
Centre for Research in Primary & Community Care  
University of Hertfordshire  
Telephone: 07733008745  
Email: [t.b.agbabiaka@herts.ac.uk](mailto:t.b.agbabiaka@herts.ac.uk)

Although we hope it is not the case, if you have any complaints or concerns about any aspect of the way you have been approached or treated during the course of this study, please contact:

Secretary and Registrar  
University of Hertfordshire  
Hatfield, AL10 9AB  
Telephone: 01707 284032  
email: [l.toon@herts.ac.uk](mailto:l.toon@herts.ac.uk)

**Thank you very much for considering participating in this study.**

## Appendix E: Literature Review Search Strategy

- 1 herb\*.ti,ab.
- 2 (plant\* adj3 (caplet\* or capsule\* or compound\* or cream\* or decoction\* or drug\* or essence\* or extract\* or formul\* or heal\* or herb\* or Infus\* or juice\* or medic\* or mixture\* or powder\* or prepar\* or prescri\* or product or products or remed\* or supplement\* or tablet\* or tea or teas or therap\* or tincture\* or tisane\* or treatment\*)).ti,ab.
- 3 (phytdrug\* or phytomed\* or phytopharmac\* or phytother\* or phytochemical\*).ti,ab.
- 4 ((natural\* or naturo\*) adj3 (caplet\* or capsule\* or compound\* or cream\* or decoction\* or drug\* or essence\* or extract\* or formul\* or herb\* or Infus\* or juice\* or medic\* or mixture\* or powder\* or prepar\* or prescri\* or product or products or remed\* or supplement\* or tablet\* or tea or teas or therap\* or tincture\* or tisane\* or treatment\*)).ti,ab.
- 5 (botanical\* adj3 (caplet\* or capsule\* or compound\* or cream\* or decoction\* or drug\* or essence\* or extract\* or formul\* or heal\* or herb\* or Infus\* or juice\* or medic\* or mixture\* or powder\* or prepar\* or prescri\* or product or products or remed\* or supplement\* or tablet\* or tea or teas or therap\* or tincture\* or tisane\* or treatment\*)).ti,ab.
- 6 (Ethnobotan\* or pharmacogno\* or Ethnopharmaco\* or ethnomedic\*).ti,ab.
- 7 ("diet\* supplement\*" or "nutri\* supplement\*" or "food supplement\*").ti,ab.
- 8 Pharmacognos\*.ti,ab.
- 9 (traditional adj3 (caplet\* or capsule\* or compound\* or cream\* or decoction\* or drug\* or essence\* or extract\* or formul\* or herb\* or Infus\* or juice\* or medic\* or mixture\* or powder\* or prepar\* or prescri\* or product or products or remed\* or supplement\* or tablet\* or tea or teas or tincture\* or tisane\*)).ti,ab.
- 10 (folk adj3 (caplet\* or capsule\* or compound\* or cream\* or decoction\* or drug\* or essence\* or extract\* or formul\* or herb\* or Infus\* or juice\* or medic\* or mixture\* or powder\* or prepar\* or prescri\* or product or products or remed\* or supplement\* or tablet\* or tea or teas or tincture\* or tisane\*)).ti,ab.
- 11 (Aloe or aloes\*).ti,ab.
- 12 ("black cohosh" or "actaea racemosa" or "Cimicifuga racemosa").ti,ab.
- 13 (Echinacea or "Coneflower").ti,ab.
- 14 ("Evening primrose" or "oenothera biennis").ti,ab.
- 15 (feverfew or "tanacetum parthenium" or "Chrysanthemum parthenium" or "Pyrethrum parthenium").ti,ab.
- 16 (garlic or "Allium sativum").ti,ab.
- 17 (ginger or "zingiber officinale").ti,ab.
- 18 (ginkgo or "fossil tree" or "maidenhair tree" or "Japanese silver apricot" or baiguo or "bai guo ye" or "kew tree" or yinhsing or "yin-hsing").ti,ab.
- 19 (ginseng or "Panax quinquefolius" or "Eleutherococcus senticosus").ti,ab.
- 20 (Grapefruit or "Citrus adj2 paradisi").ti,ab.
- 21 (Hawthorn\* or Crataegus).ti,ab.
- 22 ("John's wort" or "Johns wort" or hypericum or "Klamath weed" or "goat weed").ti,ab.
- 23 (licorice or liquorice or glycyrrhizin or "Glycyrrhiza glabra" or "sweet root" or "gan zao").ti,ab.
- 24 ("saw palmetto" or serenoa).ti,ab.
- 25 (Soursop or "Annona muricata" or "durian blanda").ti,ab.
- 26 (valerian or "valeriana officinalis" or Valerianaceae).ti,ab.
- 27 (Mint or Mentha or peppermint or menthe or Spearmint).ti,ab.
- 28 exp Plants, Medicinal/  
29 exp ethnobotany/ or exp pharmacognosy/  
30 plant preparations/ or exp plant extracts/  
31 exp Ethnopharmacology/  
32 exp Dietary Supplements/  
33 Medicine, Traditional/  
34 exp Herb-Drug Interactions/  
35 exp Plant Exudates/  
36 materia medica/ or plant extracts/  
37 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36  
38 prescri\*.ti,ab,kw.

39 ((conventional or synthetic) adj2 (drug\* or medicin\* or pharmaceut\* or medicat\*)).ti,ab,kw.  
40 "drug therap\*".ti,ab,kw.  
41 ("over-the-counter" or "over the counter" or otc).ti,ab.  
42 (("non-prescri\*" or nonprescri\*) adj2 (drug\* or medicin\* or pharmaceut\* or medicat\*)).ti,ab,kw.  
43 ("behind-the-counter" or "behind the counter" or btc).ti,ab,kw.  
44 exp Prescriptions/  
45 exp Drug Therapy/  
46 exp Prescription Drugs/  
47 exp Nonprescription Drugs/  
48 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47  
49 (elder\* or old\* or aged or geriatr\* or Gerontol\*).ti,ab,kw.  
50 exp Aged/  
51 exp Geriatrics/  
52 49 or 50 or 51  
53 37 and 48 and 52  
54 Animals/  
55 Humans/  
56 54 not (54 and 55)  
57 53 not 56

## Appendix F: Interview Guide

### Concurrent use of prescription drugs and herbal medicinal products among older adults

#### Interview Schedule

**Introduction** (Check first that all the information materials have been received, how much time they can give for the interview and if they have any further questions).

I would like to thank you for participating in this study. As you know you were invited to take part because you completed a questionnaire about medication use and specifically the use of herbal medicines. The aims of this study are to gain a better understanding of the reasons, experiences and views of UK older adults using herbal and prescription medicines. Everything you say in this interview is confidential and no one will know that you took part in the study from anything that I write in my thesis or papers. The information you share will help me to understand more about the choices people make about the medicines they use and why.

I would like to talk to you in more detail about your experience of herbal medicines and reasons for using them.

With your permission, I would like to record our conversation so as not to miss anything. This recording will be strictly confidential and used only for the purpose of this research. You can stop the interview at any time and you do not have to explain to me why (**Show person how to switch off the recorder or agree what they can do if they want to stop the interview e.g. wave their hand**).

## Interview prompts

- 1. Introductions and initial questions to confirm responses in the questionnaire and ask if there are any other herbal medicines that were not mentioned (3-5 minutes).**

## Herbal medicine

Now let's talk about your use of herbal medicine(s) as recorded in your questionnaire.

- 2. Participant's knowledge of herbal medicines (10 minutes)**

You have told me in the questionnaire that you use XX (name the herbal reported in questionnaire)?

- What do you take XX herbal medicine for?
- How did you decide to use XXX herbal medicine?
- Does anyone else in your family take herbal medicines?
- Do any of your friends take herbal medicines?

**(Repeat for each medicine)**

- 3. Source(s) of herbal medicines ( 10 minutes)**

- Where do you get this/these herbal medicines?
- Do you mind me asking how much you pay for them

- 4. Participant's experience/benefits of using herbal medicines ( 10-15 minutes)**

- You mentioned in the questionnaire that you have experienced some benefits whilst using XX herbal medicines. Can you tell me more about this?
- Did you talk to your GP or other health professional about this/these benefits?
  - What were their comments?
  - Did they ask you to stop or continue using this/these herbal medicine(s)

**5. Participant's experience/adverse effects from herbal medicines ( 10-15 minutes)**

- Have you experienced any problems whilst using herbal medicines?
- Can you tell me more about this?
- What were the symptoms you experienced?
- Why do you think the herbal medicine(s) caused this/these?
- How did you manage this/these problems?
  
- Did you talk to your GP or other health professional about this/these problems?
- Did they ask you to stop or continue using this/these herbal medicine(s)Have you ever stopped taking a herbal medicine if so why

**Concurrent use**

**6. Reasons for concurrently using prescription drugs and herbal medicines ( 10-15 minutes)**

- How do you think the herbal medicines work alongside your prescribed drugs by your GP/ other healthcare practitioner?
  
- **Would you like to add any other comments or discuss anything in particular?**

I would like to thank you so much for your time and valuable comments. This conversation is very helpful and will help us to better understand the use of herbal medicine(s) with prescription medications among older adults.

I would also want to remind you again that identities of all participants will remain strictly confidential.

## Appendix G: Interview Consent Form



### Interview Consent Form

**Patient study ID:** .....

**Project Title: Co- use of prescription medications and herbal medicinal products among older adults**

1. I confirm that I have read and I understand the information sheet (Older Adults PIS Vs 2) for the above study and have had the opportunity to ask questions and I have had these answered satisfactorily
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand that sections of my medical notes relevant to my taking part in this research may be looked at by the GP administrator. I give permission for these individuals to have access to my records.
4. I understand and agree that anonymised findings from the study might be published in journals or presented at conferences.
5. I agree to take part in this interview for the above named study and that the interview can be audio-recorded.

\_\_\_\_\_  
Name of Participant                      Signature                      Date

\_\_\_\_\_  
Name of Researcher                      Signature                      Date

*Interview consent for Participants FINAL 1 June 2015*

# Appendix H: Snapshot of Analytical Framework from NVivo

Concurrent prescription and herbed (NVivo 12).nvp - NVivo 12 Pro

Name	Files	References	Modified On	Modified By	Classification
case nodes		10	10 16/12/2017 10:45	TB	
NZ 045		0	0 05/01/2018 08:59	TB	Participants
NZ 068		0	0 05/01/2018 09:00	TB	Participants
NZ 069		1	1 05/01/2018 09:01	TB	Participants
NZ 070		1	1 05/01/2018 09:03	TB	Participants
NZ 142		1	1 05/01/2018 09:03	TB	Participants
NZ 146		1	1 05/01/2018 09:04	TB	Participants
NZ 199		1	1 05/01/2018 09:05	TB	Participants
NZ084		1	1 05/01/2018 09:08	TB	Participants
Phymed 001		1	1 05/01/2018 09:08	TB	Participants
SG 003		1	1 05/01/2018 09:08	TB	Participants
SG 070		0	0 05/01/2018 08:58	TB	Participants
SG 072		1	1 05/01/2018 09:09	TB	Participants
SG181		1	1 05/01/2018 09:10	TB	Participants

Concurrent prescription and herbed (NVivo 12).nvp - NVivo 12 Pro

Mind Map Tools

```

    graph LR
      Disclosures --- Self-management
      Disclosures --- Values and Beliefs
      Disclosures --- Decision making
      Disclosures --- Family and Friends
      Disclosures --- Healthcare practitioner
      Disclosures --- Side effects of conventional medicine
      Disclosures --- Trial and error
      Disclosures --- Information
      Disease variation --- Self-management
      Disease variation --- Values and Beliefs
      Disease variation --- Decision making
      Disease variation --- Family and Friends
      Disease variation --- Healthcare practitioner
      Disease variation --- Side effects of conventional medicine
      Disease variation --- Trial and error
      Disease variation --- Information
      Not used for serious conditions --- Self-management
      Not used for serious conditions --- Values and Beliefs
      Not used for serious conditions --- Decision making
      Not used for serious conditions --- Family and Friends
      Not used for serious conditions --- Healthcare practitioner
      Not used for serious conditions --- Side effects of conventional medicine
      Not used for serious conditions --- Trial and error
      Not used for serious conditions --- Information
      Replacement --- Self-management
      Replacement --- Values and Beliefs
      Replacement --- Decision making
      Replacement --- Family and Friends
      Replacement --- Healthcare practitioner
      Replacement --- Side effects of conventional medicine
      Replacement --- Trial and error
      Replacement --- Information
      Self-diagnosis --- Self-management
      Self-diagnosis --- Values and Beliefs
      Self-diagnosis --- Decision making
      Self-diagnosis --- Family and Friends
      Self-diagnosis --- Healthcare practitioner
      Self-diagnosis --- Side effects of conventional medicine
      Self-diagnosis --- Trial and error
      Self-diagnosis --- Information
      Supplementa son --- Self-management
      Supplementa son --- Values and Beliefs
      Supplementa son --- Decision making
      Supplementa son --- Family and Friends
      Supplementa son --- Healthcare practitioner
      Supplementa son --- Side effects of conventional medicine
      Supplementa son --- Trial and error
      Supplementa son --- Information
      Swapping and Sharing --- Self-management
      Swapping and Sharing --- Values and Beliefs
      Swapping and Sharing --- Decision making
      Swapping and Sharing --- Family and Friends
      Swapping and Sharing --- Healthcare practitioner
      Swapping and Sharing --- Side effects of conventional medicine
      Swapping and Sharing --- Trial and error
      Swapping and Sharing --- Information
  
```



2018.01.21 - Framework Matrice - Microsoft Excel

File Home Insert Page Layout Formulas Data Review View

Clipboard Font Alignment Number Styles Cells Editing

	A	B	C	D	E	F	G	H	I	J	K	L
1		<b>A : Values ans Beliefs</b>	<b>B : Decision to use HMPs/DS</b>	<b>C : Sources of information</b>	<b>D : Self management</b>	<b>E : Failings of the healthcare system</b>	<b>F : Potential interactions</b>					
2	NZ146 65-74 years	I don't take it all the time that actually. I take it, um, I mean I think, there are certain things that I take all the time because if I stop taking them my arthritis gets worse again within sort of two or three weeks of stopping taking them, so I tend to take them all the time. But I stay on the lowest doses possible that they recommend.	NZ146 ...you know, you might as well just persist with it until it stops working. If at some point it doesn't work or if, I mean if I was to get something really serious like, you know, cancer or something like that, I wouldn't be looking at the herbal side of things. I mean obviously I'd go straight to the medical profession and anything that was serious wrong with me obviously then I would do that. But I think if you're looking at things where you've just got to live along with those conditions. Interviewer So it's to maintain your day-to-day? NZ146 Yeah. To make it a little bit easier for yourself, then I will go for the herbal stuff. Interviewer	NZ146 Interviewer So not for serious conditions?	Interviewer So how did you decide to use these herbal medicines? NZ146 I didn't really want to, to be, I've got to be honest with you I've never really gone to the doctors to have my arthritis confirmed but I've had it for years now and it's progressively got slightly worse. Some bits of it have got better, particularly my knees because I've moved to a bungalow and before I could, you know, some mornings I could hardly get up and down the stairs. [Laughs] But my knees have really improved since I've moved to the bungalow and so I don't really have so much problem with them anymore. But I do get it in my hips and my wrist and sometimes in my various fingers, like my thumb joint and one of the fingers. So they, it has got progressively worse I would say over the last sort of seven or eight years. And I just think it is osteoarthritis. It's just wear and tear and I don't honestly think if I went to the doctors about it they could really	Interviewer ...in total it will be costing you everything, more up to £30, £50? NZ146 It could do, yeah. Yeah, it could do. I mean, you know, I have to say although I get my prescriptions free, when I do get them it is worth it to me because obviously I have, I have hay fever as well so I have to get that stuff from the doctors. Although I do take honey for hay fever as well but I still get it and I have to have the drops and the sprays and things. And when, so, you know, this time of year I get the most out of my free prescriptions if you like and obviously all the time I get the stuff for my reflux and the high cholesterol and the, and the other thing. [Laughs] So...						
3	NZ199											

Sheet1

Ready

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28/08/2019

## Appendix I: Invitation Letter to Study Participants



27<sup>th</sup> January 2016

### **Project Title: Co- use of prescription medications and herbal medicinal products among older adults**

Dear .....

Your GP surgery is sending you this letter on my behalf to ask if you would consider taking part in a study that looks at the different medicines people take in addition to those that are prescribed by their doctor. These include herbal remedies and medicines you might take to improve your health.

My name is Taofikat Agbabiaka and I am doing this research as part of studying for my doctorate in Health Research. I work for the NHS and have a background in complementary medicine research. I am doing this study because although it is quite common for people to take remedies in addition to medicines that have been prescribed by their GP, very little is known about the range of things that are taken and why or how people take them.

This letter is to ask if you would be kind enough to complete the attached questionnaire and return it to me in the pre- paid envelope. The questionnaire is **confidential** and your GP will not see what you write. The only time your GP would be informed is if something you have written suggests that you might be at risk or would benefit from seeing your GP. The findings from the questionnaire will be part of a report that I submit for my doctorate. No one who participates will be identifiable and it is hoped that the findings will be useful to those who are involved in prescribing medication for people like yourself.

If having read this letter, you decide you would like to know more about the study please contact me on the mobile number below or by email, so I can send you more information to help you make up your mind.

**Please kindly complete and return the questionnaire even if you do not take any herbal medicine.**

We cannot promise the study will benefit you personally in any specific way. However, it is hoped that findings from this study will provide information that helps other people in the future.

I look forward to hearing from you.

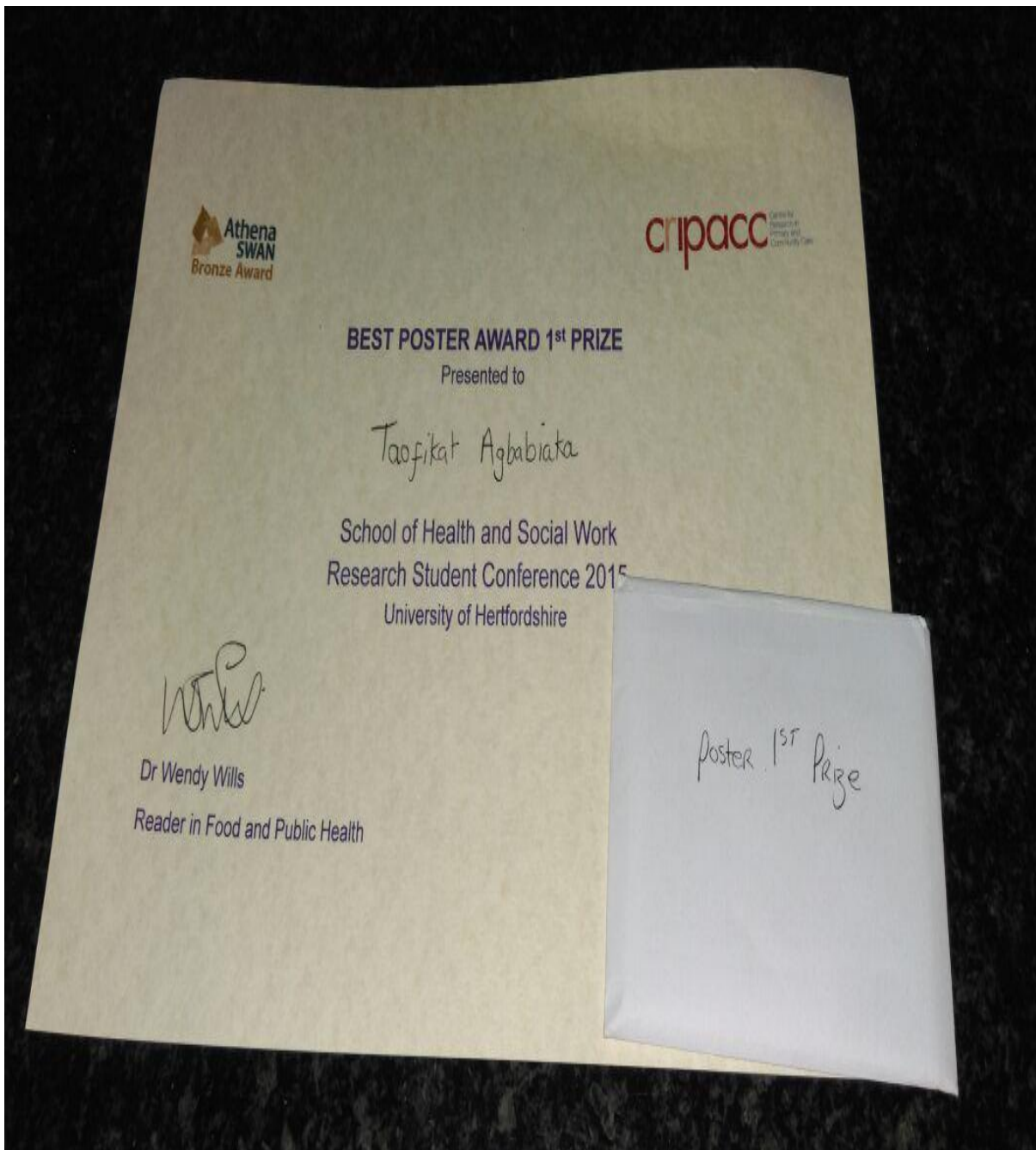
Yours sincerely,

A handwritten signature in black ink that reads "Taofikat Agbabiaka".

Taofikat Agbabiaka  
07733008745  
[t.b.agbabiaka@herts.ac.uk](mailto:t.b.agbabiaka@herts.ac.uk)

Survey Invitation Letter. FINAL. 1 June 2015

## Appendix J: School of Health & Social Care Poster Award



## Appendix J: Impact, Presentations and Papers related to the PhD

### a. Oral and Poster Presentations

- Poster presentations at the School of Health and Social Care (HSK) Research Conference in July 2015, my systematic review protocol was awarded Best Poster prize (Appendix J).
- Oral presentation of survey findings at the University of Hertfordshire School of Health and Social Care Postgraduate Research Conference in July 2017.
- Poster presentation of systematic review findings at the International Society for Pharmacovigilance Conference at Liverpool in October 2017.
- Poster presentation of survey findings at the Safer Primary Care Conference at Manchester in March 2017.
- Two Poster entries at the University of Hertfordshire Postgraduate Research Poster Competition in Oct 2017.

### b. Journal articles

- Protocol for the Phase 1 systematic review has been published (Agbabiaka et al., 2016).
- Findings from the review is published in the journal *Drugs and Aging* (Agbabiaka et al., 2017). This paper has been very well received; currently over three thousand downloads and has been cited by 13 other papers. This systematic review was one of the five most downloaded articles on the publisher (Springer Link) platform from January to December 2018.

- The phase 2 questionnaire survey has been published in published British Journal of General Practice (Agbabiaka et al., 2018)

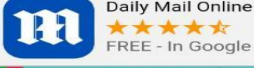
c. **Networking with Professional Bodies and Manufacturers**

- The survey paper had stimulated much discussion amongst members of the National Institute of Medical Herbalists (NIMH). A response to the paper from the Institute was published on the BJGP website(Deakin, 2018) .
- The Institute's Director of Professional and Inter-professional Development also contacted me by email to acknowledge the issues raised by the paper and what the Institute and members are doing to avoid potential herb-drug interactions and improve patient outcomes. My response to his letter was published in the Institute's newsletter.
- A leading herbal pharmaceutical company, Dr Willmar Schwabe Germany, contacted me for additional information on the potential interactions reported in the survey.

d. **Media**

- The survey paper published on the 24<sup>th</sup> of September 2018 generated huge media and public interest. It was featured by several media outlets including Daily Telegraph, Daily Mail, Daily Express, ITV, BBC and CNN.
- I also had the opportunities to talk about the study on BBC Counties Radio, BBC Radio 5 and Bob FM. Additional coverage appeared on news websites Yahoo.com and AOL (Appendix K)

## Appendix K: Some of the Media Coverage for the Study




Daily Mail Online  
★★★★★  
FREE - In Google Play

View

**DailyMail** Health

### One million over-65s could be suffering dangerous side effects from mixing 'hazardous' combinations of drugs and herbal remedies, study warns


By Kate Pickles Health Reporter For The Daily Mail  
19:03 EDT 24 Sep 2018 , updated 05:39 EDT 25 Sep 2018



296 shares

486 comments

- Hazardous combinations can increase risk of bleed or raise blood sugar levels
- Supplements such as omega-3 can interact badly with...



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### Pensioners warned not to mix statins and herbal remedies

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Scientists believe herbal remedies may lessen the effect of statins and other life-preserving drugs. CREDIT: PA

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## Concerns raised about older adults mixing prescription drugs and herbal remedies

Tuesday 25 September 2018

"One million over-65s could be suffering dangerous side effects from mixing 'hazardous' combinations of drugs and herbal remedies, study warns," reports the Mail Online.

This follows a postal survey of 149 adults aged 65 and above from southeast England. The survey wanted to see whether people were choosing to take herbal or dietary supplements while also taking prescription medication. All respondents were taking at least 1 prescription drug, and a third of them were also taking some kind of supplement.

Most of the combinations were not harmful, but

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**More than 1,000,000 are putting themselves at risk by taking alternative therapies**

Tanveer Mann Tuesday 25 Sep 2018 11:44 am

**More than one million people may be putting themselves at risk by taking alternative therapies, a new study has found.**

These therapies could potentially interact with prescribed drugs which in turn could give dangerous side effects.

The study published in the British Journal of General Practice suggested doctors ask patients about any herbal and supplement usage to identify potential side effects.

**Hertfordshire researchers find use of prescription drugs with herbal medicines could have serious consequences for older adults**

Researchers are warning more than one-million older people could be risking their health by taking herbal remedies alongside prescription drugs like statins and aspirin.

The University of Hertfordshire's found those taking medication are often also taking three or more herbal and dietary supplements, such as St John's Wort or evening primrose oil, which can reduce their effect.

They're warning the biggest problems are potentially linked to increased blood glucose concentration, risk of bleeding, and reducing the effectiveness of a prescription drug.

The study also found that some patients were taking as many as eight different alternative medicines and supplements.

Authors of the report, which has been published in the British Journal of General Practice, says patients should inform their GPs so that the risks can be explained to them.

Led by Taofiqat Agbabika, PhD Researcher at the University of Hertfordshire working in patient safety, said: "The potential risk of interactions with certain combinations of prescription drugs, herbal medicines and dietary supplements shows the need for healthcare professionals to routinely ask questions regarding the use of other medications that are not prescribed."

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**INDEPENDENT**


News > Health

# Alternative medicine use may put 1.3 million older people at risk, study suggests

One in three who take at least one prescription drug also consume herbal medicinal products or dietary supplements

**Samuel Osborne** | @SamuelOsborne93 | Tuesday 25 September 2018 00:08 |

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