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# **Improving appropriate polypharmacy in older people in primary care**

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A handwritten signature in black ink that reads "Ashleigh Gorman". The signature is written in a cursive style with a period at the end.

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Ashleigh Gorman

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## **Abstract**

### **Introduction**

People are living longer but not necessarily in better health. The ageing population coupled with the increasing prevalence of chronic conditions has resulted in many older people being prescribed polypharmacy (four or more concurrent medicines), which may not always be appropriate. An intervention to improve appropriate polypharmacy in older people was developed and tested in Northern Ireland (NI), the PolyPrime intervention. It was developed using theory following guidance from the Medical Research Council on the development of complex interventions. The aim of this research programme was to identify other theoretically derived interventions aimed at improving polypharmacy and their effectiveness, undertake a pilot cluster randomised control trial (cRCT) of the PolyPrime intervention and explore how community pharmacists could enhance their role in the management of older people with polypharmacy, in the Republic of Ireland (RoI).

### **Methods**

A systematic review was conducted to assess the effectiveness of theoretically derived interventions on appropriate polypharmacy in older people. The theories used and the extent to which they informed intervention design was established. The PolyPrime intervention, developed in NI, was refined for use in the RoI by undertaking semi-structured interviews with general practitioners (GPs) in the RoI. A pilot cRCT was conducted with six general practices from a defined area in the RoI (Cavan, Donegal, Leitrim, Louth, Monaghan, Sligo). The GP-led intervention involved four components: i) GPs watch a short online video (designed and scripted by the research team) ii) explicit plans made at weekly staff meetings to ensure that target patients prescribed appropriate polypharmacy, iii) patients are invited to attend the practice for a scheduled medication review, and iv) reception staff prompt the GP that the patient has arrived at the practice for their medication review. GP record data and patient self-reported data was collected at baseline, 6-months post initial medication review (or equivalent for control arm practices) and 9-months post initial medication review (or equivalent for control arm practices). Medication appropriateness, health-related quality of life and healthcare utilisation were measured, the fidelity of intervention delivery was assessed, participants perspectives of the intervention were ascertained and a process evaluation of the pilot RCT was undertaken. A semi-structured interview study, based on the Theoretical Domains Framework (TDF) was undertaken with community pharmacists regarding their role in the management of

appropriate polypharmacy in older people. The PolyPrime intervention was presented to community pharmacists to determine if a similar approach would be applicable in that setting.

## **Results**

Only two studies were included in the systematic review, highlighting a lack of theoretically derived interventions aimed at improving appropriate polypharmacy in older people. As a result of the qualitative interviews conducted with GPs minor amendments were made to PolyPrime intervention, notably the addition of guidelines and validated assessment tools. The pilot cRCT demonstrated that it was feasible to collect the desired data, both from GP practice records and patient self-reported, to provide outcome data. Overall, the intervention was well received by GPs, practice staff (as identified in semi-structured interviews), and patients (data collected in feedback questionnaire). The intervention was delivered as intended. The qualitative research with community pharmacists identified three strategies (medication review, communication with prescribers, access to patient records) that could be investigated to enhance their role in managing appropriate polypharmacy. TDF domains addressed in all three strategies included Beliefs about consequences and Environmental context and resources. Barriers to enhancing the role of community pharmacists in managing appropriate polypharmacy in older people included lack of resources such as staff and equipment, issues around General Data Protection Regulations and lack of financial support; facilitators included free up GP time, development of standard operating procedure and making changes public policy. The PolyPrime intervention was well received by community pharmacists.

## **Discussion/Conclusion**

The research presented in this thesis reports that there is a lack of theoretically derived interventions aimed at improving appropriate polypharmacy in older people. The pilot cRCT of the PolyPrime intervention found that such interventions are acceptable to key stakeholders. The effectiveness of the PolyPrime intervention now needs to be established via a definitive trial, considering feedback from the pilot cRCT process evaluation. There is potential to expand the role of the community pharmacist in the Rol in managing appropriate polypharmacy, including developing medication reviews and communicating more with prescribers. It is possible that the PolyPrime intervention could be refined for use in community pharmacy practice.

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## Abbreviations

<b>ACOVE</b>	Assessing Care of Vulnerable Elders
<b>AG</b>	Ashleigh Gorman
<b>APPEL</b>	Affiliation for Pharmacy Practice Experiential Learning
<b>AR</b>	Audrey Rankin
<b>BCT</b>	Behaviour change technique
<b>CC</b>	Cathal Cadogan
<b>CHITIN</b>	Cross-border Healthcare Intervention Trials in Ireland Network
<b>CHO</b>	Community Health Organisations
<b>CoMM</b>	Coordinated medication risk management
<b>CONSORT</b>	Consolidated Standards of Reporting Trials
<b>COREQ</b>	Consolidated criteria for Reporting Qualitative research
<b>CPD</b>	Continuous professional development
<b>CR</b>	Cristín Ryan
<b>cRCT</b>	Cluster randomised controlled trial
<b>CSO</b>	Central Statistics Office
<b>ECHO</b>	Economic, Clinical and Humanistic Outcomes
<b>EMA</b>	European Medicines Agency
<b>EOI</b>	Expression of interest
<b>EPOC</b>	Effective Practice and Organisation of Care
<b>GDPR</b>	General Data Protection Regulations
<b>GMS</b>	General medical scheme
<b>GP</b>	General practitioner
<b>HSE</b>	Health Service Executive
<b>ICGP</b>	Irish College of General Practitioners
<b>IloP</b>	Irish Institute of Pharmacy
<b>IPU</b>	Irish Pharmacy Union
<b>ITT</b>	Intention to treat
<b>MAI</b>	Medication Appropriateness Index
<b>MoA</b>	Mechanism of action
<b>MRB-QoL</b>	Medication-Related Burden Quality of Life
<b>MRC</b>	Medical Research Council
<b>NI</b>	Northern Ireland
<b>NICE</b>	National Institute for Health and Care Excellence

<b>NICTU</b>	Northern Ireland Clinical Trials Unit
<b>NIHR</b>	National Institute for Health Research
<b>NHS</b>	National Health Service
<b>NORGEP</b>	Norwegian general practice criteria
<b>NUIG</b>	National University of Ireland, Galway
<b>MeSH</b>	Medical Subject Headings
<b>MS Teams</b>	Microsoft Teams
<b>PARIHS</b>	Promoting Action on Research Implementation in Health Services
<b>PCNE</b>	Pharmaceutical Care Network Europe
<b>PETS</b>	Patient Experience with Treatment and Self-management
<b>PIM</b>	Potentially inappropriate medication
<b>PIP</b>	Potentially inappropriate prescribing
<b>PPO</b>	Potential prescribing omission
<b>PRISMA</b>	Preferred Reporting Items for Systematic reviews and Meta-Analyses
<b>PRISMA-P</b>	Preferred Reporting Items for Systematic reviews and Meta-Analyses- Protocols
<b>PS</b>	Practice staff
<b>PSI</b>	Pharmaceutical Society of Ireland
<b>QUB</b>	Queen’s University Belfast
<b>RCT</b>	Randomised controlled trial
<b>RoB</b>	Risk of bias
<b>ROBINS-I</b>	Risk of Bias in Non-randomised Studies-of Interventions
<b>RoI</b>	Republic of Ireland
<b>SCALE</b>	Similar, Cost-effective, Acceptable, Low-complexity, Extensible
<b>SD</b>	Standard deviation
<b>SEIPS</b>	Systems Engineering Initiative for Patient Safety
<b>SHARE</b>	Survey of Health, Ageing and Retirement in Europe
<b>SoPPS</b>	School of Pharmacy and Pharmaceutical Sciences
<b>SOP</b>	Standard operating procedure
<b>SRQR</b>	Standards for reporting qualitative research
<b>START</b>	Screening Tool to Alert doctors to Right Treatment
<b>STOPP</b>	Screening Tool of Older Persons Prescriptions
<b>TCD</b>	Trinity College Dublin
<b>TCS</b>	Theory coding scheme



<b>TDF</b>	Theoretical Domains Framework
<b>TFA</b>	Theoretical Framework of Acceptability
<b>ToC</b>	Theory of Change
<b>TPB</b>	Theory of Planned Behaviour
<b>TRA</b>	Theory of Reasoned Action
<b>TSC</b>	Trial Steering Committee
<b>TSQM</b>	Treatment Satisfaction Questionnaire for Medication
<b>UK</b>	United Kingdom
<b>VAS</b>	Visual analogue scale
<b>WHO</b>	World Health Organisation

## Publications

### Manuscripts

**Gorman, A.**, Rankin, A., Hughes, C., O'Dwyer, M., Ryan, C. 2020. Theoretically derived interventions aimed at improving appropriate polypharmacy in primary care: a systematic review. *Exploratory Research in Clinical and Social Pharmacy*, 7, pp:100166. Doi: 10.1016/j.rcsop.2022.100166

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Rankin, A., Cadogan, C.A., Barry, H.E., Gardner, E., Agus, A., Molloy, G.J., **Gorman, A.**, Ryan, C., Leathem, C., Maxwell, M., Gormley, G.J., Ferrett, A., McCarthy, P., Fahey, T., & Hughes, C.M., on behalf of the PolyPrime team. 2021. An external pilot cluster randomised controlled trial of a theory-based intervention to improve appropriate polypharmacy in older people in primary care (PolyPrime): study protocol. *Pilot and Feasibility Studies*, 7, pp:77. Doi: 10.1186/s40814-021-00822-2

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Rankin, A., **Gorman, A.**, Cole, J., Cadogan, C., Barry, H.E., Agus, A., Logan, D., McDowell, C., Molloy, G., Ryan, C., Leathem, C., Maxwell, M., Brennan, C., Gormley, G., Ferrett, A., McCarthy, P., Fahey, T., Hughes, C.M. 2022. An external pilot cluster randomised controlled trial of a theory-based intervention to improve appropriate polypharmacy in older people in primary care (PolyPrime). *Pilot and Feasibility Studies*.

*Manuscript in preparation*

Title: Enhancing community pharmacists' role in the management of appropriate polypharmacy

Target journal: International Journal of Clinical Pharmacy

### Abstracts

**Gorman A**, Rankin A, Barry H, Cadogan C, Gormley G, Fahey T, Ryan C, Gardner E, Agus A, Leathem C, Maxwell M, Molloy G, Ferrett A, McCarthy P, Hughes C. A qualitative study to refine a theory-based intervention to improve appropriate polypharmacy in older people in primary care. *International Journal of Pharmacy Practice*. 2020;28:4-43 S1. Doi: 10.1111/ijpp.12606 [Conference: Health Services Research & Pharmacy Practice Conference: Oral presentation]

**Gorman A**, O'Dwyer M, Hughes C, Honohan C, Rankin A, Ryan C. Systematic review of theoretically derived interventions aimed at improving appropriate polypharmacy in primary care. [Conference: Irish Institute of Pharmacy Conference: Poster presentation]

**Gorman A**, O'Dwyer M, Hughes C, Honohan C, Rankin A, Ryan C. Protocol for a systematic review of theoretically derived interventions aimed at improving appropriate polypharmacy in primary care. [Conference: All Ireland Schools of Pharmacy Conference: Poster presentation]

**Chapter 1**  
**Introduction**

## **1.1 Ageing**

It is widely acknowledged that the population is ageing worldwide; the number of people aged 65 years or older is expected to double to 1.5 billion by 2050 making one in six people in the global population aged 65 years or over by 2050 (United Nations 2019). This global trend is also evident in the Republic of Ireland (RoI). Data from the Central Statistics Office (CSO) showed that in 2019, there were just under 697,000 people in the RoI aged 65 years or over; this figure is expected to double to 1.56 million by 2051 (CSO 2019).

### **1.1.1 Defining an older person**

The UN Committee on Economic, Social, and Cultural Rights of Older Persons replaced the term 'elderly' with 'older persons' over 20 years ago, as the term 'elderly' can be seen to encourage ageism, such as older people being considered a burden. This shift in the use of terms has come alongside the examination of the age profile. Biological ageing is often related to a person's age in years, however some adults in their 60s can have the same mental and physical capacity as an adult in their 30s. Biological ageing can be influenced by the environmental context, both physical and social, as well as an individual's opportunity to access healthcare (Prada *et al.* 2021).

The generic consensus on a definition for an 'older person' is an individual that is 65 years or over. This definition is believed to have been generated in Germany, with the Chancellor of the German Empire (Otto von Bismarck) 1871-1890, selecting 65 years as the state pension age, assuming a small number of people would live to 65 years (Orimo *et al.* 2006). Interestingly, the state pension age in the RoI and that in many European countries was in line with this and has only recently been reviewed to increase to 66 years with a further planned increase to 68 years in 2028 (O'Brien 2014a).

The recent surge in life expectancy and population growth is a result of increased development in healthcare and medicines, with life expectancy in the RoI now 80.4 years at birth for a man and 84 years for women (Eurostat 2017a). However, the numerical value assigned to the definition of an older person is still commonly used a century and a half later, with older age still being considered 65 years.

People may be living longer, but not necessarily in better health (Jivraj *et al.* 2020). Quality of life is impacted by social and physical environment as well as noncommunicable diseases, such as diabetes, dementia, cardiovascular disease or hypertension. Noncommunicable diseases, more commonly referred to as chronic diseases or chronic conditions, tend to affect the

individual for a long period and are the result of genetic, physiological, environmental and behavioural factors (Budreviciute *et al.* 2020). The prevalence of chronic, long-term conditions [i.e. those that currently cannot be cured but are managed through medications and treatments (Yarnall *et al.* 2017)] and multimorbidity (defined below) is increasing.

## **1.2 Multimorbidity**

### **1.2.1 An overview of multimorbidity**

Multimorbidity is commonly defined as the co-existence of two or more chronic conditions (Violan *et al.* 2014). However, there is no agreement on the most appropriate definition, nor the most adequate measure of multimorbidity (Almirall *et al.* 2013). A review of definitions of multimorbidity by Johnston *et al.* (2019) concluded that most definitions of multimorbidity include the occurrence of multiple conditions, with two or more conditions being the most commonly used definition, with one definition also including biopsychosocial factors as well as physical factors (le Reste *et al.* 2013). The co-existence of two or more chronic conditions is the adopted definition for multi-morbidity throughout this thesis.

The National Institute for Health and Care Excellence (NICE) states that multimorbidity can include various types of conditions including (but not limited to) physical and mental health conditions, sensory impairment, alcohol and substance abuse, ongoing conditions such as learning disability, and symptom complexities such as frailty (NICE 2017). Multimorbidity is presenting frequently in older people globally and is common in western European countries (Prados-Torres *et al.* 2012, Violan *et al.* 2014, Woolford *et al.* 2021). Data from Scotland shows that one in four adults have multimorbidity (Barnett *et al.* 2012) and with current trends, it is expected that 17% of the UK population will have four or more chronic conditions by 2035 (Kingston *et al.* 2018). A third of people in the RoI aged  $\geq 65$  have a chronic condition (Eurostat, 2017b), and over 50% of patients with a chronic condition have multimorbidity, which puts considerable strain on the healthcare system.

Multimorbidity is not restricted to older people; approximately 35% of 55–64 year-olds live with multimorbidity (Jindai *et al.* 2016). Socio-economic status also contributes to the presence of multimorbidity. A systematic review by Violan *et al.* (2014) found that there is an association between multimorbidity and socio-economic status, people from low socio-economic areas being more likely to experience multimorbidity. Additionally, living in a low socio-economic area is the second leading cause of multimorbidity [age being the first (Violan *et al.* 2014)]. Analysis

of 15 years of hospital data, conducted by Byrne *et al.* (2019), found that patients from low socio-economic areas present to the accident and emergency department approximately 10 years earlier than people from high socio-economic areas.

### **1.2.2 Multimorbid older people and healthcare**

Multimorbidity increases pressure on healthcare resources. Long-standing health conditions account for approximately 80% of general practitioner (GP) consultations (Salisbury *et al.* 2011). People with multimorbidity account for 78% of medicines prescribed (Cassell *et al.* 2018), 70% of inpatient hospital admissions and 50% of general practitioner appointments (Woolford *et al.* 2021). As the current healthcare system is divided between primary and secondary care, it can be argued that the system is not designed, and therefore not equipped, to manage adults with multimorbidity (Colombo *et al.* 2016). There is a lack of coordination between primary and secondary care which often results in patients having to repeat discussions with a variety of healthcare professionals, and healthcare professionals can be reluctant to 'take ownership' of a patient, with the patient being referred to numerous different specialists (Wallace *et al.* 2015). GPs report that the current support for decision making in patients with multimorbidity is not sufficient (Sinnott *et al.* 2013). A systematic review of guidelines and expert consensus on the evidence supporting the best clinical management of patients with multimorbidity and polypharmacy by Muth *et al.* (2019), reported that there are eight guidelines for multimorbidity and polypharmacy, with most common recommendation being the need for individualised patient management plans. Detailed guidance is not provided on how to construct individualised patient management plans.

Patients with multimorbidity often experience a decrease in quality of life (Fortin *et al.* 2006, Makovski *et al.* 2019), a higher mortality rate (Schäfer *et al.* 2018a), are more likely to consume multiple medications daily and are more at risk of potentially inappropriate prescribing (Galvin *et al.* 2014, Schneider *et al.* 2021) than those who do not have multimorbidity (NICE 2017, Yarnall *et al.* 2017). The increase in prevalence of multimorbidity has resulted in the prescribing of multiple medications, commonly termed 'polypharmacy' (defined below).

## **1.3 Polypharmacy**

### **1.3.1 Polypharmacy: a myriad of definitions**

The increase in the prevalence of chronic conditions and multimorbidity has resulted in the prescribing of multiple medicines. Over 20% of patients with multimorbidity are prescribed 4-9

medicines (Woolford *et al.* 2021). The prescribing of multiple medicines is commonly termed 'polypharmacy', for which there is currently no accepted definition in the literature (Cadogan *et al.* 2016, Masnoon *et al.* 2017). Multiple literature reviews and systematic reviews have been conducted to define polypharmacy and explore the range of definitions used in research and within healthcare to describe the use of multiple medicines (Viktil *et al.* 2007, Masnoon *et al.* 2017, Taghy *et al.* 2020, Pazan and Wehling 2021). Masnoon *et al.* (2017) conducted a systematic review of definitions of polypharmacy and found that over 80% of 138 definitions identified were quantitative (i.e. numerical based) and the most commonly used threshold was five or more medications, with 11% of these adding a duration of therapy (for example prescribed a particular medicine for three months or more) or a particular healthcare setting to the definition. Nearly 9% of definitions examined in this review provided a descriptive approach with no numerical threshold; however, different terms were utilised when referring to the same definition (Masnoon *et al.* 2017). This can make comparing definitions, and by extension, studies that use these definitions hard to compare with other published research. Table 1.1 provides examples of definitions used for the term 'polypharmacy', including definitions identified in the systematic review conducted by Masnoon *et al.* (2017) (an exhaustive list of definitions of polypharmacy is not in the scope of this chapter).

The World Health Organisation (WHO) has moved away from defining polypharmacy using a numerical threshold, and currently defines polypharmacy as "the concurrent use of multiple medications" (WHO 2019). The occurrence of polypharmacy will vary in individuals depending on the definition used, as well as the characteristics of the population. For example, a review by Khezrian *et al.* (2020) found that the prevalence of polypharmacy in older people can vary from 10-90% in different populations. A clear definition, agreed by experts within the field of polypharmacy and gerontology, would prove useful in increasing the understanding of polypharmacy for both patients and healthcare professionals, but also in the design and comparison of research studies.

**Table 1.1 Examples of definitions of polypharmacy used in healthcare research**

	<b>Definition</b>	<b>Reference</b>
Numerical	2 or more medications to treat the same condition	Veehof <i>et al.</i> 2000, Faries <i>et al.</i> 2005
	2 to 9 regular medications	Zia <i>et al.</i> 2015
	3 to 6 regular medications	Frazier 2005
	4 or more regular medications	Trumic <i>et al.</i> 2012, McMahon <i>et al.</i> 2014, Garcia <i>et al.</i> 2015, Cadogan <i>et al.</i> 2018, Rankin <i>et al.</i> 2018a, Patton <i>et al.</i> 2021
	5 or more regular prescribed medications	Viktil <i>et al.</i> 2007, Slabaugh <i>et al.</i> 2010, Jensen <i>et al.</i> 2014, Sheehan <i>et al.</i> 2014, Prados-Torres <i>et al.</i> 2017, Fustinoni <i>et al.</i> 2015, Scott <i>et al.</i> 2015
	10 or more medications	O'Dwyer <i>et al.</i> 2013, Onder <i>et al.</i> 2013, Greiver <i>et al.</i> 2019
	Number of drug classes	Barnett <i>et al.</i> 2011
Descriptive	Potentially inappropriate medications	Bushardt <i>et al.</i> 2008
	Medications which are not clinically indicated	Fulton <i>et al.</i> 2005
	Co-prescribing multiple medications	Maher <i>et al.</i> 2014, Filkova <i>et al.</i> 2017
	Medication prescribed to treat side effects of other medication	Rambhade <i>et al.</i> 2012

For the purpose of this PhD, polypharmacy is defined as the ‘concomitant ingestion of four or more medicines’, the same definition as is used in a recent Cochrane review which investigated the effectiveness of interventions to improve appropriate polypharmacy (Rankin *et al.* 2018a). This was also the definition adopted by Cadogan *et al.* during the feasibility study (2018) of the PolyPrime project, of which the cRCT is presented in this thesis (section 1.8). This definition excludes over the counter medicines, supplements and alternative medicines (such as herbal or oriental medicines).

### **1.3.2 Appropriate polypharmacy**

The general understanding of ‘polypharmacy’ has undergone a recent paradigm shift. Historically, ‘polypharmacy’ was viewed negatively, as it was widely acknowledged that the more medicines a patient was prescribed, the more likely they were to suffer adverse effects related to the medicines prescribed (Guthrie *et al.* 2015, O'Donovan *et al.* 2019). These effects may present as increased frailty, reduced adherence to medicines and reduced quality of life, increased risk of hospitalization and of falls (Dhalwani *et al.* 2017, Khezrian *et al.* 2020). One study reported that falls were common in adults aged 60 years and over who are prescribed



polypharmacy. Adults aged 60 years and over prescribed 10 or more medicines had a 50% higher chance of experiencing a fall (Dhalwani *et al.* 2017).

Given the increase in multimorbidity and the fact that clinical guidelines advocate for the prescribing of more than one medication for the treatment and management of long-term conditions (NICE 2016), the prescribing of multiple medications is common and may be appropriate (Cadogan *et al.* 2016, Steinman 2016). The use of the term 'appropriate polypharmacy' is increasingly being adopted over 'polypharmacy' and focuses on the difference between many and too many medicines. The number of medications taken by an individual is not necessarily aligned with appropriateness as all the prescribed medications may be clinically necessary, and so are appropriate for that individual. Appropriate polypharmacy can be defined as 'the optimization of medication for patients with complex and/or multiple conditions where medicine usage agrees with best evidence' (Cadogan *et al.* 2015). As such, medications should be evaluated in relation to their indication and potential for harm towards the individual. In contrast, inappropriate prescribing occurs when medications are prescribed without clear indication, or when any harm caused by the medications outweighs the benefit of the medications (Elbeddini *et al.* 2021).

### **1.3.3 Frequency of polypharmacy**

Polypharmacy is increasing globally because people are living longer, but not necessarily in better health (Jivraj *et al.* 2020). Polypharmacy is often most challenging in older people as physiological changes associated with aging will impact on how the body responds to and handles medications, i.e. pharmacodynamics and pharmacokinetics respectively (section 1.4.1). A recent cross-sectional analysis of data from the Survey of Health, Ageing and Retirement in Europe [SHARE (Midão *et al.* 2018)] database, found that polypharmacy was present in 26-40% of older people, across 17 European countries. The prevalence of polypharmacy increased as the age groups increased: 25.3% adults aged between 65 and 74 years were prescribed polypharmacy, this increased to 36.4% adults aged between 75 and 84 years and increased further to 46.5% in adults aged 85 years and over.

Polypharmacy is common in the RoI and is increasing in prevalence. Moriarty *et al.* (2015) noted that the prevalence of polypharmacy was 17.8% in 1997 and increased to 60.4% in 2012. Richardson *et al.* (2012) reported that one in five adults over the age of 50 regularly take five or more medications whilst a study conducted by Tatum *et al.* (2019) showed that polypharmacy was evident in 38.6% of adults aged 45-54, increased to 68.2% for adults aged 65-69 and increased again to 82.6% for adults aged 75 years and over.

Polypharmacy is influenced by a variety of health-related factors, such as, obesity, frailty, chronic pain, depression, coronary heart disease and diabetes (Ersoy and Engin 2018, Rieckert *et al.* 2018, Piccoliori *et al.* 2021). There is conflicting evidence that gender influences polypharmacy. Some studies report that females are more likely to be prescribed polypharmacy (Guthrie *et al.* 2015, Pereira *et al.* 2017, Ong *et al.* 2018), however, Piccoliori *et al.* (2021) showed that polypharmacy did not have a significant association with an individual's sex. There is limited research addressing non-health related factors that might be associated with polypharmacy, however, some studies addressing socio-economic factors have been published. A retrospective study found that patients with a lower educational background are more likely to be prescribed polypharmacy (Rawle *et al.* 2018), however, Ersoy and Engin (2018) dispute this as they found education (in relation to years in education and literacy level) had a nonsignificant relationship with the number of medicines consumed daily. Adults living in areas of high deprivation are over two times more likely to be prescribed 10 or more medicines, and those living in rural areas are more likely to have polypharmacy compared to adults in an urban area (Guthrie *et al.* 2015). These socio-economic factors that influence polypharmacy contribute to the challenges of prescribing and managing polypharmacy.

## **1.4 Prescribing to older people – the challenges of polypharmacy**

### **1.4.1 Ageing process**

In addition to health-related factors influencing polypharmacy, the ageing process can also impact on the prescribing of polypharmacy. Pharmacokinetics is the process of a drug's absorption, distribution, metabolism and elimination in the body (Loucks *et al.* 2015). The physiological decline associated with ageing affects the cells, tissues and organs of the body (Soto-Perez-de-Celis *et al.* 2018) which then impacts on the body's ability to absorb and metabolise medications. As such, the pharmacokinetics of a drug's effect in an older person may be different to that of a younger person. For example, liver volume can decrease by 70% in older people which then impacts on the body's ability to metabolise medicines (Drenth-van Maanen *et al.* 2020). Also, older people experience a reduction in renal function which then impacts on medication elimination from the body (Drenth-van Maanen *et al.* 2020). Pharmacodynamics [the effect of medicines on the body (Sera and McPherson 2012)], also changes with increasing age. Drenth-van Maanen *et al.* (2020) compiled a list of medication examples that might require dosing changes, compared to a younger population, in order to result in the required outcome for older people. These include decreasing the dose of antipsychotics and benzodiazepines, for

example. The physiological change in older people means that the evidence from clinical trials may not be relevant as clinical trials often include younger participants and therefore the risk-balance information regarding the treatment or medicine may not be applicable.

#### **1.4.2 Clinical trials**

Historically, older people have been excluded from participating in clinical trials, as they often experience multimorbidity and may be excluded from specific studies based on their clinical status. Additionally, researchers anticipate communication and transport issues with this cohort (Herrera *et al.* 2010). As such, there is little evidence of clinical treatments specifically for older people. This can be a concern for prescribers as the decision to prescribe a medication to an older person is made based on the extrapolation of evidence from clinical trials involving younger adults (Bartlam *et al.* 2012, Golomb *et al.* 2012). In 2011 the European Medicines Agency (EMA) published a geriatric medicine strategy which set out to address the needs of older people in the development and evaluation of medicines (EMA 2011). It states that medicines used by older people will be extensively researched and evaluated for use in this cohort. Ten years on from this strategy, existing evidence shows that medicines used by older people are still not appropriately researched, as older people are not represented in clinical trials at levels likely to reflect potential use of the medicine being tested. A review by Florisson *et al.* conducted in 2021 found that the average participant population of a clinical trial is 7-10 years younger than the population that will likely be using the medication. For example, pneumonia is a common condition in older people but older people with pneumonia are often under-represented in clinical trials of antibiotic treatment for pneumonia (Avni *et al.* 2015).

Reasons for exclusion of older people in clinical trials often include the presence of polypharmacy, multi-morbidity and/or cognitive impairment (du Vaure *et al.* 2016, Shepherd *et al.* 2019, Tan *et al.* 2022). As these conditions are prevalent in most older people, it automatically excludes them from participating in a clinical trial. In a review of trials from 11 Cochrane Reviews of four chronic diseases (chronic obstructive pulmonary disease, diabetes, heart failure and stroke), people with comorbidity were often excluded from participating in trials. For example, 42% of heart failure trials excluded people with coronary artery disease and 44% of diabetes trials excluded people with renal insufficiency (Boyd *et al.* 2012).

Upper age limits are also common within clinical trials (Shenoy and Harugeri 2015). A systematic review of 4,341 RCTs conducted by Thake and Lowry (2017) found that 1,258 RCTs (29%) had an upper age limit but did not provide an explanation for this. 161 (3.7%) RCTs were directed towards older people and included a lower age limit of 65 years. In contrast, 12 of these 161

RCTs included unexplained upper age limits. A qualitative study by Bartlam *et al.* (2012) of older people and their carers found that neither considered age nor cognitive impairment sufficient reasons for exclusion in a clinical trial. Interestingly, the same participants agreed that multimorbidity and polypharmacy were factors for inclusion in a clinical trial. A more recent study concluded similar results, that older people would like to be involved in clinical trials (van der Cammen and Crome 2018). As older people are not represented in clinical trials for medications that they are very likely to consume, it impacts on the development of clinical guidelines on prescribing these medications to older people.

### **1.4.3 Clinical guidelines**

Clinical guidelines “systematically bring together evidence regarding a single condition or group of related conditions and provide recommendations for patient management” (Hughes *et al.* 2013). Clinical guidelines help to standardise health practices, however, most guidelines only focus on a single condition and are therefore not always reflective of the population with the condition, as many older people experience multimorbidity. Few guidelines that focus specifically on older people have been published. Those that have are disease specific and include the management of chronic kidney disease (Farrington *et al.* 2017), acute stroke (Parr *et al.* 2017), diabetes (LeRoith *et al.* 2019) and pain (Schofield *et al.* 2022) for example.

Some health groups have published their own guidelines on prescribing to older people or prescribing to adults with polypharmacy. Whilst they were developed for use in a specific healthcare context such as Wales (All Wales Medicines Strategy Group 2014) or Scotland (Scottish Government Polypharmacy Model of Care Group 2018), the guidelines can still be applied outside those healthcare jurisdictions. Whilst NICE have published a guideline on clinical assessment and management of multimorbidity, they are specific to older people (NICE 2016). To mitigate the challenges arising from the lack of guidelines for older people, researchers, clinical experts and professional groups have developed and published their own guidelines. These are not supported by organisations such as NICE but can be useful to healthcare professionals when providing healthcare for older people. Such guidelines include prescribing opioids (Guerriero 2017), managing hypertension (Parekh *et al.* 2017), and use of benzodiazepines (Conn *et al.* 2020).

In addition to the systematic review of guidelines and expert consensus on the management of patients with multimorbidity and polypharmacy by Muth *et al.* (2019), mentioned previously (section 1.2.2) another review (scoping) of prescribing guidelines for older people with

multimorbidity by Lun *et al.* (2021) identified 61 guidelines, which included tools and checklists to optimise prescribing.

Common themes arising across the guidelines included:

- Conduct comprehensive assessment before prescribing
- Identify patient's needs, goals and priorities,
- Use clinical prescribing tools
- Adopt shared decision-making
- Education and training on polypharmacy
- Broader health system related issues.

The above highlights the wide range of areas which healthcare professionals should be aware of when prescribing to older people. As some of these options mentioned by Lun *et al.* (2021) are not always available (such as shared decision-making in a single-handed general practice) following guidelines can be difficult, and may depend on the medical information available and patient preferences, which may result in inappropriate prescribing [such as over prescribing and under prescribing (Cadogan *et al.* 2021)].

#### **1.4.4 Prevalence of potentially inappropriate prescribing**

As a result of a lack of clinical guidelines for prescribing in older people, they can often be prescribed medications that are not appropriate for them and their conditions (inappropriate prescribing), or are not prescribed a medication that could be of benefit, i.e. a prescribing omission. Numerous studies have been conducted investigating the prevalence of potentially inappropriate prescribing and prescribing omissions in older people in the RoI. Cahir *et al.* (2010) reported that the prevalence of potentially inappropriate prescribing in older people aged 70 years or over was 36%. In contrast, Galvin *et al.* (2014) reported the prevalence of potentially inappropriate prescribing in adults 65 years and over to be 15%. Whilst both studies applied STOPP/START [described in section 1.6.2 (O'Mahony *et al.* 2015)] to determine the prevalence of potentially inappropriate prescribing, Galvin *et al.* (2014) applied a subset of the STOPP/START criteria, including 26 STOPP indicators and 10 START indicators, possibly accounting for the different in prevalence rates. The top three instances of potentially inappropriate prescribing identified by Galvin *et al.* (2014) are presented in Box 1.1, Box 1.2 shows the top three prescribing omissions.

**Box 1.1 Top three potentially inappropriate prescribed medications (Galvin *et al.* 2014)**

1. Non-Steroidal Anti-Inflammatory drug with moderate-severe hypertension
2. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event
3. Benzodiazepines in those prone to falls

**Box 1.2 Top three prescribing omissions (Galvin *et al.* 2014)**

1. Antihypertensive therapy where systolic blood pressure consistently >160mmHg
2. Warfarin in the presence of chronic atrial fibrillation
3. Statin therapy in diabetes mellitus if one or more co-existing major cardiovascular risk factors were present

Although not exclusively assessing potentially inappropriate prescribing in older people, Cooper *et al.* (2016) analysed data from 309,748 patients from the Health Services Executive Primary Care Reimbursement Service database using the PROMPT criteria, (Cooper *et al.* 2014) another explicit prescribing tool designed for use with middle-aged people and when healthcare professionals don't have access to clinical diagnoses. Potential inappropriate prescribing was identified in 42.9% of patients. This study found that strong opioids without co-prescription of an osmotic or stimulant laxative and proton pump inhibitors above maintenance dosage for greater than 8 weeks were the top 2 most common instances of potentially inappropriate prescribing according to PROMPT (Cooper *et al.* 2016). These results show that potentially inappropriate prescribing, and prescribing omissions, are common in the RoI.

## **1.5 Healthcare in the Republic of Ireland**

### **1.5.1 Republic of Ireland healthcare system**

The RoI has a unique healthcare system and is divided between public and private healthcare. Access to primary or secondary healthcare services are available via government funded options (i.e. public healthcare) or self-funded options (i.e. private healthcare). Various government healthcare schemes exist under which healthcare is provided for free, these schemes are described below (section 1.5.2). Primary care services (such as general practice, pharmacy, dentistry) have a contract with the Health Service Executive (HSE) to provide public services but may also provide private services. The RoI is the only country in Europe that does not offer

universal coverage of primary healthcare services (Connolly and Wren 2016; Mercille 2019) and 43% of the population hold private health insurance (Department of Health 2017). Public and private healthcare services are intertwined in that both public and private services can be delivered at the same location by the same healthcare professional (Turner 2018). This has led to resources provided by the HSE for use in public healthcare services often being utilised for patients paying privately (Henman 2020) and as such, public patients may have to wait longer for a specific service. The Health Service Capacity review conducted by the Department of Health noted that the current health system is not fit for purpose, highlighting the fragmentation of services, the hospital centric nature of care and the focus on acute care as opposed to preventive care (Department of Health 2018a). According to this report, the current system needs to change drastically cope with demand. For example to meet current international standards of hospital bed occupancy, 1260 additional beds need to be made available for hospitals throughout the country (Department of Health 2018a).

### **1.5.2 Healthcare schemes**

Support to access public healthcare is available. In 2019, 32.4% of the Irish population were eligible for free public services (Primary Care Reimbursement Service 2019). Two variations are in existence, medical card holders and non-medical card holders. Non-medical card holders are entitled to free public hospital services (but may be required to pay for in-patient and/or out-patient hospital charges), and subsidised prescribed medicines. Medical card holders are entitled to free GP services (including out-of-hours), prescribed medicines (charged €1.50 for each item dispensed to a maximum €15 per month; for people 70 years and over, it is €1 per item and a maximum €10 per month), public hospital services, dental services, maternity and infant care services and community and personal social services. Eligibility for a medical card is means tested and to qualify the individual must have a weekly income below a certain amount for their family size, for example, a couple (married/cohabiting) aged 66 years or over will qualify if they have a weekly income below €298.

There are numerous schemes to assist people with their healthcare, for example: long-term illness scheme, GP visit card, drugs payment scheme, health amendment act card and treatment benefit scheme, each is described below.

#### *Long-term illness scheme*

Those who qualify for the long-term illness scheme (i.e. those who are ordinarily resident in the ROI and have at least one of the conditions covered by the scheme) are entitled to receive the

medicines necessary for their long term illness free of charge. Illnesses covered on this scheme include (but are not limited to) spina bifida, multiple sclerosis, intellectual disability, epilepsy, cystic fibrosis (HSE 2018a).

#### *GP visit card*

Those who hold a GP visit card can visit a participating GP free of charge (not all general practices accept these or may accept a limited number of patients who hold this card), including out-of-hours. Blood tests required to diagnose or monitor a condition are provided within this scheme. However, hospital charges and prescribed medicines are not. All children six years and under, all adults 70 years and over are entitled to a GP visit card, others will need to be means tested to be deemed eligible (HSE 2018b). A married or cohabiting couple between 66-69 years old must have a weekly income limit of €492, adults younger than 66 years have a weekly limit of €441 (Citizens Information 2021).

#### *Drugs payment scheme*

Some medicines and medicine aids are included in a list published by the HSE which allows for patients to pay a maximum €80 per calendar month for their prescribed medications. Not all medicines obtained via prescription are included in this scheme (Citizens Information 2022).

#### *Health amendment act card*

All adults and children who contracted Hepatitis C from the administration of contaminated blood within the State are entitled to the Health amendment act card, allowing them access to certain services and treatments for free. These include routine dental examinations, extractions and dentures; and optician services to include routine examination and clinically prescribed lenses. All GP services are covered by the Health amendment act card and prescription medications are available free of charge (HSE 2020a).

#### *Treatment benefit scheme*

Qualification for this scheme depends on the class of social insurance an individual pays and how many social insurance contributions they have made. This scheme assists individuals pay for dental care, hair replacement products if they have hair loss from cancer or alopecia, hearing aids and optical care (McCarron 2022).

### **1.5.3 Primary care in the Republic of Ireland**

There are many definitions of primary care in the literature, most of which include the mention of diagnosis, care of common diseases, first contact advice for patients, health promotion and



health prevention. O’Dowd *et al.* (2017) comment that it is the ‘open door’ of healthcare whereby individuals can come as they choose. The WHO (2018) define primary care as “a whole society approach to health that aims at ensuring the highest possible level of health and well-being and their equitable distribution by focusing on people’s needs and as early as possible along the continuum from health promotion and disease prevention to treatment, rehabilitation and palliative care, and as close as feasible to people’s everyday environment”.

Community Health Organisations (CHO; see Table 1.2, Figure 1.1) are responsible for the delivery of primary care in their local communities. A range of services is provided through the CHO including (but not limited to) GP services, home help, addiction counselling and treatment, child health services and public health nursing.



**Figure 1.1 Map showing Community Health Organisations in the Republic of Ireland**

**Table 1.2: Community Health Organisations and the geographical areas serviced**

<b>Community Healthcare Organisation (CHO)</b>	<b>Geographical areas</b>
CHO 1	Donegal, Sligo, Leitrim, Cavan, Monaghan
CHO 2	Galway, Roscommon, Mayo
CHO 3	Clare, Limerick, North Tipperary
CHO 4	Kerry, North Cork, North Lee, South Lee, West Cork
CHO 5	South Tipperary, Carlow, Kilkenny, Waterford, Wexford
CHO 6	Wicklow, Dun Laoghaire, Dublin South East
CHO 7	Kildare, West Wicklow, Dublin West, Dublin South City, Dublin South West
CHO 8	Laois, Offaly, Longford, Westmeath, Louth, Meath
CHO 9	Dublin North

\*CHO = Community Health Organisation

### *General practice*

In the RoI, general practice is often the patients' first point of contact with the health service, the other being the community pharmacy (Hudson and Nolan 2015). GPs in the RoI are self-employed, and set their own fees for consultations which are paid for by patients. GPs sign government contracts to supply services to patients who are eligible for particular healthcare schemes, such as those mentioned above (Mercille 2019). There is currently no public register of GPs practicing in the RoI, and the number of active GPs is hard to establish. One report notes that there are currently 2932 active GPs in the RoI (Dowling *et al.* 2020), however Collins (2020, cited in Collins and Homeniuk 2021) states this number is 3496, with 25% of these GPs working on a part-time basis and it is estimated that there are approximately 25% GPs working in single-handed general practices (Collins and O'Riordan 2015).

As the population grows in the RoI, the demand for healthcare grows in tandem. It is estimated that GPs conduct approximately 21.4 million consultations per year in Ireland and this is expected to increase (Collins and Homeniuk 2021). Currently, there is an average of 0.69 GPs per 1,000 population: this figure is low given that 1.1 GPs per 1,000 population is required to meet the healthcare needs of the population (McNally 2022).

General practice is under increasing pressure due to policy changes extending free GP care, firstly to those under the age of six years and then expanding to those under the age of 12 (O'Regan 2020a), the changing population-level demography and projected changes in the GP workforce (Hutchinson 2015). One year after free GP care for children under 6 was introduced, there was a 9.4% increase in children attending general practice and an increase of 20.1% attending out-of-hours services with parents organising general practice visits for their children with minor symptoms and early stages of conditions (McGombe *et al.* 2019), not previously common before free care was introduced. The ageing population of GPs in the RoI is of concern. It is estimated that over a third of GPs are 55 years or older and thus will be retiring shortly (Comhairle na nDochtúirí Leighis Medical Council 2019). Most current GPs in training are not interested in working in a single-handed practice (O'Dowd *et al.* 2017) so it is likely that when the current single-handed GPs retire, those practices will close, potentially making it harder for individuals to access GP care, particularly in rural areas.

For GPs in the RoI, clinical consultations are their biggest workload, with the average consultation lasting just under 15 minutes (Crosbie *et al.* 2020, Pierse *et al.* 2019). It is likely that these findings may change if more people present at the general practice with more conditions present, as is likely to happen due to the ageing population and increasing multimorbidity. A

previous study by Salisbury *et al.* (2013) found that with each new additional issue, the consultation is extended by approximately 2 minutes.

#### *Pharmacy in the community*

Like general practices, community pharmacies operate as independent businesses. They are reimbursed by the government for the medicines dispensed and also paid a fee per item dispensed. Community pharmacies also provide advice, run awareness campaigns (for example in partnership with the Irish Heart Foundation), and some provide additional services such as blood pressure monitoring (87% of community pharmacies in 2016), blood glucose monitoring (38% in 2016) and smoking cessation [56% in 2016 (Henman 2020)]. Pharmacists are experts in medications and have the knowledge to reduce prescribing errors and to optimise patients' medication related outcomes (O'Dowd *et al.* 2017). As of January 2022, there are 1911 community pharmacies registered with the Pharmaceutical Society of Ireland [PSI] (PSI 2022a) and 4350 community pharmacists (PSI 2022b). However, the Irish Pharmacy Union has expressed concern as the RoI has a dearth of qualified pharmacists (Hoare 2022).

#### **1.5.4 Improving healthcare in the Republic of Ireland**

There have been numerous frameworks and strategies published in the past ten years aimed at improving healthcare in the RoI. These include Healthy Ireland (Department of Health 2013), eHealth Strategy for Ireland (HSE 2013) and the Framework for Improving Quality in our Health Service (HSE 2016); an overview of each of these is described in Box 1.3. The most important healthcare reform document, a ten-year plan on reforming the health service in the RoI, The Sláintecare Report (Houses of the Oireachtas 2017), was adopted by the Government in 2017. The proposals detailed in the report result in the formation of a universal single-tier health service with patients being treated based on need (Burke *et al.* 2018). The report provided numerous key recommendations including the expansion of health services, the reduction and removal of charges (such as reducing prescription charges and removing Emergency Department charges), and the expansion of healthcare services that are provided in primary care (see Box 1.4). Sláintecare called for the redesign of professional healthcare roles, to enable all healthcare professionals to work to the best of their ability. The implementation of Sláintecare has been slow. The report was published in 2017, however, as it was designed to be a political cross-party policy it was not officially government policy until 2018, with the publication of the Sláintecare Implementation Strategy (Department of Health 2018b). The following year, the Sláintecare Action Plan was published in 2019 which provided information on strategies and targets (Department of Health 2019). A new action plan was recently

published, setting strategies for 2021-2023 (Government of Ireland 2021). Thomas *et al.* (2021) report that Sláintecare has evolved during the years as the government implements its recommendations. For example, the phased expansion of capacity for services such as GP was acknowledged in the 2018 budget, which noted the development of a revised GP contract and expansion of community healthcare teams. The 2020 budget planned for the expansion of healthcare workforce and home-help support. These strategies were designed prior to the global pandemic: it is likely that the Coronavirus disease (COVID-19) has impacted and will continue to impact on the implementation of these strategies.

### **Box 1.3 Overview of healthcare improvement strategies in the Republic of Ireland**

#### **Healthy Ireland**

- Four goals:
  - (1) increase the proportion of people who are healthy at all stages of life
  - (2) reduce health inequalities
  - (3) protect the public from threats to health and wellbeing
  - (4) create an environment where every individual and sector of society can play their part in achieving a healthy Ireland
- Specific programmes on physical activity, obesity, smoking, alcohol, sexual health, skin cancer and vitamin D

#### **eHealth Strategy for Ireland**

- Provides an outline of eHealth and discusses how the individual, the healthcare system and the economy will benefit from eHealth as well as how it will be implemented into the Irish healthcare system

#### **Framework for Improving Quality in our Health Service**

- This document presents a strategic approach to improving quality throughout all levels of healthcare in the RoI including service delivery and management, whilst providing person centred care that is safe and effective.

#### **Box 1.4 Main components of Sláintecare**

- All Irish residents entitled to a broad package of health and social care
- Free access to GP, primary or hospital care and reduced charges for drugs
- Care provided at the lowest level of complexity and in an integrated way
- eHealth as the key tool for developing a universal health system and integrated care
- Focus on public health and health promotion
- Maximum waiting times introduced for Accident & Emergency, diagnostic tests, outpatient and inpatient appointments/procedures
- Private care phased out of public hospitals
- Community care access to diagnostics expanded
- Improved and earlier access to mental health services
- Healthcare workforce expanded, including addressing recruitment and retention issues
- Health Service Executive Board to be established
- Accountability and clinical governance to be legislated for
- Introduction of a National Health Fund

#### **1.5.5 Coronavirus COVID-19 in the Republic of Ireland**

COVID-19 is an infectious disease which commonly affects the respiratory system (Rahimi *et al.* 2020). The disease is easily spread via surface contact and via coughing, sneezing, talking or breathing. The first case of COVID-19 in the ROI was recorded on 29<sup>th</sup> February 2020 (Cazelles *et al.* 2021), and the WHO declared a global pandemic on 11<sup>th</sup> March 2020 (WHO 2020) when COVID-19 was present in 203 countries and over 720,000 cases were reported (Ohannessian *et al.* 2020). As COVID-19 is a new disease, research involving COVID-19 is still ongoing. It is known that older people are one of the groups at greatest risk of mortality as a result of COVID-19 (Bulut and Kato 2020, Onder *et al.* 2020), with severe cases of COVID-19 being strongly associated with polypharmacy (McQueenie *et al.* 2020, McKeigue *et al.* 2021), as well as the presence of multimorbidity (Huang *et al.* 2020).

In an attempt to combat the disease, numerous public health measures were advised including avoiding close contact, cough etiquette and hand hygiene, and the Irish government closed all non-essential health services (including cancer screening, outpatient clinics, elective inpatient procedures), implemented travel restrictions (Robinson *et al.* 2020) and advised older people and people considered vulnerable (such as those with lung illnesses, who had organ transplants and/or cancer or rare diseases) to 'cocoon' [i.e. to stay at home the majority of the time unless absolutely necessary to leave or advised to no longer cocoon (HSE 2020b)]. Any individual who tested positive for the disease had to self-isolate for 14 days, as did anyone who was considered

a close contact to an individual who had returned a positive test. This resulted in increased pressure on the healthcare system, both primary and secondary care, due to staff sickness, and those having to self-isolate. The supply and use of personal protection equipment, such as masks, aprons, and gloves for example, contributed to issues within healthcare and influenced particular decisions such as the prioritisation of high-risk patients (Verhoeven *et al.* 2020). Whilst healthcare services were under a lot of pressure, there was a decrease in healthcare use worldwide. A systematic review conducted by Moynihan *et al.* (2021) concluded that there was a decrease of 37% of healthcare services usage, on average. This is supported by other studies reporting similar findings (Zaninotto *et al.* 2020, Michalowsky *et al.* 2021); interestingly, those with a chronic condition were more likely to experience delays in their healthcare compared to those without a chronic condition (Zaninotto *et al.* 2020, Topriceanu *et al.* 2021). The ROI was experiencing a similar situation: in a national online survey conducted by National University of Ireland, Galway [NUIG (NUIG, 2020)], 32% of respondents reported postponing medical treatment due to the presence of COVID-19. Another study found that older people with polypharmacy and two or more chronic conditions were more likely to have their healthcare service delayed by the provider (Hennelly *et al.* 2021).

To continue to provide essential healthcare, the mode of service delivery was altered. For example, the use of telemedicine [provision of healthcare at a distance with the use of telecommunications and information technologies (Wootton *et al.* 2017)] increased, with countries across the globe removing regulatory barriers to telemedicine use (Kinoshita *et al.* 2020). General practice consultations are now commonly conducted via telephone, unless the GP invites the patient to arrive at the practice; telephone consultations increased by 106% in an 11-week period in a UK general practice, face-to-face consultations decreased by 65% (Joy *et al.* 2020) in the same period. It is likely that due to COVID-19, for the first time in general practice, remote consultations (either via telephone or video call) are conducted more frequently than face-to-face consultations. Some healthcare professionals found this mode of healthcare delivery made their job more difficult, because of difficulty in hearing patients, the loss of non-verbal communication (Verhoeven *et al.* 2020), and other factors of concern including standard of equipment and availability, broadband access, data security, inadequate training, willingness of patients to adapt to telemedicine (Bokolo 2021) and issues relating to conducting high quality assessments (Galvin *et al.* 2021). However, studies have found that patients were quick to accept the use of telemedicine (Grimes *et al.* 2020, Keesara *et al.* 2020). In relation to appropriate polypharmacy, the use of telemedicine has proved to be a barrier to deprescribing

(Elbeddini *et al.* 2020), however, it allowed healthcare professionals to access and provide healthcare to an at-risk population during a time of high concern for their health.

Healthmail was introduced in Ireland in 2014 as a secure platform to transfer patient information, however, it only became widely used in 2020 when prescriptions could be electronically transferred for the first time due to COVID-19 (Gleeson *et al.* 2022). A survey conducted by Gleeson and colleagues found that the most common workflow change in both general practice and the community pharmacy was the expansion of healthmail to facilitate the electronic transmission of prescriptions (Gleeson *et al.* 2022) and was also rated as the top new service to have the most positive effect on medication safety and management.

## **1.6 Medicine management**

As stated above in section 1.5.1, the healthcare system in the ROI is not conjoined which can make managing multiple medicines for older people challenging for healthcare professionals. However, there are several methods that can be utilised to help in the management of medicine in older people, the most common being the undertaking of a medication review. According to the Pharmaceutical Care Network of Europe, a medication review is defined as “a structured evaluation of a patient’s medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions” (Griese-Mammen *et al.* 2018). Medication reviews can be conducted by any healthcare professional with the relevant knowledge of medications, including public nurses, GPs, and pharmacists practicing in hospital or community pharmacy settings. There are a range of formats and tools that can be used to assist healthcare professionals in conducting a medication review including validated assessment tools.

### **1.6.1 Medication review**

Medication reviews can range from an opportunistic unstructured review to a more in-depth review involving discussions with patients, which have a more patient-centred approach. Clyne *et al.* (2008) present three types of medication review (see Table 1.3). Patients with different needs require different types of reviews, and their needs may vary over time.

**Table 1.3 Three types of medication reviews (according to Clyne *et al.* 2008)**

	<b>Type 1: Prescription review</b>	<b>Type 2: Concordance and compliance review</b>	<b>Type 3: Clinical medication review</b>
<b>Purpose of the review</b>	Address technical issues relating to the prescription	Address issues relating to the patient's medicine- taking behaviour	Address issues relating to the patient's use of medicines in the context of their clinical condition
<b>Requires patient to be present</b>	No	Usually	Yes
<b>Access to patient records</b>	Possibly	Possibly	Yes
<b>Includes all prescription medicines</b>	Possibly	Yes	Yes
<b>Includes prescriptions, complementary and OTC medicines</b>	No	Yes	Yes
<b>Review of medicines and/or conditions</b>	Medicines	Medicines use	Medicines and condition

OTC= over the counter

There have been various models of medication reviews published, suitable for both primary and secondary care, and can be used by any healthcare professional with the necessary knowledge and means. For example, the Scottish Government Polypharmacy Model of Care Group published 'The 7 steps medication review' (2018). This is a guide for healthcare professionals which provides a structure they can follow and is divided into six domains. A brief overview is shown in Table 1.4.



**Table 1.4 The six domains of ‘The 7 steps medication review’ (adapted from Scottish Government Polypharmacy Model of Care Group 2018)**

Domain	Steps	Process
Aims	1 What matters to the patient?	Review diagnoses and identify therapeutic objectives
Need	2 Identify essential drug therapy	Identify essential medicines
	3 Does the patient take unnecessary drug therapy?	Identify and review the need for medicines
Effectiveness	4 Are therapeutic objectives being achieved?	Identify the need for adding/intensifying drug therapy in order to achieve therapeutic objectives
Safety	5 Does the patient have ADR/side effects or is at risk of these? Does the patient know what to do if they are ill?	Identify patient ADR and safety risks
Cost-effectiveness	6 Is drug therapy cost-effective?	Identify unnecessarily costly drug therapy
Patient centeredness	7 Is the patient willing and able to take drug therapy as intended?	Does the patient understand the outcomes of the review? Ensure drug therapy changes are tailored to patient preferences Agree and communicate plan

ADR = adverse drug reaction

### 1.6.2 Validated assessment tools

Numerous assessment tools have been developed over the years and are often described as explicit (i.e., criterion-based) or implicit (i.e., judgement based). A systematic review conducted by Masnoon *et al.* (2018) concluded that there are 42 published tools to assess the appropriateness of prescribing, with only 14 of these 42 having been validated (i.e. used in an external study to prove the accuracy and usefulness of the tool). External validation of prescribing assessment tools involves at least one patient-related outcome (Masnoon *et al.* 2018). Some tools have been validated for use in the country and healthcare context in which they were developed, such as Norway - Norwegian General Practice Criteria [NORGEP (Rognstad *et al.* 2009)] or Germany - the PRISCUS list (Holt *et al.* 2010). NORGEP was developed in 2009 by Rognstad *et al.* and provides a validated list of 36 of the most relevant potentially inappropriate prescriptions in Norwegian older people aged 70 years or older (Rognstad *et al.* 2009). The PRISCUS list contains 83 potentially inappropriate medicines for older people and presents the main concerns, possible therapeutic alternatives and precautions to be taken when prescribing the medications for older people (Holt *et al.* 2010).

STOPP/START [Screening Tool of Older Persons Prescriptions/ Screening Tool to Alert doctors to Right Treatment (O'Mahony *et al.* 2015)] is an explicit prescribing tool focusing on potentially inappropriate prescriptions (STOPP) and potential prescribing omissions (START) in older adults. STOPP lists specific medicines, dosages, durations of therapy, duplication of drug classes, drug interactions as potentially inappropriate, whilst START notes medicines that should be prescribed given certain clinical situations/conditions (Kaufmann *et al.* 2014). STOPP/START was originally developed in 2008 and updated in 2014 and has been used in various intervention studies to improve prescribing appropriateness (Campins *et al.* 2017; Delgado-Silveira *et al.* 2018; Parker *et al.* 2019).

The EU(7)-PIM list referred to many published prescribing assessment tools including Beers' criteria (Fick *et al.* 2003), Canadian list (McLeod *et al.* 1997), French list (Laroche *et al.* 2007) and the PRISCUS list (Holt *et al.* 2010) during its development, and involved experts from several European countries (Estonia, Finland, France, Germany, Netherlands, Spain and Sweden). The resulting assessment tool includes 184 medications. The EU(7)-PIM list can be used with little clinical information available and as such can be used in situations where patients medical records are not available or are not up-to-date. Whilst this tool was designed for use in European countries, it is still not applicable in some countries in Central and Eastern Europe (Fialová *et al.* 2019).

### **1.6.3 Electronic support**

Recently, numerous interventions have developed their own electronic system to aid with prescribing, known as computerised clinical decision support system. Essentially, algorithms are developed that are automatically applied to patient data to produce suggested actions with the aim of improving or supporting decisions made by healthcare professionals (Gillaizeau *et al.* 2013). Electronic tools may have different inputs, for example Tamblyn *et al.* (2003) developed an algorithm to provide an alert to GPs if a patient's chart included a potential issue, the nature of the issue and possible consequences along with possible alternative treatment options. A more recent study, the cRCT OPTI-SCRIPT study (Clyne *et al.* 2013, Clyne *et al.* 2015) involved a web-based pharmaceutical treatment algorithm which guided the GP in decision making but did not incorporate the patient nor their views or goals. In comparison, the G-MEDSS© study [Goal-directed Medication review Electronic Decision Support System (O'Donnell *et al.* 2021) can be used by healthcare professionals in conjunction with their patients input, in order to modify pharmaceutical care to meet the patient's goals. Whilst electronic support with prescribing may be useful, it is not overly common in interventions aimed at improving appropriate prescribing.

An updated Cochrane review by Rankin *et al.* (2018a) identified just one intervention on improving appropriate polypharmacy in older people which included a form of electronic support (Tamblyn *et al.* 2003). This review is discussed in detail in section 1.6.4.

#### **1.6.4 Medicine management interventions**

Medicine management interventions, such as medication reviews, can be conducted in a variety of healthcare settings and include various healthcare professionals. Medicine management interventions for older people in primary care have been conducted by GPs (Jäger *et al.* 2017, Muth *et al.* 2018), nurses (Steinman *et al.* 2018) and pharmacists (van der Meer *et al.* 2018, Whitman *et al.* 2018) for example. Interventions do not always produce the results researchers would like: a cRCT by Schäfer *et al.* (2018b) on increasing GP-patient dialogue and discussing patient's goals did not lead to a reduction in medication. However, a similar intervention on encouraging patients to communicate their goals and medication concerns with their GP resulted in a reduction of high-risk prescribing (Wallis *et al.* 2018). In medicine management, it is common for similar interventions to result in varying conclusions. A recent Cochrane review conducted by Rankin *et al.* (2018a) could not determine if interventions on appropriate polypharmacy resulted in substantial clinical improvement.

The Cochrane review by Rankin *et al.* (2018a) analysed interventions to improve appropriate use of polypharmacy for older people with the aim of concluding which intervention(s) are effective. Inclusion criteria for the review included adults aged  $\geq 65$  years who are prescribed polypharmacy, a validated tool to assess prescribing appropriateness with types of studies involving RCTs, non-RCTs, controlled before-after studies and interrupted time series studies. The review included 32 studies however it was unclear if interventions to improve appropriate polypharmacy resulted in a clinically significant improvement (Rankin *et al.* 2018a). Authors stated that pharmaceutical care may slightly reduce the number of PPO, although this conclusion is only from two studies. The review was not able to determine if pharmaceutical care improves medication appropriateness, reduces the number of potentially inappropriate medications, and reduces the number of patients with one or more PPO (Rankin *et al.* 2018a). This review is an important publication in relation to this thesis as it provides a useful overview of the current evidence of what works and what does not work in interventions aiming to improve prescribing of multiple medicines in older people. Interestingly, it noted that methodology sections in the included interventions were weak with little information on development and design of the intervention. Given the vast range of guidance that now exists in developing interventions, this was an interesting finding.

## 1.7 Intervention design

Guidelines and frameworks are available to assist researchers in designing and developing healthcare interventions. A guideline is a synthesis of the best available evidence that can be used to support decision making (Gagliardi *et al.* 2011) whilst a framework refers to steps that should be followed during particular phases of intervention design (Mills *et al.* 2010). The type of intervention researchers are looking to develop, i.e. a complex intervention or a simple intervention, may influence the guidelines or frameworks they choose to follow. Complex interventions are defined as those which contain two or more interacting components, including the number of groups/ levels targeted, the number and variability of outcomes, number of interactions between components within the experimental and control groups, the number and difficulty of behaviours required by those delivering or receiving the intervention and the degree of flexibility of the intervention (Craig *et al.* 2008). However, Hawe *et al.* (2004) also state that complex interventions have different forms in different contexts yet still conform to specific theory driven processes. Throughout this thesis, theory is defined as a 'set of concepts, definitions and propositions that explain or predict... events or situations by illustrating the relationships between variables' (Glanz and Rimer 2005). A simple intervention can be described as one with a straightforward linear pathway which links the intervention and outcome (Petticrew 2011). Petticrew (2011) argues that it would be useful to not label an intervention as 'simple' or 'complex', but to focus on the research question(s) and this will determine if an intervention should be termed as 'complex' or simple. There are numerous guidelines and frameworks in the literature. This section presents an overview of Intervention Mapping (Fernandez *et al.* 2019), and the United Kingdom Medical Research Council's (MRC) framework for the development of complex interventions (Craig *et al.* 2008). A more detailed description of the MRC guidance is provided, as this was used in the development of the PolyPrime study presented in this thesis.

### 1.7.1 Intervention mapping

Intervention mapping is a systematic approach to planning and designing behaviour change interventions which provides a step-by-step decision-making guide for intervention development, implementation and evaluation (Fernandez *et al.* 2019). There are six steps in the process of intervention mapping, with each step involving specific tasks for the research group to conduct (Figure 1.2). It brings together three perspectives: i) social ecological approach, ii) inclusion of all stakeholders and iii) use of theory and evidence. The social ecological approach emphasizes not only the individual's behaviour but also the relationship between the individual,

the social, physical and policy environment (Mehtälä *et al.* 2014), allowing it to be used in various healthcare settings and conditions. Studies that have previously employed intervention mapping in their development include preventing musculoskeletal injuries (Gouttebarga *et al.* 2017) or pain (Dalager *et al.* 2019), developing an advice tool to aid return to work after knee replacement (Coole *et al.* 2020), providing a pharmaceutical discharge letter to improve communication between community and hospital pharmacists (Cornelissen *et al.* 2021) and adherence to treatment in breast cancer survivors (Moon *et al.* 2021).

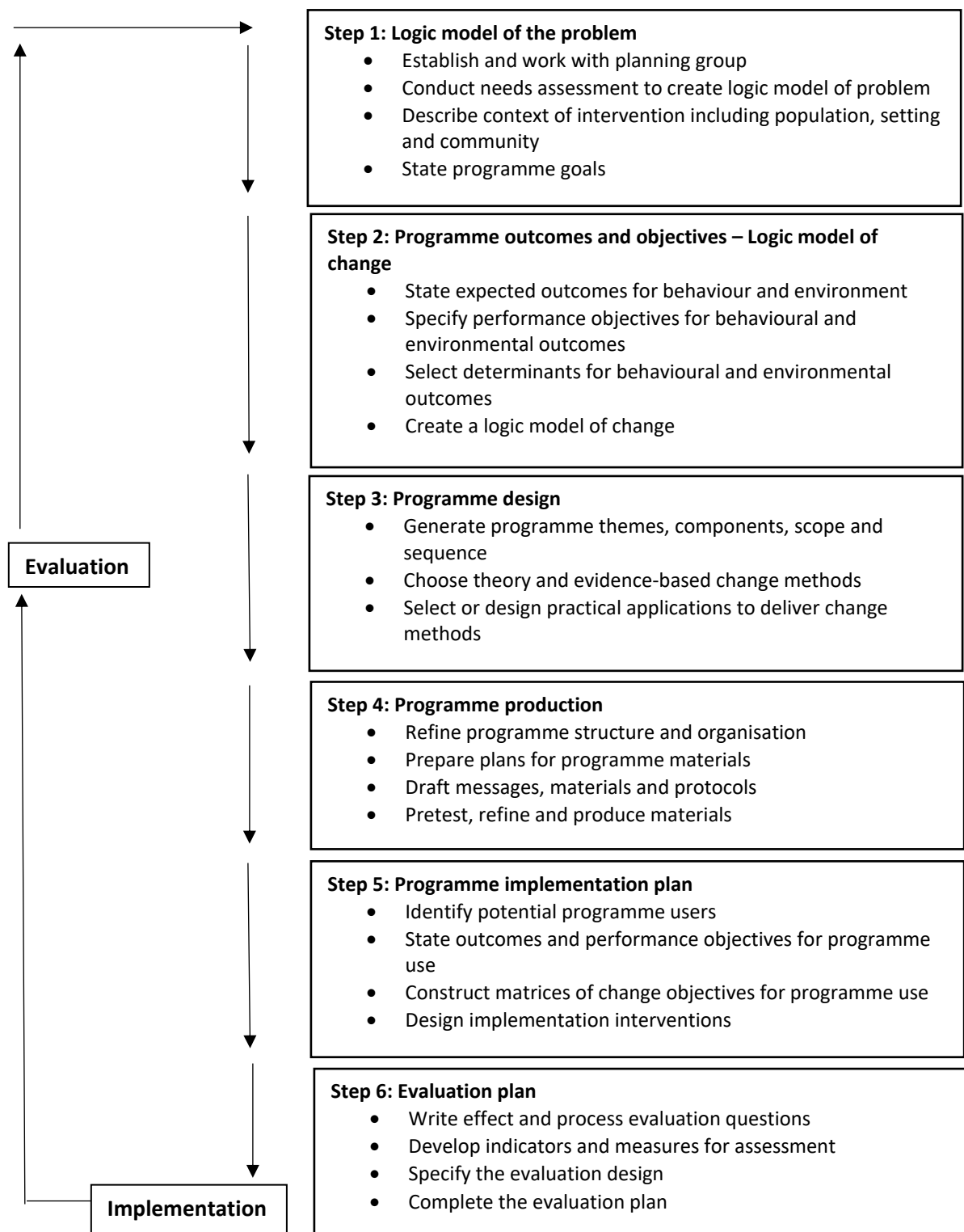


Figure 1.2 Six steps involved in intervention mapping (adapted from Fernandez *et al.* 2019)

### **1.7.2 Medical Research Council framework for the development of complex interventions**

The United Kingdom Medical Research Council (MRC) has developed a framework for the development of complex interventions, the first of which was published in 2000 (Campbell *et al.* 2000) with further updates being published in 2008 (Craig *et al.* 2008), 2015 (Moore *et al.* 2015), 2019 (O’Cathain *et al.* 2019a) and again in 2021 (Skivington *et al.* 2021). The 2008 MRC guidance document (Craig *et al.* 2008) will be discussed in detail here as this was the guidance referred to when developing the intervention presented in this thesis, the PolyPrime study. The most recent guidance by Skivington *et al.* (2021) will also be mentioned in relation to how the guidance has progressed since 2008.

The 2008 MRC guidance (Craig *et al.* 2008) advises four phases in intervention design: i) development, ii) feasibility/piloting, iii) evaluation and iv) implementation, as shown in Figure 1.3. The development phase includes all the research that occurs from the initial research question to the formal feasibility/piloting phase. The guidelines published in 2021 have not differed hugely, however, there are two important additions to note. Skivington *et al.* (2021) have identified a set of ‘core elements’ which should be considered within each of the four development phases and throughout the research project. Figure 1.4 shows these core elements in relation to the key phases of the development and evaluation process of Skivington *et al.*’s guidelines (2021). The other main addition is discussed under the development section below. Updating the guidelines involved identifying developments in methods termed a ‘gap analysis’, a workshop with experts in the field who analysed content established by the gap analysis, and an open consultation of draft framework from stakeholders. This process resulted in the move away from the 2008 guidelines which focus on effectiveness of interventions and move to acceptability, implementation, cost-effectiveness and transferability across contexts (Skivington *et al.* 2021). Limitations of the 2008 framework (Craig *et al.* 2008) as noted by Skivington *et al.* (2021) include that it focused on the effectiveness of the intervention, as opposed to the development process, it lacked information on economic evaluation and there was little to no acknowledgement of the complex systems in which interventions take place.

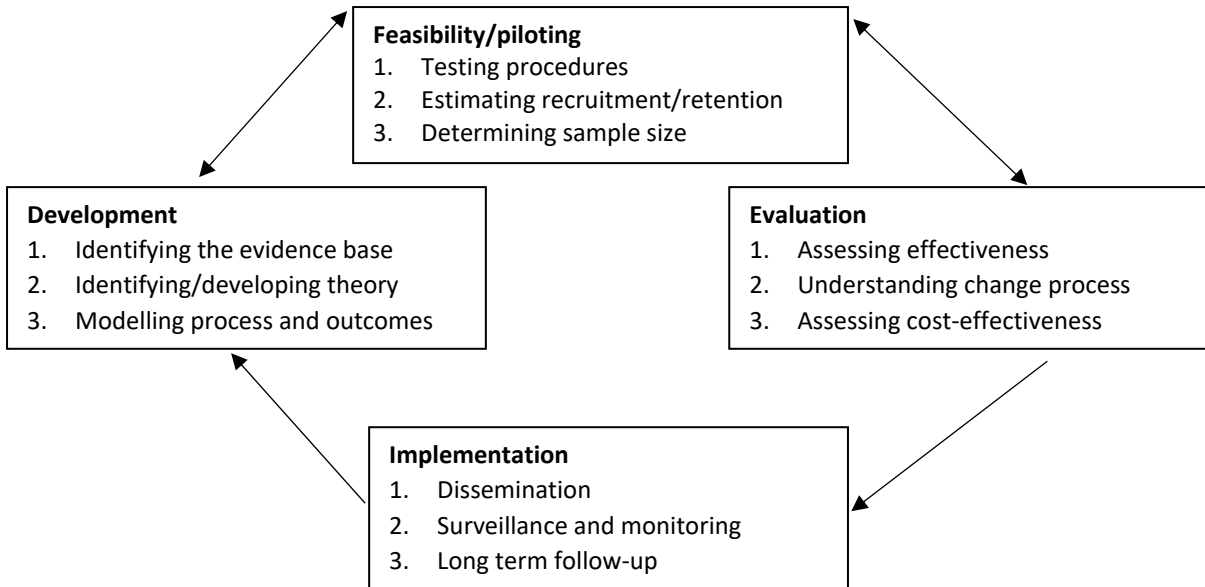


Figure 1.3 Four phases in intervention design (adapted from Craig *et al.* 2008)

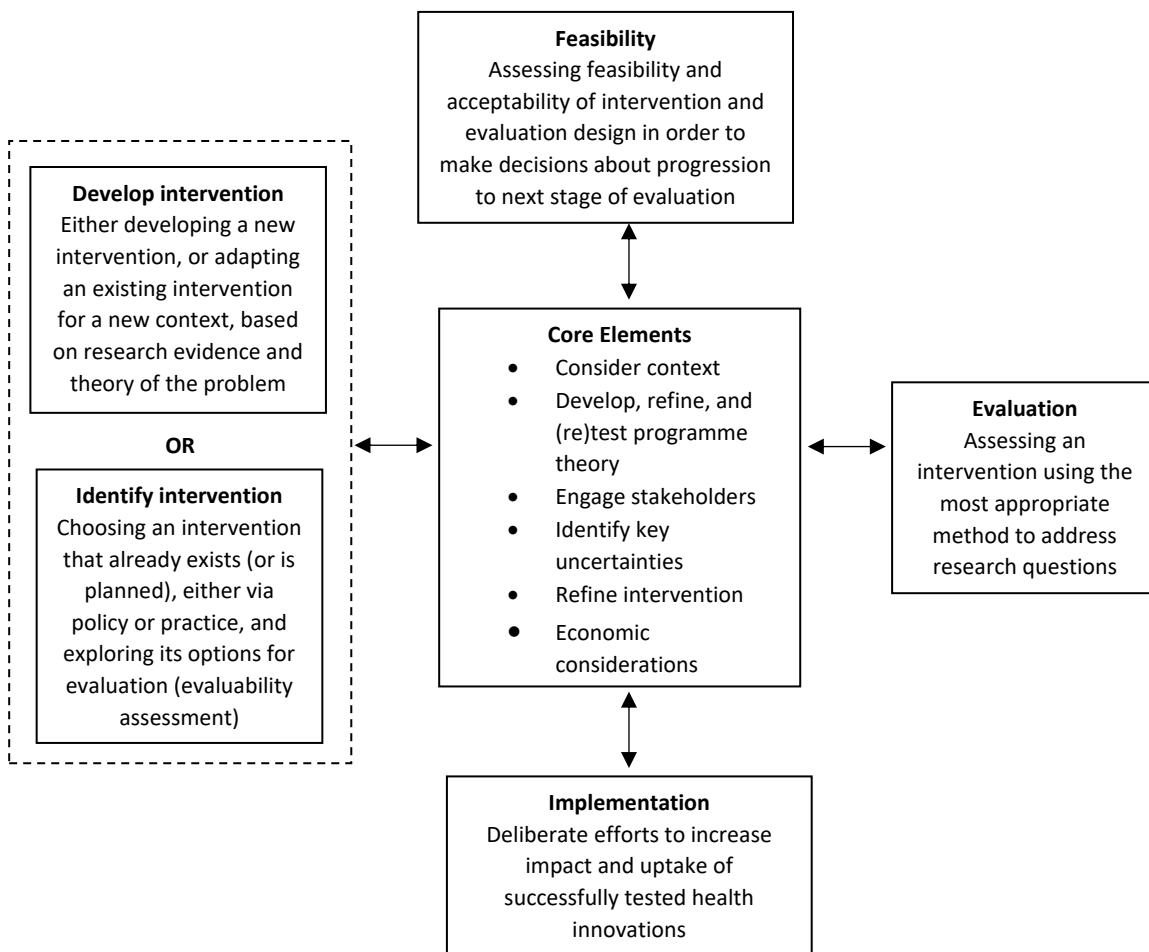


Figure 1.4 Key elements of the development and evaluation process (adapted from Skivington *et al.* 2021)



The MRC guidelines published in 2008 provided limited advice and information on how best to conduct the development phase. An important addition to the updated 2021 guidelines on developing and evaluating complex interventions (Skivington *et al.* 2021) was the inclusion of the identification of an existing intervention. This feeds into one of the core messages in the updated guidelines: that the context of the intervention is a hugely important concept, and that adapting an existing intervention for use in a new context is also an important method in intervention research. An important element in developing an intervention is the use of theory. Craig *et al.* (2008) suggests that those developing the intervention incorporate a relevant theory or theories into the design as this is more likely to lead to an intervention being effective. As there are many theories in existence and some with overlapping concepts, it would be useful to include relevant experts for example, behaviour change scientists, methodologists, or health psychologists in intervention design.

Extensive literature on guidance to intervention development has been published since the development of the PolyPrime study ranging from general guidance on healthcare intervention development (Crook *et al.* 2019, O’Cathain *et al.* 2019b, Duncan *et al.* 2020) to specific research areas (Fraser and Galinsky 2010). In 2019, O’Cathain published information (O’Cathain 2019a), in conjunction with the MRC, which extends on the guidance provided by Craig *et al.* [2008 (please note, the O’Cathain 2019a paper was not available during the development of the PolyPrime intervention)]. According to O’Cathain, aspects necessary for intervention development include a dynamic, iterative and creative process, with all researchers open to change and thinking forward to future evaluation and implementation of the intervention; numerous iterations of the interventions may be discussed and developed within this phase as well as receiving feedback from stakeholders not in the research team, possibly through both quantitative and qualitative methods (O’Cathain *et al.* 2019a). Key action points during intervention development are summarized in Table 1.5.

**Table 1.5 Key actions in intervention development (adapted from O’Cathain *et al.* 2019a)**

<b>Action</b>	<b>Procedures to consider</b>
Plan the development process	Identify the problem, is it a priority? What aspects of the problem are manageable? Assess developed intervention approaches for guidance Develop intervention protocol
Involve stakeholders	Develop a plan to integrate stakeholders into the development process and identify the best approach to working with each group of stakeholders
Establish a research team and a decision-making process	Include team members with relevant expertise Decide if decision making may only fall to certain team members
Review published evidence	At beginning and throughout process, evidence that supports and may not support the idea
Draw on existing theories	Identify relevant theories or frameworks that could inform the intervention process. Possible to include more than one existing theory or framework
Articulate the programme theory	Develop the programme theory, or draw on existing theories. Test and refine this throughout the development stage
Undertake primary data collection	Consider both quantitative and qualitative methods
Understand context	Understand the context in which the intervention will be implemented, including population, geographical setting, and socio-economic influences
Future implementation of the intervention in the real world	Understand facilitators and barriers to intervention implementation and sustainability of the intervention
Design and define the intervention	Discuss intervention with stakeholders May need to develop numerous iterations to address different factors within the intervention Ensure proposed mechanisms of action are supported
End the development phase	Write up development process and describe in detail the intervention to facilitate transferability

*Feasibility and piloting*

The second stage in designing complex interventions is the feasibility and piloting of the study. Craig *et al.* (2008) do not differentiate between a feasibility and a pilot study, instead combining the two different types of studies together in their guidelines. They state that the “feasibility and piloting stage includes testing procedures for their acceptability, estimating the likely rates of recruitment and retention of subjects, and the calculation of appropriate sample sizes” (Craig *et al.* 2008:10). However, they do not provide specific definitions of a feasibility or a pilot study. Some methodologists have worked extensively to redefine feasibility and pilot as two separate studies, and that they should be seen as two separate stages in the development of complex interventions. The UK National Institute for Health Research (NIHR) has developed a definition for both terms; a feasibility study will ask if the study can be done, should the research team

proceed with it, and if yes, how will they proceed (NIHR no date). A pilot study will ask, and should answer, the same questions, however it will also follow a specific design feature, and is conducted on a smaller scale than a RCT (NIHR 2021). This conflicts with the MRC Guidelines which note that a pilot study may not be a 'scale model' of the planned study. Eldridge *et al.* (2016a) note that pilot studies are a subset of feasibility studies and their systematic review, conducted as part of a Delphi study, and they concluded that it is not possible for feasibility and pilot studies to be given the same definition. In relation to this thesis, a feasibility study is defined as a piece of research conducted before a main study in order to answer the question 'Can this study be done?' and is used to estimate important parameters that are needed to design the main study (NIHR NETSCC 2022a). This definition was also used by Cadogan *et al.* (2018) in the development of the PolyPrime study. A pilot study is defined as "a smaller version of the main study used to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example, to ensure that recruitment, randomisation, treatment, and follow-up assessments all run smoothly" (NIHR NETSCC 2022b).

### *Evaluation*

Evaluation is the third stage in the MRC Guidelines. Numerous designs exist in relation to the vast amounts of research questions asked; the more a researcher is aware of the various evaluation methods, the more likely they are to include appropriate methodology in their intervention design. Outcome measures, both primary and secondary, are an important aspect of intervention design, and should be considered carefully. This can be achieved by researchers having a sound theoretical understanding of the intervention. Craig *et al.* (2008) note that one primary outcome and few secondary outcomes is the simplest format in relation to statistical analysis, however, researchers are to be aware that this may not be suitable for their intervention. Researchers should be mindful of the possibility of any unintended events occurring throughout the intervention as these could lead to possible adverse events, such as a patient dying, or impact particular aspects of the intervention, such as a global pandemic impacting recruitment rates in a healthcare intervention. Randomisation is a strong method of hindering selection bias however it may not be appropriate to all intervention designs (Glasziou *et al.* 2007; Craig *et al.* 2008). Secondly, a process evaluation is useful for the researchers to understand the processes around why the intervention worked well, or did not work well, and how the intervention could be improved. A process evaluation can be conducted before, alongside, or immediately after, an intervention and assesses if the intervention was implemented as planned, identifies the potential mechanism of impact as well as potential facilitators and barriers to implementing the intervention (Moore *et al.* 2015). This activity can

also identify possible environment/context factors that could have impacted on particular outcomes. Craig *et al.* (2008) recommends that an evaluation of the intervention is conducted to the same methodological standards as the actual intervention. Lastly, an economic evaluation should be conducted to assess the intervention's cost-effectiveness. An economic evaluation will estimate if the cost of the study is justified by the potential benefit (Briggs 2000). Moore *et al.* (2019) also note that it is important to bring theoretical reflection into the evaluation process and, as theory is recommended in intervention development, likewise intervention evaluation should also be driven by theory.

### *Implementation*

The fourth and final stage in Craig *et al.*'s (2008) intervention development guideline is implementation. This involves effective dissemination and the monitoring of long-term outcomes. Effective dissemination (i.e. getting results of the study into the public domain) is an important aspect of this, accompanied by ensuring the information and intervention results are accessible to all possible stakeholders. Beneficial techniques for intervention implementation in policy and practice include involving stakeholders from the beginning of the study to ensure relevance (Glasgow *et al.* 2003, Glasgow *et al.* 2006), being specific about the context in which it was conducted and discussing elements relevant to decision-making (Lavis *et al.* 2005), and stating recommendations in as much detail as possible (Michie and Johnston 2004). Monitoring long-term outcomes is an important aspect of implementation as it can determine if the changes identified as a result of the intervention, persist over a longer period. Craig *et al.* (2008) state that plans for follow-up collection of appropriate data outcome should be included at the study design phase, such as recontacting study participants after a number of years.

An important recommendation in Craig *et al.*'s (2008) guidelines on developing and evaluating complex interventions is the use of theory. Theory is also advocated for in intervention development by Skivington *et al.* (2021). The guidelines published by Craig *et al.* (2008) mention the use of theory in relation to intervention development (as discussed above), however, Skivington *et al.* (2021) advocate for the use of theory throughout the four main phases of intervention development. According to Skivington *et al.* (2021), the use of theory in intervention development is critical and can help identify key aspects of an intervention's mechanisms; in the feasibility phase theory can recommend factors that could influence the acceptability or effectiveness of the intervention, such as setting and who delivers the intervention. Theory in the evaluation phase can shape questions and also lead to theory refinement and development. Finally, theory should be applied to implementation of the

intervention from the beginning. Theory is presented here as it is an important concept throughout this thesis.

#### **1.7.4 Use of theory in intervention development**

The use of theory (defined in section 1.7) in intervention development has become increasingly popular in recent years, especially due to guidelines, such as the MRC (Craig *et al.* 2008, Skivington *et al.* 2021), advocating for its use. Theory can be beneficial in overcoming research bias and assumptions. It assists researchers and healthcare professionals in understanding the mechanisms of change underlying the intervention's effects (Cadogan *et al.* 2016), as constructs stemming from the theory can be assessed pre- and post- intervention, measuring where possible change is occurring, as well as identifying applicable fundamental factors of behaviour (Bartholomew and Mullen 2011). A theoretical basis in intervention development helps researchers identify intervention techniques (Michie *et al.* 2008), to see what techniques work and in what contexts (Jamal *et al.* 2015) and also helps in the refinement of intervention techniques (Noar *et al.* 2007). Put simply, theory can guide the research question and selection of strategies and can contextualise the study results (Birken *et al.* 2017).

Many definitions of theory exist, with some definitions being more user friendly, and therefore likely more engaging with novice researchers using theory in intervention design. Varpio *et al.* (2020) describe theory as an 'abstract description of the relationships between concepts that help us to understand the world' whilst Collins and Stockton (2018) describe theory as a 'big idea that organizes many other ideas with high degree of explanatory power'. Definitions like these, using more simple and common words, are more user friendly, which is an important aspect considering theory in intervention design, especially in healthcare, has become more frequent in recent years. Over the years, authors have discussed various attributes of theories. Wacker (1998) notes that a 'good theory' will include four aspects: (i) that it will be explanatory – providing explanations around variables and effects, being testable, predictable and verifiable, (ii) that it will be plausible – providing meaningful explanations which are consistent with existing facts, (iii) that it will be explicit – summarizing, explaining and organizing facts, and finally (iv) that it will be parsimonious – using a few variables which are arranged simply to explain effects. In a more recent publication, Kivunja (2018) has gathered numerous characteristics of theory put forward by various authors, and to qualify as theory, Kivunja (2018) notes that theory must include the following features:

- It has to be logical and coherent
- It has clear definitions of terms or variables, and has boundary conditions

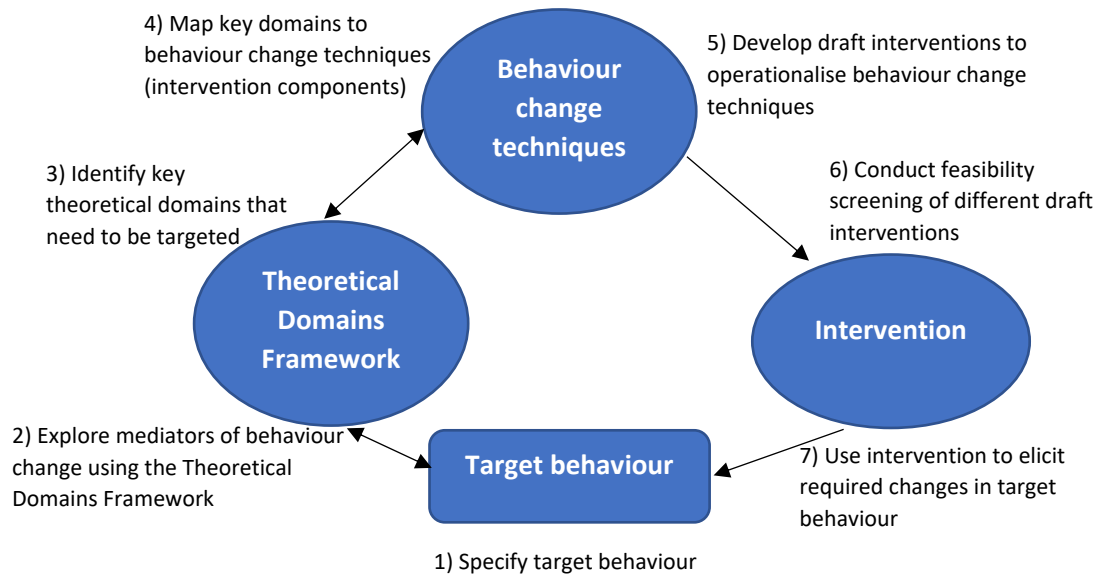
- It has a domain where it applies
- It has clearly described relationships among variables
- It describes, explains, and makes specific predictions
- It comprises concepts, themes and principles and constructs
- It must have been based on empirical data
- It must have made claims that are subject to testing, been tested and verified
- It must be clear and parsimonious
- Its assertions or predictions must be different and better than those in existing theories
- Its predictions must be general enough to be applicable to and in several contexts
- Its assertions or predictions are applicable, and if applied as predicted, will result in the predicted outcome
- The assertions and predictions are not set in concrete, but subject to revisions and improvement as social scientists use the theory to make sense of phenomena in their world
- Its concepts and principles explain what is going on and why
- Its concepts and principles are substantive enough to enable us to predict future events

It can be difficult to select the most relevant theory to the intervention being developed. Stewart and Klein (2016) note that in order to select an appropriate theory, researchers must have a knowledge of four particular factors: (i) the field of research, (ii) the research problem and its nature, (iii) available theories and their nature, (iv) how others have used the theory/theories. As theories are in abundance, researchers may not be aware of all the theories in existence. As such, the dynamics of a research team are important. A multidisciplinary team, including a health psychologist, will add more rigour to the design and development of an intervention and make it more likely that the most appropriate theory was used in the intervention development. There is no established database that holds information on all existing theories, so the onus is on the researcher to extensively search for theories and decide which is most suitable to their intervention. Currently, there is no published guidance on how to best select a theory for use in intervention development and so perhaps researchers often use the theories that they are comfortable with and have experience using (Birken *et al.* 2017). This is not surprising given that researchers often specialize in one particular area (for example, appropriate prescribing in older people or healthy eating in adolescents) and so the same theories will often be repeatedly utilized by researchers. An option for researchers to overcome choosing the most appropriate theory is to utilize a theoretical framework in intervention development.

Selecting a theoretical framework, defined as a 'logically developed and connected set of concepts and premises, developed from one or more theories' (Varpio *et al.* 2020) can be of benefit to novice users of theory as it combines multiple theories. Theoretical frameworks such as Theoretical Domains Framework [TDF (Cane *et al.* 2012)] and Systems Engineering Initiative for Patient Safety (SEIPS) 2.0 Model (Holden *et al.* 2013) are commonly used in healthcare intervention development (Campbell *et al.* 2018, Zisberg *et al.* 2018, Ogeil *et al.* 2020, Bele *et al.* 2021, Berman *et al.* 2021). Also of use to researchers are conceptual frameworks which emphasize three important factors: (i) what is currently known, often addressed by conducting a literature review, which leads to (ii) identifying gaps in the knowledge and understanding of what is being studied and (iii) summaries of methodological approaches. Conceptual frameworks, such as Promoting Action on Research Implementation in Health Services [PARIHS (Kitson *et al.* 1998, Rycroft-Malone *et al.* 2002, Rycroft-Malone *et al.* 2004) and the updated version known as i-PARIHS (Harvey and Kitson 2016, Kitson and Harvey 2016) are used extensively in healthcare implementation research (Balbale *et al.* 2015, Tian *et al.* 2017, Laycock *et al.* 2018, Meloncelli *et al.* 2020) to investigate areas which may be a barrier or facilitator to intervention implementation.

### **1.8 PolyPrime study development**

An intervention to improve appropriate polypharmacy in older people in primary care (PolyPrime) was developed using a systematic approach (see Figure 1.5), guided by theory and engagement with key stakeholders (Cadogan *et al.* 2015, Cadogan *et al.* 2016, Cadogan *et al.* 2018) in Northern Ireland (NI). GPs (n=15) and community pharmacists (n=15) were interviewed, using separate TDF based interview schedules, covering four main areas: i) views on the term 'polypharmacy', ii) assessment of a clinical scenario depicting an older patient receiving inappropriate polypharmacy (developed by GPs and pharmacists on the team), iii) perceptions of barriers and facilitators to ensure prescribing, and iv) views on potential intervention components and outcome measures (Cadogan *et al.* 2015).



**Figure 1.5 Systematic process of theory-based intervention development (adapted from Craig *et al.* 2008)**

The TDF is a collection of 33 theories of behaviour and behaviour change (Appendix 1.1) and was developed in order to make theory more accessible and usable for researchers, thus allowing for a single framework to inform intervention design and to assess implementation of the intervention (Cane *et al.* 2012). The use of the TDF in a research study enables researchers to address numerous key aspects in intervention design and implementation including theorising and testing pathways of change, and identifying appropriate process measures and problem analysis (Francis *et al.* 2012). There are two versions of the TDF in existence, version 1 contains 12 domains [TDFv1 (Michie *et al.* 2005)] and version 2 contains 14 domains [TDFv2 (Cane *et al.* 2012)], both of which are used in research. The version used often depends on the aim of the project (and therefore what particular domains are more relevant to the project as some domains are not present in both versions of the TDF – see Table 1.6) and the researchers’ familiarity with a particular version of the TDF. The TDF, a theoretical lens to view the affective, cognitive, environmental and social influences on behaviour (Atkins *et al.* 2017), has been used in various different healthcare interventions (French *et al.* 2012, Dyson *et al.* 2013, Tavender *et al.* 2015, Patton *et al.* 2021) as well as a tool to inform the design and analysis of qualitative studies (Duncan *et al.* 2012, Lawton *et al.* 2016, Volfson *et al.* 2020, Yamada *et al.* 2020). In relation to the PolyPrime study, TDFv1 was chosen over TDFv2 because members of the research team had experience in the use of TDFv1 in intervention development;



there was evidence of no difference in validity between the two versions (Huijg *et al.* 2014); and the domain ‘Nature of the behaviours’ was expected to be highly relevant to the study and this domain only appears in TDFv1 (Cadogan *et al.* 2015).

**Table 1.6 Differences between the Theoretical Domains Framework v1 and the Theoretical Domains Framework v2\***

Domain**	Construct***	Included in TDFv1	Included in TDFv2
Nature of the behaviours	Routine/automatic/habit Breaking habit Direct experience/past behaviour Representation of tasks Stages of change model	Yes	No
Optimism	Optimism Pessimism Unrealistic optimism identity	No	Yes
Reinforcement	Rewards (proximal/distal, valued/not valued, probable/improbable) Incentives Punishment Consequences Reinforcement Contingencies Sanctions	No	Yes
Intentions	Stability of intentions Stages of change model Transtheoretical model and stages of change	No	Yes

\*Please note, this table only highlights the major differences between TDFv1 and TDFv2. Some constructs from TDFv1 have been placed under a different domain in TDFv2

\*\*Domain = an area of interest; a sphere of thought, action or knowledge (Michie *et al.* 2005)

\*\*\*Construct = a concept specially devised to be part of a theory (Michie *et al.* 2005)

The aim of the qualitative interviews were to identify potential TDF domains that GPs and community pharmacists believed to be barriers or facilitators in the prescribing (GPs) or dispensing (community pharmacists) of appropriate polypharmacy in older people. The TDF domains that were considered important from the interviews were then mapped to Behaviour Change Techniques [BCTs (Michie *et al.* 2013)] from an established taxonomy and were included in the intervention as the ‘active ingredients’. BCTs are observable, replicable, and irreducible components of an intervention designed to alter or redirect processes that regulate behaviour, i.e., the ‘active ingredients’ of an intervention (Michie *et al.* 2011a, Michie *et al.* 2013). The

research team selected four BCTs for inclusion in the intervention to be delivered to GPs and/or community pharmacists: i) action planning, ii) prompts/ cues, iii) modelling or demonstrating of behaviour, and iv) salience of consequences (Cadogan *et al.* 2015), definitions of which are provided in Table 1.7 below. Three draft interventions were discussed amongst the research team (see Table 1.8), and a GP-targeted intervention was selected for further testing as it was deemed more practical than a pharmacist-led intervention (which would rely on coordination of care between GPs and pharmacists) (Cadogan *et al.* 2016).

**Table 1.7 Definitions of the four Behaviour Change Techniques included in the intervention (adapted from Michie *et al.* 2013)**

<b>Domain</b>	<b>Definition</b>
Action planning	Prompt detailed planning of performance of the behaviour (must include at least one of context, frequency, duration, and intensity). Context may be environmental (physical or social) or internal (physical, emotional, or cognitive).
Prompts/cues	Introduce or define environmental or social stimulus with the purpose of prompting or cueing the behaviour. The prompt or cue would normally occur at the time or place of performance.
Modelling or demonstrating of behaviour	Provide an observable sample of the performance of the behaviour, directly in person or indirectly e.g. via film, pictures, for the person to aspire to or imitate.
Salience of consequences	Use methods specifically designed to emphasise the consequences of performing the behaviour with the aim of making them more memorable.

**Table 1.8 Three draft interventions discussed by the PolyPrime research team (adapted from Cadogan *et al.* 2016)**

<b>Intervention</b>	<b>Target group/ target behaviour</b>	<b>Intervention description (BCT targeted)</b>
Patient targeted intervention	Patients 65 years or older receiving polypharmacy/ NA	<ul style="list-style-type: none"> <li>• Letter inviting patient to attend general practice for a review consultation (Prompts/cues)</li> <li>• Community pharmacists attach label to patients dispensed medication prompting patients to visit general practice for review consultation (Prompts/cues)</li> <li>• GPs plan to ensure patients prescribed appropriate polypharmacy (Action planning)</li> </ul>
General practice-based intervention	General practitioners/ Prescribing of appropriate polypharmacy	<ul style="list-style-type: none"> <li>• Short online video demonstrating how GPs can prescribe appropriate polypharmacy during a typical consultation with an older patient (Modelling or demonstrating of the behaviour)</li> <li>• Video last approximately the duration of an average GP consultation and include feedback from both the GP and simulated patient emphasising the positive outcomes of the consultation (Salience of consequences)</li> <li>• GPs make explicit plans at practice meetings of when and how they would ensure that target patients are prescribed appropriate polypharmacy (Action planning)</li> <li>• Prompted to carry out this plan by receptionist when target patients present at the practices (Prompts/cues)</li> </ul>
Community pharmacy-based intervention	Community pharmacists/ Dispensing of appropriate polypharmacy	<ul style="list-style-type: none"> <li>• Short online video similar to that described above for GPs and demonstrate how pharmacists can dispense appropriate polypharmacy during a typical encounter with an older patient; include feedback from both pharmacist and patient emphasising the positive outcomes (Modelling or demonstrating of the behaviour, Salience of consequences)</li> <li>• List of GP approved patients would be provided to the pharmacy which would authorise pharmacists to engage with target patients when they present at the pharmacy (Social support or encouragement)</li> <li>• Pharmacists make an explicit plan of when and how they would ensure that patients meeting the inclusion criteria are dispensed appropriate polypharmacy (Action planning)</li> <li>• Prompted to enact plan when patients present at pharmacy by support staff or a note on the patients dispensing record. Any recommendations would be communicated to the GPs (Prompts/cues)</li> </ul>

BCT = Behaviour change technique

The GP-led intervention involves four components linked to specific BCTs, as defined according to the BCT Taxonomy Version 1 (Michie *et al.* 2013): i) GPs watch a short online video (designed and scripted by the research team) (BCT: ‘Modelling or demonstrating of behaviour’ and ‘Salience of consequences’), ii) explicit plans made at weekly staff meetings to ensure that target patients prescribed appropriate polypharmacy (BCT: ‘Action planning’), iii) patients are invited to attend the practice for a scheduled medication review, and iv) reception staff prompt the GP that the patient has arrived at the practice for their medication review (BCT: ‘Prompts/cues’ (Cadogan *et al.* 2018).

### **1.8.1 Feasibility of PolyPrime**

A feasibility study is recommended prior to a RCT in the MRC guidance to developing complex interventions (Craig *et al.* 2008, Skivington *et al.* 2021). As previously mentioned, a feasibility study is concerned with whether the research can be conducted (NIHR 2012) and is often considered to be more adaptive and iterative than pilot studies (Bowen *et al.* 2009). Feasibility studies focus on the evaluation and refinement of particular study aspects including: recruitment, data collection, outcome measures, resources supplied, the evaluation of the acceptability and suitability of the intervention to stakeholders, and the research team's ability to manage the intervention (Orsmond and Cohn 2015). PolyPrime was tested in a feasibility study with two general practices in Northern Ireland. Four GPs were recruited from these practices (general practice 1: 3 GPs, general practice 2: 1 GP), and 10 patients (5 patients from each general practice). To be included in the study, patients had to be 65 years or over, receiving four or more medicines, a resident in the community and not cognitively impaired.

GPs involved in the feasibility study reported that the video would improve their effectiveness in implementing prescribing changes, make it easier for them to perform medication reviews, and increase the number of medication reviews conducted with older people in their GP practice. All four GPs reported making changes to the recruited patients’ medications. Patients involved in the feasibility study welcomed the opportunity to receive a medication review and most reported that their GP recommended changes during their scheduled review. Overall, the intervention was considered usable and acceptable by GPs, and patients were satisfied with their medication review (Cadogan *et al.* 2018). Detailed results of the study can be found in Cadogan *et al.* 2018. The next step in the PolyPrime was the cRCT conducted over two jurisdictions: NI (all six counties: Antrim, Armagh, Derry/Londonderry, Down, Fermanagh, Tyrone) and the six border counties in the RoI (Cavan, Donegal, Leitrim, Louth, Monaghan, Sligo). This defined area was chosen by project funders CHITIN (Cross-border Healthcare Intervention

Trials in Ireland Network) to conduct healthcare research as it shares common features with other border areas within Europe where developmental problems are exacerbated by the existence of borders (Bailie and Cody, no date) with the aim to deliver novel but unproven healthcare interventions to prevent and cure illness in the defined area.

### **1.9 Thesis overview**

This thesis presents a systematic review on theoretically derived interventions in appropriate polypharmacy in older people in primary care (Chapter 2). The three phases of the pilot cRCT are presented: qualitative interviews with GPs in the RoI to refine the intervention developed in NI (phase 1, Chapter 3), and a cRCT involving GP practices from the RoI including a process evaluation (phases 2 and 3, Chapter 4). Where data has been collected in both NI and the RoI jurisdictions, this thesis presents only data that was collected in the RoI. Also included in this thesis are qualitative interviews with community pharmacists on how to improve the management of appropriate polypharmacy in older people in community pharmacy (Chapter 5). The thesis ends with a discussion of the research previously presented (Chapter 6).

## **Chapter 2**

**Theoretically derived interventions to improve  
appropriate polypharmacy in primary care: a  
systematic review**

## 2.1 Introduction

This chapter presents a systematic review, which aimed to provide an overview of theoretically derived interventions developed to improve appropriate polypharmacy for older adults in primary care. As discussed in the previous chapter (Chapter 1), people are living longer but not necessarily in better health. As such, older adults may have multiple long-term health conditions (multimorbidity) which may require multiple medications, leading to the prescribing of polypharmacy. The definitions of polypharmacy and appropriate polypharmacy have been provided in the introduction, sections 1.3.1 and 1.3.2.

Rankin *et al.* (2018a) noted that included interventions (n=32) lacked detailed methodological development in a Cochrane review investigating the effectiveness of interventions to improve appropriate polypharmacy (Rankin *et al.* 2018a; (as discussed in detail in Chapter 1, section 1.6.4). As mentioned, review authors suggested referring to the United Kingdom MRC's framework for the development of complex interventions (Craig *et al.* 2008) which advocates for the use of theory at the development and evaluation stages of intervention design. Rankin *et al.* (2018a) did not establish the extent to which theory was used in the development of the interventions included in their Cochrane review.

As noted in Chapter 1 section 1.7.4, a theoretical basis in intervention development can help researchers to select intervention techniques (Michie *et al.* 2005), examine what intervention components work (Jamal *et al.* 2015) and can provide useful guidance in refining an intervention (Noar *et al.* 2007) as well as overcoming researcher bias. The same definition of theory was used for as this as defined in section 1.7., and theoretical framework was defined as a logically developed and connected set of concepts and premises developed from one or more theories (Varpio *et al.* 2020). Common theories used in healthcare interventions include the COM-B model (Capability, Opportunity, Motivation-Behaviour), Social Cognitive Theory and the Theory of Planned Behaviour. The COM-B model proposes three components which must be engaged to deliver and maintain behaviour change as the components interact with each other (Michie *et al.* 2011b). Social Cognitive Theory also notes the interactions of three components notably personal, environmental and behavioural factors and their importance in behaviour change (Bandura 2008). This is a social learning theory that proposes people will learn from their experiences but also by observing others conducting the behaviour. The Theory of Planned Behaviour (TPB; Ajzen 1991) is derived from the Theory of Reasoned Action (TRA; Fishbein *et al.* 1975) and is useful in understanding how people's behaviour changes. According to the TPB, an individual's behaviour is guided by three categories of beliefs: normative, control and

behavioural, and proposes that behaviour is not a voluntary action, and it therefore cannot always be controlled.

The extent to which theory is used in the development of interventions is often assessed using the Theory Coding Scheme [Michie and Prestwich (2010), TCS; Appendix 2.1], (Webb *et al.* 2010; Arnott *et al.* 2014; Prestwich *et al.* 2014; Farmer *et al.* 2016; Patton *et al.* 2017). It contains 19 items split into six categories and is described in more detail in in Section 2.3.5. Most older people's medications are managed in primary care, and therefore, as a setting, primary care is ideal to deliver interventions aimed at improving appropriate polypharmacy. However, to date, no review has explored the use of theory in the design of interventions aimed at improving appropriate polypharmacy in primary care.



## **2.2 Aim and objectives**

### *Aim*

The aim of this review was to establish the effectiveness of theoretically derived interventions to improve appropriate polypharmacy in primary care and to investigate the degree to which theory informed the intervention design.

### *Objectives*

The objectives of this review were to:

- Identify studies that explicitly referenced a theory in the development of interventions focusing on improving appropriate polypharmacy in primary care
- Examine the specific theory that informed the development of the intervention
- Explore how the intervention was delivered
- Determine how each study defined polypharmacy and which validated screening tool was used to assess appropriate polypharmacy
- Determine the effectiveness of theoretically derived interventions aimed at improving appropriate polypharmacy in primary care, with at least one health-related outcome (if relevant to the study design).

## **2.3 Research design and methodology**

### **2.3.1 Protocol**

The protocol was developed with reference to the Preferred Reporting Items for Systematic Review and Meta-analysis -Protocols (PRISMA-P) (Moher *et al.* 2015; Shamseer *et al.* 2015) and the Cochrane Effective Practice and Organisation of Care (EPOC) Review Group's Data Collection Checklist (EPOC 2015). The protocol was registered with PROSPERO, an international prospective register of systematic reviews [CRD42020157175]. The current systematic review follows methodologies used in two similar relevant systematic reviews: (i) a systematic review to establish the theory base of interventions to improve medication adherence in older adults (Patton *et al.* 2017) and (ii) Rankin *et al.*'s Cochrane review (Rankin *et al.* 2018a). The current review is reported in line with the PRISMA statement (Moher *et al.* 2009). A completed PRISMA checklist is provided in Appendix 2.2.

### **2.3.2 Eligibility criteria**

EPOC resources for review authors (EPOC 2015) were consulted when developing the eligibility criteria including the study designs that could be considered for inclusion and the outcomes that should be reported. All randomised controlled trials, non-randomised controlled trials, interrupted time series studies and controlled before-and-after studies involving theoretically derived interventions aimed at improving appropriate polypharmacy in primary care were eligible for inclusion in this systematic review. Feasibility studies were eligible for inclusion as it was anticipated that there would be a low number of theoretically derived RCTs focusing on appropriate polypharmacy. Study protocols, i.e., ongoing studies were also potentially eligible for inclusion if some data was available. Relevant protocols could be included once completed. Interventions had to be delivered in a primary care setting to be considered for inclusion. A theory or theoretical framework (defined above, section 2.1) had to be utilised in the development of the intervention to be considered for inclusion. If authors did not explicitly state the use of at least one theory or theoretical framework in the development of the intervention, the study was excluded. Authors had to state the use of at least one validated tool to assess prescribing appropriateness for inclusion in the systematic review. The assessment tool could be either explicit [i.e. criterion-based, for example, Assessing Care of Vulnerable Elders (ACOVE) (Wenger *et al.* 2001)] or implicit [i.e. knowledge based, for example, Cantrill Indicators of Appropriateness of long-term prescribing (Cantrill *et al.* 1998)].

The study population had to have a mean age of 65 years or over and be prescribed four or more medications (polypharmacy). Any study not written in the English language was excluded as reviewers did not have extensive knowledge of other languages, and funding was not available to support translation costs.

### **2.3.3 search strategy**

A search of seven electronic databases covering the medical and pharmaceutical peer-reviewed literature was undertaken (CINAHL, the Cochrane Library, Embase, MEDLINE, PsycINFO, SCOPUS and Web of Science). The trial registry, ClinicalTrials.gov and US National Institutes of Health were also searched. Studies published in the English language from inception of the database to the search date (original search conducted August 2019, updated in August 2020 with a further update in August 2021) were considered for inclusion. The reference lists of eligible papers, identified through the electronic search, were hand-searched.

The search strategy was developed in collaboration with a specialist subject librarian, Ms. Caitríona Honohan, and checked by another specialist librarian, Mr Andrew Jones. Search terms focused around three key areas: 'polypharmacy', 'aged' and 'primary healthcare'. All keywords were indexed to the suitable thesaurus, for example, Emtree (for Embase database) or Medical Subject Headings (MeSH) terms and modified accordingly to each database. The search strategies for each database are provided in Appendix 2.3.

### **2.3.4 Study records**

Completed searches were exported into EndNote®, where duplicates were removed and subsequently transferred into Covidence®, an online tool developed to streamline the systematic review process. References were screened and sorted into 'yes' (the study is eligible), 'maybe' (eligibility is unclear) or 'no' (the study is ineligible) categories within the Covidence® platform.

All titles and abstracts were screened by two reviewers, the PhD candidate (Ashleigh Gorman, AG) screened 100% and Audrey Rankin (AR) and Prof. Cristín Ryan (CR) screened titles and abstracts between them. Any disagreements over study inclusion were discussed and resolved between the two reviewers for that article, i.e. the PhD candidate and either AR or CR, and if agreement could not be reached, it was discussed with a third reviewer i.e. AR or CR. If information from a paper appeared missing, or the full article was not available, study authors were contacted to request the article. Full text papers of articles categorised as 'yes' or 'maybe' were reviewed by one reviewer (AG) and a random 10% sample of articles categorised for full

text review, were reviewed by a second reviewer (AR). Any disagreements or queries of inclusion were discussed and agreed with a third reviewer (CR).

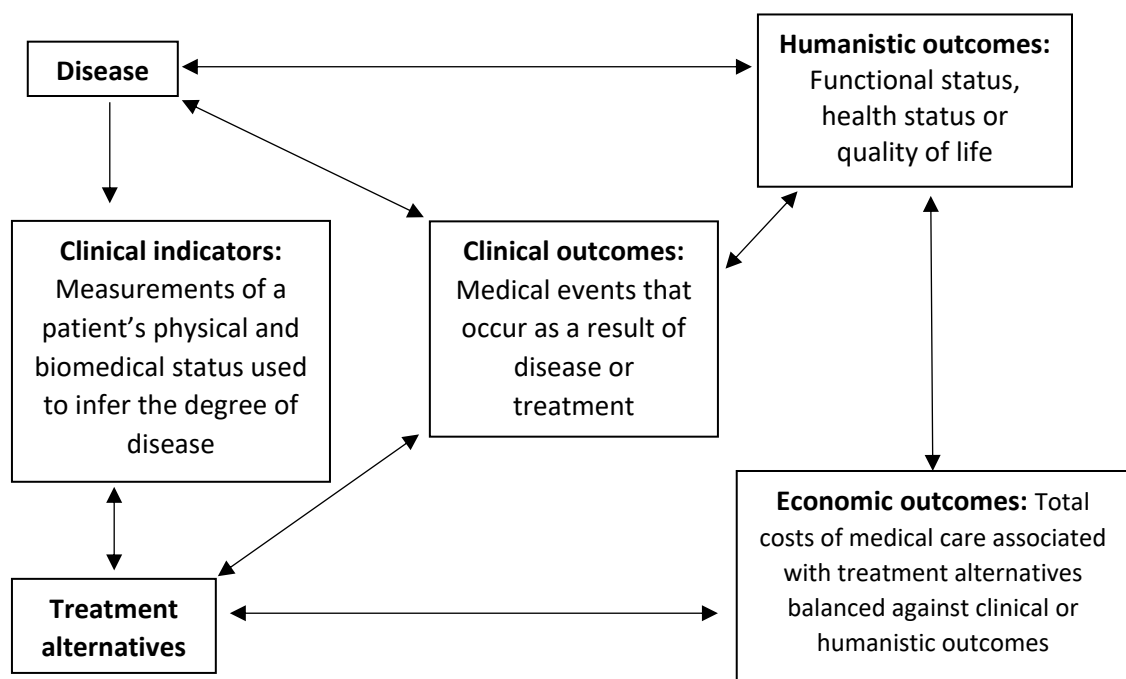
Data extraction forms were pre-defined and developed *a priori*, following an example from the Cochrane Collaboration (2020). The data extraction form was piloted independently by two reviewers (AG and AR), using two agreed studies and modifications were discussed and agreed. Data extracted included authors, country of study, study design, population characteristics, intervention type, intervention content, validated prescribing appropriateness tool used, theory used, length of follow-up, type of outcome(s) and the study conclusion. The data extraction form used in this systematic review is available in Appendix 2.4.

### **2.3.5 Study Outcomes**

The primary outcome for this review was the extent to which theory was used in the development of the intervention. Secondary outcomes of interest were the validated tool used to assess prescribing appropriateness and any economic, clinical or humanistic outcomes relevant to a prescribing intervention.

The explicit use of theory in the development of each included study was assessed using the TCS (Michie and Prestwich 2010; Appendix 2.1). The TCS contains 19 items divided into six categories: i) if a theory is mentioned, ii) the theoretical constructs targeted, iii) how the theory was used in the intervention, iv) the measurement of constructs, v) the testing of mediation effects and vi) if the intervention results were used to refine the theory. Categories 1 to 3 note the extent of theory used in the development of the intervention, and categories 4 to 6 note the testing and refinement of the theory used in the intervention. In order to evaluate the use of theory, each item is rated as yes/no/do not know, signifying if the item definition was met or not; the TCS also allows the user to note the page number/s from which information was gathered to rate each of the items. The TCS was independently applied by two reviewers (AG and AR) to the included studies. Findings were compared and an overall judgement was agreed.

Secondary outcomes of interest included the validated tool used to assess appropriate prescribing and any economic (i.e. cost-effectiveness), clinical (i.e. hospitalisation) and/or humanistic (i.e. quality of life) outcomes, guided by the ECHO (Economic, Clinical and Humanistic Outcomes) model (Kozma *et al.* 1993). The ECHO model (Figure 2.1) provides an extensive approach in decision making between economic, clinical and humanistic variables in healthcare, and as such, it provides researchers with a framework to consider all relevant outcomes. The model has been used in other systematic reviews including on drug packaging and medication adherence (Boeni *et al.* 2014), the impact of domiciliary medication reviews (McCormick *et al.* 2020) and the effectiveness of professional pharmacy services in community pharmacies (Varas-Doval *et al.* 2021).



**Figure 2.1 The Economic, Clinical and Humanistic Outcomes (ECHO) model (adapted from Barry and Hughes 2019)**

### 2.3.6 Risk of bias of included studies

Risk of bias assessments were conducted independently by two reviewers (AG and AR) for each included study using the Cochrane Risk of Bias 2.0 tool (RoB2) (Sterne *et al.* 2019) for RCTs and Risk of Bias in Non-randomized Studies – of Interventions [ROBINS-I (Sterne *et al.* 2016)] for non-RCTs. RoB2 is a result-based assessment tool containing five domains: (i) bias arising from the randomisation process, (ii) bias due to deviations from intended interventions, (iii) bias due to missing outcome data, (iv) bias in measurement of the outcome,

and (v) bias in selection of the reported result. Each domain contains numerous questions which require an answer from five possible options (i) yes, (ii) probably yes, (iii) no, (iv) probably no, or (v) no information. The answers were cumulated to provide each domain with a risk of bias judgement of low/high/some concerns. The judgements of each domain then provided an overall risk of bias of low/high/some concerns for the entire study.

ROBINS-I contains seven domains: (i) bias due to confounding, (ii) bias in selection of participants into the study, (iii) bias in classification of interventions, (iv) bias due to deviations from intended interventions, (v) bias due to missing data, (vi) bias in measurement of outcomes, and (vii) bias in selection of the reported result. Similar to RoB2, each domain in ROBINS-1 includes several questions with five possible responses of (i) yes, (ii) probably yes, (iii) probably no, (iv) no, or (v) no information. Each domain was then rated as having a low/moderate/serious/critical level of bias or no information. The judgement of each domain was then combined to provide an overall risk of bias judgement of low/moderate/serious/critical or no information. Studies were not excluded based on the risk of bias assessment.

### **2.3.7 Ethical standards**

Ethical standards for this systematic review were applied in numerous forms. Firstly, the protocol was developed in line with PRISMA-P (Moher *et al.* 2015, Shamseer *et al.* 2015) and was reported in PROSPERO, see section 2.3.1 above, ensuring the PhD student and members of the systematic review team were transparent with the work undertaken as part of the review. Transparency of study protocol and subsequent results is an important aspect of conducting a systematic review (Wager and Wiffen 2011). The study findings have been published in *Exploratory Research in Clinical and Social Pharmacy* (Gorman *et al.* 2022), which includes reference to the protocol on PROSPERO, and acknowledgement of all researchers involved in the review. Members of the systematic review team had been involved in theoretically derived interventions to improve appropriate polypharmacy; the protocol stated that, should a study they were attributed to be considered for inclusion and eligible, the study authors were not involved in the review, data extraction or analysis of the intervention in order to avoid bias.

## 2.4 Results

Electronic searches and hand searching of reference lists identified 15,402 records. Following removal of duplicates 12,416 titles and abstracts were screened. A total of 330 full text articles were retrieved and assessed for eligibility. Based on the inclusion criteria, four articles were identified as eligible [Figure 2.2 (Cadogan *et al.* 2018; Toivo *et al.* 2018; Toivo *et al.* 2019; Rankin *et al.* 2021a). Two of these articles represent the same RCT; Toivo *et al.* (2018) describes a study protocol for an RCT, while Toivo *et al.* (2019) reports the results of that RCT. As the two articles represent the same study, they are included as one study.

A protocol paper [Rankin *et al.* 2021a (the pilot study deriving from Cadogan *et al.*'s feasibility study)] was identified during the search, however, it was not included as the study was incomplete at the time of conducting this review and as such, no data had been published and it was not possible to extract data relevant for this review. Therefore, two studies are included in this systematic review, Cadogan *et al.* (2018) a feasibility study, and Toivo *et al.* (2019) a RCT. Due to the small number of studies included in this review, and their heterogeneity, a meta-analysis was not possible or appropriate. Therefore, a narrative summary of the two studies is provided. The results presented focus on the theory used in the study, the definition of polypharmacy and the validated tool used to assess prescribing.

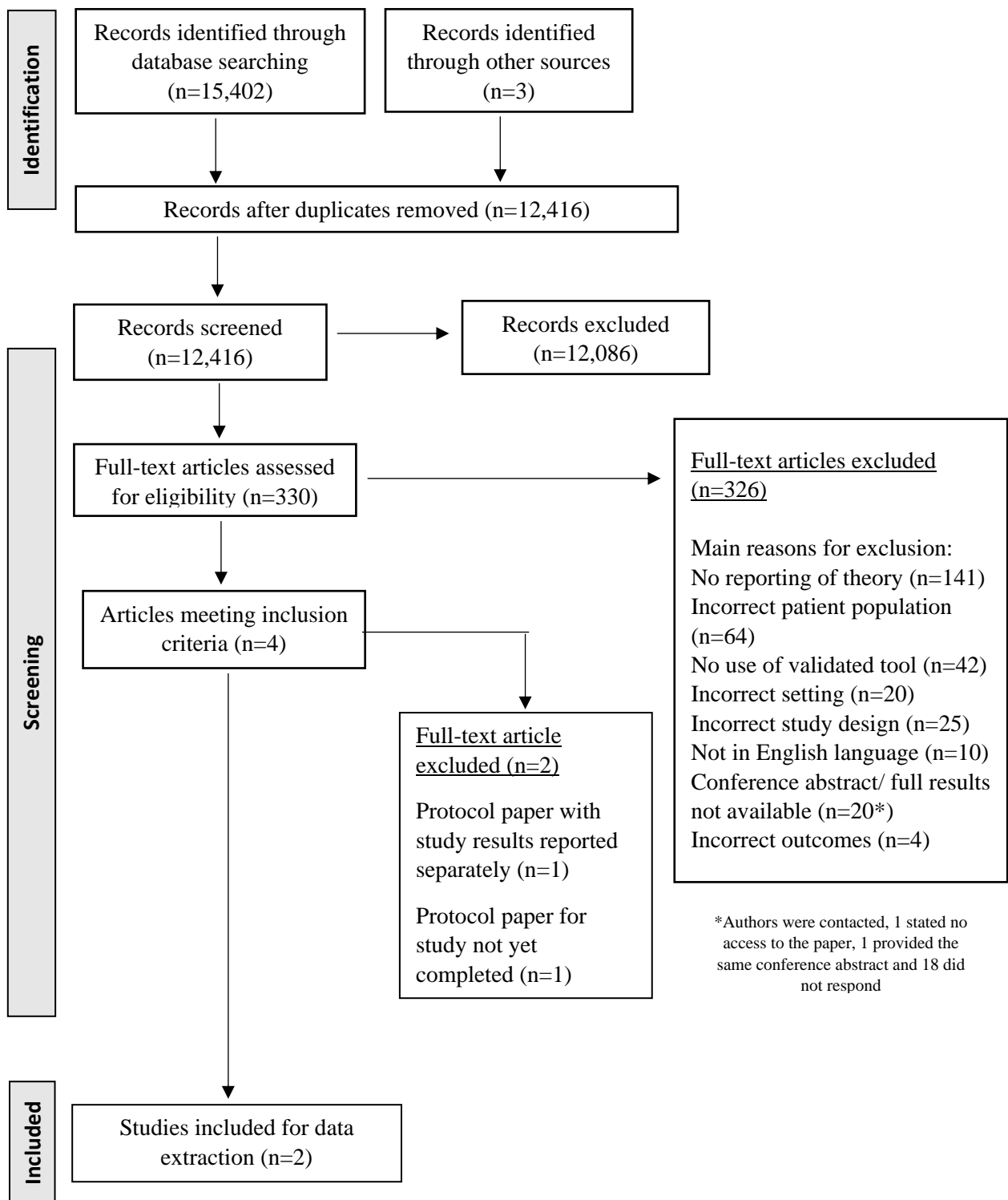


Figure 2.2 PRISMA flowchart of the systematic review process



### 2.4.1 Description of included studies

A total of 205 participants were involved in both studies, the study conducted by Cadogan *et al.* (2018) included 4 GPs and 10 patients; 191 patients were included in Toivo *et al.*'s 2019 study. In the feasibility study by Cadogan *et al.* (2018), the mean age of patients was 73 years, 60% were female and the mean number of medications per patient was 6.4 medications. In the RCT conducted by Toivo *et al.* (2019), the mean age of participants was 82 years, 70% were female and patients received a mean of 13.1 medications.

Cadogan *et al.* (2018) presented a feasibility study containing 10 participants (60% female) with an age range of 68-78 years and taking an average of 6.4 medications. The TDF (Michie *et al.* 2005) was employed as the theoretical framework in the development of this intervention. Interviews were conducted as part of the development phase of the intervention (Cadogan *et al.* 2015, Cadogan *et al.* 2016) with both GPs (n=15) and community pharmacists (n=15). Data from these interviews were mapped to Behaviour Change Techniques [BCTs (Michie *et al.* 2013)] which resulted in four BCTs being embedded within the intervention: 'Action planning', 'Prompts/cues', 'Modelling or demonstrating of behaviour' and 'Salience of consequences'. Only GPs were included in the delivery of the intervention (n=4) (Cadogan *et al.* 2018), which consisted of four components: (i) a short online video demonstrated how general practitioners (GPs) can prescribe appropriate polypharmacy during a routine consultation, (ii) practice staff made explicit plans to ensure the target patients would receive a medication review, (iii) patients attended the practice for a scheduled medication review (iv) reception staff prompted GPs to undertake the scheduled medication review. The educational tool (i.e. the online video) used in the intervention was positively received and patients (n=10) involved with the medication review component were satisfied with their consultation. All GPs involved (n=4), reported medication changes because of the medication review and were positive about the intervention.

Due to the nature of a feasibility study, Cadogan *et al.* (2018) focused on the usability and acceptability of the developed intervention to GPs and patients. The outcomes assessed in this study do not fit within the ECHO framework (Komza *et al.* 1993) as it was a feasibility study and its aim was primarily focused on the acceptability of the intervention. However, Cadogan *et al.* (2018) included the use of screening tools [the Medication Appropriateness Index (MAI: Hanlon *et al.* 1992) and STOPP/START to gauge the usability of these tools within an intervention to assess appropriate prescribing, i.e., if it was possible to apply these tools to clinical data

collected. Clinical data were extracted from patients' medical records at baseline (defined as date of scheduled consultation) and 1-month post consultation.

The RCT by Toivo *et al.* (2019) recruited 191 participants (90% female) with an age range of 65-96 years and taking an average of 13.1 medications. Toivo *et al.* (2019) used Reason's System-Based Risk Management Theory on preventing human errors (Reason 2000) to guide the development of the coordinated medication risk management (CoMM) intervention. The five main stages of the intervention involved different healthcare professionals (general practitioners, nurses and pharmacists) to resolve clinically significant medicine related problems: (i) risk assessment (via medicines reconciliation and prescription review) by nurses and pharmacists, (ii) a triage meeting between pharmacists and GP to decide on course of action e.g. type of medication review (iii) medication reviews [based on categorisation by Clyne *et al.* (2008), see Table 2.1] undertaken by pharmacists, with final decisions on any changes made by GPs, (iv) implementation of recommendations following the medication review and (v) follow-up stage involving patient monitoring. Feedback from patients and healthcare professionals was not reported. GPs' reluctance to change medications suggested by the community pharmacist and challenges when attempting to improve coordination between various healthcare professionals in relation to medication management were also noted. However, this intervention enabled healthcare professionals to dedicate time to the patients with medication concerns.

**Table 2.1 Medication review steps conducted in Toivo *et al.* (2019)**

Medication review steps	Process	Screening tool used	Healthcare professional involved
1	Prescription review: potential drug-related problems identified from lists of medications prescribed to patients. Separate report for each patient delivered to their GP by nurse.	Computerised tools integrated into dispensing system at community pharmacy.	Community pharmacist
2	Medication review: review of medication lists and medical records. Separate medication review reports delivered by nurse to relevant GP. Community pharmacist and GP discussed medication review report and recommendations.	Computerised tools integrated into dispensing system at community pharmacy. Drug Related Problem Risk Assessment Tool.	Community pharmacist GP
3	Comprehensive medication review: review of extensive medical records and medication history. Use of Beers' criteria to identify inappropriate medicines, identification of inappropriate duration. Home visit and interview with patient. Community pharmacist provided case report, including recommendations. Discussed with GP during face-to-face meeting.	Beers' criteria	Community pharmacist – specially trained for comprehensive medication reviews GP

The outcome measure focused on by Toivo *et al.* (2019) was the use of potentially inappropriate medicines for older adults [noted as a clinical outcome in reference to ECHO (Kozma *et al.* 1993)] according to Beers' criteria (American Geriatrics Society 2015) which was assessed at baseline and 12month follow-up. Beers' criteria is an explicit tool, that notes 36 drug classes to be avoided in certain incidences, 13 drug classes to be prescribed with caution and medications to avoid with 14 diseases. A summary of characteristics of both included studies is shown in Table 2.2.

**Table 2.2 Table of study characteristics**

Study (country)	Study type	Participant characteristics 1. No. of participants (% female) 2. Mean age ( $\pm$ SD) 3. Mean No. medications ( $\pm$ SD)	Intervention target and provider	Brief description of intervention	Theory used	Validated tool	Primary outcome(s)
Cadogan <i>et al.</i> 2018 (United Kingdom)	Feasibility study	1. 10 (60%) 2. 73.1 ( $\pm$ 4.04) 3. 6.4 ( $\pm$ 2.2)	Target: GP  Provider: Research team	Intervention components: (1) GPs watch educational video on prescribing appropriate polypharmacy (2) patients attend for scheduled medication review (3) explicit plans made by practice staff to target necessary patients (4) GPs prompted to carry out this plan by practice staff when the patient arrives at the practice.	TDF (Michie <i>et al.</i> 2005)	STOPP/START  MAI	Usability and acceptability of intervention to GPs and patients  Acceptability of medication review by patients
Toivo <i>et al.</i> 2019 (Finland)	RCT	1. 191 (90%) 2. 82.8 ( $\pm$ 7.1) 3. 13.1 ( $\pm$ 4.1)	Target: Nurse, Coordinating pharmacist, GP, Community pharmacist  Provider: Research team	Intervention components: (1) medication risk screening (2) triage meeting (3) collaborative medication reviews (4) implementation of required actions, changes to medications (5) follow-up.	Reason's System-Based Risk Management Theory on preventing human errors (Reason 2000)	Beers' criteria	Clinically significant medication-related risks requiring intervention using Beers' criteria

GP = General Practitioner MAI = Medication Appropriateness Index RCT = Randomised Controlled Trial SD = Standard deviation STOPP/START = Screening Tool of Older People's potentially inappropriate Prescriptions/Screening Tool to Alert doctors to Right Treatment TDF = Theoretical Domains Framework

#### 2.4.2 Theoretical underpinning of included studies

Both interventions included in this review were developed using different theoretical bases. Cadogan *et al.* (2018) used a theoretical framework, the TDF (Michie *et al.* 2005), and Toivo *et al.* (2019) used Reason's System-Based Risk Management Theory on preventing human errors (Reason 2000). Neither study opted to test and refine the underpinning theory (TCS categories 4 - 6), for example, to add or remove constructs within the chosen theory. Therefore, only categories 1 – 3 of the TCS (i.e. the extent of theory used in the intervention development) are discussed in this systematic review. The main findings from categories 1-3 are presented below and summarised in Table 2.3.

##### *Category 1: Is theory mentioned?*

Both studies mentioned theory. Cadogan *et al.* (2018) based their intervention on a framework, the TDF, while Toivo *et al.* based their intervention on a single theory, Reason's System-Based Risk Management Theory (Reason 2000). The TDF is a collection of 33 theories of behaviour and behaviour change, grouped into 14 domains (knowledge; skills; social/professional role and identity; beliefs about capabilities; optimism; beliefs about consequences; reinforcement; intentions; goals; memory, attention and decision processes; environmental context and resources; social influences; emotion and behavioural regulation). Cadogan *et al.* (2018) conducted qualitative interviews with GPs and community pharmacists, based on the TDF. These interviews aimed to identify possible theoretical domains/constructs that GPs and community pharmacists perceived as barriers or facilitators in the prescribing of appropriate polypharmacy for older people.

Reason's System-Based Risk Management Theory on preventing human error (Reason 2000) was applied to guide the construction of the CoMM procedure used by Toivo *et al.* (2019). The system approach states that humans are expected to make errors and it may not be possible to make humans error-free, however the conditions and the environment in which humans work can be altered by introducing barriers and safeguards to the work environment to enhance safety. Reason considers team work to be one type of safeguard. CoMM involved nurses, pharmacists and GPs working together to identify and resolve medication-related problems and provided additional geriatric pharmacotherapy and system-based medication risk management education to healthcare professionals involved. Toivo *et al.* did not link any specific constructs of Reason's System-Based Risk Management Theory as predictors of ensuring appropriate medication use.

*Category 2: Are relevant theoretical constructs targeted by the intervention?*

In the intervention described by Cadogan *et al.* (2018), the domains that arose during the interviews were then mapped to BCTs from an established taxonomy and embedded into the intervention as 'active ingredients' (Cadogan *et al.* 2016). A BCT is defined as a component of an intervention that is designed to alter the processes that regulate that behaviour (Carey *et al.* 2019). The BCTs embedded in the intervention include salience of consequences, modelling or demonstrating behaviour, action planning and prompts/cues. As a result, theoretical constructs are targeted by the intervention. In the study described by Toivo *et al.* (2019), Reason's system-Based Risk Management Theory was used to 'guide' the intervention development and was not used to select intervention techniques.

*Category 3: Is theory used to select intervention recipients or tailor interventions?*

In the study by Cadogan *et al.* (2016), theory was not used to select participants, nor was it used to tailor the intervention. In the study by Toivo *et al.* (2019), study participants were not recruited based on theory and the intervention was not tailored to participants based on theory.

**Table 2.3 Explanations for categories 1-3 of the Theory Coding Scheme (Michie and Prestwich 2010) for included studies**

<b>Category 1: Is theory mentioned?</b>					
<b>Study</b>	<b>Judgement<sup>a</sup></b>	<b>Item 1 – <i>Theory/model of behaviour mentioned</i></b>	<b>Item 2 – <i>Targeted construct mentioned as predictor of behaviour</i></b>		
Cadogan <i>et al.</i> (2018)	Yes	<b>Met</b> –TDF	<b>Met</b> – Targeted constructs based on TDF	<b>Met</b> – based on TDF	
Toivo <i>et al.</i> (2019)	Partially	<b>Met</b> – Reason’s System-Based Risk Management Theory	<b>Not met</b> – Authors did not explicitly state that constructs of Reason’s System-Based Risk Management Theory were predictors of prescribing appropriate polypharmacy	<b>Met</b> – based on Reason’s System-Based Risk Management Theory	
<b>Category 2: Are relevant theoretical constructs targeted by the intervention?</b>					
<b>Study</b>	<b>Judgement<sup>b</sup></b>	<b>Item 2 – <i>Targeted construct mentioned as predictor of behaviour</i></b>	<b>Item 5 – <i>Theory/predictors used to select/develop intervention techniques</i></b>	<b>Item 7, 8 or 9 – <i>Intervention technique(s) linked to theory relevant construct(s)/predictor(s)</i></b>	<b>Item 10 or 11 – <i>Theory relevant construct(s)/predictor(s) linked to intervention technique</i></b>
Cadogan <i>et al.</i> (2018)	Yes	<b>Met</b> – Targeted constructs based on TDF	<b>Met</b> – Theory was used to select intervention techniques. Domains from the TDF were mapped to Behaviour Change Techniques	<b>Met</b> – All intervention techniques are explicitly linked to theoretical constructs/predictors	<b>Met</b> – Targeted constructs were explicitly linked to at least one intervention technique
Toivo <i>et al.</i> (2019)	No	<b>Not met</b> – Authors did not explicitly state that constructs of Reason’s System-Based Risk Management Theory were	<b>Not met</b> – Theory was used to guide the intervention development, not select intervention techniques	<b>Not met</b> – Intervention techniques not explicitly linked to theoretical constructs	<b>Not met</b> – Theoretical constructs not linked to intervention techniques

		predictors of prescribing appropriate polypharmacy			
<b>Category 3: Is theory used to tailor the intervention to select the intervention recipients?</b>					
<b>Study</b>	<b>Judgement<sup>c</sup></b>	<b>Item 4 – Theory/predictors used to select recipients for the intervention</b>		<b>Item 6 – Theory/predictors used to tailor intervention techniques to recipients</b>	
Cadogan <i>et al.</i> (2018)	No	<b>Not met</b> – Participants selected on meeting pre-defined inclusion criteria		<b>Not met</b> – Intervention was not tailored to recipients	
Toivo <i>et al.</i> (2019)	No	<b>Not met</b> – Participants selected on meeting pre-defined inclusion criteria		<b>Not met</b> – Intervention was not tailored to recipients	

TDF = Theoretical Domains Framework. <sup>a</sup>Rating of ‘yes’ if study met TCS items 1, 2 and 3 in category 1. Rating of ‘partially’ if study met any of the TCS items in category 1. <sup>b</sup>Rating of ‘yes’ if study met TCS items 2 and 5 and 7, 8 or 9 and 10 or 11 in category 2. Rating of ‘no’ if study did not meet any TCS items in category 2. <sup>c</sup>Rating of ‘no’ if study did not meet any TCS items in category 3.



### **2.4.3 Use of validated prescribing tools to assess appropriate prescribing**

Pre-specified inclusion criteria noted that interventions had to include the use of a validated prescribing tool for inclusion in the systematic review to assess appropriateness of prescribing, with an objective to determine what validated screening tools are utilised. STOPP/START criteria (O'Mahony *et al.* 2015) and the MAI (Hanlon *et al.* 1992) were included by Cadogan *et al.* (2018). STOPP/START is described in Chapter 1, section 1.6.2. The MAI is an implicit tool, a framework to assess medication appropriateness. It contains 10 questions with a three-level response ('appropriate', 'marginally appropriate' or 'inappropriate') and a total MAI score is obtained by summing the scores for the individual drugs (Hanlon and Schmader 2013).

Toivo *et al.* (2019) applied Beers' criteria (American Geriatrics Society 2015), which has been utilised in numerous medication use interventions to assess the number of inappropriate medicines (Schmader *et al.* 2004, Spinewine *et al.* 2007, Pitkälä *et al.* 2014, Franchi *et al.* 2016).

### **2.4.4 The effectiveness of theoretically derived interventions aimed at improving appropriate polypharmacy in primary care**

As study design of the included studies was one feasibility study and one RCT, the effectiveness of theoretically derived interventions aimed at improving appropriate polypharmacy in primary care could not be determined.

It was not feasible for Cadogan *et al.* (2018) to apply the validated assessment tools (STOPP/START and MAI) to the prescribing data collected, notably due to insufficient level of detail of clinical diagnoses and treatment durations recorded.









Due to medication changes being only partially applied, Toivo *et al.* (2019) analysed data with the intention to treat (ITT) and per protocol analysis. Data from all participants, regardless of medication changes, was analysed for the ITT. Intervention arm participants with at least one implemented medication change and all control group participants' data was analysed for the per protocol analysis.

In the ITT analysis, no significant changes were found in any medication-related outcome between the intervention and control groups from baseline to 12-months follow-up. For example, the number of participants with potentially inappropriate medications, according to Beers' criteria, in the intervention group (N=65 participants) at baseline and 12 month's follow-up was 61 participants (93.9%) and 63 participants (96.9%) respectively; in the control group (N=64 participants) this was 58 participants (90.6%) at baseline and 57 participants (89.1%) at 12 months' follow-up.

Similarly, per protocol analysis did not identify any significant difference in medication-related outcomes between the intervention group per protocol and the control group over the 12-month follow-up period. For example, the number of potentially inappropriate medications according to Beers' criteria in the intervention group per protocol (N=27) was 26 (96.3%) at baseline and 25 (92.6%) at 12 months' follow-up. There was a notable decrease in the use of benzodiazepines in the intervention group per protocol (from 55.6 to 37.0%;  $p = 0.03$ ) and in the proportion of patients using  $\geq 3$  psychotropic medications (from 18.5 to 7.4%;  $p = 0.07$ ).

#### 2.4.5 Risk of bias of included studies

The RCT by Toivo *et al.* (2019) was judged to have a high risk of bias, largely due to the study being open-label in design, as seen in Figure 2.3. ROBINS-I could not be utilised to determine a risk of bias for Cadogan *et al.*'s feasibility study (2018) as it was a feasibility study. There is currently no available tool to assess risk of bias in a feasibility study.

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	Toivo <i>et al.</i>						
	Domains: D1: Bias arising from the randomization process D2: Bias due to deviations from intended intervention. D3: Bias due to missing outcome data. D4: Bias in measurement of the outcome. D5: Bias in selection of the reported result.						
							Judgement  High  Low

**Figure 2.3 Risk of bias summary for Toivo *et al.* (2019)**

## 2.5 Discussion

This is the first systematic review to identify interventions aimed at achieving appropriate polypharmacy for older adults in primary care whose development was informed by theory, and to examine the extent of theory usage in their intervention. Previous systematic reviews have focused specifically on the description of interventions, the healthcare professionals involved, and patient outcomes post-intervention (Kaur *et al.* 2009, Patterson *et al.* 2012, Cooper *et al.* 2015, Rankin *et al.* 2018a) but have not focused on the use of theory to develop the interventions, despite the MRC framework advocating for theory to be used in intervention development. Two studies were identified for inclusion (Cadogan *et al.* 2018 and Toivo *et al.* 2019), a feasibility study and RCT respectively, showing theoretically derived interventions aimed at improving appropriate polypharmacy in primary care are not common in this field. The effectiveness of these interventions could not be established due to the small number of studies included and their heterogeneity.

### 2.5.1 Theoretical basis

Overall, a very small number of studies used theory in the intervention development, with only three articles meeting the inclusion criteria from 12,416 titles and abstracts screened and 330 full-text articles reviewed. As noted above, two articles were discussed (Cadogan *et al.* 2018, Toivo *et al.* 2019) as the third article (Toivo *et al.* 2018) presented the protocol underpinning Toivo *et al.*'s RCT. Only one included study used theory to select constructs for use in the intervention, as assessed by the TCS (Michie and Prestwich 2010). Cadogan *et al.* (2018) employed the TDF (Michie *et al.* 2005) as part of a systematic approach to intervention development (Cadogan *et al.* 2016), as discussed in Chapter 1. The TDF covers a wide range of behaviour change areas including environmental context and resources, beliefs about capabilities, beliefs about consequences, behavioural regulations and social/professional role and identity (Cane *et al.* 2012) and has been utilised in a range of healthcare interventions (Dyson *et al.* 2013, Tavender *et al.* 2014, Cullinan *et al.* 2015, Bele *et al.* 2019).

Selecting a theory to use in the development of an intervention can be a daunting and difficult task. It is understood that some researchers may opt for a theory which they have prior knowledge and experience in using in order to ease the process of developing a theory-based intervention. There have been calls for the development of guidance documents on how to select the most appropriate theory for use in an intervention (Birken *et al.* 2017), however this could prove challenging given the wide range of theories available in the literature. Lynch *et al.* (2018), based on their own clinical and research experience, produced a pragmatic guide which

included five questions: 1) Are you looking at individuals, groups or wider settings? 2) Are you planning, conducting, or evaluating? 3) What is your aim and what do you need to understand? 4) What data will be available to use? 5) What resources do you have to support you? In order to apply these questions effectively, researchers need to have a sound knowledge of the theories proposed. They would then apply the theory to the answers of the five questions above to gauge which theory fits best with the idea they are aiming to develop. However, Moore *et al.* (2019), has advised answering four different questions in relation to including a particular theory in the intervention: 1) What is the mechanism of action, and does it fit the theory? 2) Can the theory be implemented? 3) Can the theory be used in similar contexts? 4) Can the theory be used in different contexts? Again, researchers need to be aware of numerous theories and apply the answers to the four questions to establish the most appropriate theory. The disadvantage of this is that it relies on researchers having an extensive knowledge of the existing theories which many healthcare researchers do not, emphasising the usefulness of a psychologist in the research team. The differences between Lynch *et al.*'s (2018) and Moore *et al.*'s (2019) questions regarding choosing a theory highlights the variety of opinions and recommendations that exist in the literature. Neither Cadogan *et al.* (2018) nor Toivo *et al.* (2019) used these questions in the development of their interventions, given the interventions would have been developed before Lynch *et al.* (2018) and Moore *et al.* (2019) had published.

It is crucial that authors acknowledge the use of theory in intervention development and explicitly state their reasons for selecting a theory (Helfrich *et al.* 2010, Birken *et al.* 2017). With aiming to change behaviour around prescribing, it was appropriate for Cadogan *et al.* to include a behaviour change theory as opposed to a theory that focuses on the work environment and operational processes such as Normalization Process Theory (May and Finch 2009). The TDF simplifies psychological theory in behaviour change, therefore, making the theories more accessible and user-friendly to non-health psychologists (Michie *et al.* 2005).

Toivo *et al.* only acknowledged that Reason's System-Based Risk Management Theory (Reason 2000) was a useful tool in the development of the CoMM procedure (Toivo *et al.* 2018, Toivo *et al.* 2019) but did not explicitly state their rationale for this theory in either the development work (Toivo *et al.* 2018) or the study which evaluated the intervention (Toivo *et al.* 2019), nor did they discuss how the collaborative procedures between healthcare professionals were developed in relation to the theory. This theory is often used in studies exploring the occurrence and causes of errors and has been utilised in healthcare interventions regarding prescribing errors (Coombes *et al.* 2008, Ross *et al.* 2013), non-adherence to prescribed medications (Barber *et al.* 2005) and supply of non-prescription medicines (Watson *et al.* 2006).

### **2.5.2 Intervention effectiveness**

Feasibility studies are often conducted before a main study, as recommended by the MRC framework (Craig *et al.* 2008) and are used to assess study parameters in the design of a main study, for example, recruitment rate, data collection methods and response rates (Arain *et al.* 2010). Feasibility studies are not designed to focus on the main outcomes of interest; they are often tested in a pilot study, along with ensuring that the main study components work together and complement each other. A feasibility study focuses on the acceptability of the intervention. In the study described by Cadogan *et al.* (2018), this included the educational tool for GPs and scheduled medication review for patients. This study has now progressed to an external pilot study, discussed in Chapter 1 (section 1.8.1) and with results in Chapters 3 and 4.

Toivo *et al.* (2019) did not observe a significant reduction in potentially inappropriate medications, however, per protocol analysis showed a reduction in central nervous system medications was found, along with a decrease in the use of benzodiazepines and opioids, as well as a decline in the proportion of participants using  $\geq 3$  psychotropic medications. Due to substantial negative outcomes associated with long-term benzodiazepine and opioid use (Benyamin *et al.* 2008, Ham *et al.* 2014, Airagnes *et al.* 2016, Berry *et al.* 2016, Watanabe and Yang 2019) and challenges related to deprescribing these medications (Cook *et al.* 2007, Lynch *et al.* 2020, Langford *et al.* 2021); this is a positive finding. The CoMM procedure includes working with and coordinating different healthcare professionals, and the challenges of this were acknowledged. Toivo *et al.* (2019) did not conduct a feasibility or pilot study prior to the main study, which may have identified important issues (i.e. lack of reduction in potentially inappropriate medications and challenges of various healthcare professionals working together). This could have resulted in a more efficient and effective RCT. Guidelines by the MRC recommend the use of pilot studies in complex interventions (Craig *et al.* 2008).

### **2.5.3 Measures of appropriate polypharmacy**

As appropriate polypharmacy has become a focus in prescribing research, how to measure appropriate polypharmacy is often discussed. Many research projects concentrate on developing a measure of appropriate polypharmacy. However, there is no 'gold standard' for measuring appropriate polypharmacy (Kurzewska-Michalak *et al.* 2021) and this is likely due to the lack of consensus regarding a definition of polypharmacy, as discussed in chapter 1, section 1.3.1. Given that a validated screening tool will have had to establish validity and rigor, this is a sound option to measure appropriate polypharmacy. An objective of this review was to determine which validated screening tools were included in intervention on improving

appropriate polypharmacy in older adults. This was included due to the vast options that have been published. There is no guidance in the literature on what validated tool is best suited to a certain type of intervention, however depending on the study population an appropriate tool may exist. For example, the STOPPFrail tool has been developed for a specific population – frail older adults with limited life expectancy (Lavan *et al.* 2017). Important factors to consider when choosing a validated tool include how long it is likely to take to complete and the information that will be available to complete it, and the country it was developed and validated in. However, given the lack of guidance it is likely research teams choose to incorporate a validated screening tool due to their knowledge and experience of it.

#### **2.5.4 Implications for future research**

Despite theory being recommended in intervention development, it is not routinely used in the development of interventions aimed at improving appropriate polypharmacy in primary care, as highlighted in this systematic review. It is crucial to support the use of theory in this area as there is the possibility it will lead to interventions being more effective and to less research funding wastage (Bleijenberg *et al.* 2018). Due to the development of the TDF (Michie *et al.* 2005) and other theoretical frameworks such as the Behaviour Change Wheel (Michie *et al.* 2011), theory is more accessible to and user friendly for novice researchers and non-psychologists. The use of theory should be addressed in future interventions. The TCS (Michie and Prestwich 2010), whilst developed as a theory assessment tool, could also be utilised as a guide of where and when to apply theory in intervention development and inform users of how theory can be employed in selecting and testing intervention components (Michie and Prestwich 2010). The TCS can also be used as guideline for describing interventions as it advises researchers how to articulate the extent of how they used theory in the development of the intervention. This is an important aspect of research and detailed write-ups will help determine the use of theory in intervention development.

#### **2.5.5 Strengths and limitations**

This review is the first to identify the use of theory in interventions aiming to improve appropriate polypharmacy for older people in primary care and has identified a gap in the literature involving theoretically derived interventions focusing on appropriate polypharmacy. The search strategy was developed in consultation with Trinity College's subject librarian and applied to seven databases to provide an extensive search. This coupled with the range of study types included in the predefined inclusion and exclusion criteria, and backward citation chasing via hand searching the reference list of eligible papers, ensured a wide range of studies could

be captured in the review. Backward citation chasing can potentially identify relevant articles that used different terminology and is an advantageous supplementary search method for systematic reviews (Haddaway *et al.* 2022). The TCS was utilised to analyse the extent to which theory was used in the development of the interventions, ensuring rigour in the analysis. This review has been reported in adherence with the PRISMA guidelines for systematic reviews (Moher *et al.* 2009).

As noted previously, there is no consensus on the definition of polypharmacy. This review defined polypharmacy as four or more medications, therefore, studies that defined polypharmacy as less than four, or the average number of medications prescribed per patient was less than four, were excluded. Comprehensive search strategies were conducted for this review, however, studies that met the inclusion criteria but were not adequately indexed may not have been identified in the search process. This review was limited to articles published in the English language. The TCS provides a systematic process to assess the use of theory in an intervention, however application of the TCS relies on detailed methodology supplied by the authors. Studies involving the use of theory may have been excluded from the review, or the TCS not effectively applied, if theory was not clearly stated within the article.

## **2.6 Conclusion**

This review concludes that there is a lack of theoretically derived interventions aimed at improving appropriate polypharmacy for older adults in primary care. As a result, only two studies were included in this review, and an overall conclusion on the effectiveness of theoretically derived interventions to improve appropriate polypharmacy could not be made. Additionally, one of the included studies was a feasibility study, and therefore was not designed to show effectiveness. Both included studies used different theories to underpin their development, but the reasons for including specific theories were not entirely clear. The TCS is a useful tool for assessing the extent of theory used in the development of interventions, providing sufficient detail is provided by authors. Further guidance on selecting the most appropriate theory in intervention development is needed.





## **Chapter 3**

**A qualitative study to refine a theory-based  
intervention to improve appropriate  
polypharmacy in older people in primary care  
(PolyPrime)**

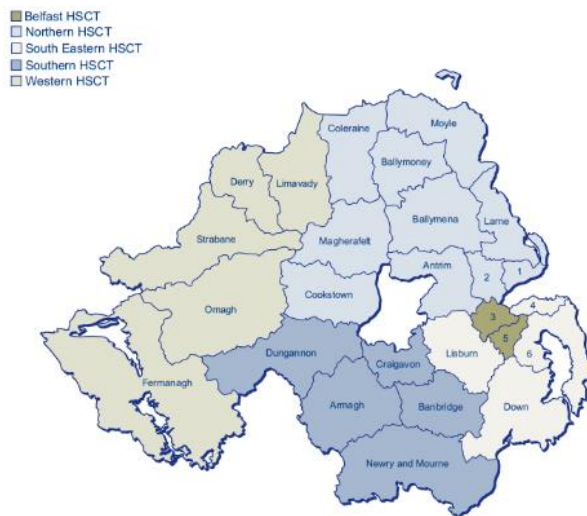
### **3.1 Introduction**

Guidelines developed by the Medical Research Council (Craig *et al.* 2008) advocate for the use of theory in intervention development, as discussed in Chapter 1, section 1.73. The systematic review presented in the previous chapter (Chapter 2), noted the lack of theoretically derived interventions to improve appropriate polypharmacy in older adults in primary care. The methodological detail provided in the publications of each of the included studies varied. Due to the low number of studies included and their heterogeneity, it was not possible to assess their effectiveness. One of the included studies was the feasibility study (Cadogan *et al.* 2018) of the PolyPrime intervention, which used the TDF as the theoretical framework to underpin intervention development (Michie *et al.* 2005). This study has been described in detail in Chapter 1, as this thesis reports on the pilot randomised controlled trial stemming from the study, however, only data from the RoI is presented in this thesis.

As noted in Chapter 1, the PolyPrime intervention was developed in Northern Ireland (NI) by Cadogan *et al.* (2015, Cadogan *et al.* 2016, Cadogan *et al.* 2018). Healthcare policies and practices vary between countries, and for this intervention to be tested in another country, such as the RoI, further refinement may be required. Therefore, this chapter presents the results from a qualitative study of semi-structured interviews with general practitioners (GPs) in the RoI, to refine the intervention.

#### **3.1.1 Healthcare in Northern Ireland**

Healthcare (primary, secondary and tertiary care) in Northern Ireland is free at the point of delivery as it operates under the National Health Service (NHS), although a small number of treatments and services are not free (such as dental services and ophthalmic services). The NHS is funded by general taxation and national insurance contributions and is available throughout the whole of the UK. The NHS in Northern Ireland is overseen by the Department of Health. Healthcare is provided within health and Social Care trusts, of which there are five, grouped according to geographical location as shown in Figure 3.1. Each trust manages its own services and staff.



**Figure 3.1 Map showing Health and Social Care Trust areas in Northern Ireland (Northern Ireland Statistics and Research Agency 2016)**

In primary care, the main healthcare provider is the GP. Patients in NI register with a particular general practice and although they may have a named GP on their records, often in a general practice with more than one GP, patients will be allocated the first GP available for their appointment. However, they can request to see a specific GP if they prefer. Patients can also request a home visit from their GP if they are unable to attend the general practice for an appointment. Services available in a general practice include (but are not limited to) medical advice and diagnosis of symptoms, physical examinations, prescribing medication, vaccinations and simple surgical operations. If a GP is unable to conduct a certain procedure or specialist knowledge is required, they will refer the patient to the necessary healthcare provider, this could be a referral to another healthcare professional within primary care or to secondary care.

The community pharmacist is the most accessible healthcare professional to patients (Department of Health 2020) in NI and provide various services including (but not limited to) dispensing of prescribed medicines, medicines use review, smoking cessation services, palliative care, needle/syringe exchange, providing vaccines. The recent development in the pharmacy profession that involves pharmacists working in general practice, i.e. practice-based pharmacists, has resulted in many pharmacists undertaking the necessary post-graduate training to become independent prescribers (Abuzour *et al.* 2018). The role of the general practice-based pharmacist is to manage patients, review and prescribe their medicines, providing the pharmacist is a trained prescriber. A recent study found that a practice-based pharmacist working part-time frees up nearly five hours of GP time per week by taking on

prescribing related tasks, and they have also been found to reduce stress levels in the practice and improve patient safety and staff morale (Maslrey *et al.* 2018). It is useful to note that at the time of development of the PolyPrime study, pharmacists were not embedded within primary care in NI, and their main role was within community pharmacy practice.

Secondary care involves more specialised treatment and includes healthcare for patients who have been referred to specialist healthcare professionals for specific care, in other words, it is not the first point of contact for the patient (Thompson 2016). Secondary healthcare is often provided in hospitals and includes both in-patients (i.e. those admitted to stay over night in the hospital) and out-patients (i.e. those who have an appointment to receive care) (Multiple Sclerosis Trust, no date). Secondary healthcare involves a wide range of care such as cardiology, dermatology, gynaecology, as well as diagnostic services such as x-ray and MRI scan. Tertiary care is for patients in need of complex and specialised treatments, for example, to receive rehabilitation after a stroke (NICE 2022) and can be accessed via referral from primary or secondary healthcare professionals. Tertiary healthcare can be delivered in the same hospital as secondary healthcare services or may be delivered in a separate hospital (Varley *et al.* 2010).

Whilst the public healthcare sector is used by the majority of people, private healthcare is also utilised in NI, however, most people rely on the NHS for their healthcare. If a patient receives a prescription through a private healthcare consultation, the prescription is still dispensed in a community pharmacy: community pharmacies do not provide private care. Services provided in secondary care are the most commonly accessed services in the private healthcare sector. There are numerous private hospitals in NI, which only provide treatment for patients that have private health insurance, or if the patient pays the treatment costs themselves; private hospitals do not provide free treatment (unless there has been a specific arrangement between the Department of Health and the individual private hospital).

### **3.1.2 General practice in Northern Ireland and the Republic of Ireland**

General practice is the main source of primary healthcare in both NI and the RoI. The healthcare system and general practice in the RoI (described in Chapter 1, section 1.5.3) are very different compared to the healthcare system and general practice in NI. As the PolyPrime intervention was developed in a specific and unique healthcare context, in order to establish if the intervention is transferable outside that context, it needs to be tested in a different healthcare jurisdiction. Movsisyan *et al.* (2019) state that for the intervention to be effective, some aspects may need to be adapted to be adequate in the new healthcare context.

Existing evidence suggests that prescribing patterns in the RoI and NI are similar. For example, using the same subset of STOPP indicators (STOPP is described in Chapter 1, section 1.6.2), the top three examples of potentially inappropriate prescribing in NI and the RoI were found to be the same – use of proton pump inhibitors at maximum therapeutic dose for over eight weeks, use of NSAIDs for longer than three months and long-term long-acting benzodiazepines (Bradley *et al.* 2012a, Bradley *et al.* 2014). There are many similarities between general practice within the two jurisdictions, with differences including the use of computer systems in NI more than RoI (Cupples *et al.* 2008). However, this study was from 2008 and it is likely that computer systems are now in widespread use in GP practices in the RoI. In the RoI a patient visits their GP an estimated 5.17 times per year (Brennan *et al.* 2019), compared to seven times in the United Kingdom (Royal College of General Practitioners 2013). However, subtle differences may exist between healthcare systems that might affect the implementation of the intervention (Campbell *et al.* 2007), for example support and availability of other general practice staff (such as a practice nurse or practice manager). As discussed in Chapter 1, section 1.8, Cadogan *et al.* interviewed GPs in NI about their prescribing practices (Cadogan *et al.* 2015, Cadogan *et al.* 2016), in order to develop an intervention to target GP prescribing, presented in Cadogan *et al.* (2018). Before implementation in a pilot cRCT involving two jurisdictions (i.e. NI and the RoI), it was necessary to test the intervention in the RoI, and refine it if necessary.

### **3.2 Aim and objectives**

#### *Aim*

The overall aim of this study was to refine a theory-based intervention (PolyPrime) targeting prescribing of appropriate polypharmacy in older people in primary care.

#### *Objectives*

The objectives of the study were to:

- Recruit up to 24 GPs (from 12 general practices) from six RoI border counties into the study;
- Conduct a semi-structured interview with each GP;
- Analyse interviews using a framework approach;
- Investigate whether refinements to the intervention are required before implementation in a pilot cRCT.

### 3.3 Research design and methodology

There are a range of designs available when collecting data, qualitative or quantitative, and a plethora of methodological options (e.g. online survey, focus groups, interviews). The choice of method used within a study can be influenced by the research question (for example, if the researcher wanted to explore participants' experiences, a qualitative method would most likely be used), what is feasible, what is within the study and funding parameters, and the researcher's knowledge and ability to employ particular methods (Whiffin 2021). This section will provide an overview of data collection methods, both quantitative and qualitative, followed by an in-depth review of qualitative methodology. The methods used in the qualitative study to refine the theory-based intervention (PolyPrime) targeting prescribing of appropriate polypharmacy will then be presented.

#### 3.3.1 Data collection methods

Often the difference between qualitative and quantitative research is narrowed down to the use of words (qualitative) or the use of numbers (quantitative) (Leppink 2017). Qualitative methods are more appropriate when exploring individuals' opinions and understanding the meaning they provide (Creswell and Creswell 2018). In comparison, quantitative methods focus on the relationship amongst variables and in providing statistical outcomes (Creswell and Creswell 2018). Common differences between qualitative and quantitative research are shown in Table 3.1.

**Table 3.1 Common differences between qualitative and quantitative research (adapted from Bryman 2012)**

<b>Aspect being compared</b>	<b>Quantitative</b>	<b>Qualitative</b>
<i>Factor</i>	Numbers	Words
<i>Point of view of</i>	Researcher	Participants
<i>Researcher involvement</i>	Researcher distant	Researcher close
<i>Use of theory</i>	Theory testing	Theory emergent
<i>Questions asked</i>	Static	Process
<i>Structure</i>	Structured	Unstructured/ semi-structured
<i>Overview</i>	Generalization	Contextual understanding
<i>Data</i>	Hard, reliable data	Rich, deep data
<i>Level of data</i>	Macro	Micro
<i>Understanding</i>	Behaviour	Meaning
<i>Setting</i>	Artificial settings	Natural settings
<i>Sample size</i>	Large	Small

There are various formats for conducting qualitative research. The most commonly used qualitative methods include focus groups and interviews. A focus group often lasts 1-2 hours and involves several participants [usually between 6-12 (Onwuegbuzie *et al.* 2009)] with emphasis on interactive responses between the group (Leung and Savithiri 2009). During a focus group, the researcher assumes the role of a ‘facilitator’ and moderates a discussion between the group participants (Nyumba *et al.* 2018). Focus groups are a useful method in discussing and collecting participants ideas, opinions, perceptions, and thoughts (Kreuger and Casey 2000).

Interviews (conducted one-to-one i.e. between the researcher and the participant) can involve various formats including: structured (all interviewees are asked exactly the same questions, regardless of their answers); semi-structured (interviewer is able to ask questions in response to interviewees answers); in-depth interviews (include open-ended questions and follow a semi-structured manner).

Structured interviews follow a strict format resulting in standardised data and are more commonly used to generate quantitative data than qualitative data (Rashidi *et al.* 2014), so are not discussed in detail here. Semi-structured and in-depth interviews allow for the researcher to adapt the order of the questions asked in relation to the interviewee responses and ask questions not on the topic guide (Bryman 2012), in order to probe for clarification on a participant’s response, to gather more information from the participant and/or to seek understanding about the participant’s response.

There are many quantitative methods of data collection, including structured interviews (the interviewee is provided with exactly the same questions and format as another interviewee, to ensure responses can be aggregated) and self-administered surveys, for example. Surveys, such as a self-completion questionnaire, can be delivered by mail or online. As a researcher is unlikely to be present during the completion of a questionnaire to provide clarification to any questions that may arise, the format must be simple and easy to follow. They often involve more ‘closed’ questions (i.e. those that require a yes/ no answer for example) and tend to be shorter in length, and therefore choosing the correct questions to ask, with the most appropriate wording, is very important (Bryman 2012). More detailed descriptions of quantitative research methodologies are provided in Chapter 4, section 4.3.1.

As noted in the introduction to this chapter (section 3.1), qualitative interviews were conducted with GPs in order to investigate if a refinement of the pre-established intervention, PolyPrime, was required before testing in a cluster pilot trial in the RoI. The remainder of this section will provide an overview of key factors to consider when undertaking qualitative research.



## *Sampling*

An important aspect of research design is sampling, i.e. selecting participants to participate in the study (Guest *et al.* 2013). Most qualitative research entails purposive sampling, a form of non-probability sampling [individuals are selected by the researcher based on their knowledge of the subject, ability to communicate experiences and opinions, and their willingness to participate (Bernard 2002, Cresswell and Plano Clark 2011)]. This can provide rich data if the researcher has limited resources (Patton 2002). There are numerous forms of purposive sampling including judgement sampling, criterion sampling and snowball sampling (Palinkas *et al.* 2015).

Judgement sampling involves the researcher selecting participants for inclusion in their study based on the researcher's judgement that they will be of use to the study (Sharma 2017), for example, that potential participants have knowledge on the subject and will be able to discuss the topic in detail. This method of sampling has been used in studies that focus on improving health and healthcare (Yeen *et al.* 2019, Berninger *et al.* 2022, Sarang and Chakrawarty 2022) but is not a particularly common sampling method in this field.

Criteria sampling is used to identify cases that meet some/all of the predetermined criteria of importance (Palinkas *et al.* 2015). It is often employed in mixed methods studies, for example, when participants complete a survey and are then selected to participate in a semi-structured interview from responses provided in the survey (Aarons *et al.* 2012, Antwi *et al.* 2021, Bilgin *et al.* 2021, Luca *et al.* 2021).

Another form of purposive sampling is snowball sampling, also called snowballing. In snowball sampling, the researcher begins with a small number of participants and these participants recommend other individuals relevant to the research, based on their opinion of who might be knowledgeable in a particular field. This sampling method is popular when recruiting hard-to-reach populations (Noy 2008) but is also a useful sampling method in healthcare research, especially when recruiting specific healthcare professionals, e.g. nurses (Horner *et al.* 2019), community pharmacists (Yong *et al.* 2021), dentists (Gallagher *et al.* 2021) and GPs (Larkin *et al.* 2021).

Another form of sampling is convenience sampling which involves participants who are close-to-hand, i.e. they are a 'convenient' source of data for the researcher and differs from purposive sampling, in that judgement is not involved in order to select participants (Jager *et al.* 2017): in

purposive sampling the researcher chooses participants with the objectives of the study in mind (Bryman 2016).

Determining an adequate sample size in qualitative research can be challenging. Many researchers choose their sample size based on previous research conducted in a similar area and manner, others note that their sample size is led by determining when data saturation is reached [when there is no new information arising from the data collected, and therefore data collection can stop (Saunders *et al.* 2018)]. Irrespective of the method chosen, detailed information on how and when sample size is deemed appropriate and when data saturation is reached is rarely published (Guest *et al.* 2013). Gerson and Horowitz (2002) advocate for between 60-150 interviews in order to produce reliable results within a manageable amount of data. Warren (2002) encourages 20-30 interviews, however, Crouch and McKenzie (2006) note less than 20 interviews is enough to reach data saturation. However, Charmaz (2006) states that sample size in qualitative research should not be defined by a numerical threshold, but dictated by the quality of data and the researcher should only stop collecting data when no new information is gathered, i.e. when data saturation has been reached. A recent systematic review conducted by Vasileiou *et al.* (2018) highlighted that not all interview studies refer to previous conducted research and recommendations to calculate a sample size, but instead some prefer to omit a numerical threshold and continue collecting data until data saturation has been reached.

### *Topic guides*

Topic guides are useful when conducting qualitative interviews as they allow for consistency across all interviews (Tracey 2012). The term 'topic guide' and 'interview schedule' are used interchangeably, although there is a subtle difference in their meaning. According to Bryman, topic guides are less specific in comparison to interview schedules (Bryman 2012). Throughout this thesis, the term 'topic guide' will be used as opposed to interview schedule. Most topic guides include several sections (introduction, main questions, conclusion) and begin with opening questions which tend to hold an introductory format of easing the interviewee into the interview and to help establish a rapport between the interviewee and the interviewer. For example, participants might be asked to describe a recent situation, and questions should be open-ended to allow for participants to provide detail in their response. Closed questions, for example, those that could be answered with a yes or no response, are not recommended. The main questions take up the bulk of the topic guide and are the main interest to the researcher. Follow-up questions, such as 'Could you explain that in more detail' and probing questions such

as 'You mentioned earlier that you prefer to... Could you tell me why?' are often used throughout a semi-structured interview but not necessarily included in a topic guide. The topic guide will usually include concluding questions. It is normal for the interviewer to signal they are approaching the end of the interview and then ask the closing question(s) which allow for the interviewee to add any additional comments or thoughts about what was discussed during the interview or provide information they feel is relevant but was not included (Bryman 2012). It is important for the interviewer to actively listen to the interviewee throughout the entire interview so they can engage effectively (McGrath *et al.* 2018).

The order of questions in a topic guide can alter from the order asked in an interview, however Bryman (2012) notes that it is useful to have a simple format so that the questions and dialogue can flow easily in the interview. A pilot test of the proposed topic guide should be conducted before the commencement of interviews as this will allow any weaknesses in the topic guide to be amended before its use in a study (Kvale 2007). This will increase the research quality, as well as allowing for the researcher to practice and estimate the length of time the interview will take (Chenail 2011). Often topic guides are iterative in semi-structured interviews whereby the topic guide can be adapted as the researcher learns more about the area and discuss matters that previous participants had brought up during their semi-structured interview (Busetto *et al.* 2020). Unlike piloting in quantitative research, there is not a specific number or method to calculate a sample size for the pilot study. Often, a pilot study in qualitative research is conducted with a small number of participants and with participants representative, or as similar as possible, of the cohort who will be officially participating in the study (Turner 2010). Pilot studies in qualitative research are rarely published (Gudmundsdottir and Brock-Utne 2010), however, some argue that they should be widely discussed and disseminated as they might present important findings in relation to research quality (van Teijlingen and Hundley 2001; Malmqvist *et al.* 2019).

#### *Data management and analysis*

Qualitative data is normally collected via audio-recordings, video-recordings or note taking. During an interview, Bryman (2012) advocates for the use of audio-recordings to ensure that a complete account of the interview will be processed (and later transcribed verbatim) and to also ensure the interviewer is not distracted by having to note interviewee responses. Following recording, the interview should be transcribed *verbatim*, and any names or locations should be pseudonymised (i.e. replaced by another name), and subsequently analysed. This is in line with current General Data Protection Regulations and would be stated in applications to ethical

committees. There are various methods by which data are analysed, the two most commonly used methods are thematic analysis and the framework approach. Thematic analysis includes six steps (defined by Braun and Clarke 2006) which include familiarisation with the data, generating initial codes, searching for themes, reviewing themes, defining and naming themes and lastly, producing the report. It has been described as a poorly demarcated yet widely used method (Roulston 2001) and Braun and Clarke (2006) describe it as a 'method for identifying, analysing, and reporting patterns (themes) within data... that minimally organises and describes your data set in (rich) detail'.

The framework approach is similar to thematic analysis, notably during the first stages of familiarisation and identification of themes and codes. Gale *et al.* (2013) provide a useful guide to implementing the framework approach, beginning with familiarisation of the data followed by identifying initial themes and categories in the data. From this, a coding scheme is developed and agreed by all researchers involved. The agreed coding scheme is then applied to the entire data set. The coded data is transferred into a file (such as Excel), accompanied by summary information from the data set, creating a framework matrix. It is important to carefully choose which analysis method to follow and to ensure that the analysis process is accurately described: both to ensure transparency and to maintain rigour.

#### *Reliability and validity*

As quantitative methods are fundamentally different from qualitative methods, alternative frameworks and definitions of reliability and validity are appropriate (Sandelowski 1993, Noble and Smith 2015). Reliability, the extent to which a study can be duplicated, is difficult to reach in qualitative research. As LeCompte and Goetz (1982) note, it is impossible to 'freeze' the setting and time in which a qualitative study takes place, and therefore problematic to replicate in future studies.

Rigour within qualitative research can be difficult due to the lack of consensus regarding standards of qualitative work (Rolfe 2006). It is important for qualitative researchers to incorporate particular strategies that can enhance the rigour of their research and to make it trustworthy [i.e. readers will have confidence in what has been reported (Stahl and King 2020)]. Noble and Smith (2015) combined a list of nine strategies to ensure the trustworthiness of data arising from qualitative work; these include: stating any personal biases (Morse *et al.* 2002) and engaging with other researchers to reduce bias (Sandelowski 1993), including rich verbatim quotations of interviewees responses (Slevin 2000), and data triangulation of different data collection methods for a comprehensive data set (Kuper *et al.* 2008). Nowell *et al.* (2017) take a

different approach to ensuring the trustworthiness of qualitative work and emphasise credibility, transferability, dependability, confirmability, and audit trails (see Box 3.1 for an overview of these terms).

Standardising reporting of qualitative studies helps to ensure rigor in the study as well as the published work by guiding researchers on the level of detail to be provided and important elements to report (Dossett *et al.* 2021). Some researchers argue that reporting guidelines are rigid and go against the nature of qualitative research, because it is often conducted in a semi-structured and iterative manner (Dunt and McKenzie 2012). Two commonly used reporting guidelines are Standards for Reporting Qualitative Research [SRQR (O'Brien *et al.* 2014b) and the Consolidated Criteria for Reporting Qualitative Research [COREQ (Tong *et al.* 2007)]. SRQR is the most recent of the two having been developed in 2014, with COREQ developed in 2007. A main difference between SRQR and COREQ is that SRQR can be applied to various qualitative studies whereas COREQ was mainly designed for use in reporting of qualitative studies using interviews and/or focus groups. The publication of COREQ has resulted in higher quality reporting of qualitative studies (de Jong *et al.* 2021).

**Box 3.1 Ensuring qualitative research is trustworthy (Nowell *et al.* 2017)**

- Credibility – the fit between the participants' views and how the researcher has presented them
- Transferability – the generalisability of the findings. It is a good idea to provide detailed descriptions so researchers can interpret if the findings may be applicable to their setting
- Dependability – ensure the methods are logical and that all aspects of the research process are traceable and documented
- Confirmability – establishing the researcher's interpretations and findings are clearly derived from the data, requiring the researcher to demonstrate how conclusions and interpretations have been reached (Tobin and Begley 2004)
- Audit trails – evidence of the decisions made by the researcher in order to get the final results. Keeping field notes and a reflexive journal can ensure evidence of decisions

This subsection has provided some detail of qualitative research methods with a short introduction on quantitative research (see Chapter 4, section 4.3.1 for more detail on quantitative research). The subsequent part of the methods section in this chapter will present the methods employed in a qualitative study conducted to refine the novel theory-based intervention, PolyPrime, which targeted the prescribing of appropriate polypharmacy, as outlined in Chapter 1, section 1.8. As already stated, semi-structured interviews (described in

section 3.1.1) were chosen as the appropriate design. Ethical approval was granted by the Research Ethics Committee in the School of Pharmacy and Pharmaceutical Sciences (SoPPS), Trinity College Dublin [TCD (Reference no: 2018-07-01, Appendix 3.1)].

### **3.3.2 Sampling and recruitment strategy**

The non-probability sampling method utilised in this study was criteria sampling. The Irish Medical Directory (Guéret 2017) was used to compile a list of all 142 general practices in the six border counties. Practices were grouped according to county, numbered 1-x, depending on the number of practices in the county, and randomised using a random number generator. Where possible, the first 20 practices per county on the randomised list were contacted by telephone. The PhD candidate (AG) and the Research Fellow (AR) (see Appendix 3.2 for research team information) each took responsibility for recruiting and conducting the interviews in three counties, as this phase was only conducted in the RoI (AG: Louth, Monaghan and Cavan; AR: Donegal, Sligo and Leitrim). Counties were allocated to the researcher based on those closest to their home location.

Practices were eligible for inclusion in the study if:

- GPs were involved in prescribing medicines for older people in primary care
- GPs were not involved in another, similar prescribing improvement research project
- The GP practice employed two or more GPs

The original protocol that was granted ethical approval, excluded single-handed practices from participating. This was due to the aim of recruiting up to two GPs per recruited practice. Once recruitment commenced, it was clear that numerous single-handed practices existed within the defined area. Therefore, an amendment to the original ethics approval was sought and granted (Appendix 3.3).

The revision stipulated that practices were eligible for inclusion if:

- GPs within the practice were involved in prescribing medicines for older people in primary care
- GPs within the practice were not involved in another, similar prescribing improvement research project.

The practice managers acted as the gatekeepers (i.e. a buffer between the researcher and the participant) for the study. The practice manager was contacted to confirm the GP practice met the inclusion criteria and to gauge if GPs would be interested in participating in the study. If

practice managers wished to receive further information on the study, or believed GPs within the practice may be interested in taking part, a letter of access (Appendix 3.4) and a practice manager consent form (Appendix 3.5) were sent directly to the practice manager. In addition, an invitation letter to the lead GP (Appendix 3.6), GP participant information leaflets (Appendix 3.7) and GP consent forms (Appendix 3.8) were also sent to the practice manager, with the understanding of delivering them to the lead GP. The lead GP was asked to distribute the study information, if appropriate, to other GPs within the practice. GPs were given ten days to decide whether or not they wished to participate in the study. If either researcher had not heard from the practice manager within fourteen days of posting the study information, the researcher contacted the practice manager via telephone to confirm interest (this allowed GPs at least 10 days to make a decision). A date and time for researcher to attend the GP practice and conduct the interview in private was then scheduled and confirmed with interested GPs.

If selected practices declined to participate, the next practice on the randomised list was contacted. Practices were recruited purposively within each county to achieve a range of practices from different geographical locations and from rural and urban locations. A rural location was defined according to the definition from the Central Statistics Office, i.e., a rural area has a population of less than 10,000 people (Department for Environment, Food & Rural Affairs 2017). If it was not possible to recruit two practices from a county, more than two practices were recruited from the other counties to ensure the target of 12 practices within the six border counties in ROI was met. Each practice was contacted with a view to recruiting two GPs per practice (where possible), providing a total GP sample of up to 24 participants. Participants were awarded with a certificate of participation (Appendix 3.9) which could be included in their continued professional development portfolio. Each GP practice was asked to invoice the research team in order to receive payment for participating in the interview (€54 per GP).

### **3.3.3 Undertaking the interviews**

The research team developed a topic guide (Appendix 3.10). The topic guide was piloted by AG and AR with a convenience sample of academics and researchers from the SoPPS, TCD; the School of Pharmacy and Biomolecular Sciences, Royal College of Surgeons in Ireland; the School of Pharmacy, Queen's University Belfast (QUB); and the School of Medicine, Dentistry and Biomedical Sciences, QUB. The interviewee assumed the role of a GP in order to pilot the topic guide. The pilot interviews were to check for understanding, acceptability and validity of the topic guide. The topic guide was modified iteratively as AG and AR discussed any comments on

the topic guide that arose during each pilot interview. This resulted in several questions being re-worded before the final topic guide was agreed. The first pilot interview conducted by AG was transcribed for learning purposes.

The amended topic guide began with a brief overview of the background to the research and why it was being conducted, followed by an overview on the existing intervention package. GPs were asked to discuss their current prescribing practices and their opinions on prescribing polypharmacy. The researcher (AG or AR) then described the existing intervention in detail and showed GPs the intervention video. GPs were then asked to comment on the content of the video, its relevance to their practice and any recommendations for improvement that they had.

When GPs were recruited, they were assigned a code, for example, GP1A. The code denoted the practice (GP1, GP2, GP3 etc.) and the GP involved in the interview (A or B). The names of participating GPs, their contact details and their assigned code were kept in a password protected file. The interviews were conducted at the participating GP's practice, at a time and date most convenient to the participant. Informed consent (Appendix 3.8) was taken by the researcher prior to commencing the interview. Interviews were audio-recorded using a dictaphone. Once each interview recording was uploaded to the TCD secure network, they were deleted from the dictaphone. All interviews, with the exception of the last interview, were transcribed verbatim by a professional company, Scribe. Scribe signed a confidentiality agreement before transcription began and followed instructions for transcription. Due to timeline restrictions, AG transcribed verbatim the last interview conducted. All interviews transcribed by Scribe were quality checked by either AG or AR. AG quality checked the transcripts of interviews that were conducted by AR, and AR quality checked the transcripts of interviews conducted by AG. AR also quality checked the transcript transcribed by AG. Quality checked transcripts were then entered into NVivo®. NVivo® is a software package that enables qualitative data to be organized and analysed in a user-friendly manner. All consent forms, from both GPs and practice managers, are currently stored in a locked filing cabinet in the SoPPS, TCD, which only AG can access. Once AG leaves TCD, this will be transferred to CR and kept for a total of five years in line with GDPR guidelines at the time of ethical approval.

#### **3.3.4 Data analysis**

The framework approach (Ritchie and Spencer 1994) was used to analyse the data and followed the analysis method employed by Gale *et al.* (2013). This method has been utilised effectively in other health research studies (Midgley *et al.* 2017; Lowthian *et al.* 2018; Potter *et al.* 2018; Bunzli *et al.* 2019). The data analysis process involved six steps, including: 1) familiarisation of



the data, 2) initial coding of three selected transcripts, 3) the development of a coding scheme, 4) application of the coding scheme to all transcripts, 5) development of a framework matrix and 6) analysis of data within the framework matrix. The in-depth familiarisation phase was conducted by AG and AR with each researcher familiarising themselves with all the interviews. This step involved repeatedly listening to the interview recordings and reading the interview transcripts. Both researchers became immersed in the interview data during this familiarisation phase. AG and AR noted ideas and/or themes that repeatedly arose, as well as initial thoughts, in the margins on the transcripts.

The second phase of the analysis involved AG and AR independently applying a 'code' to three randomly selected transcripts (GP1A, GP4A and GP5A) out of all the transcripts. The 'codes' were developed from the topic guide as well as commonly occurring themes that arose from the familiarisation phase (step one of the analysis, described above). Researchers were free to add subcategories whilst coding these three randomly selected transcripts. Following this, AG and AR met and compared the codes they had developed based on the three transcripts. The codes agreed on during this process were organised and grouped within overarching categories. The categories were titled based on the codes assembled and this resulted in a final coding scheme, which contained six categories. A third researcher, Dr Cathal Cadogan (CC) reviewed the same three transcripts and applied the coding scheme developed by AG and AR. Based on this review, a seventh overarching category was added. The developed coding scheme (containing the seven categories) was reviewed and agreed upon by the wider research team. The finalised coding scheme can be found on Appendix 3.11 and consisted of 22 codes within seven categories.

Using the finalised coding scheme, two members of the research team (AG and AR) independently coded all the transcripts, using NVivo®. For ease of use during this coding phase, all codes were assigned a number, for example 1.1: Polypharmacy definition (as seen in Appendix 3.11). All coded transcripts were checked for any differences or discrepancies, and any inconsistencies were discussed and subsequently agreed between AG and AR. Both researchers remained reflexive throughout this analytical process.

After all transcripts had been coded in NVivo, the data was charted into a framework matrix using Microsoft Excel. The framework matrix contains an overview of the data beside an illustrative quote(s). A separate matrix was made for each coding category, with one row per participant and one column per code. A screenshot of category one 'GPs definition of polypharmacy' is shown in Appendix 3.12.

After charting of the data had been completed, AG and AR analysed the framework matrix to identify key issues and patterns within each category.

### **3.3.5 Modifications to the intervention**

The findings from the qualitative interviews were discussed with members of the wider research team. Data relating to any potential modifications to the intervention was relayed to the research team and discussed in detail. This included discussions around the practicality and feasibility of making the suggested modifications within the project timeline.

### **3.3.6 Reporting the results**

The findings from this study are reported in line with COREQ reporting checklist (Tong *et al.* 2007) which is presented in Appendix 3.13.

### **3.3.7 Ethical standards**

As part of the PhD programme within TCD, the PhD student completed research and ethics training via the module 'Research integrity and impact in an open scholarship era' (see Appendix 3.14 for certificate). This allowed the student to develop an understanding in conducting ethical research and gain knowledge in collecting data, data storage and retention and ownership of data. This learning was then applied to the research process implemented within this chapter, and within the research presented in this thesis.

As mentioned above, this study received ethical approval from SoPPS research ethics committee and only commenced once approval had been received. To ensure compliance with ethical standards, informed consent was obtained prior to interviews being conducted (Appendix 3.8) and participants were provided with information regarding the project to inform their decision making via a participant information leaflet (Appendix 3.7) as discussed above. Confidentiality was observed during the research via pseudonymised transcripts and data not being attributable to recruited participants or the GP practice with which they were affiliated.

Consent forms from study participants interviewed by the PhD student, AG, were stored in a locked filing cabinet within a locked office in the SoPPS, TCD. Consent forms from participants interview by AR were stored in a locked filing cabinet within a locked office on a secure floor in the School of Pharmacy, QUB. Once the study had been completed, the consent forms stored in QUB were transferred to TCD in line with GDPR 2018 for the transferring of data and stored with the other consent forms in TCD. These will be kept for five years and then destroyed (shredded and disposed of in confidential waste bags) in line with GDPR 2018 regulations. Pseudonymised

transcripts are stored electronically on the TCD server and will also be destroyed after five years in accordance with GDPR 2018 regulations.

### 3.4 Results

Overall, 108 practices (out of a total of 142 practices in the defined area) were contacted, with 62 practices opting to receive further information with regards to the study. A letter of access and consent form were sent to the practice manager in each of these 62 practices. This was accompanied by an invitation letter to the lead GP in the practice, GP participant information leaflets and GP consent forms. As a result, 12 practices were recruited: two practices each in Cavan, Donegal and Leitrim and three practices each in Monaghan and Sligo. Recruitment in Louth was unsuccessful: hence one extra practice was recruited from Monaghan and one extra practice from Sligo. These two counties were chosen to recruit an additional practice as GP practices within these counties had already expressed an interest in taking part. Practices were contacted with the aim of recruiting up to two GPs for interview per practice, however, this only occurred in one practice. Between November 2018 and March 2019, thirteen interviews were conducted: seven by the PhD candidate and six by the postdoctoral researcher in QUB (AR). Interviews ranged from 25 minutes to 60 minutes. Table 3.2 shows the demographics of all the GPs interviewed.

**Table 3.2 Demographics of general practitioners interviewed**

Interview code	County	Rural vs Urban	Gender	Number of years practicing	Conducted by
GP1A	Donegal	Rural	M	32	AR
GP2A	Donegal	Urban	M	4	AR
GP3A	Monaghan	Rural	F	24	AG
GP4A	Cavan	Rural	F	19	AG
GP4B	Cavan	Rural	F	1.5	AG
GP5A	Sligo	Urban	M	20	AR
GP6A	Sligo	Rural	M	11	AR
GP7A	Cavan	Urban	F	10	AG
GP8A	Leitrim	Urban	M	30	AR
GP9A	Leitrim	Rural	M	20	AR
GP10A	Monaghan	Rural	M	25	AG
GP11A	Monaghan	Urban	M	13	AG
GP12A	Sligo	Rural	M	30	AG

Key: AG= Ashleigh Gorman AR= Audrey Rankin F= Female M= Male

As noted previously, a coding scheme was developed as part of the analysis process. Overarching coding categories included: GPs definitions of polypharmacy, their current prescribing practices, the intervention components [separated into three sections: i) the video, ii) making explicit plans as part of the intervention, iii) prompts to GP from practice staff noting

that patients had arrived at the practice for their scheduled medication review], GPs' views on the overall intervention package, and contextual factors (i.e. information which is of use to the study regarding how primary care operates in the RoI or how the GP practice is run). The findings from all the qualitative interviews (i.e. those conducted by both researchers) are discussed below.

#### **3.4.1 GPs definitions of polypharmacy**

Some GPs referred to polypharmacy as a numerical threshold, whilst others did not. In terms of defining polypharmacy using a numerical threshold, three GPs noted polypharmacy as three or more medicines, two GPs noted it as four or more and three GPs defined it as five or more medicines; three GPs used the term "multiple" to describe polypharmacy. There was a consensus amongst most GPs, even those that provided a numerical value, that polypharmacy should be tailored to the patient and that other factors should be considered when discussing polypharmacy, such as drug-drug interactions.

*"we would think about it all the time in terms of the numbers, but mostly in terms of the requirements, whether they need to be on them, whether they need to be stopped and we would try and review that and get it down as low as possible" [GP2A]*

*"Well I suppose the other issue is the interactions the fact that it's dangerous" [GP5A]*

*"If its two drugs too much then its polypharmacy... Polypharmacy's [sic] to me is... inappropriate use of drugs." [GP8A]*

#### **3.4.2 Current prescribing practices**

The interview schedule asked GPs to discuss their process in prescribing acute prescriptions compared to repeat prescriptions and how often they would ask patients to present at the practice if they were requesting a prescription, whether acute or repeat. GPs were also asked how they managed medications that were prescribed by another healthcare professional.

##### *Acute prescriptions*

The GPs interviewed preferred to prescribe acute prescriptions face-to-face with the patient.

*"Not often I think it's much better and safer for them to be there yeah yeah." [GP6A]*

*"I would want I personally would want to see them to determine what the need was." [GP11A]*

In describing the process for prescribing an acute prescription to an older patient, GPs refer to the patients' notes and ensure there wouldn't be any potential negative interactions with medicines they are already prescribed.

*"Uh, yeah, so I try to kind of see whether they need it, how long they need it for, um, whether or not there are any side effects associated with them and interactions, you know."* [GP3A]

*"you'd have to look at the age of the patient, and then you would look at the, well you could look at the sex of the patient as well because obviously there is differences between male and female, eh, and then you would look at the other medications that the patient is on, and then probably look at other things, other co-morbidities that they might have like renal function, diabetes etc, and then you would, and any other medications that they are on, and then you would prescribe according to, have you looked at all those things"* [GP12A]

However, GPs noted that in doing this, they rely on the patients' notes being accurate and that any previous medicines and health conditions have been recorded correctly.

*"we do rely of course on the fact that every medication they're taking is accurately documented in the notes"* [GP11A]

GPs also noted that when prescribing an acute medication, their computer software can be useful in highlighting any potential interactions with medicines previously prescribed.

*"it'll do a search against the the drugs that people are already on and flag them red, amber or green"* [GP10A]

#### *Repeat prescriptions*

GPs noted that repeat prescriptions are more commonly issued in practices, in comparison to acute prescriptions

*"so I would say probably 30% acute, 70% repeat; just for older patients"* [GP4B]

*"repeat prescribing with probably 80%"* [GP10A]

GPs described a similar approach when prescribing repeat prescriptions. Often, reception staff would print out the script, the GP reviews the script in conjunction with the patient's record and checks for potential interactions, if any blood tests are required, and if the patient appears to

be adhering to the medicine schedule (assessed by determining if their repeat prescription is early or late).

*“You know, if they’re late getting their prescription, if they’re too early, if they’re any risk of them, you know, being poorly compliant or taking too many of one medicine”*  
[GP4B]

*“Well usually they ring in and the secretary does them and then I have a look at them and just go through them and we see, you know? And then I usually look at the files to see is there anything here we can, you know, and we try every six months, that’s our, you know, and we go through it then. When we see when did we do their bloods or whatever we try and see can we – rationalise what they’re on, it doesn’t always work but we try”* [GP8A]

Some GPs noted that, due to time constraints, GPs check repeat prescriptions quickly and errors can occur.

*“you’re doing them quite quickly so your scanning quickly so there is like there is room for errors there, certainly there was an occasion not so long ago where methotrexate came up on the prescription and it was inappropriately prescribed and it went through the system”* [GP5A]

#### *Patient recalls*

The response to recalling patients to the practices for reviewing their conditions and medicines varied between the GPs interviewed from three months to one year, however, this depended on the patient, their health conditions and the medicines prescribed.

*“so we don’t have a fixed rate of reviewing them. Yeah, so just whenever they’re in usually, or when we’re signing prescriptions, maybe every three months”* [GP3A]

*“If all is going okay, annual repeat is fine”* [GP4B]

*“we would issue bloods every 3, or prescriptions rather, every 3 months. That’s the, you know, like if it’s a 3 monthly prescription, so certainly when you haven’t seen someone for 6 months, we would recall them.”* [GP12A]

#### *Prescriptions initiated by other prescribers*

GPs mentioned that they check over prescriptions initiated by other prescribers before providing the patient with a prescription for the medicine. A few GPs commented that

prescriptions from hospitals were not always clear, and sometimes confusion around whether medication changes were made deliberately or by accident existed. GPs noted that this additional check for hospital prescriptions can be time consuming.

*“You have to try and ring the the consultant yeah the team you leave a message and get them to get back to you” [GP7A]*

*“People are discharged from hospital without, with us not having any clue what was changed.” [GP11A]*

If a GP was not comfortable prescribing a medication issued originally by a hospital, it often proved challenging to explain this to the patient. In some instances, patients were not always content if the GP deviated from the hospital prescription.

*“we still take ultimate kind of control. If we don’t agree with them, we probably wouldn’t give them” [GP3A]*

*“sometimes I have some objections with the PPI [proton pump inhibitor], they pick or whatever, and, um, it is not always that easy to change that because the, the person will feel that I am, you know, that I am changing what another doctor has said” [GP4A]*

However, not all GPs interviewed have major concerns with hospital initiating medicines.

*“I suppose my view of hospital prescribing is I’m a double check on their prescribing” [GP10A]*

*“we normally would just follow whatever the hospital does. So, if they send out a prescription for a patient then we just obviously prescribe it, well, we’d look at it and make sure it goes on to their records, check in my own mind is there any reason why they shouldn’t have it, and then if I’m happy enough with it, we just prescribe it.” [GP12A]*

### **3.4.3 Clinical scenario used in the video**

The clinical scenario developed for specific use in the intervention video was received positively by GPs and described as clear and concise. The video was described as a good resource for teaching.

*“It was clear and concise and she explained the rationale behind stuff” [GP2A]*

*“very good teaching video” [GP8A]*



Some GPs however noted that that the scenario was not reflective of the majority of older patients who would visit their practices and that older patients often have more complex healthcare needs, in comparison to the simulated patient shown in the video.

*“So the ones that we would’ve on lots of medications are those with, hypertension, heart failure, arthritis, diabetes, maybe cardiovascular disease. So it would be less easy to reduce some of those medications than this example” [GP1A]*

*“I don’t think in real life a lot of patients necessarily would buy in just the same as that gentleman did” [GP10A]*

*“we would have a lot more complex, especially as patients get older” [GP12A]*

Whilst some GPs suggested that the clinical scenario and the patient needed to be more complicated, only a couple of GPs suggested a possible scenario for this

*“Yeah an option of you know dealing with the more tricky scenario maybe... especially now this flu season you know so you get a typical old man with a significant past smoking history, with chronic lung disease, and he’s come in, start of a cough, he’s bringing out green phlegm, vitals are still fine, and you listen to the chest, you know? Chest is relatively clear. But you know this patient, you know he has a bad chest, he’s probably going to end up with some, anyway you have to treat that kind of patient” [GP8A]*

*“I think a patient with chronic disease is useful, so your diabetic, your COPD patients you know, for example, would you give, can your COPD patient get a beta-blocker, for example, em, so things like that really. On a beta-blocker, is it making the COPD worse? So you can, you could have a series of patients with multiple co-morbidities because obviously, every patient on multiple meds has multiple co-morbidities, so you’re looking at, is this making this worse? So, you know, so you see your diabetic patient, do you put him on steroids for example because that is going to make his diabetes worse. So, if you had more complex patients, I think that would be helpful” [GP12A]*

The interaction between the GP and the simulated patient in the video was well received by all GPs.

*“all you want is something to show you that it is worthwhile going through, and it’s nice to see his reaction at the end, and the GP felt a bit satisfied” [GP4A]*

*“Aww no it is realistic yeah she’s a good communicator” [GP6A]*

Also, one GP discussed the difference between patients receiving free medical care and medicines from the NHS, and patients in the RoI who often pay for certain primary care services including medicines. This GP felt that patients in the RoI expect a more personalised service in comparison to patients in the NI, and therefore it could potentially be easier to change prescriptions in NI.

*“He was quite happy just to take her advice... you can intervene more easier [sic] with NHS patients than people who are coming in and having to pay €50”* [GP5A]

#### **3.4.4 Engagement with, and length of the video**

The video shown to GPs in phase 1 lasted just short of 12 minutes (including title and ending slides and relevant information). It was deemed appropriate by most GPs and the length was representative of a normal GP/ patient consultation, which GPs highlighted as an important aspect.

*“I thought it was excellent, it was the right time length”* [GP6A]

*“If it was shorter, I think it would be too fake, like it wouldn’t be real”* [GP7A]

*“I think if you are talking about something like that, it needs to be the same as a consultation would be”* [GP4A]

However, one GP stated that the length of the video was too long to ask GPs to view.

*“It would be a bit too long... GPs and doctors we’re not renowned for our focus!”*  
[GP11A]

Referring to the need to watch the video throughout an intervention study, GPs stated they would only need to watch the video once at the start of the study, as the video only included one clinical scenario. One GP noted watching the video biannually if the clinical scenario surrounding polypharmacy had changed would be beneficial. GPs believed they would refer to a video more frequently if there were several clinical scenarios provided.

*“You wouldn’t want to see the same one every time... I would like a different scenario, but only one scenario at a time... six months is okay”* [GP4A]

*“But why would they need to pop into a video that’s the same each time?”* [GP1A]

Two GPs noted that if they agreed to participate in an intervention study, that the research team should be able to clearly explain to GPs what is required from them to participate in the study.

They should be aware of the key points of the study and therefore access to the video throughout the intervention may not be required.

*“Nah, I don’t think it would make a big difference, no. Hopefully, once you’ve seen it once, once you’ve enrolled, you’d be aware of what you are doing” [GP12A]*

#### **3.4.5 Explicit plans and weekly meetings within the practice**

GPs were asked their thoughts on making plans at weekly meetings with practice colleagues to ensure that older patients who met the inclusion criteria would be invited to the GP practice for a medication review. The consensus was that weekly meetings would be hard to implement in the practice, mostly due to the time required to schedule and have the meeting.

*“some practise don’t always have the same structures or time for meetings or they may not have practise managers. Or there may be smaller single handed practices, so I think that would need to be taken into consideration” [GP1A]*

*““Yeah it could be quite time consuming. Of course its completely right thing to do and it makes sense” [GP6A]*

*“it wouldn’t be weekly meetings, it would be monthly, you know?” [GP8A]*

#### **3.4.6 Practice staff providing prompts to GPs**

Most GPs discussed that the practice would use their software to inform them that the patient had arrived at the practice for their scheduled medication review, as part of the intervention.

*“I think our software; most of us have software that allows us to this [sic] in ourselves and I think if the software was used properly, we shouldn’t need any prompts” [GP4A]*

*“It’s probably not that hard to implement having the having all the information on the computer so it’s really easy to actually find” [GP5A]*

They also added that if the study required reception staff to inform the GP that the patient has arrived at the practice for their scheduled medication review as part of the PolyPrime study, that it would not be a difficult process to implement in GP practices.

*“Be very easy to organise” [GP9A]*

*“Absolutely in this practice, and in most of the practices I’ve worked in, the reception staff are an essential component of making things work and happen, and they already*

*do, the girls will just say to me, remind, remember [GP] that's, they'll hand you the..."*  
[GP11A]

### **3.4.7 Potential enablers to intervention implementation**

GPs mentioned the addition of guidelines and validated assessment tools, such as STOPP/START (O'Mahony *et al.* 2015) and NO TEARS (Lewis 2004), to assist in the medication review process, as potential enablers to intervention implementation. Educational resources and up-to-date evidence of the most over-prescribed medicines were also suggested.

*"Possibly STOPP/START thing, you know. Just for meds"* [GP3A]

*"links to guidelines"* [GP10A]

*"A little bit more academics... a few of the commonest examples of over-prescribing"*  
[GP4A]

Separate study information for practice staff (in comparison to study information the GP would receive) and a patient recruitment poster, that could be displayed in the waiting room, informing patients about the study, were suggested as potential enablers by one GP.

*"posters in the waiting room, about polypharmacy"* [GP6A]

*"a simple pack that would say this is what you should be doing this is how you do it! This is the purpose of it"* [GP6A]

Two GPs also noted that pharmacists would be a potential enabler in an intervention on appropriate polypharmacy, including specific communication with their local pharmacy.

*"I would consider bringing in pharmacists at a stage in this"* [GP11A]

*"communication with pharmacists would be useful"* [GP12A]

### **3.4.8 Potential barriers to intervention implementation**

The time of year in which the intervention would be conducted, the lack of available time for GPs to take on extra work and potential lack of interest/ resistance from both GPs and patients to participating in an intervention on prescribing appropriate polypharmacy were considered potential barriers to implementation of the developed intervention.

The timing of the intervention delivery (i.e. conducting the medication review consultations) was of concern to some GPs interviewed, but not all. Those with concerns stated that it would

be difficult to implement an intervention during the winter months, as general practices have an increased workload, likely due to the increase of winter diseases, such as colds, flu.

*“I think in the winter months, it’s just too difficult”* [GP5A]

The majority of GPs stated that the lack of time available will be a significant barrier to GPs participating in the PolyPrime study.

*“time is the biggest issue”* [GP1A]

*“Time is what everyone is going to say to you”* [GP4A]

*“we just don’t seem to have the time would be what everyone would say to you!”* [GP9A]

Three GPs stated the extra work that would be involved in conducting specific medication reviews as a potential barrier to implementing the intervention.

*“even if I was prompted even if somebody went ahead and had like three quarters of the box is ticked – the chord that I would have to take takes up more time than I have to offer usually”* [GP11A]

*“it probably will create a certain amount of extra work, but it shouldn’t be huge”*  
[GP12A]

However, GP12A followed the above by stating that the extra work involved at the beginning could potentially level out over time.

As shown in Table 3.2 above, GPs from rural practices were interviewed and some discussed having small numbers of healthcare support staff, such as a practice nurse, meaning that GPs addressed all patient primary healthcare needs including performing blood pressure readings, changing dressings or taking blood samples.

*“we’re fairly primitive in what we’ve got there ‘cos there’s just basically a doctor doing everything... everything’s done by the doctor, all the vaccinations”* [GP5A]

The final potential barrier to intervention implementation was the possible resistance to participate in the study from both GPs and patients. GPs interviewed believed that as they are already extremely busy, i.e. have a lack of time available (as mentioned above), GPs may show some resistance to participating in an intervention involving medication reviews as this requires extra work.

*“just mentally exhaustion... actually just been blooming bothered to do it”* [GP5A]

It was mentioned by a few GPs that patients may also put-up resistance to having their medications changed or stopped, even though it would be for their benefit.

*“lots of patients probably may not wish to, err, come in for more frequent consults equally, err, they may not want to, you to touch their medicines, medications. Lots of elderly patients are very fearful of that”* [GP4B]

*“I mean there would be resistance from some patients to – having medicines stopped, some people like to take tablets and medicines”* [GP6A]

### **3.4.9 Modifications required to the intervention**

GP suggestions on how to improve the intervention were often duplicated as potential enablers to intervention implementation. Direction to validated assessment tools and prescribing guidelines, including up-to-date evidence on medications, as well as more available time for the GP were mentioned.

*“evidence-based medicine, maybe 5 or 10 bullet points”* [GP1A]

*“tools you can use with medication, you can use a, like a, STOPP/START... not all GPs are fully aware of them”* [GP2A]

*“you could use one of the algorithms for it... NO TEARS”* [GP8A]

Few GPs also highlighted that an alert from their computer software, reminding them to conduct a medication review with a patient, could be useful and may likely lead to medication reviews being more commonplace in their practice.

*“I click into someone’s file that something would flash to say medication review and then you would think of it and then be more likely that it would happen”* [GP6A]

In general, the GPs found the intervention plausible, noting its relevance and were positive about the study.

*“I think, yeah, it is a good, good study”* [GP4B]

*“I applaud what you are trying to do – and I think it’s a good thing. And certainly, anything that would benefit the patients in the long run”* [GP11A]

*“I think it’s fantastic, yeah. It’s something we really should be doing”* [GP12A]

GPs also believed that the intervention would be useable within RoI practices.

*“probably fit into most practices”* [GP5A]

*"I think it's easy done like in my point of view would be very easy done [sic], I would've no problem bringing in – not at all" [GP8A]*

### **3.5 Discussion**

As discussed in chapter one, the PolyPrime intervention was developed in NI. As a result, further exploration of the intervention and the components involved was required to assess if any refinements were required before implementation in a cross-border cluster pilot cRCT. Phase 1 of the PolyPrime project (presented in this chapter) aimed to test the theory-based intervention in a different healthcare context to which it was developed (i.e. testing it in the RoI) and to refine the intervention if necessary. Resulting from the interviews, minor additions to the intervention package were suggested based on semi-structured interviews conducted with 13 GPs along the border counties in the RoI. Based on the recommendations arising from the interviews, refinements included the addition of educational references such as guidelines, and prescribing guidance, provided in the form of validated assessment tools. The findings from this study emphasise the importance of embedding refinement procedures into interventions developed in a different healthcare context, before using an intervention in a new healthcare context to which it was developed. The sections that follow discuss GPs understanding of polypharmacy, the video component of the study, amendments to the intervention and recruitment to the study. The strengths and limitations of the study are discussed prior to the conclusion.

#### **3.5.1 GPs understanding of polypharmacy**

A systematic review by Masnoon *et al.* (2017) found that the most common definition of polypharmacy was the numerical threshold of five medicines or more. However, only three GP used this definition when asked to define polypharmacy. What is similar between the systematic review and the GPs definitions of polypharmacy is the range of definitions. Whilst GPs in this study were perhaps conservative with their definitions of polypharmacy with the largest threshold being five, in comparison to some definitions of polypharmacy in the literature, such as 10 or more medicines (Greiver *et al.* 2019). Recently, there has been a shift in the understanding of polypharmacy to mean that it is about getting the balance of medicines right. Some GPs acknowledged that it is important to understand the patient and their needs, and this comes into play when prescribing polypharmacy and therefore a definition is not necessarily just about the number of medicines prescribed.

#### **3.5.2 Video component of the PolyPrime intervention**

The video component of the intervention was well received by GPs, however, the clinical scenario was considered to be “simplistic” by some GPs. As people get older, the number of chronic diseases they have often increases in tandem (van den Akker *et al.* 1998, Salisbury *et al.* 2011, Atella *et al.* 2019) which can lead to challenges in appropriate prescribing (Cahill 2015).



The PolyPrime project aims to support GPs with this challenge. The GPs interviewed perceived prescribing and deprescribing [the process of withdrawal of an appropriate medication, supervised by a healthcare professional with the goal of managing polypharmacy and improving outcomes (Reeve *et al.* 2015)] to be a complex process which some believed was not presented in the video. This finding was discussed within the research team (which included two senior academic GPs who contributed to the development of the video), and it was felt the video still accurately portrayed how GPs can begin to deprescribe. For example, the GP provides the simulated patient with information on a medication she wishes to deprescribe, and he is able to think about this. The interviewees noted that patients might show resistance to having their medications altered or stopped, yet evidence suggests that patients are likely to support reducing the number of medications they are prescribed (Reeve *et al.* 2013, Galazzi *et al.* 2016). The length of the clinical scenario, at just under ten minutes, was considered to be appropriate by the participants and reflective of the length of a typical consultation with a patient in RoI. The entire video totalled at just under 12 minutes, which is shorter than the average duration of a GP consultation in the RoI, at 14.1 minutes (Pierse *et al.* 2019).

As only one clinical scenario was developed for the intervention, GPs stated that it was unlikely they would re-watch the same video during an intervention delivery phase. GPs would be more likely to watch videos throughout the intervention delivery phase if the clinical scenarios used varied. GPs felt that as the intervention only contains one clinical scenario, access to the video throughout the intervention may not be necessary. However, the research team decided to allow GPs assigned to the intervention arm access to the video throughout the intervention due to the modifications that have occurred as a result of the interviews. The video component now contains appropriate prescribing tools and educational materials which GPs may find useful during the intervention delivery phase. The additions to the intervention are discussed below.

### **3.5.3 Amendments to the intervention**

Numerous amendments were made to the intervention as a result of data from the 13 interviews. Educational slides have now been added to the video (see Appendix 3.15), which are shown after the clinical scenario. Website links to prescribing guidelines have been added to the webpage that supports the intervention video as, due to copyright issues, it was not possible to embed the prescribing guidelines into the actual video. The educational slides include information on commonly encountered instances of potentially inappropriate prescribing (PIP) in older people. The top five most common instances of PIP prescribed in the RoI (Moriarty *et al.* 2015) and NI (Bradley *et al.* 2012a) were compiled into one list for the video. This information

was based on studies undertaken by various members of the research team. It was felt that inclusion of this information in the video may encourage GPs allocated to the intervention arm, to specifically check if patients are prescribed a medication on that list, and review accordingly. Common instances of PIPs on the list provided include long-term use of benzodiazepines, tricyclic antidepressant with opioid or calcium channel blockers and proton pump inhibitors at maximum therapeutic dosage for over eight weeks. Guidelines from the ICGP and NICE were added as website links to the video component. NICE guidelines can be followed and applied to general practices in the ROI, even though they were not developed for specific use within the Irish context i.e. Health Service Executive; and similarly, GP practices in NI can follow guidelines issued by the ICGP. Guidelines added to the video component include: ICGP guidelines on repeat prescribing (Bradley 2013), ICGP quick reference guide on conducting a medication review (ICGP 2020) and NICE guidelines on medicines optimization (NICE 2019a).

Validated assessment tools for GPs to use during the scheduled medication reviews with their older patients were also added to the video component of the intervention (Appendix 3.16). Tools added were STOPP/START (O'Mahony *et al.* 2015) and NO TEARS (Lewis 2004) as these were the tools most commonly mentioned during the interviews. STOPP/START has performed better in detecting potentially inappropriate medications in comparison to other validated assessment tools, such as Beers' Criteria (American Geriatrics Society 2015) and has been used in several randomised controlled trials aimed at improving prescribing in this cohort (Karandikar *et al.* 2013, Boland *et al.* 2016, Brown *et al.* 2016). NO TEARS, a mnemonic tool, is explicitly designed to prompt GPs to key prescribing areas during a medication review. These areas include the need for, indication on, monitoring, evidence, adverse events, prevention, and simplification. NO TEARS has been promoted as a tool for nurses to use as a framework to explore patients' medicines (Kaufman 2016) and included in the NHS Clinical Medication Review (2014). As part of a comprehensive geriatric assessment, the British Geriatrics Society support the use of validated assessment tools, specifically NO TEARS, as a recommended reference tool (British Geriatrics Society 2019).

A single A4 sheet providing separate information for practice staff (Appendix 3.17) was also added to the material provided to practices in the intervention. Information on the sheet includes an overview of the study, patient inclusion/ exclusion criteria and tasks the practice staff are required to complete as part of the intervention, such as, scheduling patients' medication reviews and prompting the GPs to conduct a medication review as part of the PolyPrime project when the patient arrives at the practice for their scheduled review. A patient recruitment poster (Appendix 3.18) was designed for display in the waiting area with interested

patients directed to ask the reception staff for more information on the study. This is in addition to the formal recruitment procedures which involved the practice manager and research nurse screening the practice database for eligible patients.

It was recommended by two GPs interviewed that the addition of pharmacists in the intervention would be useful. Pharmacists in countries such as Australia, Canada and the United Kingdom (UK) have a wider role and more responsibility in primary care than pharmacists currently do in the RoI. Pharmacists prescribe in emergency situations (allowed to prescribe the minimum quantity of the medicine necessary to allow for the patient to visit a prescriber) and conduct medication use reviews in Australia (Roughead *et al.* 2009, Castelino *et al.* 2010, Law *et al.* 2012). They can adjust patient's prescriptions (such as altering the dose) in Canada (Tannenbaum and Tsuyuki 2013) and appropriately qualified pharmacists can independently prescribe medications in the UK (Avery and Pringle 2005, Weiss *et al.* 2015). The UK has also introduced pharmacists based in GP practices with great success. Their responsibilities include conducting medication reviews, and consulting patients with polypharmacy and medicine reconciliation after hospital discharge (Williams *et al.* 2018). A pilot study has been conducted by Cardwell *et al.* (2020) on including pharmacists in general practices within the RoI and found the integration of pharmacists in general practices to be feasible, with potential clinical and cost benefits. Practice based pharmacists have been implemented in primary care in NI and often have additional qualifications to community pharmacists as qualified independent prescribers (Ibrahim *et al.* 2022). If pharmacists were to be included in the PolyPrime study it is possible that practice-based pharmacists would be included for practices in NI, and not community pharmacists. Whilst practice-based pharmacist is not currently implemented in general practice in the RoI, pharmacists often inform the prescribing GP if they have concerns regarding the medication or dose prescribed, for example. The collaboration between pharmacist and GP, regardless of community or practice-based, shows that prescribing is a complex process and can involve multiple healthcare professionals sharing their expertise. PolyPrime was developed as a behaviour change intervention for GPs in order to conduct medication reviews as part of routine consultations. However, future research is required given the change in the initial education and training of pharmacists. These changes mean that pharmacists graduating from UK Schools of Pharmacy accredited by the Pharmaceutical Society of Northern Ireland and/or the General Pharmaceutical Council, will be qualified to prescribe from 2026 (General Pharmaceutical Council 2021).

#### **3.5.4 Recruitment**

This intervention refinement study shows that it is important to be flexible when recruiting participants (within the scope of recruitment strategy defined in the protocol). The desired number of twelve practices was successfully recruited for the study, however, the anticipated two practices per county was not achieved. It was highlighted during the recruitment process that many practices within the six border counties were single-handed practices (i.e. only one GP working in the practice). The original protocol stated single handed practices were not eligible to take part, with the intention of recruiting two GPs per recruited practice. A protocol amendment, approved by the SoPPS Research Ethics Committee, TCD, allowed for single handed practices to be included. Over-recruitment in other counties within the defined area of the project was undertaken following discussions within the research team. This was to ensure the target of 12 practices was met and to compensate for lack of recruitment in other counties (i.e. Louth).

#### **3.5.5 Strengths and limitations**

The outputs of the study are not compromised by the lack of representation of all six border counties in the RoI. As noted above in the methods section of this chapter (section 3.3.1), there is ongoing debate on adequate sample sizes within qualitative research with recommendations ranging from less than 20 interviews (Crouch and McKenzie 2006) to 150 interviews (Gerson and Horowitz 2002). This study has shown that under 20 interviews can be sufficient to reach data saturation. Data saturation should be the goal when discussing sample size, as opposed to a numerical threshold, as demonstrated here that even though an objective of the study was to recruit up to 24 GPs, data saturation was still met after interviewing 13 GPs.

This study follows recommendations by the MRC in the development of complex interventions (Craig *et al.* 2008) by using a theoretical basis in the development of the intervention, and thus enhancing the rigor of the study. Refinements have been made to the existing intervention package due to the findings arising from this study. Refinements to the interventions, based on the suggested changes, did not change the fundamental theory underpinning the intervention and were primarily focused on providing more clinical education, academic references and prescribing guidance for GPs. However, it is noted that not all suggestions were taken on board due to differences in the primary care set up in NI and the RoI (for example, practice-based pharmacists in NI), and input from two senior academic GPs. This study supports previous evidence suggesting that there is little difference between general practices in the RoI and NI

(Cupples *et al.* 2008). The refined intervention package will be used in the larger cross-border pilot cluster randomised controlled trial, the PolyPrime study.

### **3.6 Conclusion**

In conclusion, a refinement procedure was necessary to address any potential differences between the healthcare systems within the ROI and NI, as the intervention was developed in NI following interviews with GPs in NI. A number of minor amendments were made to the intervention, including the addition of educational resources, prescribing guidelines and validated tools that GPs can refer to while undertaking a medication review. As a result of the refinement process, the intervention is now ready for testing in both the ROI and NI in a pilot cRCT.



## **Chapter 4**

**A pilot cluster randomised controlled trial of a theory-based intervention to improve appropriate polypharmacy in older people in primary care: the PolyPrime study**

## 4.1 Introduction

The development of the PolyPrime study was presented in the Introduction chapter, section 1.8. As it was developed in NI, a process of intervention refinement was undertaken, as described in Chapter 3, to ensure its suitability for testing in a pilot cRCT involving two different healthcare jurisdictions, NI and RoI. This chapter focuses on the processes involved in undertaking a pilot cRCT (phase 2 of the PolyPrime study), and the process evaluation of the pilot cRCT (phase 3).

A pilot study, defined in Chapter 1, section 1.7.3, is recommended by the MRC Framework for complex intervention development to identify potential issues in the intervention such as acceptability, compliance delivery of the intervention, and recruitment and retention for example (Craig *et al.* 2008). The main purpose of a pilot study is to examine the feasibility of an approach that is intended to be used in a larger scale study, such as a RCT (Leon *et al.* 2011). It is important to note that pilot studies are not powered to show effect as the limited sample size in a pilot study can lead to an unrealistic result (Thabane *et al.* 2010). Reasons for conducting a pilot study prior to a definitive RCT are shown in Box 4.1 below.

### **Box 4.1 Reasons for conducting a pilot study (adapted from Thabane *et al.* 2010)**

- Assess recruitment, retention and refusal rates
- Check if the inclusion/exclusion criteria are sufficient
- Measure if data collection tools are fit for purpose
- Determine if the intervention processes are acceptable to key stakeholders
- Calculate sample size for a definitive RCT

RCT = randomised controlled trial

As noted in Chapter 1, section 1.7.3, there can be discrepancy between the terms ‘feasibility’ and ‘pilot’ study. Some people suggest the terms are synonymous and interchangeable (Arnold *et al.* 2009, Arain *et al.* 2010, Thabane *et al.* 2010), whilst others suggest each has a distinctive definition (Shanyinde *et al.* 2001, Donald 2018). A feasibility study should be followed by a pilot study before the intervention is implemented in a definitive RCT (Craig *et al.* 2008). RCTs are inferred as the ‘gold standard’ in intervention evaluation (Rychetnik *et al.* 2002) and it is recommended that research teams consider intervention refinement and development processes to ensure suitability of the intervention for a RCT (Campbell *et al.* 2007). Pilot RCTs are, therefore, an important aspect of intervention development as potential challenges can be identified, and feasibility can be assessed before full-scale implementation in an RCT (Feeley *et al.* 2009). Pilot RCTs help to establish if interventions can be used in a future definitive trial, such as an RCT (Bell *et al.* 2018).



A process evaluation is recommended by the MRC guidelines (Craig *et al.* 2008), as discussed in chapter one, section 1.7.3. A process evaluation is used to assess “fidelity and quality of implementation, clarify causal mechanisms and identify contextual factors associated with variation in outcomes” (Craig *et al.* 2008). Essentially, it aims to identify and understand the key processes and factors connected to successful knowledge translation in a particular setting, the relationship between these processes and factors (Rantsi *et al.* 2021) and the important aspects to pay attention to during implementation of the intervention (Proctor *et al.* 2010). Bonell *et al.* (2006) simplify this and write that process evaluations can be described in a single question, “is this intervention acceptable, effective, affordable and feasible?” and they can assist researchers in deciding if the intervention is worth progressing to an RCT, either as is or with modifications.

Process evaluations can be conducted before, during or after an intervention has been delivered, depending on the components the researchers are evaluating, and can involve a combination of different timepoints (Moore *et al.* 2015). It is common for process evaluations to follow a qualitative approach; however, some do include mixed methods or only quantitative methods (McGill *et al.* 2020). A systematic review of process evaluations by Scott *et al.* (2019) showed that qualitative methods are more commonly used in process evaluation compared to quantitative methods, with individual interviews utilised most often. Out of the 226 studies identified in the systematic review, the three most common time points to collect process evaluation data were post intervention (46%), pre and post intervention (17.7%) and, during and post intervention (12.8%). Examples of components that can be evaluated before an intervention begins included assessing how groups of potential participants are sampled and recruited, as well as who agrees to participate in the intervention. These can be evaluated by assessing recruitment numbers recorded by the research team as well as comparing the information available regarding the recruited and non-recruited groups (Grant *et al.* 2013). Other examples of possible components to evaluate, where this might occur (such as before, during or after an intervention) and their methods are shown in Table 4.1.

**Table 4.1 Possible process evaluation components, the stage of intervention best to collect the data, the research question and recommended methods (adapted from Grant *et al.* 2013)**

Component	Stage of intervention			Research question	Research method
	Before	During	After		
Context	✓	✓		What is the wider context in which the trial is being conducted?	Qualitative – interviews Data collection from policy documents
Fidelity		✓	✓	What form of the intervention is actually delivered?	Qualitative – observational, interviews
				Is the delivered intervention the one intended by the researchers?	Quantitative- measurement of intervention actions
Unintended consequences		✓	✓	Are there unintended changes in the outcomes both in relation to the intervention and the control?	Qualitative – observational, interviews Quantitative – use of routine dataset
Theory			✓	What theory has been used to develop the intervention?	Quantitative – use of framework to assess
Recruitment		✓		Is the recruitment method appropriate?	Qualitative – interviews Quantitative - questionnaire
Retention		✓	✓	Do patients stay for the course of the study?	Quantitative – number of participants who dropped out
Ability to collect outcome data		✓	✓	Can the necessary data be collected to answer outcomes	Quantitative – study data collection forms

A process evaluation is used to monitor and document intervention implementation and can assist researchers in understanding the relationship between certain intervention elements and outcomes (Saunders *et al.* 2005). Many process evaluation frameworks have been developed, some specifically for particular healthcare interventions and contexts, whilst others have been adapted from established theories (such as the Theory of Change). Previous versions of the MRC guidelines for developing and evaluating complex interventions discussed process evaluations and the benefits of inclusion in an intervention but did not provide recommendations on specific methodologies that should be adopted to undertake process evaluations (MRC 2000; Craig *et al.* 2008). Process evaluations have gained recognition and are now considered an important aspect of an intervention with specific guidance now published (Moore *et al.* 2015, Skivington *et al.* 2021). There are numerous frameworks utilised by researchers to conduct process evaluations, some are theoretically based, and some are developed by the interventions research team. What remains clear is that assessing the quality and usefulness of process evaluations is not straightforward due to the variability in methodology and of the intervention

being tested (Oakley *et al.* 2006, Grant *et al.* 2013). However, it remains an important aspect of research and study development, as does conducting a feasibility study prior to a pilot study.

A feasibility study was previously conducted in NI, and findings published in three peer reviewed journals (Cadogan *et al.* 2015, Cadogan *et al.* 2016, Cadogan *et al.* 2018). Chapter 3 presented the findings of the refinement of the work conducted by Cadogan *et al.* (2018) which resulted in amendments to the intervention. Notably, these included additions to the video component such as key issues for the prescriber to consider when conducting a medication review and guidelines that GPs could consult. The main design of the video remained unchanged as it incorporated BCTs demonstrating how GPs can prescribe appropriate polypharmacy (primarily focusing on reducing unnecessary or inappropriate medicines) during a typical consultation with an older patient. A detailed description of the BCTs included in the video component is presented in Chapter 1, section 1.8. A pilot cRCT, the second phase of the PolyPrime study was conducted between two jurisdictions: NI and the RoI. This chapter presents the findings from the pilot cRCT undertaken in the RoI and reports the findings from the process evaluation of the pilot cRCT, regarding the intervention fidelity, acceptability of the intervention and the intervention's likely mechanisms of action.

## 4.2 Aim and objectives

### *Aim*

The overall aim of the study is to undertake a pilot cRCT of a theory-based intervention targeting prescribing of appropriate polypharmacy in primary care (PolyPrime) and assess the implementation of the intervention.

### *Objectives*

The objectives of this study are to:

- Test approaches to sampling, recruitment and retention of GP practices
- Test approaches to screening, recruitment and retention of patients
- Test the feasibility of using medication appropriateness (assessed using the STOPP/START criteria) as the primary outcome in a future cRCT
- Test the feasibility of patient reported questionnaires
- Further validate the Medication-Related Burden Quality of Life (MRB-QoL) tool
- Assess if the intervention was delivered and received as intended (intervention fidelity)
- Assess the acceptability of the intervention to patients, GPs and practice staff
- Identify the intervention's likely mechanism of action

### **4.3 Research design and methodology**

The methods section that follows will present the methods employed in the pilot cRCT and its process evaluation. The methods, data collection and results presented in this chapter were mostly conducted by the PhD candidate. Some aspects crucial to the project were conducted by subject matter experts such as pharmacists, and results subsequently compiled and reported on by the PhD candidate. The pilot cRCT was undertaken in both NI and the RoI. The PhD candidate was responsible for the pilot cRCT in the RoI and only data from the RoI is presented here. The protocol describing the methods employed in the pilot cRCT has been published in *Pilot and Feasibility Studies* (Rankin *et al.* 2021a), and the protocol for the process evaluation was published in *Trials* (Rankin *et al.* 2021b), trial registration number NCT04181879. Both qualitative and quantitative methodologies were employed throughout the pilot cRCT and the process evaluation. Qualitative methods have already been described in chapter 3, section 3.3.1, the next section will provide an overview of quantitative methodologies relevant to undertaking a trial. The exact methods employed in the PolyPrime pilot cRCT will then be presented including the sampling and recruitment strategy, data collection, and data analysis.

#### **4.3.1 Quantitative research**

Key considerations when undertaking quantitative research within a trial are presented here including sampling, data collection and analysis methods, statistical significance, reliability and validity of the data.

##### *Sampling*

A sample is a subset of the population being studied and is often chosen based on a probability approach (a sample selected using random selection so that each member of the population has a known chance of being selected) or a non-probability approach [not selected using a random sample, some members of the population have a higher chance of being selected (Bryman 2016)]. Box 4.2 shows an overview of common types of probability sampling including simple random sampling and cluster sampling. Box 4.3 presents two common types of non-probability sampling: convenience and quota sampling. Often the decision of which sample method to use can be dictated by the time available to recruit participants, the money available to spend and the anticipated sample size for the study. In convenience sampling, participants are chosen

based on their convenience to the researcher. Quota sampling aims to have a sample where the groups being studied are proportional to the population being studied (Sharma 2017).

#### **Box 4.2 Types of probability sampling**

##### **Simple random sampling** (Bryman 2016)

- Each unit of the population has an equal chance of inclusion
- Each unit of the population allocated a number – numbers chosen randomly, often by a computerised number generator
- Possible to make generalisations from the results to the entire population
- Little room for human bias

##### **Cluster sampling**

- Naturally occurring groups are selected as samples (Sharma 2017)
- Allows for researchers to be more geographically concentrated if collecting data in person
- Can lead to overrepresentation of outliers – if the cluster chosen to participate has a biased opinion, then the entire population can be inferred to share this opinion which may not be representative of the population

#### **Box 4.3 Types of non-probability sampling**

##### **Convenience sampling**

- Sample drawn from group of people easily accessible to the researcher e.g. geographical proximity, availability at given time, easy accessibility (Etikan *et al.* 2016)
- Only generalised to population in which sample was taken from, if randomly selected (Andrade 2021a)
- Not costly, and less time consuming than other sampling strategies (Stratton 2021)
- Considered to lead to more bias than other forms of sampling (Mackey and Gass 2005)

##### **Quota sampling**

- Similar to convenience sampling but likely to include people underrepresented via convenience sampling (Im and Chee 2011)
- Population divided into strata based on gender or age for example. The type of strata is decided based on the area being investigated. The number of people in each strata is often determined by referring to external data such as the census and will reflect the population. The researcher will choose people to participate (Yang and Banamah 2014, Bryman 2016), often comparable with convenience sampling if the most accessible people are chosen (Lohr 2010, Górný and Napierata 2016)
- Only non-probability sampling method most likely to produce results similar to probability sampling methods (Brick 2011)
- Cheaper compared to probability sampling methods (Yang and Banamah 2014)

Sample sizes in research studies vary depending on the characteristics of the population being studied, the type of analysis that will be used and the need for results to be generalizable to the entire population or not. Regardless, it is important that the sample size represents the population being studied (Choi and Tran 2016). A sample size is necessary to determine the number of participants required to show a clinically relevant treatment effect (Noordzij *et al.* 2010) and should be calculated based on the desired primary outcome in a study. Depending on the type of study, formal calculation of sample size is not necessary, for example, a feasibility or pilot study do not require a formal sample size calculation, as the aim of these studies are focused on acceptability of the intervention being tested, and other study parameters, such as study outcomes (Eldridge *et al.* 2016b). It is common practice for the effect size [‘a quantitative reflection of a magnitude of some phenomenon that is used for the purpose of addressing a question of interest’ (Kelley and Preacher 2012)] between intervention and control arms in a pilot study to inform parameters for a sample size calculation in a full-scale study.

#### *Data collection and analysis*

There are many forms in which to collect data in quantitative research with the two most common methods being structured interviews and self-administered questionnaires. Structured interviews differ from semi-structured interviews (discussed in chapter 3, section 3.3.1) in that they must follow a specific format. Having the interviewer ask questions exactly as written and in a particular order reduces error due to the lack of variation in asking questions and often makes the processing and analysis of responses easier (Bryman 2016). Due to the defined manner which structured interviews must follow, there is no room for probing. Interviewers can repeat the question and the list of answers provided. This might occur in some circumstances, such as, if a pre-defined list is provided as potential responses to specific questions, and the answer provided by the participant does not appear on the pre-defined list. An example of a structured questionnaire is that used by The Irish Longitudinal Study on Ageing (TILDA) whereby the same questions are asked to each participant. The type of data collected here ranges from physical and cognitive health to medication use (TILDA 2022).

Self-administered questionnaires are those which are provided to the participant, and they read the information/questions and complete the questionnaire unaccompanied. Questions must be easy to understand as often there is no member of the research team present to answer any queries or explain the question. Closed questions (i.e., where a list of options is provided for the participant to choose from) are common in self-administered questionnaires. Self-administered questionnaires are inexpensive and quick to administer. A downside to self-administered questionnaires is that additional data cannot be collected once the questionnaire has been

completed, so it is recommended to trial the questionnaire to ensure that the necessary and required data is being collected. An example of data that can be collected via a self-administered questionnaire is quality of life data. Participants can complete a quality of life tool, such as the EQ-5D-5L (see section 4.3.5 for description) independently of researchers.

Analysis of quantitative data is determined by the type of data collected, such as if the variable is classified as nominal, ordinal or interval (see Box 4.4 for descriptions) and the size of the sample. There are two types of tests: parametric and nonparametric tests that are used in statistical analysis. Parametric tests assume a normal distribution of values [i.e., data is distributed either side of the mean forming a bell shape if presented on a graph, calculated using Shapiro-Wilk test (Krithikadatta 2014)] (Chin and Lee 2008). There are many types of parametric tests including regression [how the average of one variable systematically varies according to the levels of another variable (Gordon 2015)] and correlation [a measure of the monotonic association between two variables, i.e., as one variable changes so too does the other (Schober *et al.* 2018)]. The choice of test depends on the type of data and the research question that the data needs to answer. Examples of these are shown in Table 4.2 below.

#### **Box 4.4 Description of nominal, ordinal and interval variables**

**Nominal variable** - also known as a categorical variable, will have two or more categories but these cannot be rank ordered.

Example: classifying participants of a survey based on the county they live in.

**Ordinal variable** – like a nominal variable, an ordinal variable will have two or more categories however the categories can be rank ordered and the distances between the categories are not equal.

Example: level of education attained. This could be primary school, secondary school, university undergraduate, university postgraduate. The number of years in each varies, hence the categories are not equal.

**Interval variable** – also known as a numerical variable, similar to an ordinal variable except that the distances between the categories are equal.

Example: temperature measured in Celsius or Fahrenheit. The difference between 10° and 15° is the same as the difference between 20° and 25°.



**Table 4.2 Examples of parametric tests**

Type of test	Example of statistical test	Definition of statistical test	Interpretation of result	Example of research question
Regression	Linear regression	Used to model the relationship between one dependent variable and one or more explanatory variables (Maravelakis 2019)	Scatterplot – if results grouped together and in a diagonal line = positive relationship	Does a higher level of education result in a higher income?
Correlation	Pearson's <i>r</i>	Measures the relationship between two random variables and is adopted when the data follows a normal distribution (Rovetta 2020)	Number between -1 and +1. A correlation of =1.00 is a positive relationship (as one increases so does the other), correlation of -1.00 is a negative relationship (as one value increases, the other decreases). Correlation of 0 = no relationship.	What is the correlation between education and age when first married?

Normal distribution = distribution of results represents a bell shape (Krithikadatta 2014)

Non-parametric tests can be used with samples where normal distribution did not occur, or when the distribution is skewed to one side (Gomm 2008). There are numerous non-parametric tests that can be used to analyse data, depending on the type of data being analysed. Two examples of non-parametric tests, Mann-Whitney and Kruskal-Wallis are presented in Table 4.3 below.

**Table 4.3 Examples of non-parametric tests**

<b>Example of statistical test</b>	<b>Definition of statistical test</b>	<b>Interpretation of result</b>	<b>Example of research question</b>
Mann-Whitney	Assesses if there is a difference between two samples (Harris <i>et al.</i> 2008)	The U value and the significance value will determine statistical significance	Is there a statistically significant difference between the ages of men and women who participated in the trial?
Kruskal-Wallis	Used to analyse if there is a difference in median values of 3 or more samples, i.e. is there a difference between samples (Nahm 2016)	The <i>H</i> value (or chi-square value in SPSS). The significance value is also important. It is helpful to produce a boxplot to visualize results (Field 2006).	Examine the potential relationship between attendees of chair gymnastics, consumption of fruit and water intake in older adults.

*Statistical significance*

It is important to use the correct test when analysing quantitative data. An inappropriately chosen statistical test can lead to an incorrect outcome. Even with the correct test, a researcher cannot be certain of the outcome, instead, a level of confidence or statistical significance is reported. The common figure used to report statistical significance is 95%, i.e., the researcher can state with 95% certainty that variable A impacts variable B. This is often reported as the *p*-value and if the calculation of *p* is less than 0.05, it is safe for the researcher to assume statistical significance (Tenny and Abelgawad 2022). Due to a low replicability of some studies in areas such as psychology and the social sciences, there is an argument to decrease the *p* value threshold to 0.005 for statistical significance (Dreber and Johannesson 2019).

*Reliability and validity*

Reliability is the degree to which a concept is stable, i.e., the consistency of a measure (Heale and Twycross 2015). If a questionnaire for example, is to be considered to have strong reliability, it should result in little variation between responses over time. Different measures can be undertaken to assess the reliability of results, internal reliability and inter-rater reliability. Internal reliability – if indicators on scale are consistent i.e., if respondents score on one indicator are related to their scores on other indicators. The statistical test Cronbachs Alpha *α* is often used to determine internal reliability. A result of 1 shows perfect internal reliability and a result of 0 indicates no internal reliability. Often 0.80 is used as an acceptable level of internal reliability (Bryman 2016). Inter-rater reliability refers to the degree to which two or more

individuals agree about the coding of an item (Lange 2011). This is more likely to be an issue in qualitative content analysis when coding answers to open ended questions. The reliability of trial outcomes is important. Outcomes, such as patient reported quality of life, can be assessed via a questionnaire developed specifically for a trial or via an established questionnaire. A pilot study will help identify if the outcome measures are reliable (i.e. usable in a definitive trial) (Jones 2018a).

Also of importance in quantitative research is the validity of findings; validity is the extent to which a concept is accurately measured in a study (Heale and Twycross 2015). Forms of validity that are regularly calculated include internal validity and external validity. If variables have a strong internal validity, it proposes a causal relationship, i.e., that one variable causes another. This is often determined between a dependent variable (values which are influenced by other variables) and an independent variable [values which influence other valuables (Andrade 2021b)]. External validity proposes if the results of a study can be generalized beyond the specific research context in which it was conducted (Bryman 2016).

The above section provided a small insight into quantitative methods. The following section of the methods component of this chapter presents the methods employed in the PolyPrime study including sampling and recruitment strategies, COVID-19 related amendments, randomisation, data collection and data analysis.

#### **4.3.2 Sampling and recruitment strategies**

Ethical approval was granted by the ICGP on 23<sup>rd</sup> July 2019, and recruitment began end of July 2019 (Appendix 4.1). Different methods for recruitment of GP practices and patients were employed. The list of all 142 GP practices in the six border counties compiled for recruitment of GPs for phase 1, the study presented in Chapter 3, was utilised again to recruit general practices. This list contained all 142 general practices, organised per their county and numbered 1 -x, based on the number of general practices in each of the six counties. All 142 GP practice names were entered into a random number generator. The first 15 GP practices compiled in the random list per county were contacted in the first instance by the PhD candidate, who posted a brief overview of the PolyPrime study (Appendix 4.2), an expression of interest form (EOI) to complete (Appendix 4.3) and a prepaid addressed envelope to the practices. GP practices that were included in the qualitative interviews presented in Chapter 3 were not eligible to participate in the pilot cRCT. These practices were highlighted to distinguish them and ensure they would not be contacted. The aim was to recruit one general practice from each county. GP practices who had returned the expression of interest form were then sent an information pack

by the PhD candidate including an invitation letter (Appendix 4.4), a study information leaflet (Appendix 4.5), consent form (Appendix 4.6), Research Governance sign-off, Data Sharing Agreement and a GP letter of support. The research nurse working on the project, Connie Brennan (CB), contacted the general practices who had received this information to schedule a date for the PhD candidate to meet with the practice manager and/or lead GP to discuss their interest in the PolyPrime study and to sign the paperwork to confirm recruitment. GP practices that received an EOI letter but had not returned the reply slip were contacted by CB to gauge their interest and send an information pack if required.

After practices had been recruited by the PhD candidate (i.e. the PhD candidate had met with the GP practices and the necessary paperwork had been completed and returned), CB organised a site visit to screen for eligible patients. The aim was to recruit 10 patients from each practice who met the patient inclusion criteria: aged 70 years or over, prescribed four or more regular medicines, resident in the community, in receipt of a valid general medical services card, and who were registered with and/or regularly attended the practice for a minimum of 12 months. Residents of nursing homes, patients who had a terminal illness, were cognitively impaired, involved in other Investigational Medicinal Product or medicines management studies were not eligible to participate. The general practice manager, or equivalent, screened patient records with CB to identify and filter potentially eligible patients.

With assistance from practice staff, CB generated a list of patients eligible to take part and practice staff sent this to the lead GP for approval. The lead GP approved the list of patients to receive recruitment packs. These were assembled by the PhD candidate and CB prior to CB's visit to the GP practice, and handed over to the practice manager. The practice manager posted the recruitment packs in batches of 25, i.e. the first 25 patients on the list received a recruitment pack including an invitation letter (Appendix 4.7), a patient information leaflet (Appendix 4.8), two patient consent forms [one to return to AG and the other to keep for their records (Appendix 4.9)], health service use questionnaire (Appendix 4.10), EQ-5D-5L questionnaire (Herdman *et al.* 2011, Appendix 4.11) and Medication-Related Burden Quality of Life [MRB-QoL, Mohammed *et al.* 2018a (Appendix 4.12)] and a prepaid addressed envelope. The recruitment packs were to be posted in batches of 25 until either 10 patients had been recruited from the general practice, or there were no more eligible patients in the general practice to invite, whichever came first. Patients returned the necessary paperwork (i.e. consent form and questionnaires) to the PhD candidate and were assigned a unique ID code (for example, GPP21PT01 etc. where GPP indicated the GP practice and PT indicated the patient). A summary

of the sampling and recruitment roles conducted by the PhD candidate and CB are summarised in Table 4.4 below.

**Table 4.4 Summary of roles of PhD candidate and research nurse during recruitment process**

Task	Conducted by the PhD candidate	Conducted by the research nurse, CB
Brief overview and EOI letter sent to GP practices	✓	
Information pack sent to GP practices	✓	
Scheduled meeting		✓
Contact GP practices that did not return EOI		✓
Meet with GP practices and complete paperwork	✓	
Assemble patient recruitment packs	✓	✓
Site visit to screen for eligible patients		✓
Receive patient paperwork	✓	
Assign unique ID code to patient	✓	

CB= Connie Brennan EOI= Expression of Interest GP= General practitioner

#### 4.3.3 COVID-19 related amendments

Due to COVID-19, and the pressures on the health system throughout the island of Ireland, the decision was made to suspend the study on 13<sup>th</sup> March 2020, and therefore recruitment was also suspended at this time. Due to the ongoing presence of COVID-19, minor changes were made to PolyPrime study after discussions between the project management team and the trial steering committee (TSC). The TSC role in the PolyPrime intervention was to provide an objective assessment on progressing to a definitive cRCT and to oversee the conduct of the intervention. Specifically, the TSC monitored and guided the progress of the intervention, ensured compliance with scientific standards and the rights and safety of participants (Rankin *et al.* 2021a). The TSC comprised of an independent chair, two independent clinicians and one independent statistician; due to confidentiality individual names of TSC members are not presented here nor in any study output.

Minor changes made to the intervention resulting from COVID-19 included medication reviews taking place either face-to-face, in person or by video consultation (as opposed to just face-to-face). An ethical amendment was submitted to the ICGP and approved on 13<sup>th</sup> August 2020 (Appendix 4.13). Patients who had returned a consent form and questionnaires were contacted

regarding the changes made to the study (Appendix 4.14) and provided with an opt-in/opt-out form to complete (Appendix 4.15), accompanied by a prepaid addressed envelope.

The study recommenced in August 2020, however, the PolyPrime management team decided that no further recruitment would occur due to the pressure already placed on GP practices. It is also important to note that due to COVID-19, the timeline of the project altered. Three original timepoints for data collection were baseline, 6-months post initial medication review, and equivalent for control arm, and 12-months post initial medication review (equivalent for control arm), however, due to study suspension and funding limitations, 12-month follow-up had been shorted to 9-months. Numerous other ethical amendments were applied for throughout the course of the study, these are presented in Table 4.5 (ethical approval letters are in Appendices 4.16-4.19).

**Table 4.5 Information regarding ethical amendments and approval from ICGP**

<b>Date submitted</b>	<b>Date approved</b>	<b>Reason for submission</b>	<b>Overview of changes to study</b>
31 <sup>st</sup> July 2020	13 <sup>th</sup> August 2020	Study suspension due to COVID-19. Changes made to the original protocol and study timeline. Patients informed of these changes via letter and provided with an opt-in/opt-out reply slip.	Removal of 12-month follow-up replaced by follow-up at 9-months, the option to conduct medication reviews either face-to-face or via telephone, interviews with practice staff conducted via telephone, interviews with GPs conducted either face-to-face or via telephone. Patients provided with letter regarding study changes and an opt-in/opt-out reply slip. Approval of Serious Adverse Event (SAE) form and guidance document on how to complete SAE form.
20 <sup>th</sup> November 2020	25 <sup>th</sup> November 2020	Due to the study timeline adjustments, wording of patient questionnaires along with the accompanying letter required an update.	Change in study timeline reflected in: health service use diary distributed at 6 months, health service use questionnaire for use at 9-months, letter to all patients at 6-months, letter to patients in intervention arm at 9-months, letter to patients in control arm at 9-months, feedback questionnaire to patients in intervention arm and accompanying letter. Approval of topic guide for GP interviews and practice staff interviews (see Chapter 5 for more information)
30 <sup>th</sup> March 2021	21 <sup>st</sup> April 2021	Ethical approval required for letter to send to patients informing them of practice withdrawal and a patient opt-in/opt-out reply slip to return to the PhD candidate	Letter to patients and opt-in/opt-out reply slip approved
15 <sup>th</sup> June 2021	21 <sup>st</sup> June 2021	Withdrawn practice requested rewording of letter to patients informing them of withdrawal	Letter approved to inform patients of practice withdrawal
7 <sup>th</sup> July 2021	9 <sup>th</sup> July 2021	Identification of error in previously approved practice staff information leaflet	Correction to error in practice staff information leaflet (document in relation to data presented in Chapter 5)

#### **4.3.4 Randomisation and sample size**

GP practices were randomised to either the intervention arm or control arm by a Northern Ireland Clinical Trials Unit (NICTU) statistician using nQuery Advisor® software after patient recruitment had been completed. GP practices were stratified by country to ensure similar number of GP practices were allocated to the intervention and control arm in each jurisdiction. GP practices were randomised on a 1:1 allocation. Due to the nature of the intervention, it was not possible to blind GPs or the patients. GP practices randomised to the intervention arm viewed the online video, discussed scheduling medication reviews with practice staff and conducted medication reviews with recruited patients at baseline and 6-months follow-up post initial medication review. GP practices allocated to the control arm were asked to continue with providing their usual care, i.e. prescribing as per their standard practice (Rankin *et al.* 2021b). As the intervention is a pilot study, calculation of a sample size was not required. The number of GP practices and patients followed another pilot study in the literature (Patton *et al.* 2019).

#### **4.3.5 Data collection**

Numerous measures of data collection were employed throughout the PolyPrime study. Quantitative measures included self-report questionnaires, demographics, medications, and qualitative measures included semi-structured interviews.

##### *Patient data collected from the GP practice records*

Patient related data was collected from the GP practice records by CB at baseline, 6-months post initial medication review, or equivalent for control arm, and 9-months post initial medication review, or equivalent for control arm. Five documents were formulated specifically for the PolyPrime study to collect patient data from GP practice records. Documents and the information collected were as follows:

1. Patient registration form [including gender, date of birth, (Appendix 4.20)]
2. Diagnoses details [including type of condition, frequency of occurrence, date of diagnosis (Appendix 4.21)]
3. Health service use [contacts with doctor or nurse from the general practice, contact with other healthcare professionals, medication reviews, contact with hospital services including referrals and admittances to Accident and Emergency department (Appendix 4.22)]
4. Medications [including full name of medication, date medication first prescribed, strength, medication unit, dose, frequency, indication, whether it was still prescribed at



either 6-month and/or 9-month follow-up and if not prescribed at these timepoints, the date it was stopped, and reason if documented (Appendix 4.23)]

5. Queries in relation to specific medications prescribed [including if prescribed centrally acting hypertensives, phenothiazines, non-steroidal anti-inflammatories, corticosteroids, if received seasonal trivalent influenza and/or pneumococcal vaccines (Appendix 4.24)]

This information was necessary for the application of STOPP/START (O’Mahony *et al.* 2015)], already referred to in Chapter 1, section 1.6.2, available in Appendix 4.25. STOPP contains 80 criteria divided into 13 sections and START contains 34 criteria divided into nine sections (see Table 4.6 for STOPP/START sections and number of criteria in each section). STOPP identifies PIM and START identifies PPO, the results of STOPP and START combined provide information on potentially inappropriate prescribing.

**Table 4.6 Sections in STOPP/START and the number of criteria in each**

Section	Number of criteria in STOPP	Number of criteria in START
Drug indication	3	0
Cardiovascular system	13	8
Coagulation system	11	0
Central nervous system	14	6
Renal system	6	0
Gastrointestinal system	4	2
Respiratory system	4	3
Musculoskeletal system	9	7
Urogenital system	2	3
Endocrine system	6	1
Analgesics	3	2
Drugs that predictably increase the risk of falls in older people	4	0
Antimuscarinic/anticholinergic drug burden	1	0
Vaccines	0	2
Total	80	34

STOPP=Screening Tool of Older Persons Prescriptions. START=Screening Tool to Alert doctors to Right Treatment

#### *Patient self-reported data*

Numerous measures were employed to collect relevant data. As noted above, patients were provided with three questionnaires: health service use questionnaire, EQ-5D-5L (Herdman *et al.* 2011) and the Medication-Related Burden Quality of Life tool (Mohammed *et al.* 2018a).

Patients were asked to complete these questionnaires at various timepoints: baseline, 6-months post initial medication review (equivalent for control arm), and 9-months post initial medication review, or the equivalent for control arm practices. For patients allocated to the control arm, the follow-up data collection dates were calculated by the PolyPrime statistician. An average of the time between the date of baseline data collected by CB and date of the initial medication review for each patient in the intervention arm was calculated. The result was then applied to the date of baseline data collection in the control arm practices, to provide the equivalent date for 6-months and 9-months follow-up. Patients completed these questionnaires and returned them to the PhD candidate in the prepaid addressed envelope provided. If questionnaires had not been received after two weeks, the PhD candidate sent the patient a reminder letter to complete the questionnaires. If questionnaires had not been returned after a further two weeks later, the PhD candidate contacted the patient via telephone. If any of the questionnaires were missing from what the patient returned, the PhD candidate reposted the missing questionnaire along with a prepaid addressed envelope and a letter asking them to complete the unreturned questionnaire.

Health related quality of life was measured by the EQ-5D-5L tool (Herdman *et al.* 2011), a validated measure of quality of life which provides a simple, generic measure of health for clinical and economic appraisal (EuroQol Research Foundation Group 2019). The instrument consists of five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each with five statements and the respondent is asked to tick the box beside the statement that best reflects their health status. The participant also completed a visual analogue scale (VAS) as part of the EQ-5D-5L questionnaire. The VAS provides a value (0-100) for the health status of the participant on the day of completion; 0 = the worst health you can image, 100 = the best health you can imagine. Whilst another version of the EQ-5D exists, the EQ-5D-3L (Rabin and de Charro 2001) and is still in use, the EQ-5D-5L is considered the more reliable (Buchholz *et al.* 2018; Janssen *et al.* 2018; EuroQol Research Foundation Group 2019). The EQ-5D-5L takes approximately five minutes to complete (EuroQol Research Foundation Group 2019).

The MRB-QoL tool is a measure of the burden of medicines on functioning and wellbeing, developed by Mohammed *et al.* (2018a). It contains 31 items divided into five sections: routine and regimen complexity (11 items), psychological burden (six items), functional and role limitation (seven items), therapeutic relationship (three items) and social burden (four items), each item being a statement. The respondent was asked to illustrate on a five-point Likert scale the extent to which they agree or disagree with the statement; 1= strongly agree, 2= agree, 3=

neither agree nor disagree, 4= disagree, 5= strongly disagree. It is important to note that this tool has not been utilized in research in the UK or Ireland before and has only been validated for use in Australia, with further research required. Responses to this questionnaire, along with responses from patients participating in NI, were sent to the MRB-QoL research team for validation; however, this is not presented in the thesis, as the PhD candidate is not equipped to validate the tool. Both the EQ-5D-5L and the MRB-QoL are included as part of the secondary outcome of health-related quality of life.

#### *Data collected in relation to medication reviews*

Medication reviews, as part of the PolyPrime study, were only conducted by those allocated to the intervention arm. GPs were not provided with a set structure on how to conduct the medication review, however, the online video contained guidelines on conducting a medication review (ICGP 2020) and on medicines optimization (NICE 2019a). The GPs were allowed to tailor the medication review to best suit the patient and their conditions. Practice staff were asked to complete the Schedule of Medication Review form (Appendix 4.26) for each patient at both timepoints, i.e., baseline and 6-months follow-up post initial medication review. This form contained information regarding the number of medication review appointments scheduled and attended. This information is particularly pertinent to the process evaluation of the PolyPrime study. GPs were asked to record medication reviews for two patients at each timepoint. Dictaphones were provided to each practice in the intervention arm.

#### *Intervention fidelity*

Intervention fidelity was determined in relation to the delivery and enactment of the four intervention components (the online video, weekly meetings, patient recall and prompts/cues; previously described in detail in chapter 1, section 1.8). It was possible to record the number of times GPs accessed the video, and the number of times the video was played, to be recorded. Each GP was assigned a unique username and password which meant their usage could be tracked. Data was evaluated by counting (i) the number of plays on the online video, (ii) the number of weekly meetings between GPs and relevant practice staff (specific to the intervention), (iii) the number of appointments scheduled and attended (specific to the intervention), and (iv) the number of prompts GPs received from practice staff (specific to the intervention). The practice was also asked to complete a GP Practice and GP Eligibility form containing some demographic information (Appendix 4.27). This form also allowed GPs to self-report the number of times they accessed the video.

The number of weekly meetings between GPs and practice staff at which explicit plans were made to recall patients for medication reviews were self-reported on the GP Practice and GP Eligibility form (Appendix 4.27), which was completed by either the GP or practice staff. GPs and practice staff were also asked about these meetings and if and how often they occurred during the feedback interviews, described below in section 5.3.2.

Practice staff were asked to record the number of medication review appointments scheduled and the number of medication review appointments attended for each patient at both medication review timepoints, i.e., the initial medication review and 6-month follow-up medication review. The Schedule of Medication Reviews Form (Appendix 4.26) was supplied for practices to record this information and then submitted to the PhD candidate via email.

The number of prompts GPs received from practice staff to conduct medication reviews, was recorded by practice staff on the Practice Staff Input Form (Appendix 4.28). Practice staff were asked to complete this form for each patient in the study at both timepoints (i.e., initial medication review and 6-month follow-up). The form asked the practice staff to record who provided the prompt to the GP, the number of prompts given to the GP, and how the prompts were given (i.e., verbally or electronic). These forms were then submitted to the PhD candidate, via email, after the 6-month follow-up medication reviews had been completed.

#### *Acceptability of the intervention*

To ascertain the level of acceptability of the intervention to GPs, patients and practice staff, both quantitative and qualitative data were collected. Qualitative data was derived from feedback interviews conducted with GPs and practice staff, whilst quantitative data came from patient feedback questionnaires.

#### *Qualitative interviews*

All GPs and relevant practice staff were invited to take part in an interview with the research student via email. AG emailed the main contact in each intervention practice (for one practice this was the GP, and for the other practice this was the practice manager), inviting the relevant practice staff to participate in an interview. The participant information leaflet and consent form (Appendix 4.29) for practice staff were attached to the email. Practice staff were asked to read the participant information leaflet and return the completed consent form to the PhD candidate via email, along with possible dates and times which suited to participate in an interview. The PhD candidate downloaded the completed consent form and saved it to the TCD secure network.

GPs consented to participating in an interview post intervention delivery when they agreed to participate in the pilot study, therefore, GPs did not receive an additional consent form but were reminded of previously consenting to the feedback interview. Similarly to the practice staff, GPs were also asked to contact the researcher with possible dates and times for interview.

GPs and practice staff were informed that the interviews would be conducted separately, (i.e. one person interviewed at a time), via telephone and recorded using a dictaphone. Two separate topic guides were developed, one for GPs (Appendix 4.30) and the other for practice staff (Appendix 4.31). Both topic guides began with a brief overview of the interview and ensured the participants were comfortable to begin the recording. Overarching discussion points in both topic guides were: the acceptability of specific aspects of the study procedures including patient screening, patient recruitment and support provided by the research team; their experience of delivering the PolyPrime intervention (including the online video, practice meetings, prompts/cues, and the patient recall process); and the acceptability of the overall intervention. The latter set of questions were based on the Theoretical Framework of Acceptability [TFA, (Sekhon *et al.* 2017)] which is comprised of seven components (see Table 4.7), however, a question based on the component ‘ethicality’ was not included in the topic guide as the research team did not believe it was relevant due to the nature of the intervention. The topic guide for practice staff included questions in relation to 3 TFA components – affective attitude, burden and opportunity costs – as the remaining four were not deemed relevant by the research team as the intervention was GP focused. TFA based questions and its corresponding component are noted in the topic guides (Appendices 4.32 and 4.33).

**Table 4.7 Theoretical Framework of Acceptability and their definitions (adapted from Sekhon *et al.* 2017)**

<b>Component</b>	<b>Definition</b>
Affective Attitude	How an individual feels about the intervention
Burden	The perceived amount of effort that is required to participate in the intervention
Ethicality	The extent to which the intervention has a good fit with an individual’s value system
Intervention Coherence	The extent to which the participant understands the intervention and how it works
Opportunity Costs	The extent to which benefits, profits or values must be given up to engage in the intervention
Perceived Effectiveness	The extent to which the intervention is perceived as likely to achieve its purpose
Self-efficacy	The participant’s confidence that they can perform the behaviour(s) required to participate in the intervention

As each practice was already assigned an identification code (e.g., GPP21), interviewees were not assigned a new code to avoid confusion. Instead, the practice code remained and the letters 'GP' (for general practitioner) or 'PM' (for practice manager) were added to the code (e.g., GPP21GP). This was possible as there was not more than 1 GP and 1 practice staff member, involved in the study per GP practice. As soon as possible after the interview was terminated, the audio recording was uploaded to the TCD secure network and then deleted from the dictaphone. All interviews were transcribed by the PhD candidate, transcriptions were quality checked by both the PhD candidate and the research fellow (AR), followed by detailed analysis described below.

The original protocol stated that patients in the intervention arm would be invited to participate in a face-to-face semi-structured interview with the PhD candidate. However, due to the presence of COVID-19, an amendment was submitted to the ICGP ethics committee to change the semi-structured interviews to postal questionnaires (see Table 4.5 above).

#### *Patient feedback questionnaires*

A feedback questionnaire (Appendix 4.32) was posted to all participating patients in the intervention practices, accompanied with a pre-addressed stamped envelope, as soon as possible after the delivery of the intervention (i.e., after they had received their second medication review – GP or practice staff contacted the PhD candidate to inform that the second medication review had been completed). Patients were sent a reminder letter if the questionnaire had not been returned within three weeks. If this was unsuccessful, the PhD candidate then telephoned the patients to remind them to complete and return the feedback questionnaire. The questionnaire mostly contained quantitative questions with some qualitative questions in the form of open-text responses. Patients were asked to provide feedback on the study procedures such as the recruitment process and support from the research team, receiving medication reviews as part of the study and their overall experience of being involved in the PolyPrime study.

#### *Mechanisms of action*

GPs were asked to record the same patient's medication review appointments at both timepoints. The practices were provided with a dictaphone to record the medication reviews, recordings were transcribed verbatim by AG.

### **4.3.6 Data analysis**

#### *Primary outcome, medication appropriateness*

The STOPP/START tool (O'Mahony *et al.* 2015) was utilized to conduct an analysis of appropriate prescribing at baseline, 6-months post initial medication review, or equivalent for control arm, and 9-months post initial medication review, or equivalent for control arm. The assessments were carried out by senior pharmacists on the team, CR and CC, who analysed medical history, medical diagnoses and patient medication lists to conduct the STOPP/START assessment. Both CR and CC were blinded to GP practice allocation of intervention or control arm. A form specifically for the PolyPrime study was generated which included the section of STOPP/START, the description of the criteria, and a tick box for a yes or no decision on whether or not a medication was considered potentially inappropriate (Appendix 4.25). The number of patients with at least one prescription of a PIM, as identified by STOPP, and the number of patients with at least one instance of PPO, as identified by START were calculated. The instances of PIP were also calculated, identified by combining the results of STOPP and START.

#### *Secondary outcome, health related quality of life*

Health service use questionnaire answers reported by patients and those from general practice records were compared. The highest occurring answer was entered into the database for analysis, for example, a patient might have reported having two appointments at the general practice over the previous six months, yet the general practice records report this as three appointments, then three appointments was entered into the SPSS file. Descriptive statistics were generated including most used service, number of contacts with the GP practice (including with GP and/or practice nurse) and if this contact was face-to-face or via telephone, the number of visits to Accident and Emergency and the number of admissions to hospital.

For the EQ-5D-5L questionnaire (Herdman *et al.* 2011), each statement on the self-reported questionnaires was coded as a single-digit number (i.e., 1-5), reflecting the severity of the level. For example, in the mobility section the least severe statement 'I have no problems in walking about' was coded as 1 and the most severe statement 'I am unable to walk about' was coded as 5. If a patient had ticked two statements in the same dimension, this was considered missing and coded as 9, as recommended by EuroQol Research Foundation (2019). The EQ-5D-5L mean was calculated by entering questionnaire responses into a mapping function developed by van Hout *et al.* (2012), this method was recommended by NICE (2019b). The interquartile range was calculated by using the formula '=QUARTILE.EXC.(lowest excel cell: highest excel cell,1) and =QUARTILE.EXC.(lowest excel cell: highest excel cell,3)'. For the Visual Analogue Scale (VAS), the value provided by the respondent is their VAS score, missing values were coded as 999 and if the score indicated on the scale was different to that written in the box, the number in the box

was recorded as the VAS score, as recommended by EuroQol Research Foundation (2019), the mean value at each timepoint was calculated.

Inverse coding was carried out on respondent answers to the MRB-QoL, meaning if a respondent reported a statement as '5', that was coded into SPSS as 1. MRB-QoL score was calculated based on the calculation shown in Figure 4.1. An overall score of the five sections in the MRB-QoL was calculated. The equation provided by the authors of the MRB-QoL does not allow for a score for each section within the MRB-QoL. The MRB-QoL score ranges from 0-100, where 0 indicated no medication related burden (the best possible medication related quality of life) and 100 indicated the highest level of burden (the worst possible medication related quality of life). Information on how to calculate MRB-QoL does not account for patients who do not answer all the 31 statements. If a patient did not provide a response to one or more of the 31 statements, their response was marked as missing and no MRB-QoL score was calculated.

**Total MRB-QoL score =**

$$\frac{\text{Total actual raw score of each item} - \text{number of items in the sub-scale}}{\text{Maximum possible raw score of all items} - \text{number of items in the sub-scale}} \times 100$$

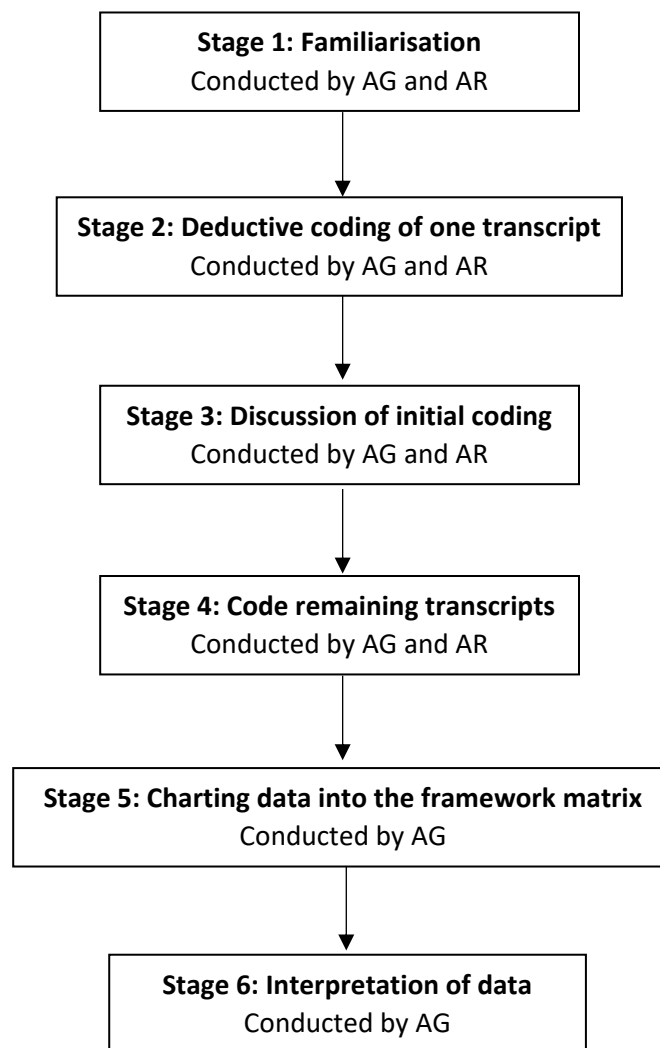
**Figure 4.1 Calculation of Medication-Related Burden Quality of Life score (adapted from Mohammed *et al.* 2018a)**

#### *Secondary outcome, acceptability of intervention*

The analysis of the qualitative interviews involved numerous steps, see Figure 4.2. After performing an in-depth familiarization phase [by listening to the recordings and reading, and re-reading, the transcripts (stage 1)], the TFA (Sekhon *et al.* 2017) was used by AG and AR to independently code one transcript by assigning the relevant seven components (see Table 4.7 above) to sections of the transcript (stage 2). AG and AR then met to compare what they had coded, discussed why it had been interpreted as meaningful and, in relation to the TFA, if the data was useful to answering the research questions (stage 3). Both researchers agreed the TFA was sufficient to analyse the interviews with GPs and practice staff. A preplanned inductive coding exercise using the Framework analysis (Ritchie and Spencer 1994, Gale *et al.* 2013) was deemed un-necessary due to the number of interviews conducted and the content. However, it was agreed to add 'acceptability' in coding subsequent transcripts as the question 'Overall, was the intervention acceptable?' was asked during the interviews. AG and AR then independently coded the remaining transcripts, using the TFA as well as the label 'acceptability', and met to discuss and agree on codes for each transcript (stage 4). AG then summarized the data in a



framework matrix (stage 5, Appendix 4.33) for each TFA component using Microsoft Excel. The data was extracted from the transcripts for each participant and TFA component, summarized alongside the verbatim quotation and placed in the corresponding cell in the matrix. The matrix comprised of one row per participant and one column per TFA component, with an additional column for 'acceptability'. An analysis of the framework matrix was then performed to identify key issues within each component (stage 6). The findings of this highlighted the intervention acceptability and potential mechanisms of action.



**Figure 4.2 Stages involved in the analysis process of feedback interviews**

The TFA was used to frame questionnaire items and included affective attitude, burden and perceived effectiveness. Due to the role of the patient in the study, TFA components ethicality, intervention coherence, opportunity costs, and self-efficacy were not included.

To determine the intervention’s likely mechanism of action, data collection measures from both intervention fidelity and acceptability of the intervention were analyzed together. Data for this included the following aspects (see Table 4.8 for overview):

- The number of weekly meetings between GPs and practice staff at which explicit plans were made to recall patients for medication reviews
- The number of prompts received by GPs from practice staff to conduct the medication reviews
- GP feedback interview
- Practice staff feedback interview

In addition to the information described above surrounding GP and practice feedback interviews, the response was also analysed to establish if the GPs and/or practice staff found the weekly meetings and receiving/delivering of prompts, to be useful components of the intervention. Transcripts of recorded medication reviews were analysed to ensure they were undertaken and delivered as intended. Additionally, a behaviour change technique (BCT; Michie *et al.* 2013) coding exercise was included to assess if any additional BCTs were performed during the medication reviews. AG completed the BCT Taxonomy online training to successfully assess BCTs in the recordings and transcripts (Appendix 4.34). BCTs were described in chapter 1 section 1.8. Recorded medication reviews were analysed to assess the patient’s attitude towards having their medications reviewed by their GP.

**Table 4.8 Summary table of each aspect of the process evaluation and the data collection measures involved**

Process evaluation area	Data collection measures involved
Intervention fidelity	<ul style="list-style-type: none"> <li>• Number of times the GPs watched the online video</li> <li>• Number of weekly meetings between GPs and practice staff</li> <li>• Number of appointments scheduled and attended</li> <li>• Number of prompts GPs received from practice staff</li> <li>• Medication review recordings</li> </ul>
Acceptability of intervention	<ul style="list-style-type: none"> <li>• GP feedback interview</li> <li>• Practice staff feedback interview</li> <li>• Patient feedback questionnaire</li> </ul>
Mechanisms of action	<ul style="list-style-type: none"> <li>• Number of prompts GPs received from practice staff</li> <li>• Number of weekly meetings between GPs and practice staff</li> <li>• GP feedback interview</li> <li>• Practice staff feedback interview</li> </ul>

### *Secondary outcome, progression criteria*

Progression criteria was developed *a priori* to determine if the PolyPrime study should proceed to a definitive cRCT, or if modifications to the study were required. The progression criteria i.e. Stop Amend Go criteria were developed by the project management team, specific for the PolyPrime study following research by Borelli *et al.* (2005) and Avery *et al.* (2017) (see Table 4.9 for definitions). The progression criteria were developed in relation to both jurisdictions (i.e. NI and the RoI) and these criteria are presented under the 'overall' section of Table 4.10. In order to present progression criteria specific to the results presented below, the progression criteria for application to one jurisdiction is also presented in Table 4.10. Borelli *et al.* (2005) note that criteria meet the 'Go' standard when >80% of the target is met, criteria meet the 'Amend' standard when 50% of the target is met and 'Stop' is applied if criteria meet less than 50% of the target. When data was available for all criteria, results were presented to the TSC and discussions relating to the progression to a definitive cRCT were held with the project management team.

**Table 4.9 Stop Amend Go definitions in the PolyPrime study (adapted from Rankin *et al.* 2021a)**

	<b>Definition</b>
<b>Stop</b>	If one or more of the criteria meet the 'Stop' thresholds, then the study should not progress towards a definitive cRCT, unless there are clear 'modifiable' contextual or design issues (i.e. related to the intervention or study procedures) which have been identified
<b>Amend</b>	If one or more of the criteria meet the 'Amend' thresholds, then these will be discussed with the trial steering committee to ascertain whether there is enough evidence that sufficient improvements can be made to proceed to a definitive cRCT.
<b>Go</b>	If all the criteria meet the 'Go' thresholds, then with the appropriate amendments (if needed), the study should proceed towards a definitive cRCT.

cRCT= cluster randomised controlled trial

**Table 4.10 Progression criteria for the PolyPrime study**

Criteria	Data source(s)	Progression criteria		
		Stop	Amend	Go
<b>Overall progression criteria</b>				
<i>GP practice recruitment</i>	Recruitment records held by research nurse	If ≤5 GP practices are recruited within 8 months	If 6-9 GP practices are recruited and/or it takes longer than predicted (6-8 months)	If ≥10 GP practices are recruited to take part in ≤6 months
<i>GP practice retention</i>	Retention records held by research nurse	If ≤5 GP practices are retained for the required period	If 6-9 GP practices can be retained for the required period	If ≥10 GP practices can be retained for the required period
<i>Patient recruitment</i>	Recruitment records held by the Research Fellow/ the PhD candidate	If ≤59 patients are recruited within 5 months	If 60-95 patients are recruited within 5 months	If ≥ 96 patients are recruited within 5 months
<i>Patient retention</i>	Retention records held by the Research Fellow/ the PhD candidate	If ≤49% of patients are retained for the required period	If 50-79% of patients are retained for the required period	If ≥80% of patients are retained for the required period
<i>Completeness of outcome data</i>	Data collected during the study (case report forms, questionnaires)	If ≤49% of each patient self-report and GP-reported outcome measure is complete	If 50-79% of each patient self-report and GP-reported outcome measure is complete	If ≥80% of each patient self-report and GP-reported outcome measure is complete
<b>Progression criteria for one jurisdiction</b>				
<i>GP practice recruitment</i>	Recruitment records held by research nurse	If ≤3 GP practices are recruited within 8 months	If 4 GP practices are recruited and/or it takes longer than predicted (6-8 months)	If ≥5 GP practices are recruited to take part in ≤6 months
<i>GP practice retention</i>	Retention records held by research nurse	If ≤3 GP practices are retained for the required period	If 4 GP practices can be retained for the required period	If ≥5 GP practices can be retained for the required period
<i>Patient recruitment</i>	Recruitment records held by the Research Fellow/ the PhD candidate	If ≤29 patients are recruited within 5 months	If 30-48 patients are recruited within 5 months	If ≥ 48 patients are recruited within 5 months
<i>Patient retention</i>	Retention records held by the Research Fellow/ the PhD candidate	If ≤49% of patients are retained for the required period	If 50-79% of patients are retained for the required period	If ≥80% of patients are retained for the required period
<i>Completeness of outcome data</i>	Data collected during the study (case report forms, questionnaires)	If ≤49% of each patient self-report and GP-reported outcome measure is complete	If 50-79% of each patient self-report and GP-reported outcome measure is complete	If ≥80% of each patient self-report and GP-reported outcome measure is complete

#### **4.3.7 Reporting of results**

The reporting of the results is presented with a Consolidated Standards of Reporting Trials [CONSORT (Schulz *et al.* 2010)] diagram presented below and a CONSORT checklist in Appendix 4.35.

#### **4.3.8 Ethics and data governance**

Both the researcher (AG) and the research nurse (CB) had completed training in Good Clinical Practice (Appendix 4.36) before the PolyPrime study began. The NICTU also developed a standard operating procedure (SOP) which included aspects of clinical data management, ensured standardization between researchers in RoI and those working in NI. This SOP adhered to the International Conference of Harmonisation Good-Clinical Practice guidelines and regulatory requirements (Dixon Jr 1998, International Conference on Harmonisation, no date). As well as receiving ethical approval from the ICGP (see above), the trial was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (World Medical Association 2001).

Personal data, including patient consent forms and completed questionnaires, and GP consent documents (consent form, research governance form, data sharing agreement and GP letter of support) were held in a locked filing cabinet in a locked office within the SoPPS, TCD, as only hard copies of these documents existed. The documents will be transferred to Professor Carmel Hughes (CH), the Principal Investigator, in Queen's University Belfast (QUB), in line with GDPR guidelines for transferring of data upon study completion (Article 32), following award of PhD. All participants (GPs, patients and practice staff) were aware of this transfer and information was provided in the relevant participant information leaflets (Appendices 4.5, 4.8 and 4.29). Electronic data, for example, typed pseudonymized transcripts from process evaluation interviews, were transferred through encrypted email to CH. GP and patient consent forms, pseudonymized transcripts from GPs and practice staff, patient questionnaires and patient health data will be securely stored for five years in a locked cabinet in QUB and then destroyed, in line with GDPR guidelines at time of protocol development and as per ethical approval by the ICGP.

As the grant holder for the PolyPrime study was QUB, they acted as the sponsor for the study and took overall responsibility for the conduct of the trial. A collaboration agreement was put in place between QUB and TCD, and other partner universities, and was signed and dated by representatives of all universities prior to the study commencing. The Research Governance

office at QUB monitored the study to ensure compliance with Research Governance Framework. CHITIN (project funders, see above) received quarterly reports on progress made during the project.

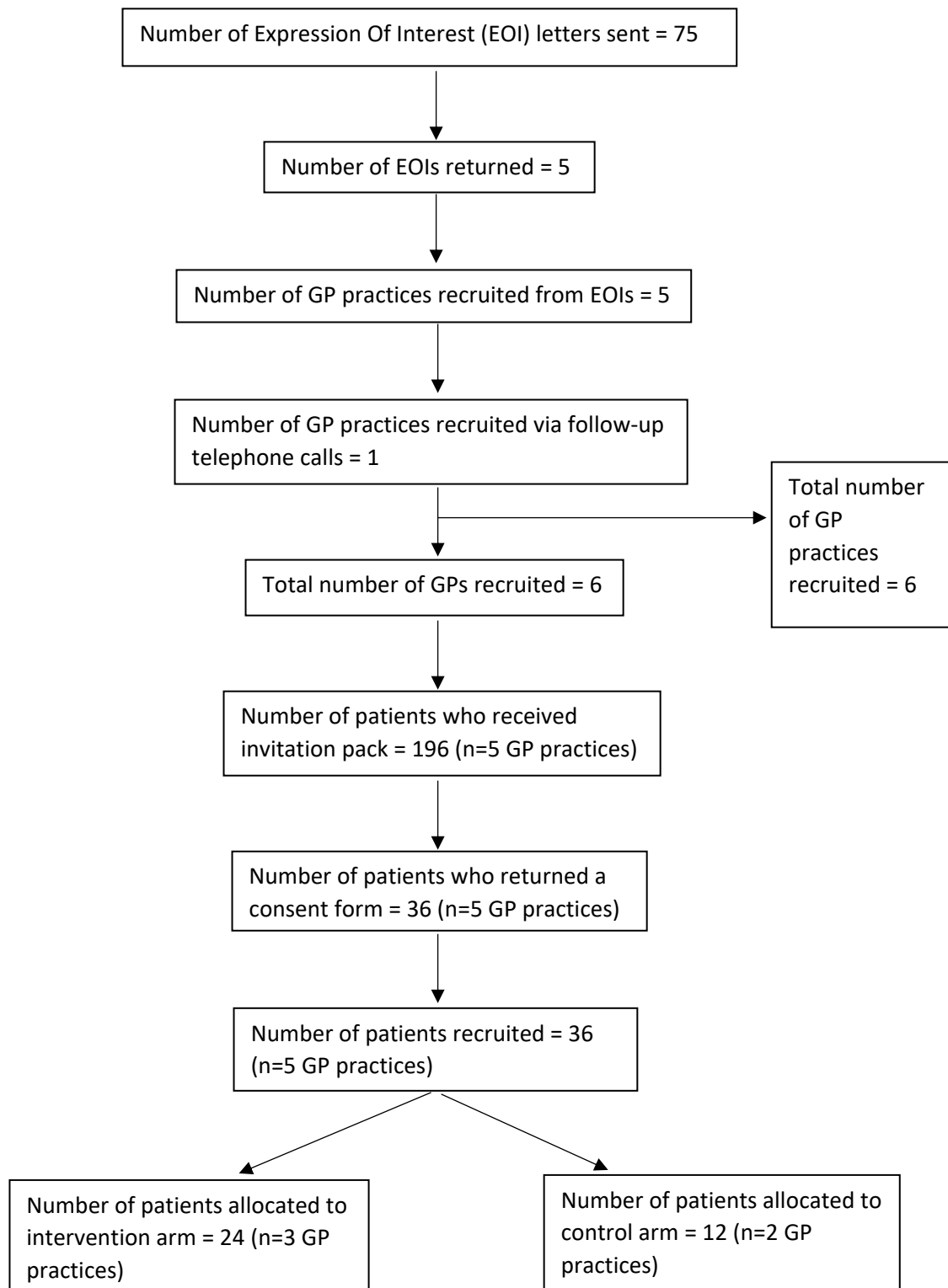
## 4.4 Results

This section presents the results of the process of recruiting GP practices, GPs and patients to the PolyPrime study, alongside the demographics of the GP practices, GPs and patients. The primary outcome of medication appropriateness (assessed by STOPP/START) is presented followed by the secondary outcomes of health-related quality of life, the acceptability of the intervention (only applicable to GP practices, GPs and patients allocated to the intervention arm) and the progression criteria.

### 4.4.1 Recruitment

In total, 75 EOI letters were sent to GP practices; up to 15 letters per county with the aim of recruiting one general practice per county. Only six and nine EOI letters were posted to Leitrim and Monaghan respectively (counties Cavan, Donegal, Louth and Sligo all received 15 EOI letters). This was due to GP practices being involved in phase 1 of the PolyPrime study (see Chapter 3) or the practice already being involved in a medicine management study and therefore did not meet the study's inclusion criteria. Five EOIs were returned from four counties [Cavan =2, Donegal =1, Louth =1, Sligo =1]. CB contacted practices, via telephone, in Monaghan and Leitrim that had received an EOI letter but had not returned the reply, with one general practice in Leitrim opting to receive an information pack. As no general practices located in Monaghan expressed an interest in participating, the second practice in Cavan to receive the information pack was contacted to schedule a meeting with AG. Six practices across five counties were recruited [Cavan =2, Donegal =1, Leitrim =1, Louth =1, Sligo =1 (Figure 4.3)]. The study allowed for multiple GPs from the recruited practice to join the study, to spread the workload of the intervention. Only one GP from each practice consented to take part in the study. A flowchart of the recruitment process and recruitment numbers is presented in Figure 4.3. The demographics of the GP practices and the recruited GP are shown in Table 4.11. Data regarding GPs' demography and GP practices was collected after baseline data collection was completed at the GP practices, hence there is numerous data missing, particularly for the two GP practices that withdrew: GPP23 and GPP25 (described below). Most practices were in a rural setting with only one of the six GP practices located in an urban setting. Rural setting was defined as settlement with less than 10,000 resident population (Department for Environment, Food & Rural Affairs 2017). Due to missing data, the average number of GPs in the GP practice, the average length of time practicing as a GP (for recruited GPs), and the average number of patients registered to the GP practice could not be calculated. Out of the four practices that provided demographic data, all employ a minimum of two administrative/ support staff and at

least one nurse; only one other GP practice (GPP24) employed a further staff member, a phlebotomist.



**Figure 4.3 Flowchart of recruitment process and recruitment numbers**



**Table 4.11 Demographics of the recruited GP practices and the general practitioners**

	Allocation					
	Intervention			Control		
	GPP22	GPP24	GPP25	GPP21	GPP23	GPP26
Number of GPs in the GP practice	2	3	M	1	M	5
Number of other staff members	2 administrative/ support, 1 nurse	6 administrative/ support, 3 nurses	M	4 (2 nurses, 2 administrative/ support)	M	5 administrative/ support, 2 nurses
Patient list size	950	400	M	850	M	7700
Currently conduct medication reviews (Yes/No)	Y	N	M	Y	M	M
Total years practicing as a GP	6	30	M	22	M	37
Location	Rural	Rural	Rural	Rural	Rural	Urban

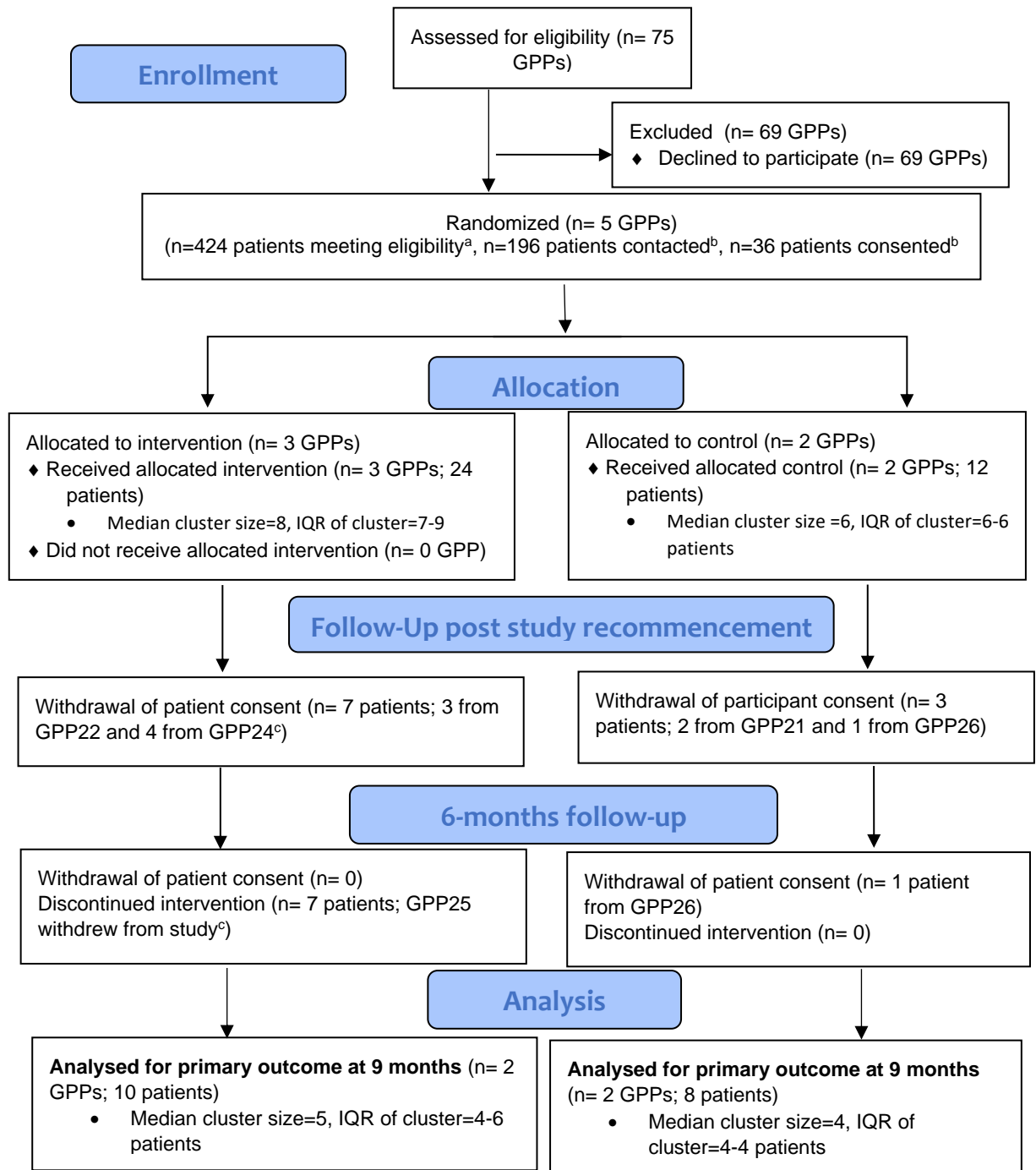
GP= General practitioner M= Missing

Before patient recruitment began, one practice (GPP23) withdrew from the study because of COVID-19, therefore, patient recruitment occurred in five general practices. As discussed in section 4.2, CB oversaw the screening and recruitment of patients alongside the general practice manager, or equivalent. A total of 36 patients were initially recruited (see Table 4.12), and baseline questionnaires were returned at this point. Before patient recruitment was completed, the study was suspended due to COVID-19. After study recommencement, recruited patients were informed of changes made to the study in response to COVID-19, and provided with the option to remain in the study or to withdraw. At this point, 10 patients opted to withdraw leaving 26 remaining across the five GP practices (see Table 4.12). Reasons given for withdrawal being: hearing loss (n=1), no longer interested (n=6), opt-in/opt-out letter no reason stated (n=1), having a recent hospital visit (n=1), not interested in engaging with healthcare more than necessary due to COVID-19 (n=1). GPP25 withdrew after baseline data collection stating increased work-load pressures directly resulting from COVID-19 as the reason for withdrawal. The seven patients recruited from this practice were provided with a letter from the practice explaining their withdrawal and inviting the patients to continue participation in the study by completing questionnaires at the pre-defined dates of 6-month follow-up and 9-month follow-up. Three patients opted to continue in the study (Table 4.12), however data collected from the GP practice did not occur at 6-months post initial medication review and 9-months post initial medication review due to the practice withdrawing from the study. This information is included in the CONSORT diagram below (Figure 4.4).

**Table 4.12 GP practice patient numbers and recruitment**

<b>General practice ID</b>	<b>Number of patients meeting inclusion criteria</b>	<b>Total number of recruitment packs sent</b>	<b>Number of consent forms returned</b>	<b>Number of patients remaining after study recommenced</b>	<b>GP practice record data available for patients at 9 months</b>
GPP21	200	25	6	4	4
GPP22	174	25	9	6	6
GPP24	50	50	8	4	4
GPP25	M <sup>a</sup>	50	7	7	3 <sup>b</sup>
GPP26	M	46	6	5	4 <sup>c</sup>
<b>TOTAL</b>	NA	196	36	26	21

GP=general practice M=missing NA=not available <sup>a</sup>Practice withdrew before this information was collected <sup>b</sup>Practice withdrew after baseline data collection <sup>c</sup>Patient withdrew due to health reasons



GPP=General practitioner practice IQR=Interquartile range

<sup>a</sup>The number of patients meeting eligibility criteria relates to three GPPs as information was not available for two GPPs. <sup>b</sup>The number of patients contacted and consented related to five GPPs as one GPP withdrew from the study before patient recruitment commenced. <sup>c</sup>One GPP allocated to the intervention arm withdrew from the study after being informed of allocation to the intervention. No patients in this GPP received medication reviews, however, 3 patients opted to be followed up for the patient reported questionnaires.

**Figure 4.4 CONSORT flow diagram for the PolyPrime study**

Demographics at baseline are provided for all patients recruited, regardless of withdrawal at study recommencement or at another point in the study. Demographics of patients are shown in Table 4.13. The average age of patients across both intervention and control arms was 76.3 years, with the average age of patients in the intervention arm being slightly older at 76.71 years and control arm patients slightly younger than study average at 75.5 years. Over half of patients in the PolyPrime study were male (55.5%). The average number of medications at baseline was similar between intervention arm and control arm patients with patients prescribed 5.1 and 5.2 medicines respectively. The most common category of medical conditions present at baseline was in relation to the cardiovascular system (for example, hypertension) with 30 instances from both intervention (14 instances) and control arm (16 instances) noted. In total, 14 instances (9 intervention arm, 5 control arm) had a condition in the musculoskeletal system at baseline data collection. Examples of conditions reported in the musculoskeletal system are gout and osteoporosis. The ocular system was the least common with only one instance (control arm) of an ocular condition presenting at baseline (glaucoma).

**Table 4.13 Demographics of all recruited patients at baseline**

	<b>Intervention (n=24)</b>	<b>Control (n=12)</b>	<b>Total (n=36)</b>
<b>Average age</b>	76.7 years	75.5 years	76.3 years
<b>Gender (%)</b>			
Female	12 (50%)	4(33.3%)	16 (44.4%)
Male	12	8	20
<b>Total number of prescribed medicines</b>			
Baseline	124	63	187
Average number of prescribed medicines per patient	5.1	5.2	5.1
<b>Medical conditions at baseline</b>			
Cardiovascular system	14	16	30
Central nervous system	0	4	4
Endocrine system	6	1	7
Gastrointestinal system	5	3	8
Musculoskeletal system	9	5	14
Ocular system	0	1	1
Respiratory system	2	3	5
Urogenital system	5	3	8
Other	26	21	47

#### **4.4.2 Results of STOPP/START assessment**

As STOPP/START (O'Mahony *et al.* 2015) was calculated based on GP practice record data, the number of patients at baseline is smaller compared to the number of patients at baseline who completed the health service use, the EQ-5D-5L (Herdman *et al.* 2011) and the MRB-QoL

(Mohammed *et al.* 2018a) questionnaires. GP record data was available for 26 patients at baseline, 19 patients at 6-months post initial medication review, or equivalent for control arm (GPP25 withdrew prior to 6-months post medication review data collection), and 18 patients at 9-months post initial medication review, or equivalent for control arm, (one patient had withdrawn due to health reasons). The results of PIM, PPO and PIP are presented below.

#### *Potentially inappropriate medication (STOPP)*

At baseline, a total of 37 instances of PIM was recorded, 26 instances in GP practices allocated to the intervention arm and 11 instances in GP practices allocated to the control arm. The most common reason for PIM was 'Any drug prescribed without an evidence-based clinical indication' (STOPP section A1) with this arising in a total of 17 patients across both intervention and control arm GP practices. A total of 19 instances of PIM was recorded at 6-months, eight instances from five patients allocated to the intervention arm and 11 instances from six patients allocated to the control arm. The most common reason for PIM at 6-months was the same at baseline, with nine patients having a PIM due to lack of evidence-based clinical indication (STOPP section A1). At 9-months follow-up post initial medication review, or equivalent, 18 instances of PIM were recorded. Nine instances of PIM were recorded in both intervention and control arm patients, in six patients and five respectively. At 9-months the most common reason for instance of PIM was prescription without evidence-based clinical indication (STOPP section A1). Table 4.14 presents the proportion of patients with, and the number of instances of, potentially inappropriate prescribing at baseline, 6 months and 9 months

#### *Potential prescribing omissions (START)*

At baseline, a total of 27 instances of PPO were recorded with 18 instances in the intervention arm patients and 9 in control arm patients. Ten patients in the intervention arm and seven patients in the control arm were assessed to have PPO. The most common reason for PPO was the omission of the 'Pneumococcal vaccine at least once after age 65 according to national guidelines' (START section I2). A total of 20 instances of PPO was analysed at 6-months, 11 instances in seven patients allocated to the intervention arm and nine PPO instances in eight control arm patients. The most common instance of PPO at 6-months was the lack of pneumococcal vaccine (n=13), as in baseline results. The total number of instances of PPO at 9-months was 21. A total of 12 instances of PPO were recorded in seven intervention arm patients and nine instances in seven control arm patients. The most common reason for PPO was no pneumococcal vaccine (n=13). Table 4.14 presents the results of the number of patients with PPO at all three timepoints.

*Potentially inappropriate prescribing (STOPP and START combined)*

At baseline, 44 instances of PIP were recorded from GP intervention practices in 15 patients and 20 instances from control GP practices in eight patients, providing a total of 64 instances of PIP in 28 patients at baseline. The number of instances of PIP at 6-months post initial medication review, or equivalent, totals at 39. 19 instances of PIP were reported in eight patients from intervention GP practices and 20 instances of PIP in nine patients from control arm GP practices. At 9-months, both the number of instances of PIP and the number of patients with PIP increases in the intervention GP practices to 21 instances and nine patients. Control arm GP practices had a decrease in the number of instances of PIP to 18 and the number of patients reporting PIP to eight. At 9-months follow-up, the total number of instances across intervention and control arm GP practices was 39 instances, reported in 18 patients.

**Table 4.14 Proportion of patients with, and the number of, potentially inappropriate prescribing at baseline, 6-months and 9-months follow-up**

	Intervention		Control	
<b>Potentially inappropriate medications (STOPP)</b>				
	Patients n(%)	PIM n	Patients n(%)	PIM n
Baseline	n=17 13(76.5)	26	n=9 7(77.8)	11
6-months	n=10 5(50)	8	n=9 6(66.7)	11
9-months	n=10 6(60)	9	n=8 5(62.5)	9
<b>Potential prescribing omissions (START)</b>				
	Patients n(%)	PPO n	Patients n(%)	PPO n
Baseline	n=17 10(58.8)	18	n=9 7(77.8)	9
6-months	n=10 7(70)	11	n=9 8(88.9)	9
9-months	n=10 7(70)	12	n=8 7(87.5)	9
<b>Potentially inappropriate prescribing (STOPP, START combined)</b>				
	Patients n(%)	PIP n	Patients n(%)	PIP n
Baseline	n=17 15(88.2)	44	n=9 8(88.9)	20
6-months	n=10 8(80)	20	n=9 8(88.9)	20
9-months	n=10 9(90)	21	n=8 8(100)	18

PIM= potentially inappropriate medications PIP= potentially inappropriate prescribing PPO= potential prescribing omissions

#### 4.4.3 Health service use

The most common health care professional patients had contact with was their GP. Patients had contact with their GP a total of 185 times (either with an in-person consultation, a home visit from their GP, or a telephone conversation) in the six months prior to baseline data collection. The second most common healthcare professional patients came into contact with was the practice nurse, with patients across the intervention and control arms having contact with their practice nurse (by attending an appointment with them at the GP practice or speaking to them via the telephone) a total of 74 times. Patients came into contact with their pharmacist 68 times, however this could have included picking up their medications and may not have received any specific advice from them. Health services utilisation is presented in Table 4.15 below.

**Table 4.15 Patients contacts with healthcare professionals**

		Contacts with healthcare professionals			
		GP	Nurse	Pharmacist	Other
<b>Baseline</b>	Intervention (n=23)	107	40	53	14
	Control (n=12)	78	29	15	16
<b>6-months</b>	Intervention (n=13)	58	19	53	10
	Control (n=9)	40	22	18	8
<b>9-months</b>	Intervention (n=13)	47	16	34	15
	Control (n=8)	43	17	25	7

GP = general practitioner

The frequency of medication reviews was captured in the patient self-reported health service use questionnaire and the GP record of patient health service use. Patients were asked if attending the community pharmacy was to discuss or review their medications; the patient health service use form completed by CB with the GP practice record, asked if the patient had any medication reviews recorded in their notes. For baseline and 6-months follow-up post initial medication review (or equivalent for control arm) this applied to the patient's health record for the previous six months, at 9-months data collection this applied to the previous three months health record.

Patients in the intervention arm received medication reviews as part of the PolyPrime intervention, however, data collected from GP records showed that patients in the control arm also received medication reviews as part of their usual care. Patients in the control arm dropped from 12 at baseline to nine at 6-months follow-up, however, medication reviews increased from three medications reviews recorded across all control arm patients at baseline data collection to five medication reviews at 6-months follow-up post initial medication review (or equivalent for control arm). At baseline data collection only one of these was conducted by the GP; at 6-months follow-up all five medication reviews were conducted by the GP. At 9-months follow-up data collection, four patients in the control arm had received a medication review, conducted by their GP, in the previous three months. In the intervention arm, nine of 17 patients had received a medication review in the previous six months up to baseline data collection; four medication reviews were conducted by their GP. At 6-months follow-up post initial medication review, nine of 13 patients had medication review in their GP record, all of which were conducted by their GP, and at 9-months eight patients in the intervention arm had received a



medication review in the previous three months. The number of medication reviews according to GP practice record data is presented in Table 4.16.

**Table 4.16 Medication reviews according to GP practice record data**

		Medication review conducted by	
		GP n(%)	Other healthcare professional n(%)
<b>Baseline</b>	Intervention (n=17)	4 (23.5)	5 (29.4)
	Control (n=9)	2 (22.2)	1 (11.1)
<b>6-months</b>	Intervention (n=13)	9 (69.2)	0 (0)
	Control (n=9)	5 (55.5)	0 (0)
<b>9-months</b>	Intervention (n=10)	8 (80)	0 (0)
	Control (n=8)	4 (50)	0 (0)

GP = general practitioner

In the previous six months prior to baseline data collection, patients in the control arm had contact with hospital services a total of thirteen times. Two patients visited their local A&E department, both of which resulted in the patients being admitted to hospital. A further two patients were admitted to hospital, not via A&E, with one spending a total of 28 nights in hospital, and the other patient being admitted and discharged on the same day. Patients in the control arm visited seven clinics in the hospital including cardiology clinic, dermatology and for immunoglobulin infusion once a month, this decreased to five clinics at 6-months follow-up and remained at five at 9-months follow-up data collection. At 6-months follow-up, the number of patients that made a visit to A&E in the previous six months decreased to one, in the three months following up to nine months data collection, this number increased to two. One patient had been admitted to hospital for 10 nights between baseline and 6-months follow-up data collection and another was admitted for nine nights between 6-months and 9-months follow-up data collection.

Of the 17 patients in the intervention arm, three patients had a visit to A&E in the previous six months to baseline data collection, two of which called an ambulance and were admitted. At 6-months follow-up post initial medication review, three patients had visited A&E with only one being admitted; no patients had a visit to A&E in the three months between 6-months and 9-months follow-up. In total, six patients were admitted to hospital for a total of 17 nights at baseline, and one patient admitted for four nights at 6-months data collection. At baseline, 13 clinics were being used by patients in the intervention arm including eye clinic, urology and cardiac. This decreased to four clinics at 6-months follow-up but increased to eight clinics at 9-months follow-up post initial medication review.

#### 4.4.4 EQ-5D-5L

EQ-5D-5L utility scores were available for 35 patients at baseline (1 questionnaire missing), 20 patients at 6-months follow-up (1 questionnaire missing) and 19 patients at 9-months follow-up (2 questionnaires missing), Table 4.17 presents the mean and interquartile range for these three timepoints, divided by patients allocated to the intervention or control arm. A total of 19 patients returned EQ-5D-5L completed utility scores at all three timepoints. Patients in the control arm showed an increase in utility score between baseline and 6-months follow-up (from 0.75 to 0.82) and again from 6-months to 9-months (0.82 to 0.85). The EQ-5D-5L utility was 0.79 at baseline and decreased to 0.76 at 6-months follow-up post initial medication review and increased to 0.78 at 9-months follow-up. Control patients showed an increase from 73.85 EQ-5D-5L VAS at baseline, 81 at 6-months follow-up and 83.75 at 9-months follow-up. In contrast, the VAS score for intervention patients fluctuated in the same manner as the utility score in that 6-months follow-up post initial medication review saw an increase from 71.96 to 80, however this decreased to 66.82 at 9-months follow-up post initial medication review (see Table 4.17). The mean utility score for this group of patients at baseline, 6-months post initial medication review or equivalent for control arm, and 9-months post initial medication review (or equivalent for control arm) was the same at 0.81.

**Table 4.17 EQ-5D-5L utility and VAS scores at baseline, 6-months and 9-months follow-up**

EQ-5D-5L Utility score (IQR)						
	Baseline		6-months		9-months	
	Intervention (n=23)	Control (n=12)	Intervention (n=12 <sup>a</sup> )	Control (n=8)	Intervention (n=11 <sup>b</sup> )	Control (n=8)
		0.79 (0.69-1.00)	0.75 (0.65-0.96)	0.76 (0.80-0.88)	0.82 (0.71-0.97)	0.78 (0.69-0.88)
EQ-5D-5L-VAS						
<b>Median</b>	75.0	73.6	83.5	81.0	66.8	83.8
<b>-25<sup>th</sup> percentile</b>	65.0	58.75	75.0	67.5	50.0	63.8
<b>-75<sup>th</sup> percentile</b>	90.0	96.0	95.0	97.3	85.0	98.8

<sup>a</sup>1 questionnaire missing

<sup>b</sup>2 questionnaires missing

#### 4.4.5 Medication-Related Burden Quality of Life

At baseline, 35 out of a possible 36 MRB-QoL questionnaires were returned. Scores were available for 29 participants with scores for six patients not calculated as they did not provide a

response to every statement, and one participant did not return a questionnaire. At 6-months post initial medication review (or equivalent for control arm), one MRB-QoL questionnaire was not returned, and a score could not be calculated for six returned questionnaires, therefore, the mean and range is calculated for 10 patients in the intervention arm and 4 patients in the control arm. In total, 19 MRB-QoL questionnaires were returned at 9-months post medication review with two missing. It was not possible to calculate a score for 5 patients, three in the control arm and two in the intervention arm. The mean and range at 9-months post medication review is calculated from five patients in the control arm and six patients in the intervention arm, see Table 4.18 for results.

**Table 4.18 Medication-Related Burden Quality of Life scores at baseline, 6-months and 9-months follow-up**

	Intervention			Control		
	Missing (%)	Mean	Range	Missing (%)	Mean	Range
Baseline (nI=24 nC=12)	5	20.9	0-53.2	2	20.6	0-55.6
6-months (nI=13 nC=8)	3	15.3	0-30.6	4	5.4	0-19.3
9-months (nI=13 nC=8)	4	17.6	0-41.1	3	9.0	0-28.2

nI=number of participants in the intervention arm after withdrawals nC=number of participants in the control arm after withdrawals

The statements that did not receive a response varied, and there was no clear pattern amongst the uncompleted MRB-QoL questionnaires regarding the statements most frequently not answered. For example, at baseline the most commonly omitted statement was statement 17 (“my medicines signify me as being not healthy”), at 6-months post initial medication review (or equivalent) it was statement 22 (“because of my medicine/s I feel too tired to perform physical activities”) and at 9-months post medication review (or equivalent) statements 18 (“I am sometimes sexually frustrated because of my medicine/s”) and 19 (“I am unable to relax and enjoy sex because of my medicine/s”) were the most common blank statement.

#### **4.4.6 Intervention fidelity**

The four intervention components i.e., the online video, weekly meetings, patient recall and prompts/cues (previously described in detail in chapter 1, section 1.8) were assessed for fidelity i.e., if they were delivered as intended. The online platform showed that the video was accessed an average of 5 times per GP, with the GP from GPP22 accessing it 6 times and the GP from

GPP24 accessing it 4 times (see table 4.19). The video was played an average of 14.5 times per GP, with GP22 pressing 'play' 22 times and GP24 pressing 'play' 7 times. It cannot be determined if the video was watched from the beginning straight through to the end, or if the viewer was interrupted, 'paused' the video then pressed 'play' to resume watching it. The GPs reported the number of times they accessed the video, twice and three times for GP22 and GP24 respectively.

Practice staff were asked to record the number of weekly meetings between themselves and the GPs in which they would discuss explicit plans regarding the recall of patients for medication review. Across both intervention practices, this came to a total of three weekly meetings over the course of the study, one practice reported having two such meetings and the other practice reported having one meeting (see Table 4.19). Qualitative feedback on this process is presented below in section 4.4.7. Practice staff recorded medication review appointment scheduling details for both the initial and 6-month follow-up reviews. All 10 patients in the intervention practices attended medication reviews at both timepoints. One patient missed their 6-month follow-up appointment but did attend the re-scheduled appointment; neither intervention practice experienced any drop-out after the initial medication review (see Table 4.19).

The fourth intervention component involved practice staff delivering a prompt to the GP, indicating that the patient had arrived at the practice for their scheduled medication review. As one practice did not have a practice manager, the GP involved in the study did the recruitment tasks allocated to practice staff within the study protocol. For this practice (GPP22), information regarding prompts for the initial medication review were not recorded on the practice staff time input, however, it was noted that the secretary prompted the GP for the 6-month follow-up medication reviews, but no information was provided regarding how they were delivered and how many prompts the GP received. A staff time input form was required to be completed as part of a cost-effectiveness analysis that was being conducted by a health economist and is not presented in this thesis. Information on this form included the time taken for the staff member to schedule the medication reviews, the time taken to prompt the GP to conduct the medication reviews and any other activity conducted by the staff member in relation to the PolyPrime study. In the other intervention practice, GPP24, the practice manager provided prompts to the GP for both the initial and the 6-month follow-up medication reviews, all prompts were delivered verbally, and the number of prompts delivered in relation to each patient ranged from 1-2 prompts (see Table 4.19).

**Table 4.19 Intervention fidelity data counts**

Data collected	Self-reported	Collected by research team	GPP22	GPP24
Number of times GPs accessed the video	✓		6	4
Number of times the video was played	✓	✓	22	7
Number of weekly meetings discussing medication reviews held across the study	✓		2	1
Number of initial medication reviews scheduled	✓		6	4
Number of initial medication reviews attended	✓		6	4
Number of 6-month follow-up medication reviews scheduled	✓		6	4
Number of 6-month follow-up medication reviews attended	✓		6	4
Total number of prompts delivered	✓		6	14
- Verbal prompts			0 <sup>a</sup>	14
- Electronic prompts			0 <sup>a</sup>	0

<sup>a</sup>method of delivering prompts was not recorded GP=general practitioner

#### 4.4.7 Acceptability of intervention

Intervention acceptability was assessed via feedback interviews with both GPs recruited from the intervention practices. Only one practice staff interview was conducted as the staff member that participated in a small number of study activities from practice GPP22 did not wish to participate in an interview. Responses in feedback questionnaires delivered to patients recruited from intervention arm GP practices were also analysed to assess intervention acceptability.

##### *Feedback interviews*

Feedback interviews were conducted with recruited GPs from practices GPP22 and GPP24 and with the practice manager from GPP24. Results for intervention acceptability are presented in terms of the TFA components, as well as an additional section presenting the overall acceptability of the intervention. Responses relating to the intervention (i.e., the four intervention components: the online video, weekly meetings, patient recall and prompts/cues) and the procedures relating to the overall study (i.e., recruitment, support from researchers) are presented here.

##### *Affective attitude*

Overall, the intervention and the study were well received by the three interviewees.

*“yes it was a pretty straightforward em study to take part in” [GPP22]*

*“we actually found eh the process to be a pleasure to do, because you’ve assisted us ehh ye know all along” [GPP24]*

*“I thought it was a fantastic study - it’s a pity it couldn’t be rolled out [research assistants name] to everybody” [GPP24PM]*

Participating in the study and conducting medication reviews as part of the intervention reinforced that medication reviews can be conducted during routine care in GP practice and reminded the GP to complete them.

*“it’s probably brought it further up in my mind, that that’s something that can be part of routine practice” [GPP22]*

The video was well received by both GPs, who referenced the clinical relevance of medication reviews being conducted during a typical consultation.

*“I thought it was realistic kinda of em consultation from that point of view and you also demonstrated how you can actually do it in a pretty time pretty time efficient manner as well that you know it’s not it doesn’t require you know three quarters of an hour sitting down with a BNF, that you can run through these things kinda with the patient in front of you” [GPP22]*

*“I think that was very realistic ye know I mean eh eh it it sort of struck me that ye know the list of medication the patient was taking was very reflective of, be very typical of a lot of general practice patients” [GPP24]*

However, one GP stated that it would not be possible to conduct a medication review in every consultation with every patient they see, due to time constraints, but was overall positive about the study and the video.

*“the only reservation there would be with we’d rarely have enough time to do that with each and every patient” [GPP24]*

As part of the intervention, GPs were asked to have a weekly meeting with practice staff. Weekly meetings only occurred while study activities were taking place (for example, 6-month follow-up medication reviews) or only once as in the case of GPP22. The lack of weekly meetings was reported due to COVID-19 and the small number of patients involved in the study.

*“I know it mentioned the weekly meeting to be honest that that fell by the way side we were dealing with six named people” [GPP22]*

GP practices found the patient recall process straightforward to execute, especially as they are used to scheduling appointments and it was not an unfamiliar task for the GP practice to undertake, including the GP receiving the prompt that the patient was at the practice for their scheduled medication review as part of the PolyPrime study.

*“It wasn’t a problem we do that all the time. We schedule everybody for appointments so there wasn’t a bother to actually just add in the extra four people” [GPP24PM]*

Conducting medication reviews was well received by both GPs and the protected time to conduct a medication review was beneficial as there were no other issues to discuss, such as acute illnesses, during the consultation.

*“apply this as an opportunity to reduce polypharmacy you know so just focusing just on the actual medication or the chronic illness as opposed to kinda well saying maybe you could do without that” [GPP22]*

*“well eh the thought it was eh very straightforward, I suppose the fact that we didn’t have ye know any other issues to to eh discuss during the consultation, the patients weren’t coming to see me for any particular medical problem...it was purely for for this so we had like full fifteen to twenty minutes to do to do the medication review” [GPP24]*

One GP noted that not all recruited patients were assigned to him in the GP practice, as such, no medication changes were made but instead his review was passed on to the patients assigned GP and it was left to them to follow-up with the patient and make any necessary medication changes.

*“the only difficulty I had was the in looking at these four patients’ medication, I didn’t want to obviously or wouldn’t make any change without consulting with their own GP” [GPP24]*

Study procedures, such as patient screening and recruitment as well as the support the GP practice received from the research team were also discussed during the interviews with GPs and practice staff. The patient screening and recruitment process was considered the most time-consuming aspect of participating in the PolyPrime study by one GP. Whilst the other noted that the recruitment process was fair and ensured that the patients did not feel obliged to participate in the study.

*“Probably the the the most time-consuming part was just was just identifying the patients in the first place” [GPP22]*

*“I think it did ehh I think patients didn’t feel eh you know sort of ehh forced to eh eh to enrol as such eh so I think that was, that was satisfactory” [GPP24]*

The practice manager stated that if there had been an element of face-to-face interaction, or researchers having personal communication with potential participants at some point in the recruitment process, that possibly more patients would have consented to participate in the study. This may also have prevented the high drop-out rate that was seen across the study. The practice manager also noted that patients may have found the questionnaires to be long.

*“that’s my only point, even if [research nurses name] had been able to speak to them for five minutes I think it would be lovely, and they would be well on board and they would meet somebody and they’d put a face to the study right” [GPP24PM]*

*“some of them found them quite long-winded or couldn’t be bothered filling all this stuff out” [GPP24PM]*

GPP24 also discussed the questionnaires that patients were asked to complete at three separate time points, and suggested that after returning their consent forms, patients could then be asked to complete the questionnaires. The recruitment pack received by patients [including invitation letter, patient information leaflet, two consent forms and three questionnaires (EQ-5D-5L, MRB-QoL, health service use questionnaire), may have discouraged some patients to participate.

*“possibly ehh ye know introducing it at the recruitment stage, maybe not to have too many questions... It might just have deterred some people from er who would otherwise maybe have agreed to take part” [GPP24]*

The PhD candidate was in contact at various timepoints throughout the intervention to inform the GP practice of the next steps involved in the intervention and what was required from the GPs and/or practice staff. This was well received by the GPs and practice manager.

*“It was absolutely the great there wasn’t any point were I felt we were kinda em all at sea or anything you know” [GPP22]*

*“I think that was very good we we we understood exactly what we had to do, and eh yes of course support was eh eh was excellent really... I think you you were with us on a regular basis eh taking us through each step so we knew exactly what was involved” [GPP24]*

*Burden*



GPs did not consider participating in the study to be burdensome because of the few numbers of recruited patients.

*“It was a little bit different because of everything that’s been going on but not not in anyway time consuming. I suppose again it’s something that could be different with a larger practice or with a larger cohort where you had to make em a more a more kinda regiment plan about how you were going to deal with it” [GPP22]*

The practice manager noted that the only real effort required with participating in the intervention was that patients were identified as their given ID code and not their name and due to patient drop-out the ID codes were no longer in numerical order. The practice manager had to refer to the patient identification list each time to complete a task as part of the intervention, such as contacting patients to schedule a medication review or completing intervention paperwork for each individual patient.

*“It was their number and that is understandable but it was just a little bit of effort to work it, like [GP name] was who’s number 1 again?” [GPP24PM]*

#### *Ethicality*

Although there was no specific question in relation to ‘ethicality’ in either the topic guide for GPs or practice staff, the interpretive summary identified relevant information regarding how the PolyPrime intervention has good fit on the individuals value system. GPs noted that medication reviews are something that should be happening in GP practice as standard, but often they are not conducted.

*“well you should be doing that anyway but the reality is it often takes something just to eh just to focus on it” [GPP22]*

*“it’s not something that we eh probably do systematically... Because of time restraints, but we do try to review the patients’ medications as often as we can, and yes, the the intervention it’s perfect time.” [GPP24]*

#### *Intervention coherence*

GPs understood how the intervention aimed to improve appropriate polypharmacy in older adults and specified the usefulness of the video.

*“the point was definitely made in the video and there’s, there’s obviously, there’s appropriate polypharmacy and then there’s times in a medication review where you might have to increase rather than decrease the dose, or the number of tablets that are*

*involved, so yeah, I think again it's just making you think about the, the intent behind the prescription just that in that each of them is having the intended effect, and not having adverse effects" [GPP22]*

The practice manager reported that it was also useful for the practice staff to be aware of the importance of appropriate polypharmacy.

*"it's just handy to look at that, and just, when ye do have patients whether there's all or fine, ye know doing a prescription, I could ring a doctor and say just to say does he still need to be on Calcichew or still need to be on..." [GPP24PM]*

#### *Opportunity costs*

Both GPs detailed that they did not have to deprioritize anything, such as work tasks or extend their working hours to participate in the PolyPrime study, particularly when there were so few patients involved.

*"Eh no it wasn't disruptive because eh as I said we were we were just dealing with four patients" [GPP24]*

#### *Perceived effectiveness*

GPs stated that they believe the intervention would be effective in improving appropriate polypharmacy in older patients and that patients not involved in the study also benefitted as the study served as a reminder to think about reviewing medications for their patients.

*"you're looking to focus the doctor on what needs to be done, you're looking to get the patients involved in it. Em, yeah, I think it is, I found it quite effective anyway em, as I said, it did em, it did, it did focus me on something that I maybe wasn't paying as much attention to as previously" [GPP22]*

*"I suppose in our four patients it merely eh ye know, and eh it would mainly have just confirmed that they were on appropriate medications, but I'm sure as I said before that there were probably other patients not in...study, where hopefully ehh the the medications were eh aimed to be ehh reduced" [GPP24]*

The practice manager also noted that the study encouraged patients involved to take ownership of their medications and ask questions about their prescriptions.

*“Where and ye know I think the older people as well, they might mention there like ‘Look, do I need to still be on that?’ or, the people who were involved in the study... I think that’s eh a good thing” [GPP24PM]*

### *Self-efficacy*

GPs reported that they felt confident to conduct the medication reviews after watching the online video and that it reinforced the need to conduct medication reviews.

*“Em pretty confident, I think like most, most of the actual kind communication skills, clinical acumen that is demonstrated in the video I think is something that most GPs would be pretty self-confident about. Em so again, I think it’s just having the em, the opportunity and the time and whether that’s time to do it opportunistically or making the time as part of routine healthchecks. Em, but that’s, that probably would be the main thing that, just, not being focused on and being able to do it at the appropriate time” [GPP22].*

### *Overall acceptability of the study*

The TFA does not include a section on overall acceptability, however, it was important to ask both GPs and practice staff if they believed the whole intervention was acceptable or not. All three interviewees stated that the intervention was acceptable.

*“obviously there was a lot of work involved, both for you and for us, and eh a lot of questions which you had to ask, I I think we understood why ye had to answer you had to ask ye know many questions many times... but my overall impression was that it was very professional professionally conducted eh survey” [GPP24]*

### *Feedback questionnaires*

Feedback questionnaires were received from seven of the 10 patients (70%) recruited from both intervention GP practices, however, not all patients answered each question. The remaining patients claimed to have posted the questionnaires to the PhD candidate, but these were not received. Based on the seven responses received, the patients’ experiences of participating in the PolyPrime intervention were positive with four reporting their experience as ‘Good’, and one reporting it as ‘Average’ (two did not respond) and six patients would recommend being involved in the PolyPrime study to a family or friend and one would not. Patients were asked how much effort was required for them to take part in the study, two patients stated ‘No effort

at all', four stated 'A little effort' and one patient did not provide an answer. The quantitative findings from the feedback questionnaires are presented in Table 4.20. Five patients reported that they were happy with the overall experience of participating in the study and that nothing could be improved, with one patient noting that longer appointment times would improve the study, as well as feedback, and another stating that they could benefit from understanding their medications more.

*"more formal feedback from the GP on potential follow up actions" [GPP24PT05]*

*"I feel I could benefit from understanding my medications better" [GPP2PT07].*

In terms of the medication review appointments, three patients reported that they liked attending for their appointments, three did not respond and one patient did answer with one of the given options but wrote

*"looked forward to review but felt it was not constructive. LIKE the idea. DISLIKE lack of focus" [GPP24PT05].*

The effect of medication reviews as part of the study was generally positive from the seven patients. Three patients were reassured that their medicines have been reviewed, and a further fourth patient has a better understanding of the medicines they take. Two patients reported it made no difference and with one of these two patients reporting that they are still concerned about the medicines they take, and one did not respond.

*"understand the medication I am now taking and what they are for" [GPP22PT01]*

*"the follow up was efficient" [GPP24PT08].*

Study procedures, such as recruitment, completing questionnaires and research team support were also included in the feedback questionnaire. Four patients responded with 'Like' when asked how they felt about the first time they were contacted about the study, via post, with two patients stating they had 'No opinion' and one did not respond. All seven patients stated that they were happy with the number of questionnaires they were asked to complete during the study, with explanations including:

*"the study was efficient. Enough questions asked (easy to answer)" [GPP22PT04]*

*"There were no questions regarding narrative in the answer and responding was not time consuming" [GPP24PT05].*

Five patients were happy with the support provided by members of the research team

*“the questions asked were fully explained”* [GPP22PT04]

*“always pleasant and willing to answer any questions I had”* [GPP22PT07].

One patient responded with ‘N/A’ as they

*“did not require assistance from the research team”* [GPP24PT05]

and the seventh patient did not tick a given response but stated

*“never contacted the research team directly”* [GPP22PT01].

**Table 4.20 Quantitative responses from feedback questionnaires**

<b>Feedback questionnaire item</b>	<b>Response</b>
Number of questionnaires posted	10
Number of questionnaires returned	7
<i>Did you like or dislike the way you were contacted about the study?</i>	
Like	4
No opinion	2
Missing	1
<i>Were you happy with the number of questionnaires you were asked to complete?</i>	
Yes	7
<i>Were you happy with the support from members of the research team?</i>	
Yes	5
Not contacted	1
Missing	1
<i>What did you hope would happen as a result of having your medicines reviewed by your GP?</i>	
The number of medicines I take would decrease	1
I would have a better understanding about the medicines I take	2
I would feel happier about my medicines I take	2
I would feel reassured that my medicines have been reviewed	6
<i>Based on my experience, the PolyPrime intervention is likely to improve how many medicines are prescribed for older people.</i>	
Agree	3
No opinion	1
Missing	3
<i>What has been the effect of having your medicines reviewed by your GP?</i>	
I have a better understanding about the medicines I take	1
I feel reassured that my medicines have been reviewed	3
I am still concerned about my medicines	1
No difference	2
<i>How would you sum up your experience of the PolyPrime study?</i>	
Good	4
Average	1
Missing	2
<i>How much effort was required for you to take part in the PolyPrime study?</i>	
No effort	2
Little effort	4
Missing	1
<i>What would have improved your overall experience of being involved in the PolyPrime study?</i>	
Longer appointments	1
Nothing, I was happy with the overall experience	4
<i>Would you recommend being involved in the PolyPrime study to a friend or family member?</i>	
Yes	6
No	1

#### 4.4.8 Mechanisms of action

The mechanisms of action (MoA) 'mediate' intervention effects (Carey *et al.* 2019), which are activated as a result of the BCTs. The findings in relation to the BCTs and their intended MoA are discussed below, presented with the relevant intervention component. Results presented here are to emphasise the response to each included BCT. As some medication reviews were conducted via telephone and the face-to-face appointments required face masks to be worn by both the GP and patient (COVID-19 guidelines), it was not possible for either GP to record any medication review appointments. Consequently, it is not possible to determine if any additional BCTs were delivered during the medication review.

*Intervention component: BCT: Demonstration of the behaviour – Online video (MoA: GPs beliefs about capabilities/ Skills)*

The feedback interviews were analysed to assess if watching the online video brought about changes in the GPs beliefs about capabilities, regarding conducting medication reviews. Both GPs stated that they felt confident in conducting medication reviews after watching the video.

*“I would say I was very confident, increasingly confident, ehh I would have been confident to conduct such an interview in any case, but the eh the the video was of enhanced system.” [GPP24]*

*Intervention component: Weekly meetings between GPs and practice staff, BCT: Action planning (MoA: Memory, attention, and decision processes/ Behavioural regulation)*

As noted above, GPs were asked to record the number of weekly meetings they had with practice staff. This alongside data from the feedback interviews from GPs and practice staff showed that meetings took place during the intervention delivery stages of the study. Self-reported quantitative data shows that three meetings took place across both practices throughout the study. However, it is clear that the weekly meetings were not deemed necessary by the practices and were conducted as an add on to a pre-arranged meeting or as a discussion as opposed to an official meeting specifically for the study.

*“That was fine. [Pause] Fine, again we’re a very small practice so it was it was just basically myself and [GP name] involved ... like we’d have a meeting on a Monday, we’d just afterwards have a quick mention about PolyPrime” [GPP24PM]*

*“I know it mentioned the weekly meeting to be honest that that fell by the way side, we were were dealing with six named people we were pretty familiar with so we were able to say look this is how we are able to manage that we’ll bring them back” [GPP22]*

It was acknowledged that holding meetings as part of the PolyPrime study was beneficial and did not disrupt the work schedule in the GP practice.

*“I thought it was useful and ehh it wasn’t at all disruptive I mean it was one, was one meeting per week” [GPP24].*

*Intervention component: Simulated patient and GP feedback in online video, BCT: Salience of consequences (MoA: Salience about consequences)*

As noted previously, the video was well received by GPs. The specific part of the video in relation to this BCT involved the simulated patient and GP providing their thoughts on receiving/providing a medication review during the scheduled consultation. Whilst the GPs did not comment on this reflection process, they stated that the video was useful and could be used as part of a continued training programme.

*“I think it would have been a eh a directive video that could be used for training and continuing education” [GPP24]*

*Intervention component: Practice staff delivering prompts to GP, BCT: Prompts/ cues (MoA: Memory, attention, and decision processes/ Behavioural regulation)*

Quantitative data from the self-report forms GP practices were asked to complete and qualitative data from the GP and practice manager feedback interviews revealed numerous verbal prompts were provided to the GP in one general practice for both the initial and 6-month follow-up medication reviews; average 1.75 verbal prompts delivered by the practice manager to the recruited GP per patient at both reviews. However, the interview with the practice manager highlighted that it was also recorded in the GP practices appointment system that the patient was attending for their scheduled medication review as part of the PolyPrime study. The other GP stated that the prompts were not frequently used. This GP discussed that he did not want to bring the patients into the practice, if possible, due to the COVID-19 Coronavirus situation, and so identified free time periods in the schedule to call them himself. Both GP practices received a reminder from AG that the 6-month follow-up medication reviews were due and to organize these with the recruited patients in their practice.



“so we weren’t like yeh (secretary name) wasn’t prompting me for for appointments, because kinda I just identified right well actually we just need to we just need to do this by phone, I don’t really want to call this person in you know” [GPP22]

#### 4.4.9 Progression criteria

As noted in section 4.3.6, the progression criteria were developed for the overall trial including both healthcare jurisdictions (i.e. NI and the RoI), however, the results of the progression criteria are presented in relation to the RoI only, see Table 4.21. Two progression criteria met ‘Go’ (GP practice recruitment and Completeness of outcome data) and three progression criteria met ‘Amend’ (GP practice retention, Patient recruitment and Patient retention). The results of the progression criteria were discussed between the TSC and the management team. As two GP practices from the RoI withdrew due to COVID-19, the opinion of the TSC was that this criterion would have met ‘Go’ as both the practices had consented to participate, if COVID-19 was not an issue. The TSC was not able to determine if the progression criteria Patient recruitment and Patient retention would have met ‘Go’ if COVID-19 had not been present.

**Table 4.21 Progression criteria results**

<b>Progression criteria</b>	<b>Met</b>	<b>Result</b>
GP practice recruitment	<i>Go</i> (If $\geq 5$ GP practices are recruited to take part in $\leq 6$ months)	6 GP practices were recruited to take part in $\leq 6$ months
GP practice retention	<i>Amend</i> (If 4 GP practices can be retained for the required period)	4 GP practices were retained for the required period
Patient recruitment	<i>Amend</i> (If 30-48 patients are recruited within 5 months)	36 patients were recruited within 5 months
Patient retention	<i>Amend</i> (If 50-80% of participants are retained for the required period)	58.3% of participants were retained for the required period
Completeness of outcome data	<i>Go</i> (If $\geq 80\%$ of each patient self-report and GP-reported outcome measure is complete)	90.5% of each patient self-report and GP-reported outcome measure is complete

## **4.5 Discussion**

A pilot study should not focus on the comparison of outcomes between intervention and control groups (Kistin and Silverstein 2015). Therefore, this discussion focuses on the study outcomes, in particular the results of the progression criteria (including possible amendments required for a definitive cluster RCT) and the ability to collect the necessary data both from GP record data and patient self-report. The impact of COVID-19 on the study and the strengths and limitations are also addressed.

### **4.5.1 Progression criteria**

The recruitment strategy for GP practices was successful with six GP practices recruited within a six month timeframe, meeting the 'Go' progression criteria. Two GP practices withdrew from the study therefore four GP practices were retained for the required period, meeting the 'Amend' GP practice retention progression criteria. However, both practices cited the increasing demand and pressure on general practice because of COVID-19. After discussions between the TSC and management team, it was agreed that this criterion would have met 'Go' had it not been for COVID-19. As a result, no modifications to the GP recruitment strategy are required for progression to a definitive cluster RCT.

CB had begun patient screening and recruitment prior to COVID-19, which halted due to study suspension in March 2020. As COVID-19 was still present when the study recommenced, it was not possible to continue with patient recruitment due to government restrictions and access to GP practices. If patient recruitment had continued at the same rate before study suspension, it is likely that this progression criteria would have met 'Go'. However, it is not certain that this would have occurred, and the criterion was therefore not adjusted from 'Amend' to 'Go'. Possible amendments to patient recruitment were addressed in the process evaluation interviews with GPs and practice staff which are discussed below. Patient retention was 58.3% which met 'Amend' (50-80% patients retained for the required period). After the study recommenced, a large drop-out was experienced. Amendments for this criterion might be addressed with a varying recruitment strategy, as mentioned during the process evaluation interviews. This could involve researchers having face-to-face time with potential participants during the recruitment phase as suggested during the interviews with practice staff and GPs. Progression to a definitive cRCT would require researching recruitment methods that have been successful in primary care in Ireland.

The final progression criterion was the completeness of outcome data which met 'Go'. This pilot study showed that it was feasible to collect the necessary data from GP practice record and

patient self-reports with 90.5% of data being collected. Due to the nature of the quality of life tools (i.e. EQ-5D-5L and MRB-QoL), it was not possible to calculate scores if the full questionnaire was not completed, impacting on the completeness of data.

#### **4.5.2 Application of STOPP/START**

Data collection forms designed specifically for the PolyPrime study to collect GP practice data allowed for the application of STOPP/START (O'Mahony *et al.* 2015) and therefore this is a feasible primary outcome for definitive cluster RCT. There are numerous validated assessment tools assessing appropriate prescribing. It was decided to include STOPP/START as the validated assessment tool in the PolyPrime study as it has been widely used in clinical practice and used in studies conducted in NI and the RoI (Gallagher *et al.* 2008, Galvin *et al.* 2014, Dalton *et al.* 2019, Inch *et al.* 2019). The main concern with STOPP/START in the PolyPrime study was whether or not enough patient data could be gleaned from the medical notes to apply the tool in its entirety. It had not been possible to apply the STOPP/START tool in the assessment of appropriate prescribing during the feasibility study (Cadogan *et al.* 2018) due to insufficient patient record data.

Lam and Cheung (2012) provided an overview of both STOPP/START (version 1, Gallagher *et al.* 2008) and Beers' criteria (Fick *et al.* 2003) and noted that STOPP/START is a more sensitive tool, in that it identifies more potentially inappropriate prescribing compared to the Beers' criteria. Studies conducted in the primary care setting have found that the prevalence of potentially inappropriate prescribing to be higher with the use of STOPP/START compared to Beers' criteria (Conejos Miquel *et al.* 2010, Lafuente Gonzalez *et al.* 2015, van der Stelt *et al.* 2016). Hamilton *et al.* (2011) found STOPP/START detected at least one instance of potentially inappropriate prescribing in 56% of hospitalized patients and Beers' criteria detected 29% in the same population.

STOPP/START has proven to identify more instances of potentially inappropriate prescribing compared to Beers' Criteria (Steinman and Fick 2019) in various countries including Spain (Ubeda *et al.* 2012), Australia (Curtain *et al.* 2013), and the Netherlands (Rongen *et al.* 2016). STOPP and Beers criteria have also been used in conjunction to identify instances of potentially inappropriate medications to positive effect (Khera *et al.* 2019, Buda *et al.* 2021). However, a systematic review conducted by Thomas and Thomas (2019) concluded that Beers' criteria identified at least one instance of potentially inappropriate prescribing in nearly 47% of older adults living in the community whilst STOPP identified at least one instance of potentially inappropriate prescribing in 40% of the same cohort. As this systematic review brought together

assessments of STOPP/START and Beers criteria from across the world, the results should be interpreted with caution as different countries may have varying prescribing guidelines.

As presented in Table 4.16 (section 4.4.3) patients in both the control arm and intervention arm had received a medication review in the previous six months prior to baseline data collection for the PolyPrime study. Interestingly, the number of control arm patients that received a medication review increased during the PolyPrime study. Medication reviews have been shown to be effective in ensuring appropriate prescribing of multiple medications (van Summeren *et al.* 2017, Lenander *et al.* 2018) which might explain why GPs in the control arm provided their patients with a medication review. Alternatively, this could be a result of the Hawthorne effect, when individuals consciously alter their natural behaviour because they are aware they are being studied (Sedgwick 2015). It is possible that participating in an intervention focusing on appropriate prescribing and medication reviews, may have encouraged GPs to conduct medication reviews to ensure their patients are receiving appropriate medications.

Interestingly, the data collected from GP records showed that not all patients allocated to the intervention arm had received a medication review at 6-months and 9-months follow-up post initial medication review, however, all PolyPrime documentation was completed and returned indicating that they did occur. This could highlight a potential concern with practices not documenting all interactions with their patients and what was discussed during this time, a possible factor to consider if the PolyPrime study was to progress to a definitive RCT.

#### **4.5.3 Quality of life tools included in the PolyPrime study**

Definitions of quality of life vary, however, common concepts across the literature include cultural, societal, psychological and physical dimensions as well as general satisfaction (Post 2014). In relation to health-related quality of life, Krahn *et al.* (2014) state that five dimensions are required: physical health (e.g. energy/fatigue), mental health (e.g. distress), social health (e.g. relationships), life satisfaction/beliefs (e.g. meaningful activities) and environment (e.g. safety and security). The variation of definitions then impacts on the dimensions included in quality of life tools. Therefore, it was important to investigate the range of quality of life tools available to ensure that the most appropriate tool/tools were included in the study and that it reflected the aim and objectives of the PolyPrime study. It is important to note here that although quality of life measures were collected, they are only presented in this thesis in relation to the completeness of outcome data measure. The quality of life measures collected were also part of a separate health economic analysis, conducted by an health economist in the NICTU.

Results of the health economic analysis in the PolyPrime intervention have been published in Rankin *et al.* (2022).

The EQ-5D-5L (Herdman *et al.* 2011) was included as one of the quality of life tools in the PolyPrime study, the second specifying medication and quality of life, the MRB-QoL tool (Mohammed *et al.* 2018a). Three versions of the EQ instruments exist: EQ-5D-3L (Rabin and de Charro 2001), EQ-5D-5L (Herdman *et al.* 2011) and the EQ-5D-Y (Wille *et al.* 2010). The EQ-5D-Y (Wille *et al.* 2010) was designed for children and adolescents to self-complete and was therefore not suitable for use in the PolyPrime study. Choosing between the EQ-5D-3L (Rabin and de Charro 2001) and EQ-5D-5L (Herdman *et al.* 2011) requires thought as both have been used to good effect in numerous studies focusing on older adults with polypharmacy (Cardwell *et al.* 2020, Kang *et al.* 2020, Patton *et al.* 2021, McCarthy *et al.* 2022, Salari *et al.* 2022). A study by Bhadhuri *et al.* (2020) concluded that either the EQ-5D-3L (Rabin and de Charro 2001) or the EQ-5D-5L (Herdman *et al.* 2011) are suitable to be included in a study on older adults with polypharmacy. The EQ-5D-5L (Herdman *et al.* 2011) was chosen over the EQ-5D-3L (Rabin and de Charro 2001) due to the response options in relation to each dimension. The EQ-5D-5L (Herdman *et al.* 2011) has five options for each domain (see section 4.3.5) with the EQ-5D-3L only having three (no problems, some problems, extreme problems). Given that the population of the study were 70 years or over and prescribed a minimum of four medications, as part of the inclusion criteria, the EQ-5D-5L (Herdman *et al.* 2011) provided a wider range of response options to assess the quality of life of patients over the course of the study. The small number of patients that participated in the study meant that the analysis of results was limited to what was presented above, however, the high response rate at the three timepoints indicates that the tool was straightforward for patients to complete. As this was self-completed by the patient and returned via post, we do not know if the patient required assistance to complete the EQ-5D-5L. A systematic review of 17 studies using either the EQ-5D-5L (Herdman *et al.* 2011) or the EQ-5D-3L (Rabin and de Charro 2001) to assess quality of life in older adults, concluded that a completion rate of 90% is common when the tool is completed by an older adult (Marten *et al.* 2021). Studies have shown that it generates a lower missing value than other quality of life tools that are often included in studies with an older adult population such as the ICECAP-O (Davis *et al.* 2013) and SF-36 (Grund *et al.* 2017). The popularity of the EQ-5D tool has led to it being validated for use in various different countries including Spain (Hernandez *et al.* 2018) Singapore (Seng *et al.* 2020) and Poland (Młyńczak and Golicki 2021), indicating that it is usable by a range of people in various different social environments and healthcare contexts.

Numerous medication related quality of life tools were considered for use in the PolyPrime study, including the Medication-Related Quality of Life Scale (Tseng *et al.* 2016), and Living with Medicines Questionnaire (Krska *et al.* 2017, Katusiime *et al.* 2018), alongside the MRB-QoL (Mohammed *et al.* 2018a) that was the quality of life tool included in the PolyPrime study. The Living with Medicines Questionnaire was developed and validated within the UK which made it potentially suitable for use in the PolyPrime study. Interviews were conducted with 21 patients to discuss a range of potential dimensions to include in the tool (Krska *et al.* 2013), alongside free text comments from tool participants (Krska *et al.* 2017) and preliminary testing in an English primary care setting (Krska *et al.* 2014) ensuring extensive research was put into the development of the tool which can impact on its likelihood of being acceptable. The Living with Medicines Questionnaire has been used in numerous studies and was concluded as useful (van der Laan *et al.* 2018, Zidan *et al.* 2018, Tordoff *et al.* 2019, Awad *et al.* 2020). This tool does not focus on older adults and was developed with participants aged 18-90 years old, nor is polypharmacy a focus in the tool. Instead, participants can include those with only one medicine: as patients in the PolyPrime study are older adults taking multiple medicines, the Living with Medicines Questionnaire was not deemed to fit with the aim of the study.

The Medication-Related Quality of Life Scale was developed in Taiwan and as such, it was believed that it may not have been transferable for use in NI and the RoI. This tool focuses on patients with medication problems. Whilst the PolyPrime study aimed to improve appropriate prescribing for older adults, it could not be assumed that participants would have had medication problems and therefore it was not the most appropriate quality of life questionnaire to include in the study. A recent study by Jennings *et al.* (2021) found that it was not a suitable tool to assess medication-related quality of life for geriatric patients. However, Tegegn *et al.* (2019) found that the tool was usable and concluded that patients who report a lower quality of life are prescribed a higher number of medicines in Ethiopia. Interestingly, a study aiming to validate the Danish version of the Medication-Related Quality-of-Life Scale tool concluded that further work was required to be suitable in the Danish setting (Lech *et al.* 2020). The Danish healthcare system is similar to the healthcare system in NI and the RoI, compared to Ethiopia and Taiwan healthcare systems. This coupled with the knowledge that the acceptability and feasibility of the Medication-Related Quality of Life Scale tool was not fully explored, a small sample size was used with no qualitative data collected in the development process (which might have led to more relevant dimensions included in the tool) and the test-retest reliability was not fully established (Tseng *et al.* 2016), leads to the conclusion that the MRB-QoL tool (Mohammed *et al.* 2018a) was likely a better tool to include in the study.

The MRB-QoL tool (Mohammed *et al.* 2018a) used in the PolyPrime study was considered to be the most appropriate given that the development of the tool involved patients prescribed at least three medicines on a regular basis however, participants had to be 18 years or over which did not fit with the population of the PolyPrime study. With the tool developed in Australia, similarities between populations of Australia, NI and the RoI exist making it potentially more suited for use in a study conducted in NI and the RoI. The Principal Investigator was a colleague of a member of the MRB-QoL development team and so an agreement was made for the tool to be included in the PolyPrime study and the data would inform the validation of the tool outside Australia. Extensive research was conducted to inform the development of the MRB-QoL including two systematic reviews (Mohammed *et al.* 2016a, Mohammed *et al.* 2018b) and a systematic review of qualitative studies (Mohammed *et al.* 2016b) making the included domains more likely to be relevant. Whilst the MRB-QoL tool (Mohammed *et al.* 2018a) has not been utilised in many healthcare studies to date, it has been included in reviews of quality of life tools focusing on medication and was concluded to cover seven of 14 content domains. Domains not assessed in the MRB-QoL include perceived effectiveness of medicines, relationship with healthcare professionals about medicines, general satisfaction with medicines, self-control, accessibility of medicines, willingness to de-prescribe, and patients perceived healthcare professional knowledge about medicines (Kotronoulas *et al.* 2019). Overall, the MRB-QoL was found to be robust with criterion validity and floor/ceiling effects reported (Mohammed *et al.* 2018a). Other medicine related quality of life tools identified in the review by Kotronoulas *et al.* (2019) included the Treatment Satisfaction Questionnaire for Medication (TSQM, Atkinson *et al.* 2005) and Patient Experience with Treatment and Self-management (PETS, Eton *et al.* 2017). TSQM was found to be fit for purpose in various populations with numerous conditions (Delestras *et al.* 2013, Vermersch *et al.* 2017, Shilbayeh *et al.* 2018, Liberato *et al.* 2020) as was the PETS tool (Rogers *et al.* 2017, Eton *et al.* 2020, Lee *et al.* 2021). However, neither of these tools fit with the aim of the PolyPrime study making the MRB-QoL tool (Mohammed *et al.* 2018a) the best available medication related quality of life tool.

#### **4.5.4 Acceptability of the intervention**

GPs, practice staff and patients were very positive about the intervention. GPs felt the intervention enabled them to conduct medication reviews as well as reinforced that there is benefit to conducting them where possible. Videos have been used in other healthcare studies and have been well received in these settings (Kim *et al.* 2017; Myhill *et al.* 2017; Mian *et al.* 2020; Pisani *et al.* 2021). Many people are visual learners and therefore it can be easier for them to learn via a video, as opposed to reading. The video format allows GPs to watch it in their own

time and watch it again, with all the necessary information in one place. The video, and the general concept of the intervention in terms of conducting medication reviews, reminded GPs that these are an important part of a GPs role, and that they should be conducted. Other interventions focusing on GPs conducting medication reviews have been well received by GPs (Clyne *et al.* 2016; Sinnott *et al.* 2017). Patients were also positive towards receiving a medication review, and reported that they were reassured that their medications had been reviewed. This supports previous studies on patients' thoughts on medication reviews conducted by their GP, which have been positive (Clyne *et al.* 2016; Uhl *et al.* 2018; van Blijswijk *et al.* 2018).

The process evaluation showed that weekly meetings were not implemented to the extent intended by the research team. GPs and practice staff stated that this was mainly due to the small number of patients included in the study. As discussed in Chapter 1 (Introduction) and Chapter 4 (the PolyPrime study), the implementation of behaviour change technique 'Action Planning' was included in the PolyPrime study in the form of weekly meetings between GPs and practice staff. Whilst there is evidence to suggest that some BCTs work more effectively than others (Michie *et al.* 2009; Compernelle *et al.* 2019) there is need for further research into this claim (Peters *et al.* 2015), especially due to the BCTs implemented in various types of health care interventions such as prescribing, physical activity, and health eating which may impact the effectiveness of different BCTs. 'Action planning' has been found to have had no overall effect or moderate effect (Schroé *et al.* 2020), however the authors state that this may be due to the intention to do an activity can have an effect on some individuals, in terms of changing their behaviour, as opposed to forming a specific plan regarding how the intervention activity will be conducted. 'Action planning' is not one of the more commonly used BCTs in behaviour change interventions, with only 11 out of 86 studies incorporating the BCT into their intervention (Scott *et al.* 2020). Other behaviour change interventions have found it to be effective (Cradock *et al.* 2017; Howlett *et al.* 2019). It is important to note, that if the PolyPrime study was to proceed to a larger trial, according to feedback from both GPs and practice staff, that the weekly meetings may have more use if a larger number of patients were participating and it is therefore an important aspect of the intervention to keep.

Other BCTs delivered in the intervention included demonstration of the behaviour, salience of consequences and prompts/cues. Training is a common factor in healthcare interventions, either for the healthcare professionals or the patients. BCTs normally featuring in this part of an intervention include social support, information about consequences, self-belief, and comparison of outcomes. Demonstration of the behaviour has been the most commonly used



BCT in a variety of healthcare interventions with various types of participants including: increasing physical activity among breast cancer survivors (Hailey *et al.* 2022), hand washing in children (Watson *et al.* 2021), complimentary feeding (Webb Girard *et al.* 2020), and fall prevention programmes delivered to healthcare professionals (McHugh *et al.* 2018). This BCT has also shown to be effective in interventions, or is likely to be effective, if implemented to a larger cohort (Brierley *et al.* 2019). In the PolyPrime study, this BCT was delivered in the online video for GPs. Both GPs were very positive about this aspect of the intervention and how it reinforced that medication reviews can be conducted during routine consultations, although it would not be possible to conduct one during every routine consultation.

Salience of consequences was included as the feedback from the GP and simulated patient on the video. This particular aspect of the video was not discussed during the feedback interviews, a learning point for this researcher. However, it is an important component of the video and supports the BCT demonstration of behaviour. Salience of consequences reinforces the benefit of medication reviews for older adults on polypharmacy and so is relevant to the PolyPrime study on affecting prescribing behaviour change. The final BCT included, Prompts/cues, was also well received by the GPs and practice staff notably because it is something they already implement in the GP practice. A recent survey by O'Regan *et al.* (2020b) on GP practices found that all use computerized systems, which is likely the case across Ireland. This means that including the BCT Prompts/cues should be relatively straight forward for GP practices involved in a definitive RCT. The process evaluation has proved that the BCTs involved in the PolyPrime intervention are acceptable to GPs to improve appropriate polypharmacy in older adults, however, due to the limited data the BCTs effectiveness could not be assessed.

#### **4.5.5 Possible amendments arising from the process evaluation**

This pilot cRCT and its process evaluation informed the PolyPrime research team that there is scope for possible changes to be made to the intervention, if a full RCT is to occur. Recommendations from GPs and practice staff included changing the recruitment strategy and recommendations from patients included longer medication review times, a specific format for the medication review and to have the medication review conducted by the patient's assigned GP within the practice.

Firstly, the screening and recruitment process was discussed as an area for possible improvement. One GP noted that a new recruitment option could be to wait until the patients either present at the practice or contact the practice to provide them with information about the study, and invite them to participate. It is not uncommon for healthcare interventions to

use healthcare professionals to recruit participants (Messerli *et al.* 2016; Fathima *et al.* 2019; Patton *et al.* 2021). There are limitations associated with healthcare professionals recruiting for a study being conducted on their site, with previous studies noting that there are time constraints (Fathima *et al.* 2019), recruitment paperwork and procedures can be seen as burdensome (Patton *et al.* 2021), and staff might forget they are participating in a study and not remember to bring it to the attention of an eligible patient (van den Brink *et al.* 2020). Many healthcare professionals do not fully understand the time and commitment that is often required to recruit target numbers as they are rarely involved in trials. If the PolyPrime study was to proceed to a definitive pilot trial, it is unlikely this suggestion will be adopted.

Whilst it is well documented that recruitment to healthcare interventions can be challenging (CISCRP 2019), the practice manager at GPP24 noted a face-to-face approach may help with recruitment and retention in this study. Axén *et al.* (2021) recommend a face-to-face meeting between researchers and potential participants during the recruitment phase. This could potentially be added to the recruitment process of the PolyPrime intervention, however, not all GP practices will be able to provide space for this, and the researchers involved would have to be approachable and not persuasive to allow potential participants sufficient time to consider participating in the study and ensure consent is freely given, as is required by the current General Data Protection Regulations (European Parliament 2016). Research into improving recruitment in clinical trials ranked moving information from the participant information leaflet to a face-to-face meeting as a top 3 improvement strategy (Bower *et al.* 2014), however it is important to note that this recommendation was made prior to COVID-19 and that, regardless of government guidelines at the time of recruitment, some practices may not be happy to host face-to-face recruitment sessions, and some patients may not be comfortable with attending their GP practice for this purpose. Potential participants should still receive a participant information leaflet after an initial face-to-face meeting with a researcher to ensure that they have substantial information, and that informed consent [the procedure of informing participants of the potential risks of partaking in a study and receiving their agreement to partake (Perrault and Keating 2018)] is given (Innes *et al.* 2018).

Both practices allocated to the intervention arm had at least 2 GPs working within the GP practice, however only one GP within each practice consented to participate in the study. This meant that it was likely that some patients received medication reviews from the GP they do not normally see. This was the case with one patient who felt the communication between the GP involved in the study and their own GP was not optimal as recommendations were provided to their GP and no changes were made. This finding may only be relevant to one patient from a

possible ten, however, it is important that all patients are comfortable and satisfied with the healthcare they receive regardless of whether it is part of a healthcare intervention or their normal healthcare schedule. Mohammed *et al.* (2016) found that lack of an established relationship with the GP can lead a patient to have a negative attitude towards their prescribed treatment and conduct inappropriate medication related behaviour. Research has been conducted regarding patient's familiarization with the GP, what the patient gets out of the consultation, and the healthcare they feel they have received from the consultation. A Polish study found a positive correlation between having a pre-established relationship with the GP conducting the consultation and their perceived ability to cope with the condition discussed and understand the health problem (Pawlikowska *et al.* 2009). This study supports previous work by Nutting *et al.* (2003) and Guthrie *et al.* (2008) who found that older adults benefit from continuity of healthcare professionals, notably due to the likelihood of multiple conditions being present. More recently, improving continuity of care has become a research priority, due to patients receiving care from multiple different healthcare professionals and in various settings (Haggerty *et al.* 2013). This is important for people in Ireland, given the disjointed nature of the healthcare system in the RoI (as discussed in chapter 1, section 1.5). Whilst having an assigned GP in a GP practice is often welcomed by patients and has been shown to decrease the risk of mortality (Maarsingh *et al.* 2016), in a move to see all adults aged 75 years or over in England have a named accountable GP in their practice, Barker *et al.* (2016a) found that it did not improve the care received. It might be beneficial, more so to the patients than GPs, to include a caveat in a definitive RCT that patients should receive the medication review from the GP they see most often.

A patient also recommended that the study could benefit from longer appointment times. GPs were not provided with any guidance as to how long a medication review meeting should last, but the video showed that they could be completed during a typical consultation. A typical consultation with a GP in Ireland lasts just over 14 minutes (Pierse *et al.* 2019) whilst the entire PolyPrime video lasted 13 minutes. Duncan *et al.* (2019) found that many GPs, as well as community pharmacists who conduct medication reviews, often conduct a medication review without the patient being present, but recognize the usefulness and need for involving the patient in their medication review. This study supports the set-up of the PolyPrime intervention whereby the patient is present at the GP practice with their GP and involved in the process of having their medications reviewed.

Another suggestion, again only from one patient, was for GPs to provide feedback on the consultation. This was provided in the feedback questionnaire, so we are unable to determine

if the feedback is in reference to how the GP felt the medication review went and why they made the suggestions or changes that they did. Parker *et al.* (2021) comment that providing information to the patient on taking medication, explaining how the medication works, any side effects, as well as inviting questions, is an important aspect of communication between a GP and their patient.

The MRC guidelines, which have been referred to throughout the development of the PolyPrime study, note that evaluating the acceptability of an intervention is a key aspect of a process evaluation; however, the guidelines provide little guidance for doing so. Definitions of acceptability in evaluation research range from treatment acceptability, such as patient opinions on the interventions effectiveness on addressing the clinical issue (Sidani *et al.* 2009), to person/social context focused, such as patient attitudes towards the facility in which an intervention occurs (Dillip *et al.* 2012). Whilst developing the TFA, Sekhon *et al.* also constructed their own definition of acceptability, “a multi-faceted construct that reflects the extent to which people delivering or receiving a healthcare intervention consider it to be appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention” (Sekhon *et al.* 2017:4). The TFA allowed for researchers to provide a deeper assessment of participants’ view on the acceptability of the intervention, with topic guide questions based on the TFA in comparison to asking a closed question such as ‘was the intervention acceptable?’ This was an important factor in determining the acceptability of the PolyPrime intervention as acceptability is not a fixed construct (Deja *et al.* 2021). The TFA has been used to great success in other healthcare interventions (Murphy and Gardner 2019, Pavlova *et al.* 2020, Bartlett *et al.* 2021, Sekhon *et al.* 2021)

#### **4.5.6 Scale-up of the PolyPrime study**

The PolyPrime intervention was deemed to be acceptable overall by the staff in the two GP practices in which it was implemented. Health literature argues that the intervention should be ‘scaled up’ and implemented on a wider scale (WHO 2010, Milat *et al.* 2013). To scale-up an intervention can mean the “deliberate efforts to increase the impact of successfully tested health interventions so as to benefit more people and to foster policy and program development on a lasting basis” (WHO 2010). Assessing the scalability of a health intervention, i.e., “the ability of a health intervention shown to be efficacious on a small scale or under controlled conditions to be expanded under real-world conditions to reach a greater proportion of the eligible population, while retaining effectiveness” (Milat *et al.* 2013), is a fundamental process in scaling-up an intervention.

Numerous frameworks have been developed to facilitate intervention scale up of healthcare interventions; many of which are defined by either the intervention focus [such as HIV/AIDS (Hirschhorn *et al.* 2013), mental health (Belkin *et al.* 2011), chronic respiratory diseases (Bousquet *et al.* 2016)] or if they had been conducted in a low-middle income country (Atun 2010; Yamey 2011; Bradley *et al.* 2012b; Barker 2016b; Cooley *et al.* 2016) or a high-income country (Victoria *et al.* 2012; Milat *et al.* 2016; Greenhalgh *et al.* 2017). Others are more general: Zamboni *et al.* (2019) published a literature review identifying five factors to consider when planning a scale-up: (i) attributes of the intervention, (ii) attributes of the implementers, (iii) attributes of the adopting community, (iv) socio-political context, (v) scale-up strategy. Another literature review conducted by Milat *et al.* 2020 identified twelve concepts that are common in published scalability checklists or frameworks (including comparison against similar interventions, evidence of effectiveness, intervention reach and acceptability, scale-up and implementation considerations for example). The twelve concepts were used to develop the Intervention Scalability Assessment Tool, a three-part tool that can be used not only for decision making regarding scale-up of an intervention but also as a support to receive additional funding, and document key learnings for quality improvement activities. However, a common criticism of scale-up frameworks is that they lack a theoretical basis. Nguyen *et al.* 2020 have developed a framework based on three theories: diffusion of innovation, complex adaptive systems, and organisational readiness for change. This contains three phases: (i) groundwork preparation, (ii) implementing scale-up, (iii) sustaining the scaled-up health intervention, and acknowledges that intervention components of context, capacity and stakeholders can be interdependent on the other as well as constantly changing and influencing each scale-up phase.

A scale-up framework that might be more applicable to the PolyPrime intervention is from Saeri *et al.* (2021) who conducted two studies, the first being a qualitative synthesis identifying fifteen articles and identifying five factors for scale -up (i) complexity, (ii) measured and perceived effectiveness, (iii) adaptability, (iv) congruence, (v) compatibility and acceptability. The second study consisted of twelve interviews with behaviour science experts and discussed what the interviewees deemed to be relevant factors to scale-up and why, as well as the activities involved. The results from these two studies developed SCALE framework for improving scale up of behaviour change interventions. SCALE is an acronym for the framework: **S**imilar (scale up is more effective when the intervention is tested in contexts similar to those that it will be scaled into and by similar deployment teams); **C**ost-effective (scale up is more effective when the intervention is perceived to be cost-effective by those required to propagate and adopt it); **A**ceptable (scale up is more effective when the intervention to be scaled is acceptable,

compatible and affordable to the supporting organisation and target audience); Low-complexity (scale up is more effective when the intervention is low-complexity and does not require specialised expertise, setting or equipment for design, testing or implementation); Extensible (scale up is easier when the intervention is designed to be extensible: easily expanded and adapted to new deployment contexts).

Researchers involved in the PolyPrime intervention will discuss if there is sufficient evidence of acceptability and effectiveness within the two jurisdictions of the RoI and NI to seek funding to support a scale up to a full defined RCT, possibly using one of the above frameworks that is suitable to the intervention and the data that has been collected. It is important to note that significant challenges may impede a successful scale-up of the PolyPrime intervention, such as cultural, political or institutional factors (Lawoyin and Lawoyin 2013). Liu *et al.* (2016) states that often there is a lack of understanding of implementation issues for the various stakeholders involved in the intervention. However, as all stakeholders (GPs, practice staff and patients) were included in data collection specifically for the process evaluation, it is likely that the research team has a sound understanding of the potential concerns regarding the intervention, such as those discussed above, to bring to a potential scale-up of the PolyPrime intervention. A potential negative factor was conducting the pilot study during a COVID-19 pandemic, when a definitive RCT is unlikely to be conducted in similar circumstances.

#### **4.5.7 Impact of COVID-19**

The COVID-19 pandemic had a tremendous impact on healthcare research with many non-covid trials being affected by the pandemic. Approximately 80% of non-covid trials were interrupted as a result of COVID-19, mainly due to the studies being unable to proceed with their original protocol due to the presence of COVID-19 (Milton *et al.* 2021) and the additional safety measures put in place such as social distancing. The National Institute for Health Research encouraged the reallocation of academic and clinical healthcare professionals from non-covid clinical trials and healthcare research projects to return to clinical care (Mitchell *et al.* 2020) thus impacting the conduct of non-covid research further. Whilst the PolyPrime project was able to be completed, a study suspension was required at the height of the pandemic. When the study recommenced, patients were offered the opportunity to opt-out after being informed of protocol amendments which ensured the study complied with COVID-19 guidelines; the PolyPrime study experienced the largest number of patients withdrawing at this stage. Patient drop-out as a result of COVID-19 was common in other healthcare studies (Mitchell *et al.* 2020).

The presence of COVID-19 meant that some medication reviews were conducted remotely, via telephone, whilst others were conducted during a face-to-face consultation. Murphy *et al.* (2021) conducted a longitudinal study with 21 GP practices in England and found that GPs conducted three times more remote consultations in 2020 compared to 2019. A similar pattern was also seen in Ireland with face-to-face appointments decreasing by over half and consultations via telephone increased from 10% to 57% (Homeniuk and Collins 2021). Despite older adults regularly using GP services, Homeniuk and Collins (2021) reported a significant drop in non-COVID 19 related consultations. The PolyPrime study was possibly then a useful intervention for older adults during COVID-19, despite not focusing on the virus, as it gave older adults the opportunity to receive one-on-one healthcare in relation to their medicines that they may not have been given otherwise.

#### **4.5.8 Strengths and Limitations**

The PolyPrime trial has been developed using a systematic, theory-based approach as recommended by the MRC. Progression criteria were developed *a priori* ensuring an objective assessment on progressing further with the PolyPrime intervention. A TSC was established specifically for the trial, they ensured the study was applying the protocol and guided project decisions.

The PolyPrime pilot cRCT and its subsequent process evaluation had some limitations. Recruitment targets were not met for patients, and we did not retain GP practices throughout the entire study, however, the recruitment target was met for GP practices. The small number of participants may impact the interpretation of the feasibility of patient self-reported questionnaires. Whilst participant numbers were small in the process evaluation, the feedback was valuable.

COVID-19 had a fundamental impact on the study. The trial was suspended, and recruitment was not recommenced after suspension. Intended methods of data collection changed because of COVID-19, and some practices and patients withdrew specifically because of COVID-19. It is not possible to determine what the recruitment would have been, if the COVID-19 had not occurred. We can hypothesize, however, that recruitment and retention issues would not have been as great if COVID-19 had not been present.

#### **4.6 Conclusion**

The pilot cRCT presented above showed it is possible to conduct a theory-based intervention aimed at improving appropriate polypharmacy in primary care which had been developed in a

different healthcare context. Despite study suspension due to, and many issues arising as a result of COVID-19, the progression criteria findings support further testing of the PolyPrime intervention. However, issues surrounding patient recruitment and patient retention would need to be overcome.





## **Chapter 5**

# **Community pharmacists' role in the management of appropriate polypharmacy for older people in the Republic of Ireland**

## 5.1 Introduction

As discussed in Chapter 1 (Introduction), the global population is ageing. People are living longer but not necessarily in better health. Multi-morbidity is common in older people as is polypharmacy. Also discussed in Chapter 1, was the unique healthcare setting in the RoI, notably the division between public and private healthcare and individuals' access to healthcare professionals. Older people have access to the GMS card which enables them to visit their GP free of charge. The presence of COVID-19 has made having face-to-face access in general practice more difficult and changes in presentations to healthcare services were noted. For example, Brick *et al.* (2020) reported a 32.5% reduction in the number of people presenting at emergency departments, and a national online survey conducted by the National University of Ireland Galway (2020) found that 32% of respondents opted to postpone a medical check-up appointment. Community pharmacies continued to operate as normal throughout the COVID-19 pandemic, with patients able to walk in and/ or contact the pharmacy via telephone to speak to their local pharmacist. Whilst the community pharmacy is an important aspect of primary healthcare, the services available in the community pharmacy in the RoI are limited in comparison to those provided by pharmacies in other countries.

### 5.1.1 Community pharmacy internationally

The current role of the pharmacist practising in community pharmacy and in primary care varies internationally. This is partly due to approaches taken by Governments to deal with pressures on primary health care systems because of the expanding populations and the advancement of technology, research and education (Sadek *et al.* 2016). In 2015, the Department of Health in England introduced the concept of pharmacists working as part of the general practice team (Torjesen 2015) and funded the employment of 500 pharmacists in general practice. This has been well received and continues to expand throughout England and the rest of the UK with main roles of the practice-based pharmacist being medicine reconciliation, telephone support and face-to-face medication review (Alshehri *et al.* 2021). Similarly, in Northern Ireland, the Department of Health recently provided £13 million funding to allow for practice-based pharmacists to support GPs (Bostock 2019). There is no comparable policy-driven initiative in the RoI.

Governments internationally are facilitating the expansion of the role of the pharmacists via their policy and legislative changes. In community pharmacy for example, pharmacists practicing in the UK can prescribe medications, providing they have the appropriate post-graduate qualifications (Stewart *et al.* 2012). In Canada, community pharmacists are considered

part of the Family Health Team (a multidisciplinary health team in local areas) and can conduct medication reviews if patients meet particular criteria [such as prescribed three medications and have a chronic condition] (Allin *et al.* 2021). In Australia, community pharmacists can perform a home medicine review for older people and identify possible medicines to deprescribe (Liacos *et al.* 2020), develop medication management plans in association with the patient's GP and provide support to patients with chronic disease (Buss *et al.* 2018). In the RoI, pharmacists cannot prescribe or adjust patients' prescriptions. They perform the traditional role of a community pharmacist in the supply of medications, providing information on side effects and medication interactions, and some monitoring services, for example, blood pressure and cholesterol testing and vaccination services (Henman 2020). It is possible that pharmacists could play a greater role in the management of appropriate polypharmacy.

### **5.1.2 Expanding community pharmacy in the Republic of Ireland**

In the RoI, evidence in support of pharmacists having an official role in managing appropriate polypharmacy in older people is limited largely to general practice. For example, Cardwell *et al.* (2020) assessed the feasibility of pharmacists working within general practices to optimise prescribing. The intervention was found to be feasible with the potential to improve prescribing and provided the rationale for a pilot cluster RCT, which is ongoing (Croke *et al.* 2021). Even though pharmacists practising in community pharmacy in other countries have more clinical autonomy in their role and are therefore in a better position to manage appropriate polypharmacy, there is little ongoing research or action by the Irish Government to support role expansion of pharmacists practising in the community pharmacy setting. The Irish Pharmacy Union (IPU 2019a) reported that over 80% of respondents to a national survey of pharmacists, felt that more services need to be available via the community pharmacy setting. This finding coupled with the rise in GP workload due to an ageing population, and challenges arising from multi-morbidity (Dowling *et al.* 2020) indicates that it is time for scope of the community pharmacist in managing appropriate polypharmacy to be enhanced.

It is clear from comparisons with the role of the community pharmacist internationally, those practising in the community sector in the RoI could potentially have an enhanced role in the management of appropriate polypharmacy in this setting. In order to establish what this enhanced role might involve, it is important to firstly understand what pharmacists currently do to ensure the prescribing of polypharmacy is appropriate, how pharmacists would like to see their role in the management of appropriate polypharmacy evolve, and what the perceived barriers and facilitators to enhancing their role are. This study aims to achieve this. This study

will also explore community pharmacists' views on the PolyPrime intervention (described in Chapter 4) and its adaptability for the community pharmacy setting.

## 5.2 Aim and objectives

### *Aim*

The aim of this study is to explore community pharmacists' current involvement in the management of appropriate polypharmacy for older people and their views of how their current role in the management of appropriate polypharmacy for older people could be enhanced.

### *Objectives*

The specific objectives are to:

- Recruit 15-20 community pharmacists from across the RoI
- Conduct a semi-structured interview with each recruited community pharmacist
- Explore community pharmacists' experiences of managing appropriate polypharmacy for older people in community pharmacy
- Establish community pharmacists' views on how the management of appropriate polypharmacy for older people in community pharmacy settings could expand
- Explore the barriers and facilitators of enhancing the management of appropriate polypharmacy for older adults in community pharmacy (using the TDF)
- Identify which theoretical domains to target in order to enhance the management of appropriate polypharmacy for older people in community pharmacy (using the TDF)
- Explore community pharmacists' views on a theory-based intervention designed for GPs to improve the prescribing of appropriate polypharmacy in older people in primary care (PolyPrime),
- Determine if the PolyPrime intervention would be of benefit to community pharmacists, and explore any recommended refinements.

### **5.3 Research design and Methodology**

For this qualitative study, semi-structured interviews were selected as the approach for data collection. Semi-structured interviews allow the researcher to ask further questions in relation to responses provided by the interviewee and therefore facilitate the collection of a large amount of data from the interviews, including themes that the researcher may not have deemed relevant during the development of the interview schedule (Bryman 2012). Essentially, semi-structured interviews allow the researcher to be flexible with the questions asked to the interviewee, whilst maintaining structure to the interview, via the development of a topic guide, to ensure the research question will be answered. Detail on qualitative research was provided in Chapter 3.

#### **5.3.1 Sampling and Recruitment Strategy**

Ethical approval for this study was approved by the SoPPS on 27<sup>th</sup> August 2021 (Appendix 5.1). The study was advertised via the SoPPS' Twitter page (Appendix 5.2). The initial sampling frame encompassed community pharmacists who have access to, and who follow, the School's Twitter account as well as the Twitter accounts of the organisations who post and retweet the initial tweet placed on the School's Twitter account. Pharmacy organisations including the IPU, the Pharmaceutical Society of Ireland (PSI), Irish Pharmacy Forum, the Irish Institute of Pharmacy (IloP) and Affiliation for Pharmacy Practice Experiential Learning (APPEL) were specifically asked to re-tweet the original tweet, so that the study would be highlighted to their followers. A link to a news article about the study, published on the SoPPS' website, provided a brief overview of the study (Appendix 5.3), which also included a privacy notice. Community pharmacists interested in participating were asked to contact the PhD candidate (AG), via email. AG asked the interested pharmacist a small number of screening questions (Appendix 5.4) to determine their eligibility to take part (e.g. currently provide care to older patients prescribed polypharmacy) as well as some questions about where they work (e.g. independent/ chain pharmacy, urban/rural location). To be eligible for inclusion in this study, participants had to be employed in a community pharmacy on a full-time or part-time basis or as a locum, registered as a community pharmacist within the RoI and provide care for patients prescribed polypharmacy (i.e. four or more medicines), aged 65 years or over. Registered pharmacists not working in a community pharmacy in the RoI, and/or those who do not provide care for patients prescribed polypharmacy aged 65 years or over, were not eligible for inclusion in this study.

The responses to the screening questions from community pharmacists who met the eligibility criteria were entered into a sampling matrix in chronological order (Appendix 5.5). Responses

were assessed to ensure a range of participants from different locations and types of pharmacies. Potential participants were formally asked to take part via email (Appendix 5.6). The Participant information leaflet (Appendix 5.7) and consent form (Appendix 5.8) were attached to the email. Potential participants were asked to read the participant information leaflet and to complete and return the consent form via email if they wished to participate in an interview. If the pharmacist had not responded within seven days, AG contacted them again. After confirmation of participation and consent, community pharmacists were assigned a unique identifier (e.g. CP01, CP02 etc.). An ethical amendment was approved by the SoPPS research ethics committee on 28<sup>th</sup> October 2021 (Appendix 5.9), to expand the recruitment strategy and allow for advertisement of the study in the e-newsletters and/or magazines of the IloP, the PSI, the IPU and the Irish Pharmacy News. The Twitter advertisement was altered to reflect this. Details of why this was required are presented in the results, section 5.4.

### **5.3.2 Undertaking the interviews**

A topic guide was developed and used to guide the interviews and to ensure consistency throughout. The topic guide was developed and tested *a priori* via pilot interviews (n=4) with academic pharmacists, who also practise as community pharmacists, from the SoPPS, Trinity College Dublin. Those eligible were contacted via email by the PhD candidate and invited to participate in the pilot study, conducted by the PhD candidate. Each pilot interview was discussed with the project supervisory team and changes were made to the topic guide iteratively. The finalized topic guide (Appendix 5.10) began with a brief introduction and demographic questions, the way in which the pharmacist currently manages appropriate polypharmacy for older patients, if and subsequently how they would like their role in the management of polypharmacy to evolve. Questions pertaining to barriers and facilitators to implementing changes in their role were based on the TDFv1 [Appendix 5.11 (Michie *et al.* 2005)]. Following discussion within the team, it was decided to use the TDFv1 (Michie *et al.* 2005) rather than TDFv2 (Cane *et al.* 2012). This was because the domain 'Nature of the Behaviours' and its constructs were believed to be relevant to the study aim and objectives, and these do not form part of TDFv2. Additionally, the TDFv1 had been used in the development of the PolyPrime study (Cadogan *et al.* 2015), which was presented to community pharmacists in this study to ascertain their views on it. The interview was scheduled to take place at a date and time that suited the community pharmacist and researcher via Microsoft Teams or telephone. Remote interviews were preferable to minimize travel for the researcher and to maintain safety in line with COVID-19 related public health guidance in place at the time of data collection (Department of the Taoiseach 2021). Participants were asked to be in a quiet space for the



interview. Interviews conducted online were recorded via Microsoft Teams recording option, which provides both an audio and visual recording of the participant and researcher, following permission of the participant. Interviews conducted via telephone were recorded using a dictaphone and all interviews were transcribed *verbatim* by the researcher. Participants were given the opportunity to review their transcript. Participants received a certificate of participation (Appendix 5.12) following completion of the interview.

### **5.3.3 Data analysis**

Data analysis was undertaken in parallel with data collection. Data analysis was conducted using both a deductive and inductive approach, as is recommended by McGowan *et al.* (2020). The deductive approach [analysis guided by theory (Bryman 2012)] was applied using the TDFv1 as the analytical framework, whereby each of the 12 domains acted as the coding categories. The inductive approach [deriving concepts or themes via the data collected (Thomas 2006)] was applied using the framework method (Ritchie *et al.* 1994), following a similar approach adopted by Gale *et al.* (2013). The use of both a deductive and inductive approach involved a number of steps as detailed below:

#### *Step 1: The Familiarization Phase*

Following transcription of interview recordings, an in-depth familiarisation process was undertaken. All interview transcripts were repeatedly read, and the audio-recordings were listened to again. The PhD candidate noted initial thoughts regarding possible themes and interpretation of findings in the margin of the transcripts.

#### *Step 2: Identification of main themes*

The second step involved identifying the overarching main themes, using the framework method (Ritchie *et al.* 1994), following a similar approach adopted by Gale *et al.* (2013), which allowed for further analysis outside of the TDFv1 framework, i.e. the inductive approach. Where possible, the TDFv1 acted as the analytical framework, whereby each of the 12 domains were defined as a coding category, i.e. the deductive approach. A random sample of three transcripts were analysed by the PhD candidate and a second member of the research team, AR. Coding for the three randomly selected transcripts was compared and any discrepancies were resolved through discussion. The emergent coding scheme (Appendix 5.13) comprised of overarching categories and sub-categories, including the 12 domains that comprise the TDFv1.

#### *Step 3: Applying the coding scheme*

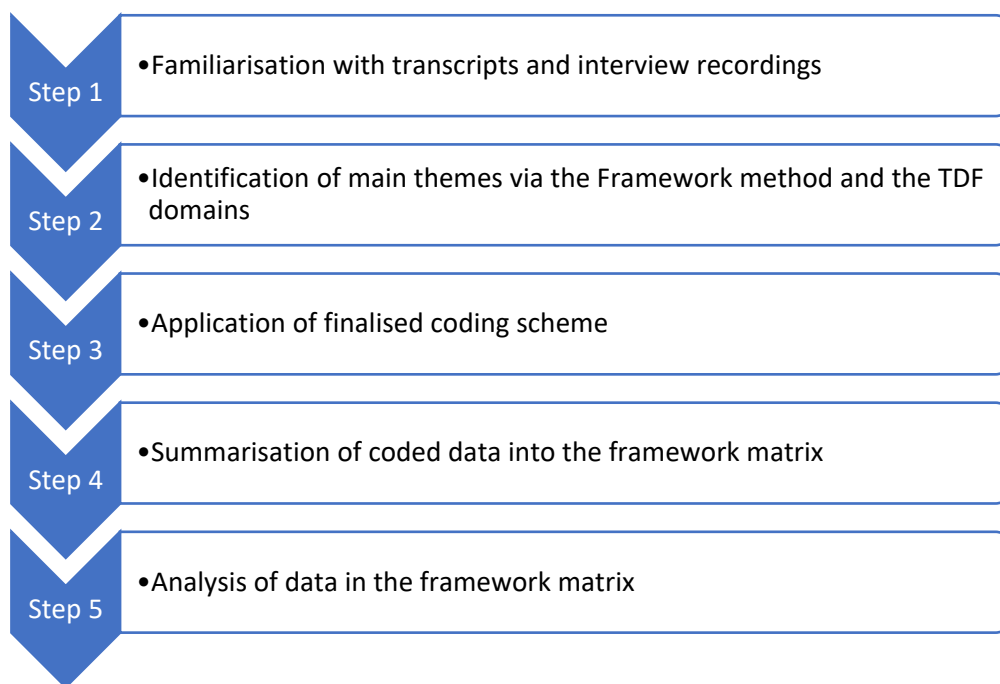
In the third analysis step, AG applied the finalized coding scheme to all subsequent transcripts. Each code was assigned a number for easy identification.

*Step 4: Framework matrix*

When all transcripts were coded and agreed, AG summarized the data into a framework matrix for each code in Microsoft Excel. This constituted the fourth step in the data analysis process. The matrix comprised of one row per participant and one column per code. Each overarching category was represented on a separate sheet. Relevant data (i.e. quotations) from the transcript were extracted for each participant and coded alongside an overview of the quotation and positioned into the corresponding cell in the matrix.

*Step 5: Analysis of the framework matrix*

Lastly, an analysis of the framework matrix was performed to identify key responses within each category. An interpretive summary of the data within each category was produced, highlighting the main findings regarding community pharmacist's current management of polypharmacy for older people, how their role in the management of polypharmacy could evolve and the barriers and facilitators to these. An overview of each analytical step is shown in Figure 5.1 below.



**Figure 5.1** Flow diagram indicating each analytical step

### **5.3.4 Reporting of Data**

This study has been reported in line with the COnsolidated criteria for REporting Qualitative research (COREQ: Tong *et al.* 2007) and a completed checklist can be found in Appendix 5.14.

### **5.3.5 Ethics**

Ethical standards for this research are similar to that in Chapter 3, section 3.3.7 as they were both qualitative studies. Name and email addresses of participants are stored in a password protected document [sampling matrix (Appendix 5.5)], stored on the PhD student's TCD OneDrive account, accessed via their TCD double encrypted laptop. OneDrive was used throughout the PhD thesis as recommended secure data storage by IT services in TCD; documents stored on TCD OneDrive account are automatically backed up. IT services can retrieve 'lost' documents if required. No data has been stored on a personal computer/laptop. The code key is also stored here in a separate password protected document. Each original electronic copy of the consent forms, as well as the pseudonymised transcripts in a word document, have their own unique password and are stored on the PhD's student TCD OneDrive account, accessed via their TCD double encrypted laptop. Each MS Teams recording was downloaded onto the PhD student's TCD OneDrive account as soon as possible after the interview had ended. For interviews conducted via telephone, interviews were uploaded to the same account as soon as possible after the interview. Both recordings were then deleted from the original source. Once the interview had been transcribed and quality checked, the recording on the PhD student's TCD OneDrive account was also deleted. This was to ensure participants could not be identified via their voice or image, or both.

TCD was the data controller for the study and the PhD student had primary responsibility for data protection. QUB only had access to securely sent pseudonymised transcripts. All members involved in this study (PhD supervisors and AR) were the data processors. The PhD student is responsible for storing data securely on their TCD OneDrive account, as noted above. Data collected and retained for this study (consent forms and transcripts) will be destroyed after seven years. A log of when personal data has been accessed/changed is kept in a password protected document on the PhD student's TCD OneDrive account. Responsibility of data storage and deletion, e.g. consent forms and transcripts, will be transferred to CR following PhD attainment, in line with current General Data Protection Regulations and Health Research Regulations, and as per SoPPS ethical approval (Appendix 5.1). The code key will be destroyed once the PhD candidate has graduated. Following discussion with the chair of the SoPPS REC, an

amendment has been submitted to the SoPPS REC to this effect. The code key will not be destroyed until written approval from the SoPPS REC is in place.

## 5.4 Results

In total, 17 community pharmacists expressed interest in participating in an interview. All 17 community pharmacists met the inclusion criteria. Out of this 17, three opted not to participate after receiving the formal email invitation, participant information leaflet and consent form. All three reported this was due to their lack of availability and the time estimated to complete an interview, therefore 14 community pharmacists (six female, eight male) were included in the study. Community pharmacists who participated in an interview, referred to from here as participants, mostly practiced in a community pharmacy located in an urban location (n=13) with one pharmacist located in a rural community pharmacy. Most participants worked full-time (n=9), followed by part-time (n=3) with the fewest working as a locum (n=2). Participants were practicing as a community pharmacist for an average of 15.1 years (range 3 months – 46 years). Eight participants worked in independent community pharmacies, three in chain pharmacies and a further three in independent pharmacies that are part of a larger buying group. Demographics of participants are shown in Table 5.1. Recruitment to the study was slow, resulting in the ethics amendment mentioned in 5.3.1. After the ethics amendment had been approved, the PhD candidate contacted the necessary organisations (IIoP, PSI, IPU and the Irish Pharmacy News) via email to advertise. However, no reply was received, and so no further pharmacists were recruited via this advertising method. This resulted in a total of 14 interviews being conducted. Four of these interviews were conducted via MS Teams with the remaining 10 conducted via telephone. Interviews ranged from 40 minutes to 75 minutes.

**Table 5.1 Demographics of participants**

Interview code	Gender	Number of years practicing	Full/part-time or locum	Location	Type of pharmacy
CP01	Male	23	Full-time	Urban	Independent, part of buying group
CP02	Female	1	Locum	Urban	Chain
CP03	Female	11	Part-time	Urban	Independent, part of buying group
CP04	Female	35	Full-time	Rural	Independent
CP05	Male	9	Full-time	Urban	Independent
CP06	Male	1	Part-time	Urban	Chain
CP07	Male	9	Part-time	Urban	Independent
CP08	Male	7	Full-time	Urban	Independent, part of buying group
CP09	Male	46	Full-time	Urban	Independent
CP10	Female	25	Full-time	Urban	Independent
CP11	Female	30	Full-time	Urban	Independent
CP12	Female	4	Full-time	Urban	Independent
CP13	Male	3 months	Locum	Urban	Chain
CP14	Male	8	Full-time	Urban	Independent

The coding scheme developed as part of the analysis process resulted in 53 codes (Appendix 5.13). Codes were organized into overarching categories: demographics, definitions, experiences managing polypharmacy, how management of appropriate polypharmacy could be expanded, and each of the 12 TDF domains. Overarching categories relating to data surrounding the PolyPrime intervention included: video, scheduled medication review, and the intervention as a whole. The findings from the semi-structured interviews with community pharmacists on their role in the management of appropriate polypharmacy for older people are discussed below. Section 5.4.1 relates to the participants understanding of some terminology, namely polypharmacy and appropriate polypharmacy, section 5.4.2 presents the participants' current experiences of managing appropriate polypharmacy for older people, section 5.4.3 relates to the ideas to expand the management of appropriate polypharmacy for older people and the barriers and facilitators to this, and sections 5.4.4 presents the participants views on a similar intervention to the PolyPrime study and if this could be of benefit to them.

#### **5.4.1 Community pharmacists' definitions of polypharmacy**

Most community pharmacists defined polypharmacy using a numerical value, ranging from 3 medications to ten medications, with 5 medications being the most common response (n=5).

Two remarked that polypharmacy constitutes the prescribing of multiple medications but did not apply a numerical threshold.

*“So, polypharmacy, I would understand it as the use of 5 or more drugs, regularly eh in one patient” [CP07]*

All 14 community pharmacists provided similar definitions of appropriate polypharmacy, that the medications had to be in line with the patient’s requirements and health conditions being managed.

*“It would be a case of focusing on the minimum amount of medicines that they can be and they should be on” [CP01]*

*“Appropriate polypharmacy would be only using medicines that were necessarily prescribed with indications and part of a current degree to review treatment programmes” [CP14]*

#### **5.4.2 Experiences managing polypharmacy**

This section of the results presents the participants’ experiences in managing polypharmacy including how they dispense polypharmacy, any issues they have experienced in managing appropriate polypharmacy, resources they use to identify appropriate polypharmacy and their confidence in identifying appropriate polypharmacy. The role of the community pharmacist in the healthcare team on managing older people and polypharmacy, and how they communicate effectively with patients or healthcare professionals are also presented.

##### *Dispensing multiple medicines*

Most participants discussed reviewing the patient’s dispensing history, checking the dosage is correct, the length of time the patient has been prescribed the medication, and making sure it is appropriate for older people and their conditions.

*“so first of all you would look at their history and why different things were started... to make sure everything they are taking is absolutely appropriate. Em, I’d also, even if the formulations are appropriate, I think that’s another quite an important thing you know in the dispensing process, and then the dosage as well” [CP03]*

If a patient is new to the pharmacy or if a repeat patient was prescribed a new medication, many participants noted that they would discuss the new medication with the patient.

*“we just have a protocol in place were the pharmacists check the new medicines, make sure they are safe” [CP08]*

Two participants stated that they would have discussed with older people who are prescribed multiple medicines, to ensure they are still able to manage their medication. One locum mentioned that they just ensure the medicine is correct and appropriate as they are often only in that pharmacy for one day so are unlikely to contact prescribers to make changes, however, if they had a major concern, they would contact the prescriber.

#### *Issues in managing appropriate polypharmacy*

Participants experienced many challenges in managing appropriate polypharmacy for older people. The most frequently discussed issue was not having diagnosis information/ access to patient notes, making dispensing appropriate polypharmacy more time consuming.

*“By and large we are left you know in the dark quite a lot because we don’t get any background to what they are being treated for what, their treatment regime is or anything like that... we have to do all these drug reviews and make recommendations and we don’t have the, we are not given the basic information” [CP11]*

Also discussed by some participants was how busy the community pharmacy is and how much bureaucracy and paperwork community pharmacies must deal with and it therefore can be difficult to spend a lot of time talking to patients, which is then challenging to manage polypharmacy.

*“we are inundated with paperwork and all of that, em, you know it’s really hard to have enough time to talk to a certain patient to go through their medication problems and all of that” [CP06]*

Issues also discussed by participants included blister packing as participants could not be sure patients know the medicines, and also blister packing is a time-consuming process that they do not get reimbursed for.

*“And if we could get like paid for doing those blister packs and stuff that would be good” [CP12]*

Changes can be made to the patients’ medications when they are in hospital and the only way for participants to check if the changes are deliberate or an error, is to contact the prescriber which can be a long process and may take numerous phone calls before they talk to the prescriber, and this can make it difficult when managing polypharmacy.



*“getting on to Drs, getting on to hospitals is a very time consuming process” [CP09]*

One participant mentioned that older people who take multiple medicines often do not collect their medicines, instead they are delivered to them, or a family member collects the medicines which can be difficult for the community pharmacist to talk to the patient and see how they are experiencing their medication and therefore it can be challenging to manage polypharmacy.

*“a lot of these older patients wouldn’t necessarily come to the pharmacy themselves... You don’t get a lot of personal contact with them. That’s definitely one challenge” [CP06]*

#### *Resources used to manage appropriate polypharmacy*

A wide range of resources are used by participants in managing appropriate polypharmacy. The most common resource mentioned was the British National Formulary, followed by Stockleys and the Summary of Product Characteristics. All resources mentioned are shown in Box 5.1.

*“if I want to check an interaction or something I would go on to the BNF or medicines Complete, there is sort of an interaction checker called Stockley’s, interaction checker, sometimes I would look at the SPCC” [CP05]*

#### **Box 5.1 Resources used to manage appropriate polypharmacy**

- British National Formulary (n=7)
- Stockley’s (n=4)
- Summary of Product Characteristics (n=4)
- Own professional judgement (n=3)
- Interaction checkers (n=3)
- Patients (n=2)
- National Medicine Information Centre (n=1)
- Twitter (n=1)
- Pharma Buddy (n=1)
- Irish Medicines Formulary (n=1)
- Medicines complete (n=1)
- NEWT guidelines (n=1)

#### *Confidence in identifying appropriate polypharmacy*

The majority of participants felt confident in identifying appropriate polypharmacy.

*“I’d be reasonably confident because I’m very experienced and because the pharmacy I work in, most of the patients would be well known to me from over the years, so em, you’d know a good bit about them, about their medical and their social history” [CP04]*

*“I would be very confident, yeah absolutely. I understand, I’ve been qualified for some time and I’ve worked with some fantastic pharmacists, but I am quite confident when it comes to things like that. I’ll always do a double check... so in administration and in the knowledge, yeah, I’d be quite confident” [CP10]*

The few participants who did not feel confident in identifying appropriate polypharmacy felt this was mostly due to not having access to the patients’ medical records and therefore did not always have the full picture of their diagnoses.

*“I would say not very confident because we don’t have their full medical history and we don’t have their diagnosis” [CP06]*

#### *The role of community pharmacist in the healthcare team in managing polypharmacy*

When asked to discuss what participants see as the role of the community pharmacist in the healthcare team, several roles were mentioned. The most common role was to ensure that patients receive the correct medication, the most appropriate medication for the patient and to ensure no therapeutic duplications.

*“I think the pharmacist has a really valuable role in assessing what medicines people are on and their correct dose” [CP02]*

*“accurately dispense medication to patients” [CP14]*

The second most common role discussed was seeing community pharmacists as the link between all healthcare professionals and prescribers.

*“We have to be the link between everyone. The GP can be one angle, the prescribing nurse can be another, the public health nurse, loads of people but we have to be the link between them all and if we are not the link between them all then there will be gaps and mistakes made” [CP08]*

Participants see themselves as an educator- they are more accessible than the GP, and provide a free service for patients to ask questions about their medications and health conditions. Educating patients about their medications can help with managing appropriate polypharmacy. Two participants discussed the community pharmacist as having a very limited role in that they

dispense medication but that they have the ability to do more for patients and provide more services than they offer currently, due to their knowledge and accessibility.

*"We are available anywhere without an appointment, as opposed to a GP that you might need to make an appointment to see a GP" [CP01]*

*"In some aspects it's very limited, you're limited to what is in front of you. I often think we come in too late in the process, the prescription has already been written, often the person is already taking the medicines then the problems come up, you know, so you don't have the input before they actually prescribe" [CP04]*

#### *Communication and managing polypharmacy*

Discussion on communication focused on communication with patients, and communication with other healthcare professionals. Nearly half of the participants stated that knowing the patients in their pharmacy makes it easier to approach them and have a conversation about their medicines; participants believed it makes it easier for the patient to communicate effectively with the pharmacist and tell them information that they should know.

*"I'd be more comfortable in approaching someone if I knew them...as opposed to someone just walking in off the street you know in the same situation" [CP01]*

*"Because they have a relationship with you, they are more likely to disclose how they feel rather than just take them home and maybe throwing them in a corner" [CP04]*

Pharmacists also discussed challenges when contacting the prescriber after hospital discharge or the patient's GP. Some participants spend a lot of their time in the pharmacy attempting to contact hospital prescribers.

*"It can be very hard to get in contact with anyone at a hospital level. Getting in contact with a GP is hard enough but when it's at a hospital level then that can be even more difficult so getting that, so that's what I have had the most difficulty with, but we got a result in the end through with enough time but yeah" [CP13]*

#### **5.4.3 How the management of appropriate polypharmacy could expand**

Numerous strategies were generated by the participants as potential ways to expand their management of appropriate polypharmacy for older people including conducting medication reviews, access to patient health records and an enhanced communication system with prescribers. All strategies are presented in Box 5.2 alongside the number of participants that suggested the strategy. Out of the strategies the participants suggested, they were asked to

choose the strategy they thought could make the most important change to how they manage appropriate polypharmacy. From this, five different strategies were discussed – patient records, medication reviews, utilisation of dispensing software, national database with information regarding inappropriate/appropriate prescribing, and enhanced communication system with prescribers. As the strategy of a national database is not within the reach of a behaviour change intervention for whom the community pharmacist would be the direct target, this strategy is not presented below. The barriers and facilitators discussed in relation to the four strategies are presented under the TDF domains. One TDF domain was not considered to be relevant to strategies on expanding the community pharmacists' role in managing appropriate polypharmacy: 'Emotions'.

**Box 5.2 Suggestions to improve the management of appropriate polypharmacy in older people**

- Access to patient records (n=10)
- Medication reviews (n=10)
- Enhanced communication system with prescriber (n=5)
- Blister packing (n=4)
- General practice-based pharmacists (n=3)
- Utilisation of dispensing software (n=3)
- Medication use review (n=2)
- Hospital discharge prescription/letter checked by hospital pharmacist (n=2)
- Independent prescribing rights (n=2)
- Indication for medication on prescription (n=2)
- Multidisciplinary team involved in prescribing (n=2)
- National database with information regarding inappropriate/appropriate prescribing (n=2)
- Minor ailment services/ health checks (n=2)
- Patient card with regular medications (n=1)
- Compliance aids (n=1)
- Re-design of medication boxes to be identifiable (n=1)
- Interconnected pharmacy records (community and hospital) (n=1)
- System to know medication changes/concerns have been acknowledged or addressed (n=1)
- Re-structuring of community pharmacy payment scheme (n=1)
- E-prescribing (n=1)

*Theoretical domains to enhance the management of appropriate polypharmacy*

Most theoretical domains were common across the strategies discussed to expand the role of the community pharmacist in managing appropriate polypharmacy in older people. One TDF domain ('Emotions') was not deemed to be relevant. An overview of the barriers and facilitators are presented in Table 5.2 alongside the relevant TDF domain.

**Table 5.2 Barriers and facilitators to expanding the role of the community pharmacist in managing appropriate polypharmacy in older people**

<b>TDF domain</b>	<b>Barriers</b>	<b>Facilitators</b>
<b>Knowledge</b>	Need to recap on how to interpret results as currently not part of their job Do not have knowledge to conduct medication review	Clinical knowledge Patient knowledge Expert in different medicines
<b>Skills</b>	Some younger CPs do not have the required communication skills	CPD course Communication skills
<b>Social/professional role and identity</b>	GPs would need to be accepting of expanding role Necessary information not always provided	More recognition of CP
<b>Beliefs about capabilities</b>	Not confident to interpret medical results	
<b>Beliefs about consequences</b>	GDPR and consent Other prescribers may not approve	Speed up the process of dispensing Benefits for patient, healthcare system, the government Patients encouraged to use pharmacy more often Free up GP time Ease communication
<b>Motivation and goals</b>	Not making money	Make job easier by having more information about patient More time efficient Payment
<b>Environmental context and resources</b>	Lack of resources Lack of operational support Burden of access to confidential information Staff shortage/ availability Cost of providing services Use of different software systems	Extra pharmacist Public policy implemented Develop SOP Standardised equipment supplied
<b>Social influences</b>	Difficult relationship with prescriber/ patient may influence decision to conduct medication review	Evidence of benefits
<b>Behavioural regulation</b>	Paperwork associated with procedures in pharmacy	Support from Unions, government, regulatory bodies Develop SOP Review of procedures in pharmacy
<b>Nature of the behaviours</b>	Cannot make changes without GP	DoH driven campaign for change Time efficient Public policy Extra staff

<b>Memory attention and decision processes</b>	Paperwork associated with procedures in pharmacy	
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CP= Community pharmacist CPD= Continuing Professional Development DoH= Department of Health GDPR= General data protection regulations GP= General practitioner SOP= Standard Operating Procedure TDF=Theoretical Domains Framework

*TDF domain: Knowledge*

All participants discussed knowledge as an important domain. Community pharmacists often have a lot of knowledge about their patients and know them well, which helps them in managing appropriate polypharmacy. Having more in-depth information regarding patient’s health conditions, results and diagnoses can help community pharmacists manage appropriate polypharmacy in older people.

*“people do build up a relationship whether they like it or not their customers, patients or whatever you wish to call them, and that relationship is very much in key to improving and making sure that the service they get is appropriate and effective” [CP09]*

*“we would do sort of a mini drug review every time somebody comes in... and go through their meds and why are you on this and why aren't you taking that... you know and that would be with the people we would know well and are familiar with their things so the more information you have, information is power” [CP11]*

Some participants noted they believe community pharmacists have the clinical knowledge to understand and interpret patient records (also noted as TDF: Beliefs about capabilities). Access to patient records would enable expansion of their role in managing appropriate polypharmacy in older people.

*“we do have a degree in pharmacy, we do have the knowledge, we do have the skills in pharmacy to understand patient notes and to understand appropriate care for it so it wouldn’t be wasted on us to receive those notes” [CP05]*

Few participants mentioned that they do not currently have the clinical knowledge to expand their role to access patient records or conduct medication reviews (also noted as TDF: Beliefs about capabilities).

*“I feel like, em the population has different needs compared to the general public I guess. If you ask me to provide the service I definitely wouldn’t feel very confident in*

*providing a very good service because I feel like I'd need a bit more support in terms of what their needs are and what to look out for" [CP06]*

*TDF domain: Skills*

Most participants believed it would be useful to develop a continuing professional development (CPD) course alongside expanding the role of the community pharmacist in managing appropriate polypharmacy.

*"I suppose further professional development, further continued professional development in clinical pharmacy... I think it would be easy enough for them to do the training. There's a system of, eh, training in pharmacy already that we are expected to do cont, continued professional development, eh, pharmacist's do that every year. Clinical training in that shouldn't be that hard to implement. There's eh, it's easy to do online courses" [CP05]*

In relation to community pharmacists conducting medication reviews, it would be useful if the CPD course informed them of specific factors to be aware of in patients prescribed polypharmacy and how to provide a medication review. One participant stated that younger community pharmacists do not always have great communication skills and might struggle to provide clinical information in a manner that patients understand.

*"perhaps in the form of CPD training could be organized, I don't know by the IloP perhaps... the course would tell you, you know, this is how you complete a medication review, this is what it entails and these are the other things you should be looking out for in polypharmacy and so and so and then upon completion you are sort of qualified to provide the intervention" [CP06]*

*"I notice in younger pharmacists, is trying to help them with translating their clinical knowledge into much better way for the patient to understand, and that is sometimes what people have to learn. They may know exactly what it is they are talking about, but I can see that the patient, it has gone straight over their head" [CP10]*

*TDF domain: Social/professional role and identity*

The strategies discussed could improve the standing of the community pharmacist as part of the healthcare team. For example, by facilitating community pharmacists to conduct medication reviews and employing an enhanced communication system with prescribers, this would improve their standing in the healthcare team. However, one participant thought that providing



community pharmacists with access to patient records would not improve the recognition that community pharmacists receive.

*“we might feel like we are appreciated because we are asked to provide a clinical based service, not just sort of, you know we usually do dispensing which can be very repetitive, very manual kind of work whereas with medication review its kinda like recognizing ‘you are the medication expert, we want you to like em, we want your input and we want you consultancy and everything so I feel like that could be a form of recognition for pharmacists” [CP06]*

*“I don’t know the government will recognise anything because so far at the moment all they have done is em given us more to do and less money” [CP11]*

A barrier to expanding the role of community pharmacist in managing appropriate polypharmacy is that they currently cannot change patients’ prescriptions (also noted as TDF: Beliefs about capabilities, Beliefs about consequences). If community pharmacists were to conduct medication reviews, they would have to communicate any necessary changes to the prescriber, such as the GP. It has been suggested that trying to contact GPs and especially hospital doctors is a very time-consuming activity, therefore a communication channel between community pharmacists and prescribers may need to be implemented, or community pharmacists may need to become independent prescribers.

*“you’re still referring back to your GP afterwards so that would maybe tie in with independent prescribing, but I think that would be much harder to implement” [CP03]*

*“I think it should be a collaborative process, em, but I think it goes back to the structural problems. How do we contact prescribers? How do we have a channel of communication that is always open, easy to access? We don’t have to go through the secretary who might not have medical knowledge. You know I feel like there are a lot of systematic issues that need to be addressed for the intervention to be working really well” [CP06]*

The expansion of community pharmacist role would require a national system to be implemented with the HSE and regulatory bodies to be supportive of the process and ensure all prescribers and community pharmacists have the supports they need to expand their role.

*“I think, em we would need, I think we would need like you know regulatory bodies like the PSI and operational bodies like the HSE to review and protect community pharmacists clinical time and what they expect to be done in that time versus what is being done at a bureaucratic level” [CP07]*

*TDF domain: Beliefs about capabilities*

Barriers and facilitators under this domain are also relevant to other TDF domains of Knowledge and Social/professional role and identity and so are presented there.

*TDF domain: Beliefs about consequences*

Some participants discussed General Data Protection Regulations (GDPR) as a barrier to expanding community pharmacist management of appropriate polypharmacy via access to patient records and enhanced communication system with prescribers.

*"I think you would have to have the allowance for GDPR to be looked at so you want to make sure that the, that the patient was like aware of information sharing and that the allowance is there for hospital, for information to flow in all directions where it's needed by all the healthcare professionals" [CP07]*

*"GDPR issues, sharing medicines information inappropriately without patient consent" [CP14]*

All participants anticipated many benefits to the expansion of the community pharmacist managing appropriate polypharmacy in older people. For example, saving healthcare professionals time, economic benefits, a reduction in incorrect medications and/or unused medications being prescribed and dispensed and better care for patients: patients would receive better care and care that is more appropriate to their medications and health conditions. The enhanced communication system would free-up community pharmacist time, allowing for them to interact more, and for longer, with their patients. Medication reviews may allow patients to gain a better understanding of their medications.

*"for the patient, it's going to improve patient safety" [CP05]*

*"people taking the right medication that saves money, treatment of adverse side effects, medication is missed or someone was on a steroid and wasn't taking their calcium or vitamin D, you know they had a stomach ulcer or something later on down the line... that costs money, all of that domino effect. Happier health care workers, not as burnt out" [CP12]*

*"we can clinically check prescriptions with access to full medication records which reduces the likelihood of personally have an oversight or maybe missing something ..... we can do our job more effectively and quickly. We don't have to waste our time*

*jumping from one department to the next in the hospital trying to find a prescriber to get access to certain information” [CP14]*

*TDF domain: Motivation and goals*

In order for community pharmacists to engage with the expansion of their role in managing appropriate polypharmacy via medication reviews, communicating with prescribers and accessing patient records for example, most participants stated necessary payment was required.

*“the obvious one is money! It’s always a good incentive! If you want someone to do something you pay them!” [CP04]*

*“It’s all an extra cost and it’d be great to get help with that... Yeh, it is the stumbling block. It’s why it’s why it isn’t happening” [CP10]*

However, a few participants stated that if community pharmacists understood the reasons resulting in the expansion of their role and the possible benefits to patients, that this would encourage them to expand their role.

*“Pharmacists tend to get in the role of a healthcare professional to help patients and if this helps patients and helps patient safety, em, that would be enough to motivate pharmacists” [CP05]*

*TDF domain: Environmental context and resources*

Most participants discussed a lack of resources that would be a barrier to expanding the role of community pharmacists in managing appropriate polypharmacy in older people. These barriers include lack of staff, lack of suitable equipment including computers, broadband, and a private room in which to speak to patients. Participants noted that every pharmacy will have a consultation room, however, if a community pharmacist is using that room to conduct a medication review as part of their role expansion, other services may be impacted such as providing vaccines.

*“In rural areas we tend to have problems with broadband and so on and it can slow things down” [CP04]*

*“You would need extra personnel which would have financial implications” [CP09]*

*“you would have to have that space dedicated” [CP10]*

Some pharmacists discussed the development of a standard operating procedure (SOP) for conducting medication reviews for example.

*“I suppose some sort of SOP you know standard operating procedure, and so just every pharmacist who is working in the same pharmacy would know that what kind of characteristics of a patients prescription would be considered high risk and then what they need to do in terms of intervention, you know, just kind of standardizing the process” [CP06]*

Some participants discussed that unions and regulatory boards would also need to support the implementation of community pharmacists expanding their role via medication reviews, communication channel with prescribers and accessing patient records. An official campaign organised by the Department of Health would help to ensure community pharmacists having access to patient records becomes part of the healthcare system (also TDF: Behavioural regulation and Nature of the behaviours).

*“so it would be important just to even to get the PSI, the IPU on board, just to say look it’s important, it might be a little bit of extra work because you have this access now an extra few minutes or whatever on each patient, but, in theory it will be better for the patient in the long run, they will be getting a more holistic service” [CP04]*

#### *TDF domain: Social influences*

Few participants discussed how social influences would impact on them accessing patient records, contacting the prescriber or conducting a medication review. In relation to conducting medication reviews, if community pharmacists thought it was unlikely that the prescriber would listen to their findings from the medication review and take their recommendations on board, this might affect their willingness to conduct a medication review as they could interpret the task as time wasting.

*“Like if you know you are dealing with a difficult colleague and you know ‘oh I could do the medication review, provide the recommendations but they are not going to be taken on board, that might kind of effect how willing you are you know because you are putting in all this effort and you don’t see anything getting changed” [CP06]*

#### *TDF domain: Behavioural regulation*

Few participants noted the large amount of paperwork that community pharmacists already have to complete and expanding the role of the community pharmacist in managing appropriate

polypharmacy in older people may also lead to more paperwork, which they considered a barrier to expanding their role. This is also relevant to the domain Memory, attention and decision processes, as community pharmacists are spending a lot of their time on paperwork which could possibly affect their attention and desire to conduct a new task within the pharmacy and expand the services on offer to patients.

*“the amount of paperwork kind of like is overwhelming to the point that it makes it hard to focus on doing new thing things because you have so much to catch up on” [CP13]*

A facilitator to the expansion of their role could be a review of existing procedures within the pharmacy which may allow for existing processes to be streamlined or more efficient processes put in place.

*“I think it would require a like a review of the requirements and the operational, the simplification of the operational process around the running of the community pharmacy. If major efficiencies were made there it would allow community pharmacies to run more, to run more efficiently and less bureaucratically and I think that would make, that would make the space” [CP07]*

The facilitators of development of an SOP and implementation of public policy discussed under TDF domain Environmental context and resources are also relevant under this domain.

*TDF domain: Nature of the behaviours*

No new barriers or facilitators were identified under this domain. However, barriers and facilitators previously presented are also relevant here. Facilitators of extra staff and public policy (presented under TDF domain Environmental context and resources), time efficient processes (presented under TDF domains Behavioural regulation and Beliefs about consequences), and government backed campaign (presented under TDF domain Social/professional role and identity) are also relevant here. The barrier discussed by some participants under this domain was the community pharmacists’ inability to make changes to patients’ prescriptions, presented under TDF domain Social/professional role and identity.

#### **5.4.4 Community pharmacist views on the PolyPrime intervention**

*Intervention component-video*

The PolyPrime intervention video was not watched by any of the participants, and instead the same description was used to describe the video to all participants. For interviews conducted via Microsoft Teams, participants were invited to watch the video, however, they opted to hear

the description of the video instead. The description of the video was well received by participants, and they highlighted how beneficial a video can be in this instance, having a visual of how to conduct a medication review, and that it is a useful learning tool and different to reading information.

*"I think a video is a great, eh are excellent at informing and educating, it's the best tool"*  
[CP05]

*"Yes, it would definitely be better than reading reams of PSI legislation type guidelines, a video might be a more professional tool"* [CP12]

However, one participant could not see the benefit of including an educational video in an intervention as they believed that community pharmacists would not watch it.

*"I genuinely don't believe a lot of people would watch it"* [CP08]

Participants felt that there were several components of the PolyPrime video that would be useful to include in a similar educational video tailored for community pharmacists. These include: validated assessment tools, prescribing guidelines, simulated patient feedback and tips on communicating with reluctant patients.

*"those guidelines it would be beneficial to have access. The whole resource material as such for the video"* [CP14]

*"it would be good to know how they persuaded them to change their behaviour... I think that would be useful to kind of, to learn how they would manoeuvre that"* [CP03]

Some changes were suggested by participants to adapt the PolyPrime video for the community pharmacy setting. These include expanding the types of patients, clinical scenarios and drug interactions. Further suggestions are provided in Box 5.3.

**Box 5.3 Possible additions to the PolyPrime video for community pharmacists**

- Include different types of people, e.g. people with a learning disability, migrant, different socio-economic backgrounds
- Transcript of video
- Framework of medication review/ list of possible questions to ask
- Suite of different clinical scenarios
- Most common drug-drug interactions

*"like diversity in terms of older adults, like their profiles, their clinical conditions, the issues they are dealing with" [CP06]*

*"I think a suite of videos would be useful. Where they would look at potential various disease states that are being managed" [CP07]*

*"a comprehensive covered of the most common drug interactions. Something that would be, you don't keep Stockley's in your head but you might keep major, you might keep a smaller more precise and more common occurrences of drug interactions. It is something like that in review in a video format that I think would be very helpful" [CP09]*

#### *Intervention component-scheduled medication review*

Overall, participants were positive about conducting medication reviews and believed a medication review could be conducted within a community pharmacy. However, the time of year may impact delivery due to annual leave, or vaccine season for example.

*"for it to be effective, it needs to be consistent and it might not always be possible at certain times of year, maybe in the summer or maybe in the, maybe at Christmas time or something like that" [CP01]*

A locum pharmacist felt they may not be in a good position to conduct medication reviews due to the nature of their temporary role.

*"as a locum I'm constantly in different pharmacy environments, in the majority of places, I'm not sure you'd have the time or the resources to go through a medication review, with the patient" [CP02]*

Most participants thought that a scheduled medication review would be of benefit and that any employee could schedule a medication review, building on experience of arranging vaccination appointments.

*"you could run it very like the vaccination, once you have a template set up like that" [CP03]*

*"That would have to be the structured way to ensure sufficient time would be put aside to do it" [CP09]*

Only two participants believed that a walk-in medication review service would be more beneficial than a scheduled medication review. One participant stated this was because patients

are used to their community pharmacy being accessible at any time and another noted that it would be better conducted at the time when patients are collecting their prescriptions.

*"I think you might run in to the problem that patients are used to pharmacies being available all the time, they don't know they need an appointment. I know people doing vaccinations have ran into that 'why do I need an appointment?'"* [CP04]

*"it could be at the point where they collect their medicines and I think that would be at a better time"* [CP05]

Numerous barriers and facilitators were discussed in relation to community pharmacists conducting medication reviews in the community pharmacy. The two most common barriers identified by most community pharmacists included the lack of staff and time pressures. Other barriers identified included lack of access to patient records, lack of space available within the pharmacy, and a perception that recommending changes might impact on their relationships with local GPs.

*"in the present context where there's not a lot we can do about it, even if we got the agreement from the patient, you still have to go back to the prescriber, you know, I think people might feel like you are putting the cart before the horse"* [CP04]

*"the staffing issue would be a big barrier to us"* [CP05]

*"I just think it would be a hugely demanding thing to do at present, where they would be hard pressed to find the time, eh so that they could run you know a functional business"* [CP07]

*"space could actually be an issue in the sense that there is one consultation room so if there is anything else happening then there is nowhere really to talk to in private with the patient"* [CP13]

The most common facilitator to conducting medication reviews in the community pharmacy include having more staff and also having an established framework/ standard operating procedure for community pharmacists to follow when conducting the review.

*"well I think it's something that you really need 2 pharmacists because you can't interfere with the normal work. Usually we just have 1 pharmacist there at a time"* [CP04]

*"like a template I suppose would be helpful, like questions to ask or something"* [CP12]



Payment, protected time and physical space within the community pharmacy would also help. Some participants also noted that GPs would need to be supportive of community pharmacists conducting medication reviews as otherwise the participants could not see the benefit of conducting medication reviews if GPs would not heed their advice and recommendations.

*"Financed is the big one. Definitely if it was financed it would be put into play" [CP10]*

*"if it was once a week or something like that. I couldn't do it for big numbers, but it would be a case of if you'd one morning a week and you did four appointments or something like that" [CP01]*

*"I think we could certainly provide that service... the GPs are on board with receiving the information that would be gathered" [CP14]*

#### *Intervention as a whole*

All pharmacists felt that the PolyPrime intervention would be of potential benefit to numerous cohorts including patients, healthcare providers and the government.

*"There would be greater assurance that the right medication is getting to the patient in the right way and that there is a facility there for shall we say inappropriate medicines entering into the system" [CP09]*

*"I just think that it would be a great idea, that there is a huge need for it" [CP10]*

*"It's of benefit for government, Doctors, and us" [CP14]*

Similar barriers and facilitators were identified to implementing a similar intervention to the PolyPrime intervention in community pharmacy compared to conducting medication reviews in the community pharmacy (presented above). The most common barrier to implementing a similar intervention was the lack of staff, followed by lack of time available, lack of funding and the range of people possibly involved in the patients prescribing.

*"you know I think that the two barriers are always going to be time and money! You know, if you get around them you get around everything else!" [CP04]*

*"I just think community pharmacies in so many places are so hard pressed on what they are trying to fit in clinically into an over burgeoning system, is too demanding... there are more pressing issues that need to be addressed" [CP07]*

*"very often with polypharmacy there are a number of people involved in the prescribing the medicines from hospitals GPs to dispensing pharmacists and it's that triangle that*

*needs to be polished in order to ensure that communications are the way they should be, or where they should be, so that appropriate prescribing and dispensing takes place"*  
[CP09]

Facilitators to implementing the intervention in the community pharmacy were similar to conducting a medication review; examples of facilitators were funding to participate in the intervention, staff available to conduct medication reviews and for normal services to continue in the community pharmacy, and protected time to enable the intervention.

*"very protected time for medication review and you know or even like conducting one review everyday like you know from 12 to 12.30 is for medication review we are not going to be dispensing any medications during this time so there are definitely some ways to get around it"* [CP06]

*"yea like if the pharmacist is away for half of the day then there needs to be another pharmacist in. And then that's two pharmacist wages there needs to be two methods of income to make up for that"* [CP13]

Two facilitators to help implement the intervention in the community pharmacy not discussed during the facilitators to conduct a medication review, were the integration within a Continuous Professional Development programme and the inclusion of prescribers or establishment of a formal communication channel to transfer findings of the medication review to ensure they are applied to the patient if necessary and appropriate.

*"if you were able to do the training packs, have access to them, if they could also be used as part of your CPD"* [CP03]

*"if it was something as simple as it would be compulsory for a GP to get back to us... or they had some sort of training to get back to pharmacies you know"* [CP05]

*"There is no reason why any pharmacist couldn't sign up to do this on behalf of the patients. Some sort of company set up to relay the findings back to GPs"* [CP14]

#### *Changes required to the PolyPrime intervention to be applicable for community pharmacists*

Possible additions to make the PolyPrime intervention applicable to community pharmacists were discussed by participants. Few suggestions were made here as most changes suggested were in relation to a specific aspect of the intervention, such as the video component or the medication review and presented above. One participant mentioned that a community pharmacist could be employed to conduct medication reviews and even visit patients in their

homes, whilst another noted that it might be more beneficial for a pharmacist to be involved at the point of prescribing as opposed to when the medications are being dispensed or after they have been dispensed.

*"you did have a community pharmacist say you had a spare pharmacist to go round to someone's house to review their medication" [CP14]*

*"I would think primarily the importance of it would be at the point of prescribing with complex patients... that then the pharmacist is brought on board and that can be managed at that point. I think it would be more meaningful then because it would be starting at the point from the prescribing" [CP07]*

## **5.5 Discussion**

As noted in the introduction to this chapter, the role of the community pharmacist in managing appropriate polypharmacy in older people revolves around dispensing their medications. The aim of this study was to explore community pharmacists' current involvement in the management of appropriate polypharmacy for older people and their views of how their current role in the management of appropriate polypharmacy for older people could be enhanced. This section discusses participants understanding of polypharmacy, the experiences of community pharmacists in managing appropriate polypharmacy and the strategies to expand their role via medication reviews, access to patient records and communication with prescribers. Recruiting community pharmacists via Twitter to participate in research is also discussed. The strengths and limitations of this study are discussed, followed by the conclusions. The findings from this study emphasise that community pharmacists in the ROI conduct many tasks but there is appetite to expand their role in the management of appropriate polypharmacy in older people. The identification of facilitators and barriers to overcome is an important starting point.

### **5.5.1 Participants understanding of polypharmacy**

As discussed in chapter 1, section 1.3.1, there are numerous definitions of polypharmacy in the literature, and this was reflected by the participants. The most common definition of polypharmacy in the literature is the use of five or more medications (Masnoon *et al.* 2017, Sirois *et al.* 2019) and this was the most common definition supplied by the participants. As a recent review of definitions of polypharmacy conducted by Pazan and Wehling (2021) found that 112 out of 143 definitions were numerical, and descriptive definitions of polypharmacy are much less common. Only two participants did not apply a numerical threshold to how they would define polypharmacy. Participants' described appropriate polypharmacy in line with definitions used in the literature (Payne and Duerden 2015, Mair *et al.* 2021), referring to medicines being prescribed for the appropriate clinical indications.

### **5.5.2 Confidence in managing appropriate polypharmacy**

Participants discussed different levels of confidence in identifying inappropriate prescribing, lower confidence was mainly due to lack of information as a result of not having access to patient records, whilst a higher level of confidence was due to their experience. Similar findings were found by Hansen *et al.* (2019) in a TDF based interview with 18 community pharmacists in Cork, Ireland. A survey conducted by community pharmacists in Finland (Kallio *et al.* 2021) concluded that community pharmacists are extremely confident in many tasks including identifying drug interactions and checking the dosage of medications (which participants in this

study also reported confidence in). The study reported that there is a high need to develop community pharmacist's confidence in medication risk management [a strategy aiming to decrease, or prevent, the risks associated with the use of medicines (Kallio *et al.* 2020)]; such a strategy could also be developed in Ireland which might improve community pharmacists' confidence in identifying and managing appropriate polypharmacy for older people. There is little information on community pharmacist's confidence in identifying appropriate prescribing in the literature, mostly a paragraph or two included as part of a wider study. However, there are numerous publications focusing on community pharmacist's confidence and ability to prescribe (Hanna *et al.* 2014, Abuzour *et al.* 2018, Woit *et al.* 2019, Cope *et al.* 2020).

### **5.5.3 Expanding the role of the community pharmacist in managing appropriate polypharmacy in older people**

Participants saw their role of the community pharmacist as ensuring the patient receives their correct medication and as an educator in enhancing patient's knowledge about their medications, the latter being as they are more accessible to patients than GPs. The community pharmacist was also seen as the link between all healthcare professionals; these descriptions of the community pharmacists are coherent with Rakvaag *et al.* (2020). The community pharmacist is in a prime position to expand their role in managing appropriate polypharmacy, due to their existing knowledge, both clinical and knowledge of their patients, and their accessibility, as is evident from the interviews presented above. As mentioned in the introduction to this chapter, section 5.1.1, the role of the community pharmacist in other countries has expanded and progressed to provide various services, however, the role of the community pharmacist remains limited in the RoI. The strategies discussed by participants in this study to enhance their management of appropriate polypharmacy in older people could help expand their role. This section will discuss the strategies to enhance their management in appropriate polypharmacy in comparison to the role of the community pharmacist internationally.

#### Medication reviews

Community pharmacists are in a unique position to offer medication reviews as their role in dispensing medication provides them with an insight into patients' use of both prescription and over-the-counter medications and may be in a better position to investigate patient's adherence to their medication than prescribers (Korenvain *et al.* 2020). Community pharmacists are highly regarded in the RoI with a recent report, the Pharmacy Usage and Attitudes Survey, showing 84% of respondents believed that community pharmacists could manage day-to-day healthcare issues (IPU 2019b). The same survey identified that 63% of the respondent's believed GPs were

capable of the same. Numerous studies have been conducted into various healthcare professionals conducting medication reviews, such as nurses (Bergqvist *et al.* 2009, Johansson-Pajala *et al.* 2018), pharmacists (Lexow *et al.* 2022, Uitvlugt *et al.* 2022), GPs (Cadogan *et al.* 2018, Prados-Torres *et al.* 2020, Gedde *et al.* 2022), and multidisciplinary medication reviews (Toivo *et al.* 2019, Dellinger *et al.* 2020). These studies have had varying results: two have shown effectiveness (Bergqvist *et al.* 2009, Lexow *et al.* 2022), other studies were shown to be acceptable and feasible (Cadogan *et al.* 2018, Dellinger *et al.* 2020, Prados-Torres *et al.* 2020, Gedde *et al.* 2022) whilst others acknowledge the need for further research to ensure a favourable outcome (Toivo *et al.* 2019).

Medication reviews conducted by community pharmacists have been shown to improve blood pressure (Geurts *et al.* 2016), optimise drug therapy (Messerli *et al.* 2016), resolve drug related problems (Geurts *et al.* 2016, Verdoorn *et al.* 2019) and improve health related quality of life (Verdoorn *et al.* 2019). Evidence shows that patients who receive a medication review from their community pharmacist are satisfied and believe it to be a valuable service (Cardosi *et al.* 2018, Messerli *et al.* 2018). It also a service commonly offered in community pharmacies internationally, for example, a survey by Imfeld-Isenegger *et al.* (2020) found that 19 out of 34 European countries provided a medication review conducted by community pharmacists, conducted in a community pharmacy. The types of medication reviews provided were classified according to the Pharmaceutical Care Network Europe (PCNE) definitions (PCNE 2018) of Type 1 (medication history), Type 2a (medication history and patient interview), Type 2b (medication history and clinical data), and Type 3 (medication history, patient interview and clinical data). The most common type of medication review provided was Type 1 and Type 2a, notably due to the lack of clinical data that community pharmacists have access to. Remuneration was identified as a facilitator to conducting medication reviews in community pharmacies in the RoI. Imfeld-Isenegger *et al.* (2020) found that the different types of medication reviews are supported by different amounts of remuneration, for example, 15% of Type 1 medication reviews received remuneration compared to 36% of Type 2a medication reviews. The type of medication review that could be offered by community pharmacists in the RoI was not discussed; further research is required on this and the type that is best suited to older people to ensure they receive appropriate polypharmacy. A systematic review by Michel *et al.* (2022) found that adequate remuneration was essential for the service to be frequently implemented in community pharmacy. It is evident from the interviews that medication reviews conducted by community pharmacists in the RoI would need to be supported by remuneration. This finding is reciprocated in a recent survey completed by 426 community pharmacists in the RoI that

focused on community pharmacists' attitudes towards deprescribing. Identifying deprescribing opportunities during medication reviews was considered part of the role of the community pharmacist by 85.4% of participants, with one of the top ranked barriers to deprescribing being lack of remuneration (Heinrich and Donovan 2022). However, pay for performance (i.e. remuneration received for every medication review conducted) does not result in appropriate prescribing (Ödesjö *et al.* 2017) and therefore may not be an appropriate remuneration method. It is important that the medication review and remuneration work for both the patient and community pharmacist and the result improves the management of appropriate polypharmacy in older adults.

The IPU are eager to progress the role of the community pharmacist and in 2018, they proposed a 'New medication' service (IPU 2018) where the community pharmacist would provide advice and support for patients taking a newly prescribed medication, within two weeks of commencing new medication. The IPU states that this service would save the health system an estimated €2.5million over 5 years with potential to save more as inappropriate medications may be identified leading to a decrease in medication related hospitalisations (IPU 2018). This service was implemented in England and led to a decrease in adverse events alongside a decrease in complex treatments (Elliott *et al.* 2017). Much work needs to be done to implement the 'New medication' service but it would be a useful step to introducing medication reviews conducted by community pharmacists, and progressing the role of the community pharmacist in the management of appropriate polypharmacy.

Validated prescribing and medication review tools were discussed in Chapter 1, section 1.6.2. The tools discussed were either developed for GPs or for general use by healthcare professionals and often require the patient's medical records to complete, such as STOPP/START (O'Mahony *et al.* 2015). Tools have been developed, and validated, for community pharmacists in the implementation of health promotion programmes (Truong *et al.* 2012), assessing ambulatory care (Bradley *et al.* 2018) and providing care to patients with heart failure (Riester *et al.* 2021). Few tools have been developed specifically for use by community pharmacists in a medication review, or to assess appropriate prescribing acknowledging that in some countries, community pharmacists do not have access to patient records. An example of a medication review tool developed specifically for use by community pharmacists is ReMeDo (Quintana-Barcena *et al.* 2022), however this has been developed for use in the patient's home, and not strictly in the pharmacy. The tool provides an outline of information to be collected before the community pharmacist's visit (including demographic information, health conditions and current prescriptions), during the visit (including storage of medication, review of all their medication

present at home) and after the visit (including drug related problems with patient's medication at home). This tool has been found to be easy to use and necessary to optimize medication use. A tool similar to ReMeDo could be developed for community pharmacists to use in the pharmacy and expand their role in the management of appropriate polypharmacy in older adults.

#### Access to patient records

A patient medical record is defined as 'the document that explains all detail about the patient's history, clinical findings, diagnostic test results, pre and postoperative care, patient's progress and medication' (Bali *et al.* 2011) and contains a lot of critical information that can be crucial to ensuring appropriate prescribing in older people. Studies show that community pharmacists are hindered in their role and the advice they can provide by not having access to patient medical records (Roberts *et al.* 2019). The Rx-SafeNet study, a randomised controlled pilot study with 37 patients and 4 community pharmacists, showed that community pharmacists who have access to patient records are able to identify medication-related problems as well as PPO (Gernant *et al.* 2018). Access to patient records has been shown to improve confidence in identification of drug therapy problems, with access to laboratory results acknowledged as the most useful type of information from patient records (van Lint *et al.* 2015). Medication-related problems and PPOs are important aspects in appropriate prescribing and community pharmacists have the knowledge to identify these (as stated above), therefore, the access to patient records would be helpful in expanding their role in managing appropriate polypharmacy.

Few countries allow community pharmacists access to patient records, the UK and Australia two examples of countries that do provide community pharmacists access. The Summary Care Records system in the UK is an electronic record of important patient information created from GP records and is created automatically unless an individual opts out (NHS Digital 2022). The My Health Record used in Australia is also an electronic record of key health information that is designed to be utilised in conjunction with existing local clinical information (Pires 2022). These initiatives have shown to be time effective, enhance patient safety and identify medication discrepancies in a timely manner (Jones 2015, Salmi *et al.* 2020). These studies show the importance and usefulness of community pharmacists having access to patient records and future research should investigate developing this in the RoI. As GP practices act as independent businesses and do not share patient records (except if requested by the hospital for example) this process may take longer to implement than in other countries. Some progress has been made in order for community pharmacists to have access to patient records with the



development of the electronic health record in the RoI, stemming from the 'ehealth strategy for Ireland' (Department of Health 2013), discussed in Chapter 1, section 1.5.4.

Access to patient records may be considered useful, however, similar initiatives on a smaller scale can also be effective. A recent study conducted in Norway found that an electronically shared medication list between GPs, community pharmacists and home care services significantly reduced the number of discrepancies between the medication lists of the three healthcare professions and therefore reduce prescription errors (Josendal *et al.* 2021). Due to the Covid-19 virus, a national electronic prescription transfer to community pharmacy was implemented (as discussed in Chapter 1, section 1.5.5). This has since been reviewed via an online survey completed by 494 community pharmacists which concluded that the process of electronic prescription transfer should continue after the pandemic and that it was seen as a positive step for community pharmacy practice (Kenny and Dalton 2021). However, this study also reported that over half of the community pharmacists believed the electronic transfer of prescription has led to patients feeling that they are not as involved in their medication. If this practice is to continue, future work is required to ensure patients feel involved in their medication. Whilst this is not the same as having access to patient records, it must be noted as an important development in community pharmacy.

### Communication

The lack of a direct communication channel with prescribers was an important factor in helping participants to improve their management of appropriate polypharmacy in older people. A study in Canada found that a lack of an appropriate communication channel with prescribers was a barrier for community pharmacists in providing all possible services that are in their remit (Hussein *et al.* 2021). To the research student's knowledge, there has been little investigation into developing an effective, user-friendly communication channel between prescribers and community pharmacists. Instead, many studies that include a communication channel focus on the collaborative process between community pharmacists and prescribers, the latter predominantly GPs in the literature (Van *et al.* 2012, Rathbone *et al.* 2016, Saha *et al.* 2021).

Communication between community pharmacist and GP in Ireland is traditionally conducted via telephone or healthmail, yet telephone calls in particular can disturb workflow and be disruptive (Renfro *et al.* 2018). The implementation of a shared electronic health record (see above) could be acknowledged as a communication channel between community pharmacists and prescribers. As it is not widely implemented in community pharmacies, it's use as a communication tool is unknown but has shown to be of use in one study (Renfro *et al.* 2018). A

survey conducted in 2019 by the IPU, found that 95% of the 310 community pharmacist respondents believed that community pharmacists and GPs needed to work more closely together (IPU 2019a). GP-community pharmacist organised cooperation can improve the effectiveness of drug therapy (Waszyk-Nowaczyk *et al.* 2021) and GPs welcome collaboration with community pharmacists in relation to medicine management, although both professions have noted tensions regarding contact in relation to minor prescribing errors (Bidwell and Thompson 2015). An official communication channel between GPs and community pharmacists could potentially ease the tension resulting from contact over minor prescribing errors, especially in the RoI where community pharmacists do not have the authority to alter or change prescriptions.

Community pharmacists provide care for patients after they have been discharged from hospital and return home, however, community pharmacists are rarely included in the discharge process nor any communications between healthcare professionals regarding this process (Urban *et al.* 2013). Two systematic reviews have highlighted the importance of the community pharmacist during transitions of care (Ensing *et al.* 2015, Nazar *et al.* 2015) and evidence shows that involvement of the community pharmacist decreases the rate of adverse drug events (Guilcher *et al.* 2020) and hospital readmissions (Wright *et al.* 2019). It is evident that the RoI is not the only country with need of an official communication channel between community pharmacists and prescribers. Communication with prescribers is an important aspect of the role of the community pharmacist and it is clear that a communication channel would be useful in expanding the role of community pharmacists managing appropriate polypharmacy in older adults.

#### **5.5.4 TDF domains to target to enhance the community pharmacist role in managing appropriate polypharmacy**

The TDF was used in this study as it is a useful tool in detecting factors that influence an individual's behaviour and therefore identify factors that should be addressed in order for change to occur (Lynch *et al.* 2018). In this instance, the TDF highlighted the barriers and facilitators to participant's strategies in expanding the management of appropriate polypharmacy in older people. As the research student is not an expert in theory, the TDF was a useful tool to inform the topic guide as it incorporates 33 theories in relation to behaviour change. A survey conducted by Birken *et al.* (2017) found that the most common reason for use of theory was to identify key factors that act as barriers and facilitators; the TDF is a useful tool in identifying this.

Whilst some studies solely use the TDF as their analytical framework to analyse the TDF based interviews, this research followed recommendations by McGowan *et al.* (2020) which advocates for the use of both an inductive and deductive approach to analysis. This means that no important aspect of the interviews was lost during the analysis process because it did not fit within a TDF domain. Most barriers and facilitators identified during the interviews sat within the domains of the TDF, supporting comments by Burgess *et al.* (2015) and Haith-Coper *et al.* (2018) that a deductive approach to analysis using the TDF is sufficient.

Two TDF domains were addressed in all strategies to enhance community pharmacist's role in the management of appropriate polypharmacy in older people: Environmental context and resources, and Motivation and goals, and are therefore important TDF domains to target. The most discussed TDF domain was Environmental context and resources (i.e., the most barriers and facilitators discussed were categorised under this domain), this aligns with other TDF based studies (Gerlach *et al.* 2020, Alenezi *et al.* 2022). The barriers identified were lack of time, staff shortages and lack of resources (such as free space in the pharmacy, spare equipment). These barriers have also been identified in TDF based studies with community pharmacists providing antimicrobial stewardship in England and Wales (Jones *et al.* 2018), providing cognitive services during Covid-19 in Turkey (Okuyan *et al.* 2021), promoting physical activity in Portuguese community pharmacies (Viegas *et al.* 2021) and managing opioid therapy in the UK (Alenezi *et al.* 2022) proving that these barriers are not unusual to the community pharmacy practice in the RoI. Lack of time to conduct extra activities in the pharmacy (such as medication reviews) and lack of resources have been identified as issues in the community pharmacy setting internationally continually for the past 20 twenty years (Dunlop *et al.* 2002, Roberts *et al.* 2008, Costa *et al.* 2017). This issue is therefore not unique to the RoI, however, it is clear that community pharmacists in the RoI, and internationally, do require more resources and perhaps a clear structure of job activities which they are to complete. This research has shown that community pharmacists would welcome more staff in order to help with their workload. A clear outline of staff members and their tasks could help time management in the pharmacy though more research is required on how, and if, this could work in the community pharmacy setting in the RoI.

Version 1 of the TDF was used for this study, however, the TDF domain Motivation and goals was split into two domains in version 2 – Intentions (a conscious decision to perform a behaviour or a resolve to act in a certain way) and Goals (mental representations of outcomes or end states that an individual wants to achieve) (Cane *et al.* 2012). Barriers and facilitators identified under the Motivation and goals domain by participants included the community pharmacist being

more accessible than the GP, remuneration, government support and to provide better healthcare. Quality of care and improving patient safety have been identified under this domain in other TDF based research (Lawton *et al.* 2016) showing that the barriers and facilitators from this study are comparable to other TDF research in primary care, even if the focus was not on enhancing how community pharmacists manage appropriate polypharmacy in older people. As this study used version 1 and participants identified the domain Motivation and goals to be important in enhancing community pharmacists' management of appropriate polypharmacy in older people, studies that used TDF version 2 were not included in the examples provided.

The TDF domain Memory, attention, and decision processes was seen to be an important TDF domain in a study on implementing pharmacist-led pharmacogenomic testing (Luke *et al.* 2021), community pharmacists providing reproductive health services to women receiving opioid substitution treatment (Alhusein *et al.* 2021) and has been included in a community pharmacy intervention to improve older people's medication adherence (Patton *et al.* 2020). This TDF domain was not deemed to be as important in comparison to other domains when enhancing the community pharmacist's role in the management of appropriate polypharmacy as it was only discussed by one participant. However, the domain should therefore be considered when developing a future intervention. Whilst participants in this study did not identify the TDF domain Emotion as an important domain to target to enhance community pharmacist's management of appropriate polypharmacy, it has been acknowledged as an important aspect in other studies. Examples include community pharmacists caring for people who are homeless (Paudyal *et al.* 2019), enhancing the public health role of community pharmacists (Agomo *et al.* 2020), and community pharmacists providing reproductive health services to women receiving opioid substitution treatment (Alhusein *et al.* 2021). The researcher acknowledges that some quotations provided in the results are emotions, for example, 'happy' and 'overwhelming'. However, given the context from which the quotation was derived, they fit more appropriately in other domains and as such Emotion has not been included as a domain to target in an intervention to enhance community pharmacists management of appropriate polypharmacy in older people in primary care. There is a possibility that the questions posed did not result in participants identifying this domain as relevant, however, as the topic guide had been piloted before implementation in the study this is unlikely. Emotion was not deemed to be a relevant domain in other TDF based studies including improving appropriate polypharmacy for older people (Cadogan *et al.* 2015), GP's perspectives on prescribing to older people (O'Riordan *et al.* 2017), using a screening tool in medicine use review (Cardwell *et al.* 2018) and deprescribing in older adults (Evrard *et al.* 2022).

### 5.5.5 The PolyPrime intervention for community pharmacists

Overall, the PolyPrime video (albeit the description of the PolyPrime video), was well received by participants and they could see the potential of showing a video to community pharmacists on how to conduct a medication review within the pharmacy. A qualitative study conducted by Barry *et al.* (2020) which developed an intervention using BCTs (see Chapter, section 1.8 for definition), identified a video to deliver the BCT 'Modelling or demonstrating the behaviour'. Although this decision was supported by the development work completed for the PolyPrime study (Cadogan *et al.* 2015, Cadogan *et al.* 2018) it shows that a video can be a useful component in an intervention due to its accessibility. A study to enhance asthma care by community pharmacists also included educational videos which were found to be helpful (Serhal *et al.* 2022). The inclusion of different scenarios was mentioned by both GPs (see Chapter 3) and participants in this study which is an important factor to consider both for the future use of the PolyPrime intervention in a GP setting, and if the intervention is to be amended and delivered to community pharmacists.

Participants stated that they would likely find the inclusion of validated assessment tools, prescribing guidelines, patient feedback and how to navigate a patient showing resistance as useful components of the video. It is important to note here that the video discussed in this study was different to the video shown to GPs in Chapter 3. The participating community pharmacists were described the amended video that resulted from GP feedback presented in Chapter 3, i.e., the video that was included as part of the PolyPrime trial presented in Chapter 4, and so the results presented above are not necessarily comparable to those in Chapter 3. As noted in section 5.5.3 above, there are few publications in the literature on validated assessment tools for community pharmacists to use during a medication review. A comprehensive educational video (similar to that in the PolyPrime intervention), alongside a medication review framework, could be developed and tested as part of a feasibility study on community pharmacists conducting a medication review in the pharmacy. Weir *et al.* (2019) have developed the Medicines Conversation Guide, a one-page tool to guide healthcare professionals in conversations about medicines. Elements in the guide include health priorities, patient goals and fears, and general health understanding. If the PolyPrime intervention is to be adapted and tested for feasibility in community pharmacy, the Medicines Conversation Guide could be a useful addition. The addition of the most common drug-drug interactions was also noted. Hughes *et al.* (2021) identified the top 10 most frequently dispensed (co-prescribed) drug-drug interactions, the ten most frequent drug-drug interactions involving medications dispensed  $\pm$  seven days of each other, and the drugs most commonly involved in the

identification of drug-drug interactions, in older people who participated in The Irish Longitudinal study on Ageing (TILDA). These findings could be added to the information section of the video.

Barriers identified by participants to implementing the PolyPrime intervention in their pharmacy included a lack of available time, lack of space, no access to patient records and lack of ability to make changes to prescriptions. Lack of available time and lack of space are common issues in community pharmacy, as identified above. Consultation rooms in the ROI are mandatory in a pharmacy since 2008 (PSI 2015). However, as medication reviews can be lengthy, private and confidential interactions with patients may have to wait until the consultation rooms becomes available and this may not be ideal, given that community pharmacies are considered an easily accessible healthcare site (Henman 2020). Lack of access to patient records could be addressed by community pharmacists conducting a Type 2a medication review (see section 5.5.3) as medication history would be available via the pharmacy database, and the patient's dispensing records and consultation rooms to conduct a patient interview in private are available in every pharmacy. To address the need and scheduling of medication reviews alongside availability of staff and space, criteria could be employed to qualify for the service (such as the inclusion criteria for patients in the PolyPrime study, addressed in Chapter 4 section 4.3.2). Canada utilises a similar method whereby patients have to be receiving five or more medicines (Carter *et al.* 2012) or have three chronic conditions (Pammett and Jorgenson 2014) to qualify for the intervention.

Literature suggests that patients can correctly identify their medication (Hoisnard *et al.* 2019), however the more medications an older person is prescribed, the knowledge of their medications decreases (Hoisnard *et al.* 2019). Patients can often be discouraged from talking to their community pharmacist due to having to wait for their prescription and the noisy environment of the pharmacy (Qudah *et al.* 2021). Protected time for community pharmacists in order to provide a medication review could increase the patient's knowledge of their medications.

#### **5.5.6 Recruitment**

A novel approach to recruitment was adopted by this study. Pharmacists were recruited via social media, notably Twitter, which has not previously been done by the research team. Whilst Twitter is not a new social media, its use in healthcare research recruitment is relatively young. However, it is gaining traction as a useful recruitment method and has been used to recruit healthcare professionals such as GPs (Panahi *et al.* 2016, White *et al.* 2022), community

pharmacists (Rolf von den Baumen *et al.* 2020), and medical students (Friedman *et al.* 2022). Twitter was often used in conjunction with another recruitment method, such as advertising via forums and direct invitation (Panahi *et al.* 2016); a study recruiting family caregivers solely on Twitter found it enhanced the recruitment process (Wasilewski *et al.* 2019). Recruitment via Twitter offered benefits including being cost-effective (the PhD candidate did not have to spend money on advertising or postal charges), and increased exposure through people sharing and commenting on the post. Nevertheless, recruitment was slow and perhaps if the study had employed another advertising method at the beginning of the study recruitment would have been quicker and the recruitment aim met.

Potential participants were provided with some detail about the study before agreeing (or disagreeing) to take part. They were informed that the interview would take approximately one hour, which perhaps was a deterrent for some potential participants. However, this could not be shortened as all questions on the topic-guide were considered important to ensure the research question could be answered by the study. This timeframe is in-keeping with other semi-structured interviews conducted with healthcare professionals based on the TDF (Debono *et al.* 2017, Jones *et al.* 2018, Barry *et al.* 2020, Tang *et al.* 2020, Ly *et al.* 2021, Patton *et al.* 2021, Leather *et al.* 2022). The objective of recruiting 15 participants reflected other semi-structured studies with healthcare professionals conducted by the research team (Cadogan *et al.* 2015, Patton *et al.* 2021).

The number of interviews required in qualitative studies to ensure the research question is answered, is a well debated topic. Analysis of qualitative health research in three journals (British Medical Journal, British Journal of Health Psychology, Sociology of Health & Illness) from the past 15 years has shown that the mean number of interviews in qualitative publications ranges from 18 to 44 interviews and the median number of interviews spans from 15-31; six was the smallest number of interviews conducted (Vasileiou *et al.* 2018). Some researchers are guided by the concept of 'data saturation' (described in chapter 3, section 3.3.1) which would mean that data analysis would take place in tandem to data collection. Identifying when data saturation is reached is challenging. To overcome this challenge, Francis *et al.* (2010) recommend researchers apply a set of four systematic principles to justify an appropriate sample size has been reached. The principles are as follows: (i) specify *a priori* the number of interviews to have taken place before the first round of analysis, (ii) specify *a priori* how many additional interviews will be conducted without new themes emerging, (iii) initial analysis is conducted by a minimum of two researchers independently, (iv) reporting of data saturation methods and findings (Francis *et al.* 2010).

Community pharmacists in the RoI are not regularly invited to take part in semi-structured interview studies, however this is beginning to change with numerous qualitative studies recently published (Hansen *et al.* 2019, Morcos and Dalton 2021). In the UK, the Royal Pharmaceutical Society launched a Research Resource Hub to encourage pharmacists to become involved in research and to provide support to those who wish to be involved in research (Royal Pharmaceutical Society 2017). Previous research has found that community pharmacists have not participated in research due to lack of available time (Peterson *et al.* 2009) and lack of payment for involvement (Rosenbloom *et al.* 2000). A more recent study, conducted by Crilly *et al.* (2017) found that 57% of participants considered research to be important with 45% noting that research should be a priority. However, over a quarter of participants did not believe research to be part of their role as a community pharmacist. Crilly *et al.* (2017) noted that lack of time and remuneration were the most common reasons cited by community pharmacists for not taking part in research studies. Training tools to enable pharmacists to take part as well as protected time to participate in research would encourage pharmacists to take part (Crilly *et al.* 2017). This research was conducted in England but similar findings have been found in other countries including Canada (Hébert *et al.* 2013), Sweden (Frisk *et al.* 2019) and Australia (Saini *et al.* 2006, Bertilsson *et al.* 2021). There is a desire for community pharmacists to be involved in research (Li *et al.* 2020), however, as of writing this thesis, no similar research regarding community pharmacists views on participating in research has been conducted in the RoI.

### **5.5.7 Strengths and limitations**

The topic guide for this study was based on the TDF with questions deriving from previous TDF based topic guides and was also piloted numerous times to ensure validity and that questions were understandable. The research team involved in this study had previous experience of using the TDF (Cadogan *et al.* 2015, Cullinan *et al.* 2015, Barry *et al.* 2020, Patton *et al.* 2021), ensuring its appropriate use and were able to guide the novice student. This study has been reported in line with the Consolidated criteria for reporting qualitative research (CORE-Q), see Appendix 5.14 for completed checklist.

There are some limitations to this study. Firstly, the target recruitment of a minimum of 15 participants was not achieved. However, given the wide range of responses it is unlikely that one extra participant would have added much to the findings. The nature of the topic guide (i.e. suggestions to improve the management of appropriate polypharmacy) requires a larger number of participants to reach data saturation, likely over 30 participants. Due to time



pressures, it was not possible to continue with recruitment until data saturation had been reached. Secondly, given that there was little representation from locum and relief as well as community pharmacists, the findings may not be representative of all community pharmacists. Thirdly, the use of two interview methods (Microsoft Teams and telephone) might have influenced the findings as the interviewer could not pick up non-verbal social cues such as facial reaction during telephone interviews, and the interviewee, knowing they could not be seen on the telephone, may not have given the interview their full attention. However, Brustad *et al.* (2003) found differences in results from telephone or virtual interviews not to be substantial. Finally, using the TDF to formulate questions may have limited the identification of barriers and facilitators to the ideas suggested.

## **5.6 Conclusion**

Further research is required on how the community pharmacists' role in the management of appropriate polypharmacy for older people in primary care could be improved in the RoI, and how this could be achieved. More interviews need to be conducted in order to ensure data saturation is reached in relation to enhancing the management of appropriate polypharmacy in older people. Nonetheless, this study has identified one TDF domain that community pharmacists do not deem to be relevant –Emotions, and two TDF domains that they deem to be relevant to enhancing the management of appropriate polypharmacy, regardless of the idea discussed (Environmental context and resources, Motivation and goals). To make the PolyPrime intervention suitable for community pharmacists, the addition of the most common drug-drug interactions and a medication review framework would be useful additions. However, lack of staff, lack of quiet and confidential space in the pharmacy, and their inability to make any changes to prescriptions are barriers to community pharmacists conducting medication reviews.

## **Chapter 6**

### **General discussion and conclusion**

## 6.1 General discussion

The research presented in this thesis has focused on examining methods of improving appropriate prescribing for older people in primary care, and focused primarily on a theory-based intervention, the PolyPrime intervention. This was developed by the research team in a systematic manner, following the MRC framework (Craig *et al.* 2008) for complex intervention development, prior to the commencement of this research PhD. As the population ages, problems arising from inappropriate medication usage in older people are set to increase, as older people are more susceptible to adverse effects of medicines than their younger counterparts. Polypharmacy is often essential for older people, given the presence of multimorbidity. The research presented in this thesis lays out a clear pathway for additional research to be carried out on how to best improve appropriate polypharmacy in primary care, in terms of the next steps required for the PolyPrime intervention itself and other potential methods for improving appropriate polypharmacy that should be investigated. This section provides a general discussion on the chapters presented in this thesis including the key findings and implications for further research and practice where relevant.

Chapter 1 introduces the topic of polypharmacy and related aspects of polypharmacy, such as defining appropriate polypharmacy, noting the types and prevalence of adverse effects associated with polypharmacy and presents the concepts for systematic and theoretically based intervention development. It also presents the concepts and theories associated with behaviour change interventions. The development of the PolyPrime intervention was also discussed here, noting that it followed a systematic approach and was guided by theory. Interviews were conducted with GPs and community pharmacists using the TDF which identified barriers and facilitators in prescribing (GPs) or dispensing (community pharmacists) of appropriate polypharmacy in older people. The TDF domains were then mapped to BCTs, and four BCTs were selected for inclusion in an intervention (i) action planning, ii) prompts/ cues, iii) modelling or demonstrating of behaviour, and iv) salience of consequences (Cadogan *et al.* 2015). The resulting, GP-led intervention was tested in a feasibility study and found to be acceptable (Cadogan *et al.* 2018).

The intervention consisted of four components: i) GPs watch a short online video (designed and scripted by the research team) (BCT: 'Modelling or demonstrating of behaviour' and 'Salience of consequences'), ii) explicit plans made at weekly staff meetings to ensure that target patients prescribed appropriate polypharmacy (BCT: 'Action planning'), iii) patients are invited to attend the practice for a scheduled medication review, and iv) reception staff prompt the GP that the

patient has arrived at the practice for their medication review (BCT: 'Prompts/cues' (Cadogan *et al.* 2018)).

The findings of a systematic review of theory-based interventions to improve appropriate polypharmacy in older adults in primary care are presented in Chapter 2. There is a clear dearth of such interventions, adding weight to the need for interventions such as the PolyPrime intervention. A narrative review was provided as the effectiveness of theory-based interventions on improving appropriate polypharmacy in older adults in primary care could not be determined because of the few studies identified.

A qualitative study to refine the PolyPrime intervention is presented in Chapter 3. This study involved investigating any updates required as well as necessary amendments to use the PolyPrime intervention in the RoI, given that it was developed in NI. The main amendments arising from this research included the addition of educational slides containing website links to prescribing guidelines and conducting a medication review, and information on commonly encountered instances of potentially inappropriate prescribing in older people. Validated assessment tools of STOPP/START (O'Mahony *et al.* 2015) and NO TEARS (Lewis 2004) were also included alongside information for practice staff. The required changes were made following discussions with the wider research team.

Chapter 4 presents the outcomes, including a process evaluation for a pilot cRCT of the PolyPrime intervention. The pilot cRCT was undertaken in NI and in the RoI, but only data from the RoI sites involved are presented. The data supports the possibility of proceeding to a full RCT of the PolyPrime intervention, however some minor amendments may be required to the patient recruitment strategy to ensure patient retention.

In the final research chapter, Chapter 5, various approaches to how community pharmacists in the RoI could enhance their role in the management of appropriate polypharmacy in older adults are presented, along with the perceived barriers and facilitators to each approach. This study was guided by the TDF. The barriers and facilitators for all strategies were presented as one under the TDF domains as many barriers and facilitators were similar regardless of the strategy being discussed, and when considered by the research team collectively, the strategies seemed interdependent.

Recommendations arising from the thesis including the use of theory in intervention development and recruitment of healthcare professionals for a qualitative interview via social media are then discussed. This is followed by the implications for policy and practice, discussing

enhancing the role of the community pharmacist in the RoI as well as expanding the scope of the PolyPrime intervention. A final conclusion is then provided.

### **6.1.1 Theory in intervention development: what is the evidence?**

Guidance from the MRC in developing and evaluating complex interventions (Campbell *et al.* 2000, Craig *et al.* 2008, Skivington *et al.* 2021) recommend the use of theory in intervention development. Key principles and actions for consideration during intervention development, resulting from a consensus exercise, also advocated for the use of theory (O’Cathain *et al.* 2019). Various authors suggest that a theoretically derived intervention will likely be more effective than an intervention that does not include theory (Craig *et al.* 2008, Bleijenberg *et al.* 2018). Theory-based healthcare interventions have been shown to be effective in enhancing self-care in people with type 2 diabetes (Al-Washali *et al.* 2018), improving physical activity in people with several mental illnesses (Romain *et al.* 2020), and medication adherence in patients with rheumatoid arthritis (Asgari *et al.* 2021). However, there is conflict in the literature regarding which approach, i.e. to include theory in intervention development or not, is the best approach to follow. Some authors advocate for more research before the argument can be concluded (Gourlan *et al.* 2016, Patton *et al.* 2017, Xing *et al.* 2019, Rigby *et al.* 2020)). A review of systematic reviews concluded that interventions developed using theory are not more effective than interventions developed without theory (Dalgetty *et al.* 2019). It is important to note that the authors of the review made this conclusion on the overall evidence base and do not dismiss the inclusion of theory in intervention development. Other research has also concluded that theory does not increase intervention effectiveness (Alageel *et al.* 2017, Garnett *et al.* 2018).

The systematic review presented in Chapter 2 identified only two theory-based interventions aimed at improving appropriate polypharmacy in older adults in primary care (Cadogan *et al.* 2018, Toivo *et al.* 2019). The search strategy was conducted across seven databases in August 2019, updated in August 2020 with a further update in August 2021. One of the retrieved studies described the PolyPrime intervention, the intervention developed by the research team involved in the current research and that which was investigated for refinement and piloted in a cRCT presented in this thesis. The outcomes from the systematic review did not provide evidence for effect of theoretically derived interventions due to the small number retrieved and the relative infancy at which the reported studies were at. The systematic review was not established to compare theoretically derived interventions to those that were not theoretically derived, and was simply designed to establish the effectiveness of theoretically derived interventions. Disappointingly, given the lack of studies retrieved, this was not possible.

Information gleaned from this systematic review noted that, according to the TCS, theory was not applied to its full extent in either of the two retrieved studies as neither study opted to test and refine the underpinning theory. Therefore, only categories 1-3 of the TCS (i.e. the extent of theory used in the development of the intervention) were reported on and discussed. Categories 4-6 (i.e. the testing and refinement of the theory used in the development of the intervention) are not commonly used when assessing the extent of theory used in healthcare intervention development (Prestwich *et al.* 2014, Patton *et al.* 2017, Lycett *et al.* 2018, Garnett *et al.* 2018, Nili *et al.* 2020) as information on refining or developing theory is often not reported in descriptions of how interventions are developed.

As mentioned above, it was not possible to discuss the effectiveness of theory-based interventions. Consequently, this systematic review cannot recommend that theory based interventions should be developed to enhance effectiveness of interventions targeting appropriate polypharmacy, but it can and does recommend that, given the lack of published theoretically derived interventions, more are required to answer the effectiveness question. Including theory in intervention development can help researchers to identify the key aspects of their intervention's mechanisms (Cadogan *et al.* 2016, Skivington *et al.* 2021) and helps to refine the intervention (Noar *et al.* 2007).

There are various ongoing studies investigating different approaches to healthcare, with key comparisons being made based on whether interventions are theoretically derived or not. One such study, by Morrow and colleagues aims to compare the effectiveness of a theory-based implementation approach against a non-theory-based approach for improving detection of Lynch syndrome amongst patients with colorectal cancer (Morrow *et al.* 2019). Whilst this study focuses on referral practices in cancer genetics, it's findings in relation to theory will be important for all healthcare interventions, and help to establish the true role of theory in intervention development, and its place within the MRC framework. A similar comparison of interventions, i.e., theoretically derived versus non-theoretically derived, to improve appropriate polypharmacy would be valuable to determine the effectiveness of theoretically derived interventions for appropriate polypharmacy.

### **6.1.2 The PolyPrime intervention: its transferability to other healthcare jurisdictions and healthcare settings**

Theory was used in the development of the PolyPrime intervention (Cadogan *et al.* 2015, Cadogan *et al.* 2016, Cadogan *et al.* 2018). Barriers and facilitators of prescribing appropriate polypharmacy were categorised under the 12 domains of the TDF version 1 (Michie *et al.* 2005).

Identified key theoretical domains perceived to influence GP prescribing behaviour were used to develop a behaviour change intervention, whereby key domains were mapped to behaviour change techniques (Cadogan *et al.* 2015). GPs interviewed to develop the intervention were practicing in NI. The developed intervention was tested in a feasibility study, which found that the intervention was acceptable to GPs and patients in NI (Cadogan *et al.* 2018). Whilst there are other behaviour frameworks which could have been utilised in the development of the PolyPrime intervention, such as the COM-B model of behaviour (Michie *et al.* 2011b), its use in the context of this current study was potentially limited. For example, the TDF allowed for the barriers and facilitators of prescribing appropriate polypharmacy to be explored in detail and to identify domains that influence prescribing. It is possible that the COM-B model would not have been able to explore the wide range of domains to the same extent as the TDF. It was felt that the TDF, was the most suitable given that it was focused and fitted appropriately with the PolyPrime project framing prescribing as the behaviour. The TDF has been utilised in the development of numerous interventions (see Chapter 5, section 5.5.4 for examples), however, it remains unclear how successful the interventions were and if any were implemented within the healthcare system in which they were tested. Further research could investigate the effectiveness of interventions that were theoretically derived using the TDF.

Another way of improving patient safety within the healthcare environment is to use a human factors system approach. This approach is well recognised as critical to improving patient safety across healthcare domains (Carayon *et al.* 2015). One of the most widely used models of work systems is the Systems Engineering Initiative for Patient Safety [SEIPS (Carayon *et al.* 2014, Carayon *et al.* 2020)]. SEIPS is now on its third iteration and focuses on the patient journey as having multiple stages and that interactions within different work systems occur at each stage. An exploration of these work systems involved in a patient's journey in the healthcare system could be used to identify how improvement to patient safety could be made and to address appropriate prescribing. SEIPS has been used in various studies exploring different components of healthcare provision, including administration of medicines. For example, Odberg *et al.* (2020) investigated the processes involved in medication administration in a nursing home ward, using SEIPS. The authors illustrated the complexity of the process, and the barriers and facilitators within the work system linked to the administration process, thereby noting clear targets for improvement in medication administration in a ward in a nursing home. SEIPS has also been used by Odukoya *et al.* (2015) to examine the barriers and facilitators to recovery from e-prescribing errors in community pharmacies, and the solutions to ensure recovery from errors. The results of this study note several barriers and facilitators to recovery from e-

prescribing errors, including level of experience, knowledge of pharmacy personnel, availability of tools and technologies, and the physical environment. Interestingly, these key themes are each specific independent components of the TDF, the framework used in this thesis that describes actions as behaviours. However, a comparison of behavioural approaches versus a system-based approach to healthcare was beyond the scope of this thesis.

Undertaking a refinement phase between a feasibility and a pilot study is also consistent with the guidance from MRC and has become a regular aspect in the research process (Skivington *et al.* 2021). Other programmes of research which contain refinement processes, using qualitative interviews as the chosen research methodology, include cardiac rehabilitation (Winder *et al.* 2017), long-acting injectable antipsychotic medication (Blixen *et al.* 2020), communication in paediatric oncology (Dewez *et al.* 2021), and adherence to therapy after breast cancer (Jacobs *et al.* 2021). In the case of the PolyPrime intervention, given that the pilot study was to be conducted in two jurisdictions, a refinement phase was considered necessary because of the increasing divergence of healthcare services provided in NI and the RoI, as described in Chapter 3, section 3.1.2 and was undertaken.

Minor amendments resulted from the refinement phase, such as the addition of educational slides involving the most common instances of potentially inappropriately prescribed medications and the inclusion of other reference tools. This is consistent with research which reports that the most common topic in continuing medical education is prescribing updates (Dowling *et al.* 2020). Overall, the intervention was considered acceptable to the GPs interviewed, and no jurisdictional-specific changes were recommended or made. Therefore, it can be concluded that whilst the intervention was developed in NI, it was transferrable to the RoI, and could be transferrable to other healthcare jurisdictions outside the RoI and NI. However, it will be important to consider the healthcare context especially in relation to prescribing and also looking at prescribing in its totality as a system. The PolyPrime intervention has framed prescribing as a behaviour, as have many other studies (Bannan *et al.* 2019, Kunstler *et al.* 2019, Bannan *et al.* 2021, Pan *et al.* 2022). It is possible that in certain contexts patients may expect to receive a prescription from a GP. This is likely more common in Ireland than in Northern Ireland as most patients in RoI have to pay for a consultation with their GP. To date, there has been little research conducted on this, nonetheless, Murphy and colleagues conducted a study on differences in antibiotic prescribing between those who pay a fee for their GP consultation and those attend on a government scheme. The results showed that private patients were more likely to receive a prescription for antibiotics (Murphy *et al.* 2011). A possible reason for this is that GP's decision to prescribe may be influenced by the payment



method, thus, the argument can be made that prescribing is also in relation to the healthcare system and not solely as a behaviour conducted by the GP. This may need to be considered in future prescribing interventions focusing on behaviour change.

Other important contextual factors to consider are the communication and influence of other healthcare prescribers on the action of the GP. For example, a community pharmacist may not feel a prescription is appropriate and contact the GP to discuss their concerns. If a GP decides to change the prescription after this discussion, the prescribing would then be a result of more than one healthcare professional's behaviour, i.e. the pharmacist's intervention and the GP's prescribing. Some prescribing studies involving multidisciplinary teams have shown effectiveness, especially in relation to reducing therapeutic duplication (Maher *et al.* 2014), reducing medications prescribed with no indication of benefit (Liu *et al.* 2019), deprescribing in older adults with polypharmacy (Seto *et al.* 2022), whilst other researchers suggest frequent collaboration between GP and other healthcare prescribers to be of benefit (Baruth *et al.* 2020).

The PolyPrime intervention was described to community pharmacists (see Chapter 5 section 5.4.4) and was well received in this cohort. They discussed several components of the PolyPrime video that would be useful to community pharmacists in a similar intervention. These included access to validated assessment tools, prescribing guidelines and information on how to communicate with reluctant patients (in the PolyPrime video, the simulated patient showed some reluctance to have a medication stopped), and how to proceed in such a situation. Community pharmacists interviewed believed that a medication review could be scheduled and conducted within a community pharmacy, however, there are some barriers to be addressed for this to occur. They are in a good position to conduct medication reviews to improve appropriate polypharmacy given that communication and knowledge (both personal and clinical) are key aspects to their role (Ilardo and Speciale 2020, O'Sullivan *et al.* 2020) and important when conducting medication reviews. The PhD candidate believes that the PolyPrime intervention has potential to be implemented in the community pharmacy. However, a feasibility study would have to be conducted after adapting the video to be more community pharmacist focused and align with the scope of community pharmacists in the RoI (and consequently practice-based pharmacists in NI).

### **6.1.3 The pilot cluster randomised controlled trial of the PolyPrime intervention**

Two core outcome sets have been developed which are of use to the PolyPrime intervention. The first is by Rankin *et al.* (2018b) and includes 16 outcomes aimed at improving appropriate polypharmacy in older people in primary care. The second core outcome set includes seven

outcomes for use in clinical trials of medication review in multi-morbid older people (Beuscart *et al.* 2018). Both core outcome sets are discussed below. In total, the PolyPrime study includes six outcomes included in the core outcome set by Rankin *et al.* (2018b) including serious adverse drug reactions, mortality, hospitalisations, medication appropriateness, number of regular medicines prescribed, and quality of life. Two of the outcomes overlap with outcomes from Beuscart *et al.* (2018): potentially inappropriate medications, and health-related quality of life. As the PolyPrime intervention encompasses outcomes from two core outcome sets, this will ease future research in assessing the effectiveness of the study in comparison to other theory-based interventions to improve appropriate prescribing.

### *Medication appropriateness*

Medication appropriateness is one of 16 outcomes included in a core outcome set for trials aimed at improving appropriate polypharmacy in older people in primary care (Rankin *et al.* 2018b) and one of seven outcomes in a core outcome set for clinical trials of medication review in multi-morbid older people (Beuscart *et al.* 2018). Beuscart *et al.* (2018) include two outcomes similar to potentially inappropriate medications: overuse, and underuse. Both these outcomes are arguably part of the PolyPrime study as STOPP (O'Mahony *et al.* 2015) identifies potentially inappropriate medications, such as those prescribed without an evidence-based clinical indication and medication used beyond the recommended duration, which are defined under the outcome 'overuse'. START (O'Mahony *et al.* 2015) identified PPOs which falls under Beuscart *et al.*'s (2018) definition of 'underuse' (a failure to prescribe drugs that are indicated, including 1) omission of an evidence-based drug; 2) too short a duration). Therefore, one of the main objectives of the PolyPrime pilot study was to assess the feasibility of using medication appropriateness as the primary outcome in a definitive RCT. The pilot found that it was feasible to use medication appropriateness, measured using the validated, explicit prescribing tool STOPP/START (O'Mahony *et al.* 2015) as the primary outcome. STOPP/START was applied to the patient record data, collected via documents formulated specifically for the PolyPrime study, by academic pharmacists on the research team (CR and CC). Whilst the study wasn't powered to show effect, interesting trends were noted in the outcomes of the application of the STOPP/START tools. The most common instance of PIM, identified by STOPP, was 'Any drug prescribed without an evidence-based clinical indication'; the most common instance at all three data collection timepoints (baseline, 6-months and 9-months post initial medication review or equivalent). The drop of PIM from baseline (37 instances) to 9-months post initial medication review (18 instances) is positive, however, a GP practice did withdraw after baseline data collection impacting the findings. The number of instances of PPO at baseline was 27,

compared to 21 at 9-months post initial medication review or equivalent. Similar to PIM, the withdrawal of a GP practice and the accompanying GP record data for seven patients will have had an impact on this. The most common instance of PPO was 'Pneumococcal vaccine at least once after age 65 according to national guidelines'. It is important to note that many older people will receive this vaccine in their community pharmacy and not via their GP. It is not common practice for the pharmacy to inform the patients GP that they have received the vaccine. Due to GP data records, it is possible that some patients may have wrongly been identified as having not received the pneumococcal vaccine. This is important to remember when applying STOPP/START in a definitive RCT.

### *Quality of life*

As part of understanding the feasibility of the PolyPrime study, patients completed two questionnaires to assess their quality of life – the EQ-5D-5L (Herdman *et al.* 2011) and the MRB-QoL (Mohammed *et al.* 2018a) (core outcome: quality of life). The pilot cRCT presented in Chapter 4 was not designed to measure effect, however, potential trends can be identified from the two quality of life measures. Both the EQ-5D-5L and MRB-QoL reported high rates of return, yet if the entire questionnaire was not completed, a score could not be calculated for either. At all three timepoints, more completed EQ-5D-5Ls were returned compared to MRB-QoL. This is possibly due to the number of items on each questionnaire with the EQ-5D-5L containing a total of six items [five statements on their health and one self-rated scale (EuroQol Research Foundation Group 2019)] compared to the 31 items on the MRB-QoL (Mohammed *et al.* 2018a). MRB-QoL scores were not able to be calculated for six patients at baseline and 6-months post initial medication review or equivalent, and for five patients at 9-months due to incomplete questionnaires. There was no clear pattern on items not scored on the returned MRB-QoL, with the item most not completed varying at the three timepoints. However, a selection of sub-scales to use in a future definitive RCT may have merit and may result in an increase in the level of completed questionnaires returned. It may also be of use to develop a method of calculating MRB-QoL score for patients who returned an incomplete questionnaire; this would require collaboration with the MRB-QoL research team (Mohammed *et al.* 2018a).

### *Relevant policy changes*

During the course of the PolyPrime study, the Chronic Disease Management Programme was implemented in the RoI in 2019, after recruitment for the PolyPrime study had begun. To qualify for this programme, patients must have a medical or GP visit card as well as a diagnosis of asthma, cardiovascular disease (including heart attack/failure, irregular heartbeat, stroke),

chronic obstructive pulmonary disease or type 2 diabetes (Tandan *et al.* 2022). This programme involves two reviews within one year, with the patient seeing their GP and the practice nurse (if one is employed in the GP practice). Patients receive a written care plan after each visit with steps they can complete to improve their management of their condition(s). The aim of this programme is to help patients recognise if their condition is deteriorating, how they can manage a deteriorating condition and to support the patient to remain living in the community for as long as possible (O'Reilly and Hanlon 2017). As the Chronic Disease Management Programme is relatively new in the RoI, there is no evidence on its effectiveness, nor summary findings on its perceived usefulness for both patients and the healthcare professionals involved. However, this programme is likely to have an impact on quality of medications prescribed and thus may reduce the need for the PolyPrime intervention to be developed further for use in GP practice.

#### *Progression to a definitive randomised controlled trial*

The cRCT of the PolyPrime intervention, presented in Chapter 4 alongside the process evaluation, reported the findings from the RoI jurisdiction. The recruitment goal of six GP practices was met, meeting 'Go' on the progression criteria. However, the presence of Covid-19 resulted in the withdrawal of two GP practices, resulting in GP practice retention meeting 'Amend' on progression criteria. Patient recruitment and patient retention progression criteria both met 'Amend' 21 patients remaining in the study at 9-month data collection point. The PolyPrime study was found to be acceptable by GPs, GP practice staff and patients who received the intervention, yet due to certain progression criteria not being met, further modifications are required to meet patient recruitment targets and ensure a high level of patient retention. It may also be useful to assess the level of patient burden in participating, and decrease this if necessary. Some research has been conducted on how to improve patient recruitment and retention in trials which might be of use if progressing the PolyPrime intervention to a definitive RCT (Bower *et al.* 2014, Duncan *et al.* 2020, Gillies *et al.* 2021). Patient recruitment was not continued until the target of 10 patients per GP practice had been met due to Covid-19. Discussions with the trial steering committee noted that whilst it is important to acknowledge the impact COVID-19 has had, it cannot be assumed that patient retention is solely down to COVID-19 and modifications here are required before progressing to a definitive pilot RCT. This emphasises the importance of conducting pilot trials before implementing an intervention in a definitive RCT. An internal pilot study may be required as part of a future definitive RCT. This would be used to assess the effectiveness of amendment to patient recruitment strategy, and patient retention. Key findings of this pilot cRCT also included the feasibility of patient reported questionnaires which were completed by most participants at each timepoint, indicating that it

is feasible for them to be included in a definitive pilot RCT. Whilst the PolyPrime intervention has potential to be useful, some modifications are required such as patient recruitment and given recent changes in the healthcare system in RoI, the future of the PolyPrime study may be more appropriate in a different primary healthcare setting, such as the community pharmacy.

#### **6.1.4 Community pharmacist and their role in managing appropriate polypharmacy**

Community pharmacists in other countries have more responsibility and greater roles in the management of prescribing, as presented in Chapter 5 section 5.1, than the pharmacists practising in the RoI. It is widely acknowledged that pressure on GPs is increasing, because of the aging population and workforce shortages in general practice (McCombe *et al.* 2019). Given that pharmacists are specialists in medicines and are readily accessible to patients, pharmacists in the RoI could potentially have a greater role in managing appropriate polypharmacy. Strategies to enhance role of the community pharmacist in the management of appropriate polypharmacy in older adults were discussed with community pharmacists, using the TDF to identify barriers and facilitators to each strategy (Chapter 5). Pharmacists suggested that they could provide additional support to patients to manage polypharmacy if they had (i) access to patient records (ii) if communication with prescribers was enhanced and (iii) if they undertook medication reviews. Common barriers were noted across all the strategies and included lack of resources, lack of available time, staff shortages and potential cost to the pharmacy (TDF: Environmental context and resources). Facilitators discussed included knowledge of the patient (TDF: Knowledge), benefits for patients (TDF: Beliefs about consequences) and payment for services (TDF: Motivation and goals). Indeed, it could be argued, that the strategies mentioned by the pharmacists are interdependent. In other words, if medication reviews were undertaken where pharmacists had access to patient records and an enhanced method of communicating with prescribers was in place, pharmacists would indeed be able to provide more support to patients and prescribers in the management of appropriate polypharmacy. These ideas form the basis of a future research programme, where a behaviour change intervention will be developed targeting community pharmacists. Interestingly, the barriers and facilitators noted in the current study were identified in other TDF based studies involving expansion of community pharmacists' roles in deprescribing, antimicrobial stewardship and in chronic pain management (Jones *et al.* 2018, Gerlach *et al.* 2020, Alenezi *et al.* 2022) This suggests that a strategic view of community pharmacy practice by policy makers to address the commonly identified barriers and target the commonly identified facilitators could see enhanced services being developed more quickly and efficiently on a large scale.

### **6.1.5 The impact of COVID-19**

Due to the Covid-19 pandemic, GPs and patients in the intervention arm of the PolyPrime study were provided with the option to conduct medication reviews either in-person or via telephone. Previous research has found that medication reviews conducted via telephone are accepted by patients (Hanjani *et al.* 2020a) and show evidence of improving clinical and cost outcomes (Hanjani *et al.* 2020b). Due to the changing nature of general practice, brought on by the Covid-19 pandemic, the PolyPrime trial has shown the acceptability from both patients and GPs of conducting medication reviews via telephone. It is acknowledged, however, that the number of participants receiving the intervention was small and these findings may differ if conducted on a larger scale. It is likely COVID-19, and the study suspension as a result of the pandemic, impacted on GP retention and both patient recruitment and retention. Other clinical trials also reported similar issues in recruitment and retention of participants arising from COVID-19 (Thorton 2020, Shiely *et al.* 2021).

Recruitment of community pharmacists to participate in an interview was conducted via Twitter. This was a novel approach for the research team and, as noted in Chapter 5 section 5.5.6, recruitment to the study was slow. Lack of time has been documented as one reason for community pharmacists not taking part in research (Peterson *et al.* 2009, Crilly *et al.* 2017). During COVID-19, community pharmacists were declared to be an essential service and therefore had to adapt their pharmacy and working schedules to ensure safety of staff and patients (Hayden and Parkin 2020). This resulted in many working longer hours whilst dealing with personal issues, perhaps such as lack of childcare, leading to stress and burnout (McNicholas *et al.* 2020). The increased pressures on community pharmacists during COVID-19 to continue to provide the high level of care patients are used to could have attributed to a lack of availability to participate in a one-hour interview.

### **6.1.6 Patient and public involvement**

Patient and public involvement, also known as PPI, aims to improve the quality and appropriateness of research and to ensure it meets the needs of those who may benefit from the findings and study outputs (Carroll *et al.* 2021). It is accepted that PPI relates to activity that is done 'with' or 'by' patients or members of the public rather than 'about' or 'for' them (INVOLVE 2012, Ocloo *et al.* 2021). PPI can take many forms including, but not limited to, aiding researchers to develop and define their research question, reviewing funding applications, offering advice as members of steering group, collaborating on the development of dissemination materials (Jackson *et al.* 2020). In order to better understand how to incorporate

PPI in this thesis, the researcher completed training in PPI 'Involving the public in the design and conduct of research: building research partnerships' (Appendix 6.1). Two members of the PolyPrime management team, which met monthly, were PPI representatives. These representatives were older males, who lived in the community and were prescribed polypharmacy. Their main task in relation to the work in this thesis, was to review patient facing documents before submission to ethics for approval, to ensure that the documents were user friendly, and that the language used was understandable. This included the invitation letter, information leaflet, consent form, and all patient reported questionnaires. An example of their contribution was the inclusion of the word 'chemist' in the patient reported health service use questionnaire (Appendix 4.10) as this was likely the common term used by the cohort, as opposed to pharmacist. The PPI members for the PolyPrime intervention were also involved in developing the funding application and research protocol.

PPI was not utilised in the systematic review as the question was related to the PolyPrime intervention and theoretically derived interventions. As such, involving PPI in a methodology focused systematic review was collectively agreed by the supervision team to be unnecessary and would only be tokenistic in nature. The 'public' component of PPI was not involved in the systematic review either. This could have included non-academic GPs, or other primary healthcare professionals for example. The project was discussed openly with academic GPs on the wider PolyPrime team, who were supportive of the approach. It is possible that non-academic GPs may have had additional recommendations. Whilst there is no evidence of association with PPI in a systematic review and the impact or benefit of a systematic review (Pollock *et al.* 2021), there are other circumstances where PPI can make a valuable contribution to a systematic review. These would be circumstances where the research question does not include a complex exploration of theoretically underpinned interventions. In some appropriate circumstances, PPI representatives could be involved in designing a protocol, identifying articles which fit the inclusion criteria for the review and also to support the interpretation of findings. The ACTIVE framework (Pollock *et al.* 2021) guides researchers in involving PPI at various stages of a systematic review. This framework was published after the systematic review research question in this thesis was developed.

PPI representatives were not involved in chapters 3 and 5 of this thesis. A purpose of PPI is to provide a meaningful contribution to the research from an end user's perspective (Hardavella *et al.* 2015). With this in mind, the end user for the work described in chapters 3 and 5 would be patients, however the focus of the research was on the healthcare professional, GPs and community pharmacists respectively, and a knowledge of the internal structure of the

healthcare setting was required in order to achieve the aim of each study. A follow-on, separate but linked study involving only patients is planned by the research team to allow for overall triangulation of findings. Findings from the interview study with community pharmacists will be presented to patients in order to get their opinions of the findings. PPI will be involved in the development of this study protocol. PPI involvement would increase the possibility that the research will be meaningful, have a potential impact on policy and improve the quality of research (Hoddinott *et al.* 2018).



## **6.2 Recommendations for future research**

### **6.2.1 What next for the PolyPrime intervention?**

As three of the five progression criteria met 'Amend' in the Stop Amend Go criteria, the PolyPrime intervention requires further amendment before progression to a definitive cRCT. The criterion of GP practice retention, patient recruitment and patient retention will have to be addressed (discussed above). It is entirely possible that COVID-19 was responsible for shortcomings in these areas, however, further discussions within the team and with the trial steering committee will be required prior to progression. Future trials and recruitment to trials should be planned for with the knowledge that should COVID-19 re-surge, or indeed another pandemic occur, recruitment could be impacted. Aspects of recruitment and retention could be altered and tested in an internal pilot study.

Changes to the healthcare system in NI (addition of practice-based pharmacists) and the RoI (introduction of the Chronic Disease Management Programme) will need consideration. This is discussed below in section 6.3.2. Essentially, the PolyPrime intervention could be amended to be pharmacist-led, whether the pharmacist is practice-based or community-based.

### **6.2.2 Methodological aspects of behaviour change intervention studies**

#### *The use of theory in intervention development*

Whilst this thesis has not provided evidence for effectiveness of theoretically derived interventions to improve the management of appropriate polypharmacy, following established frameworks such as the MRC framework for complex interventions (Craig *et al.* 2008, Skivington *et al.* 2021), is a methodologically robust approach to intervention development and has a greater potential for success than a less robust approach (Skivington *et al.* 2021). It has been noted in the scientific literature that a theoretical approach to intervention design is useful as it is likely to lead to the intervention being effective (Craig *et al.* 2008, de Silva *et al.* 2014). Incorporating theory into intervention development is challenging, particularly to a researcher without a psychology background. However, this challenge has been well recognised in the literature and is the reason why health psychologists developed the TDF and other frameworks that distil complex psychological theories into user friendly and stepwise approaches. The TDF [Chapter 1, section 1.8 (Michie *et al.* 2005, Cane *et al.* 2012)] is a useful theoretical framework to include in intervention development as it incorporates 33 theories of behaviour and behaviour change into one user-friendly conceptual aid. The Behaviour Change Wheel (Chapter 2, section 2.5.4) can be easily implemented in the intervention design process and provides a

comprehensive eight step approach to intervention development (Michie *et al.* 2011). As discussed in Chapter 2, section 2.5.1, selecting the optimal theory to guide intervention development can be challenging. Due to the lack of guidelines on how to select the most appropriate theory, researchers have opted to publish their recommendations, such as Lynch *et al.* (2018) who encourage intervention developers to ask five questions: 1) Are you looking at individuals, groups or wider settings? 2) Are you planning, conducting, or evaluating? 3) What is your aim and what do you need to understand? 4) What data will be available to use? 5) What resources do you have to support you? However, the intervention developer would require knowledge of theory which may be discouraging. In this instance, a theoretical framework, such as the TDF may be more suited to the intervention developers. In future behaviour change development studies, it is important to continue to include theory until definitive evidence for or against this approach is available.

#### *Inclusion of a refinement phase*

Chapter 3 presented the refinement phase of the PolyPrime intervention. Recruitment targets were met in the defined timeline and the intervention was well received by GPs. The refinement study resulted in the addition of prescribing and medication review information for GPs, making the educational component stronger and more useful in the pilot cRCT. Refinement of an intervention is recommended by the MRC framework in developing and evaluating complex interventions and is discussed as part of the feasibility phase (Skivington *et al.* 2021). The feasibility study of the PolyPrime intervention did not result in any refinements (Cadogan *et al.* 2018), however, as the intervention was not developed in the RoI a refinement study was required. This thesis has shown the merits of conducting a refinement phase when the intervention being tested was developed in a different healthcare jurisdiction or indeed targeting a different healthcare professional group. It would also be important to undertake a refinement phase if there was a time-lapse between intervention development and its testing, or if significant healthcare policy changes that might impact on the intervention delivery were implemented in the healthcare jurisdiction where the intervention is being tested.

#### *Involvement of control arm practices during a process evaluation*

It is not common practice to include participants allocated to the control arm in a process evaluation, notably because they did not receive the intervention. However, there are aspects of a study that participants allocated to the control arm can still provide useful feedback on. These include the recruitment process and any paperwork completed. In the context of the PolyPrime study, this involved feedback on receiving a recruitment pack which included the

study questionnaires (EQ-5D-5L, MRB-QoL and the health service use questionnaires) and receiving and completing the questionnaires at three timepoints. As a result of the small number of participants remaining in the PolyPrime study, only 10 patients remained from the GP practices allocated to the intervention arm with only 6 of these 10 returning feedback questionnaires. Whilst the recruitment process and paperwork were well received by the patients who received the intervention, it cannot be assumed that patients who were allocated to the control arm would have provided the same feedback. Including a control arm receiving usual care is important to establish the efficacy of the intervention treatment (Karlsson and Bergmark 2015). Having activities between both intervention and control arm as equal as possible, such as the length of patient involvement, engagement with research team members (e.g. data collectors) can assist in ensuring the same level of engagement and as such improve the credibility of the study (Tock *et al.* 2022). Therefore, patients allocated to the control arm can provide useful feedback information about the study procedures and should be considered for inclusion in study feedback.

#### *Recruitment of healthcare professionals via social media*

Chapter 5 presented a semi-structured interview study undertaken with community pharmacists. Recruitment was planned to take place using social media alone, via an advertisement on Twitter, because social media has been acknowledged as a useful and promising advertising channel to recruit participants for research (Gelinis *et al.* 2017). However, recruitment using Twitter alone was poor, and an amendment to the ethics application to allow for advertisement and recruitment in pharmacy newsletters was necessary. Our challenges in recruiting via social media alone have been experienced by others. Whilst recruitment via social media has been effective in some studies (Khatri *et al.* 2015), a systematic review of 30 studies reported that less than half of the included studies found social media recruitment to be the most effective method of recruitment (Topolovec-Vranic and Natarajan 2016). When planning recruitment via social media alone, it may also be useful to consider advice from those who found it effective (i.e. those who recruited via social media and met their recruitment targets) and guidance in the literature. For example, Arigo *et al.* (2018) have provided four considerations: i) identify the platform most relevant to the target population, ii) be selective with information presented, iii) include the name of sites frequented by the target population, and iv) use relevant hashtags for the advertisement to gain traction. These four recommendations were followed to recruit community pharmacists: responses to Arigo *et al.* (2018) recommendations are i) Twitter was found to be the common social media platform in healthcare (Chen and Wang 2021, Yeung *et al.* 2021), ii) study advertisements were reviewed

by the research team and care was taken to ensure only basic information was provided, iii) important organisations in relation to community pharmacy in the RoI, such as the Irish Institute of Pharmacy were asked to retweet the study advertisement (see Appendix 5.2), and lastly, iv) relevant hashtags relating to research and polypharmacy were added to the post.

In the qualitative study presented in chapter 5, the recruitment of 15 participants could potentially have been met had there not been a timeline restriction, as there was in this study (in this case 12 weeks). Increasing the time for recruitment might ensure more participants are recruited successfully. From experience in this study, it is also recommended that several approaches to recruitment be considered, i.e. using more than one social media channel, recruiting via professional newsletters and mailing lists for example.

## **6.3 Implications for policy and practice**

### **6.3.1 Expanding the scope of the PolyPrime intervention**

The PolyPrime intervention was piloted in the border counties of the RoI, perhaps limiting the evidence compared to if the trial was piloted in other counties such as Dublin, which would have a higher population, and afford a different type of GP practice to be recruited. Patient recruitment and retention of GP practices and patients will need to be addressed in a definitive pilot study. These minor concerns of the three criteria meeting 'Amend' resulting the Stop Amend Go criteria should be addressed before implementing the PolyPrime intervention in a definitive RCT, perhaps in an internal pilot to confirm effectiveness. Possible amendments for patient recruitment can be taken from findings from the process evaluation, such as including an element of face-to-face with the research team, which may also lead to improved retention rates of patients.

There is the potential to pilot the study in the community pharmacy setting. Community pharmacists are eager to expand their role and one idea to help them do this, specifically in their role in managing appropriate polypharmacy in older adults, is to conduct medication reviews. The PolyPrime intervention was well received by community pharmacists interviewed in Chapter 5, however, some amendments are required to make it community pharmacist focused, as opposed to GP focused. Currently, research is ongoing to integrate clinical pharmacists within general practice in the RoI (Croke *et al.* 2021) with a non-randomised trial showing it has the possibility to improve prescribing in primary care (Cardwell *et al.* 2020). In time, there might be an opportunity to adapt the PolyPrime intervention for practice-based pharmacists to conduct medication reviews with older adults to improve appropriate polypharmacy.

As it stands, pharmacists will continue to work in the community pharmacy and therefore future funding could seek to amend the PolyPrime intervention and test it in a pilot RCT in community pharmacy in the RoI. This could lead to the both the role of the community pharmacist expanding as well as the introduction of medication reviews conducted by community pharmacists. Given the implementation of the Chronic Disease Management Programme, the PolyPrime trial could likely be of more use if amended to be piloted for use in community pharmacies.

### **6.3.2 Healthcare research conducted in Northern Ireland and the Republic of Ireland**

Despite NI and the RoI operating very different healthcare systems (as described in Chapter 3, section 3.1.3), evidence suggests that prescribing patterns between the two jurisdictions are

comparable (Bradley *et al.* 2012a, Bradley *et al.* 2014). Developments in the healthcare system in NI, with the implementation of practice-based pharmacists since the conception of the PolyPrime study in 2015 (Cadogan *et al.* 2015, Cadogan *et al.* 2016) and the recent Chronic Disease Management Programme (discussed above) in the RoI, have increased the differences between the two healthcare systems. The PolyPrime intervention may be more suited to being led by practice-based pharmacists in the NI, with a comparison to a GP-led medication review in the RoI. Practice-based pharmacists in NI are well established with their role incorporating medication reconciliation, medication reviews, clinical audits, repeat prescribing, and educating and counselling patients on their medication (Ibrahim *et al.* 2022). As many practice-based pharmacists conduct medication reviews with patients which has shown to reduce inappropriate prescribing (Syafhan *et al.* 2021), they will need to be considered in any adaptations to the PolyPrime intervention. The Chronic Disease Management Programme in the RoI may affect conducting medication review research as part of the programme involves receiving a medication review twice yearly from the patients GP. The Chronic Disease Management Programme only accepts patients with certain conditions (see above), so if progressing the PolyPrime intervention is to be delivered in the GP practice setting, patients not included in the Chronic Disease Management Programme may be an additional inclusion criterion to consider.

### **6.3.3 Enhancing the role of the community pharmacist in the Republic of Ireland**

Community pharmacists globally have a wider role as part of the healthcare team compared to community pharmacists in the RoI. For example, community pharmacists in Canada can renew prescriptions initiated by GPs (Tannenbaum and Tsuyuki 2013), and in NI they have the opportunity to train as independent prescribers and work as a pharmacist in general practice (Bostock 2019). However, the role of the community pharmacist in the RoI focuses on traditional roles of dispensing, clinical checking, responding to minor ailments and providing some additional services such as the flu vaccine. The findings presented in Chapter 5 show that community pharmacists in the RoI would welcome the expansion of their role, particularly in relation to enhancing their management of appropriate polypharmacy in older adults. The role can be enhanced through development of procedures to allow community pharmacists to conduct medication reviews with findings passed on to the prescriber, an official communication system with prescribers which could enable prescription queries to be dealt with in a timely manner, and having access to patient records could help the community pharmacist determine if a medicine is appropriate or not. These role enhancing strategies have been implemented, or have been tested, in various other countries and have been received positively. Given the expansion of the role of community pharmacists in other countries, and

the ideas generated by participants in Chapter 5 to enhance their role are not novel to the profession, it is possible to enhance the role of the community pharmacist in managing appropriate polypharmacy in older adults. The HSE and pharmacy unions should support the enhancement of the community pharmacist role in managing appropriate polypharmacy and should strive to deliver the necessary funding in order for community pharmacy to continue dispensing medications but also to provide additional services, such as the medication review.

## 6.4 General conclusion

The need to improve appropriate polypharmacy for older patients is widely acknowledged and is due to the aging population and the increased prevalence of multimorbidity in older patients. The research presented in this thesis aimed to add to the research literature on theoretically derived interventions to improve appropriate polypharmacy in older patients in primary care, specifically the PolyPrime intervention, which was initially developed by some members of the current research team in Northern Ireland.

Initially, a systematic review was conducted to establish the extent to which theory is used in interventions to improve appropriate prescribing in older adults in primary care. The outcome of this systematic review showed that a small number of interventions used theory in their development, and consequently the effectiveness of theoretically derived interventions to improve appropriate polypharmacy in older adults in primary care could not be established.

One of the studies identified in this systematic review was the PolyPrime intervention, which used the TDF as its theoretical basis and incorporates behaviour change techniques as the active ingredients of the intervention. Within the current programme of research, the PolyPrime intervention underwent a refinement phase, in line with recommendations from the MRC. This was undertaken by interviewing GPs in the RoI prior to implementation in a pilot cRCT. Minor amendments resulted from this refinement phase, mostly the inclusion of educational information such as prescribing guidelines and validated assessment tools as additional reference materials for GPs. The refined intervention was then tested in a pilot cRCT. Findings from the pilot cRCT and the process evaluation of the pilot cRCT demonstrated that the intervention was acceptable to patients, GPs and practice staff. It also demonstrated that it was possible to collect sufficient data to measure the primary outcome, medication appropriateness, using a validated screening tool. It also demonstrated that other patient outcomes, such as quality of life, as measured by EQ-5D-5L and MRB-QoL could be measured and reported on. The pilot cRCT was undertaken while COVID-19 broke, was suspended and then restarted. This had an impact on important study parameters such as patient and GP recruitment. Despite this, the study progressed in line with our pre-specified progression criteria.

The process evaluation phase also demonstrated that it would be possible for the PolyPrime intervention to progress to a definitive RCT, with consideration given to some modifications, such as patient recruitment and the development of a process to ensure that recruited patients receive medication reviews from the GP with whom they are registered.



The final research chapter in this thesis presented a TDF-based qualitative study involving community pharmacists to determine their perceptions on what they could do to enhance the appropriate management of polypharmacy in primary care. Suggestions included undertaking medication reviews, having more access to patient records and an enhanced mode of communication with prescribers. Numerous barriers and facilitators were identified under the domains of the TDF. These could be mapped to BCTs to develop a behaviour change intervention rooted in community pharmacy in the future. The PolyPrime intervention was discussed during interview with the participants. It was well received and the potential for it to be amended for a community pharmacy focus was endorsed.

Further research should establish the effectiveness of the PolyPrime intervention on improving appropriate polypharmacy via a definitive RCT. Additionally, sufficient time should be dedicated to developing community pharmacy focused behaviour change interventions to improve the use of appropriate polypharmacy, building on data presented in this thesis.

## **References**

- Aarons, G.A., Green, A.E., Palinkas, L.A., *et al.* 2012. Dynamic adaptation process to implement an evidence-based child maltreatment intervention. *Implementation Science*, 7, pp:32.
- Abuzour, A.S., Lewis, P.J., Tully, M.P. 2018. Practice makes perfect: a systematic review of the expertise development of pharmacist and nurse independent prescribers in the United Kingdom. *Research in Social and Administrative Pharmacy*, 14, pp:6-17. Doi: 10.1016/j.sapharm.2017.02.002
- Agomo, C.O., Ogunleye, J., Portlock, J., *et al.* 2020. Enhancing the public health role of community pharmacists – a qualitative research utilizing the theoretical domains framework. *Innovations in Pharmacy*, 11, pp:3. Doi: 10.24926/iip.v11i4.3393
- Airagnes, G., Pelissolo, A., Lavallée, M., *et al.* 2016. Benzodiazepine misuse in the elderly: risk factors, consequences, and management. *Current Psychiatry Reports*, 18, pp:89. Doi:10.1007/s11920-016-0727-9.
- Ajzen, I. 1991. The theory of planned behaviour. *Organizational behaviour and human decision processes*, 50, pp:179-221. Doi: 10.1016/0749-5978(91)90020-T
- Alageel, S., Gulliford, M.C., McDermott, L., *et al.* 2017. Multiple health behaviour change interventions for primary prevention of cardiovascular diseases in primary care: systematic review and meta-analysis. *BMJ Open*, 7, pp:e015375. Doi: 10.1136/bmjopen-2016-015375
- Alenezi, A., Yahyouche, A., Paudyal, V. 2022. Roles, barriers and behavioural determinants related to community pharmacists' involvement in optimizing opioid therapy for chronic pain: a qualitative study. *International Journal of Clinical Pharmacy*, 44, pp:180-191. Doi: 10.1007/s11096-021-01331-1
- Alhusein, N., Scott, J., Neale, J., *et al.* 2021. Community pharmacists' views on providing a reproductive health service to women receiving opioid substitution treatment: a qualitative study using the TDF and COM-B. *Exploratory Research in Clinical and Social Pharmacy*, 4, pp:100071. Doi: 10.1016/j.rcsop.2021.100071
- Allin, S., Martin, E., Rudoler, D., *et al.* 2021. Comparing public policies impacting prescribing and medication management in primary care in two Canadian provinces. *Health Policy*, 125, pp:1121-30. Doi: 10.1016/j.healthpol.2021.06.002
- All Wales Medicines Strategy Group. 2014. *Polypharmacy: guidance for prescribing*. Available at: <https://awmsg.nhs.wales/files/guidelines-and-pils/polypharmacy-guidance-for-prescribing-pdf/> accessed 11/03/2022.

- Almirall, J., Fortin, M., *et al.* 2013. The coexistence of terms to describe the presence of multiple concurrent diseases. *Journal of Comorbidity*, 3, pp:4-9. Doi: 10.15256/joc.2013.3.22.
- Alshehri, A.A., Cheema, E., Yahyouche, A., *et al.* 2021. Evaluating the role and integration of general practice pharmacists in England: a cross-sectional study. *International Journal of Clinical Pharmacy*, 43, pp:1609-18. Doi: 10.1007/s11096-021-01291-6
- Al Washali, A.Y.A., Kadri, H., Ismail, S., *et al.* 2018. Systematic review on effectiveness of theory-based intervention on self-care behaviors among patients with type 2 diabetes. *Clinical Trials in Degenerative Diseases*, 3, pp:88-94. Doi: 10.41032542-3975.242955
- American Geriatrics Society, 2015. Updated Beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, 63, pp:2227-2246. Doi: 10.1111/jgs.13702.
- Andrade, C. 2021a. The inconvenient truth about convenience and purposive samples. *Indian Journal of Psychological Medicine*, 43:86-88. Doi: 10.1177/0253717620977000
- Andrade C. 2021b. A student's guide to the classification and operationalization of variables in the conceptualization and design of a clinical study: part 1. *Indian Journal of Psychological Medicine*, 43:177-179. Doi: 10.1177/0253717621994334
- Antwi, W.K., Reeves, P., Christine, F., *et al.* 2021. A qualitative description of how Ghanaian radiographers identify suspected child physical abuse. *Radiography*, 27, pp:1073-7. Doi: 10.1016/j.radi.2021.04.007.
- Arain, M., Campbell, M.J., Cooper, C.L., *et al.* 2010. What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Medical Research Methodology*, 10, pp:67.
- Arigo, D., Pagoto, S., Carter-Harris, L., *et al.* 2018. Using social media for health research: methodological and ethical considerations for recruitment and intervention delivery. *Digital Health*, 4, pp:1-15. Doi: 10.1177/2055207618771757
- Arnold DM, Burns KE, Adhikari NK *et al.* 2009. The design and interpretation of pilot trials in clinical research in critical care. *Critical Care Medicine*, 37, pp:S69-S74. Doi: 10.1097/CCM.0b013e3181920e33.
- Arnott, B., Rechackova, L., Errington, L., *et al.* 2014. Efficacy of behavioural interventions for transport behaviour change: systematic review, meta-analysis and intervention coding. *International Journal of Behavioural Nutrition and Physical Activity*. 11, pp:133. Doi:10.1186/s12966-014-0133-9.

- Asgari, S., Abbasi, M., Hamilton, K., *et al.* 2021. A theory-based intervention to promote medication adherence in patients with rheumatoid arthritis: a randomized controlled trial. *Clinical Rheumatology*, 40, pp:101-111. Doi: 10.1007/s10067-020-05224-y
- Atella, V., Piano Mortari, A., Kopinska, J., *et al.* 2019. Trends in age-related disease burden and healthcare utilization. *Aging Cell*, 18, pp:e12861. Doi:10.1111/acer.12861.
- Atkins, L., Francis, J., Islam, R., *et al.* 2017. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. *Implementation Science*, 12, pp:77. Doi:10.1186/s13012-017-0605-9.
- Atkinson, M.J., Kumar, R., Cappelleri, J.C., *et al.* 2005. Hierarchical construct validity of the Treatment Satisfaction Questionnaire for Medication (TSQM version II) among outpatient pharmacy consumers. *Value in Health*, 8, pp:S9-S24. Doi: 10.1111/j.1524-4733.2005.00066.x
- Atun, R., de Jongh, T., Secci, F., *et al.* 2010. Integration of targeted health interventions into health systems: a conceptual framework for analysis. *Health Policy and Planning*, 25, pp:104-111.
- Avery, A.J., Pringle, M., 2005. Extended prescribing by UK nurses and pharmacists: with more evidence and strict safeguards, it could benefit patients. *British Medical Journal*, 331, pp:1154. Doi: 10.1136/bmj.331.7526.1154
- Avery, K.N.L., Williamson, P.R., Gamble, C., *et al.* 2017. Informing efficient randomised controlled trials: exploration of challenges in developing progression criteria for internal pilot studies. *BMJ Open*, 7, pp:e013537. Doi: 10.1136/bmjopen-2016-013537.
- Avni, T., Shiver-Ofer S., Leibovici, L., *et al.* 2015. Participation of elderly adults in randomized controlled trials addressing antibiotic treatment of pneumonia. *Journal of the American Geriatrics Society*, 63, pp:233-243. Doi: 10.1111/jgs.13250
- Awad, A., Alhadab, A., Albassam, A. 2020. Medication-related burden and medication adherence among geriatric patients in Kuwait: a cross-sectional study. *Frontiers in Pharmacology*. Doi: 10.3389/fphar.2020.01296
- Axén, I., Björk Brämberg, E., Galaasen Bakken, A., *et al.* 2021. Recruiting in intervention studies: challenges and solutions. *BMJ Open*, 11, pp:e044702. Doi: 10.1136/bmjopen-2020-044702

Bailie, J., Cody, A. No date. *INTERREG VA Programme – An update for the R&D Strategic Advisory Group*. Available at: <https://research.hscni.net/cross-border-healthcare-intervention-trials-ireland-network-chitin-0> accessed 01/08/2022.

Balbale, S.N., Hill, J.N., Guihan, M., *et al.* 2015. Evaluating implementation of methicillin-resistant *Staphylococcus aureus* (MRSA) prevention guidelines in spinal cord injury centers using the PARIHS framework: a mixed methods study. *Implementation Science*, 10, pp:130. Doi: 10.1186/s13012-015-0318-x.

Bandura, A., 2008. *Social foundations of thought and action: A social cognitive theory*. Englewood Cliffs, NJ: Prentice-Hall.

Bannan, D.F., Aseeri, M.A., AlAzmi, A. *et al.* 2019. Understanding the causes of prescribing errors from a behavioural perspective. *Research in Social and Administrative Pharmacy*, 15, pp:546-57. Doi: 10.1016/j.sapharm.2018.07.007

Bannan, D.F., Aseeri, M.A., AlAzmi, A. *et al.* 2021. Prescriber behaviours that could be targeted for change: an analysis of behaviours demonstrated during prescription writing in children. *Research in Social and Administrative Pharmacy*, 17, pp:1737-49. Doi: 10.016/j.sapharm.2021.01.007

Barber, N., Safdar, A., Franklin, B.D., 2005. Can human error theory explain non-adherence? *Pharmacy World & Science*. 27, pp:300-304. Doi: 10.1007/s11096-005-0355-7.

Barker, I., Lloyd, T., Steventon, A. 2016a. Effect of a national requirement to introduce named accountable general practitioners for patients aged 75 or older in England: regression discontinuity analysis of general practice utilization and continuity of care. *BMJ Open*, 6, pp:e011422. Doi: 10.1136/bmjopen-2016-011422

Barker, P.M., Reid, A., Schall, M.W. 2016b. A framework for scaling up health interventions: lessons from large-scale improvement initiatives in Africa. *Implementation Science*, 11, pp:12. Doi: 10.1186/s10312-016-0374-x

Barnett, K., McCowan, C., Evans, J.M., *et al.* 2011. Prevalence and outcomes of use of potentially inappropriate medicines in older people: cohort study stratified by residence in nursing home or in the community. *BMJ Quality & Safety*, 20, pp:275-281. Doi: 10.1136/bmjqs.2009.039818.

- Barnett, K., Mercer, S.W., Norbury, M., *et al.* 2012. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *The Lancet*, 380, pp:37-43. Doi: 10.1016/S0140-6736(12)60210-2
- Barry, H.E., Hughes, C.M., 2019. Economical, clinical and humanistic outcomes, in: Costa, A., Alvarez Risco, A., van Mil, F. (eds). *The Pharmacist Guide to Implementing Pharmaceutical Care*. Springer.
- Barry, H.E., Bedford, L.E., McGrattan, M., *et al.* 2020. Improving medicines management for people with dementia in primary care: a qualitative study of healthcare professionals to develop a theory-informed intervention. *BMC Health Services Research*, 20, pp:120. Doi: 10.1186/s12913-020-4971-7.
- Bartlett, Y.K., Kenning, C., Crosland, J., *et al.* 2021. Understanding acceptability in the context of text messages to encourage medication adherence in people with type 2 diabetes. *BMC Health Services Research*, 21:608. Doi: 10.1186/s12913-021-0663-2
- Bartholomew, L.K., Mullen, P.D. 2011. Five roles for using theory and evidence in the design and testing of behaviour change interventions. *Journal of Public Health Dentistry*, 71, pp:S20-S33. Doi:10.1111/j.1752-7325.2011.00223.x.
- Bartlam, B., Cromie, P., Lally, F., *et al.* 2012. The views of older people and carers on participation in clinical trials: the PREDICT study. *Clinical Investigation*, 2, pp:327-336. Doi: 10.4155/CLI.12.4
- Baruth, J.M., Gentry, M.T., Rummans, T.A., *et al.* 2020. Polypharmacy in older adults: the role of the multidisciplinary team. *Hospital Practice*, 48, pp:56-62. Doi: 10.1080/21548331.2019.1706995
- Bele, S., Cassidy, C., Curran, J., *et al.* 2019. Barriers and enablers to implementing a virtual tertiary-regional Telemedicine Rounding And Consultation (TRAC) model of inpatient pediatric care using the Theoretical domains framework (TDF) approach: a study protocol. *BMC Health Services Research*, 19, pp:29. Doi: 10.1186/s12913-018-3859-2.
- Bele, S., Cassidy, C., Curran, J., *et al.* 2021. Using the theoretical domains framework to identify barriers and enablers to implementing a virtual Tertiary-Regional Telemedicine Rounding and Consultation for Kids (TRaC-K) model: qualitative study. *Journal of Medical Internet Research*, 23, pp:e28610. Doi: 10.2196/28610.

- Belkin, G.S., Unützer, J., Kessler, R.C., *et al.* 2011. Scaling up for the “bottom billion”: “5x5” implementation of community mental health care in low-income regions. *Psychiatric Services*, 62:1494-1502. Doi: 10.1176/appi.ps.000012011
- Bell, M.L., Whitehead, A.L., Julious, S.A. 2018. Guidance for using pilot studies to inform the design of intervention trials with continuous outcomes. *Clinical Epidemiology*, 10, pp:153-157. Doi: 10.2147/CLEP.S146397
- Benyamin, R., Trescot, A.M., Datta, S., *et al.* 2008. Opioid complications and side effects. *Pain Physician Opioid*, 11, pp:S105-S120.
- Bergqvist, M., Ulfvarson, J., Andersén Karlsson, E. 2009. Nurse-led medication reviews and the quality of drug treatment of elderly hospitalized patients. *European Journal of Clinical Pharmacology*, 65, pp:1089-96. Doi: 10.1007/s00228-009-0728-2
- Berman, L., Kavalier, M., Gelana, B., *et al.* 2021. Utilizing the SEIPS model to guide hand hygiene interventions at a tertiary hospital in Ethiopia. *PLoS One*, 16, pp:e0258662. Doi: 10.1371/journal.pone.0258662.
- Bernard, H.R., 2002. *Research methods in anthropology: qualitative and quantitative approaches*. 3<sup>rd</sup> edn. California: Alta Mira Press.
- Berninger, N.M., Plasqui, G., Crutzen, R., *et al.* 2022. The effects of UPcomply on office workers’ sedentary behaviour, quality of life and psychosocial determinants: a stepped-wedge design. *International Journal of Behavioral Medicine*. Doi: 10.1007/s12529-022-10054-0
- Berry, S.D., Placide, S.G., Mostofsky, E., *et al.* 2016. Antipsychotic and benzodiazepine drug changes affect acute falls risk differently in the nursing home. *Journal of Gerontology: Series A*, 71, pp:273-278. Doi: 10.1093/Gerona/glv091.
- Bertilsson, E., Serhal, S., Emmerton, L., *et al.* 2021. Pharmacists experience of and perspectives about recruiting patients into a community pharmacy asthma service trial. *Research in Social & Administrative Pharmacy*, 17, pp:595-605. Doi: 10.1016/j.sapharm.2020.05.012
- Beuscart, J-B., Knol, W., Cullinan, S., *et al.* 2018. International core outcome set for clinical trials of medication review in multi-morbid older patients with polypharmacy. *BMC Medicine*, 16, pp:21. Doi: 10.1186/s12916-018-1007-9
- Bhadhuri, A., Kind, P., Salari, P., *et al.* 2020. Measurement properties of EQ-5D-3L and EQ-5D-5L in recording self-reported health status in older patients with substantial multimorbidity



and polypharmacy. *Health and Quality of Life Outcomes*, 29, pp:317. Doi: 10.1186/s12955-020-01564-0.

Bidwell S, Thompson L. 2015. GPs, community pharmacists and shifting professional boundaries. *New Zealand Medical Journal*, 128, pp:19-26.

Bilgin, A., Kesik, G., Ozdemir, L., *et al.* 2021. 'The body seems to have no life': The experiences and perceptions of fatigue among patients after COVID-19. *Journal of Clinical Nursing*, 0, pp:1-11. Doi: 10.1111/jocn.16153

Birken, S.A., Powell, B.J., Shea, C.M. *et al.* 2017. Criteria for selecting implementation science theories and frameworks: results from an international survey. *Implementation Science*, 12, pp:124. Doi:10.1186/s13012-017-0656-y

Bleijenberg, N., de Man-van Ginkel, J.M., Trappenburg, J.C.A., *et al.* 2018. Increasing value and reducing waste by optimizing the development of complex interventions: enriching the development phase of the Medical Research Council (MRC) Framework. *International Journal of Nursing Studies*, 79, pp:86-93. Doi: 10.1016/j.ijnurstu.2017.12.001

Blixen, C., Lema, I., Mbwambo, J., *et al.* 2020. Community perceptions of barriers to management of chronic psychotic disorders and knowledge and attitudes about long-acting injectable antipsychotic medication: qualitative study in Dar es Salaam, Tanzania. *BJPsycho Open*, 6, pp:e27. Doi: 10.1192/bjo.2020.4

Boeni, F., Spinatsch, E., Suter, K., *et al.* 2014. Effect of drug reminder packaging on medication adherence: a systematic review revealing research gaps. *Systematic Reviews*, 3, pp:29. Doi: 10.1186/2046-4053-3-29.

Boland, B., Guignard, B., Dalleur, O., *et al.* 2016. Application of STOPP/START and Beers criteria: compared analysis on identification and relevance of potentially inappropriate prescriptions. *European Geriatric Medicine*, 7, pp:416-23. Doi: 10.1016/j.eurger.2016.03.010

Bokolo, A.J. 2021. Exploring the adoption of telemedicine and virtual software for care of outpatients during and after COVID-19 pandemic. *Irish Journal of Medical Science*, 190, pp:1-10. Doi: 10.1007/s11845-020-02299-z

Bonell, C., Oakley, A., Hargreaves, J., *et al.* 2006. Assessment of generalizability in trials of health interventions: suggested framework and systematic review. *BMJ*, 333, pp:346-349. Doi: 10.1136/bmj.333.7563.346.

- Borrelli, B., Sepinwall, D., Ernst, D., *et al.* 2005. A new tool to assess treatment fidelity and evaluation of treatment fidelity across 10 years of health behavior research. *Journal of Consulting and Clinical Psychology*, 73, pp:852-860. Doi: 10.1037/0022-006X.73.5.852
- Bostock N. 2019. Northern Ireland unveils £27m GP funding boost for 2019/20. *GP*. Available at: <https://www.gponline.com/northern-ireland-unveils-27m-gp-funding-boost-2019-20/article/1660263#:~:text=A%20total%20of%20%C2%A32.19,than%20%C2%A313m%20a%20year>. Accessed 25/10/2020 [checked 28/08/2022]
- Bousquet, J., Farrell, J., Crooks, G., *et al.* 2016. Scaling up strategies of the chronic respiratory disease programme of the European Innovation Partnership on Active and Healthy Ageing (Action Plan B3: Area 5). *Clinical and Translational Allergy*, 6, pp:29. Doi: 10.1186/s13601-016-0116-9
- Bower, P., Brueton, V., Gamble, C., *et al.* 2014. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. *Trials*, 15:399.
- Bowen, D.J., Kreuter, M., Spring, B., *et al.* 2009. How we design feasibility studies. *American Journal of Preventive Medicine*, 36, pp:452-457. Doi: 10.1016/j.amepre.2009.02.002
- Boyd, C.M., Vollenweider, D., Puhan, M.A. 2012. Informing evidence-based decision-making for patients with comorbidity: availability of necessary information in clinical trials for chronic diseases. *PLoS One*, 7, pp:e41601. Doi: 10.1371/journal.pone.0041601.
- Bradley, M.C., Fahey, T., Cahir, C., *et al.* 2012a. Potentially inappropriate prescribing and cost outcomes for older people: a cross-sectional study using the Northern Ireland Enhanced Prescribing Database. *European Journal of Clinical Pharmacology*, 68, pp:1425-33. Doi: 10.1007/s00228-012-1249-y.
- Bradley, E.H., Curry, L.A., Taylor, L.A., *et al.* 2012b. A model for scale-up of family health innovations in low-income and middle-income settings: a mixed methods study. *BMJ Open*, 2, pp:e000987. Doi: 10.1136/bmjopen-2012-000987
- Bradley, C. 2013. Repeat Prescribing. Dublin: ICGP. [online] Available at: [www.icgp.ie](http://www.icgp.ie) accessed 13/4/2020
- Bradley, M.C., Motterlini, N., Padmanabhan, S., *et al.* 2014. Potentially inappropriate prescribing among older people in the United Kingdom. *BMC Geriatrics*, 14, pp:72. Doi: 10.1186/1471-2318-14-72.

- Braun, V., Clarke, V., 2006. Using thematic analysis in psychology. *Qualitative Research in Psychology*, 3, pp:77-101. Doi: 10.1191/1478088706qp063oa
- Brennan, J., Bourke, M., O'Donnchadha, R., *et al.* 2019. What really matters to you? A study of public perspectives on General Practice in Ireland. *Irish Medical Journal*, 112, pp:854.
- Brick, M. 2011. The future of survey sampling. *Public Opinion Quarterly (Special Issue)*, 75, pp:872-888. Doi: 10.1093/poq/nfr045
- Brick, A., Walsh, B., Keegan, C., *et al.* 2020. COVID-19 and emergency department attendances in Irish public hospitals. *Economic and Social Research Institute (ESRI)*. [online] Available at: [https://www.esri.ie/system/files/publications/QEC2020SUM\\_SA\\_lyons.pdf](https://www.esri.ie/system/files/publications/QEC2020SUM_SA_lyons.pdf) accessed 02/01/2022
- Brierley, M.L., Chater, A.M., Smith, L.R. *et al.* 2019. The effectiveness of sedentary behaviour reduction workplace interventions on cardiometabolic risk markers: a systematic review. *Sports Medicine*, 49, pp:1739-1767. Doi: 10.1007/s40279-019-01168-9
- Briggs, A. 2000. Economic evaluation and clinical trials: size matters. *BMJ*, 321, pp:362-363. Doi: 10.1136/bmj.321.7273.1362
- British Geriatrics Society. 2019. *CGA in primary care settings: medication review*. Available at: <https://www.bgs.org.uk/resources/6-cga-in-primary-care-settings-medication-review#anchor-nav-no-tears-tool> accessed 29/10/20 Checked 26/08/2022
- Brown, J.D., Hutchison, L/C/, Li, C., *et al.* 2016. Predictive validity of the Beers and Screening Tool of Older Person's Potentially Inappropriate Prescriptions (STOPP) criteria to detect adverse drug events, hospitalizations, and emergency department visits in the United States. *Journal of the American Geriatrics Society*, 64, pp:22-30. Doi: 10.1111/jgs.13884.
- Brustad, M., Skeie, G., Braaten, T., *et al.* 2003. Comparison of telephone vs face-to-face interviews in the assessment of dietary intake by the 24 h recall EPIC SOFT program – the Norwegian calibration study. *European Journal of Clinical Nutrition*, 57, pp:107-13. Doi: 10.1038/sj.ejcn.1601498.
- Bryman, A. 2012. *Social Research Methods*. 4<sup>th</sup> edn. Oxford: Oxford University Press.
- Bryman, A. 2016. *Social Research Methods*. 5<sup>th</sup> edn. Oxford: Oxford University Press.

- Buchholz, I., Janssen, M.F., Kohlmann, T., *et al.* 2018. A systematic review of studies comparing the measurement properties of the three-level and five-level versions of the EQ-5D. *Pharmacoeconomics*, 36, pp:645-661. Doi: 10.1007/s40273-018-0642-5.
- Buda, V., Prelipcean, A., Cristescu, C., *et al.* 2021. Prescription habits related to chronic pathologies of elderly people in primary care in the western part of Romania: current practices, international recommendations and future perspectives regarding the overuse and misuse of medicines. *International Journal of Environmental Research and Public Health*, 18, pp:7043. Doi: 10.3390/ijerph18137043
- Budreviciute, A., Damiati, S., Sabir, D.K., *et al.* 2020. Management and prevention strategies for non-communicable diseases (NCDs) and their risk factors. *Frontiers in Public Health*, 8, pp:574111. Doi: 10.3389/fpubh.2020.574111
- Bulut, C., Kato, Y. 2020. Epidemiology of COVID-19. *Turkish Journal of Medical Sciences*, 50, pp:563-570. Doi: 10.3906/sag-2004-172
- Bunzli, S., O'Brien, P., Ayton, D., *et al.* 2019. Misconceptions and acceptance of evidence-based nonsurgical interventions for knee osteoarthritis: A qualitative study. *Clinical Orthopaedics and Related Research*, 477, pp:1975-83. Doi: 10.1097/CORR.0000000000000784.
- Burgess, C., Wright, A.J., Foster, A., *et al.* 2015. Influences on individuals' decisions to take up the offer of a health check: a qualitative study. *Health Expectations*, 18, pp:2437-48. Doi: 10.1111/hex.12212
- Burke, S., Barry, S., Siersbaek, R., *et al.* 2018. Sláintecare – a ten-year plan to achieve universal health care in Ireland. *Health Policy*, 122, pp:1278-1282. Doi: 10.1016/j.healthpol.2018.05.006
- Busetto, L., Wick, W., Gumbinger, C., 2020. How to use and assess qualitative research methods. *Neurological Research and Practice*, 2, pp:14. Doi: 10.1186/s42466-020-00059-z
- Bushardt, R.L., Massey, E.B., Simpson, T.W., *et al.* 2008. Polypharmacy: misleading, but manageable. *Clinical Interventions in Aging*, 3, pp:383-389. Doi: 10.2147/cia.s2468
- Buss, V.H., Shield, A., Kosari, S., *et al.* 2018. The impact of clinical services provided by community pharmacies on the Australian healthcare system: a review of the literature. *Journal of Pharmaceutical Policy and Practice*, 11, pp:22. Doi: 10.1186/s40545-018-0149-7
- Byrne, D., Cournane, S., Conway, R., *et al.* 2019. Socio-economic status and multioriginal morbidity – fact or fiction? *Acute Medicine Journal*, 18, pp:64-70. Doi: 10.52964/AMJA.0753

Cadogan, C.A., Ryan, C., Francis, J.J., *et al.* 2015. Improving appropriate polypharmacy for older people in primary care: selecting components of an evidence-based intervention to target prescribing and dispensing. *Implementation Science*, 10, pp:161. Doi: 10.1186/s13012-015-0349-3

Cadogan, C.A., Ryan, C., Francis, J.J., *et al.* 2016. Development of an intervention to improve appropriate polypharmacy in older people in primary care using a theory-based method. *BMC Health Services Research*, 16, pp:661. Doi:10.1186/s12913-016-1907-3

Cadogan, C.A., Ryan, C., Gormley, G.J., *et al.* 2018. A feasibility study of a theory-based intervention to improve appropriate polypharmacy for older people in primary care. *Pilot and Feasibility Studies*, 4, pp:23. Doi: 10.1186/s40814-017-0166-3

Cadogan, C.A., Murphy, M., McLean, S., *et al.* 2021. Development of criteria for identifying potentially inappropriate prescribing in older adults with cancer receiving palliative care (PIP-CPC). *Journal of Geriatric Oncology*, 12, pp:1193-1199. Doi: 10.1016/j.jgo.2021.06.003

Cahill, P. 2015. Prescribing for patients with multimorbidity: aiming to tailor to patient-set goals. *British Journal of General Practice*, 65, pp:114-5. Doi: 10.3399/bjgp15X683857

Cahir, C., Fahey, T., Teeling, M., *et al.* 2010. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. *British Journal of Clinical Pharmacology*, 69, pp:543-552. Doi: 10.1111/j.1365-2125.2010.03628.x

Campbell, M., Fitzpatrick, R., Haines, A., *et al.* 2000. Framework for design and evaluation of complex interventions to improve health. *BMJ*, 321, pp:694-696. Doi: 10.1136/bmj.321.7262.694

Campbell, N.C., Murray, E., Darbyshire, J., *et al.* 2007. Designing and evaluating complex interventions to improve health care. *BMJ*, 334, pp:455-9. Doi: 10.1136/bmj.39108.379965.BE

Campbell, K.A., Fergie, L., Haynes-Coleman, T., *et al.* 2018. Improving behavioral support for smoking cessation in pregnancy: what are the barriers to stopping and which behaviour change techniques can influence these? Application of theoretical domains framework. *International Journal of Environmental Research and Public Health*, 17, pp:359. Doi: 10.3390/ijerph15020359.

Campins, L., Serra-Prat, M., Gozalo, I., *et al.* 2017. Randomized controlled trial of an intervention to improve drug appropriateness in community-dwelling polymedicated elderly people. *Family Practice*, 34, pp:36-42. Doi: 10.1093/fampra/cmw073.

- Cane, J., O'Connor, D., Michie, S. 2012. Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implementation Science*, 7, pp:37.
- Cantrill, J.A., Sibbald, B., Buetow, S. 1998. Indicators of the appropriateness of long-term prescribing in general practice in the United Kingdom: consensus development, face and content validity, feasibility, and reliability. *International Journal for Quality in Health Care*, 7, pp:130-5. Doi: 10.1136/qshc.7.3.130.
- Carayon, P., Wetterneck, T.B., Rivera-Rodriguez, A.J., et al. 2014. Human factors systems approach to healthcare quality and patient safety. *Applied Ergonomics*, 45, pp:14-25. Doi: 10.1016/j.apergo.2013.04.023
- Carayon, P., Kianfar, S., Yagiong, L., et al. 2015. A systematic review of mixed methods research on human factors and ergonomics in health care, *Applied Ergonomics*, 51, pp:291-321. Doi: 10.1016/j.apergo.2015.06.001
- Carayon, P., Wooldridge, A., Honnakker, P., et al. 2020. SEIPS 3.0: Human-centered design of the patient journey for patient safety. *Applied Ergonomics*, 84, pp:103033. Doi: 10.1016/j.apergo.2019.103033
- Cardosi, L., Hohmeier, K.C., Fisher, C., et al. 2018. Patient satisfaction with a comprehensive medication review provided by a community pharmacist. *Journal of Pharmacy Technology*, 34, pp:48-53. Doi: 10.1177/8755122517752158.
- Cardwell, K., Hughes, C.M., Ryan, C. 2018. Community pharmacists' views of using a screening tool to structure medicines use reviews for older people: findings from qualitative interviews. *International Journal of Clinical Pharmacy*, 40, pp:1086-95. Doi: 10.1007/s11096-018-0659-2
- Cardwell, K., Smith, S.M., Clyne, B., et al. 2020. Evaluation of the General Practice Pharmacist (GPP) intervention to optimise prescribing in Irish primary care: a non-randomised pilot study. *BMJ Open*, 10, pp:e035087. Doi:10.1136/bmjopen-2019-035087.
- Carey, R.N., Connell, L.E., Johnston, M., et al. 2019. Behaviour change techniques and their mechanisms of action: a synthesis of links described in published intervention literature. *Annals of Behavioral Medicine*, 53, pp:693-707. Doi:10.1093/abm/kay078
- Carroll, P., Dervan, A., Maker, A., et al. 2021. Patient and Public Involvement (PPI) in preclinical research: a scoping review protocol. [version 2; peer review: 2 approved]. *HRB Open Research*, 4, pp:61. Doi: 10.12688/hrbopenres.13303.2

Carter, S.R., Chen, T.F., White, L. 2012. Home medicines reviews: a quantitative study of the views of recipients and eligible non-recipients. *International Journal of Pharmacy Practice*, 20, pp:209-17. Doi: 10.1111/j.2042-7174.2011.00180.x

Cassell, A., Edwards, D., Harshfield, A., *et al.* 2018. The epidemiology of multimorbidity in primary care: a retrospective cohort study. *British Journal of General Practice*, 68, pp:e245. Doi: 10.3399/bjgp18X695465

Castelino, R.L., Bajorek, B.V., Chen, T.F., 2010. Retrospective evaluation of home medicines review by pharmacists in older Australian patients using the medication appropriateness index. *The Annals of Pharmacotherapy*, 44, pp:1922-9. Doi: 10.1345/aph.1P373.

Cazelles, B., Nguyen-Van-Yen, B., Champagne, C., *et al.* 2021. Dynamics of the COVID-19 epidemic in Ireland under mitigation. *BMC Infectious Diseases*, 21, pp:735. Doi: 10.1186/s12879-021-06433-9

Central Statistics Office. 2019. *Mortality Differentials in Ireland 2016-2017*. Cork: CSO.

Charmaz, K., 2006. *Constructing grounded theory*. Thousand Oaks, California: SAGE.

Chen, R., Lee, B.Y. 2008. Principles and practice of clinical trial medicine. *Academic Press*. Doi: 10.1016/B978-0-12-373695-6.X0001-4

Chen, J., Wang, Y. 2021. Social media use for health purposes: systematic review. *Journal of Medical Internet Research*, 23, pp:e17917. Doi: 10.2196/17917

Chenail, R.J., 2011. Interviewing the investigator: strategies for addressing instrumentation and researcher bias concerns in qualitative research. *The Qualitative Report*, 16, pp:255-62.

Choi, S.W., Tran, D.H.D. 2016. Calculating sample size. Alpha, beta, mu and sigma - it's all Greek. *Anaesthesia*, 71:462-464. Doi: 10.1111/anae.13369

CISCRP. 2019. Patient engagement in clinical trials. Available at: <https://www.ciscrp.org/patient-engagement-in-clinical-trials/> accessed 7/1/21 [checked 27/08/2022]

Citizens Information. 2021. *GP visit cards*. Available at: [https://www.citizensinformation.ie/en/health/medical\\_cards\\_and\\_gp\\_visit\\_cards/gp\\_visit\\_cards.html](https://www.citizensinformation.ie/en/health/medical_cards_and_gp_visit_cards/gp_visit_cards.html) accessed 23/08/2022.

Citizens Information. 2021. *Drugs payment scheme*. Available at: [https://www.citizensinformation.ie/en/health/drugs\\_and\\_medicines/drugs\\_payment\\_scheme.html](https://www.citizensinformation.ie/en/health/drugs_and_medicines/drugs_payment_scheme.html) accessed 23/08/2022.

Clyne, W., Blenkinsopp, A., Seal, R. 2008. *A guide to medication review 2008*. The National Prescribing Centre, the Medicines Partnership Programme 2.1. Available at: <https://www.cff.org.br/userfiles/52%20-%20CLYNE%20W%20A%20guide%20to%20medication%20review%202008.pdf> accessed 15/03/2022

Clyne, B., Bradley, M.C., Smith, S.M., *et al.* 2013. Effectiveness of medicines review with web-based pharmaceutical treatment algorithms in reducing potentially inappropriate prescribing in older people in primary care: a cluster randomised trial (OPTI-SCRIPT study protocol). *Trials*, 14, pp:72. Doi: 10.1186/1745-06215-14-72.

Clyne, B., Smith, S.M., Hughes, C.M., *et al.* 2015. Effectiveness of a multifaceted intervention for potentially inappropriate prescribing in older patients in primary care: a cluster-randomised controlled trial (OPTI-SCRIPT study). *Annals of Family Medicine*, 13, pp:545-553. Doi: 10.1370/afm.1838

Clyne, B., Cooper, J.A., Hughes, C.M., *et al.* 2016. A process evaluation of a cluster randomised trial to reduce potentially inappropriate prescribing in older people in primary care (OPTI-SCRIPT study). *Trials*, 17, pp:386. Doi: 10.1186/s13063-016-1513-z.

The Cochrane Collaboration. Data extraction Forms. 2020. Available at: <https://dplp.cochrane.org/data-extraction-forms> accessed 27<sup>th</sup> March 2020

Collins, C., O’Riordan, M. 2015. *The future of Irish general practice: ICGP member survey 2015*. Available at: <https://www.icgp.ie/speck/properties/asset/asset.cfm?type=LibraryAsset&id=E21D6E5F%2DD02B%2D6BC2%2DB065BD5083304AB4&property=asset&revision=tip&disposition=inline&app=icgp&filename=The%5FFuture%5Fof%5FIrish%5FGeneral%5FPractice%5F%2D%5FICGP%5FMember%5FSurvey%5F2015%2Epdf> accessed 26/01/2022

Collins, C.S., Stockton, C.M. 2018. The central role of theory in qualitative research. *International Journal of Qualitative Methods*, 17, pp:1-10. Doi: 10.1177/1609406918797475



Collins, C., Homeniuk, R. 2021. How many general practice consultations occur in Ireland annually? Cross-sectional data from a survey of general practices. *BMC Family Practice*, 22, pp:40. Doi: 10.1186/s12875-021-01377-0

Colombo, F., García-Goñi, M., Schwierz, C. 2016. Addressing multimorbidity to improve healthcare and economic sustainability. *Journal of Comorbidity*, 6, pp:21-27. Doi: 10.15256/joc.2016.6.74

Comhairle na nDochtúirí Leighis Medical Council. 2019. *Medical workforce intelligence report: a report on the 2016 and 2017 annual registration retention & voluntary registration withdrawal surveys. Summary document*. Available at: <https://medicalcouncil.ie/news-and-publications/press-releases/press-release/medical-workforce-intelligence-report-summary.pdf> accessed 25/01/2022

Compennolle, S., DeSmet, A., Poppe, L., *et al.* 2019. Effectiveness of interventions using self-monitoring to reduce sedentary behaviour in adults: a systematic review and meta-analysis. *International Journal of Behavioral Nutrition and Physical Activity*, 16, pp:63. Doi: 10.1186/s12966-019-0824-3

Conejos Miquel, M.D., Sanchez Cuervo, M., Delgado Silveira, E., *et al.* 2010. Potentially inappropriate drug prescription in older subjects across health care settings. *European Geriatric Medicine*, 1, pp:9-14. Doi: 10.1016/j.eurgerr.2009.12.002

Conn, D.K., Hogan, D.B., Amdam, L., *et al.* 2020. Canadian guidelines on benzodiazepine receptor agonist use disorder among older adults title. *Canadian Geriatrics Journal*, 23, pp:116-122. Doi: 10.5770/cgj.23.419

Connolly, S., Wren, M-A. 2016. The 2011 proposal for Universal Health Insurance in Ireland: potential implications for healthcare expenditure. *Health Policy*, 120, pp:790–796. Doi: 10.1016/j.healthpol.2016.05.010.

Cope, L.C., Tully, M.P., Hall, J. 2020. An exploration of the perceptions of non-medical prescribers, regarding their self-efficacy when prescribing, and their willingness to take responsibility for prescribing decisions. *Research in Social and Administrative Pharmacy*, 16, pp:249-56. Doi: 10.1016/j.sapharm.2019.05.013.

Cook, J.M., Marshall, R., Masci, C., *et al.* 2007. Physicians' perspectives on prescribing benzodiazepines for older adults: a qualitative study. *Journal of General Internal Medicine*, 22, pp:303-307. Doi: 10.1007/s11606-006-0021-3.

Coole, C., Baker, P., McDaid, C., *et al.* 2020. Using intervention mapping to develop and occupational advice intervention to aid return to work following hip and knee replacement in the United Kingdom. *BMC Health Services Research*, 20, pp:523. Doi: 10.1186/s12913-020-05375-3

Cooley, L., Kohl, R., Ved, R. 2016. *Scaling up – from vision to large scale change: a management framework for practitioners*. Available at: [https://www.msiworldwide.com/sites/default/files/additional-resources/2018-11/ScalingUp\\_3rdEdition.pdf](https://www.msiworldwide.com/sites/default/files/additional-resources/2018-11/ScalingUp_3rdEdition.pdf) accessed 07/02/2022

Coombes, I.D., Stowasser, D.A., Coombes, J.A., *et al.* 2008. Why do interns make prescribing errors? A qualitative study. *Medical Journal of Australia*, 188, pp:88-94. Doi: 10.5694/j.1326-5377.2008.tb01529.x.

Cooper, J.A., Ryan, C., Smith, S.M., *et al.* 2014. The development of the PROMPT (Prescribing Optimally in Middle-aged People's Treatments) criteria. *BMC Health Services Research*, 14, pp:484.

Cooper, J.A., Cadogan, C.A., Patterson, S.M., *et al.* 2015. Interventions to improve the appropriate use of polypharmacy in older people: a Cochrane systematic review. *BMJ Open*. 2015:e009235. Doi:10.1136/bmjopen-2015-009235.

Cooper, J.A., Moriarty, F., Ryan, C., *et al.* 2016. Potentially inappropriate prescribing in two populations with differing socio-economic profiles: a cross-sectional database study using the PROMPT criteria. *European Journal of Clinical Pharmacology*, 72, pp:583-591. Doi: 10.1007/s00228-015-2003-z

Cornelissen, N., Karapinar-Çarkit, F., En-nasery-de Heer, S., *et al.* 2021. Application of intervention mapping to develop and evaluate a pharmaceutical discharge letter to improve information transfer between hospital and community pharmacists. *Research in Social and Administrative Pharmacy*, 18, pp:3297-3302. Doi: 10.1016/j.sapharm.2021.10.001

Costa, F.A., Scullin, C., Al-Taani, G., *et al.* 2017. Provision of pharmaceutical care by community pharmacists across Europe: Is it developing and spreading? *Journal of Evaluation in Clinical Practice*, 23, pp:1336-1347. Doi: 10.1111/jep.12783

Cradock, K.A., Ólaighin, G., Finucane, F.M., *et al.* 2017. Behaviour change techniques targeting both diet and physical activity in type 2 diabetes: a systematic review and meta-analysis.

- International Journal of Behavioral Nutrition and Physical Activity*, 14, pp:18. Doi: 10.1186/s12966-016-0436-0
- Craig, P., Dieppe, P., Macintyre, S., *et al.* 2008. Developing and Evaluating Complex Interventions: The New Medical Research Council Guidance. *BMJ*, 337, pp:a1655. Doi:10.1136/bmj.a1655
- Cresswell, J.W., Plano Clark, V.L., 2011. *Designing and conducting mixed method research*. Thousand Oaks, California: SAGE.
- Creswell, J.W., Creswell, J.D., 2018. *Research design: qualitative, quantitative, and mixed methods approaches*. Los Angeles: SAGE Publications.
- Crilly, P., Patel, N., Ogunrinde, A., *et al.* 2017. Community pharmacists' involvement in research in the United Kingdom. *Pharmacy*, 5, pp:48. Doi: 10.3390/pharmacy5030048
- Croke, A., Moriarty, F., Boland, F., *et al.* 2021. Integrating clinical pharmacists within general practice: protocol for a pilot cluster randomised controlled trial. *BMJ Open*, 11, pp:e041541. Doi: 10.1136/bmjopen-2020-041541.
- Croot, L., O'Cathain, A., Sworn, K., *et al.* 2019. Developing interventions to improve health: a systematic mapping review of international practice between 2015 and 2016. *Pilot and Feasibility Studies*, 5, pp:127. Doi:10.1186/s40814-019-0512-8
- Crosbie, B., O'Callaghan, M.E., O'Flanagan, S., *et al.* 2020. A real-time measurement of general practice workload in the Republic of Ireland: a prospective study. *British Journal of General Practice*, 70, pp:e489-496. Doi: 10.3399/bjgp20X710429
- Crouch, M., McKenzie, H., 2006. The logic of small samples in interview-based qualitative research. *Social Science Information*, 45, pp:18. Doi:10.1177/0539018406069584.
- Cullinan, S., Fleming, A., O'Mahony, D., *et al.* 2015. Doctors' perspectives on the barriers to appropriate prescribing in older hospitalized patients: a qualitative study. *British Journal of Clinical Pharmacology*, 79, pp:860-869. Doi: 10.1111/bcp.12555.
- Cupples, M.E., Byrne, M.C., Smith, S.M., *et al.* 2008. Secondary prevention of cardiovascular disease in different primary healthcare systems with and without pay-for-performance. *Heart*, 94, pp:1594-600. Doi: 10.1136/hrt.2008.145912.

- Curtain, C.M., Bindoff, I.K., Westbury, J.L., *et al.* 2013. A comparison of prescribing criteria when applied to older community-based patients. *Drugs & Aging*, 30:935-943. Doi: 10.1007/s40266-013-0116-6.
- Dalager, T., Højmark, A., Jensen, P.T., *et al.* 2019. Using an intervention mapping approach to develop prevention and rehabilitation strategies for musculoskeletal pain among surgeons. *BMC Public Health*, 19, pp:320. Doi: 10.1186/s12889-019-6625-4.
- Dalgetty, R., Miller, C.B., Dombrowski, S.U. 2019. Examining the theory-effectiveness hypothesis: a systematic review of systematic reviews. *British Journal of Health Psychology*, 24, pp:334-356. Doi: 10.1111/bjhp.12356.
- Dalton, K., O'Mahony, D., O'Sullivan, D., *et al.* 2019. Prescriber implementation of STOPP/START recommendations for hospitalized older adults: a comparison of a pharmacist approach and a physician approach. *Drugs & Aging*, 36, pp:279-288.
- Davis, J.C., Liu-Ambrose, T., Richardson, C.G., *et al.* 2013. A comparison of the ICECAP-O with the EQ-5D in a falls prevention clinical setting: are they complements or substitutes? *Quality of Life Research*, 22, pp:969-977. Doi: 10.1007/s11136-012-0225-4
- Debone, D., Taylor, N., Lipworth, W., *et al.* 2017. Applying the theoretical domains framework to identify barriers and targeted interventions to enhance nurses' use of electronic medication management systems in two Australian hospitals. *Implementation Science*, 12, pp:42. Doi: 10.1186/s13012-017-0572-1
- Deja, E., Peters, M.J., Khan, I., *et al.* 2021. Establishing and augmenting views on the acceptability of a paediatric critical care randomized controlled trial (the FEVER trial): a mixed methods study. *BMJ Open*, 11, pp:e041952. Doi: 10.1136/bmjopen-2020-041952
- de Jong, Y., van der Willik, E.M., Milders, J., *et al.* 2021. A meta-review demonstrates improved reporting quality of qualitative reviews following the publication of COREQ- and ENTREQ-checklists, regardless of modest uptake. *BMC Medical Research Methodology*, 21, pp:184. Doi: 10.1186/s12874-021-01363-1.
- Delestras, S., Roustit, M., Bedouch, P., *et al.* 2013. Comparison between two generic questionnaires to assess satisfaction with medication in chronic diseases. *PLoS ONE*, 8, pp:e56247. Doi: 10.1371/journal.pone.0056247

Delgado-Silveira, E., Albiñana-Pérez, M.S., Muñoz-García, M., CRONOS Group *et al.* 2018. Pharmacist comprehensive review of treatment compared with STOPP-START criteria to detect potentially inappropriate prescription in older complex patients. *European Journal of Hospital Pharmacy*, 25, pp:16-20. Doi: 10.1136/ejhpharm-2016-001054

Dellinger, J.K., Pitzer, S., Schaffler-Schaden, D., *et al.* 2020. Improving medication appropriateness in nursing homes via structured interprofessional medication-review supported by health information technology: a non-randomized controlled study. *BMC Geriatrics*, 20, pp:506. Doi: 10.1186/s12877-020-01895-z

Department for Environment, Food & Rural Affairs. 2017. *Defining rural areas using the rural urban classification*. Available at: <https://www.gov.uk/government/statistics/defining-rural-areas> Accessed 30/07/2022

Department of Health. 2013. *Healthy Ireland*. Available at: <https://assets.gov.ie/7555/62842eef4b13413494b13340fff9077d.pdf> accessed 26/01/2022

Department of Health. 2017. *Health in Ireland, Key Trends 2017*. Dublin, Ireland: Department of Health.

Department of Health. 2018a. *Health service capacity review 2018 executive report. Review of health demand and capacity requirements in Ireland to 2031 – findings and recommendations*. Available at: <https://www.gov.ie/en/publication/26df2d-health-service-capacity-review-2018/> accessed 26/0/2022

Department of Health. 2018b. *Sláintecare implementation strategy*. Dublin: Department of Health

Department of Health. 2019. *Sláintecare action plan 2019*. Available at: <https://www.gov.ie/en/publication/109e2b-slaintecare-action-plan-2019/> accessed 23/07/2022

Department of Health. *Pharmacy Workforce Review*. 2020. Available at: <https://www.health-ni.gov.uk/sites/default/files/publications/health/doh-pharmacy-workforce-review.pdf>. Accessed 09/07/2021 checked 26/08/2022

Department of Health. 2021. *Sláintecare implementation strategy & action plan*. Available at: <https://www.gov.ie/en/publication/6996b-slaintecare-implementation-strategy-and-action-plan-2021-2023/> accessed 23/07/2022

De Silva, M.J., Breuer, E., Lee, L., *et al.* 2014. Theory of change: a theory-driven approach to enhance the Medical Research Council's framework for complex interventions. *Trials*, 15, pp:267.

Dewez, S., Laurin, C., Ogez, D., *et al.* 2021. Elaboration and refinement of a motivational communication training program for healthcare professionals in pediatric oncology: a feasibility and acceptability study. *Health Psychology and Behavioral Medicine*, 9, pp:220-238. Doi: 10.1080/21642850.2021.1903326

Dhalwani, N.N., Fahami, R., Sathanapally, H., *et al.* 2017. Association between polypharmacy and falls in older adults: a longitudinal study from England. *BMJ Open*, 7, pp:e016358. Doi:10.1136/bmjopen-2017-016358

Dillip, A., Alba, S., Mshana, C., *et al.* 2012. Acceptability – a neglected dimension of access to health care: findings from a study on childhood convulsions in rural Tanzania. *BMC Health Services Research*, 12:113.

Dixon Jr, J.R. The international conference on harmonization good clinical practice guideline. 1998. *Quality Assurance*, 6, pp:65-74. Doi: 10.1080/105294199277860

Donald, G. 2018. A brief summary of pilot and feasibility studies: exploring terminology, aims, and methods. *European Journal of Integrative Medicine*, 24, pp:65-70. Doi: 10.1016/j.eujim.2018.10.017

Dossett, L.A., Kaji, A.H., Cochran, A., 2021. SRQR and COREQ reporting guidelines for qualitative studies. *JAMA Surgery*, 156, pp:875-6. Doi: 10.1001/jamasurg.2021.0525

Dowling, S., Last, J., Finnegan, H., *et al.* 2020. What are the current 'top five' perceived educational needs of Irish general practitioners? *Irish Journal of Medical Science*, 189, pp:381-388. Doi: 10.1007/s11845-019-02047-y

Dreber, A., Johannesson, M. 2019. Statistical significance and the replication crisis in the social sciences. *Economics and Finance*. Doi: 10.1093/acrefore/9780190625979.013.461

Drenth-van Maanen, A.C., Wilting, I., Jansen, P.A.F. 2020. Prescribing medicines to older people – how to consider the impact of ageing on human organ and body functions. *British Journal of Clinical Pharmacology*, 86, PP:1921-1930. Doi: 10.1111/bcp.14094.

Duncan, E.M., Francis, J.J., Johnston, M., *et al.* 2012. Learning curves, taking instructions, and patient safety: using a theoretical domains framework in an interview study to investigate

prescribing errors among trainee doctors. *Implementation Science*, 7, pp:86.

Doi:10.1186/1748-5908-7-86.

Duncan, P., Cabral, C., McCahon, D., *et al.* 2019. Efficiency versus thoroughness in medication review: a qualitative interview study in UK primary care. *British Journal of General Practice*, 69, pp:E190-E198. Doi: 10.3399/bjgp19X701321

Duncan, E., O’Cathain, A., Rousseau, N., *et al.* 2020. Guidance for reporting intervention development studies in health research (GUIDED): an evidence-based consensus study. *BMJ Open*, 10, pp:e033516. Doi:10.1136/bmjopen-2019-033516

Dunlop, J.A., Shaw, J.P. 2022. Community pharmacists’ perspectives on pharmaceutical care implementation in New Zealand. *Pharmacy World and Science*, 24, pp:224-30. Doi: 10.1023/a:1021526425458.

Dunt, D., McKenzie, R., 2012. Improving the quality of qualitative studies: do reporting guidelines have a place? *Family Practice*, 29, pp:367-9. Doi: 10.1093/fampra/cms041

du Vaure, C.B., Dechartres, A., Battin, C., *et al.* 2016. Exclusion of patients with concomitant chronic conditions in ongoing randomised controlled trials targeting 10 common chronic conditions and registered at ClinicalTrials.gov: a systematic review of registration details. *BMJ Open*, 6, e012265. Doi: 10.1136/bmjopen-2016-012265

Dyson, J., Lawton, R., Jackson, C., *et al.* 2013. Development of a theory-based instrument to identify barriers and levers to best hand hygiene practices among healthcare practitioners. *Implementation Science*, 8, pp:111. Doi:10.01186/1748-5908-8-111.

Effective Practice and Organisation of Care (EPOC). 2015. EPOC Resources for review authors, Norwegian Knowledge Centre for the Health Services. Available at:

<https://epoc.cochrane.org/resources/epoc-resources-review-authors> Accessed 7.07.19

[checked 27/08/2022]

Elbeddini, T., Prabakaran, T., Almasalkki, S., *et al.* 2020. Barriers to conducting deprescribing in the elderly population amid the COVID-19 pandemic. *Research in Social and Administrative Pharmacy*. 17, pp:1942-1945. Doi: 10.1016/j.sapharm.2020.05.025

Elbeddini, A., Sawhney, M., Tayefehchamani, Y., *et al.* 2021. Deprescribing for all: a narrative review identifying inappropriate polypharmacy for all ages in hospital settings. *BMJ Open Quality*, 10, pp:e001509. Doi: 10.1136/bmjopen-2021-001509

- Eldridge, S.M., Lancaster, G.A., Campbell, M.J., *et al.* 2016a. Defining feasibility and pilot studies in preparation for randomized controlled trials: development of a conceptual framework. *PLoS ONE*, 11, pp:e0150205. Doi:10.1371/journal.pone.0150205
- Eldridge, S.M., Chan, C.L., Campbell, M.J., *et al.* 2016b. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ*, 355, pp:i5239. Doi: 10.1136/bmj.i5239
- Elliott, R.A., Tanajewski, L., Gkountouras, G., *et al.* 2017. Cost effectiveness of support for people starting a new medication for a long-term condition through community pharmacies: an economic evaluation of the New Medicine Service (NMS) compared with normal practice. *PharmacoEconomics*, 35, pp:1237-55. Doi: 10.1007/s40273-017-0554-9
- Ensing, H.T., Stuijt, C.C.M., van den Bemt, B.J.F., *et al.* 2015. Identifying the optimal role for pharmacists in care transitions: a systematic review. *Journal of Managed Care & Specialty Pharmacy*, 21, pp:614-36.
- Ersoy, S., Engin, V.S., 2018. Risk factors for polypharmacy in older adults in a primary care setting: a cross-sectional study. *Clinical Interventions in Aging*, 13, pp:2003-2011. Doi:10.2147/CIA.S176329
- Etikan, I., Musa, S.A., Alkassim, R.S. 2016. Comparison of convenience sampling and purposive sampling. *American Journal of Theoretical and Applied Statistics*, 5:1-4. Doi: 10.11648/j.ajtas.20160501.11
- Eton, D.T., Yost, K.J., Lai, J.S., *et al.* 2017. Development and validation of the Patient Experience with Treatment and Self-management (PETS): a patient-reported measure of treatment burden. *Quality of Life Research*, 26:489-503. Doi: 10.1007/s11136-016-1397-0
- Eton, D.T., Lee, M.K., Sauer, J.L.S., *et al.* 2020. Known-groups validity and responsiveness to change of the Patient Experience with Treatment and Self-management (PETS vs 2.0): a patient-reported measure of treatment burden. *Quality of Life Research*, 29:3143-54. Doi: 10.1007/s11136-020-2546-x.
- European Medicines Agency. 2011. *MEA geriatric medicines strategy*. 2011. Available at: <https://ema.europa.eu/en/documents/other/geriatric-medicines-strategy-en.pdf> accessed 04/03/2022
- European Parliament. 2016. *Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 65/46/EC*



- (General Data Protection Regulation). Available at: <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679> accessed 09/02/2022
- EuroQol Research Foundation Group. 2019. EQ-5D-5L user guide. Available at: <https://euroqol.org/publications/user-guides/> accessed 13/12/2021 [checked 26/08/2022]
- Eurostat. 2017a. *Life expectancy by age and sex and healthy life years statistics*. Available at [https://ec.europa.eu/eurostat/databrowser/view/tepsr\\_sp320/default/table?lang=en](https://ec.europa.eu/eurostat/databrowser/view/tepsr_sp320/default/table?lang=en) accessed 10/11/21.
- Eurostat. 2017b. *Self-perceived long-standing limitations in usual activities due to health problem by sex, age and income quintile*. Available at: <https://ec.europa.eu/eurostat/web/health/data/database> accessed 10/11/21
- Evrard, P., Péteïn, C., Beuscart, J-B., *et al.* 2022. Barriers and enablers for deprescribing benzodiazepine receptor agonists in older adults: a systematic review of qualitative and quantitative studies using the theoretical domains framework. *Implementation Science*, 14, pp:41. Doi: 10.1186/s13012-022-01206-7.
- Faries, D., Ascher-Svanum, H., Zhu, B., *et al.* 2005. Antipsychotic monotherapy and polypharmacy in the naturalistic treatment of schizophrenia with atypical antipsychotics. *BMC Psychiatry*, 5, pp:26. Doi: 10.1186/1471-244X-5-26
- Farmer, A.J., McSharry, J., Rowbotham, S., *et al.* 2016. Effects of interventions promoting monitoring of medication use and brief messaging on medication adherence for people with Type 2 diabetes: a systematic review of randomised trials. *Diabetic Medicine*, 33, pp:565-579. Doi: 10.1111/dme.12987.
- Farrington, K., Covic, A., Nistor, I., *et al.* 2017. Clinical practice guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR<45mL/min/1.73m<sup>2</sup>): a summary document from the European Renal Best Practice Group. *Nephrology Dialysis Transplantation*, 32, pp:9-16. Doi: 10.1093/ndt/gfw411
- Fathima, M., Saini, B., Foster, J.M., *et al.* 2019. A mixed methods analysis of community pharmacists' perspectives on delivering COPD screening service to guide future implementation. *Research in Social and Administrative Pharmacy*, 15:662-672. Doi: 10.1016/j.sapharm.2018.08.007
- Feeley, N., Cossette, S., Côté, J., *et al.* 2009. The importance of piloting an RCT intervention. *The Canadian Journal of Nursing Research*, 41:85-99.

- Fernandez, M.E., Ruiter, R.A.C., Markham, C.M., *et al.* 2019. Intervention mapping: theory – and evidence-based health promotion program planning: perspective and examples. *Frontiers in Public Health*, 7, pp:209. Doi: 10.3389/fpubh.2019.00209
- Fialová, D., Brkić, J., Laffon, B., *et al.* 2019. Applicability of EU(7)-PIM criteria in cross-national studies in European countries. *Therapeutic Advances in Drug Safety*, 10, pp:2042098619854014. Doi: 10.1177/2042098619854014.
- Fick, D.M., Cooper, J.W., Wade, W.E., *et al.* 2003. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Archives of Internal Medicine*, 163, pp:2716-24. Doi: 10.1001/archinte.163.22.2716.
- Field A. 2006. *Discovering statistics using SPSS*. 2<sup>nd</sup> ed. London: SAGE Publications
- Filkova, M., Carvalho, J., Norton, S., *et al.* 2017. Polypharmacy and unplanned hospitalizations in patients with rheumatoid arthritis. *Journal of Rheumatology*, 44, pp:1786-1793. Doi: 10.3899/jrheum.160818.
- Fishbein, M., Ajzen, I. 1975. *Belief, attitude, intention and behaviour: An introduction to theory and research*. Reading, MA: Addison-Wesley
- Florisson, S., Aagesen, E.K., Bertelsen, A.S., *et al.* 2021. Are older adults insufficiently included in clinical trials? – An umbrella review. *Basic and Clinical Pharmacology and Toxicology*, 128, pp:213-223. Doi: 10.1111/bcpt.13536
- Fortin, M., Bravo, G., Hudon, C., *et al.* 2006. Relationship between multimorbidity and health-related quality of life of patients in primary care. *Quality of Life Research*, 15, pp:83-91. Doi: 10.1007/s11136-005-8661-z.
- Franchi, C., Tettamanti, M., Djade, C.D. *et al.* 2016. E-learning in order to improve drug prescription for hospitalized older patients: a cluster-randomized controlled study. *British Journal of Clinical Pharmacology*, 82, pp:53-63. Doi: 10.1111/bcp.12922.
- Francis, J.J., Johnston, M., Robertson, C., *et al.* 2010. What is an adequate sample size? Operationalising data saturation for theory-based interview studies. *Psychology and Health*, 25, pp:1229-45. Doi: 10.1080/08870440903194015
- Francis, J.J., O'Connor, D., Curran, J. 2012. Theories of behaviour change synthesis into a set of theoretical groupings: introducing a thematic series on the theoretical domains framework. *Implementation Science*, 7, pp:35. Doi:10.1186/1748-5908-7-35.

- Fraser, M.W., Galinsky, M.J., 2010. Steps in intervention research: designing and developing social programs. *Research on Social Work Practice*, 10, pp:459-466.  
Doi:10.1177/1049731509358424
- Frazier, S.C., 2005. Health outcomes and polypharmacy in elderly individuals: an integrated literature review. *Journal of Gerontological Nursing*, 31, pp:4-11. Doi: 10.3928/0098-9134-20050901-04.
- French, S.D., Green, S.E., O'Connor, D.A., *et al.* 2012. Developing theory-informed behaviour change interventions to implement evidence into practice: a systematic approach using the theoretical domains framework. *Implementation Science*, 7, pp:38.
- French, S.D., McKenzie, J.E., O'Connor, D.A., *et al.* 2013. Evaluation of a theory-informed implementation intervention for the management of acute low back pain in general medical practice: the IMPLEMENT cluster randomised trial. *PLoS One*, 8, pp:e65471.  
Doi:10.1371/journal.pone.0065471.
- Friedman, B.J., Chen, I., Asantey, K., *et al.* 2022. Twitter engagement of medical students applying to urology residency during COVID-19: a mixed methods study. *Urology*, 165, pp:120-7. Doi: 10.1016/j.urology.2021.11.046
- Frisk, P., Holtendal, C., Bastholm-Rahmner, P., *et al.* 2019. Competence, competition and collaboration: perceived challenges among Swedish community pharmacists engaging in pharmaceutical services provision and research. *International Journal of Pharmacy Practice*, 27, pp:346-54. Doi: 10.1111/ijpp.12518
- Fulton, M.M., Allen, E.R. 2005. Polypharmacy in the elderly: a literature review. *Journal of the American Association of Nurse Practitioners*, 17, pp:123-132. Doi: 10.1111/j.1041-2972.2005.0020.x.
- Fustinoni, S., Renard, D., Santos-Eggimann, B., *et al.* 2015. Polypharmacy and associated factors among community-dwelling older persons in a Swiss canton. *Clinical Therapeutics*, 37, pp:39-40. Doi: 10.1016/j.clinthera.2015.05.119
- Gagliardi, A.R., Brouwers, M.C., Palda, V.A., *et al.* 2011. How can we improve guideline use? A conceptual framework of implementability. *Implementation Science*, 6, pp:26.
- Galazzi, A., Lusignani, M., Chiarelli, M.T., *et al.* 2016. Attitudes towards polypharmacy and medication withdrawal among older inpatients in Italy. *International Journal of Clinical Pharmacy*, 38, pp:454-61. Doi: 10.1007/s11096-016-0279-4.

Gale, N.K., Heath, G., Cameron, E., *et al.* 2013. Using the Framework Method for the analysis of qualitative data in multi-disciplinary health research. *BMC Medical Research Methodology*, 13, pp:117.

Gallagher, P., Ryan, C., Byrne, S., *et al.* 2008. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. *International Journal of Clinical Pharmacology and Therapeutics*, 46, pp:72-83. Doi: 10.5414/cpp46072.

Gallagher, J.E., Colonio-Salazar, F.B., White, S., 2021. Supporting dentists' health and wellbeing – workforce assets under stress: a qualitative study in England. *British Dental Journal*, 20, pp:1-12. Doi: 10.1038/s41415-021-3130-9

Galvin, R., Moriarty, F., Cousins, G., *et al.* 2014. Prevalence of potentially inappropriate prescribing and prescribing omissions in older Irish adults: findings from The Irish Longitudinal study on Ageing study (TILDA). *European Journal of Clinical Pharmacology*, 70, pp:599-606. Doi: 10.1007/s00228-014-1651-8

Galvin, E., Desselle, S., Gavin, B., *et al.* 2021. Implementation of telemedicine consultations for people with mental health conditions in the community: a protocol for a systematic review [version 1; peer review: awaiting peer review]. *HRB Open Research*, 4, pp:125. Doi: 10.12688/hrbopenres.13435.1

Garcia, J., Vaz, M., Poggi, M. 2015. Estimated prevalence of contraindicated, severe and moderate interactions in ambulatory patients with polypharmacy in a healthcare provider in Uruguay. *Clinical Therapeutics Journal*, 1, pp:145.

Garnett, C., Crane, D., Brown, J., *et al.* 2018. Reported theory use by digital interventions for hazardous and harmful; alcohol consumption, and association with effectiveness: meta-regression. *Journal of Medical Internet Research*, 20, pp:e69. Doi: 10.2196/jmir.8807

Gedde, M.H., Husebo, B.S., Mannseth, J., *et al.* 2022. The impact of medication reviews by general practitioners on psychotropic drug use and behavioral and psychological symptoms in home-dwelling people with dementia: results from the multicomponent cluster randomized controlled LIVE@Home.Path trial. *BMC Medicine*, 20, pp:186. Doi: 10.1186/s12916-022-02382-

5

Gelinas, L., Pierce, R., Winkler, S., *et al.* 2017. Using social media as a research recruitment tool: ethical issues and recommendations. *American Journal of Bioethics*, 17, pp:3-14. Doi: 10.1080/15265161.2016.1276644

General Data Protection Regulations. *Article 32*. Available at:

[www.gdprhub.eu/Article\\_32\\_GDPR](http://www.gdprhub.eu/Article_32_GDPR) accessed 23/12/22

General Pharmaceutical Council. 2021. *Standards for the initial education and training of pharmacists*. Available at: [standards-for-the-initial-education-and-training-of-pharmacists-january-2021\\_final-v1.3.pdf](https://www.pharmacyregulation.org/sites/default/files/standards-for-the-initial-education-and-training-of-pharmacists-january-2021-final-v1.3.pdf) (pharmacyregulation.org) accessed 13/03/23

Gerlach, N., Michiels-Corsten, M., Viniol, A., *et al.* 2020. Professional roles of general practitioners, community pharmacists and specialist providers in collaborative medication deprescribing – a qualitative study. *BMC Family Practice*, 21, pp:183. Doi: 10.1186/s12875-020-01255-1

Gernant, S.A., Zillich, A.J., Snyder, M.E. 2017. Access to medical records' impact on community pharmacist-delivered medication therapy management: a pilot from the medication safety research network of Indiana (Rx-SafeNet). *Journal of Pharmacy Practice*, 31, pp:642-50. Doi: 10.1177/897190017735422

Gerson, K., Horowitz, R. 2002. Observation and interviewing: options and choices. In May T (ed) *Qualitative Research in Action*. London: SAGE.

Geurts, M.M.E., Stewart, R.E., Browsers, J.R.B.J., *et al.* 2016. Implications of a clinical medication review and a pharmaceutical care plan of polypharmacy patients with a cardiovascular disorder. *International Journal of Clinical Pharmacy*, 38, pp:808-15. Doi: 10.1007/s11096-016-0281-x

Gillaizeau, F., Chan, E., Trinquart, L., *et al.* 2013. Computerized advice on drug dosage to improve prescribing practice. *Cochrane Database of Systematic Reviews*. 11, pp:CD002894. Doi: 10.1002/14651858.cd002894.pub3

Gillies, K., Kearney, A., Keenan, C., *et al.* 2021. Strategies to improve retention in randomised trials. *Cochrane Database of Systematic Reviews*, 3, pp:MR000032. Doi: 10.1002/14651858.MR000032.pub3.

Glanz, K., Rimer, B.K. 2005. *Theory at a glance: a guide for health promotion practice*. San Francisco: NIH National Cancer Institute.

- Glasgow, R.E., Lichtenstein, E., Marcus, A.C. 2003. Why don't we see more translation of health promotion research into practice? Rethinking the efficacy-to-effectiveness transition. *American Journal of Public Health*, 93, pp:1261-7. Doi: 10.2105/ajph.93.8.1261.
- Glasgow, R.E., Davidson, K.W., Dobkin, P.L., *et al.* 2006. Practical behavioral trials to advance evidence-based behavioral medicine. *Annals of Behavioral Medicine*, 31, pp:5-13. Doi:10.1207/s15324796abm3101\_3.
- Glasziou, P., Chalmers, I., Rawlins, M., *et al.* 2007. When are randomized trials unnecessary? Picking signal from noise. *BMJ*, 334, pp:349-51. Doi: 10.1136/bmj.39070.527986.68
- Gleeson, L.L., Ludlow, A., Wallace, E., *et al.* 2022. Changes to primary care delivery during the COVID-19 pandemic and perceived impact on medication safety: a survey study. *Exploratory Research in Clinical and Social Pharmacy*, 6, pp:100143. Doi: 10.1016/j.rcsop.2022.100143
- Golomb, B.A., Chan, V.T., Evans, M.A., *et al.* 2012. The older the better: are elderly study participants more non-representative? A cross-sectional analysis of clinical trial and observational study samples. *BMJ Open*, 2, pp:e000833. Doi: 10.1136/bmjopen-2012-000833
- Gordon, R.A. 2015. Regression analysis for the social sciences. 2<sup>nd</sup> edn. New York: Routledge
- Gorman, A., Rankin, A., Hughes, C. *et al.* 2022. Theoretically derived interventions aimed at improving appropriate polypharmacy in primary care: a systematic review. *Exploratory Research in Clinical and Social Pharmacy*, 7, 100166. Doi: 10.1016/j.rcsop.2022.100166
- Górny, A., Napierała, J. 2016. Comparing the effectiveness of respondent-driven sampling and quota sampling in migration research. *International Journal of Social Research Methodology*, 19:645-661. Doi: 10.1080/13645579.2015.1077614
- Gomm, R. 2008. Social Research Methodology: a critical introduction. 2<sup>nd</sup> edn. New York: Palgrave Macmillan
- Gourlan, M., Bernard, P., Bortolon, C., *et al.* 2016. Efficacy of theory-based interventions to promote physical activity. A meta-analysis of randomised controlled trials. *Health Psychology Review*, 10, pp:50-66. Doi: 10.1080/17437199.2014.981777.
- Gouttebauge, V., van Sluis, M., Verhagen, E., *et al.* 2017. The prevention of musculoskeletal injuries in volleyball: the systematic development of an intervention and its feasibility. *Injury Epidemiology*, 4, pp:25. Doi: 10.1186/s40621-017-0122-y

Government of Ireland. 2021. Sláintecare Implementation Strategy & Action Plan 2021-2023. Available at: <https://www.gov.ie/en/publication/6996b-slaintecare-implementation-strategy-and-action-plan-2021-2023/> accessed 19/08/2022

Grant, A., Treweek, S., Dreischulte, T., *et al.* 2013. Process evaluations for cluster-randomised trials of complex interventions: a proposed framework for design and reporting. *Trials*, 14, pp:15

Greenhalgh, T., Wherton, J., Papoutsi, C., *et al.* 2017. Beyond adoption: a new framework for theorizing and evaluating nonadoption, abandonment, and challenge to the scale-up, spread, and sustainability of health and care technologies. *Journal of Medical Internet Research*, 19, pp:e367. Doi: 10.2196/jmir.8775

Greiver, M., Dahrouge, S., O'Brien, P., *et al.* 2019. Improving care for elderly patients living with polypharmacy: protocol for a pragmatic cluster randomized trial in community-based primary care practices in Canada. *Implementation Science*, 14, pp:55. Doi: 10.1186/s13012-019-0904-4

Griese-Mammen, N., Hersberger, K.E., Messerli, M., *et al.* 2018. PCNE definition of medication review: reaching agreement. *International Journal of Clinical Pharmacy*, 40, pp:1199-208. Doi: 10.1007/s11096-0180696-7

Grimes, C.L., Balk, E.M., Crisp, C.C., *et al.* 2020. A guide for urogynecologic patient care utilizing telemedicine during the COVID-19 pandemic: review of existing evidence. *International Urogynecology Journal*, 31, pp:1063-1089. Doi: 10.1007/s00192-020-04314-4

Grund, S., Breiting, E., Fricke, S., *et al.* 2017. Health-related quality of life measurement inpatient geriatric rehabilitation: a comparison of the feasibility and suitability between the SF-36 and EQ-5D-5L questionnaires. *Journal of Gerontology & Geriatric Research*, 6, pp:458. Doi: 10.4172/2167-7182.1000458

Gudmundsdottir, G.B., Brock-Utne, B., 2010. An exploration of the importance of piloting and access as action research. *Educational Action Research*, 18, pp:359-72. Doi:10.1080/09650792.2010.499815.

Guéret, M. 2017. *Irish Medical Directory: The Directory of Irish Healthcare 2017-2018*. Dublin: IMD.

Guerriero, F., 2017. Guidance on opioids prescribing for the management of persistent non-cancer pain in older adults. *World Journal of Clinical Cases*, 5, pp:73-81. Doi: 10.12998/wjcc.v5.i3.73.

Guest, G., Namey, E.E., Mitchell, M.L., 2013. *Collecting qualitative data: a field manual for applied research*. United States of America: SAGE Publications.

Guilcher, S.J.T., Fernandes, O., Luke, M.J., *et al.* 2020. A developmental evaluation of a intraprofessional Pharmacy cOMmunication ParTnership (PROMPT) to improve transitions in care from hospital to community: a mixed-methods study. *BMC Health Services Research*, 20, pp:99. Doi: 10.1186/s12913-020-4909-0.

Guthrie, B., Saultz, J.W., Freeman, G.K., *et al.* 2008. Continuity of care matters. *BMJ*, 337, pp:a867. Doi: 10.1136/bmj.a867.

Guthrie, B., Makubate, B., Hernandez-Santiago, V., *et al.* 2015. The Rising Tide of Polypharmacy and Drug-Drug Interactions: Population Database Analysis 1995-2010. *BMC Medicine*, 13, pp:74. Doi:10.1186/s12916-015-0322-7

Haddaway, N.R., Grainger, M.J., Gray, C.T., *et al.* 2022. Citation chaser: a tool for transparent and efficient forward and backward citation chasing in systematic searching. *Research Synthesis Methods*, 13, pp:533-545. Doi: 10.1002/jrsm.1563

Haggerty, J.L., Roberge, D., Freeman, G.K., *et al.* 2013. Experienced continuity of care when patients see multiple clinicians: a qualitative metasummary. *Annals of Family Medicine*, 11, pp:262-271. Doi: 10.1370/afm.1499.

Hailey, V., Rojas-Garcia, A., Kassianos, A.P. 2022. A systematic review of behaviour change techniques used in interventions to increase physical activity among breast cancer survivors. *Breast Cancer*. Doi: 10.1007/s12282-021-01323-z.

Haith-Cooper, M., Waskett, C., Montague, J., *et al.* 2018. Exercise and physical activity in asylum seekers in Northern England; using the theoretical domains framework to identify barriers and facilitators. *BMC Public Health*, 18, pp:762. Doi: 10.1186/s12889-018-5692-2.

Ham, A.C., Swart, K.M.A., Enneman, A.W., *et al.* 2014. Medication-related fall incidents in an older, ambulant population: the B-PROOF study. *Drugs & Aging*, 31, pp:12. Doi: 10.1007/s40266-014-0225-x.



- Hamilton, H., Gallagher, P., Ryan, C., *et al.* 2011. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Archives of Internal Medicine*, 171, pp:1013-109. Doi: 10.1001/archinternmed.2011.215.
- Hanjani, L.S., Caffery, L.J., Freeman, C.R., *et al.* 2020a. A scoping review of the use and impact of telehealth medication reviews. *Research in Social and Administrative Pharmacy*, 16:1140-1153. Doi: 10.1016/j.sapharm.2019.12.014
- Hanjani, L.S., Bell, J.S., Freeman, C.R. 2020b. Undertaking medication review by telehealth. *Australian Journal of General Practice*. 2020;49:826-31. Doi: 10.31128/AJGP-06-20-5461
- Hanlon, J.T., Schmader, K.E., Samsa, G.P., *et al.* 1992. A method for assessing drug therapy appropriateness. *Journal of Clinical Epidemiology*, 45, pp:1045-1051. Doi: 10.1016/0895-4356(92)90144-c.
- Hanlon, J.T., Schmader, K.E. 2013. The Medication Appropriateness Index at 20: where it started, where it has been and where it may be going. *Drugs and Aging*, 30, pp:893-900. Doi: 10.1007/s40266-013-0118-4.
- Hanna, T., Bajorek, B., LeMay, K.S., *et al.* 2014. Using scenarios to test the appropriateness of pharmacist prescribing in asthma management. *Pharmacy Practice*, 12, pp:390.
- Hansen, C.R., Byrne, S., O'Mahony, D., *et al.* 2019. Qualitative analysis of community pharmacists' opinions on their involvement in reducing potentially inappropriate prescribing. *European Journal of Clinical Pharmacology*, 75, pp:265-74. Doi: 10.1007/s00228-018-2578-2
- Hardavella, G., Bjerg, A., Saad, N., *et al.* 2015. How to optimise patient and public involvement in your research. *Breathe*, 11, pp:223-7. Doi: 10.1183/20734735.007615
- Harris, J.E., Boushey, C., Bruemmer, B., *et al.* 2008. Publishing nutrition research: a review of nonparametric methods, part 3. *Research Perspectives in Practice*, 108, pp:1488-1496. Doi: 10.1016/j.jada.2008.06.426
- Harvey, G., Kitson, A., 2016. PARIHS revisited: from heuristic to integrated framework for the successful implementation for knowledge into practice. *Implementation Science*, 11, pp:13. Doi: 10.1186/s13012-016-0398-2
- Hawe, P., Shiell, A., Riley, T. 2004. Complex interventions: how "out of control" can a randomized controlled trial be? *BMJ*, 328, pp:1561-1563. Doi:10.1136/bmj.328.7455.1561

- Hayden, J.C., Parkin, R. 2020. The challenges of COVID-19 for community pharmacists and opportunities for the future. *Irish Journal of Psychological Medicine*, pp:1-6. Doi: 10.1017/ipm.2020.52
- Heale, R., Twycross, A. 2015. Validity and reliability in quantitative studies. *Evidence Based Nursing*, 18:66-67. Doi: 10.1136/eb-2015-102129
- Health Service Executive. 2013. *eHealth Strategy for Ireland*. Available at: <https://assets.gov.ie/16174/092e7c62f97b472b83cdb6dfdcd5c7.pdf> accessed 26/01/2022.
- Health Service Executive. 2016. *Framework for improving quality in our health service*. Available at: <https://www.hse.ie/eng/about/who/qid/framework-for-quality-improvement/framework-for-improving-quality-2016.pdf> accessed 26/01/2022.
- Health Service Executive. 2018a. *Long-term illness scheme*. Available at: <https://www2.hse.ie/services/long-term-illness-scheme/long-term-illness.html> accessed 23/08/2021
- Health Service Executive. 2018b. *GP visit cards*. Available at: <https://www2.hse.ie/services/gp-visit-cards/gp-visit-cards.html> accessed 23/08/2021
- Health Service Executive. 2020a. *Information guide to HSE primary care hospital services for persons who contracted Hepatitis C through the administration within the State of contaminated blood or blood products, arrangements for the provision of services 2020*. Available at: <https://www.hse.ie/eng/national-hepatitis-c-treatment-programme/haa-information-guide.pdf> accessed 21/07/2022
- Health Service Executive. 2020b. *Coronavirus COVID-19 Cocooning Public Health Advice*. Available at: <https://www.hse.ie/eng/services/news/newsfeatures/covid19-updates/partner-resources/a-guide-to-cocooning-easy-read-.pdf> accessed 27/01/2022
- Hébert, J., Laliberté, M-C., Berbiche, D., *et al.* 2013. The willingness of community pharmacists to participate in a practice-based research network. *Canadian Pharmacists Journal*, 146, pp:47-54. Doi: 10.1177/1715163512473240
- Heinrich, C.H., Donovan, M.D. 2022. Assessing community pharmacists' attitudes towards identifying opportunities for deprescribing in clinical practice in Ireland. *International Journal of Pharmacy Practice*, 30, pp:28-35. Doi:10.1093/ijpp/riab079

Helfrich, C.D., Damschroder, L.J., Hagedorn, H.J., *et al.* 2010. A critical synthesis of literature on the promoting action on research implementation in health services (PARIHS) framework. *Implementation Science*, 5, pp:82.

Henman, M.C., 2020. Primary health care and community pharmacy in Ireland: a lot of visions but little progress. *Pharmacy Practice (Granada)*, 18, pp:2224.

Doi:10.185499/PharmPract.2020.4.2224.

Hennelly, N., Lalor, G., Gibney, S., *et al.* 2021. A cross-sectional study of the relationship between delayed healthcare utilisation and chronic conditions among older adults during the COVID-19 pandemic in Ireland [version 1; peer review: 1 approval]. *HRB Open Research*, 4, pp:112. Doi: 10.12688/hrbopenres.13336.1

Herdman, M., Gudex, C., Lloyd, A., *et al.* 2011. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research*, 20, pp:1727-36. Doi: 10.1007/s11136-011-9903-x.

Hernandez, G., Garin, O., Pardo, Y., *et al.* 2018. Validity of the EQ-5D-5L and reference norms for the Spanish population. *Quality of Life Research*, 27:2337-2348. Doi: 10.1007/s11136-018-1877-5.

Herrera, A.P., Snipes, S.A., King, D.W., *et al.* 2010. Disparate inclusion of older adults in clinical trials: priorities and opportunities for policy and practice change. *American Journal of Public Health*, 100, pp:S105-12. Doi: 10.2105/AJPH.2009.162982

Hirschhorn, L.R., Talbot, J.R., Irwin, A.C., *et al.* 2013. From scaling up to sustainability in HIV: potential lessons for moving forward. *Globalization and Health*, 9:57

Hoare, P. 2022. Dedicated pharmacy school is needed to avert community pharmacy 'crisis'. *Irish Examiner*. 14<sup>th</sup> February. Available at: <https://www.irishexaminer.com/news/arid-40807341.html> accessed 23/08/2022

Hoddinott, P., Pollock, A., O'Cathain, A. *et al.* 2018. How to incorporate patient and public perspectives into the design and conduct of research. *F1000 Research*, 18, pp:752. Doi: 10.12688/f1000research.15162.1.

Hoisnard, L., Santos-Eggimann, B., Chauvin, P., *et al.* 2019. Do older adults know the purpose of their medications? A survey among community-dwelling people. *European Journal of Clinical Pharmacology*, 75, pp:255-63. Doi: 10.1007/s00228-018-2575-5

- Holden, R.J., Carayon, P., Gurses, A.P., *et al.* 2013. SEIPS 2.0: a human factors framework for studying and improving the work of healthcare professionals and patients. *Ergonomics*, 56, pp:1669-1686. Doi: 10.1080/00140139.2013.838643.
- Holt, S., Schmiedl, S., Thürman, P.A. 2010. Potentially inappropriate medications in the elderly: the PRISCUS list. *Deutsches Ärzteblatt International*, 107, pp:543-551. Doi: 10.3238/arztebl.2010.0543
- Homeniuk, R., Collins, C. 2021. How COVID-19 has affected general practice consultations and income: general practitioner cross-sectional population survey evidence from Ireland. *BMJ Open*, 11, pp:e044685. Doi: 10.1136/bmjopen-2020-044685
- Horner, G., Daddona, J., Burke, D.J., *et al.* 2019. "You're kind of at war with yourself as a nurse": perspectives of inpatient nurses on treating people who present with a comorbid opioid use disorder. *PLoS One*, 14, pp:e0224335. Doi: 10.1371/journal.pone.0224335
- Houses of the Oireachtas. 2017. Committee on the Future of Healthcare: Sláintecare Report. Available at: <https://assets.gov.ie/22609/e68786c13e1b4d7daca89b495c506bb8.pdf> accessed 25/10/20 [checked 26/08/2022]
- Howlett, N., Trivedi, D., Troop, N.A., *et al.* 2019. Are physical activity interventions for healthy inactive adults effective in promoting behaviour change and maintenance, and which behaviour change techniques are effective? A systematic review and meta-analysis. *TBM*, 9:147-157. Doi: 10.1093/tbm/iby010
- Huang, C., Wang, Y., Li, X., *et al.* 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*, 395, pp:497-506. Doi: 10.1016/S0140-6736(20)30183-5
- Hudson, E., Nolan, A. 2015. Public healthcare eligibility and the utilization of GP services by the older population in Ireland. *Journal of the Economics of Ageing*, 6, pp:24-43. Doi: 10.1016/j.jeoa.2014.08.005
- Hughes, L.D., McMurdo, M.E.T., Guthrie, B. 2013. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. *Age and Ageing*, 42, pp:62-69. Doi: 10.1093/ageing/afs100
- Hughes, J.E., Russo, V., Walsh, C., *et al.* 2020. Prevalence and factors associated with potential drug-drug interactions in older community-dwelling adults: a prospective cohort study. *Drugs & Aging*, 38, pp:1025-37. Doi: 10.1007/s40266-021-009-898-8

- Huijg, J.M., Gebhardt, W.A., Crone, M.R. *et al.* 2014. Discriminant content validity of a theoretical domains framework questionnaire for use in implementation research. *Implementation Science*, 9, pp:11.
- Hussein, R., Whaley, C.R.J., Lin, E.C.J., *et al.* 2021. Identifying barriers, facilitators and behaviour change techniques to the adoption of the full scope of pharmacy practice among pharmacy professionals: using the theoretical domains framework. *Research in Social and Administrative Pharmacy*, 17, pp:1396-406. Doi: 10.1016/j.sapharm.2020.10.003
- Hutchinson, A. 2015. Ireland. In: Kringos, D.S., Boerma, W.G.W., Hutchinson, A., *et al.* (eds). *Building primary care in a changing Europe: Case studies*. World Health Organization, United Kingdom Available at: <https://www.ncbi.nlm.nih.gov/books/NBK459019/?report=reader> accessed 25/10/2020 [checked 26/08/2022]
- Ibrahim, A.S.H., Barry, H.E., Hughes, C.M. 2022. General practitioners' experiences with, views of, and attitudes towards, general practice-based pharmacists: a cross-sectional survey. *BMC Primary Care*, 23, pp:6. Doi: 10.1186/s12875-021-01607-5
- Ilardo, M.L., Speciale, A. 2020. The community pharmacist: perceived barriers and patient-centered care communication. *International Journal of Environmental Research and Public Health*, 17, pp:536. Doi:10.3390/ijerph17020536
- Imfeld-Isenegger, T.L., Soares, B.I., Makovec, U.N., *et al.* 2020. Community pharmacist-led medication review procedures across Europe: characterization, implementation and remuneration. *Research in Social and Administrative Pharmacy*, 16, pp:1057-66. Doi: 10.1016/j.sapharm.2019.11.002
- Ims, E.-O., Chee, W. 2011. Quota sampling in internet research. *Computers Informatics Nursing*, 29:381-385. Doi: 10.1097/NCN.0b013e3181f9dc45
- Inch, J., Notman, F., Bond, C.M., *et al.* 2019. The Care Home Independent Prescribing Pharmacist Study (CHIPPS)-a non-randomised feasibility study of independent pharmacist prescribing in care homes. *Pilot and Feasibility Studies*, 5, pp:89. Doi: 10.1186/s40814-019-0465-y
- Innes, K., Cotton, S., Campbell, M.K., *et al.* 2018. Relative importance of informational items in participant information leaflets for trials: a Q-methodology approach. *BMJ Open*, 8:e023303. Doi: 10.1136/bmjopen-2018-023303

International Conference on Harmonisation. No date. Available at: [www.ich.org](http://www.ich.org) Accessed 23/12/23

INVOLVE. 2012. *Briefing notes for researchers: involving the public in NHS, public health and social care research*. Available at: [https://www.invo.org.uk/wp-content/uploads/2014/11/9938\\_INVOLVE\\_Briefing\\_Notes\\_WEB.pdf](https://www.invo.org.uk/wp-content/uploads/2014/11/9938_INVOLVE_Briefing_Notes_WEB.pdf) accessed 25/02/23

Irish College of General Practitioners Quick Reference Guide (ICGPQRG). 2020. Medication review – A guide for GPs. Dublin: ICGP.

Irish Pharmacy Union. 2018. Vision for community pharmacy in Ireland. [online] Available at: [https://ipu.ie/wp-content/uploads/2018/04/PwC\\_IPU-report.pdf](https://ipu.ie/wp-content/uploads/2018/04/PwC_IPU-report.pdf) accessed 16/02/2021

Irish Pharmacy Union. 2019a. Perspective of community pharmacy. [online] Available at: <https://ipu.ie/wp-content/uploads/2014/11/IPU-Community-Pharmacy-Consultancy-Report.pdf> accessed 17/02/2021

Irish Pharmacy Union. 2019b. Pharmacy Usage & Attitudes Survey. [online] Available at: <https://banda.ie/wp-content/uploads/Pharmacy-Usage-and-Attitudes-Survey-IPU-BA-2019.pdf> accessed 17/02/2021

Jackson, T., Pinnock, H., Liew, S.M., *et al.* 2020. Patient and public involvement in research: from tokenistic box ticking to valued team members. *BMC Medicine*, 18, pp:79. Doi: 10.1186/s12916-020-01544-7

Jacobs, J.M., Walsh, E.A., Rapoport, C.S., *et al.* 2021. Development and refinement of a telehealth intervention for symptom management, distress, and adherence to adjuvant endocrine therapy after breast cancer. *Journal of Clinical Psychology in Medical Settings*, 28, pp:603-618. Doi: 10.1007/s10880-020-09750-4.

Jäger, C., Freund, T., Steinhäuser, J., *et al.* 2017. Impact of a tailored program on the implementation of evidence-based recommendations for multimorbid patients with polypharmacy in primary care practices - results of a cluster-randomized controlled trial. *Implementation Science*, 12, pp:8.

Jager, J., Putnick, D.L., Bornstein, M.H., 2017. More than just convenient: the scientific merits of homogeneous convenience samples. *Monographs of the Society for Research in Child Development*, 82, pp:13-30. Doi: 10.1111/mono.12296

- Jamal, F., Fletcher, A., Shackelton, N., *et al.* 2015. The three stages of building and testing mid-level theories in a relevant RCT: a theoretical and methodological case-example. *Trials*, 16, pp:466. Doi: 10.1186/s13063-015-0980-y
- Janssen, M.F., Bonsel, G., Luo, N. 2018. Is EQ-5D-5L better than EQ-5D-3L? A head-to-head comparison of descriptive systems and value sets from seven countries. *Pharmacoeconomics*, 36, pp:675-697. Doi: 10.1007/s40273-018-0623-8.
- Jennings, E.L.M., O'Mahony, D., Gallagher, P.F. 2021. Medication-related quality of life (MRQoL) in ambulatory older adults with multimorbidity and polypharmacy. *European Geriatric Medicine*. Doi: 10.1007/s41999-021-00573-6
- Jensen, L.D., Andersen, O., Hallin, M., *et al.* 2014. Potentially inappropriate medication related to weakness in older acute medical patients. *International Journal of Clinical Pharmacy*, 36, pp:570-580. Doi: 10.1007/s11096-014-9940-y.
- Jindai, K., Nielson, C.M., Vorderstrasse, B.A., *et al.* 2016. Multimorbidity and functional limitations among adults 65 or older, NHANES 2005-2021. *Preventing Chronic Disease*, 13, pp:e151. Doi: 10.5888/pcd13.160174.
- Jivraj, S., Goodman, A., Pongiglione, B., *et al.* 2020. Living longer but not necessarily healthier: the joint progress of health and mortality in the working-age population of England. *Population Studies*, 74, pp:399-414. Doi: 10.1080/00324728.2020.1767297.
- Johnston, M.C., Crilly, M., Black, C., *et al.* 2019. Defining and measuring multimorbidity: a systematic review of systematic reviews. *European Journal of Public Health*, 29, pp:182-189. Doi: 10.1093/eurpub/cky098
- Jones EW. 2015. How summary care records can improve patient safety. *Emerging Nurse*, 23, pp:20-2. Doi: 10.7748/en.23.1.20.s27.
- Jones, G. 2018a. Raising the profile of pilot and feasibility studies in relation to the development, evaluation and implementation of patient-reported outcome measures. *Pilot and Feasibility Studies*, 4:3. Doi: 10.1186/s40814-017-0151-x
- Jones, L.F., Owens, R., Sallis, A., *et al.* 2018. Qualitative study using interviews and focus groups to explore the current and potential for antimicrobial stewardship in community pharmacy informed by the Theoretical Domains Framework. *BMJ Open*, 8, pp:e025101. Doi: 10.1136/bmjopen-2018-025101

- Josendal, A.V., Bergmo, T.S., Granas, A.G. 2021. Implementation of a shared medication list in primary care – a controlled pre-post study of medication discrepancies. *BMC Health Services Research*, 21, pp:1335. Doi: 10.1186/s12913-021-07346-8
- Joy, M., McGagh, D., Jones, N., *et al.* 2020. Reorganisation of primary care for older adults during COVID-19: a cross-sectional database study in the UK. *British Journal of General Practice*, 70, pp:e547. Doi: 10.3399/bjgp20x710933
- Kallio, S., Eskola, T., Pohjanoksa-Mäntylä, M., *et al.* 2020. Medication risk management in routine dispensing in community pharmacies. *International Journal of Environmental Research and Public Health*, 17, pp:8186. Doi: 10.3390/ijerph17218186
- Kallio, S., Eskola, T., Airaksinen, M., *et al.* 2021. Identifying gaps in community pharmacist's competence in medication risk management in routine dispensing. *Innovations in Pharmacy*, 12, pp:8. Doi: 10.24926/iip.v12i1.3510
- Kang, M.-G., Kang, C.-H., Lee, H., *et al.* 2020. A medical care model using comprehensive geriatric assessment for community-dwelling older Korean adults. *Archives of Gerontology and Geriatrics*, 89, pp:104064. Doi: 10.1016/j.archger.2020.104064
- Karandikar, Y.S., Chaudhari, S.R., Dalal, M., *et al.* 2013. Inappropriate prescribing in the elderly: a comparison of two validated screening tools. *Journal of Clinical Gerontology and Geriatrics*, 4, pp:109-114. Doi: 10.1016/j.jcgg.2013.04.004
- Karlsson, P., Bergmark, A. 2015. Compared with what? An analysis of control-group types in Cochrane and Campbell reviews of psychosocial treatment efficacy with substance use disorders. *Addiction*, 110, pp:420-428. Doi: 10.1111/add.12799
- Katusiime, B., Corlett, S.A., Krska, J. 2018. Development and validation of a revised instrument to measure burden of long-term medicines use: the Living with Medicines Questionnaire version 3. *Patient Related Outcome Measures*, 9:155-1568. Doi: 10.2147/PROM.S151143
- Kaufmann, C.P., Tremp, R., Hersberger, K.E., *et al.* 2014. Inappropriate prescribing: a systematic overview of published assessment tools. *European Journal of Clinical Pharmacology*, 70, pp:1-11. Doi: 10.1007/s00228-013-1575-8
- Kaufman, G. 2016. Identifying polypharmacy in the primary care setting. *Practice Nursing*, 27, pp:28-33. Doi: 10.12968/pnur.2016.27.1.28



- Kaur, S., Mitchell, G., Vitetta, L., *et al.* 2009. Interventions that can reduce inappropriate prescribing in the elderly. *Drugs and Ageing*, 26, pp:1013-1028. Doi: 10.2165/11318890-000000000-00000.
- Keesara, S., Jonas, A., Schulman, K. 2020. Covid-19 and health care's digital revolution. *The New England Journal of Medicine*, 382, pp:e82. Doi: 10.1056/NEJMp2005835
- Kelley, K., Preacher, K.J. 2012. On effect size. *Psychological Methods*, 17, pp:137-152. Doi: 10.1037/a0028086
- Kenny, C., Dalton, K. 2021. Community pharmacists' views on the implementation of a national electronic prescription transfer system to pharmacies. *International Journal of Clinical Pharmacy*, 43, pp:1736. Doi: 10.1007/s11096-021-01352-w
- Khatri, C., Chapman, S.J., Glasby, J., *et al.* 2015. Social media and internet driven study recruitment: evaluating a new model for promoting collaborator engagement and participation. *PLoS One*, 10, pp:e0118899. Doi: 10.1371/journal.pone.0118899.
- Khera, S., Abbasi, M., Dabravolskaj, J., *et al.* 2019. Appropriateness of medications in older adults living with frailty: impact of a pharmacist-led structured medication review process in primary care. *Journal of Primary Care and Community Health*, 10, pp:1-8. Doi: 10.1177/2150132719890227
- Khezrian, M., McNeil, C.J., Murray, A.D., *et al.* 2020. An overview of prevalence, determinants and health outcomes of polypharmacy. *Therapeutic Advances in Drug Safety*, 11, pp:1-10. Doi: 10.1177/2042098620933741
- Kim, Y.H., Yoo, K.H., Yoo, J.H. *et al.* 2017. The need for a well-organised, video-assisted asthma education program at Korean primary care clinics. *Tuberculosis & Respiratory Diseases*, 80:169-178. Doi: 10.4046/trd.2017.80.2.169
- Kingston, A., Robinson, L., Booth, H., *et al.* 2018. Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model. *Age and Ageing*, 47, pp:374-380. Doi: 10.1093/ageing/afx201.
- Kinoshita, S., Cortright, K., Crawford, A., *et al.* 2020. Changes in telepsychiatry regulations during the COVID-19 pandemic: 17 countries and regions' approaches to an evolving healthcare landscape. *Psychological Medicine*, pp:1-8. Doi: 10.1017/S0033291720004584
- Kistin, C., Silverstein, M. 2015. Pilot studies: a critical but potentially misused component of interventional research. *JAMA*, 314:1561-1562. Doi: 10.1001/jama.2015.10962

- Kitson, A., Harvey, G., McCormack, B. 1998. Enabling the implementation of evidence based practice: a conceptual framework. *Quality in Health Care*, 7, pp:149-158. Doi: 10.1136/qshc.7.3.149.
- Kitson, A., Harvey, G. 2016. Methods to succeed in effective knowledge translation in clinical practice. *Journal of Nursing Scholarship*, 48, pp:294-302. Doi: 10.1111/jnu.12206
- Kivunja, C. 2018. Distinguishing between theory, theoretical framework, and conceptual framework: a systematic review of lessons from the field. *International Journal of Higher Education*, 7, pp:6. Doi: 10.5430/ijhe.v7n6p44
- Korenvain, C., MacKeigan, L.D., Dainty, K.N., *et al.* 2020. Exploring deprescribing opportunities for community pharmacists using the Behaviour Change Wheel. *Research in Social and Administrative Pharmacy*, 16, pp:1746-53. Doi: 10.1016/j.sapharm.2020.01.019.
- Kotronoulas, G., Cooper, M., Johnston, B. 2019. Core Patient-Reported Outcomes (PROs) and PRO Measures (PROMs) for polypharmacy medicines reviews: a sequential mixed-methods study. *Patient Preference and Adherence*, 13:2071-2087. Doi: 10.2147/PPA.S236122
- Kozma, C.M., Reeder, C.E., Schulz, R.M., 1993. Economic, clinical and humanistic outcomes: a planning model for pharmaco-economic research. *Clinical Therapeutics*, 15, pp:1121-1132.
- Krahn, G.L., Horner-Johnson, W., Hall, T.A., *et al.* 2014. Development and psychometric assessment of the function-neutral health-related quality of life measure. *American Journal of Physical Medicine & Rehabilitation*, 93:56-74. Doi: 10.1097/PHM.0b13e3182a517e6.
- Krithikadatta, J. 2014. Normal distribution. *Journal of Conservative Dentistry*, 17:96-97. Doi: 10.4103/0972-0707.124171
- Krueger, R.A., Casey, M.A. 2000. *Focus groups: a practical guide for applied researchers*. 3<sup>rd</sup> edn. Thousand Oaks, California: SAGE.
- Krska, J., Morecroft, C.W., Poole, H., *et al.* 2013. Issues potentially affecting quality of life arising from long-term medicines use: a qualitative study. *International Journal of Clinical Pharmacy*, 35:1161-1169. Doi: 10.1007/s11096-013-9841-5
- Krska, J., Morecroft, C.W., Rowe, P.H., *et al.* 2014. Measuring the impact of long-term medicines use from the patient perspective. *International Journal of Clinical Pharmacy*, 36, pp:675-678. Doi: 10.1007/s11096-014-9970-5.

- Krska, J., Katusiime, B., Corlett, S.A. 2017. Validation of an instrument to measure patients' experiences of medicine use: the Living with Medicines Questionnaire. *Patient Preference and Adherence*, 11, pp:671-679. Doi: 10.2147/PPA.S126647
- Kunstier, B.E., Lennox, A., Bragge, P. 2019. Chasing prescribing behaviours with educational outreach: an overview of evidence and practice. *BMC Medical Education*, 19, pp:311. Doi: 10.1186/s12909-019-1735-3
- Kuper, A., Lingard, L., Levinson, W. 2008. Critically appraising qualitative research. *BMJ*, 337, pp:a1035. Doi: 10.1136/bmj.a1035
- Kurczewska-Michalak, M., Lewek, P., Jankowska-Polńska, B., *et al.* 2021. Polypharmacy management in the older adults: a scoping review of available interventions. *Frontiers in Pharmacology*, 12, pp:734045. Doi: 10.3389/fphar.2021.734045
- Kvale, S. 2007. *Doing interviews*. Thousand Oaks, California: Sage.
- Lafuente Gonzalez, M., Ferrit Martin, M., De Amezua, F.O.C., *et al.* 2015. PS-069 Potentially inappropriate medications in primary care older patients in Toledo (Spain): the stop-start criteria compared with the beers criteria. *European Journal of Hospital Pharmacy*, 22, pp:a163.
- Lange, R.T. 2011. Inter-rater reliability. In: Kreutzer JS, DeLuca J, Caplan B (eds). *Encyclopedia of Clinical Neuropsychology*. New York, NY: Springer. Doi: 10.1007/978-0-387-79948-3
- Langford, A.V., Gnjidic, D., Lin, C-W. C., *et al.* 2021. Challenges of opioid deprescribing and factors to be considered in the development of opioid deprescribing guidelines: a qualitative analysis. *BMJ Quality & Safety*, 30, pp:133-140. Doi: 10.1136/bmjqs-2020-010881
- Lam, M.P.S., Cheung, B.M.Y. 2012. The use of STOPP/START criteria as a screening tool for assessing the appropriateness of medications in the elderly population. *Expert Review of Clinical Pharmacology*, 5:187-197. Doi: 10.1586/ecp.12.6
- Larkin, J., Pericin, I., Collins, M., *et al.* 2021. GPs' perceptions of their relationship with the pharmaceutical industry: a qualitative study. *BJGP Open*, 5, pp:BJGPO.2021.0057. Doi: 10.3399/BJGPO.2021.0057.
- Laroche, M.L., Charmes, J.P., Merle, L. 2007. Potentially inappropriate medications in the elderly: a French consensus panel list. *European Journal of Clinical Pharmacology*, 63, pp:725-731. Doi: 10.1007/s00228-007-0324-2.

Lavis, J., Davies, H., Oxman, A., *et al.* 2005. Towards systematic reviews that inform healthcare management and policy-making. *Journal of Health Services Research and Policy*, 10, pp:35-48. Doi: 10.1258/1355819054308549.

Lavan, A.H., Gallagher, P., Parsons, C., *et al.* 2017. STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy): consensus validation. *Age and Ageing*, 46, pp:600-607. Doi: 10.1093/ageing/afx005.

Law, M.R., Ma, T., Fisher, J., *et al.* 2012. Independent pharmacist prescribing in Canada. *Canadian Pharmacists Journal*, 145, pp:17-23. Doi: 10.382/1913-701X-145.1.17

Lawoyin, T.O., Lawoyin, O.O. 2013. Translation of research into reality in sub-Saharan Africa. *Lancet*, 381:2146-2147. Doi: 10.106/S0140-6736(13)60601-7.

Lawton, R., Heyhoe, J., Louch, G., *et al.* 2016. Using the Theoretical Domains Framework (TDF) to understand adherence to multiple evidence-based indicators in primary care: a qualitative study. *Implementation Science*, 11, pp:113. Doi:10.1186/s13012-016-0479-2.

Laycock, A., Harvey, G., Percival, N., *et al.* 2018. Application of the i-PARIHS framework for enhancing understanding of interactive dissemination to achieve wide-scale improvement in Indigenous primary healthcare. *Health Research Policy and Systems*, 16, pp:117. Doi: 10.1186/s12961-018-0392-z

Leather, J.Z., Keyworth, C., Kapur, N., *et al.* 2022. Examining drivers of self-harm guideline implementation by general practitioners: a qualitative analysis using the theoretical domains framework. *British Journal of Health Psychology*, 00:1-21. Doi: 10.1111/bjhp.12598

Lech, L.V.J., Jónsdóttir, E.D., Niclasen, J., *et al.* 2020. Translation and psychometric validation of a Danish version of the medication-related quality of life scale. *International Journal of Clinical Pharmacology*, 42:667-676. Doi: 10.1007/s11096-020-00979-5.

LeCompte, M.D., Goetz, J.P. 1982. Problems of reliability and validity in ethnographic research. *Review of Educational Research*, 52, pp:31-60. Doi: 10.3102/00346543052001031

Lee, M.K., Sauver, J.L.S., Anderson, R.T., *et al.* 2021. Confirmatory factor analyses and differential item functioning of the Patient Experience with Treatment and Self-management (PETS vs2.0): a measure of treatment burden. *Patient Related Outcome Measures*, 11:249-263. Doi: 10.2147/PROM.S282728.

- Lenander, C., Bondesson, Å., Viberg, N., *et al.* 2018. Effects of medication reviews on use of potentially inappropriate medications in elderly patients; a cross-sectional study in Swedish primary care. *BMC Health Services Research*, 18, pp:616. Doi: 10.1186/s12910-018-3425-y.
- Leon, A.C., Davis, L.L., Kraemer, H.C. 2011. The role and interpretation of pilot studies in clinical research. *Journal of Psychiatric Research*, 45:626-629. Doi: 10.1016/j.jpsychires.2010.10.008
- Leppink, J. 2017. Revisiting the quantitative-qualitative mixed methods labels: research questions, developments, and the need for replication. *Journal of Taibah University Medical Sciences*, 12, pp:97-101. Doi: 10.1016/j.jtumed.2016.11.008
- Le Reste, J.Y., Nabbe, P., Mancasu, B., *et al.* 2013. The European General Practice Research Network presents a comprehensive definition of multimorbidity in family medicine and long term care, following a systematic review of relevant literature. *Journal of the American Medical Directors Association*, 14, pp:319-325. Doi: 10.1016/j.jamda.2013.01.001.
- Le Roith, D., Biessels, C.J., Braithwaite, S.S., *et al.* 2019. Treatment of diabetes in older adults: an endocrine society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism*. 104, pp:1520-1574. Doi: 10.1210/jc.2019-00198.
- Leung, F-H., Savithiri, R., 2009. Spotlight on focus groups. *Canadian Family Physician*, 55, pp:218-9.
- Lewis, T., 2004. Using the NO TEARS tool for medication review. *BMJ*, 329, pp:434. Doi: 10.1136/bmj.329.7463.434
- Lexow, M., Wernecke, K., Sultzer, R., *et al.* 2022. Determine the impact of a structured pharmacist-led medication review – a controlled intervention study to optimize medication safety for residents in long-term care facilities. *BMC Geriatrics*, 22, pp:307. Doi: 10.1186/s12877-022-03025-3.
- Li, J.S., Blake, V., George, S., *et al.* 2020. Formation of a statewide community pharmacy practice-based research network: pharmacist opinions on research participation and engagement. *Journal of the American Pharmacists Association*, 60, pp:951-6. Doi: 10.1016/j.japh.2020.07.008
- Liacos, M., Page, A.T., Etherton-Beer, C. 2020. Deprescribing in older people. *Australian Prescriber*, 43, pp: 114-20. Doi: 10.18773/austprescr.2020.033

- Liberato, A.C.S., São João, T.M., Jannuzzi, F.F., *et al.* 2020. Treatment Satisfaction Questionnaire for Medication (TSQM version 1.4): ceiling floor effects, reliability, and known-group validity in Brazilian outpatients with hypertension. *Value in Health Regional Issues*, 23:150-156. Doi: 10.1016/j.vhri.2020.07.578
- Liu, H., Muhunthan, J., Hayek, A., *et al.* 2016. Examining the use of process evaluations of randomized controlled trials of complex interventions addressing chronic disease in primary health care -a systematic review protocol. *Systematic Reviews*, 5:138. Doi: 10.1186/s13643-016-0314-5
- Liu, Y.L., Chu, L.L., Su, H.C. *et al.* 2019. Impact of computer-based and pharmacist-assisted medication review initiated in the emergency department. *Journal of the American Geriatrics Society*, 67, pp:2298-304. Doi: 10.1111/jgs.16078.
- Lohr, A.L. 2010. Sampling design and analysis. Boston, MA: Cengage Learning
- Loucks, J., Yost, S., Kaplan, B. 2015. An introduction to basic pharmacokinetics. *Transplantation*, 99, pp:903-7. Doi: 10.1097/TP.0000000000000754
- Lowthian, J.A., Lennox, A., Curtis, A., *et al.* 2018. Hospitals and patients WoRking in Unity (HOW R U?): Telephone peer support to improve older patients' quality of life after emergency department discharge in Melbourne, Australia – A multicentre prospective feasibility study. *BMJ Open*, 8, pp:e020321. Doi:10.1136/bmjopen-2017-020321.
- Luca, C.E., Cavicchioli, A., Bianchi, M. 2021. Nurses who assume the role of advocate for older hospitalized patients: a qualitative study. *SAGE Open Nursing*, 7, pp:1-14. Doi: 10.1177/23779608211030651
- Luke, M.J., Krupetsky, N., Liu, H., *et al.* 2021. Pharmacists as personalized medicine experts (PRIME): experiences implementing pharmacist-led pharmacogenomic testing in primary care practices. *Pharmacy*, 9, pp:201. Doi: 10.3390/pharmacy9040201
- Lun, P., Law, F., Ho, E., *et al.* 2021. Optimising prescribing practices in older adults with multimorbidity: a scoping review of guidelines. *BMJ Open*, 11, pp:e049072. Doi: 10.1136/bmjopen-2021-049072
- Ly, A., Zemek, R., Wright, B., *et al.* 2021. "What is the actual goal of the pathway?": examining emergency department physician and nurse perspectives on the implementation of a pediatric concussion pathway using the theoretical domains framework. *BMC Health Services Research*, 21, pp:119. Doi: 10.1186/s12913-021-06110-2

- Lycett, H.J., Raebel, E.M., Wildman, E.K., *et al.* 2018. Theory-based digital interventions to improve asthma self-management outcomes: systematic review. *Journal of Medical Internet Research*, 20, pp:e293. Doi: 10.2196/jmir.9666
- Lynch, E.A., Mudge, A., Knowles, S., *et al.* 2018. "There is nothing so practical as a good theory": a pragmatic guide for selecting theoretical approaches for implementation projects. *BMC Health Services Research*, 18, pp:857. Doi: 10.1186/s12913-018-3671-z
- Lynch, T., Ryan, C., Hughes, C.M., *et al.* 2020. Brief interventions targeting long-term benzodiazepine and Z-drug use in primary care: a systematic review and meta-analysis. *Addiction*, 115, pp:1618-1639. Doi:10.1111/add.14981.
- Maarsingh, O.R., Henry, Y., van de Ven, P., *et al.* 2016. Continuity of care in primary care and association with survival in older people: a 17-year prospective cohort study. *British Journal of General Practice*, 66, pp:e531-539. Doi: 10.3399/bjgp16X686101
- Mackey, A., Gass, S. 2005. Second language research: methodology and design. New Jersey: Lawrence Erlbaum Associates, Inc.
- Maher, R.L., Hanlon, J.T., Hajjar, E.R., *et al.* 2014. Clinical consequences of polypharmacy in elderly. *Expert Opinion on Drug Safety*, 13. Doi: 10.1517/14740338.2013.827660.
- Mair, A., Antoniadou, E., Hendry, A., *et al.* 2021. Appropriate polypharmacy: a barometer for integrated care. *Journal of Integrated Care*, 29, pp:204-14. Doi: 10.1108/JICA-04-2020-0019
- Makovski, T.T., Schmitz, S., Zeegers, M.P., *et al.* 2019. Multimorbidity and quality of life: systematic literature review and meta-analysis. *Ageing Research Reviews*, 53, pp:100903. Doi: 10.1016/j.arr.2019.04.005
- Malmqvist, J., Hellberg, K., Möllås, G., *et al.* 2019. Conducting the pilot study: a neglected part of the research process? Methodological findings supporting the importance of piloting in qualitative research studies. *International Journal of Qualitative Methods*, 18, pp:1-11. Doi:10.1177/1609406919878341.
- Maravelakis P. 2019. The use of statistics in social sciences. *Journal of Humanities and Applied Social Sciences*, 1, pp:87-97. Doi: 10.1108/JHASS-08-2019-0038
- Marten, O., Brand, L., Greiner, W. 2021. Feasibility of the EQ-5D in the elderly population: a systematic review of the literature. *Quality of Life Research*, 31, pp:1621-1637. Doi: 10.1007/s11136-021-03007-9

- Maskrey, M., Johnson, C.F., Cormack, J., *et al.* 2018. Releasing GP capacity with pharmacy prescribing support and new ways of working: a prospective observational cohort study. *British Journal of General Practice*, 68, pp:e735 Doi: 10.3399/bjgp18X699137
- Masnoon, N., Shakib, S., Kalisch-Ellett, L., *et al.* 2017. What is polypharmacy? A systematic review of definitions. *BMC Geriatrics*, 17, pp:230. Doi:10.1186/s12877-017-0621-2
- Masnoon, N., Shakib, S., Kalisch-Ellett, L., *et al.* 2018. Tools for assessment of the appropriateness of prescribing and association with patient-related outcomes: a systematic review. *Drugs and Aging*, 35, pp:43-60. Doi: 1007/s40266-018-0516-8
- May, C., Finch, T., 2009. Implementing, embedding, and integrating practices: an outline of normalization process theory. *Sociology*, 43, pp:535-554. Doi: 10.1177/0038038509103208
- McCarron J. 2022. Treatment benefit scheme for dental works, hearing aids and glasses extended by 80,000 people. *The Journal*. 30<sup>th</sup> May. Available at: <https://www.thejournal.ie/treatment-benefit-young-prsi-5777881-May2022/> accessed 23/07/2022
- McCarthy, C., Clyne, B., Boland, F., *et al.* 2022. GP-delivered medication review of polypharmacy, deprescribing, and patient priorities in older people with multimorbidity in Irish primary care (SPPiRE Study): a cluster randomised controlled trial. *PLoS Medicine*, 19, pp:e1003862. Doi: 10.1371/journal.pmed.1003862
- McCombe, G., Conneally, N., Harold, A., *et al.* 2019. How does the introduction of free GP care for children impact on GP service provision? A qualitative study of GPs. *Irish Journal of Medical Science*, 188, pp:1245-1249. Doi: 10.1007/s11845-019-01997-7.
- McCormick, P., Chennells, R., Coleman, B., *et al.* 2020. The outcome of domiciliary medication reviews and their impact: a systematic review. *International Journal of Pharmacy Practice*, 28, pp:417-427. Doi: 10.1111/ijpp.12649
- McGill, E., Marks, D., Er, V., *et al.* 2020. Qualitative process evaluation from a complex systems perspective: a systematic review and framework for public health evaluators. *PLoS Medicine*, 17, pp:e1003368. Doi: 10.1371/journal.pmed.1003368
- McGowan, L.J., Powell, R., French, D.P. 2020. How can use of the theoretical domains framework be optimized in qualitative research? A rapid systematic review. *British Journal of Health Psychology*, 25, pp:677-94. Doi: 10.1111/bjhp.12437



- McGrath, C., Palmgren, P.J., Liljedahl, M. 2018. Twelve tips for conducting qualitative research interviews. *Medical Teacher*, 41, pp:1002-6. Doi: 10.1080/0142159X.2018.1497149
- McHugh, S., Sinnott, C., Racine, E., *et al.* 2018. 'Around the edges': using behaviour change techniques to characterize a multilevel implementation strategy for a fall prevention programme. *Implementation Science*, 13, pp:113. Doi: 10.1186/s13012-018-0798-6.
- McKeigue, P.M., Kennedy, S., Weir, A., *et al.* 2021. Relation of severe COVID-19 to polypharmacy and prescribing of psychotropic drugs: the REACT-SCOT case-control study. *BMC Medicine*, 19, pp:51. Doi: 10.1186/s12916-021-01907-8
- McLeod, P.J., Huang, A.R., Tamblyn, R.M., *et al.* 1997. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. *Canadian Medical Association Journal*, 156, pp:385-391.
- McMahon, C.G., Cahir, C.A., Kenny, R.A., *et al.* 2014. Inappropriate prescribing in older fallers presenting to an Irish emergency department. *Age and Ageing*, 43, pp:44-50. Doi: 10.1093/ageing/aft114.
- McNally T. 2022. Over 1,600 GPs need to be hired before 2028 as concern grows over shortage. *The Journal*. 26<sup>th</sup> January. Available at: <https://www.thejournal.ie/more-gps-needed-5664914-Jan2022/> accessed 23/07/2022
- McNicholas, F., Sharma, S., O'Connor, C., *et al.* 2020. Burnout in consultants in child and adolescent mental health services (CAMHS) in Ireland: a cross-sectional study. *BMJ Open*, 10, pp:e030354. Doi: 10.1136/bmjopen-2019-030354.
- McQueenie, R., Foster, H.M.E., Jani, B.D., *et al.* 2020. Multimorbidity, polypharmacy and COVID-19 infection within the UK Biobank cohort. *PLoS ONE*, 15, pp:e0238091. Doi: 10.1371/journal.pone.0238091
- Medical Research Council. 2000. *A framework for development and evaluation of RCTs for complex interventions to improve health*. Available at: <https://mrc.ukri.org/documents/pdf/rcts-for-complex-interventions-to-improve-health/> accessed 13<sup>th</sup> December 2021 [checked 27/08/2022]
- Mehtälä, M.A.K., Sääkslahti, A.K., Inkinen, M.E., *et al.* 2014. A socio-ecological approach to physical activity interventions in childcare: a systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, 11, pp:22. Doi: 10.1186/1479-5868-11-22

Meloncelli, N., Barnett, A., de Jersey, S. 2020. An implementation science approach for developing and implementing a dietitian-led model of care for gestational diabetes: a pre-post study. *BMC Pregnancy and Childbirth*, 20, pp:661. Doi: 10.1186/s12884-020-03352-6.

Mercille, J. 2019. The public-private mix in primary care development: the case of Ireland. *International Journal of Health Services*, 49, pp:412-430. Doi: 10.1177/0020731419836079.

Messerli, M., Blozik, E., Vriends, N., *et al.* 2016. Impact of a community pharmacist-led medication review on medicines use in patients on polypharmacy – a prospective randomised controlled trial. *BMC Health Services Research*, 16, pp:145. Doi: 10.1186/s12913-016-1384-8

Messerli, M., Vriends, N., Hersberger, K.E., *et al.* 2018. Humanistic outcomes and patient acceptance of the pharmacist-led medication review “Polymedication Check” in primary care in Switzerland: a prospective randomized controlled trial. *Patient Preference and Adherence*, 12, pp:1071-8. Doi: 10.2147/PPA.S160789

Mian, N.D., Pincus, D.B., Perrin, E.C., *et al.* 2020. Identifying and making recommendations for pediatric anxiety disorders in primary care settings: a video-based training. *MedEdPORTAL*, 16, pp:11033. Doi: 10.15766/mep\_2374-8265.11033

Michalowsky, B., Hoffmann, W., Bohlken, J., *et al.* 2021. Effect of the COVID-19 lockdown on disease recognition and utilization of healthcare services in the older population in Germany: a cross-sectional study. *Age and Ageing*, 50, pp:317-325. Doi: 10.1093/ageing/afaa260

Michel, D.E., Tonna, A.P., Dartsch, D.C., *et al.* 2022. Experiences of key stakeholders with the implementation of medication reviews in community pharmacies: a systematic review using the Consolidated Framework for Implementation Research (CFIR). *Research in Social and Administrative Pharmacy*, 18, pp:2944-61. Doi: 10.1016/j.sapharm.2021.07.017

Michie, S., Johnston, M. 2004. Changing clinical behaviour by making guidelines specific. *British Medical Journal*, 328, pp:343-345. Doi: 10.1136/bmj.328.7435.343

Michie, S., Johnston, M., Abraham, C., *et al.* 2005. Making psychological theory useful for implementing evidence based practice: a consensus approach. *Quality & Safety in Health Care*, 14, pp:26-33. Doi: 10.1136/qshc.2004.011155

Michie, S., Johnston, M., Francis, J., *et al.* 2008. From theory to intervention: mapping theoretically derived behavioural determinants to behavior change techniques. *Applied Psychology: an international review*, 57, pp:660-80. Doi:10.1111/j.1464-0597.2008.00341.x

Michie, S., Abraham, C., Whittington, C., *et al.* 2009. Effective techniques in healthy eating and physical activity interventions: a meta-regression. *Health Psychology*, 28, pp:690-701. Doi: 10.1037/a0016136

Michie, S., Prestwich, A., 2010. Are interventions theory-based? Development of a theory coding scheme. *Health Psychology*, 29, pp:1-8. Doi: 10.1037/a0016939.

Michie, S., Abraham, C., Eccles, M.P., *et al.* 2011a. Strengthening evaluation and implementation by specifying components of behaviour change interventions: a study protocol. *Implementation Science*, 6, pp:10.

Michie, S., van Stralen, M.M., West, R. 2011b. The behaviour change wheel: a new method for characterizing and designing behaviour change interventions. *Implementation Science*, 6, pp:42.

Michie, S., Richardson, M., Johnston, M., *et al.* 2013. The Behavior Change Technique Taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Annals of Behavioral Medicine*, 46, pp:81. Doi: 10.1007/s12160-013-9486-6.

Midão, L., Giardini, A., Menditto, E., *et al.* 2018. Polypharmacy prevalence among older adults based on the survey of health, ageing and retirement in Europe. *Archives of Gerontology and Geriatrics*, 78, pp:213-20. Doi:10.1016/j.archger.2018.06.018

Midgley, N., Parkinson, S., Holmes, J., *et al.* 2017. "Did I bring it on myself?" An exploratory study of the beliefs that adolescents referred to mental health services have about the causes of their depression. *European Child and Adolescent Psychiatry*, 26, pp:25-34. Doi: 10.1007/s00787-016-0868-8.

Milat, A.J., King, L., Bauman, A., *et al.* 2013. The concept of scalability: increasing the scale and potential adoption of health promotion interventions into policy and practice. *Health Promotion International*, 28, pp:285-298. Doi: 10.1093/heapro/dar97

Milat, A.J., Newson, R., King, L., *et al.* 2016. A guide to scaling up population health interventions. *Public Health and Research Practice*, 26, pp:e261104

Milat, A., Lee, K., Conte, K., *et al.* 2020. Intervention scalability assessment tool: a decision support tool for health policy makers and implementers. *Health Research Policy and Systems*, 18:1. Doi: 10.1186/s12961-019-0494-2

- Mills, A.J., Durepos, G., Wiebe, E. 2010. Encyclopedia of case study research. United States of America: SAGE Publications
- Milton, S., McIntosh, J., Boyd, L., *et al.* 2021. Commentary: pivoting during a pandemic: developing a new recruitment model for a randomised controlled trial in response to Covid-19. *Trials*, 22:605. Doi: 10.1186/s13063-021-05567-0
- Mitchell, E.J., Ahmed, K., Breeman, S., *et al.* 2020. It is unprecedented: trial management during the covid-19 pandemic and beyond. *Trials*, 21, pp:784. Doi: 10.1186/s13063-020-04711-6
- Młyńczak, K., Golicki, D. 2021. Validity of the EQ-5D-5L questionnaire among the general population of Poland. *Quality of Life Research*, 30, pp:817-829. Doi: 10.1007/s11136-020-02667-3.
- Mohammed, M.A., Moles, R.J., Chen, T. 2016a. Impact of pharmaceutical care interventions on health-related quality-of-life outcomes: a systematic review and meta-analysis. *Annals of Pharmacotherapy*, 50, pp:862-881. Doi: 10.1177/1060028016656016
- Mohammed, M.A., Moles, R.J., Chen, T.F. 2016b. Medication-related burden and patients' lived experience with medicine: a systematic review and metasynthesis of qualitative studies. *BMJ Open*, 6, pp:e010035. Doi: 10.1136/bmjopen-2015-010035
- Mohammed, M.A., Moles, R.J., Hilmer, S.N., *et al.* 2018a. Development and validation of an instrument for measuring the burden of medicine on functioning and well-being: the Medication-Related Burden Quality of Life (MRB-QoL) tool. *BMJ Open*, 8, pp:e018880. Doi: 10.1136/bmjopen-2017-018880
- Mohammed, M.A., Moles, R.J., Chen, T.F. 2018b. Pharmaceutical care and health related quality of life outcomes over the past 25 years: Have we measured dimensions that really matter? *International Journal of Clinical Pharmacy*, 40, pp:3-14. Doi: 10.1007/s11096-017-0582-8
- Moher, D., Liberati, A., Tetzlaff, J., *et al.* 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*, 339, pp:b2535. Doi: 10.1136/bmj.b2535
- Moher, D., Shamseer, L., Clarke, M., *et al.* 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*, 4, pp:1. Doi:10.1186/2046-4053-4-1.

- Moon, Z., Moss-Morris, R., Hunter, M.S., *et al.* 2021. Development of a self-management intervention to improve tamoxifen adherence in breast cancer survivors using an intervention mapping framework. *Supportive Care in Cancer*, 26, pp:3329-3338. Doi: 10.1007/s00520-020-05850-x.
- Moore, G.F., Audrey, S., Barker, M., *et al.* 2015. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ*, 35, pp:h1258. Doi: 10.1136/bmj.h1258
- Moore, G., Gambon, L., Michie, S., *et al.* 2019. Population health intervention research: the place of theories. *Trials*, 20, pp:285. Doi: 10.1186/s13063-019-3383-7
- Morcos, P., Dalton, K. 2021. Exploring pharmacists' perceptions of integrating pharmacists into the general practice setting. *Exploratory Research in Clinical and Social Pharmacy*, 2, pp:100027. Doi: 10.1016/j.rcsop.2021.100027
- Moriarty, F., Hardy, C., Bennett, K., *et al.* 2015. Trends and interaction of polypharmacy and potentially inappropriate prescribing in primary care over 15 years in Ireland: a repeated cross-sectional study. *BMJ Open*, 5, pp:e008656. Doi:10.1136/bmjopen-2015-008656
- Morrow, A., Hogden, E., Kang, Y.-J., *et al.* 2019. Comparing theory and non-theory based implementation approaches to improving referral practices in cancer genetics: a cluster randomised trial protocol. *Trials*, 20, pp:373. Doi: 10.1186/s13063-019-3457-6
- Morse, J., Barrett, M., Mayan, M., *et al.* 2002. Verification strategies for establishing reliability validity in qualitative research. *International Journal of Qualitative Research*, 1, pp:1-19. Doi: 10.1177/160940690200100202
- Moynihan, R., Sanders, S., Michaleff, Z.A., *et al.* 2021. Impact of COVID-19 pandemic on utilization of healthcare services: a systematic review. *BMJ Open*, 11, pp:e045343. Doi: 10.1136/bmjopen-2020-045343
- Movsisyan, A., Arnold, L., Evans, R., *et al.* 2019. Adapting evidence-informed complex population health interventions for new contexts: a systematic review of guidance. *Implementation Science*, 14, pp:105. Doi:10.1186/s13012-019-0956-5.
- Multiple Sclerosis Trust. No date. *Care in the NHS*. Available at: <https://mstrust.org.uk/az/care-in-the-nhs> accessed 07/08/2022

Murphy, M., Byrne, S., Bradley, C.P. 2011. Influence of patient payment on antibiotic prescribing in Irish general practice: a cohort study. *British Journal of General Practice*, e549. Doi: 10.3399/bjgp11X593820

Murphy, A.L., Gardner, D.M. 2019. Pharmacists' acceptability of a men's mental health promotion program using the Theoretical Framework of Acceptability. *AIMS Public Health*, 6, pp:195-208. Doi: 10.3934/publichealth.2019.2.195

Murphy, M., Scott, L.J., Salisbury, C., *et al.* 2021. Implementation of remote consulting in UK primary care following the COVID-19 pandemic: a mixed-methods longitudinal study. *British Journal of General Practice*, 71, pp:e166-e177. Doi: 10.3399/BJGP.2020.0948

Muth, C., Uhlmann, L., Haefeli, W.E., *et al.* 2018. Effectiveness of a complex intervention on PRIoritising MULTimedication in Multimorbidity (PRIMUM) in primary care: results of a pragmatic cluster randomized controlled trial. *BMJ Open*, 8, pp:e017740. Doi: 10.1136/bmjopen-2017-017740

Muth, C., Blom, J.W., Smith, S.M., *et al.* 2019. Evidence supporting the best clinical management of patients with multimorbidity and polypharmacy: a systematic guideline review and expert consensus. *Journal of Internal Medicine*, 285, pp:272-288. Doi:10.1111/joim.12842

Myhill, T., Coulson, W., Nixon, P., *et al.* 2017. Use of supplementary patient education material increases treatment adherence and satisfaction among acne patients receiving adapalene 0.1%/benzoyl peroxide 2.5% gel in primary care clinics: a multicenter, randomized, controlled clinical study. *Dermatology and Therapy*, 7, pp:515-524. Doi: 10.1007/s13555-017-0203-4

Nahm, F.S. 2016. Nonparametric statistical tests for the continuous data: the basic concept and the practical use. *Korean Journal of Anesthesiology*, 69:8-14. Doi: 10.4097/kjae.2016.69.1.8

National health Service (NHS). 2014. *Medicines optimisation: Clinical medication review A practice guide*. Available at: <https://www.sps.nhs.uk/wp-content/uploads/2016/08/Brent-CCG-Medication-Review-Practice-Guide-2014.pdf> accessed 13/4/2020

National Health Service Digital. 2022. Summary care record in community pharmacy. [online] Available: <https://digital.nhs.uk/services/summary-care-records-scr/summary-care-record-scr-in-community-pharmacy> accessed 21/03/2022

National Institute for Health and Care Excellence (NICE). 2016. *Multimorbidity: Clinical Assessment and Management*. Available at: [www.nice.org.uk/guidance/ng56](http://www.nice.org.uk/guidance/ng56) accessed 10/11/2021 [checked 26/08/2022]

National Institute for Health and Care Excellence (NICE). 2017. *Multimorbidity and polypharmacy*. Available at: <http://www.nice.org.uk/guidance/ktt18> accessed 10/11/2021

National Institute for health and Care Excellence Guidelines. 2019a. *Medicines Optimization: The safe and effective use of medicines to enable the best possible outcomes (NG5)*. Available at: [www.nice.org.uk/guidance/ng5](http://www.nice.org.uk/guidance/ng5) accessed 26/08/2022

National Institute of Health and Care Excellence. 2019b. Position statement on use of the EQ-5D-5L values set for England. Available from: <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technologyappraisal-guidance/eq-5d-5l> accessed 06/01/2022 [checked 26/08/2022]

National Institute for Health and Care Excellence NICE. 2022. Glossary – tertiary care. Available at: <https://www.nice.org.uk/glossary?letter=t> accessed 07/08/2022

National Institute for Health Research. No date. *NIHR evaluation, trials and studies coordination centre: Glossary*. Available at: <https://www.nihr.ac.uk/glossary?letter=F&postcategory=-1> accessed 25/01/2022 [checked 26/08/2022]

National Institute for Health Research (NIHR). 2021. *Guidance on applying for feasibility studies*. Available at: <https://www.nihr.ac.uk/documents/nihr-research-for-patient-benefit-rfpb-programme-guidance-on-applying-for-feasibility-studies/20474> accessed: 20/08/2021 [checked 26/08/2022]

National Institute for Health Research (NIHR). 2022a. *NIHR Evaluation, Trials and Studies Coordinating Centre: Glossary*. Available at: <https://www.nihr.ac.uk/glossary?letter=F&postcategory=-1> accessed: 27/02/2022

National Institute for Health Research (NIHR). 2022b. *NIHR Evaluation, Trials and Studies Coordinating Centre: Glossary*. Available at: <https://www.nihr.ac.uk/glossary?letter=P&postcategory=-1> accessed: 27/02/2022

National University of Galway. 2020. *Corona citizens science project – wave 2 results*. Available at: <https://www.nuigalway.ie/corona-study/results2/> accessed 27/01/2022 [checked 26/08/2022]

- Nazar, H., Nazar, Z., Portlock, J., *et al.* 2015. A systematic review of the role of community pharmacies in improving the transition from secondary to primary care: community pharmacist's role in transfer of care. *British Journal of Clinical Pharmacology*, 80, pp:936-48.
- Nguyen, D.T.K., McLaren, L., Oelke, D., *et al.* 2020. Developing a framework to inform scale-up success for population health interventions: a critical interpretive synthesis of the literature. *Global Health Research and Policy*, 5:18. Doi: 10.1186/s41256-020-00141-8
- Nili, M., Mohamed, R., Kelly, K.M. 2020. A systematic review of interventions using health behavioral theories to improve medication adherence among patients with hypertension. *Translational Behavioral Medicine*, 10, pp:1177-1186. Doi: 10.1093/tbm/ibaa020
- Noar, S.M., Benac, C.N., Harris, M.S. 2007. Does tailoring matter? Meta-analytic review of tailored print health behavior change interventions. *Psychological Bulletin*, 133, pp:673-693. Doi: 10.1037/0033-2909.133.4.673.
- Noble, H., Smith, J. 2015. Issues of validity and reliability in qualitative research. *Evidence Based Nursing*, 18, pp:34-5. Doi: 10.1136/eb-2015-102054
- Noordzij, M., Tripepi, G., Dekker, F.W., *et al.* 2010. Sample size calculation: basic principles and common pitfalls. *Nephrology Dialysis Transplantation*, 25:1388-1393. Doi: 10.1093/ndt/gfp732
- Northern Ireland Statistics and Research Agency. 2016. *Maps of Northern Ireland's Health and social care trust and local government districts*. Available at: <https://www.nisra.gov.uk/publications/maps-northern-irelands-health-and-social-care-trust-and-local-government-districts> accessed 27/08/2022
- Nowell, L.S., Norris, J.M., White, D.E., *et al.* 2017. Thematic analysis: striving to meet the trustworthiness criteria. *International Journal of Qualitative Methods*, 16, pp:1-13. Doi: 10.1177/1609406917733847
- Noy, C. 2008. Sampling knowledge: the hermeneutics of snowball sampling in qualitative research. *International Journal of Social Research Methodology*, 11, pp:327-44. Doi: 10.1080/13645570701401305
- Nutting, P.A., Goodwin, M.A., Flocke, S.A., *et al.* 2003. Continuity of primary care: to whom does it matter and when? *Annals of Family Medicine*, 1:149-155.



- Nyumba, T.O., Wilson, K., Derrick, C.J., *et al.* 2018. The use of focus group discussion methodology: insights from two decades of application in conservation. *Methods in Ecology and Evolution*, 9, pp:20-32. Doi:10.1111/2041-210X.12860.
- Oakley, A., Strange, V., Bonell, C., *et al.* 2006. Process evaluation in randomized controlled trials of complex interventions. *BMJ*, 332:413-416. Doi: 10.1136/bmj.332.7538.413
- O'Brien C. 2014a. State pension age increases to 66. *The Irish Times*. 2<sup>nd</sup> January. Available at: <https://www.irishtimes.com/news/social-affairs/state-pension-age-increases-to-66-1.1641529> accessed 04/08/2022
- O'Brien, B., Harris, I., Beckham, T. *et al.* 2014b. Standards for Reporting Qualitative Research: a synthesis of recommendations. *Academic Medicine*, 89, pp:1245-51. Doi: 10.1097/ACM.0000000000000388
- O'Cathain, A., Croot, L., Duncan, E., *et al.* 2019a. Guidance on how to develop complex interventions to improve health and healthcare. *BMJ Open*, 9, pp:e029954. Doi:10.1136/bmjopen-2019-029954
- O'Cathain, A., Croot, L., Sworn, K., *et al.* 2019b. Taxonomy of approaches to developing interventions to improve health: a systematic methods overview. *Pilot and Feasibility Studies*, 5, pp:41. Doi: 10.1186/s40814-019-0425-6
- Ocloo, J., Garfield, S., Dean Franklin, B., *et al.* 2021. Exploring the theory, barriers and enablers for patient and public involvement across health, social care and patient safety: a systematic review of reviews. *Health Research Policy and Systems*, 19, pp:8. Doi: 10.1186/s12961-020-00644-3
- Odberg, K.R., Hansen, B.S., Aase, K., *et al.* 2020. A work system analysis of the medication administration process in a Norwegian nursing home ward. *Applied Ergonomics*, 86, pp:103100. Doi: 10.1016/j.apergo.2020.103100.
- Ödesjö, H., Anell, A., Boman, A., *et al.* 2017. Pay for performance associated with increased volume of medication reviews but not with less inappropriate use of medications among the elderly – an observational study. *Scandinavian Journal of Primary Health Care*, 35, pp:271-8. Doi: 10.1080/02813432.2017.1358434
- O'Donnell, L.K., Reeve, E., Hilmer, S.N. 2021. Development, validation and evaluation of the Goal-directed Medication review Electronic Decision Support System (G-MEDSS)©. *Research in Social and Administrative Pharmacy*, 18, pp:3174-3183. Doi: 10.1016/j.sapharm.2021.09.004

O'Donovan, B., Rodgers, R.M., Cox, A.R., *et al.* 2019. 'You feel like you haven't got any control': A qualitative study of side effects from medicines. *Journal of Patient Safety and Risk Management*, 24, pp:13-24. Doi: 10.1177/2516043518821499

O'Dowd T, Ivers J-H, Handy D. 2017. *A future together building a better GP and primary care service*. Available at: <https://www.lenus.ie/handle/10147/622643> accessed 26/01/2022

Odukoya, O.K., Stone, J.A., Chui, M.A. 2015. Barriers and facilitators to recovering from e-prescribing errors in community pharmacies. *Journal of the American Pharmacists Association*, 55, pp:52-8. Doi: 10.1331/JAPhA.2015.13239.

O'Dwyer, M., Peklar, J., McCarron, M., *et al.* 2013. Prevalence, patterns and factors associated with polypharmacy and excessive polypharmacy in an ageing population with intellectual disability in Ireland. *Irish Journal of Medical Science*, 182, pp:210. Doi: 10.1111/jir.12391.

Ogeil, R.P., Chakraborty, S.P., Young, A.C., *et al.* 2020. Clinician and patient barriers to the recognition of insomnia in family practice: a narrative summary of reported literature analysed using the theoretical domains framework. *BMC Family Practice*, 21, pp:1. Doi: 10.1186/s12875-019-1070-0.

Ohannessian, R., Duong, T.A., Odone, A. 2020. Global telemedicine implementation and integration within health systems to fight the COVID-19 pandemic: a call to action. *JMIR Public Health and Surveillance*, 6, pp:e18810. Doi: 10.2196/18810

Okuyan, B., Bektay, M.Y., Kingir, Z.B., *et al.* 2021. Community pharmacy cognitive services during the COVID-19 pandemic: a descriptive study of practices, precautions taken, perceived enablers and barriers and burnout. *International Journal of Clinical Practice*, 75, pp:e14834. Doi: 10.1111/ijcp.14834

O'Mahony, D., O'Sullivan, D., Byrne, S., *et al.* 2015. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age and Ageing*, 44, pp:213-218. Doi:10.1093/ageing/afu145.

Onder, G., Liperoti, R., Foebel, A., *et al.* 2013. Polypharmacy and mortality among nursing home residents with advanced cognitive impairment: results from the shelter study. *Journal of the American Medical Directors Association*, 14, pp:4507-4512. Doi: 10.1016/j.jamda.2013.03.014.

Onder, G., Rezza, G., Brusaferro, S. 2020. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*, 323, pp:1775-1776. Doi: 10.1001/jama.2020.4683

Ong, S.M., Lim, Y.M.F., Sivasampu, S., *et al.* 2018. Variation of polypharmacy in older primary care attenders occurs at prescriber level. *BMC Geriatrics*, 18, pp:59. Doi:10.1186/S12877-018-0750-2

Onwuegbuzie, A.J., Dickinson, W.B., Leech, N.L., *et al.* 2009. A qualitative framework for collecting and analyzing data in focus group research. *International Journal of Qualitative Methods*, 8, pp:1-21. Doi: 10.1177/160940690900800301

O'Regan E. 2020a. Free GP care to be extended to children under 12 and medical card income for over-70s widened. *Irish Independent*. 26<sup>th</sup> June. Available at: <https://www.independent.ie/irish-news/health/free-gp-care-to-be-extended-to-children-under-12-and-medical-card-income-for-over-70s-widened-39318218.html> accessed 20/11/20 [checked 26/08/2022]

O'Regan, A., Hayes, P., O'Connor, R., *et al.* 2020b. The University of Limerick Education and Research Network for General Practice (ULEARN-GP): practice characteristics and general practitioner perspectives. *BMC Family Practice*, 21, pp:25. Doi: 10.1186/s12875-020-1100-y

O'Reilly, O., Hanlon, D. 2017. Irish integrated care programmes for chronic disease – supporting general practice. *International Journal of Integrated Care*, 17, pp:a55. Doi: 10.5334/ijic.3167

Orimo, H., Ito, H., Suzuki, T., *et al.* 2006. Reviewing the definition of 'elderly'. *Geriatrics and Gerontology International*, 6, pp:149-158. Doi:10.1111/j.1447-0594.2006.00341.x

O'Riordan, D., Byrne, S., Fleming, A., *et al.* 2017. GPs' perspectives on prescribing for older people in primary care: a qualitative study. *British Journal of Clinical Pharmacology*, 83, pp:1521-1531. Doi: 10.1111/bcp.13233

Orsmond, G.I., Cohn, E.S. 2015. The distinctive features of a feasibility study: objectives and guiding questions. *OTJR: Occupation, Participation and Health*, 35, pp:169-177. Doi: 10.1177/1539449215578649

O'Sullivan, T.A., Sy, E., Bacci, J.L. 2020. Essential attributes for the community pharmacist as care provider. *American Journal of Pharmaceutical Education*, 84, pp:106-117. Doi: 10.5688/ajpe7125

Palinkas, L.A., Horwitz, S.M., Green, C.A., *et al.* 2015. Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Administration and Policy*

in *Mental Health and Mental Health Services Research*, 42, pp:533-44. Doi: 10.1007/s10488-013-0528-y

Pammett, R., Jorgenson, D. 2014. Eligibility requirements for community pharmacy medication review services in Canada, 147, pp:1. Doi: 10.1177/1715163513514006

Pan, L., Zhao, R., Zhao, N. *et al.* 2022. Determinants associated with doctors' prescribing behaviours in public hospitals in China. *Annals of the New York Academy of Sciences*, 1507, pp:99-107. Doi: 10.1111/nyas.14677

Panahi, S., Watson, J., Partridge, H. 2016. Social media and physicians: exploring the benefits and challenges. *Health Informatics Journal*, 22, pp:99-112. Doi: 10.1177/146045821454907

Parekh, N., Page, A., Ali, K., *et al.* 2017. A practical approach to the pharmacological management of hypertension in older people. *Therapeutic Advances in Drug Safety*, 8, pp:117-132. Doi: 10.117/2042098616682721.

Parker, K., Bull-Engelstad, I., Benth, J.Š., *et al.* 2019. Effectiveness of using STOPP/START criteria to identify potentially inappropriate medication in people aged  $\geq 65$  years with chronic kidney disease: a randomized clinical trial. *European Journal of Clinical Pharmacology*, 75, pp:1503-11. Doi: 10.1007/s00228-019-02727-9.

Parker, L., Ryan, R., Young, S., *et al.* 2021. Medications and doctor-patient communication. *Australian Journal of General Practice*, 50, pp:709-714. Doi: 10.31128/AJGP-05-21-5973

Parr, E., Ferdinand, P., Roffe, C. 2017. Management of acute stroke in the older person. *Geriatrics*, 2, pp:27. Doi: 10.3390/geriatrics2030027

Patterson, S.M., Hughes, C., Kerse, N., *et al.* 2012. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database of Systematic Reviews*, 5, pp:CD008165. Doi: 10.1002/14651858.CD008165.pub2.

Patton, M.Q. 2002. *Qualitative research and evaluation methods*. 3<sup>rd</sup> edn. Thousand Oaks, California: SAGE.

Patton, D.E., Hughes, C.M., Cadogan, C.A., *et al.* 2017. Theory-based interventions to improve medication adherence in older adults prescribed polypharmacy: a systematic review. *Drugs and Ageing*, 34, pp:97-113. Doi: 10.1007/s40266-016-0426-6.

Patton, D.E., Francis, J.J., Clarke, E., *et al.* 2019. A pilot study of the S-MAP (Solutions for Medications Adherence Problems) intervention for older adults prescribed polypharmacy in

primary care: study protocol. *Pilot and Feasibility Studies*, 5, 16. Doi: 10.1186/s40814-019-0506-6

Patton, D.E., Ryan, C., Hughes, C.M. 2020. Development of a complex community pharmacy intervention package using theory-based behaviour change techniques to improve older adults' medication adherence. *BMC Health Services Research*, 20, pp:418. Doi: 10.1186/s12913-020-05282-7

Patton, D.E., Pearce, C.J., Cartwright, M., *et al.* 2021. A non-randomised pilot study of the Solutions for Medication Adherence Problems (S-MAP) intervention in community pharmacies to support older adults adhere to multiple medications. *Pilot and Feasibility Studies*, 7, pp:18. Doi: 10.1186/s40814-020-00762-3.

Paudyal, V., Smith, K.G., MacLure, K., *et al.* 2019. Perceived roles and barriers in caring for the people who are homeless: a survey of UK community pharmacists. *International Journal of Clinical Pharmacy*, 41, pp:215-27. Doi: 10.1007/s11096-019-00789-4

Pavlova, N., Teychenne, M., Olander, E.K. 2020. The concurrent acceptability of a postnatal walking group: a qualitative study using the Theoretical Framework of Acceptability. *International Journal of Environmental Research and Public Health*, 17:5027. Doi: 10.3390/ijerph17145027

Pawlikowska, T.R.B., Walker, J.J., Nowak, P.R., *et al.* 2009. Patient involvement in assessing consultation quality: a quantitative study of the patient enablement instrument in Poland. *Health Expectations*, 13, pp:13-23. Doi: 10.1111/j.1369.7625.2009.00554.x

Payne, R., Duerden, M. 2015. Polypharmacy – appropriate, problematic or both? [online]. Available at: <https://wileymicrositebuilder.com/trends/wp-content/uploads/sites/29/2015/12/Polypharmacy-appropriate-problematic-or-both.pdf> accessed 21/03/2022

Pazan, F., Wehling, M. 2021. Polypharmacy in older adults: a narrative review of definitions, epidemiology and consequences. *European Geriatric Medicine*, 12, pp:443-452. Doi: 10.1007/s41999-021-00479-3

Pereira, K.G., Peres, M.A., Iop, D., *et al.* 2017. Polypharmacy among the elderly: a population-based study. *Revista Brasileira de Epidemiologia*, 20, pp:335-344. Doi:10.1590/1980-5497201700020013

- Perrault, E.K., Keating, D.M. 2018. Seeking ways to inform the uninformed: improving the informed consent process in online social science research. *Journal of Empirical Research on Human Research Ethics*, 13, pp:50-60. Doi: 10.1177/1556264617738846
- Peters, G.J., de Bruin, M., Crutzen, R. 2015. Everything should be as simple as possible, but no simpler: towards a protocol for accumulating evidence regarding the active content of health behaviour change interventions. *Health Psychology Review*, 9, pp:1-14. Doi: 10.1080/17437199.22013.848409
- Peterson, G.M., Jackson, S.L., Fitzmaurice, K.D., *et al.* 2009. Attitudes of Australian pharmacists towards practice-based research. *Journal of Clinical Pharmacy and Therapeutics*, 34, pp:397-405. Doi: 10.1111/j.1365-2710.2008.01020.x
- Petticrew, M. 2011. When are complex interventions 'complex'? When are simple interventions 'simple'? *European Journal of Public Health*, 21, PP:397-399. Doi: 10.1093/eurpub/ckr084.
- Pharmaceutical Care Network Europe. 2018. PCNE definition of medication review: reaching agreement. *International Journal of Clinical Pharmacy*, 40, pp:1199-208. Doi: 10.1007/s11096-018-0696-7
- Pharmaceutical Society of Ireland. 2015. Guidelines on patient consultation areas in retail pharmacy business. [online]. Available at: [https://www.thepsi.ie/Libraries/Folder\\_Pharmacy\\_Practice\\_Guidance/01\\_2\\_Patient\\_consultation\\_areas\\_AW1.sflb.ashx#:~:text=Since%201996%20there%20have%20been,Pharmacy%20Businesses%20Regulations%202008%20\(S.I.](https://www.thepsi.ie/Libraries/Folder_Pharmacy_Practice_Guidance/01_2_Patient_consultation_areas_AW1.sflb.ashx#:~:text=Since%201996%20there%20have%20been,Pharmacy%20Businesses%20Regulations%202008%20(S.I.) accessed 21/03/2022
- Pharmaceutical Society of Ireland. 2022a. *Pharmacy statistics*. Available at: [https://www.thepsi.ie/Libraries/Monthly\\_Statistics/Pharmacies\\_-\\_Website\\_Statistics.sflb.ashx](https://www.thepsi.ie/Libraries/Monthly_Statistics/Pharmacies_-_Website_Statistics.sflb.ashx) accessed 26/01/2022
- Pharmaceutical Society of Ireland. 2022b. *Pharmacists statistics*. Available at: [https://www.thepsi.ie/Libraries/Monthly\\_Statistics/Pharmacists\\_-\\_Website\\_Statistics.sflb.ashx](https://www.thepsi.ie/Libraries/Monthly_Statistics/Pharmacists_-_Website_Statistics.sflb.ashx) accessed 26/01/2022
- Piccoliori, G., Mahlknecht, A., Sandri, M., *et al.* 2021. Epidemiology and associated factors of polypharmacy in older patients in primary care: a northern Italian cross-sectional study. *BMC Geriatrics*, 21, pp:197. Doi:10.1186/s12877-021-02141-w

- Pierse, T., Barry, L., Glynn, L., *et al.* 2019. A pilot study of the duration of GP consultations in Ireland. *Pilot and Feasibility Studies*, 5, pp:142. Doi: 10.1186/s40814-019-0532-4
- Pires, C. 2022. Medical records in community pharmacies: the cases of UK and Australia. *Foundations*, 2, pp:399-408. Doi: 10.3390/foundations2020027
- Pisani, A.R., Cross, W.F., West, J.C., *et al.* 2020. Brief video-based suicide prevention training for primary care. *Family Medicine*, 53:104-110. Doi: 10.22454/FamMed.2021.367209
- Pitkälä, K.H., Juola, A.L., Kautiainen, H., *et al.* 2014. Education to reduce potentially harmful medication use among residents of assisted living facilities: a randomized controlled trial. *Journal of the American Medical Directors Association*, 15, pp:892-898. Doi: 10.1016/j.jamda.2014.04.002.
- Pollock, A., Campbell, P., Synnot, A. *et al.* 2021. Patient and public involvement in systematic reviews. In GIN Public Toolkit: *Patient and Public Involvement in Guidelines*. 2021 Guidelines International Network.
- Post, M.W.M. 2014. Definitions of quality of life: what has happened and how to move on. *Topics in Spinal Cord Injury Rehabilitation*, 20, pp:167-180. Doi: 10.1310/sci2003-167
- Potter, C., Kelly, L., Hunter, C., *et al.* 2018. The context of coping: A qualitative exploration of underlying inequalities that influence health services support for people living with long-term conditions. *Sociology of Health and Illness*, 40, pp:130-45. Doi: 10.1111/1467-9566.12624.
- Prada, D., Belsky, D., Baccarelli, A.A. 2021. Is this environment making you older? Molecular biomarkers and new approaches to investigate the influences of environmental chemicals through aging. *La Medicina del Lavoro Work, Environment and Health*, 112, pp:8-14.
- Prados-Torres, A., Poblador-Plou, B., Calderon-Larrañaga, A., *et al.* 2012. Multimorbidity patterns in primary care: interactions among chronic diseases using factor analysis. *PLoS One*, 7, pp:e32190.
- Prados-Torres, A., del Cura-González, I., Prados-Torres, D., *et al.* 2017. Effectiveness of an intervention for improving drug prescription in primary care patients with multimorbidity and polypharmacy: study protocol of a cluster randomized clinical trial (Multi-PAP project). *Implementation Science*, 12, pp:54. Doi:10.1186/s13012-017-0584-x
- Prados-Torres, A., del Cura-González, I., Prados-Torres, J.D., *et al.* 2020. MULTIPAP Study: improving healthcare for patients with multimorbidity. *British Journal of General Practice*, 70, pp:bjgp20X711257. Doi: 10.3399/bjgp20X711257

- Prestwich, A., Sniehotta, F.F., Whittington, C., *et al.* 2014. Does theory influence the effectiveness of health behaviour interventions? Meta-analysis. *Health Psychology*, 33, pp:465-474. Doi: 10.1037/a0032853.
- Primary Care Reimbursement Service. 2019. *Statistical analysis of claims and payments 2019*. Available at: <https://www.hse.ie/eng/staff/pccrs/about-pccrs/> accessed 13/07/21 [checked 26/08/2022]
- Proctor, E., Silmere, H., Raghavan, R., *et al.* 2010. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Administration and Policy in Mental Health*, 38, pp:65-76. Doi: 10.1007/s10488-010-0319-7
- Qudah, B., Thankur, T., Chewing, B. 2021. Factors influencing patient participation in medication counseling at the community pharmacy: a systematic review. *Research in Social and Administrative Pharmacy*, 17, pp:1863-76. Doi: 10.1016/j.sapharm.2021.03.005
- Quintana-Barcena, P., Sinner, C., Berger, J. 2022. Domiciliary medication review (ReMeDo): development, reliability and acceptability of a tool for community pharmacists. *International Journal of Pharmacy Practice*, 30, pp:129-35. Doi: 10.1093/ijpp/riab078
- Rabin, R., de Charro, F. 2001. EQ-5D: a measure of health status from the EuroQol Group. *Annals of Medicine*, 33:337-343. Doi: 10.3109/07853890109002087
- Rahimi, B., Vesal, A., Edalatifard, M. 2020. Coronavirus and its effect on the respiratory system: is there any association between pneumonia and immune cells. *Journal of Family Medicine and Primary Care*, 9, pp:4729-4735. Doi: 10.4103/jfmpc.jfmpc\_763\_20
- Rakvaag, H., Søreide, G.E., Meland, E., *et al.* 2020. Complementing or conflicting? How pharmacists and physicians position the community pharmacist. *Pharmacy practice*, 18, pp:2078. Doi: 10.18549/PharmPract.2002.3.2078
- Rambhade, S., Chakarborty, A., Shrivastava, A., *et al.* 2012. A survey on polypharmacy and use of inappropriate medications. *Toxicology International*, 19, pp:68-73. Doi: 10.4103/0971-6580.94506
- Rankin, A., Cadogan, C.A., Patterson, S.M., *et al.* 2018a. Interventions to improve the appropriate use of polypharmacy in older people. *Cochrane Database of Systematic Reviews*, 9, pp:CD008165. Doi: 10.1002/14651858.CD008165.pub4



Rankin A, Cadogan CA, Ryan C *et al.* 2018b. Core outcome set for trials aimed at improving the appropriateness of polypharmacy in older people in primary care. *Journal of the American Geriatrics Society*, 66, pp:1206-1212. Doi: 10.1111/jgs.15245.

Rankin, A., Cadogan, C.A., Barry, H.E., *et al.* 2021a. An external pilot cluster randomised controlled trial of a theory-based intervention to improve appropriate polypharmacy in older people in primary care (PolyPrime): study protocol. *Pilot and Feasibility Studies*, 7, pp:77. Doi: 10.1186/s40814-021-00822-2

Rankin, A., Molloy, G.J., Cadogan, C.A., *et al.* 2021b. Protocol for a process evaluation of an external pilot cluster randomised controlled trial of a theory-based intervention to improve appropriate polypharmacy in older people in primary care: the PolyPrime study. *Trials*, 22, pp:449. Doi: 10.1186/s13063-021-05410-6

Rankin, A., Gorman, A., Cole, J., *et al.* 2022. An external pilot cluster randomised controlled trial of a theory-based intervention to improve appropriate polypharmacy in older people in primary care (PolyPrime). *Pilot and Feasibility Studies*, 8, pp:203. Doi: 10.1186/s40814-022-01161-6

Rantsi, M., Hyltinen, V., Jyrkkä, J., *et al.* 2021. Process evaluation of implementation strategies to reduce potentially inappropriate medication prescribing in older population: a scoping review. *Research in Social and Administrative Pharmacy*. Doi: 10.1016/j.sapharm.2021.04.012

Rashidi, M.N., Begum, R.A., Mokhtar, M., *et al.* 2014. Conduct of structured interviews as research implementation method. *Journal of Advanced Research Design*, 1, pp:28-34.

Rathbone, A.P., Mansoor, S.M., Krass, I., *et al.* 2016. Qualitative study to conceptualise a model of interprofessional collaboration between pharmacists and general practitioners to support patients' adherence to medication. *BMJ Open*, 6, pp:e010488. Doi: 10.1136/bmjopen-2015-010488

Rawle, M.J., Richards, M., Davis, D., *et al.* 2018. The prevalence and determinants of polypharmacy at age 69: a British birth cohort study. *BMC Geriatrics*, 18, pp:118. Doi: 10.1186/s12877-018-0795-2

Reason, J. 2000. Human error: models and management. *BMJ*, 320, pp:768-770. Doi: 10.1136/bmj.320.7237.768

Reeve, E., Wise, M.D., Hendrix, I., *et al.* 2013. People's attitudes, beliefs, and experiences regarding polypharmacy and willingness to deprescribe. *Journal of American Geriatric Society*, 61, pp:1508-14. Doi: 10.1111/jgs.12418.

Reeve, E., Gnjidic, D., Long, J., *et al.* 2015. A systematic review of the emerging definition of 'Deprescribing' with network analysis: implications for future research and clinical practice. *British Journal of Clinical Pharmacology*, 80, pp:1254-68. Doi: 10.1111/bcp.12732

Renfro, C.P., Ferreri, S., Barber, T.G., *et al.* 2018. Development of a communication strategy to increase interprofessional collaboration in the outpatient setting. *Pharmacy*, 6, pp:4. Doi: 10.3390/pharmacy6010004

Richardson, K., Moore, P., Peklar, J., on behalf of the TILDA team. 2012. *Polypharmacy in adults over 50 in Ireland: opportunities for cost saving and improved healthcare*. Available at: [https://tilda.tcd.ie/publications/reports/pdf/Report\\_Polypharmacy.pdf](https://tilda.tcd.ie/publications/reports/pdf/Report_Polypharmacy.pdf) accessed 26/08/2022

Rieckert, A., Trampisch, U.S., Klaatzen-Mielke, R., *et al.* 2018. Polypharmacy in older patients with chronic diseases: a cross-sectional analysis of factors associated with excessive polypharmacy. *BMC Primary Care*, 19, pp:113. Doi: 10.1186/s12875-018-0795-5

Riester, M.R., McAuliffe, L., Collins, C., *et al.* 2021. Development and validation of the tool for pharmacists to predict 30-day hospital readmission in patients with health failure (ToPP-HF). *American Journal of Health-system Pharmacy*, 78, pp:1691-700. Doi: 10.1093/ajhp/zxab223.

Rigby, R.R., Mitchell, L.J., Hamilton, K., *et al.* 2020. The use of behaviour change theories in dietetics practice in primary health care: a systematic review of randomized controlled trials. *Journal of the Academy of Nutrition and Dietetics*, 120, pp:1172-1197. Doi: 10.1016/j.jand.2020.03.019.

Ritchie, J., Spencer, L. 1994. Qualitative data analysis for applied policy research. In Bryman, A., Burgess, T.D. (eds) *Analyzing Qualitative Data*. London, Routledge.

Roberts, A.S., Benrimoj, S., Chen, T.F. *et al.* 2008. Practice change in community pharmacy: quantification of facilitators. *Annals of Pharmacotherapy*, 42, pp:861-8. Doi: 10.1345/aph.1K617.

Roberts, M.F., Reeves, K., Divine, H. 2019. Community pharmacists' lack of access to health records and its impact on targeted MTM interventions. *Journal of the American Pharmacists Association*, 59, pp:s81-4. Doi: 10.1016/j.japh.2019.04.023.

Robinson, K., O'Neill, A., Conneally, M., *et al.* 2020. Exploring the beliefs and experiences of older Irish adults and family carers during the novel coronavirus (COVID-19) pandemic: a qualitative study protocol. *HRB Open Research*, 3, pp:16. Doi: 10.12688/hrbopenres.13031.1

Rogers, E.A., Yost, K.J., Rosedahl, J.K., *et al.* 2017. Validating the Patient Experience with Treatment and Self-management (PETS), a patient-reported measure of treatment burden, in people with diabetes. *Patient Related Outcome Measures*, 8:143-156. Doi: 10.2147/PROM.S140851.

Rognstad, S., Brekke, M., Fetveit, A., *et al.* 2009. The Norwegian General Practice (NORGE) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study. *Scandinavian Journal of Primary Health Care*, 27, pp:153-159. Doi: 10.1080/02813430902992215.

Rolfe, G., 2006. Validity, trustworthiness and rigour: quality and the idea of qualitative research. *Journal of Advanced Nursing*, 53, pp:304-10. Doi: 10.1111/j.1365-2648.2006.03727.x

Romain, A.J., Bernard, P., Akkrass, Z., *et al.* 2020. Motivational theory-based interventions on health of people with several mental illness: a systematic review and meta-analysis. *Schizophrenia Research*, 222, pp:31-41. Doi: 10.1016/j.schres.2020.05.049

Rongen, S., Kramers, C., O'Mahony, D., *et al.* 2016. Potentially inappropriate prescribing in older patients admitted to psychiatric hospital. *International Journal of Geriatric Psychiatry*, 31:137-145. Doi: 10.1002/gps.4302.

Rosenbloom, K., Taylor, K., Harding, G. 2000. Community pharmacists' attitudes towards research. *International Journal of Pharmacy Practice*, 8, pp:103-110. Doi: 10.1111/j.2042-7174.2000.tb00994.x

Ross, S., Ryan, C., Duncan, E.M., *et al.* 2013. Perceived causes of prescribing errors by junior doctors in hospital inpatients: a study from the PROTECT programme. *BMJ Quality and Safety*, 22, pp:97-102. Doi: 10.1136/bmjqs-2012-001175.

Roughead, E.E., Barratt, J.D., Ramsay, E., *et al.* 2009. The effectiveness of collaborative medicines reviews in delaying time to next hospitalization for patients with heart failure in the practice setting: results of a cohort study. *Circulation: Heart failure*, 2, pp:424-8. Doi: 10.1161/CIRCHEARTFAILURE.109.861013.

Roulston, K., 2001. Data analysis and 'theorizing as ideology'. *Qualitative Research*, 1, pp:279-302. Doi: 10.1177/146879410100100302

Rovetta, A. 2020. Raiders of the lost correlation: a guide on using pearson and spearman coefficients to detect hidden correlation in medical sciences. *Cureus*, 12:e11794. Doi: 10.7759/cureus.11794

Royal College of General Practitioners. 2013. The 2022 GP: Compendium of evidence. Available at: <https://www.rcgp.org.uk/campaign-home/~media/Files/Policy/A-Z-policy/The-2022-GP-Compendium-of-Evidence.ashx> accessed 13/07/21 [checked 26/08/22]

Royal Pharmaceutical Society. 2017. Research, evidence and evaluation toolkit (REET). [online]. Available at: <https://www.rpharms.com/publications/member-resources#?Sort=Title&Tags=toolkit> accessed: 03/06/22

Rychetnik, L., Frommer, M., Hawe, P., *et al.* 2002. Criteria for evaluating evidence on public health interventions. *Journal of Epidemiology and Community Health*, 56:119-1127. Doi: 10.1136/jech.56.2.119.

Rycroft-Malone, J., Kitson, A., Harvey, G., *et al.* 2002. Ingredients for change: revisiting a conceptual framework. *Quality and Safety in Health Care*, 11, pp:174-180. Doi: 10.1136/qhc.11.2.174

Rycroft- Malone, J., Harvey, G., Seers, K., *et al.* 2004. An exploration of the factors that influence the implementation of evidence into practice. *Journal of Clinical Nursing*, 13, pp:913-924. Doi: 10.1111/j.1365-2702.2004.01007.x.

Sadek, M.M., Elnour, A.A., Al Kalbani, N.M.S., *et al.* 2016. Community pharmacy and the extended community pharmacist practice roles: the UAE experience. *Saudi Pharmaceutical Journal*, 24, pp:563-70. Doi: 10.1016/j.jsps.2015.03.023.

Saeri, A.K., Slattery, P., Tear, M.J., *et al.* 2021. Scale up of behaviour change interventions: a rapid review of evidence and practice. *OSF Preprints*. Doi: 10.31219/osf.io/scd3k

- Saha, S.K., Kong, D.C.M., Thursky, K., *et al.* 2021. Divergent and convergent attitudes and views of general practitioners and community pharmacists to collaboratively implement antimicrobial stewardship programs in Australia: a nationwide study. *Antibiotics (Basel)*, 10, pp:47. Doi: 10.3390/antibiotics10010047.
- Saini, B., Brillant, M., Filipovska, J., *et al.* 2006. Factors influencing Australian community pharmacists' willingness to participate in research projects – an exploratory study. *International Journal of Pharmacy Practice*, 14, pp:179-88. Doi: 10.1211/ijpp.14.3.0004
- Salari, P., O'Mahony, C., Henrard, S., *et al.* 2022. Cost-effectiveness of a structured medication review approach for multimorbid older adults: within-trial analysis of the OPERAM study. *PLoS ONE*, 17, pp:e0265507. Doi: 10.1371/journal.pone.0265507
- Salisbury, C., Johnson, L., Purdy, S., *et al.* 2011. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. *British Journal of General Practice*, 61, pp:e12-21. Doi: 10.3399/njgp11X548929.
- Salisbury, C., Proctor, S., Stewart, K., *et al.* 2013. The content of general practice consultations: cross-sectional study based on video recordings. *British Journal of General Practice*, 63, pp:e751-759. Doi: 10.3399/bjgp13X674431
- Salmi, L., Brudnicki, S., Isono, M., *et al.* 2020. Six countries, six individuals: resourceful patients navigating medical records in Australis, Canada, Chile, Japan, Sweden and the USA. *BMJ Open*, 10, pp:e037016. Doi: 10.1136/bmjopen-2020-037016
- Sandelowski, M. 1993. Rigor or rigor mortis: the problem of rigor in qualitative research revisited. *Advances in Nursing Science*, 16, pp:1-8.
- Sarang, S., Chakrawarty, A. 2022. Study of outcome in intracapsular fracture of neck of femur in elderly patient treated by hemiarthroplasty. *European Journal of Molecular and Clinical Medicine*, 9, pp:239-45.
- Saunders, R.P., Evans, M.H., Joshi, P. 2005. Developing a process-evaluation plan for assessing health promotion program implementation: a how-to guide. *Health Promotion Practice*, 6, pp:134-47. Doi: 10.1177/1524839904273387

Saunders, B., Sim, J., Kingstone, T., *et al.* 2018. Saturation in qualitative research: exploring its conceptualization and operationalization. *Quality and Quantity*, 52, pp:1893-1907.

Doi:10.1007/s11135-017-0574-8.

Schäfer, I., Kaduszkiewicz, H., Nguyen, T.S., *et al.* 2018a. Multimorbidity patterns and 5-year overall mortality: results from a claims data-based observational study. *Journal of Comorbidity*, 8, pp:2235042X18816588. Doi: 10.1177/2235042X18816588

Schäfer, I., Kaduszkiewicz, H., Mellert, C., *et al.* 2018b. Narrative medicine-based intervention in primary care to reduce polypharmacy: results from the cluster-randomized controlled trial MultiCare AGENDA. *BMJ Open*, 8, pp:e017653. Doi: 10.1136/bmjopen-2017-017653.

Schmader, K.E., Hanlon, J.T., Pieper, C.F., *et al.* 2004. Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly. *The American Journal of Medicine*, 116, pp:394-401. Doi: 10.1016/j.amjmed.2003.10.031.

Schneider, J., Algharably, E.A.E., Budnick, A., *et al.* 2021. High prevalence of multimorbidity and polypharmacy in elderly patients with chronic pain receiving home care are associated with multiple medication-related problems. *Frontiers in Pharmacology*, 12, pp:686990. Doi: 10.3389/fphar.2021.686990

Schober, P., Boer, C., Schwarte, L.A. 2018. Correlation coefficients: appropriate use and interpretation. *Anesthesia & Analgesia*, 126, pp:1763-1768. Doi: 10.1213/ANE.0000000000002864

Schofield, P., Dunham, M., Martin, D., *et al.* 2022. evidence-based clinical practice guidelines on the management of pain in older people – a summary report. *British Journal of Pain*, 16, pp:6-13. Doi: 10.1177/2049463720976155

Schroé, H., van Dyck, D., de Paepe, A., *et al.* 2020. Which behaviour change techniques are effective to promote physical activity and reduce sedentary behaviour in adults: a factorial randomized trial of an e- and m- health intervention. *International Journal of Behavioral Nutrition and Physical Activity*, 17, pp:127. Doi: 10.1186/s12966-020-01001-x

Schulz, K.F., Altman, D.G., Moher, D., for the CONSORT group. 2010. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ*, 340, pp:c332. Doi: 10.1136/bmj.c332

- Scott, I.A., Hilmer, S.N., Reeve, E., *et al.* 2015. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Internal medicine*, 175, pp:827-834. Doi: 10.1001/jamainternmed.2015.0324
- Scott, S.D., Rotter, T., Flynn, R., *et al.* 2019. Systematic review of the use of process evaluations in knowledge translation research. *Systematic Reviews*, 8, pp:266. Doi: 10.1186/s13643-019-1161-y
- Scott, C., de Barra, M., Johnston, M., *et al.* 2020. Using the behaviour change technique taxonomy v1 (BCTTv1) to identify the active ingredients to improve non-hospitalised patient health outcomes. *BMJ Open*, 10, pp:e036500. Doi: 10.1136/bmjopen-2019-036500.
- Scottish Government Polypharmacy Model of Care Group. 2018. Polypharmacy guidance, realistic prescribing. Available at: <https://therapeutics.scot.nhs.uk/wp-content/uploads/2018/04/Polypharmacy-Guidance-2018.pdf> accessed 15/03/2022
- Sedgwick, P. 2015. Understanding the Hawthorne effect. *BMJ*, 351, pp:h4672. Doi: 10.1136/bmj.h4672
- Sekhon, M., Cartwright, M., Francis, J.J. 2016. Acceptability of health care interventions: a semi-structured interview study. *The European Journal of Health Psychology*, 18, pp:565.
- Sekhon, M., Cartwright, M., Francis, J.J. 2017. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. *BMC Health Services Research*, 17, pp:88. Doi: 10.1186/s12913-017-2031-8
- Sekhon, M., van der Straten, A. 2021. on behalf of the MTN-041/MAMMA study team. Pregnant and breastfeeding women's prospective acceptability of two biomedical HIV prevention approaches in Sub Saharan Africa: a multisite qualitative analysis using the Theoretical Framework of Acceptability. *PLoS ONE*, 16, pp:e0259779. Doi: 10.1371/journal.pone.0259779
- Seng, J.J.B., Kwan, Y.H., Fong, W., *et al.* 2020. Validity and reliability of EQ-5D-5L among patients with axial spondyloarthritis in Singapore. *European Journal of Rheumatology*, 7, pp:71-78. Doi: 10.5152/eurjrheum.2020.19043.
- Sera, L.C., McPherson, M.L., 2012. Pharmacokinetics and pharmacodynamic changes associated with aging and implications for drug therapy. *Clinics in Geriatric Medicine*, 28, pp:273-286. Doi: 10.1016/j.cger.2012.01.007.

- Serhal, S., Saini, B., Bosnic-Anticevich, S., *et al.* 2022. A multi-mode education program to enhance asthma care by pharmacists. *American Journal of Pharmaceutical Education*, 86, pp:8633. Doi: 10.5688/ajpe8633
- Seto, H., Ishimaru, N., Ohnishi, J., *et al.* 2022. Multidisciplinary team deprescribing intervention for polypharmacy in elderly orthopedic inpatients: a propensity score-matched analysis of a retrospective cohort study. *Internal Medicine*, 61, pp:2417-26. Doi: 10.2169/internalmedicine.8929-21
- Shamseer, I., Moher, D., Clarke, M., *et al.* 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*, 350, pp:g7647. Doi: 10.1136/bmj.g7647
- Shanyinde, M., Pickering, R.M., Weatherall, M. 2011. Questions asked and answered in pilot and feasibility randomized controlled trials. *BMC Medical Research Methodology*, 11, pp:117.
- Sharma, G. 2017. Pros and cons of different sampling techniques. *International Journal of Applied Research*, 3, pp:749-752.
- Sheehan, K., O'Shea, D., Crowe, M., *et al.* 2014. Potentially inappropriate medications in older hospitalized patients. *Irish Journal of Medical Science*, 1, pp:328.
- Shenoy, P., Harugeri, A. 2015. Elderly patients' participation in clinical trials. *Perspectives in Clinical Research*, 6, pp:184-189. Doi: 10.4103/2229-3485.167099
- Shepherd, V., Wood, F., Griffith, R., *et al.* 2019. Protection by exclusion? The (lack of) inclusion of adults who lack capacity to consent to research in clinical trials in the UK. *Trials*, 20, pp:474. Doi: 10.1186/s13063-019-3603-1
- Shilbayeh, S.A.R., Alyahya, S.A., Alshammari, N.H., *et al.* 2018. Treatment Satisfaction Questionnaire for Medication: validation of the translated Arabic version among patients undergoing warfarin therapy in Saudi Arabia. *Value in Health Regional Issues*, 16, pp:14-21. Doi: 10.1016/j.vhri.2018.01.007
- Shiely, F., Foley, J., Stone, A., *et al.* 2021. Managing clinical trials during COVID-19: experience from a clinical research facility. *Trials*, 22, pp:62. Doi: 10.1186/s13063-020-05004-8
- Sidani, S., Epstein, D.R., Bootzin, R.R., *et al.* 2009. Assessment of preferences for treatment: validation of a measure. *Research in Nursing & Health*, 32, pp:419-431. Doi: 10.1002/nur.20329.



- Sinnott, C., McHugh, S., Browne, J., *et al.* 2013. GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. *BMJ Open*, 3, pp:e003610. Doi: 10.1136/bmjopen-2013-003610
- Sinnott, C., Byrne, M., Bradley, C.P. 2017. Improving medication management for patients with multimorbidity in primary care: a qualitative feasibility study of the MY COMRADE implementation intervention. *Pilot and Feasibility Studies*, 3, pp:14. Doi: 10.1186/s40814-017-0129-8
- Sirois, C., Domingues, N.S., Laroche, M-L. *et al.* 2019. Polypharmacy definitions for multimorbid older adults need stronger foundations to guide research, clinical practice and public health. *Pharmacy*, 7, pp:126. Doi: 10.3390/pharmacy7030126
- Skivington, K., Matthews, L., Simpson, S.A., *et al.* 2021. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *BMJ*, 374, pp:n2061. Doi: 10.1136/bmj.n2061
- Slabaugh, S.L., Maio, V., Abouzaid, S., *et al.* 2010. Prevalence and predictors of polypharmacy amongst elderly patients: a population-based cohort study. *Value in Health*, 13, pp:181. Doi: 10.2165/11584990-000000000-00000.
- Slevin, E., 2000. Enhancing the truthfulness, consistency, and transferability of a qualitative study: using a manifold of approaches. *Nurse Researcher*, 7, pp:79-98. Doi: 10.7748/nr2000.01.7.2.79.c6113
- Soto-Perez-de-Celis, E., Daneng, L., Yuan, Y., *et al.* 2018. Functional versus chronological age: geriatric assessments to guide decision making in older patients with cancer. *Lancet Oncology*, 19, pp:e305-316. Doi: 10.1016/S1470-2045(18)30348-6.
- Spinewine, A., Swine, C., Dhillon, S., *et al.* 2007. Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. *Journal of the American Geriatrics Society*, 55, pp:658-665. Doi: 10.1111/j.1532-5415.2007.01132.x.
- Stahl, N.A., King, J.R., 2020. Understanding and using trustworthiness in qualitative research. *Journal of Developmental Education*, 44, pp:26-28.
- Steinman, M., 2016. Polypharmacy-time to get beyond numbers. *JAMA Internal Medicine*, 176, pp:482-483. Doi: 10.1001/jamainternmed.2015.8597

Steinman, M.A., Low, M., Balicer, R.D., *et al.* 2018. Impact of a nurse-based intervention on medication outcomes in vulnerable older adults. *BMC Geriatrics*, 18, pp:207. Doi: 10.1186/s12877-018-0905-1.

Steinman, M.A., Fick, D.M. 2019. Using wisely: a reminder on the proper use of the American Geriatrics Beers Criteria. *Journal of the American Geriatrics Society*, 67, pp:644-6. Doi: 10.1111/jgs.15766

Sterne, J.A.C., Hernán, M.A., Reeves, B.C., *et al.* 2016. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. *BMJ*, 355, PP:i4919. Doi: 10.1136/bmj.i4919

Sterne, J.A.C., Savović, J., Page, M.J., *et al.* 2019. RoB2: a revised tool for assessing risk of bias in randomised trials. *BMJ*, 366, pp:14898.

Stewart, D., MacLure, K., George, J. 2012. Educating non-medical prescribers. *British Journal of Clinical Pharmacology*, 74, pp:662-7. Doi: 10.1111/j.1365-2125-2012.04204.x

Stewart, D., Klein, S. 2016. The use of theory in research. *International Journal of Clinical Pharmacy*, 38, pp:615-619. Doi:10.1007/s11096-015-0216-y

Stratton, S.J. 2021. Population research: convenience sampling strategies. *Prehospital and Disaster Medicine*, 36, pp:4. Doi: 10.1017/S1049023x21000649

Syafhan, N.F., Azzam, S.A., Williams, S.D., *et al.* 2021. General practitioner practice-based pharmacist input to medicines optimisation in the UK: pragmatic, multicenter, randomised, controlled trial. *Journal of Pharmaceutical Policy and Practice*, 14, pp:4. Doi: 10.1186/s40545-020-00279-3

Taghy, N., Cambon, L., Cohen, J.M., *et al.* 2020. Failure to reach a consensus in polypharmacy definition: an obstacle to measuring risks and impacts – results of a literature review. *Therapeutics and Clinical Risk Management*, 16, pp:57-73. Doi: 10.2147/TCRM.S214187

Tamblyn, R., Huang, A., Perreault, R., *et al.* 2003. The medical office of the 21<sup>st</sup> Century (MOXXI): effectiveness of computerized decision-making support in reducing inappropriate prescribing in primary care. *Canadian Medical Association Journal*, 169, pp:549-556.

Tan, Y.Y., Papez, V., Chang, W.H., *et al.* 2022. Comparing clinical trial population representativeness to real-world populations: an external validity analysis encompassing 43 895 trials and 5, 685, 738 individuals across 989 unique drugs and 286 conditions in England. *The Lancet*. Doi: 10.1016/S2666-7568(22)00186-6.

- Tandan, M., Twomey, B., Twomey, L., *et al.* 2022. National chronic disease management programmes in Irish general practice-preparedness and challenges. *Journal of Personalized Medicine*, 12, pp:1157. Doi: 10.3390/jpm12071157
- Tang, J., Toma, M., Gray, N.M., *et al.* 2020. Pharmacist and Data-Driven Quality Improvement in Primary care (P-DQIP): a qualitative study of anticipated implementation factors informed by the theoretical domains framework. *BMJ Open*, 10, pp:e033574. Doi: 10.1136/bmjopen-2019-033574
- Tannenbaum, C., Tsuyuki, R.T. 2013. The expanding scope of pharmacists' practice: implications for physicians. *Canadian Medical Association Journal*, 185, pp:1228-332. Doi: 10.1503/cmaj.121990
- Tatum, T., Curry, P., Dunne, B., *et al.* 2019. Polypharmacy rates among patients over 45 years. *Irish Medical Journal*, 112,893.
- Tavender, E.J., Bosch, M., Gruen, R.L., *et al.* 2014. Understanding practice: the factors that influence management of mild traumatic brain injury in the emergency department – a qualitative study using the Theoretical Domains Framework. *Implementation Science*, 9, pp:8. Doi:10.1186/1748-5908-9-8.
- Tavender, E.J., Bosch, M., Gruen, R.L., *et al.* 2015. Developing a targeted, theory-informed implementation intervention using two theoretical frameworks to address health professional and organisation factors: a case study to improve the management of mild traumatic brain injury in the emergency department. *Implementation Science*, 10, pp:74. Doi:10.1186/s13012-015-0264-7.
- Tegegn, H.G., Erku, D.A., Sebsibe, G., *et al.* 2019. Medication-relation quality of life among Ethiopian elderly patients with polypharmacy: a cross-sectional study in an Ethiopia university hospital. *PLoS ONE*, 14, pp:e0214191. Doi: 10.1371/journal.pone.0214191
- Tenny, S., Abdelgawad, I. 2022. *Statistical Significance*. In: StatPearls [online]. 2022. StatPearls Publishing, Treasure Island, Florida. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK459346/>
- Thabane, L., Ma, J., Chu, R., *et al.* 2010. A tutorial on pilot studies: the what, why and how. *BMC Medical Research Methodology*, 10, pp:1.

Thake, M., Lowry, A. 2017. A systematic review of trends in the selective exclusion of older participant from randomised clinical trials. *Archives of Gerontology and Geriatrics*, 72, pp:99-102. Doi: 10.1016/j.archger.2017.05.017

The Irish Longitudinal Study on Ageing. 2022. *Documentation*. Available at:

<https://tilda.tcd.ie/data/documentation/> accessed 28/08/2022

Thomas, D.R. 2006. A general inductive approach for analyzing qualitative evaluation data. *American Journal of Evaluation*, 27, pp:237-46. Doi: 10.1177/1098214005283748

Thomas, R.E., Thomas, B.C. 2019. A systematic review of studies of the STOPP/START 2015 and American Geriatrics Society Beers 2015 criteria in patients  $\geq 65$  years. *Current Aging Science*, 12, pp:121-54. Doi: 10.2174/1874609812666190516093742.

Thomas, S., Johnston, B., Barry, S., *et al.* 2021. Sláintecare implementation status in 2020: limited progress with entitlement expansion. *Health Policy*, 125, pp:277-83. Doi: 10.1016/j.healthpol.2021.01.009

Thompson, J. 2016. *Transforming health and social care in Northern Ireland – services and governance*. Available at:

<http://www.niassembly.gov.uk/globalassets/documents/raise/publications/2016-2021/2016/health/4016.pdf> accessed 07/08/2022 [checked 26/08/22]

Thornton, J. 2020. Clinical trials suspended in UK to prioritise covid-19 studies and free up staff. *BMJ*, 368, pp:m1172. Doi: 10.1136/bmj.m1172.

Tian, L., Yang, Y., Sui, W., *et al.* 2017. Implementation of evidence into practice for cancer-related fatigue management of hospitalized adult patients using the PARIHS framework. *PLoS One*, 12, pp:e0187257. Doi: 10.1371/journal.pone.0187257.

Tobin, G.A., Begley, C.M., 2004. Methodological rigour within a qualitative framework. *Journal of Advanced Nursing*, 48, pp:388-96. Doi: 10.1111/j.1365-2648.2004.03207.x.

Tock, W., Maheu, C., Johnson, N.A. 2022. Considerations of control conditions designs in randomized controlled trials of exercise interventions for cancer survivors. *Canadian Journal of Nursing Research*, 0, pp:1-15. Doi: 10.1177/084456212111062467

Toivo, T., Dimitrow, M., Puustinen, J., *et al.* 2018. Coordinating resources for prospective medication risk management of older home care clients in primary care: procedure development and RCT study design for demonstrating its effectiveness. *BMC Geriatrics*, 18, pp:74. Doi:10.1186/s12877-018-0737-z.

- Toivo, T., Airaksinen, M., Dimitrow, M., *et al.* 2019. Enhanced coordination of care to reduce medication risks in older home care clients in primary care: a randomized controlled trial. *BMC Geriatrics*, 1, pp:332. Doi:10.1186/s12877-019-1353-2
- Tong, A., Sainsbury, P., Craig, J. 2007. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 19, pp:349-357.
- Topolovec-Vranic J, Natarajan K. 2016. The use of social media in recruitment for medical research studies: a scoping review. *Journal of Medical Internet Research*, 18, pp:e286. Doi: 10.2196/jmir.5698.
- Topriceanu, C.C., Wong, A., Moon, J.C., *et al.* 2021. Evaluating access to health and care services during lockdown by the COVID-19 survey in five UK national longitudinal studies. *BMJ Open*, 11, pp:e045813. Doi: 10.1136/bmjopen-2020-045813
- Tordoff, J.M., Brenkley, C., Krska, J., *et al.* 2019. Exploring medicines burden among adults in New Zealand: a cross-sectional study. *Patient Preference and Adherence*, 13, pp:2171-84. Doi: 10.2147/PPA.S231202
- Torjesen, I. 2015. More than 400 pharmacists will be recruited to GP surgeries by next year. *BMJ*, 351, pp:h6167.
- Tracy, S.J. 2012. *Qualitative research methods: collecting evidence, crafting analysis, communicating impact*. Massachusetts, Wiley-Blackwell.
- Truong, H.A., Taylor, C.R., DiPietro, N.A. 2012. The assessment, development, assurance pharmacist's tool (ADAPT) for ensuring quality implementation of health promotion programs. *American Journal of Pharmaceutical Education*, 76, pp:12. Doi: 10.5688/ajpe76112.
- Trumic, E., Pranjic, N., Begic, L., *et al.* 2012. Idiosyncratic adverse reactions of most frequent drug combinations longterm use among hospitalized patients with polypharmacy. *Medical Archives*, 66, pp:243-248. Doi: 10.5455/medarh.2012.66.243-8.
- Tseng, H.-M., Lee, C.-H., Chen, Y.-J., *et al.* 2016. Developing a measure of medication-related quality of life for people with polypharmacy. *Quality of Life Research*, 25, pp:1295-302. Doi: 10.1007/s11136-015-1177-2

Turner, D.W. 2010. Qualitative interview design: a practical guide for novice investigators. *The Qualitative Report*, 15, pp:754-60. Doi: 10.46743/2160-3715/2010.1178

Turner, B. 2018. Putting Ireland's health spending into perspective. *The Lancet*, 391, pp:833–834. Doi: 10.1016/S0140-6736(18)30461-6

Ubeda, A., Ferrándiz, L., Maicas, N., *et al.* 2012. Potentially inappropriate prescribing in institutionalised older patients in Spain: the STOPP-START criteria compared with the Beers criteria. *Pharmacy Practice (Granada)*, 10, pp:83-91. Doi: 10.4321/s1886-36552012000200004

Uhl, M., Muth, C., Gerlach, F.M., *et al.* 2018. Patient-perceived barriers and facilitators to the implementation of a medication review in primary care: a qualitative thematic analysis. *BMC Family Practice*, 19, pp:3. Doi: 10.1186/s12875-017-0707-0

Uitvlugt, E.B., En-nasery-de Heer, S., van den Bemt, B.J.F., *et al.* 2022. The effect of a transitional pharmaceutical care program on the occurrence of ADEs after discharge from hospital in patients with polypharmacy. *Research in Social and Administrative Pharmacy*, 18, pp:2651-8. Doi: 10.1016/j.sapharm.2021.05.009.

United Nations, Department of Economic and Social Affairs, Population Division. 2019. *World Population Ageing 2019: Highlights*. Available at: <https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Highlights.pdf> accessed 19/08/2022

Urban, R., Paloumpi, E., Rana, N., *et al.* 2013. Communicating medication changes to community pharmacy post-discharge: the good, the bad, and the improvements. *International Journal of Clinical Pharmacy*, 35, pp:813-20.

Van, C., Costa, D., Abbott, P., *et al.* 2012. Community pharmacist attitudes towards collaboration with general practitioners: development and validation of a measure and a model. *BMC Health Services Research*, 12, pp:320. Doi: 10.1186/1472-6963-12-320.

van Blijswijk, S.C.E., de Waard, C.S., van Peet, P.G., *et al.* 2018. Wishes and needs of community-dwelling older persons concerning general practice: a qualitative study. *PLoS One*, 13, pp:e0200614. Doi: 10.1371/journal.pone.0200614

van den Akker, M., Buntinx, F., Metsemakers, J.F. *et al.* 1998. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *Journal of Clinical Epidemiology*, 51, pp:367-375. Doi: 10.1016/s0895-4356(97)00306-5.

van der Cammen, T.J.M., Crome, P. 2018. Persistent exclusion of older people from clinical trials of cardiovascular and antithrombotic medicinal products. *European Geriatric Medicine*, 9, pp:413-414. Doi: 10.1007/s41999-018-0080-0

van der Laan, D.M., Elders, P.J.M., Boons, C.C.L.M., *et al.* 2018. The impact of cardiovascular medication use on patients' daily lives: a cross-sectional study. *International Journal of Clinical Pharmacy*, 40, pp:412-20. Doi: 10.1007/s11096-018-0601-4

van der Meer, H., Wouters, H., Pont, L.G., *et al.* 2018. Reducing the anticholinergic and sedative load in older patients on polypharmacy by pharmacist-led medication review: a randomized controlled trial. *BMJ Open*, 8, pp:e019042. Doi: 10.1136/bmjopen-2017-019042.

van der Stelt, C.A.K., Vermeulen Windsent-van den Tweel, A.M.A., Egberts, A.C.G., *et al.* 2016. The associations between potentially inappropriate prescribing and medication-related hospital admissions in older patients: a nested case control study. *Drug Safety*, 39, pp:79-87. Doi: 10.1007/s40264-015-0361-1.

van Hout, B., Janssen, M.F., Feng, Y.S., *et al.* 2012. Interim scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value in Health*, 15, pp:708-15. Doi: 10.1016/j.val.2012.02.008.

van Lint, J.A., Sorge, L.A., Sorensen, T.D. 2015. Access to patients' health records for drug therapy problem determination by pharmacists. *Journal of the American Pharmacists Association*, 55, pp:278-81. Doi: 10.1331/JAPhA.2015.14102

van Summeren, J.J., Schuling, J., Haajer-Ruskaamp, F.M., *et al.* 2017. Outcome prioritisation tool for medication review in older patients with multimorbidity: a pilot study in general practice. *British Journal of General Practice*, 67, pp:e501-6. Doi: 10.3399/bjgp17X690485.

van Teijlingen, E.R., Hundley, V., 2002. The importance of pilot studies. *Nursing Standard*, 16, pp:33-6. Doi: 10.7748/ns2002.06.16.40.33.c3214.

Varas-Doval, R., Saéz-Benito, L., Gastelurrutia, M.A., *et al.* 2021. Systematic review of pragmatic randomised control trials assessing the effectiveness of professional pharmacy

- services in community pharmacies. *BMC Health Services Research*, 21, pp:156. Doi: 10.1186/s12913-021-06150-8
- Varley, J., Delanty, N., Normand, C., *et al.* 2010. Epilepsy in Ireland: towards the primary-tertiary care continuum. *Seizure*, 19, pp:47-52. Doi: 10.1016/j.seizure.2009.11.002
- Varpio, L., Paradis, E., Uijtdehaage, S., *et al.* 2020. The distinctions between theory, theoretical framework and conceptual framework. *Journal of the Association of American Medical Colleges*, 95, pp:989-994. Doi: 10.1097/ACM.0000000000003075
- Vasileiou, K., Barnett, J., Thorpe, S. *et al.* 2018. Characterising and justifying sample size sufficiency in interview-based studies: systematic analysis of qualitative health research over a 15-year period. *BMC Medical Research Methodology*, 18, pp:148. Doi: 10.1186/s12874-018-0594-7
- Veehof, L.J.G., Meyboom-De Jong, B., Haaijer-Ruskamp, F.M. 2000. Polypharmacy in the elderly – a literature review. *European Journal of General Practice*, 6, pp:98-106. Doi: 10.3109/13814780009069956
- ven den Brink, M.J., Hummel, M., Lemstra, M., *et al.* 2020. Factors affecting patient recruitment to trials: qualitative research in general practice. *BJGP Open*, 4, pp:bjgopen20X101056. Doi: 10.3399/bjgpopen20X101056
- Verdoorn, S., Kwint, H-F., Blom, J.W., *et al.* 2019. Effects of a clinical medication review focused on personal goals, quality of life, and health problems in older persons with polypharmacy: a randomised controlled trial (DREAMeR-study). *PLoS Medicine*, 16, pp:e1002798. Doi: 10.1371/journal.pmed.1002798.
- Verhoeven, V., Tsakitzidis, G., Philips, H., *et al.* 2020. Impact of the COVID-19 pandemic on the core functions of primary care: will the cure be worse than the disease? A qualitative interview study in Flemish GPs. *BMJ Open*, 10, pp:e039674. Doi: 10.1136/bmjopen-2020-039674
- Vermersch, P., Hobart, J., Dive-Pouletty, C., *et al.* 2017. Measuring treatment satisfaction in MS: Is the Treatment Satisfaction Questionnaire for Medication fit for purpose? *Multiple Sclerosis Journal*, 23, pp:604-13. Doi: 10.1177/1352458516657441
- Victoria, C.G., Barros, F.C., Assuncao, M.C., *et al.* 2012. Scaling up maternal nutrition programs to improve birth outcomes: implementation issues. *Food and Nutrition Bulletin*, 33, pp:S6



- Viegas, R., Godinho, C.A., Romano, S. 2021. Physical activity promotion in community pharmacies: pharmacists' attitudes and behaviours. *Pharmacy Practice*, 19, pp:2413. Doi: 10.18549/PharmPract.2021.3.2413
- Viktil, K.K., Blix, H.S., Moger, T.A., *et al.* 2007. Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. *British Journal of Clinical Pharmacology*, 63, pp:187-195. Doi: 10.1111/j.1365-2125.2006.02744.x
- Violan, C., Foguet-Boreu, Q., Flores-Mateo, G., *et al.* 2014. Prevalence, determinants and patterns of multimorbidity in primary care: A systematic review of observational studies. *PLoS ONE*, 9, pp:3–11. Doi: 10.1371/journal.pone.0102149
- Volfson, Z., McPherson, A.C., Tomasone, J.R., *et al.* 2020. Examining factors of physical activity participation in youth with spina bifida using the Theoretical Domains Framework. *Disability and Health Journal*, 13, pp:100922. Doi:10.1016/j.dhjo.2020.100922.
- Von den Baumen, T., Lake, J., Everall, A.C., *et al.* 2020. "Clearly they are in the circle of care, but...": A qualitative study exploring perceptions of personal health information sharing with community pharmacists in an integrated care model. *Canadian Pharmacists Journal/Revue des Pharmaciens du Canada*, 153, pp:378-98. Doi: 10.1177/1715163520956686
- Wacker, J.G. 1998. A definition of theory: research guidelines for different theory-building research methods in operations management. *Journal of Operations Management*, 16, pp:361-385.
- Wager, E., Wiffen, P.J. 2011. Ethical issues in preparing and publishing systematic reviews. *Journal of Evidence-based Medicine*, 4, 130-4. Doi: 10.1111/j.1756-5391.2011.0112.x
- Wallace, E., Salisbury, C., Guthrie, B., *et al.* 2015. Managing patients with multimorbidity in primary care. *BMJ*, 350, pp:h176. Doi: 10.1136/bmj.h176
- Wallis, K.A., Elley, C.R., Moyes, S., *et al.* 2018. Safer Prescribing and Care for the Elderly (SPACE): a pilot study in general practice. *BJGP Open*, 2, pp:bjgpopen18X101594. Doi: 10.3399/bjgpopen18X101594.
- Warren, C.A.B. 2002. Qualitative Interviewing. In Gubrium, J.F., Holstein, J.A. (eds) *Handbook of Interview Research: Context and Method*. Thousand Oaks California: SAGE.

- Wasilewski, M.B., Stinson, J.N., Webster, F., *et al.* 2019. Using Twitter to recruit participants for health research: an example from a caregiving study. *Health Informatics Journal*, 25, pp:1485-97. Doi: 10.1177/1460458218775158
- Waszyk-Nowaczyk, M., Guzenda, W., Kamasa, K., *et al.* 2021. Cooperation between pharmacists and physicians – whether it was before and is it still ongoing during the pandemic? *Journal of Multidisciplinary Healthcare*, 14, pp:2101-10.
- Watanabe, J.H., Yang, J., 2019. Hospitalization and combined use of opioids, benzodiazepines, and muscle relaxants in the United States. *Hospital Pharmacy*, 55, pp:5.  
Doi:10.1177/0018578719894702.
- Watson, M.C., Bond, C.M., Johnston, M., *et al.* 2006. Using human error theory to explore the supply of non-prescription medicines from community pharmacies. *Quality & Safety in Health Care*, 15, pp:244-250. Doi: 10.1136/qshc.2005.014035.
- Watson, J., Cumming, O., MacDougall, A., *et al.* 2021. Effectiveness of behaviour change techniques used in hand hygiene interventions targeting older children – a systematic review. *Social Science and Medicine*, 281, pp:114090. Doi: 10.1016/j.socscimed.2021.114090.
- Webb, T., Joseph, J., Yardley, L., *et al.* 2010. Using the internet to promote health behaviour change: a systematic review and meta-analysis of the impact of theoretical basis, use of behaviour change techniques, and mode of delivery on efficacy. *Journal of Medical Internet Research*, 12, pp:e4. Doi: 10.2196/jmir.1376.
- Webb Girard, A., Waugh, E., Sawyer, S., *et al.* 2020. A scoping review of social-behaviour change techniques applied in complementary feeding interventions. *Maternal and Child Nutrition*, 16, pp:e12882. Doi: 10.1111/mcn.12882.
- Weir, K.R., Bonner, C., McCaffery, K., *et al.* 2019. Pharmacists and patients sharing decisions about medicines: development and feasibility of a conversation guide. *Research in Social and Administrative Pharmacy*, 15, pp:682-90. Doi: 10.1016/j.sapharm.2018.08.009
- Weiss, M.C., Platt, J., Riley, R., *et al.* 2015. Medication decision making and patient outcomes in GP, nurse and pharmacist prescriber consultations. *Primary Health Care Research and Development*, 16, pp:513-27. Doi: 10.1017/S146342361400053X.

- Wenger, N.S., Shekelle, P.G., 2001. Assessing care of vulnerable elders: ACOVE project overview. *Annals of Internal Medicine*, 135, pp:642-646. Doi: 10.7326/0003-4819-135-8\_part\_2-200110161-00002.
- Whiffin, C.J., 2021. *Choose your methodology: little quick fix*. Thousand Oaks, California: SAGE.
- White, C., Alton, E. 2022. The interface between primary care and care homes: general practitioner experiences of working in care homes for older people. *Health & Social Care in the Community*, 30, pp:e2896-904. Doi: 10.1111/hsc.13734
- Whitman, A., DeGregory, K., Morris, A., *et al.* 2018. Pharmacist-led medication assessment and deprescribing intervention for older adults with cancer and polypharmacy: a pilot study. *Supportive Care in Cancer*, 26, pp:4105-4113. Doi: 10.1007/s00520-018-4281-3.
- Wille, N., Badia, X., Bonsel, G., *et al.* 2010. Development of the EQ-5D-Y: a child-friendly version of the EQ-5D. *Quality of Life Research*, 19, pp:875-86. Doi: 10.1007/s11136-010-9648-Y.
- Williams, S., Hayes, J., Brad, L., 2018. Clinical pharmacists in general practice: a necessity not a luxury? *British Journal of General Practice*, 68, pp:85. Doi:10.3399/bjgp18X694697.
- Winder, R., Richards, S.H., Campbell, J.L., *et al.* 2017. Development and refinement of a complex intervention within cardiac rehabilitation services: experiences from the CADENCE feasibility study. *Pilot and Feasibility Studies*, 3, pp:9. Doi: 10.1186/s40814-017-0123-1
- Woit, C., Yuksel, N., Charrois, T.L. 2019. Competence and confidence with prescribing in pharmacy and medicine: a scoping review. *International Journal of Pharmacy Practice*, 28, pp:312-25. Doi: 10.1111/IJPP.12595
- Woolford, S.J., Aggarwal, P., Sheikh, C.J., *et al.* 2021. Frailty, multimorbidity and polypharmacy. *Medicine*, 49, pp:166-172. Doi:10.1016/j.mpmed.2020.12.010
- Wootton, R., Craig, J., Patterson, V. 2017. *Introduction to telemedicine*. 2<sup>nd</sup> edition. London: CRC Press
- World Health Organization. 2010. *Nine steps for developing a scaling-up strategy*. available at: [https://www.who.int/immunization/hpv/deliver/nine\\_steps\\_for\\_developing\\_a\\_scalingup\\_strategy\\_who\\_2010.pdf](https://www.who.int/immunization/hpv/deliver/nine_steps_for_developing_a_scalingup_strategy_who_2010.pdf) accessed 07/02/2022

World Health Organisation and United Nations Children's Fund (UNICEF). 2018. *A vision for primary health care in the 21<sup>st</sup> century: towards universal health coverage and the Sustainable Development Goals*. Available at:

<https://apps.who.int/iris/bitstream/handle/10665/328065/WHO-HIS-SDS-2018.15-eng.pdf?sequence=1&isAllowed=y> accessed 26/01/2022

World Health Organisation. 2019. *Medication safety in polypharmacy*. Available at:

<https://www.who.int/publications/i/item/WHO-UHC-SDS-2019.11> accessed 19/08/2022

World Health Organisation. 2020. Coronavirus disease 2019 (COVID-19) Situation Report – 51.

Available at: [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf?sfvrsn=1ba62e57\\_10](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf?sfvrsn=1ba62e57_10) accessed 27/01/2022

World Medical Association. 2001. WMA Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bulletin of the World Health Organisation*, 79, 373-4.

Wright, E.A., Graham, J.H., Maeng, D., *et al.* 2019. Reductions in 30-day readmission, mortality, and costs with inpatient-to-community pharmacist follow-up. *Journal of the American Pharmacists Association*, 59, pp:178-86.

Xing, Z., Wang, Y., Li, H., *et al.* 2019. Theory-based interventions to promote fluid intake adherence among dialysis patients: a systematic review. *Research and Theory for Nursing Practice*, 33, pp:357-391. Doi: 10.1891/1541-6577.33.4.357.

Yamada, J., Kouri, A., Simard, S.-N., *et al.* 2020. Barriers and enablers to using a patient-facing electronic questionnaire: a qualitative theoretical domains framework analysis. *Journal of Medical Internet Research*, 22, pp:e19474. Doi:10.2196/19474.

Yamey, G. 2011. Scaling up global health interventions: a proposed framework for success. *PLoS Medicine*, 8, pp:e1001049. Doi: 10.1371/journal.pmed.1001049

Yang, K., Banamah, A. 2014. Quota sampling as an alternative to probability sampling? An experimental study. *Sociological Research Online*, 2014. Doi: 10.5153/sro.3199

Yarnall, A.J., Sayer, A.A., Clegg, A., *et al.* 2017. New horizons in multimorbidity in older adults. *Age and Ageing*, 46, pp:882-888. Doi:10.1093/ageing/afx150

Yeen, Y.L., Arulanandam, L.T., Lai, M.M., *et al.* 2019. Quality assurance of HIV rapid testing: a cross-sectional interlaboratory comparison. *Medical Journal of Malaysia*, 74, pp:S2.

Yeung, A.W.K., Kletecka-Pulker, M., Eibensteiner, F., *et al.* 2021. Implications of Twitter in health-related research: a landscape analysis of the scientific literature. *Frontiers in Public Health*, 9, pp:654481. Doi: 10.3389/fpubh.2021.654481

Yong, F.R., Hor, S.-Y., Bajorek, B.V. 2021. Considerations of Australian community pharmacists in the provision and implementation of cognitive pharmacy services: a qualitative study. *BMC Health Services Research*, 21, pp:906. Doi: 10.1186/s12913-021-06838-x

Zamboni, K., Schellenberg, J., Hanson, C., *et al.* 2019. Assessing scalability of an intervention: why, how and who? *Health Policy and Planning*, 34, pp:544-552. Doi: 10.1093/heapol/czz068

Zaninotto P, Di Gessa G, Steel N. 2020. The experience of older people with multimorbidity during the COVID-19 pandemic. Available at: [https://11a183d6-a312-4f71-829a-79ff4e6fc618.filesusr.com/ugd/540eba\\_bb1d692cf19a4b79bf68b2c5dd9a3d1f.pdf](https://11a183d6-a312-4f71-829a-79ff4e6fc618.filesusr.com/ugd/540eba_bb1d692cf19a4b79bf68b2c5dd9a3d1f.pdf) accessed 27/01/2022

Zia, A., Kamaruzzaman, S.B., Tan, M.P. 2015. Polypharmacy and falls in older people: balancing evidence-based medicine against falls risk. *Postgraduate Medical Journal*, 127, pp:330-337. Doi: 10.1080/00325481.2014.996112.

Zidan, A., Awaisu, A., El-Hajj, M.S., *et al.* 2018. Medication-related burden among patients with chronic disease conditions: perspectives of patients attending non-communicable disease clinics in a primary healthcare setting in Qatar. *Pharmacy*, 6, pp:85. Doi: 10.3390/pharmacy6030085

Zisberg, A., Agmon, M., Gur-Yaish, N., *et al.* 2018. No one size fits all-the development of a theory-driven intervention to increase in-hospital mobility: the “WALK-FOR” study. *BMC Geriatrics*, 18, pp:91. Doi: 10.1186/s12877-018-0778-3.