DEVELOPMENT OF AN INTERVENTION TO SUPPORT MEDICATION MANAGEMENT IN PATIENTS WITH MULTIMORBIDITY IN PRIMARY CARE

A thesis submitted to the National University of Ireland, Cork for the degree of Doctor of Philosophy in General Practice

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LIST OF ABBREVIATIONS

ACE	Adverse childhood experience
ADR	Adverse drug reaction
APEASE	Affordability, practicability, effectiveness and cost effectiveness, acceptability, side effects/safety and equity: criteria used for selecting intervention strategies.
BCW	Behaviour Change Wheel
BMI	Body mass index
CDC	Centre for Disease Control
CES-D	Centre for Epidemiologic Studies Depression questionnaire
COM-B	Capability, Opportunity, Motivation – Behaviour: refers to a model of behaviour.
CSR	Chart simulated recall
FEMPI	Financial Emergency Measures in the Public Interest Act 2009
GMS	General Medical Services
GP	General Practitioner
HADS-A	Hospital Anxiety and Depression Scale- Anxiety component
HCP	Healthcare professional
ICGP	Irish College of General Practitioners
IQR	Interquartile range
LMIC	Low and middle income countries
MRC	Medical Research Council
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
RWA	Recommended weekly allowance
SD	Standard deviation
UK	United Kingdom
US	United States

DECLARATION

I declare that this thesis has not been submitted for another degree either at University College Cork or elsewhere. The work, upon which this thesis is based, was carried out in collaboration with a team of researchers and supervisors who are duly acknowledged in the text of the thesis. The Library may lend or copy this thesis upon request.

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Signed Date

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I am extremely grateful to many individuals who shared their expertise and support during the course of this thesis. To start, I would like to acknowledge my supervisor Professor Bradley for his constant guidance in both the research and clinical aspects of my fellowship. I would like to thank the South East GP training scheme who facilitated my combined GP training/research fellowship at every stage, especially Dr. Martin Rouse, Ms. Patricia Drennan, the assistant directors and my GP trainers Dr. Liam Meagher, Dr. Joseph Meehan, Dr. Mark Rowe and Dr. Ita Creavin.

I am indebted to the twenty GPs who participated in the qualitative interview study, and the additional fifteen GPs who participated in the feasibility study. I thank the participants, the study nurses, the administrators and clinical staff at the Living health primary care centre, Mitchelstown, Cork (source of data for Chapter 8). I would like to thank all my co-researchers and co-authors: Sheena Mc Hugh, John Browne, Maria Boyce, Martina Kelly, Patricia Kearney, Molly Byrne, Stewart Mercer, Martin Duerden and Rupert Payne.

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THESIS ABSTRACT

Background

Amongst patients who have chronic disease, the majority have multiple chronic diseases (multimorbidity). Because medical evidence and guidelines are structured around single diseases, multimorbidity can lead to problems for general practitioners (GPs) when prescribing medications. The overarching aim of this thesis is to develop an intervention to support patient-centred prescribing in the context of multimorbidity in primary care.

Methods

A range of research methods were used to address different components of the Medical Research Council, UK (MRC) guidance on the development and evaluation of complex interventions in health care. The existing evidence on GPs' perceptions of the management of multimorbidity was systematically reviewed and synthesized. This was supplemented with new evidence by conducting a qualitative interview study and a cross-sectional study. In qualitative interviews, chart-stimulated recall was used to explore the challenges experienced by GPs when prescribing for multimorbid patients. The utility of chart-stimulated recall as a clinical research method was also systematically reviewed. In the cross-sectional study, data from the Mitchelstown Cohort Study was used to understand the psychosocial issues that can occur with and complicate the management of multimorbidity. To develop the complex intervention, the Behaviour Change Wheel (BCW) was used to integrate behavioural theory with the findings of the systematic review, qualitative interviews and cross-sectional study. A feasibility study of the new intervention was then conducted with GPs.

Results

The systematic review revealed GPs' isolation in decision-making for multimorbid patients, which resulted from difficulties in four areas: disorganization and fragmentation of health care; inadequacy of guidelines and medical evidence; challenges delivering patient-centred care; and barriers to shared decision-making. The qualitative interview study showed that GPs responded to these difficulties by 'satisficing': accepting care that they deemed satisfactory and sufficient for a particular patient. In multimorbid patients perceived as stable, GPs preferred to 'maintain the status quo' rather than actively change medications. In the cross-sectional study, the significant association between multimorbidity and a range of negative psychosocial factors was shown. The findings of these three studies were used to guide the development of the 'Multimorbidity Collaborative Medication Review and Decision-making' (MY COMRADE) intervention. This intervention primarily involves peer support: two GPs review the medications prescribed to a complex multimorbid patient together. In the feasibility study, pairs of GPs reviewed medications using the MY COMRADE approach. They reported that the intervention was appropriate for the context of general practice; was widely applicable to their patients with multimorbidity; and recommendations for optimising medications arose from all collaborative reviews.

Conclusion

This work responds to the call for interventions to improve patient-centred medication management in multimorbidity. Applying theory to empirical data has led to an intervention that fits well into clinical practice, and has the potential to positively change GPs' behaviour to support the conduct of medication review for patients with multimorbidity.

CHAPTER 1. INTRODUCTION

1.1. Introduction

Multimorbidity is the co-occurrence of two or more chronic medical conditions in one person. In general practice, individual chronic conditions are common: approximately one third of Irish adults have a chronic condition such as hypertension, cardiovascular disease, diabetes or stroke (1). However, more patients have multimorbidity than even the most common individual chronic condition (2, 3). Healthcare systems and clinical evidence remain overwhelmingly orientated towards the management of individual conditions with relatively few initiatives addressing the reality that the majority of people with chronic disease have multimorbidity (4).

This mismatch can lead to problems in the management of patients with multimorbidity in general practice, especially in the management of medications. Combining clinical practice guidelines in the treatment of patients with multimorbidity can lead to burdensome and even harmful polypharmacy (5). Individual medications may be effective for a specific condition, but higher numbers of medications are associated with adverse effects, interactions and poor adherence (6).

Therefore, there is a need for new patient-centred approaches to chronic disease management that acknowledge the predominance of multimorbidity. Rather than considering diseases in isolation, a patient-centred approach advocates consideration of the patient's illnesses in a whole-person, biopsychosocial context (7). Regarding medication management, interventions that support proactive chronic disease care while avoiding medication-related harm are required. The question is how to develop an intervention which facilitates care that is consistent with the best available evidence *and* tailored to the needs and preferences of the individual patient.

The Medical Research Council, UK (MRC) has issued a widely used framework for the development of interventions in healthcare (8). This framework advocates using the best available (and if necessary, new) evidence and appropriate theory to develop interventions. It states that a thorough understanding of existing practice is required prior to intervention development and implementation, as inadequate consideration of participants' perspectives or context can diminish an intervention's clinical impact. If information on existing practice is lacking, primary research should be conducted. This framework provides a useful starting point for developing interventions to improve medication management in multimorbidity because, despite the high prevalence of multimorbidity, the specific challenges experienced by general practitioners (GPs) in relation to prescribing for these patients, and their responses to those challenges, have been poorly described.

1.2. Aim

The overarching aim of this thesis is to develop an intervention to support patient-centred prescribing for patients with multimorbidity in general practice. Broadly, this involves gaining insights into GPs' current practice, and then integrating these insights with behavioural theory to develop a behaviour change intervention to support and improve prescribing.

1.3. Objectives

Adhering to the phases outlined in the MRC guidance on the development of interventions in health care, the specific objectives of this thesis are:

1. To identify and review the existing evidence on the challenges experienced by GPs in the management of patients with multimorbidity.

2. To generate new information on the complexities of clinical decision-making for patients with multimorbidity in primary care by
    a. exploring the challenges experienced by GPs when prescribing for these patients, using case-based data.
    b. examining the social, behavioural and psychological factors that can occur with, and complicate the management of, patients with multimorbidity.
3. To develop an intervention targeted at GPs, by combining behavioural theory with evidence gained from objectives 1 and 2, and using the input of an expert panel.
4. To evaluate the feasibility and implementation of the new intervention in a study with GPs.

1.4. Thesis outline

This thesis contains eleven chapters, six of which are studies that address the aims and objectives (Figure 1).

In Chapter 2, the context for this research, including the role of general practice in the Irish healthcare system and recent changes to the landscape of Irish general practice are described.

Chapter 3 provides an introduction to the problem of multimorbidity, and the related issues of polypharmacy and clinical practice guidelines. Existing approaches to improve medication management in primary care are reviewed.

Chapter 4 gives an overview of the research methods used in this thesis to address different phases of the MRC guidance on the development and evaluation of complex interventions in health care.

Chapters 5, 6, 8, 9 and 10 represent phases of the MRC framework. In Chapter 5, the existing evidence on GPs' perceptions of the management of multimorbidity is

systematically reviewed and synthesized. This evidence had not been systematically collated prior to this thesis. Chapter 6 describes qualitative research on the complexities of clinical decision-making for patients with multimorbidity. Chapter 8 details new findings on the negative psychosocial factors which can occur with and may complicate the management of multimorbidity, and therefore warrant consideration in the development of patient-centred interventions. In Chapter 9, the process of developing a theory-based intervention is described. Chapter 10 is the feasibility study of the new theory-based intervention, which was conducted with GPs.

Chapter 7 details a scoping review of chart-stimulated recall. This method was used in the qualitative interviews in Chapter 6, and its application to clinical research had not been systematically reviewed prior to this thesis.

Chapter 11 provides an overall discussion of the research, including strengths and limitations, and makes suggestions for future research and policy implications.

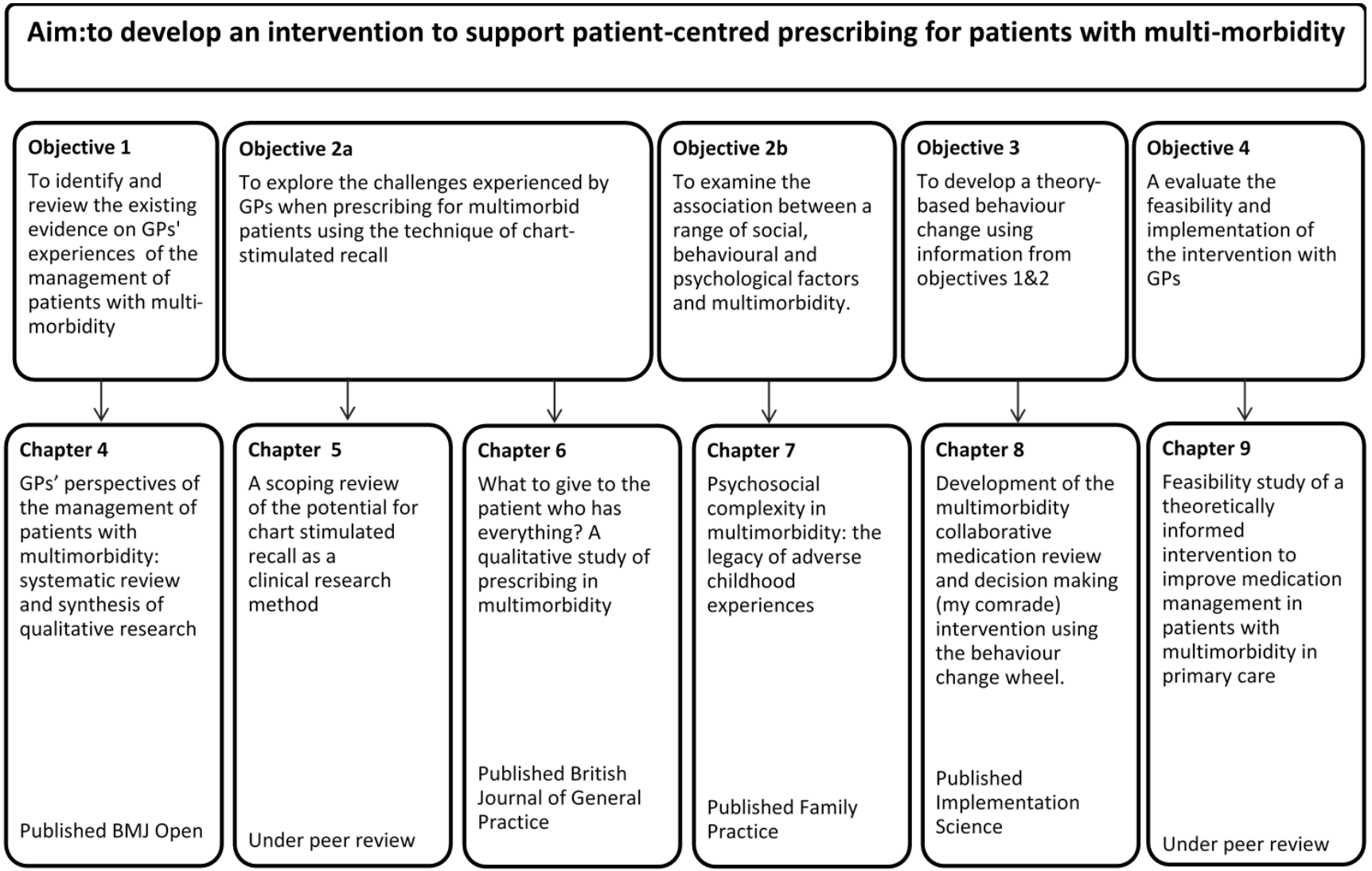

Figure 1. Thesis outline

1.5. Author's contribution to the included studies

I was the lead author of the research papers in Chapters 5 to 10. This involved writing the protocol for each study, literature searching, collecting, managing and analysing data, and drafting each manuscript. Professor Colin Bradley supervised the drafting of the original proposal for this PhD, and guided the design, conduct and write-up of each of the studies.

Additional expertise was gained from the following individuals:

- Dr Sheena Mc Hugh, Research Fellow, Department of Epidemiology and Public Health, UCC
    - Second coder for the qualitative synthesis (Chapter 5) and qualitative interview study (Chapter 6), assistance with formulation of research question and drafting of manuscript (Chapter 8).
- Professor John Browne, Department of Epidemiology and Public Health, UCC
    - Expertise on methods for systematic review (Chapter 5)
- Dr Maria Boyce, Postdoctoral researcher, UCC (2013-14)
    - Critically reviewed interview techniques, and carried out data coding, analysis and interpretation for qualitative interview study (Chapter 6)
- Dr Martina Kelly, Associate Professor, Department of Family Medicine, University of Calgary, Canada
    - Second reviewer for study selection, data extraction, quality appraisal, and analysis (Chapter 7)
- Professor Patricia Kearney, Department of Epidemiology and Public Health, UCC
    - Expertise on formulation of research question, methods for secondary analysis and drafting of research paper using the Mitchelstown cohort study (Chapter 8)

- Dr Anthony Fitzgerald, Senior Lecturer, School of Mathematical Sciences, UCC.
    - Expertise on formulation of research question and regression analysis (Chapter 8)
- Dr Molly Byrne, Senior Lecturer, Health Behaviour Change Research Group, School of Psychology, National University of Ireland, Galway
    - Expertise on behavioural science and intervention design, and member of expert panel (Chapter 9); second coder for evaluation interviews in feasibility study (Chapter 10)
- Professor Stewart Mercer, Chair in Primary Care Research, University of Glasgow, Scotland
    - Expertise on intervention development in multimorbidity and member of expert panel (Chapter 9)
- Dr Martin Duerden, Senior Clinical Lecturer in Health Technology Assessment, Centre for Health Economics and Medicines Evaluation, Bangor University, Wales
    - Expertise on clinical pharmacology and prescribing in multimorbidity and member of expert panel (Chapter 9)
- Dr Rupert Payne, Clinical Lecturer in General Practice, University of Cambridge
    - Expertise on clinical pharmacology and prescribing in multimorbidity and member of expert panel (Chapter 9)

1.6. Author's professional role

I conducted the research for this thesis in tandem with GP training, as a fellow on the National Specialist Registrar Academic Fellowship Programme (NSAFP). The fellowship spanned five years during which I completed my final two years of GP training (on a part-time basis over four years) while simultaneously gaining training in and conducting

research for a PhD degree. As a GP trainee, my GP training practices were Killenaule Family Practice, Co. Tipperary (three days a week over six months); Ardmore Health Centre, Co. Waterford (three days a week over one year); and the Rowe Creavin General Practice, Waterford city (two days a week over two years). When not in practice, I was based in the Department of General Practice, University College Cork. I conducted the qualitative interview study and the feasibility study in GP practices in Cork and surrounding counties between 2013 and 2015. Overall, twenty seven practices and thirty five GPs participated. I used data from the Mitchelstown Cohort Study for the cross-sectional paper. This study recruited a representative sample of over two thousand middle-aged adults from a single large primary care centre in 2010. The funders of the NSAFP (the Health Service Executive and the Health Research Board of Ireland) and the funders of the Mitchelstown Cohort Study (the Health Research Board of Ireland) had no influence or input into the conduct of the research or study findings.

CHAPTER 2. MAPPING THE TERRAIN: THE CONTEXT FOR THIS RESEARCH

This research is based in primary care, specifically the setting of general practice. Healthcare systems with strong primary care have better health outcomes for patients with chronic illness, at a lower cost and with less health inequality (9). There are multiple professionals involved in medication management (e.g. GPs, pharmacists, specialists, practice nurses etc.), but as GPs are the most commonly seen physician for patients with multimorbidity (9), I focus on the perspective and role of the GP.

In this chapter, I describe briefly the context for the research that follows: the role of primary care and general practice in the Irish healthcare system, and changes that have occurred in the landscape of Irish general practice since I commenced this thesis in 2012.

2.1. Government policy on primary care in the Irish health system

In 2001, the Irish government publication "Primary Care: A New Direction" acknowledged the central role of primary care in the Irish health service (10). It outlined a vision for primary care services whereby the health of the population is managed, as far as possible, within a primary care setting. In 2013, the government's framework for achieving a "Healthy Ireland" was also aligned with this approach (11). Current government strategies promote the expansion of chronic disease prevention and management in primary care, with a specific emphasis on diabetes, chronic respiratory disease and heart failure. These strategies include the recent launch of integrated care programmes for chronic disease, implementation plans for activity based funding and the establishment of a Medicines Management programme to promote cost-effective prescribing, especially for long-term medications (12).

2.2. Structure of Irish general practice

Although primary care is the location of choice for the management of chronic disease, Ireland is unique in being the only health system in the European Union that does not offer patients universal coverage for primary care at the point of access (13). GPs play a central role in the delivery of primary care services. The majority of GPs are self-employed private practitioners but a large proportion also provide free GP care at the point of access through the state-funded General Medical Services (GMS) programme (14). Approximately 40% of the population is covered by the GMS, and the remainder generally pay their GP an out-of-pocket fee of approximately €50 per consultation (13). Individual patients are means tested to determine their eligibility for the GMS programme; if eligible, they are given either a Medical Card or a GP Visit Card. Medical Cards may also be granted on a discretionary basis in the case of serious illness. Medical Card and GP Visit Card holders are entitled to free GP care at the point of access, for which the GP is paid annual capitation of the order of €43 to €270, depending on the age and gender of the patient (15). In 2015, free GP care at the point of access was extended to all people aged over 70 regardless of income and all children aged under six years, with further expansion of coverage planned for 2016.

As gatekeepers to hospital services, GPs play an important role in controlling costs at secondary and tertiary level. The Irish College of General Practitioners (ICGP) reports that 95% of patients are managed solely in general practice with only a 5% referral rate (16). However, recent figures show that only 2.3% of the total health budget is allocated to general practice (17).

2.3. The impact of austerity

In 2008, Ireland faced an economic crisis caused by a combination of international factors, poor national fiscal and public policy choices (18). In December 2010, Ireland entered into an international bailout worth €85 billion. In response to this crisis, there were a series of austerity budgets which led to public expenditure on health falling by 9% (19).

The budgetary responses included the Financial Emergency Measures in the Public Interest (FEMPI) Act 2009. This act allowed the then Minister for Health, Mary Harney to reduce government payments to GPs (19). The first reductions were of the order of 8%, and affected GMS services such as capitation, care of temporary residents, out of hour's care, special items of service, distance allowances, immunisation and nursing home care, dispensing fees, and practice management expenses. In 2010, Minster Harney announced further reductions in GMS payments to GPs of between 8-15%. In July 2013, the new Minister for Health, Dr James O Reilly (also a GP), reduced payments to GPs by a further 7.5%.

Simultaneously, as personal incomes fell with the recession, there was a 70% increase in the numbers of people eligible for state-provided GP care (13).

The impact of increasing demand in the face of reduced payments has challenged the financial viability of many general practices. Some practices have closed, while others have struggled to find young GPs to take over practices on the retirement of GP principals. As of May 2015, there were 21 general practice lists in Ireland without a GP (16).

2.4. Withdrawal of the ICGP from Clinical Care Programmes

In July 2013, in response to the diminishing resources available to general practice, the ICGP withdrew from the National Clinical Care Programmes (20). The Clinical Care Programmes were established by the Health Service Executive (HSE) to streamline the management of chronic conditions. One of the aims of the programmes was to develop more effective shared care of patients between hospitals and GPs. However, in the face of increasing workload and on-going cuts to funding, the ICGP stated that GPs were not in a position to offer structured chronic disease care unless funding was diverted from secondary to primary care (20).

2.5. New contract and cycle of diabetes care

The contract currently held by GPs for the provision of GMS care was written in 1989, and was originally designed for acute medical care without mention of chronic disease (21). From the perspective of GPs and the Department of Health, there has long been a need to revise the terms of this contract (22). In January 2014, the government released a draft contract for the provision of free GP care at the point of access without any prior consultation with the ICGP or medical unions. The contract was received unfavourably by GPs, and the ICGP's formal response branded it "deficient in areas of clinical appropriateness, patient-centredness, quality and safety of care, evidence based care, outcomes focussed care, patient privacy, the clinical independence of doctors and ultimately the viability or sustainability of a general practice service"(23). Contract negotiations ensued and a revised contract was announced in July 2015. In addition to detailing the capitation payments and requirements of GPs in the provision of care to all children aged under six years, it includes a new cycle of care for patients with diabetes. GPs are paid a once-off registration fee of €30 per registered patient

with diabetes who holds a Medical Card, and receive enhanced capitation payments of €100 per registered patient for two annual reviews. Despite the fierce early opposition, this initiative seems to have been welcomed by GPs as the first step in adequately resourcing primary care to provide high quality chronic disease management.

Figure 2 outlines the temporal relationship between some of these events and the qualitative research described in this thesis.

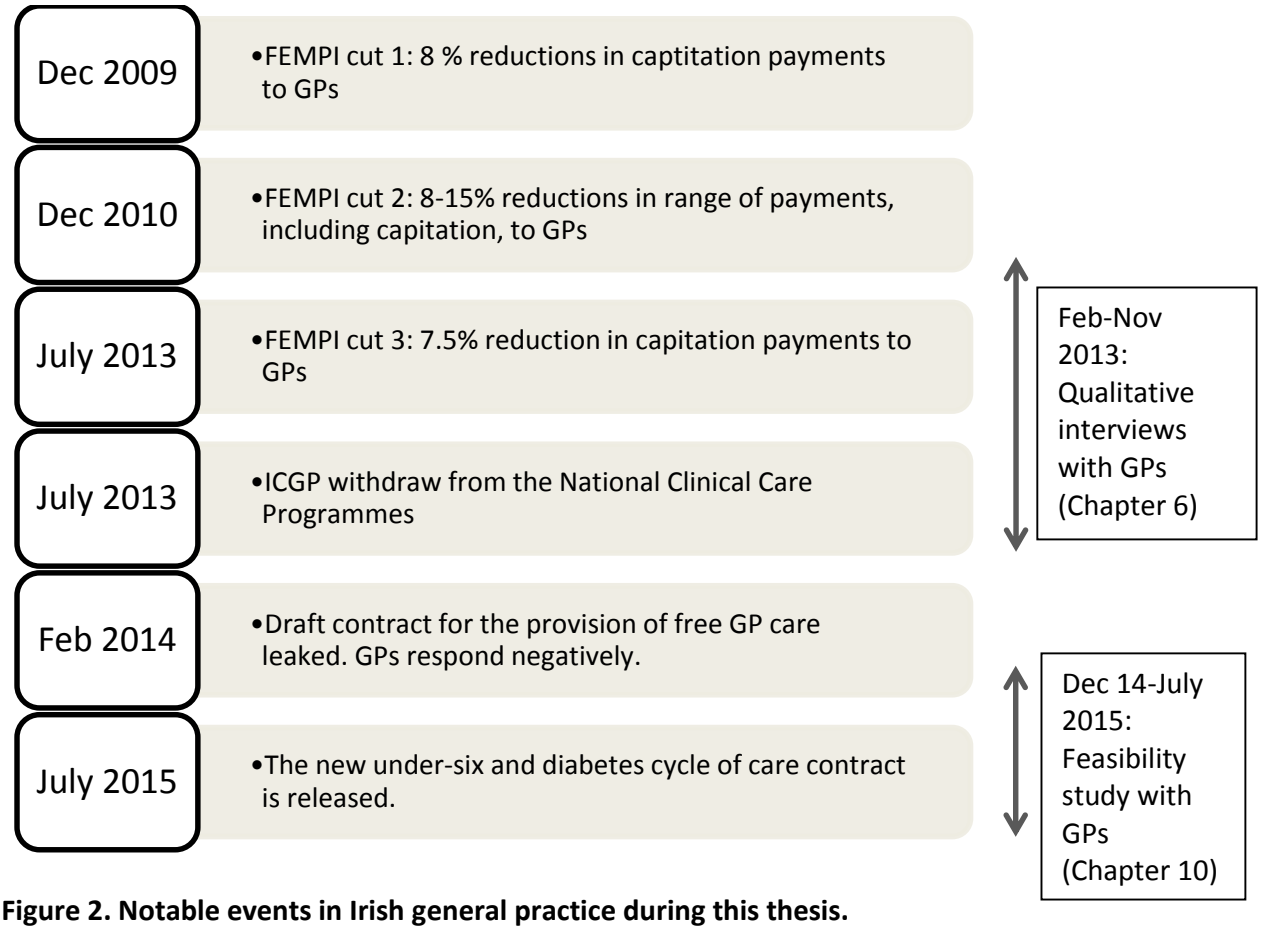

Figure 2. Notable events in Irish general practice during this thesis.

CHAPTER 3. A REVIEW OF THE LITERATURE

3.1. Introduction

This chapter provides an overview of the literature which has informed my work. I begin by describing the problem of multimorbidity: its definition, epidemiology, short and long term health consequences, and wider economic costs. Then I review the related issues of polypharmacy and the influence of clinical practice guidelines. Lastly, I describe existing interventions to improve multimorbidity care, their limitations and lessons that can be learned from interventions in related fields.

3.2. Multimorbidity: what's in a word?

The basic definition of multimorbidity is the co-occurrence of multiple chronic conditions within the one person without any reference to an index condition (24). This is conceptually different to comorbidity, which refers to any additional condition in a patient who has an index condition (25). The term multimorbidity tends to be used in a generalist context (i.e. by GPs and geriatricians) where the identification of an index condition may not be obvious or useful. Comorbidity better captures the views of specialists and what is designated as the index condition depends on the speciality in question (26). Starfield et al. suggested that acute conditions, some of which persist or recur over time, be included in the definition of multimorbidity but this application is not widespread (26, 27).

3.3. Measures of multimorbidity

Patients with multimorbidity are a heterogeneous group. Some have co-occurring but otherwise uncomplicated conditions while others, for a range of biopsychosocial reasons, are more difficult to manage. Numerous operational measures of

multimorbidity have been used in research. Some are broad and inclusive, while others try to capture the more complicated multimorbid patients that most need intervention.

3.3.1. Counts of conditions

In two separate systematic reviews, the most commonly used measure of multimorbidity was the presence of two or more chronic conditions (28, 29). While this measure appears to be straightforward, what constitutes a condition varies between studies. Fortin et al. have suggested that the term "condition" is more encompassing than "disease" (which denotes a condition with signs and symptoms) or "illness" (which refers to a person's perception of their health) (30). Some researchers count anything that is listed as a chronic condition in a patient's medical record (31) or coded as a chronic condition in a recognised classification system (such as the International Classification of Primary Care) (32, 33). Others use lists or indices of pre-specified conditions. In 2011, Diederichs et al. reviewed 39 such indices (34). On average, there were 18 conditions listed per index. The rationale for including conditions in an index varied from high prevalence, to inclusion in other indices of multimorbidity, or association with mortality, physical function, or other health outcomes. In the majority of indices (59%), there was no rationale given for the selection of conditions. Diederichs et al. recommended four criteria to govern the inclusion of conditions in indices of multimorbidity: conditions of long duration, a need for continuous medical treatment, severe impact on affected people, and high prevalence. They suggested eleven conditions that they believe should be included as a minimum: cancer, diabetes, hypertension, myocardial infarction, chronic ischaemic heart disease, cardiac arrhythmias, cardiac insufficiency, stroke, chronic obstructive airways disease, depression and arthritis (34). Fortin et al. (28) have suggested that indices should

include the twelve most prevalent chronic conditions at a minimum, as there is less variation in prevalence estimates using at least this number of conditions.

While two or more conditions is the most commonly used measure of multimorbidity, Harrison et al. (35) compared this to three or more conditions, and found the latter had greater specificity for identifying patients with substantial health needs.

When counting conditions, the source of the data (i.e. patient-reported, administrative data or medical records) is an important consideration. Diederichs et al. suggested that patient-reported data is better for establishing the effects of multimorbidity because it reduces the impact of excessive labelling of disease (34). Fortin and others have proposed that using a combination of sources gives more reliable estimates than relying on one source alone (28, 35, 36).

3.3.2. Weighted classification systems

More elaborate systems try to account for severity or the complexity that can occur due to non-biomedical factors. These systems attach weights to different conditions using mortality risk, presence of complications, or impact on physical function or quality of life (29, 34). They allow calculation of summary measures for the combined burden of a patient's conditions. Examples include the Charlson Comorbidity Index, the Cumulative Illness Rating Scale, the Index of Coexisting Disease, the Kaplan–Feinstein Index and the Duke Severity of Illness Checklist (26, 37). Other systems combine the type and severity of diseases with age and gender to classify patients into groups that signify expected healthcare need (e.g. Adjusted Clinical Groups) (38).

3.3.3. Measures that use medications

Given the lack of consensus on what constitutes a chronic condition, the number of long-term medications prescribed to an individual has been suggested as an alternative proxy measure of multimorbidity (39). This may involve simply counting the subclasses of medications prescribed to a patient or may be weighted by age, gender and the severity of conditions the medications are used to treat, as in the Chronic Disease Score (40). While these measures are useful for predicting outcomes like hospitalisation and mortality (39), medications cannot capture function or quality of life, or the presence of disease that is not being pharmacologically treated. Therefore, these measures may under-estimate morbidity burden in samples of older, frailer and cognitively impaired people where less active disease management is pursued (41).

3.3.4. The concept of complex multimorbidity

In 2014, Harrison et al. proposed the concept of "complex multimorbidity" for identifying high-need individuals who would benefit from more intensive intervention (35). They defined complex multimorbidity as the co-occurrence of three or more chronic conditions affecting three or more different body systems within one person without defining an index chronic condition. This “stepped care” approach is promising: targeting interventions at patients by profiling their level of complexity has led to improvements in the management of individual chronic conditions, and it is not a difficult measure to replicate or interpret (42, 43).

3.3.5. Which measure to choose?

Although different measures lead to different prevalence estimates of multimorbidity (discussed further below), the predictive validity of different measures for the same

outcome (e.g. hospitalisation or mortality) differ only slightly, and simple counts of conditions or medications perform almost as well as complex measures in predicting most outcomes (35, 36).

In this thesis, the term multimorbidity is used to represent the co-occurrence of two or more chronic conditions. There are two exceptions. In the qualitative interview study (Chapter 6), I asked participating GPs to discuss multimorbid patients with at least three chronic conditions in order to get cases where difficult decisions, particularly those regarding medications, were more likely to arise. In the feasibility study (Chapter 10), I asked GPs to choose multimorbid patients prescribed ten or more medications or five or more medications with another complicating factor, in order to get cases where recommendations for changes in medications were more likely to emerge.

The concepts of patient complexity and frailty are more common in and complicate the management of patients of multimorbidity, but are distinct from multimorbidity as it is defined in this thesis (30). Patient complexity acknowledges that morbidity burden is influenced not only by health-related characteristics, but also by socioeconomic, cultural, environmental, and patient behaviour characteristics. These interactions between disease factors and socio-economic factors can make the clinical management of multimorbidity more or less challenging, time-consuming, and resource intensive. However, approaches to capturing and measuring complexity are lacking. Frailty represents a state of increased vulnerability to physical stressors that results from decreased physiologic reserves of multiple physiological systems (44). It has been estimated that frailty affects 46% of patients with multimorbidity, and substantially increases the risk of falls, disability, long-term care, and death in this population. However, 26% of patients with frailty do not have co-existing multimorbidity, which highlights the distinction between the concepts (45).

3.4. How common is multimorbidity?

Unsurprisingly, estimates for the prevalence of multimorbidity vary according to the age and location of the study population, the data source and the measure of multimorbidity used. This variation has been demonstrated in three systematic reviews. The first review, published in 2011, included twelve prevalence studies, and showed multimorbidity affected 20-30% of all adults and 55-98% of older adults (46). The second review, published a year later, included 21 prevalence studies with estimates ranging from 3% to 98% (28). Three years on, a third review found double the number of studies (reflecting the interest in the topic) and found consistent variation in prevalence estimates (47).

In all three reviews, the majority of included studies defined multimorbidity as two or more conditions. The main source of variation between studies was the total number of conditions considered. For example, a Dutch study used data on only five conditions to show a prevalence of multimorbidity of 15% in patients aged over 65 years (48), but another Dutch study considered 335 conditions and found a prevalence of over 60% in the same age group (33).

Comparing population level data to primary care data, prevalence estimates are generally the same for people aged up to 60 years; after this, prevalence estimates are 10 to 20 points higher in primary care data (29).

In studies using similar measures of multimorbidity (i.e. two or more conditions), prevalence estimates for adults in high-incomes countries are similar e.g. 48% in Spain (47), and 46% to 52% in Canada (2). In Ireland, it is estimated that multimorbidity affects two thirds of patients aged over 50 years attending primary care (3).

Low and middle income countries (LMICs) appear to have lower rates of multimorbidity. In a pooled analysis of data on adults from China, Ghana, India, Mexico, Russia, and South Africa, the overall prevalence of multimorbidity was 22%; the highest rates were in Russia (35%) and the lowest rates were in China (20%) (49). The lower prevalence may be explained by a higher burden of infectious diseases and lower life expectancy in these countries. Alternatively, prevalence estimates may be biased by limitations in the data available, and under diagnosis of chronic disease (50).

3.4.1. Association with age

All studies included in the three systematic reviews show a significant positive association between age and multimorbidity, but the relationship is s-shaped rather than linear, plateauing after 70 years at around 75% (28, 29, 46).

The association with age explains in part the increasing burden of multimorbidity, and the need for interventions to improve medication management for these patients. Nevertheless, the absolute number of people with multimorbidity is higher in those younger than 65 years (51). This places additional demands on GPs: whereas patients aged 65 and over can be referred to geriatricians, sub-specialisation of physicians in secondary care has led to a situation where generalist services seldom exist for the increasing number of multimorbid patients aged less than 65 years (52).

3.4.2. Association with gender

Studies from high income countries show that the prevalence of multimorbidity is higher in women than in men of a similar age, with an odds ratios of 1.12 (1.07-1.17) in the Netherlands (33), 1.23 (1.06-1.42) in Ireland (3), and 1.41 (1.4-1.42) in Scotland (51). This has been explained by women's greater longevity, because men who survive

longer are healthier than women, and because women are more affected by non-fatal conditions (i.e. osteoarthritis) than men (46). It may also relate to reporting differences between the genders. However, to appropriately tailor interventions to patients' needs, more research into the risk factors for, mechanisms of and natural history of multimorbidity between genders is warranted (46).

3.4.3. Association with socio-economic status

In high income countries, socio-economic status (measured using deprivation scores, health insurance status or lower educational attainment) is inversely associated with multimorbidity (29). This was most strikingly shown in a Scottish study where the onset of multimorbidity occurred on average ten years earlier in deprived areas than in more affluent areas (51). This is important because people living in areas of deprivation tend to experience more social problems and have more complex health needs that those in affluent areas.

In low or middle income countries, this association between multimorbidity and socio-economic status is inconsistent or inverted (49, 53). In lower income countries, affluent individuals tend to have higher levels of health risks like high body mass index and reduced physical activity, which can lead to higher levels of chronic disease in these groups. Additionally, under-diagnosed disease and relatively shorter life-expectancy with less opportunity to develop chronic disease disproportionately affects lower social classes in lower-income countries (54).

3.5. Patterns of multimorbidity

The level of difficulty associated with medication management in multimorbidity is influenced by the combination of conditions involved. Conditions can co-occur for

reasons of chance, detection bias, or common pathology (26, 46). Common pathology includes shared risk factors (e.g. smoking as a cause for lung disease and vascular disease), co-occurring risk factors (e.g. smoking and alcohol can lead to lung disease and hepatic disease in the one person), or one condition or its treatment causing another condition (e.g. inflammatory arthritis or non-steroidal anti-inflammatories leading to chronic kidney disease) (55).

More generally, conditions may be described as "concordant" if they share the same overall pathophysiological risk profile or management (i.e. diabetes and hypertension); or "discordant" if not directly related in either pathogenesis, management or predisposing factors (i.e. diabetes and irritable bowel syndrome) (56). Discordant conditions cause more problems for medication management than concordant conditions, due to the risk of interactions between agents indicated for individual conditions, lack of synergies in management, and the additional time required to manage each distinct condition (57, 58).

In their 2014 systematic review of prevalence studies, Violan et al. also examined the patterns of co-occurring conditions. The most frequently observed dyad of conditions was hypertension and osteoarthritis, followed by different combinations of cardiovascular conditions (29). Using cluster or factor analysis to group conditions in a meaningful way, the most commonly observed groupings were 1) cardio-metabolic conditions, 2) anxiety, depression and other psychiatric conditions and 3) painful conditions (including mechanical pain). Since that review, others groups have published similar findings (59, 60). The consistency of these patterns suggests that they should be accounted for in relevant clinical practice guidelines (61), especially the common synergies or interactions that may occur.

Guidelines aside, the importance of disease patterns should not be over-emphasized (62). In a study of patients with hypertension, only one third of their consultations were for that diagnosis. The next most common reason for consultation was their diabetes but this accounted for only 3% of consultations. Thus, almost two thirds of consultations were for a wide variety of reasons, with no one of them accounting for more than 1% of visits (63).

3.5.1. Co-occurring physical and mental health conditions

There is a unique relationship between physical and mental health conditions in multimorbidity, particularly in areas of deprivation (51, 64). It has been estimated that approximately one third of people with multimorbidity have both a physical and a mental health disorder, with the odds of a mental health condition increasing as the number of physical morbidities increase (51). Furthermore, serious mental illness is associated with elevated mortality compared to the general population; the majority of this excess is attributable to co-occurring common physical health conditions (65). It has been suggested that worse outcomes ensue for those with serious mental illness and co-occurring physical disease due to adverse health behaviours of patients with serious mental illness, suboptimal access to and utilisation of healthcare by this patient group, and the delivery of inferior healthcare to those that do.

The relationship between physical and mental health conditions may be causal, with physical conditions contributing to the development of mental health conditions or vice-versa. Medications, and their side effects, may also be implicated (e.g. medications for psychiatric conditions contributing to cardiovascular disease or medications for epilepsy or hypertension leading to depression). Multimorbid patients with mental health issues have poorer health outcomes and greater functional deterioration than

those with mental health conditions or physical multimorbidity alone (43). However, ensuring that both the physical and the mental health conditions receive adequate attention can be a challenge in consultations in general practice, and highlights why interventions that aim for whole-person care are needed in this field (64).

3.6. The impact of multimorbidity

Interventions are needed to reduce the negative effects exerted by multimorbidity on patients and on healthcare systems. The degree to which individuals are affected by multimorbidity depends on the diseases involved, and the patient's personal, physical and social resources (66). Health system effects are seen to vary by the relative strength of and accessibility to continuous, generalist primary care (9).

3.6.1. Quality of life and function

Quality of life declines with increasing numbers of and severity of chronic conditions (46, 67-69). This association persists even after controlling for confounders such as education, self-perception of economic status, and social support (70). Depression and chronic pain are associated with the greatest reductions in quality of life in multimorbidity (68, 71), suggesting that these conditions should be prioritised for intervention.

To date, most studies examining this relationship have measured quality of life using short form questionnaires (70, 72) or the EQ5D (67, 68). Some authors have questioned the value of these measures in multimorbidity, arguing that they obscure the longer term benefits patients may receive from using chronic disease medications and may not capture all the domains of disease (68). While this may be true, others argue that

quality of life is of greater importance than measures of disease progression (73), and interventions that aim to improve these patient-reported measures in the context of multimorbidity should be a priority.

Functional limitation causes additional challenges for many people with multimorbidity and their carers. In the Survey of Health, Ageing and Retirement in Europe (with data on over 40,000 patients from ten European countries), 65% of multimorbid patients reported established functional decline, frailty or pre-frailty (74).

In a review of nine cohort studies, multimorbidity at baseline predicted future functional decline (75). People with multimorbidity are more likely to become dependent on long-term care, with the highest risks for functional deterioration in multimorbid patients with neuropsychiatric disorders (76).

3.6.2. Treatment burden, experience of healthcare and self-management

Treatment burden relates to the demands that are placed on patients in the management of their chronic disease. It includes adherence to medications, attendance for medical reviews, and lifestyle modifications. Overburdening patients can lead to poor adherence and poorer health outcomes and there is evidence that this is more often the case in patients with multimorbidity (77). In a cross-sectional survey of multimorbid patients in England, two thirds of patients reported “hassles” in their medical care, such as lacking information about their treatment options, poor communication and disagreements between individual doctors involved (78). Multimorbid patients who were younger, were in active employment and had less frequent contact with their GP were more likely to experience these hassles. A synthesis of qualitative research showed that multimorbid patients find it more difficult to engage in self-management if they receive conflicting information from or

experienced difficulties communicating with healthcare professionals (79). Interventions that accommodate greater consideration of treatment burden, facilitate the provision of consistent information to patients and improve doctor-patient communication are needed to address these deficits.

3.6.3. Quality of health care

A systematic review of studies examining the association between multimorbidity and quality of care showed mixed results (73). When quality is measured using process indicators, higher numbers of conditions are associated with higher quality scores. This relationship is only partially explained by the increased use of healthcare by patients with more conditions or care processes that satisfy multiple quality indicators (80, 81). In one study from the United States (US), quality scores for each additional condition increased more for patients who had seen a relevant specialist than for those who had not. However, for patients who received only generalist care, the relationship between the quality score and the number of conditions remained positive (80).

When quality is assessed using patient-reported outcomes like continuity of care (82), or doctor-patient communication (83), higher numbers of conditions are associated with lower quality scores. This negative association was magnified in those with higher numbers of annual hospital outpatient attendances (82). So, care that is measurably better using process indicators may be perceived as worse by patients (84). The combinations of conditions are also relevant here: studies focusing on index conditions show that the quality of care is better if comorbidities are concordant, but worse if they are discordant (85, 86).

3.6.4. Healthcare utilisation and costs

Patients with multimorbidity are major drivers of healthcare costs, as well as economic losses. Data from the Survey of Health, Ageing and Retirement in Europe shows that, everything else being equal, a multimorbid patient sees doctors 23% more often, and has 1.43 times greater risk of hospitalisation in a given year, than those without multimorbidity (74). However, the magnitude of this effect varies by health system. If GPs play a gate keeping role in the healthcare system, patients with higher numbers of conditions have large increases in primary care visits, but less significant increases in more expensive hospital visits, and shorter hospital admissions (3, 87). In contrast, when patients can self-refer to secondary care, multimorbidity is associated with larger increases in the demand for more intensive and more expensive secondary care (88). In the US, the 65% of aged Medicare beneficiaries who have multimorbidity account for 95% of Medicare expenditure (4, 60). Unscheduled care and hospital admissions for ambulatory care sensitive conditions also increase with multimorbidity: for example, Medicare beneficiaries with four or more chronic conditions were ninety nine times more likely than a beneficiary without any chronic conditions to have an admission for an ambulatory care sensitive condition (4). Patients with multiple chronic conditions also use a greater array of services: patients with five or more chronic conditions see on average fourteen different healthcare professionals (89). As the number of healthcare professionals increases, co-ordinating care becomes more difficult for physicians and for patients who find it increasingly challenging to understand, remember, and reconcile the various instructions they have been given (78, 90).

3.6.5. Mortality

Estimates of the effect of multimorbidity on mortality vary by patient age and physical function. Marengoni et al. found only three out of five studies showed an increased risk of mortality in multimorbid patients. However, the other two studies involved the oldest old, where age rather than number of chronic conditions may have been a greater risk for mortality (46). In studies of index conditions, mortality rates are higher if comorbidities are discordant rather than concordant (91). Multimorbid patients with functional limitation have consistently higher levels of mortality than multimorbid patients without functional limitation (92, 93).

3.6.6. Summary

Increasing numbers of chronic conditions have an incremental negative impact on patient-reported and system level outcomes (46, 75). Negative effects are greatest in patients with more complex, discordant combinations of conditions or existing functional impairment. In light of the varying associations with mortality, re-configuring care to help patients live well with multimorbidity appears more appropriate than striving to reduce mortality alone (84). Attuning healthcare systems to the existence and needs of patients with multimorbidity is needed to address these disproportionate effects. Interventions that enhance the role of GPs as co-ordinators of care and empower them to provide care that is based on patients' symptoms, values and preferences may help reverse these trends.

3.7. Medications and multimorbidity

Polypharmacy is one of the most important consequences of multimorbidity (94). Similar to multimorbidity, polypharmacy has also been defined in numerous ways, but threshold numbers of medications (e.g. four or more (95), six or more (96) etc.) are commonly used. The term polypharmacy has also been used to represent undesirable medication use. Certainly, higher numbers of medications are associated with greater risk of preventable drug-related morbidity (97, 98). However, using multiple medications for the control of chronic disease may also benefit the patient by reducing morbidity and improving quality of life. This has led the Kings Fund (an independent think-tank in England) (99), and others (95) to make a distinction between appropriate and inappropriate (or problematic) polypharmacy. Methods for assessing the appropriateness of polypharmacy are reviewed below.

3.7.1. The epidemiology of polypharmacy

In 2010, 21% of Scottish adults were prescribed five or more medications (100). This is very close to the 23% of Scottish patients estimated to have multimorbidity (51). The proportion receiving a higher threshold of ten or more drugs was 6%. As with multimorbidity, there are strong associations between polypharmacy and older age. In an Irish study of patients aged 65 years and over, 60% received five or more medications, while 22% received ten or more (101).

Rates vary in low and middle income countries: 6% of Chinese but 43% of Brazilian primary care patients receive five or more medications (102). Explanations for the high prevalence of polypharmacy include increased availability of treatment, improved access to health care, the promotion of adherence to clinical practice guidelines, and patient expectation for active management (103).

3.7.2. When good medicines are bad for your health

Polypharmacy can lead to preventable drug-related morbidity via medication errors and adverse drug reactions (ADRs) (104, 105). In the Practice Study (106), Avery et al. found medication errors were more common as the number of prescribed medications increased; errors occurred in 32% of patients on five or more medications, and in 48% of patients on ten or more medications. ADRs are more common in older multimorbid patients because of their lower physiological ability to metabolize and tolerate medications (98). A large proportion of ADRs are due to interactions, either between medications or between medications and other chronic conditions (107). In the aforementioned Scottish study, the number of drugs dispensed was strongly associated with potential interactions: 81% of people on 15 or more medications had at least one potentially serious drug-drug interaction (100). This is important because 6% to 17% of hospital admissions are due to ADRs, with the majority of these admissions deemed avoidable (107, 108). In the US, ADRs are amongst the top five causes of death in hospital (84).

Medication regimens in multimorbidity can be demanding and restrictive, leading to poor adherence by some patients for reasons of impaired social and cognitive ability, beliefs about using multiple medications, and fear of side effects (109). As these issues may not stop patients from filling their prescriptions, poor adherence represents waste from the cost of unused medications, and the costs associated with progressive chronic disease (110).

3.7.3. Measuring the "appropriateness" of medications

While polypharmacy is associated with risk of hospitalisation, if the polypharmacy is appropriate for the individual patient's multiple conditions, this association is less

pronounced (111). The difficulty lies in determining what is and what is not appropriate.

A number of tools have been developed to assess medication appropriateness, and are broadly categorized as explicit (criterion-based) or implicit (judgment-based) (112). Explicit tools, such as the Beers criteria and the Screening Tool of Older Persons Prescriptions (STOPP) (113, 114), list medicines which should be avoided in older people because the potential risks are considered to outweigh the potential benefits. They are applied without clinical judgment, and do not take into account other factors that define high quality healthcare for an individual, such as patient preference or the presence of comorbidity. The lists themselves are criticized for a lack of transparency and reliability in their development and the dating of indicators as new medical evidence emerges (115). Despite these weaknesses, they have been widely applied to patient data to demonstrate substantial levels of "inappropriate prescribing" in primary care settings (112). In Ireland, approximately one third of medications prescribed to older people are reported to be potentially inappropriate using the STOPP criteria (101, 116). These studies did not explore prescribers' reasons for issuing potentially inappropriate medications but they did show an association between the offending medications and the presence of multimorbidity (116).

With implicit tools, each medication is assessed across a range of prescribing domains and a summary score of appropriateness is generated (e.g. the Medication Appropriateness Index) (112). Although more patient-focused than explicit tools, implicit tools are time-consuming, dependent on user knowledge and generally do not address under-prescribing (112).

Tools for inappropriate omissions (e.g. the Screening Tool to Alert doctors to Right Treatment (START)) have also been developed. They show omissions occur in 30-50% of older patients (117-119), and are more likely in patients on polypharmacy (120). Studies linking explicit and implicit tools with outcomes such as mortality, morbidity and quality of life show mixed results and are weakened by inadequate consideration of confounders like multimorbidity (112). A leading group of researchers have suggested that the existing tools overlook the needs of individual patients (112). They, and others, have recommended that future methods of assessing medication appropriateness should consider patients' comorbidities, preferences, life-expectancy and function (95). Medication appropriateness is also a function of time; ensuring that polypharmacy remains appropriate necessitates regular and comprehensive medication review (121).

3.8. Clinical practice guidelines: the source of the problem?

The evidence-based medicine movement has achieved safer, more consistent and more cost-effective care (122). However, combining evidence-based guidelines in patients with multiple chronic conditions can lead to burdensome and even harmful polypharmacy (123). For instance, the Guidelines International Network database currently lists more than 3,700 guidelines from 39 countries (124). Since 2002, over 2,500 peer-reviewed guidelines have been published which relate specifically to cardiovascular disease alone (125). Guideline duplication is common, quality is variable, and there are many potential interactions between guidelines aimed at different conditions.

3.8.1. An example case

An example of how clinical practice guidelines complicate care for patients with multimorbidity was described by Boyd et al. in 2005 (126). The patient was a 79 year old woman with chronic obstructive airways disease, diabetes, hypertension, osteoarthritis and osteoporosis. Implementing the clinical practice guidelines in the simplest way possible for each of these conditions led to prescription of twelve medications, nineteen doses of medication per day and fourteen non-pharmacological management techniques (126). Multiple drug-drug, drug-disease and drug-food interactions were identified. Had the patient's blood pressure remained uncontrolled, the guidelines did not give the marginal benefit of adding yet another medication to her existing regimen. The annual cost of the medications was estimated to be over four thousand American dollars. The authors noted that guidelines incorporated poor quality or no evidence relating to older or multimorbid patients. Reviews of Canadian and Australian guidelines show similar findings: few guidelines account for the presence of multimorbidity or address treatment for older patients with multimorbidity (127, 128).

3.8.2. Evidence underpinning guidelines

The recommendations issued in most clinical practice guidelines often depend on lower levels of evidence or expert opinion (129). Even when clinical trial data do exist, they rarely represent multimorbid patients or their needs (130). Most trials focus on the benefit of one drug in one condition so exclude patients with multimorbidity (130). There is an over reliance on surrogate outcomes (i.e. blood pressure, lipids, albuminuria) rather than outcomes that matter to multimorbid patients (131). Short

follow-up, and under-appreciation and under-reporting of harms make valid assessments of time to benefit (or harm) difficult (6, 125).

These limitations cast doubt on even high-quality clinical evidence, which in turn weakens prescribers' confidence in "evidence-based guidelines". In older complex patients, interpretation of the potential risks and benefits associated with guidelines is even more problematic (26).

A short term solution is to re-analyse existing trial datasets to determine the outcomes for multimorbid participants that were recruited. In the longer term, recruiting patients with higher levels of multimorbidity, and following outcomes that are important to them, will be essential in building an evidence base that is relevant to the majority of people with chronic disease (6).

3.8.3. The use of guidelines to measure quality of care

Guidelines are increasingly used to define standards and focus efforts to improve quality and effectiveness (6, 126). The English model of general practice is acclaimed internationally for providing universal, free access to community-based health care. Over the past decade, the quality outcomes framework (QOF) has helped drive primary care services there in a uniformly evidence-based direction (132). QOF is a pay for performance programme that incentivizes adherence to guidelines to promote quality and effectiveness. However, the programme has had some undesirable effects (133). There has been a decline in non-incentivized care, and less continuity of care. Consultations are increasingly booked for the patient, rather than by the patient; focus solely on chronic disease management; and are often governed by computerised tick box templates (134).

Guidelines are not developed with quality assessment in mind; they are intended to be used in conjunction with professional judgement and patient preferences (135). But balancing these dimensions becomes complicated when adherence to guidelines is linked to quality and physician re-imbursement. Most pay for performance programmes target conditions in isolation, which can lead to inappropriate and inefficient care in people with multimorbidity (126). They can lessen the patient's and even the physician's role in decision-making, by highlighting the best option but rarely offering alternatives to this course (136).

If pay for performance systems are to continue, they need to evolve to match the needs of patients with multimorbidity (134). Ideally, this evolution would facilitate a modified approach to guideline implementation in multimorbidity, which would allow balancing of the risks and benefits of medications with a patient's health priorities (66).

3.8.4. Guidelines and deprescribing

Deprescribing is the process of tapering or stopping drugs, aimed at minimizing polypharmacy and improving patient outcomes (137). Deprescribing is difficult for physicians, and guidelines rarely advise on when or how to stop medications (138). However, evidence of efficacy for deprescribing is emerging. In observational studies, mortality is higher in octogenarians if systolic blood pressure is treated to below 130mmHg, even after adjusting for cardiovascular history and excluding patients without a diagnosis of hypertension who receive anti-hypertensive agents (139). In a study of US Veterans aged 70 years and over, those with very low levels of HbA1c or blood pressure underwent de-intensification of treatment; less than 0.8% had follow-up measurements that were elevated (140). While deprescribing reduces costs and potentially lowers the risk of adverse drug events, there is also evidence that it is

acceptable to patients. In a survey of older patients on polypharmacy, 92% stated that they would be willing to stop one or more of their current medications if possible (141). Interventions that facilitate more effective communication with patients on deprescribing are a first step in this process.

3.9. What interventions specific to multimorbidity have been developed so far?

Despite numerous international advisory groups emphasizing the need for interventions to improve the patient outcomes in multimorbidity (123, 142, 143), a paucity of such interventions exist, specifically in the area of medication management.

3.9.1. Comprehensive care programmes

The chronic care model addresses healthcare systems as the main barrier to effective care of long term conditions. Developed by Wagner in 2001, this model suggests that comprehensive care programmes ideally comprise of six interrelated components. Four components refer to the care delivered by healthcare professionals: provision of self-management support to patients; organisational systems that are designed to deliver effective, efficient patient care through involvement of the multidisciplinary team; decision support by evidence-based guidelines; and clinical information systems that provide feedback and reminders to healthcare professionals. The two remaining components refer to the context in which chronic care is provided: a well-organised motivated healthcare system and community resources that support or expand care for chronically ill patients.

In 2012, de Bruin et al. reviewed the effect of comprehensive care programmes on management of patients with multiple chronic conditions (144). They only included interventions that incorporated at least two or more components of the chronic care model. Out of the 33 studies included, only six reported on measures of medication use (i.e. medication appropriateness, use of high-risk or unnecessary medications). The results of these six studies were inconsistent, leading the authors to conclude that there is insufficient evidence for a beneficial effect of comprehensive care on the management of medications in multimorbidity. The other results of the review showed insufficient or no evidence for benefits in health-related quality of life, outpatient healthcare utilization and costs, functional status, mortality, and caregiver burden (144). The authors suggested that better descriptions of interventions and their implementation are needed to enhance comparability between studies, and generate consistent evidence that will support decision-making for patients with multimorbidity.

3.9.2. Other complex interventions

Also in 2012, in a review for the Cochrane Collaboration, Smith et al. (145) reviewed ten interventions designed to improved physical, psychological and care utilisation outcomes in patients with multimorbidity in primary care. Six were organisational interventions and involved case management, co-ordination of care or the enhancement of skill mix in multidisciplinary teams. The other four interventions focused on patient behaviours, rather than healthcare professionals. Individual study results were either insignificant or mixed, with little impact on physical health, mental health, or care utilisation. Three studies found benefits relating to prescribing and medication use (secondary outcomes), which signal the potential of these interventions to improve other health outcomes over longer periods.

Based on the characteristics of the included studies, the authors made suggestions for future interventions. First, interventions targeting specific risk factors or "areas where patients have difficulties such as management of medication were more likely to be effective" than interventions with a broader focus (e.g. case management, changes in care delivery). Second, interventions that were integrated into the healthcare system tended to show better results. Third, the review highlighted the need for theoretical frameworks to guide intervention development, to allow assessment of what worked and why.

Since then a number of other relevant studies have emerged. In the OPTISCRIPT study, Clyne et al. evaluated a multifaceted intervention which incorporated web-based treatment algorithms for GPs, academic detailing with a pharmacist and tailored patient information leaflets. Participating patients were prescribed, on average, ten regular long-term medications. Although the intervention led to reductions in the use of inappropriately high doses of proton-pump inhibitors, no significant changes in other classes of medications occurred and there were no positive effects in patient-reported outcomes (146).

Bregnhøj et al. found that interactive educational meetings with feedback from pharmacists but not educational meetings alone improved medication appropriateness in older patients prescribed more than five regular medications. However, their findings were weakened by very low GP participation rates (14%) possibly because of the time-consuming, and thus impractical, nature of the intervention (147).

3.9.3. Interventions using information technology

Clinical decision support systems (CDSS) have been suggested as a solution to the problem of excess information in the management of medications in patients with

multimorbidity (121). These systems use inbuilt prescribing information to alert prescribers to indicated or interacting medications. While CDSS can improve process measures, the evidence for clinical, economic, workload and patient related outcomes remains sparse (148, 149).

The application of CDSS to the management of patients with multimorbidity was recently reviewed (150). Twenty studies met the inclusion criteria, with ten focusing on medication management. In four studies, the recommendations of individual guidelines were merged, but the possible interactions between these recommendations were not considered. Only pairwise combinations of guidelines were used, which is too simplistic for most patients with multimorbidity, and none of the CDSS interventions incorporated patient preference in decision-making. Evaluations of the usability or effectiveness of the interventions were either of poor quality or absent. The authors highlighted the risks of uncritical integration of guidelines in CDSS and called for more research about how conditions interact to inform better programming of these interventions (150).

3.10. Learning from interventions in related fields

Although there is a lack of interventions in the specific field of medication management in multimorbidity, lessons can be learned from other interventions designed to improve or support prescribing in primary care.

3.10.1. Interventions involving pharmacists

Patterson et al. (95) included eleven pharmacist-based interventions in their Cochrane review of interventions to improve prescribing appropriateness. In these studies, pharmacists conducted medication reviews, gave advice on adherence and safe use,

and provided patient and physician education. Overall, the interventions led to small improvements in scores of medication appropriateness but they had little effect on hospital admissions and no effect on health-related quality of life. The authors recommended that consideration of practice norms and cultures is a prerequisite for intervention success; interventions should focus on appropriate prescribing rather than simple reductions in numbers of drugs or scores; and interventions must account for the complexity of clinical situations, the patient's wishes, and the individuality of prescribers.

Rollason et al. conducted a similar review, but restricted it to pharmacist-based interventions that aimed to reduce numbers of medications (151). Fourteen studies were included. Overall, the studies were effective in reducing numbers of medications, but the authors were unable to determine if they improved patient-related outcomes or other clinical consequences of polypharmacy. They commented that direct involvement between the pharmacist and physician achieved more changes in medicines than written recommendations.

In 2012, the pharmacist-led information technology intervention for medication errors (PINCER) trial was conducted with the aim of reducing medication error in general practice (152). In control practices, GPs were sent computerised feedback on patients identified as high risk for medication error plus information on each type of error. In intervention practices, GPs received this feedback and also had an opportunity to discuss it with a pharmacist who attended the practice thrice weekly over twelve weeks. Although the intervention reduced medication errors, the qualitative evaluation showed tensions within practices that impacted on effectiveness (153). For example, not all errors were necessarily seen as failings by GPs, especially if patients had multimorbidity (e.g. the prescription of beta-blockers to a patient with asthma). As the

intervention did not individualize risk assessments, some GPs over-ruled pharmacists' advice on the basis of clinical experience and in-depth knowledge of the patient. Integration of pharmacists into practices was an issue: while the face-to-face contact was appreciated by GPs, the pharmacists themselves reported feeling isolated from the clinical team. These issues arose in a similar study conducted in an Irish setting (154). In summary, while pharmacists have valuable expertise to contribute to medication management in multimorbidity, existing interventions do not seem to have utilised this expertise in a way that leads to improvements in clinically meaningful outcomes. Further research on the context and dynamics of pharmacists and physicians working in close liaison, with shared access to patients' medical records, may lead to greater and sustained success in this field.

3.10.2. Interventions in primary care involving geriatricians

Interventions involving geriatricians offer potential advantages for tailoring management plans to the needs of elderly, frailer patients. However, in a review of interventions to improve inappropriate prescribing in the elderly, only two out of three interventions that involved geriatricians in a primary-care based team led to improvements in prescribing appropriateness and none of the interventions improved other patient-reported or clinical outcomes (112, 155).

In the Dutch Geriatrics Intervention Programme (156), nurses visited vulnerable older patients at home under the collaborative supervision of GPs and geriatricians. The GP retained primary responsibility for care of the patient and made the final decisions on referrals, medication changes etc. The published results did not report on changes in medications, but the intervention did lead to improvements in functional performance and mental well-being at 3-month and 6-month follow-up. The qualitative evaluation

showed that GPs valued the input of geriatricians for issues such as cognition, mood and mobility but difficulties occurred in communication between providers and achieving agreement on the goals of care (157).

While harnessing the expertise of geriatricians is a promising approach for select groups of older community-dwelling patients, these interventions will not be accessible for the majority of multimorbid patients that are aged less than 65 years. Furthermore, there are logistical challenges to implementing multidisciplinary reviews in the community, namely resourcing, staffing and communication issues.

3.10.3. Interventions involving other healthcare professionals

In 2009, Boult et al. published a review of models of comprehensive healthcare for older persons with chronic conditions (158). Out of the 123 high-quality studies included, only six specifically addressed medication management or pharmaceutical care. Five of these six focused on prescribers at secondary care level, and only one improved patient-reported outcomes (a study that used a pharmacist in a hospital heart failure clinic).

In 2001, a Canadian study examined the effect of team-based medication reviews on reducing the number of potentially inappropriate prescriptions given to elderly patients (159). The team included two hospital physicians, a pharmacist and a nurse, who made written recommendations to the patient's primary care physician. Although the intervention led to significantly fewer inappropriate medications, this difference was not statistically significant in the intention-to-treat analysis. Extrapolating the conclusion of the Cochrane review by Patterson et al. (95), perhaps if greater attention was given to the role of the primary care prescriber, more significant effects would have been seen.

In a review of interventions to reduce preventable drug-related morbidity, Royal et al. assessed protocol-based, nurse-led interventions that aimed to improve prescribing for single chronic conditions such as diabetes, heart failure and asthma. Even with this narrow focus, no significant improvements in medication management occurred (160). Although not focusing directly on prescribing, the recent Collaborative Interventions for Circulation and Depression (COINCIDE) trial provides a useful example of the benefits of integrated collaborative care in multimorbidity (43). The trial showed that depression scores improved in patients with long-term conditions (diabetes or chronic heart disease) after integrating low-intensity psychological interventions with the routine primary care management of the chronic conditions (161). Patients in intervention practices received up to eight sessions with psychological wellbeing practitioners, two of which were delivered jointly with the practice nurse. This study highlights the role for interventions that facilitate collaboration between the healthcare professionals involved in an individual patient's care, with potential benefits in the co-ordination of care, self-management and patient-centredness.

3.10.4. Educational interventions

As multimorbidity is infrequently incorporated into medical training curricula, educational interventions have the potential to address an important learning need for GPs. Educational interventions have been used to improve prescribing in other areas of general practice with varying degrees of success. In a review of initiatives to optimize the use of antibiotics, passive educational initiatives directed at GPs were unsuccessful (162). This failure was attributed to a didactic approach that did not acknowledge the context and complexities involved in prescribing. In contrast, interactive educational meetings on antibiotic use led to significant changes in prescribing behaviour, perhaps

through better engagement of the prescribing physician (162). Similarly, in an educational intervention study on inappropriate prescribing in Norwegian general practice, Rognstad et al. found that engaging GPs in critical review of their prescribing by using audit and feedback at continuing medical education meetings significantly reduced potentially inappropriate medications for patients aged 70 years are over (163).

3.11. New opportunities

Ideally, interventions in multimorbidity would help physicians achieve a balance between patient-centred care and guideline adherence; however, none of interventions described above have tackled this issue. Some interventions achieved success in medication-related outcomes such as prescribing appropriateness and medication errors. Although these outcomes may not be a priority for patients with multimorbidity, lessons can still be learned from their success. Future interventions should integrate well into existing practice, focus on specific areas of difficulty, facilitate tailoring to patient complexity, and involve face-to-face interaction between clinical decision-makers. This information presents a huge opportunity to develop interventions that not only improve medication use in patients with multimorbidity, but also improve patient-related outcomes such as treatment burden, patient satisfaction and health-related quality of life.

CHAPTER 4. METHODOLOGICAL FRAMEWORK AND OVERVIEW OF STUDY METHODS

This chapter provides a description of the MRC framework and its application in this thesis. An *overview* of methods used to address each phase of the framework is provided here; greater detail on each method is provided in the relevant chapter.

4.1. The Medical Research Council guidance on complex interventions

Complex interventions use behavioural rather than pharmacological approaches to improve health outcomes. They can involve several interacting components, target one or multiple behaviours, involve individuals or organisations, and may aim to achieve a range of different outcomes. In the past, the evaluation of complex interventions has proved difficult because of problems defining, identifying, documenting, and reproducing the intervention. Therefore, the MRC proposed a phased approach to the development and evaluation of complex interventions, which is akin to that used for the development of pharmacological interventions. Broadly, this approach involves using the best available evidence (supplemented if necessary by new primary research) and appropriate theory in intervention development, testing it using pilot and feasibility studies to resolve key uncertainties in the design, before moving on to an exploratory and then a definitive evaluation (see Figure 3). These phases do not necessarily occur in a linear order, but the framework can help researchers define where they are in the research process. Detailed description of the intervention facilitates better replication, evidence synthesis and wider implementation.

This thesis focuses mainly on the first two phases of the MRC framework: intervention development and assessing feasibility.

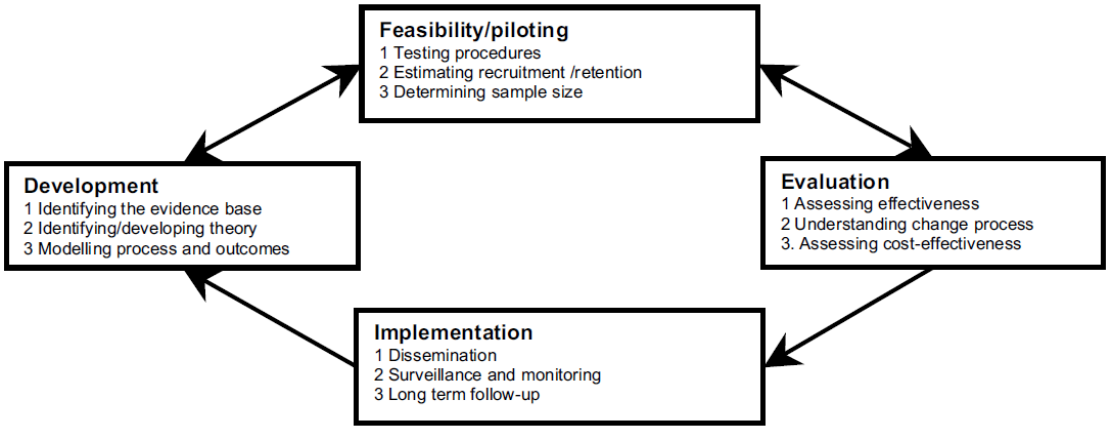

Figure 3. The Medical Research Council (UK) framework for developing and evaluating complex interventions

4.2. MRC phase 1: Intervention development

Because of the paucity of research on medication management in multimorbidity (described in Chapter 3), there is a need for pre-intervention research to inform the development of an intervention that will meet the needs and expectations of patients and the capabilities of healthcare professionals (164, 165).

4.2.1. Identifying the evidence base

4.2.1.1. Existing evidence

I. The existing evidence on GPs' perceptions of the management of multimorbidity was systematically reviewed and synthesized using a meta-ethnographic approach, as described by Noblit and Hare. Meta-ethnography is the most commonly used method of reviewing and synthesizing qualitative health literature, and is described in detail in Chapter 5.

4.2.1.2. New evidence

The existing evidence on multimorbidity was supplemented with new information generated by three studies:

II. The first was a qualitative interview study to explore the challenges experienced by GPs when prescribing for multimorbid patients. The methods of data collection and analysis in the qualitative interview study were informed by grounded theory as described by Charmaz (166) and are discussed in detail in Chapter 6.

III. I used the technique of chart-stimulated recall during qualitative interviews with GPs, and afterwards conducted a review of prior use of this technique in other clinical research. The five step approach for scoping reviews described by Arksey and O'Malley (167) was used to guide this study, and is described in detail in Chapter 7.

IV. Stewart et al. have stated that quantitative research can enhance our understanding of patient complexity and context, and can inform the delivery of patient-centred care (7). To examine the association between psychosocial complexity and multimorbidity reported by GPs in the qualitative study further, I conducted secondary analysis of quantitative data from the Mitchelstown Cohort Study in Chapter 8. The Center for Disease Control Adverse Childhood Experience (ACE) pyramid was used to inform the multivariable ordinal logistic regression analysis (168). The ACE pyramid links adverse childhood experiences to other social and behavioural risk factors in adulthood, which in turn can lead to health consequences such as chronic disease higher up the pyramid (169).

4.2.2. Identifying theory, and modelling process and outcomes

Developing an intervention using robust knowledge and theory can increase its success in improving clinical outcomes (170).

V. The Behaviour Change Wheel (BCW) and related models were used to explicitly integrate behavioural theory with data from Chapters 5, 6 and 8 to develop a complex intervention (171). The model of behaviour at the core of the BCW supposes that the interaction between one's capability (C), opportunity (O) and motivation (M) provides explanations for why a particular behaviour (B) is or is not performed (COM-B). The COM-B behavioural analysis guides the choice of intervention strategies most likely to achieve behaviour change, and highlights the behaviour change techniques particularly suitable for each intervention strategy. Following this structured approach lends transparency to the process of intervention development, and facilitates its subsequent implementation and evaluation [12]. The application of these models to our data is described in detail in Chapter 9. An expert panel informed modelling of intervention characteristics (e.g. which multimorbid patients should be targeted, choice of prescribing tool etc.). This process is also described in Chapter 9 with additional details provided in Appendix V.

4.3. MRC phase 2: Assessing feasibility

A key question in evaluating complex interventions is whether they are effective in everyday practice. Interventions to improve the quality of healthcare often fail or have only modest impact if there is inadequate attention paid to the target population or subject matter (172), and interventions may work better if a specified degree of adaption to local settings is allowed. Regardless of this flexibility, the implementation

of and fidelity to the various components of the intervention should be monitored, to see what works, where it works and why (8).

VI. The acceptability of the intervention, key uncertainties identified during development, and the impact of context on implementation is evaluated in the feasibility study described in Chapter 10. The approach was informed by the work of a group of researchers who are developing CONSORT guidelines for pilot and feasibility studies (173-176), and the National Institute for Health Research guidance on feasibility studies (177). Within the study, I explored feasibility by focusing the analysis on a core set of implementation outcomes: acceptability, adoption, appropriateness, cost, feasibility, fidelity, penetration, and sustainability (178, 179).

4.4. Philosophical orientation

Clinical research traditionally fits with the biomedical model of positivism. However, as I intended to examine physicians' thought processes and decision-making behaviours, a constructivist approach was required for the first phase of intervention development. Following the suggestions of Hammersley on subtle realism, I have assumed that an independent reality exists, but one which cannot be directly accessed; knowledge of this reality is a human construction, based on assumptions and purpose (180). Beyond this, I also agree with the suggestions of Patton: that practical research questions can be addressed without definite allegiance to a specific philosophical stance and that 'methods of qualitative inquiry now stand on their own as reasonable ways to find out what is happening in programmes and other human settings' (181).

In qualitative research, the aim determines the most appropriate methodology and type of analysis (182). However, in my experience, different methodologies offered diverse but potentially useful perspectives on how GPs face the issue of multimorbidity. Qualitative methods are generally not 'pure' but textured with features and 'hues' of many possible approaches (183). So during this thesis, I have come to appreciate the need for a 'situated methodology': adopting a research-centred view of the place of methodological rules and adapting methodology to the research situation (184). I have taken a 'bricoleur' approach by first synthesizing existing qualitative studies but then conducting a qualitative interview study that incorporated many features of grounded theory (which traditionally eschews prior systematic reviews). The coding of data using theoretical frameworks in the intervention development and feasibility studies is more akin to framework analysis (185). Thus, rather than adopting one qualitative method across the thesis, I have used different approaches depending on the study or phase of research (186).

CHAPTER 5. GPS' PERSPECTIVES ON THE MANAGEMENT OF PATIENTS WITH MULTIMORBIDITY: A SYSTEMATIC REVIEW AND SYNTHESIS OF QUALITATIVE RESEARCH

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5.1. Abstract

Objective

To synthesize the existing published literature on the perceptions of GPs or their equivalent on the clinical management of multimorbidity and determine targets for future research that aims to improve clinical care in multimorbidity.

Design

Systematic review and meta-ethnographic synthesis of primary studies that used qualitative methods to explore GPs' experiences of clinical management of multimorbidity or multiple chronic diseases.

Data sources

EMBASE, Medline, CINAHL, PsycInfo, Academic Search Complete, SocIndex, Social Science Full Text, and digital theses/online libraries (database inception to September 2012) to identify literature using qualitative methods (focus groups or interviews).

Review methods

The seven step meta-ethnographic approach described by Noblit and Hare, which involves cross-interpretation between studies while preserving the context of the primary data.

Results

Of 1805 articles identified, 37 were reviewed in detail and ten were included, including a total of 275 GPs in seven different countries. Four areas of difficulty specific to the management of multimorbidity emerged from these papers: disorganization and

fragmentation of health care; the inadequacy of guidelines and evidence based medicine; challenges in delivering patient-centred care; and barriers to shared decision-making. A 'line of argument' was drawn which described GPs' sense of isolation in decision-making for multimorbid patients.

Conclusions

This systematic review shows that the problem areas for GPs in the management of multimorbidity may be classified into four domains. There will be no 'one size fits all' intervention for multimorbidity but these domains may be useful targets to guide the development of interventions to assist healthcare professionals and improve the provision of care to patients with multimorbidity.

5.2. Introduction

Multimorbidity, the co-existence of two or more long-term conditions in an individual patient, is increasingly the norm in chronic disease management in primary care (2, 33). The management of patients with multiple morbidities presents unique challenges for healthcare professionals, and there is evidence that patients with multimorbidity receive a lower quality of care than those with single diseases (85, 187). Healthcare utilisation, hospitalization rates and total healthcare costs are higher among multimorbid patients, even in systems where access to secondary care is restricted to referral by a primary care physician (3, 4, 188).

The epidemiology of multimorbidity is thus well described and there is now a need for interventions to improve healthcare in this patient group (145, 189). A necessary step in the development of interventions is to understand why problems arise and what processes in the delivery of care are amenable to change. Interviews with stakeholders such as healthcare professionals can be important sources of this information (8). To date, qualitative studies from a range of countries have elicited GPs' views on challenges in the clinical management of multimorbidity, with diverse and sometimes conflicting findings. A synthesis of these studies has the potential to achieve a greater conceptual understanding of the challenges associated with multimorbidity than a single empirical study.

Meta-ethnography, one of the most commonly used methods for synthesizing qualitative research studies, employs a process of comparison and cross-interpretation between studies while preserving the context of primary data (190). Similar to traditional systematic reviews, this process can generate new insights, highlight gaps in our knowledge and show areas of data saturation where no further primary research is required (191).

An awareness of the overall picture of challenges faced by GPs in multimorbidity is needed to direct research efforts and intervention development in this field. To achieve this, we synthesised and analysed the existing literature on the views of GPs on the management of multimorbid patients and determined targets for future research to improve multimorbidity care.

5.3. Methods

The seven step model of meta-ethnography described by Noblit and Hare was used to guide the search and synthesis (192). (The study protocol is provided in Supplementary material 1.)

The first step involved a clear statement of the specific research question and the contribution it will make to the field.

In step two, a search strategy was devised to retrieve papers related to this aim. We focused our search to locate primary studies that used qualitative methods to explore the clinical management of multimorbidity or multiple chronic conditions by GPs or their equivalent. We searched seven databases using database specific search terms and validated methods for retrieving qualitative studies: EMBASE (Elsevier), Medline (Ovid), CINAHL, PsycInfo, Academic Search Complete, SocIndex, Social Science Full Text(all Ebsco) (search terms provided in Supplementary material 2)(193-196). We supplemented this by searching databases of grey literature and reference lists. The search was not limited by language or dates of publication. The titles and abstracts of retrieved citations were read by one reviewer (CS). Full papers were ordered for all potentially relevant abstracts (197). These papers were reviewed by two researchers (CS, CB) and included if they met our inclusion criteria. Studies that examined the management of multimorbidity as part of a wider research question were included. We assessed the quality of included studies using the Critical Appraisal Skills Programme (CASP) for qualitative research (198). Assessment of study quality was not used to exclude studies that otherwise met the inclusion criteria, but gave useful insights into the methods used for data collection and analysis.

Step three of the meta-ethnographic synthesis involved reading the studies. Initially two reviewers (CS and CB) read and re-read the included studies, and independently

listed the main findings from each one. Study findings were defined as all data in the results and discussion sections of the included papers – including both the first order interpretations (views of the participants) and second order interpretations (views of authors). In studies where GPs were interviewed with another healthcare professional, the analysis was restricted to the views of the GP where possible. We abstracted data on standard fields such as study aims, design, methods, setting and participants (data abstraction form provided in Supplementary material 3) (199). Data was entered in to QSR International's NVivo 9 software to assist our qualitative analysis and synthesis (200).

In step four, we determined how the studies were related to each other by comparing individual study findings. Four key concepts were chosen which reflected the main findings of all included studies.

In step five, studies were translated into each other by examining the contribution of each study to a key concept. Within the key concepts, similarities and differences in study findings and contexts were noted, and deviant cases were sought. To address the potential for clinical bias a third reviewer with a non-medical background (SMH) independently read all included papers and cross-checked the derivation and development of the key concepts.

In step six, we synthesized the translations in each key concept to develop third order interpretations, or higher levels of abstraction of the data for each key concept. We linked the third order interpretations using a 'line of argument', which represented the overarching perspective of GPs towards multimorbidity.

The final step involved expressing the results of the synthesis, for which we used tables, figures and text. The 'Enhancing transparency in reporting the synthesis of qualitative research' (ENTREQ) statement was used to inform the reporting of our

results (provided in Supplementary material 4) (201). Additionally, a summary of our findings were supplied to the first authors of all included papers, in order to validate our findings as representative of the original sources.

5.4. Results

The electronic database search returned 2,005 citations, leaving 1805 citations after removal of duplicates (Figure 4). A further 1768 citations were excluded by reading the title or abstract: 48 did not concern primary care, 891 were not qualitative studies, 769 did not concern multimorbidity, and 60 did not concern the GP's perspective. Full text articles were retrieved for 37 citations. Eleven of these were excluded because they did not use qualitative methods. A further 16 articles were excluded because, although they concerned patients with multiple chronic conditions, their exploration was focused on the management of an index condition. One possible relevant citation was in abstract form only (the study authors were contacted and the full account of this data has not been published yet) (details on excluded full texts are available in Supplementary material 5). One additional study was retrieved from reference searching of the nine remaining studies. Ten studies were included in the final synthesis.

The included studies were conducted in seven countries: Belgium, England, Germany, Ireland, Scotland, the Netherlands and the United States (Table 1). A total of 275 GPs were involved; five studies used focus groups and five used interviews with individual GPs. One of the included articles was published in German. The authors were contacted for an English translation and as none was available, the article was translated by a native German speaker in collaboration with CS.

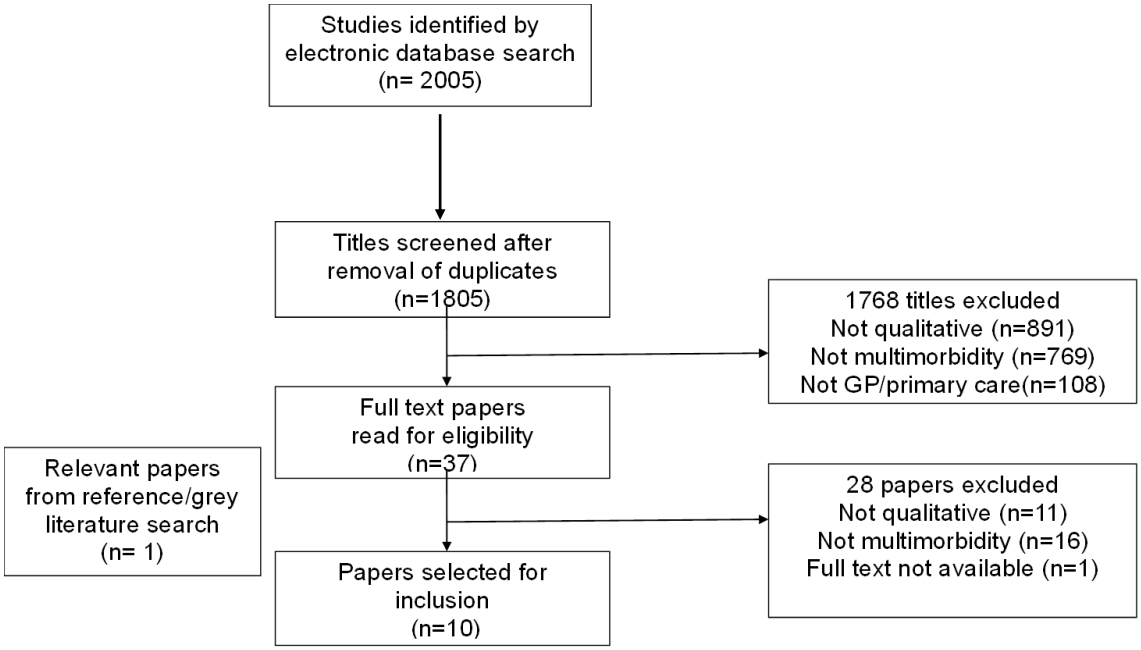

Figure 4. Flow chart of studies in the systematic review

The overall quality of the ten included studies was high, with all papers meeting the majority of CASP criteria (details available in Supplementary material 6). The most common weaknesses related to data saturation (not reported in six studies) (202-207) and reflexivity (not discussed in five studies) (204-206, 208, 209). GPs with academic/research affiliations were over-represented as research subjects in five studies, representing a potential source of bias (202, 205, 208-210).

Six studies primarily focused on multimorbidity. In these studies, multimorbidity was defined for study participants as two or more chronic conditions (203, 205, 208, 211) or introduced to participants using a multimorbid case vignette (209) or an editorial on multimorbidity (202). Four studies retrieved by our search did not focus primarily on multimorbidity but were included as multimorbidity emerged as an important issue for study participants; two studies addressed polypharmacy (207, 210) and two explored the role of guidelines in primary care (204, 206).

Table 1. Characteristics of studies included in the systematic review (n=10)

First Author	Objective	Data Collection	Participants (n)	Qualitative methodology /analysis	Country	Year of pub
Smith (202)	To explore the views and attitudes of GPs and pharmacists managing patients with multimorbidity in primary care.	Focus group with topic guide; participants were given a published editorial on multimorbidity before hand	GPs (13) & pharmacists. GPs were tutors to undergraduate medical students, worked in a mix of rural/urban, deprived/affluent practice and varied by gender and years of experience	Framework	Ireland	2010
O'Brien (203)	To understand GPs and practice nurses' experiences of managing multimorbidity in deprived areas and elicit views on what might help.	Individual semi-structured interview facilitated by researched topic guide	GPs (15) & nurses, working in areas of high deprivation in Scotland	Constant comparison	Scotland	2011
Steinman (204)	To investigate clinician attitudes about the usefulness of heart failure guidelines in patients of various ages/morbidity	Telephone based interview using Likert scales followed by open ended questions	Primary Care Practitioners (48/58) and Internists (10/58) responsible for sub-optimally managed patients with heart failure.	Content analysis	US	2012
Fried (205)	To explore clinicians' perspectives of and experiences with therapeutic decision-making for older persons with multiple medical conditions	Focus groups with broad discussion initially, then focused questions on polypharmacy, side effects, and evidence based medicine in multimorbidity	GPs (36) purposively sampled to vary on academic, community and Veteran Affair settings	Content analysis	US	2011
Solomen (206)	To explore the relationship between prescribing guidelines and patient-partnership by exploring the attitudes of patients, GPs and prescribing advisors	Semi-structured interviews	GPs (8) sampled using maximum variation by location, gender, single vs. group practice	Framework	England	2012

Anthierens (207)	To describe GPs' views and beliefs on polypharmacy	Semi-structured interviews	65 GPs working in mixed rich/poor urban environment	Content Analysis	Belgium	2010
Bower (208)	To explore GP and nurse perceptions of multimorbidity and the influence on service organization and clinical decision-making	Individual semi-structured interview using topic guide with questions and case vignettes.	GPs (15) & nurses, working in a pay for performance system. Purposively sampled from research network, to vary on list size and deprivation.	Framework	England	2011
Schuling (209)	To explore how experienced GPs feel about deprescribing medication in older patients with multimorbidity and to what extent they involve patients in these decisions.	Focus groups	GPs (29) split into 3 groups. All were GP trainers of at least 5yrs experience 'used to reflecting on their practice'	Thematic	Netherlands	2012
Marx (210)	To explore the 'dilemma of polypharmacy' in primary care	Focus groups	GPs (21) in three focus groups. Fulltime GPs, junior and senior academic GPs, conducted at an academic GP conference.	Mind maps and grounded theory	Germany	2009
Luijks (211)	To explore GPs' considerations and main aims in the management of multimorbidity, and factors influencing this management in daily practice.	Focus groups using an interview guide	Purposively sampled GPs (25), with/out involvement in training/academia, in five focus groups.	Constant comparison	Netherlands	2012

Translation of included studies

GPs in all studies reported challenges in multimorbidity, which they faced with "moderate optimism to something close to despair" (209). Even in the context of deprivation, some participants reported feeling like a "wrung out rag" after complex multimorbidity consultations while others felt "energised" by the "privilege and rewards" that could be obtained from working in such a complex environment (203). Four key concepts that reflected the principal findings of all included studies were determined (Figure 5). The key concepts are described below and with quotations in Table 2. The subthemes in each key concept are highlighted in bold in the text and are shown in tabular form in Supplementary material 7.

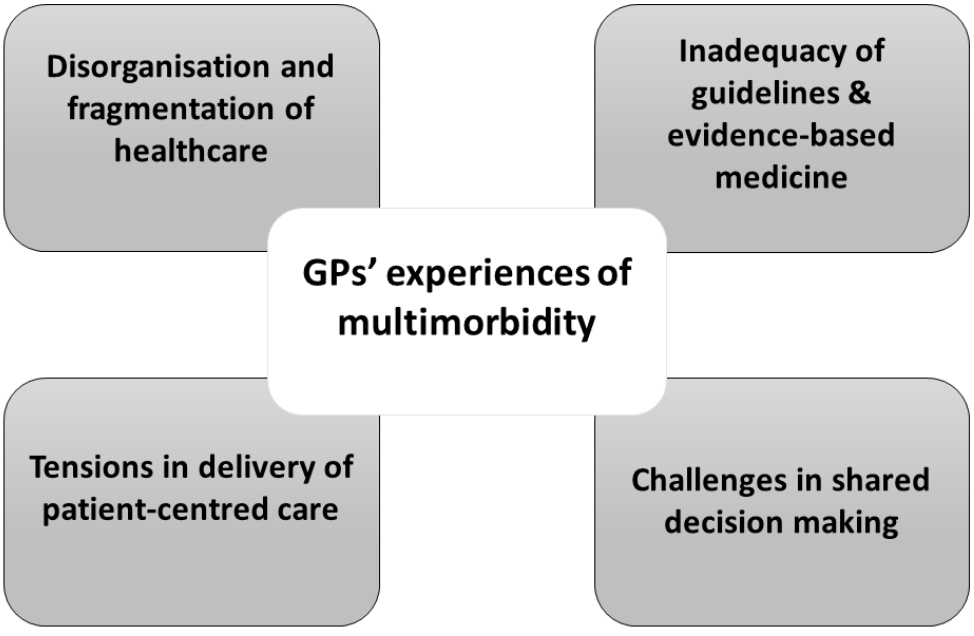

Figure 5. Four domains in which GPs experience difficulties in the management of patients with multimorbidity.

Disorganisation and fragmentation of health care

The included studies covered a range of different health systems, all of which lacked specific systems for treating patients with multimorbidity. In most studies this lack of organisation hampered care by causing logistical difficulties and excessive consultation demands on the patient and their GP. Only one study mentioned that these problems were not serious enough to warrant a change in service organisation (208).

The prevailing **structure of primary healthcare** reduced GPs' ability to respond to the needs of patients with multimorbidity. Insufficient consultation **time** led to amended or suboptimal approaches in many cases (202, 203, 208). It was suggested that weighting consultation lengths according to the complexity of multimorbidity would facilitate more effective management (202, 208).

Fragmented care resulted from "the involvement of several medical specialists, who each emphasize the importance of 'their' guideline" (209) and "poor communication from specialists and hospitals to the family physician" (210) which meant that "co-ordination and overview on medication were hard to maintain" (211). In some studies, GPs had a broad sense of responsibility towards overseeing and screening patients' medications (207, 210, 211); others were unsure about their role in screening prescriptions and felt that a clear line of responsibility was required (202). It was suggested that specialists did not "consider the wider harms and benefits of organ-specific intervention", thereby adding to the problems of multimorbidity, in contrast to GPs who had a "holistic" view of the patient; "The cardiologists, you know, don't mind if they bleed to death" (205).

Despite these reservations, the input of specialists was desired. A "balance of equals" was called for, that would allow GPs and specialists to discuss complex patients, and improve the awareness of complexity in multimorbidity amongst specialists (202, 210).

This would help all doctors involved “to speak with one voice. Different stories provoke distrust”(209).

The inadequacy of guidelines and evidence based medicine

There was concern amongst GPs about clinical guidelines, which are “generally written for sole conditions” and do not account for “the unique circumstances of each patient” (204, 206). Most GPs felt guidelines were less useful in multimorbidity and that they actually **added to the complexity** in some cases: “no one can tell you the added benefit of an additional agent for blood pressure if you are already on ten” (205, 209). However, others felt that using guidelines in multimorbidity ensured patients received the best quality care: “why should their asthma be treated any differently just because they've got asthma and heart disease and you know osteoporosis or whatever” (208). GPs doubted if the **evidence underpinning guidelines** could be extrapolated to patients with multimorbidity: “The guidelines are going to be set for optimum situations, and someone with multiple comorbidities [is] not going to be optimum”(204-206, 210). They also questioned the **relevance of disease specific outcomes** and guideline recommendations for the use of **primary prevention** (i.e. antihypertensive or lipid lowering agents) in multimorbidity, preferring to orient management to symptoms or quality of life (202, 204).

GPs adopted **modified approaches** to guidelines, such as estimating the risk associated with particular diseases/treatments (205, 209). However, some felt this modification was in conflict with “best practice” and felt guilt for not implementing guidelines fully (203, 209). Initiatives that linked **physician reimbursement** with adherence to guidelines were seen as a threat to GPs’ ability to deliver patient-centred care (203, 205).

Challenges in delivering patient-centred care

In response to the many demands of multimorbidity, GPs recognized the importance of delivering patient-centred care, which incorporated two principal concepts: **individualised** management and a **generalist** approach (202-205, 207-211). Delivering patient-centred care was seen as a useful approach by some but a challenge for others. For instance, some GPs felt that taking a broader view of the patient, incorporating nonmedical or psychosocial issues, increased the level of complexity in their management (203). However, for others adopting a patient-centred approach was seen as a way of resolving the conflicts and uncertainty that can occur, particularly with co-implementation of multiple sets of guidelines (203, 211).

In most studies, the **longitudinal nature of the patient-GP relationship** was seen as a "major facilitator" and "elementary component" of patient-centred care in multimorbidity (202, 203, 207-211). Within the specific context of deprivation, longitudinal care was "potentially transformative" by giving "time to build relationships with patients" but it was also was a source of problems, by creating dependence and increased demands by patients for consultations (203).

The impact of **treatment burden** was an important consideration given the greater costs and risk of adverse drug events associated with the use of multiple medications (202, 208, 211). This burden was compounded by **certain patient characteristics** such as cognitive or memory problems, poor social supports and finances, and low levels of motivation (202-205, 207, 208) which were likely to affect a patient's ability to understand and adhere to treatment (204, 205, 209-211).

Challenges in shared decision-making

Shared decision-making was considered to be more complicated in the context of multimorbidity due to many of the issues discussed above. The importance of eliciting a patient's preferences was widely acknowledged, but GPs had difficulties doing this in practice (209, 211). GPs reported that many patients actively participate in decision-making, can prioritize and are "good with trial and error" (208, 209). However, for certain patients making choices could be a "source of distress" and contributed to them becoming "over the top anxious about their conditions" (208). Discussing **the risks and outcomes associated with treatment options** in a way that facilitated patient involvement was particularly challenging, as was discussing the balance between quantity and quality of life (203-205, 209, 211). In response to difficulties in shared decision-making, GPs employed a range of techniques including **prioritization** of the doctor's or the patient's agenda (207, 208, 210), **avoidance** of decision-making (202, 209), drawing on one's own **personal experience** (210) or using **additional investigations** to support a decision (205).

Enhanced **communication skills** were needed in multimorbidity to facilitate clear and concise discussion with patients on the interplay between their chronic conditions and to help with **deprescribing** medications, which if done badly could be interpreted as withdrawing care (205, 209, 210). GPs felt they had a pivotal role to play in patients who were in the advanced stages of a chronic disease but due to multimorbidity may no longer be receiving specialist input. In this setting, adopting a palliative approach was useful when making decisions on medications (209, 211).

Third order interpretations and the 'line of argument'

By synthesizing the individual contributions of each study to the key concepts, third order interpretations were generated and linked using a 'line of argument' (Table 2).

1) Disorganisation and fragmentation of health care: The involvement of multiple specialists and the emphasis on single disease care is antagonistic to the 'holistic' goals of GPs. This problem is compounded by poor co-ordination and communication within the health service, leaving GPs feeling excluded from their patients' care and with a sense of uncertainty regarding their role.

2) The inadequacy of guidelines and evidence based medicine: Guidelines offer GPs less support in the management of multimorbid patients and may in fact cause additional problems when they try to adhere to them.

3) Challenges in delivering patient-centred care: Patient-centredness is an overriding principal for GPs in multimorbidity but trying to achieve this increases the complexity of care in some cases, and can lead the GP into additional conflict with specialist services or evidence based medicine.

4) Challenges in shared decision-making: The patient's role in decision-making in multimorbidity is limited by difficulties in communicating risk-benefit and outcomes in a field where there is much more uncertainty on these issues.

These key concepts represent four problematic domains in the provision of healthcare in multimorbidity, as seen by GPs. The line of argument linking these domains suggests that GPs feel isolated in the management of patients with multimorbidity, a group that they are specifically tasked with caring for.

Table 2. Translations between studies with third order interpretations.

First Author	Disorganisation & Fragmentation of health care	The inadequacy of guidelines & evidence based medicine	Challenges in patient-centred care	Challenges in shared decision-making
Smith (202)	'*lines of communication need time and nobody appears to have time*' '*collusion of anonymity, which is, you know, this is not my patient, not my patient*'	'the paradox faced by conscientious GPs in attempting to balance the potentially competing demands of health promotion, evidence-based medicine, and the use of multiple medications'	'a focus on function and quality of life was preferable to considering specific disease outcome measures'	'*..decision-making very difficult to achieve*.' 'decisions were linked to the theme of avoidance of complex issues which...can appear to become increasingly problematic and unsolvable'
O'Brien (203)	' adaptation of existing practice systems, particularly appointment length, relationship continuity, and referral systems for resources outside primary care, may improve services from the perspectives of professionals'	'*need .. to demonstrate that we are interested in (patients) as a person, not someone who has heart failure*'	'wanted to develop relationships with patients because she thought that greater understanding of their circumstances would help her get to the root of (medical) problems'	'*there was a need to address 'a bit of the patient's agenda and our agenda' within consultations*'
Steinman (204)	-	'...those with multiple comorbid conditions were more likely to experience harm from aggressive guideline based treatments' 'guidelines represent a criterion standard of evidence-based care....regardless of patient age or comorbid burden'	'*Each patient is a unique situation and is not going to be the same as another patient…. We have to go by the individual patient, by the patient's comfort, how is he feeling, and how is he doing*.'	'a suggested approach to decision-making for older adults that provides guidance on prioritizing care, accounting for comorbid conditions, and factoring in the role of estimated life expectancy'
Fried (205)	'fragmentation of care for patients who receive care for their multiple conditions from many physicians.' 'the limitations imposed by current reimbursement systems, which fail to	'*If they cannot manage... I am not going to complicate it further by adding something to get to the goal range*.' 'other clinicians believed that	'Tailoring their approach …from a consideration of such factors as patients' cognition and availability of social support'	'...conflicts between what they wanted to do for the patient and what the patient wanted' '...patients' and families' inaccurate understanding of harms and benefits,

	acknowledge the complexities of caring for older persons with multiple conditions'	guideline-directed care would produce the best outcomes'		and they described performing testing to help patients understand their risk.'
Solomen (206)	-	'there was a perception that real patients differ from those recruited to the trials that inform guidelines'	'Many GPs felt they needed to be able to interpret guidelines in the context of individual patients'	' to reach a compromise by following guidelines and accommodating patient factors, such as patient preferences or the patient's ability to tolerate medicines'
Anthierens (207)	*' The co-ordination of the medication regime of different disciplines is a tough job..."*	'preventive aims are often minimal considering their age and polypathology, which is in contrast with guidelines talking about one specific disease. '	'*As a GP you have a broader view of your patient. You look at him/her from his own life.*'	'They have a holistic view of the patient because of the long standing doctor-patient relationship….. a very tough job for GPs with major implications for their workload'
Bower (208)	'clash between services and the needs of patients was most salient in terms of logistics and inconvenience' 'Difficulties in information sharing between professionals meant that patients often had to co-ordinate care'	'...ambivalence about the need to consistently change clinical practice to reflect multimorbidity' '...*why should their asthma be treated any differently just because they've got asthma and heart disease and you know, osteoporosis or whatever*'	*'Weighing up what that patient can manage on the conditions they have, as to what it actually says to do.*' 'benefits of continuity of care in patients with multimorbidity'	'Dealing with multiple competing agendas in multimorbidity was important.' 'limited impact of multimorbidity on clinical decision-making'
Schuling (209)	'...medication lists of the doctors involved are not exchanged and are consequently inconsistent.' '...several healthcare providers are involved in a patient's treatment and communication is sometimes poor'	'*guidelines are kind of a hindrance. At the moment they do not cater for older patients.'* ' I have difficulty not following the guidelines if I don't have good reasons to do so. '	'GPs report to support the concept of a patient-centred management as best practice' *'take her quality of life into account and ask myself will she live long enough to benefit from this (preventive) drug? '*	'the importance of exploring patient preferences about treatment goals, in practice GPs appear hesitant.' '… GPs tend to avoid discussing withdrawal of preventive medication with their elderly patients'
Marx (210)	'poor communication from specialists and hospitals to the family physician' 'highlights the need for professional	'The desire of family doctors to deliver the best possible patient care quickly leads to	'conflict arose in the actions of GPs trying to deliver personalized care to individuals and trying to	'uncertainty could be counteracted by good communication between the doctor and patient.'

	discussion on the one hand and avoiding unnecessary medication by multiple prescribers on the other hand.'	polypharmacy, if guidelines are used'	delivering guideline orientated care'	'the patient and the doctor are in an interactive process, which necessitates careful negotiation'
Luijks (211)	'in multimorbidity, fragmentation of care is a pitfall.... stimulated by disease-centred reimbursement systems' ' impeding multimorbidity management... insufficient time and compensation'	'adhering to standard regimens or strict guidelines was unwanted, as it contradicts their integrated perception of a unique person with a specific combination of diseases'	'A personal patient–doctor relationship was considered a major facilitator in the management of multimorbidity' 'patient-centredness can be regarded as 'tool' to counteract multimorbidity's potential pitfalls'	'GPs agreed that they want to involve their patients' perspectives and preferences into the decision-making process'
TOIs	The involvement of multiple specialists each operating on a single disease paradigm without an overview of the 'whole patient' leads to fragmented care in multimorbidity. Single disease care is antagonistic to the goals of GPs in primary care. This problem is compounded by poor co-ordination and communication within the health service, leaving GPs feeling excluded from their patients care and with a sense of uncertainty regarding their role.	GPs have reservations about the outcomes and risk-benefit of guidelines in multimorbid patients. Although useful as a template, GPs feel that guidelines offer them less guidance or support for multimorbid patients and may in fact cause additional problems when they try to adhere to them.	Patient-centred care is an overriding principal for GPs in multimorbidity and incorporates the principles of individualization and generalism. Trying to achieve this aim increases the complexity of care in some cases, and can lead the GP into additional conflict with specialist services or evidence based medicine.	While GPs recognize the importance of involving patients in decision-making process, they have difficulties in doing so. Communicating risk and outcomes in way that will engage patients in the decision-making process is an area that GPs feel unskilled in, thereby limiting the patients influence as factor that would help the decision-making process

Italicized extracts represent first order interpretations (views of participants in included studies). Non-italicized extracts represent second order interpretations (views of authors of included studies). TOIs= third order interpretations.

5.5. Discussion

The studies presented here used a bottom-up approach to explore the management of patients with multimorbidity. This paper is the first to our knowledge to systemically review and synthesize their findings, and demonstrates the diversity in how GPs see this issue. The difficulties that GPs encounter span a number of clinical domains including system factors, the evidence base for chronic disease management and their own communication skills in the context of multiple physician and patient agendas. These findings are important because they highlight the separate but interacting areas of clinical practice that require intervention to improve care in multimorbidity. Thus, this study is additive to the findings of the individual studies reviewed; synthesizing the contributions of existing qualitative investigations in this area has led to a broader description and fuller understanding of the range of challenges that exist. Given the considerable overlap and repetition of data that emerged from the primary studies, it is unlikely that further scoping work on the challenges of multimorbidity will be useful. However, despite the commonalities, the significance of each domain varied between settings. Further research should focus on the reasons why some domains matter more in particular settings and how local factors modify and influence these domains, with a view to exploring what solutions exist and what those solutions may be (212). There will not be a 'one size fits all' intervention to support and improve the quality of care in multimorbidity. However, the domains that have emerged from this review give a useful framework for future work in this field.

Comparison with other research

Disorganisation and fragmentation of care

Integrating patient care across services is important in all aspects of medicine, but there is a pressing need to address this in multimorbidity. Patients attending four or more doctors experience problems such as conflicting medical advice, unavailable test results and duplication of tests more commonly (213). Our study indicates that, across settings, GPs receive poor communication from other care providers in multimorbidity, leaving them guessing about the course of management. Enhanced use of information technology may support more seamless multimorbidity care, by allowing bi-directional communication and local integration between care providers.

Satisfaction with prevailing health systems also varied between studies. Generalisations relating to a health system cannot be made from one single study, but this divergence is worthy of further exploration. For instance, a comparative analysis, using a multimorbidity perspective, of the strengths and weaknesses of the UK system (which uses explicit quality frameworks for chronic disease management) and a health system without such an approach may help inform policy and the development of interventions at health system level.

The inadequacy of guidelines and evidence based medicine

GPs in the studies reviewed here desired evidence on which to base their management but had mixed feelings on the clinical utility of guidelines as they currently stand. This finding is supported by prior studies showing that, internationally, few guidelines offer modified advice for patients with multimorbidity (126, 127). To increase the relevance of clinical guidelines for multimorbid patients, our findings support the call for greater representation of multimorbid patients in trials and greater involvement of GPs in the writing of guidelines (130).

Chronic conditions can occur in combinations that are concordant (have synergies in treatment) or discordant (conflicting treatments or interactions) (85). Although the synergies between certain conditions were discussed in the papers reviewed here, examples of specific discordant conditions were rare. It would be useful to explore what discordant combinations commonly occur in practice. This information could be used to inform the development of caveats in guidelines, educational initiatives or prioritization tools that would support safe approaches to competing diseases (121).

Delivering patient-centred care

This domain emerged as an intuitive and over-riding goal of GPs in all studies, thus interventions in multimorbidity must help GPs deliver patient-centred care. Continuity of care emerged as an important tenet of patient-centredness and should be promoted in any such interventions. Three subtypes of continuity of care have been previously described (214). Informational and management continuity were seen here as necessary for patient safety and cohesive management. However, it was relational continuity that appeared to most facilitate care in multimorbidity, by allowing GPs to foster trust, anticipate preferences, and empower their patients over time. GPs felt that multimorbid patients with cognitive impairment, mental health issues or low social support require greater attention, and may benefit from more nuanced interventions to support their care.

Challenges in shared decision-making

Shared decision-making is facilitated by many aspects of primary care (215-217). Nevertheless, GPs reported a need for additional skills in shared decision-making in multimorbid patients, especially for complex decisions that involve not prescribing or

discontinuing medications. It is known that interventions to improve shared decision-making may fail due to barriers such as lack of time and perceived lack of suitability of the patient (218, 219). Given the overlap between these barriers and those that GPs encounter in multimorbidity, it is likely that special attention is warranted for the development of models of decision-making for multimorbid patients. Evaluating existing models of shared decision-making, such as the choice talk/option talk/decision talk model described by Elwyn and colleagues, in clinical encounters with multimorbid patients may be a useful place to start this process (220).

Usefulness of meta-ethnography

The systematic approach of meta-ethnography as applied in this study has a number of strengths. It gives a fuller description of multimorbidity care while preserving the important contextual features that are inherent in general practice research. Our themes, developed from the experiences of 275 participants, indicated considerable overlap from each of the primary studies. Nevertheless, different opinions within particular themes gave useful insights into how system factors and context can influence practice. The step by step approach used in our analysis generated themes in a transparent and reproducible way. The robustness of our findings is supported by several features. First, the quality of the studies reviewed was assessed using a published framework and quality levels were uniformly high. Secondly, there was concordance in the themes derived by non-clinical and the clinical reviewers on the research team. Thirdly, the findings from our analysis were disseminated to the authors of the primary studies. In the resulting feedback, the authors felt their results were represented within the findings of the synthesis.

Limitations and challenges

Retrieving qualitative studies from biomedical databases is challenging despite recent advances in the indexing of qualitative literature. We used validated combinations of qualitative search terms to optimize the list of citations returned (193-196). Furthermore, we also used non-biomedical databases to ensure that articles of relevance in the sociology or psychology literature were not missed (197).

Multimorbidity is not a MeSH (Medical Subject Heading) term and there is a lack of consensus on what the term means or encompasses with regard to diseases and disease severity (36). We used a broad but less specific search strategy to account for this (detailed in Supplementary material 2) which resulted in the retrieval of papers with important information on multimorbidity, despite their original focus not being on this issue. Achieving consensus on the definition of multimorbidity will be important for the generalisability of findings and evaluation of future interventions in this field.

The term 'multimorbidity' was first discussed in the literature in 1976. However, the first article that we found investigating this issue with GPs using qualitative methods was published in 2009. There has been a surge in quantitative research on multimorbidity, which may be explained by the increasing prevalence and economic impact of multimorbid patients (51).

There was no language restriction used for inclusion of studies, and translations of potentially relevant titles and papers were conducted. However, we could have missed papers not listed on English language databases.

Although the quality of included studies was generally good, the over-representation of academic GPs as participants was a potential source of bias and may limit the generalisability of our findings to the overall GP population. Future studies should

endeavour to include GPs outside of the academic field to ensure the full range of clinical challenges is explored.

The primary data in our review originated from focus groups or clinical vignettes, reflecting what clinicians say rather than what they do. It would be valuable to use case-based data in future studies, to see for example what specific conflicts arise between guidelines and how shared decision-making is currently broached in practice. Such data would also help inform educational programmes in multimorbidity for GPs and GP trainees.

Our findings are limited to the challenges experienced by healthcare professionals in management of multimorbidity; the patient perspective also requires consideration. Elderly patients report functional decline, poor quality of life, and high healthcare costs as major consequences of multimorbidity, therefore these issues should be addressed in the development of interventions in this field (46).

5.6. Conclusions

This systematic review shows that the problem areas for GPs in the management of multimorbidity may be classified into four domains: disorganization and fragmentation of health care; the inadequacy of guidelines and evidence based medicine; challenges in delivering patient-centred care; and barriers to shared decision-making. There will be no 'one fits all' intervention for multimorbidity but these domains may be useful targets to guide the development of interventions that will assist and improve the provision of care to multimorbid patients.

CHAPTER 6. WHAT TO GIVE TO THE PATIENT WHO HAS EVERYTHING? A QUALITATIVE STUDY OF PRESCRIBING IN MULTIMORBIDITY

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6.1. Abstract

Background

Using clinical guidelines in the management of patients with multimorbidity can lead to the prescription of multiple and sometimes conflicting medications.

Aim

To explore how GPs make decisions when prescribing for multimorbid patients, with a view to informing intervention development in this field.

Design and Setting

In-depth qualitative interviews incorporating chart stimulated recall (CSR) with purposively sampled GPs in the Republic of Ireland.

Methods

Grounded theory analysis with iterative theory development.

Results

Twenty GPs were interviewed about 51 multimorbid cases. In these cases, GPs integrated information from multiple sources including the patient, specialists and evidence based medicine. Difficulties arose when recommendations or preferences conflicted. GPs responded to these conflicts by 'satisficing': accepting care that they deemed satisfactory and sufficient for a particular patient. Satisficing was manifest as relaxing targets for disease control, negotiating compromise with the patient, or making 'best guesses' about the most appropriate course of action to take. In multimorbid patients perceived as stable, GPs preferred to 'maintain the status quo'

rather than rationalize medications, even in cases with significant polypharmacy. GPs took this approach due to the potential negative repercussions associated with changing medications. Proactive changes in medications were facilitated by continuity of care, sufficient consultation time and open lines of communication with the patient, other healthcare professionals and other GPs.

Conclusion

GPs respond to conflicts in the management of multimorbidity by satisficing, which involves making compromises between patient-centred and evidence-based care. These findings will help inform the development of interventions that aim to improve medication management and patient-centred care in multimorbidity.

6.2. Introduction

Multimorbidity, the co-occurrence of two or more chronic conditions, affects over 50% of patients with chronic disease in primary care and leads to increased mortality, higher rates of disability, and lower quality of life (51, 87). For healthcare systems, multimorbidity leads to higher rates of healthcare utilization, especially high cost services such as hospitalisations and emergency department visits (3, 46, 221). Due to the aging demographic, this burden continues to rise and optimizing the management of multimorbidity is a major concern for health research, policy and education (59). Multimorbid patients are also more likely to experience polypharmacy and potentially inappropriate prescribing than patients with single conditions (222, 223). However, prescribing 'appropriately' in multimorbidity is not always straight forward (111, 116). Guidelines exist for most common chronic conditions and offer benefits associated with the best available evidence, but adhering to guidelines in the management of a patient with multimorbidity almost invariably leads to multiple medications, resulting in increased risk of drug interactions, adverse effects and poor adherence (103, 224). Furthermore, most guidelines do not address patient preferences, quality of life or the expected time to benefit (66). Thus prescribing in multimorbidity poses a dilemma: to prescribe a recommended medication that may, via polypharmacy, lead to adverse effects or not to prescribe a medication that may have potential benefits (225). Despite the prevalence of multimorbidity, there have been few professional-orientated interventions developed to improve patient outcomes in this field (145). Prescribing behaviour appears to be a worthy candidate for such an intervention. We know that GPs question the usefulness of single disease guidelines in multi-disease patients (Chapter 5) (226). However, we know little about how GPs choose what to do when faced with guidelines that indicate that multiple and sometimes conflicting medicines

should be prescribed. An important first step in intervention design is to gain a thorough understanding of existing behaviour (8, 227). Thus, our aim in this study was to explore how and why GPs make the decisions they do when prescribing for multimorbid patients, with a view to informing the development of interventions to assist prescribing in multimorbidity care.

6.2. Methods

Design

We conducted a qualitative study using a grounded theory approach. We performed in-depth interviews with GPs using chart stimulated recall (CSR), a clinical assessment tool that uses a medical chart to stimulate a physician's recall of a case and its management (228, 229).

Setting

We conducted this study in the Republic of Ireland, where GPs play a gate keeping role in the healthcare system. Most GPs in Ireland are private practitioners, but the majority also provide public health services to people with the means tested medical card which allows free GP care at the point of access (15).

Sampling

A purposive sample of GPs was selected from attendees at two regional continuing professional development meetings and supplemented by snowball sampling where necessary to gain representation of GPs by: length of time qualified (over/under ten years); practice location (rural/urban); and practice size (single/group practice).

Data collection

Interviews took place in participants' clinics between February and November 2013. Prior to the interview, we requested GPs to choose patients from their practice that had three or more chronic diseases, and were prescribed five or more long-term medications for the purpose of CSR. We asked GPs to choose, where feasible, patients seen on the day of or the day preceding the interview, to maximise their recollection of

the case details. During the interview, the GP was asked to give a summary of each patient case including demographics, diagnoses and prescribed medications, and then describe the patient's recent consultations using the medical notes as an aide memoire. The interview followed the participant's description of a chosen patient's sequential consultations as far as possible. A topic guide, which was derived from the key findings of a systematic review of the literature (i.e. Chapter 5) (226), was referred to during interviews. The topic guide included prompts on the use of clinical guidelines, goals of care and shared decision-making, and was modified after each interview to pursue emergent themes (the evolution of the topic guides is shown in Supplementary material 8). All interviews were conducted by CS, audio-recorded and transcribed in full.

Analysis

Coding was data driven according to the grounded theory approach described by Charmaz (166). The first stage involved open coding of GPs' actions in multimorbidity, and the causes, conditions and consequences of these actions. The second stage of coding involved categorization of the coded data based on conceptual similarity. Divergent cases were actively sought. This approach to coding was agreed a priori by team consensus. The first three transcripts were read, coded and compared by CS and MB, focusing on interviewing technique and the development of preliminary codes. The next three interviews were coded and compared by CS and CB. CS coded all remaining interviews as they took place, adhering to the principles of constant comparison. Once data collection was complete, the other members of the team (CB, SMH, MB) independently coded an additional three randomly assigned interviews. Field notes, memos, coding and theoretical development were discussed at regular

team meetings. NVivo 10 was used for data management (230). Demographic and chronic disease information of the cases discussed were analysed descriptively using Microsoft Excel. The consolidated criteria for reporting qualitative research (COREQ) statement was used to inform the reporting of our findings (provided in Supplementary material 9). Ethical approval was granted by the Clinical Research Ethics Committee of the Cork University Teaching Hospitals (reference ECM 4(t) 12/6/12) and from the Research Ethics Committee of the Irish College of General Practitioners.

6.3. Results

Twenty GPs were interviewed. Characteristics of participating GPs are shown in Table 3. A total of fifty one patients with multimorbidity were discussed during the twenty interviews. The median patient age was 75 years (range 39-92) and 55% were female. Patients had an average of 8.3 chronic conditions and were prescribed an average of 10.6 regular medications (detail on the each patient's list of conditions is provided in Supplementary material 10). Interviews lasted on average 42 minutes (range 32 to 65 minutes). Conceptual data saturation occurred at interview 18, as subsequent interviews did not contribute to the development of new themes.

We have selected participant quotations representative of typical responses to illustrate our qualitative findings, supplemented with relevant case details where applicable.

Table 3. Characteristics of GP participants in qualitative interview study (total number of participants=20)

	% of participants (n)
Practice Location	
-Rural	45% (9)
-Urban	35% (7)
-Mixed	20% (4)
Type of practice	
-Single handed	30% (6)
-Group practice	70% (14)
Length qualified	
<10years in practice	30% (6)
>10years in practice	70% (14)

Factors influencing decisions in multimorbidity

Figure 6 shows the diverse range of medical and psychosocial influences on GPs' decisions in multimorbidity. GPs considered and integrated the factors deemed relevant to a particular case in order to make an appropriate decision for that patient. Multiple chronic conditions did not always lead to difficult decisions, even when multiple medications and complex combinations were present.

> "*I have a lot of patients with hypertension, lipid disorder and thyroid disease but I wouldn't classify those as multimorbid. They are most of the time fairly straight forward. It is only when you add something else into the mix that it gets complicated*" (gp15)

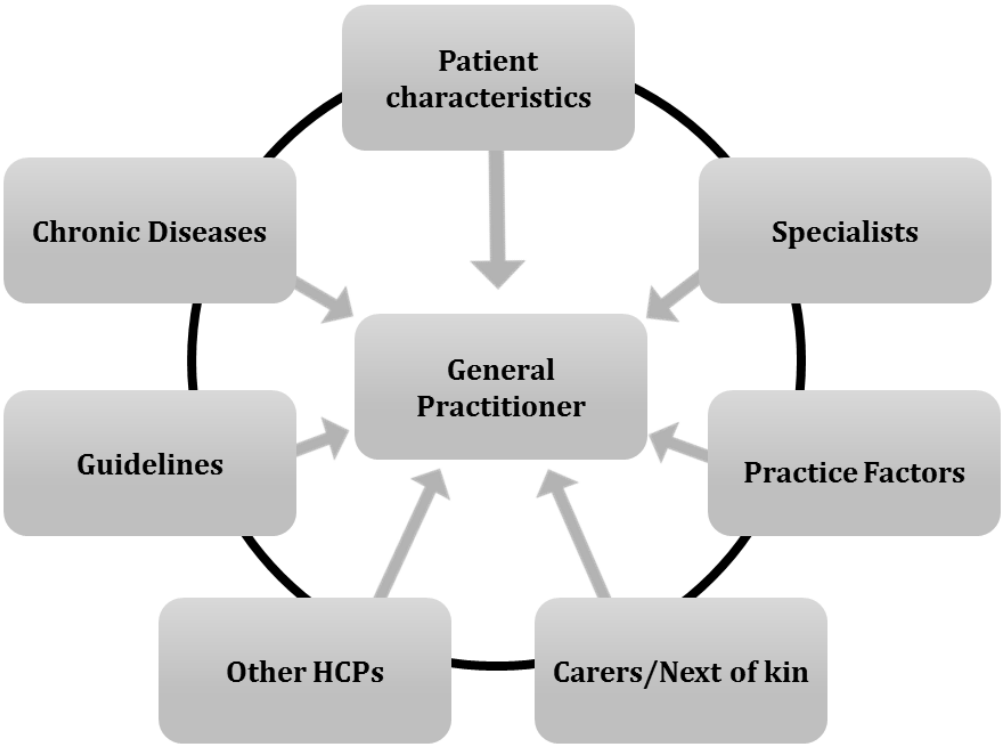

Figure 6. Influences on GPs' decision-making in multimorbidity.

Satisficing: An approach to decision-making in multimorbidity

Conflicts arose in cases due to potential interactions between diseases and medications; discrepancies between the patient's preferences and best practice recommendations; or lack of an evidence base relevant to multimorbidity. In response to these conflicts, GPs tried to find a balance between optimal disease management and patient-centred care using a process of satisficing: settling for chronic disease management that was satisfactory and sufficient, given the particular circumstances of that patient. Figure 7 shows the different manifestations of satisficing that were observed; the approach taken by GPs depended on the patient's disease trajectory or level of stability.

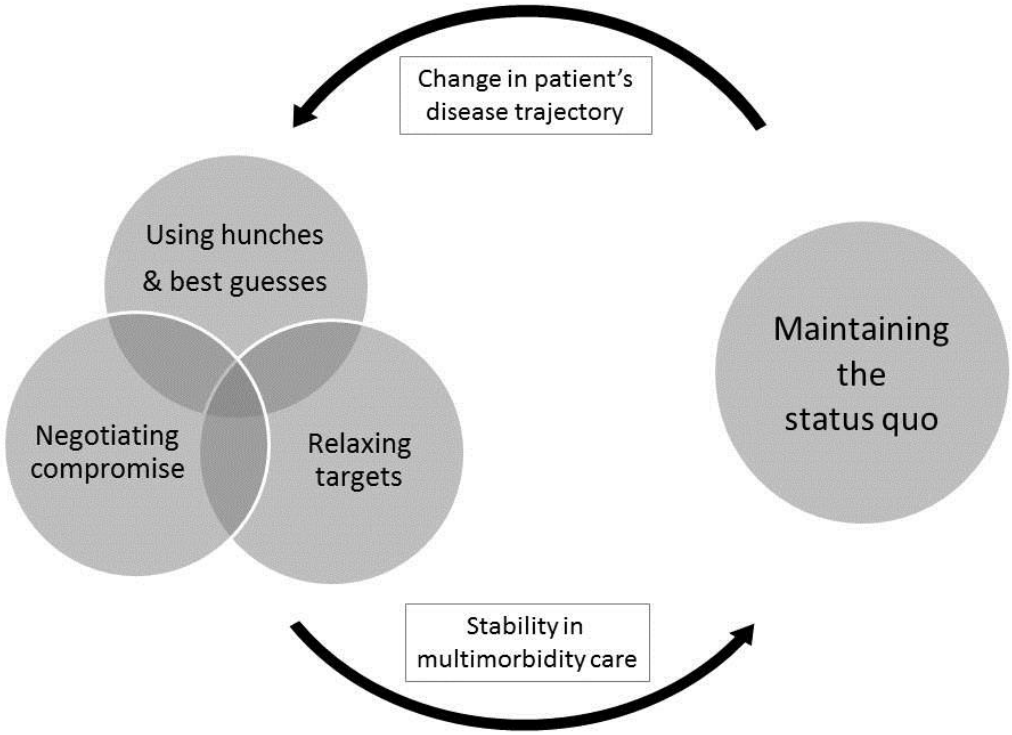

Figure 7. GPs' approaches to decision-making in patients with complicated multimorbidity

Relaxing targets

Satisficing meant that GPs accepted less stringent levels of disease control than was advised by guidelines. This was seen in cases where the management of one disease was prioritized over others because of severity or symptoms.

> "*I'm not aiming for very tight control - I'm happy if his sugars are running a little higher than normal. I mean he has got cardiac failure as well, his life expectancy isn't brilliant - so long term I think, I don't think it's his type 2 diabetes that's going to kill him*" (gp7 discussing a 77 year old man with nine chronic diseases prescribed sixteen regular medications)

Suboptimal targets were also accepted in patients with poor adherence in whom GPs felt that, due to the impact of multiple medications, disease "*control is as good as he (patient) will allow it to be, he's not madly compliant*" (gp17).

When patients developed side effects from guideline recommended medications, GPs considered other factors before deciding whether to relax disease targets or continue the drug:

> "*if we increase her drugs for her cardiac failure and she is getting more dizzy, then we will always go back to the last stage before she had symptoms."* (gp20 discussing her decision to prioritize patient comfort in a 71 year old woman with cardiac failure, orthostatic hypotension, seven other chronic diseases and nine regular medications)
>
> "*I think, I suppose, at the end of it his cardiac and renal function are what are going to kill him, not getting up at night to pee*"(gp17 discussing his decision to prioritize disease control in a 64 year old man with ten chronic diseases and thirteen regular medications, whose urinary symptoms are exacerbated by diuretics)

Negotiating compromise

Conflicts sometimes arose between what the GP thought best for a patient and the patient's requests or a specialist's recommendations. Here, GPs negotiated to find a satisfactory compromise, using techniques such as concessions over drug dose or duration, gradual weaning of medications, or substitution with lower risk alternatives.

> "*Well it wouldn't be 'my way or the highway'; you need to negotiate it, because as you know people have all sorts of kind of fixed ideas about things really and it can be difficult to dislodge them."* (gp14 on an 81 year old man with a recent myocardial infarction and hypertension who requested anti-inflammatories for increasing joint pain.)

Hunches and best guesses

When presented with a range of options, none of which were clearly right or wrong, many GPs used a "*hunch"* or made a "*best guess"* as to which option to take. This occurred in situations where the reason for a patient's symptoms was unclear, potentially attributable to many of the patient's existing diagnoses.

> "*he has lots of reasons to be short of breath -so his pulmonary emboli can do it; his anaemia can do it, his lobectomy can do it, his CCF could do it and his COPD could do it; so ah, it's basically a case of trying to figure out and sort them out. I know him quite well, and what his baseline is, so it's a case of trying to figure out what is the major cause each time he comes in... we generally try and make a best guess at it*" (gp7 discussing 77 year old man with nine chronic diseases on sixteen regular medications)

Best guesses were also required because "*you don't have guidelines for every situation-there are times when you just have to make a decision as best you can*" (gp6). GPs relied heavily on their prior knowledge and experience of the patient in this process.

Maintaining the status quo

Once a multimorbid patient appeared to be stable, GPs' default approach was to "*maintain the status quo*" (gp1) rather than interfere with drug regimens, unless they saw clear evidence of adverse drug effects.

> "*really didn't entertain changing them because why stir things up*?"(gp19)
>
> "*look she's on it, she's fine, it doesn't bother her, its suiting her fine*" (gp12)
>
> "*like he is very stable on them all but it does seem like an awful lot*." (gp2)
>
> "*she's doing better than she has in a long time-I'm not going to rock the boat at all*" (gp11)

Although concerned about polypharmacy, GPs had a greater fear of medico-legal repercussions or negative responses from the patient or their next of kin if rationalizing medications led to adverse clinical events:

> "*I think litigation is a huge issue: as I say the wife is on the ball; okay I say 'look let's get rid of his aspirin and his statin - he has no ischemic heart disease'. And then say, he gets a myocardial infarction in four months' time and you say 'should I have left him on the statin?'*"(gp6 discussing an 84 year old man with hypertension, hyperlipidaemia, osteoarthritis, recent deep venous thrombosis, prostate cancer, osteoporosis and constipation on thirteen medications)

GPs were reassured that the on-going use of some medications was "*justified*" (gp7) because they were commenced by a specialist or due to best practice guidelines, in many cases years before:

"*There is very little we can get away with in terms of manoeuvring with her. She has a lot of pathology and she probably needs virtually everything she is on there*."(gp9 discussing an 86 year old lady with anxiety, osteoporosis, stage 3 kidney disease, hypothyroidism, coronary artery disease, atrial fibrillation, cardiac failure, osteoarthritis, stress urinary incontinence, COPD, diverticular disease, aortic stenosis and constipation on fourteen medications)

Resources to assist decision-making in multimorbidity

Figure 8 shows the key facilitators to resolving conflicts in prescribing decisions: "broadening the loop" of communication to involve others in the decision-making process and the availability of time. Deficiencies in these processes were common which left GPs less comfortable with their decisions.

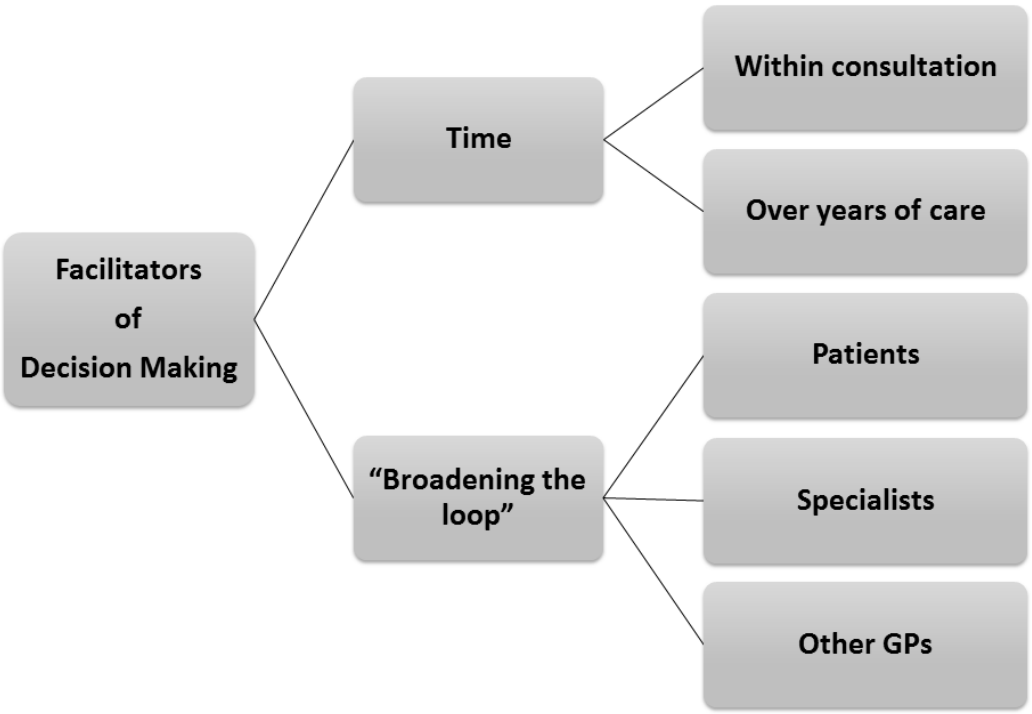

Figure 8. Facilitators of decision-making in multimorbidity

Broadening the loop to patients

GPs believed that many multimorbid patients preferred not to be involved in decisions, where "*the more complex their needs, the more they rely on you to be the final arbitrator or the over-seer*" (gp19). Some GPs felt that patients would be unable to understand the various conflicts and uncertainties faced, and so would "*just worry about it myself … rather than imparting a huge amount of knowledge*" (gp16). This contrasted with cases where the GP shared the uncertainty and responsibility for a decision with the patient, evident in situations involving younger GPs or those with a shorter professional relationship with the patient.

> "*you have to go 'this is your life, your decision' and then give them my advice but they have to make the decision for themselves*"(gp3 discussing primary prevention in a 54 year old man with six chronic diseases on six regular medications)

GPs had specific difficulties talking to multimorbid patients about stopping medications; they feared this could be interpreted by the patient as a withdrawal of care and potentially damage the doctor-patient relationship.

> "*what you are saying by stopping it [a statin] is 'I'm stopping this now because really now you are so old so if you get a heart attack at this stage… whatever*."(gp5 discussing the message he feared he would give by stopping a statin in an 84 year old lady with seven chronic diseases on eighteen medications)

Broadening the loop to other healthcare professionals

GPs liked to "*share the onus of responsibility*" (gp16) with specialists and pharmacists in complicated multimorbid patients "*rather than flying solo on it*" (gp14). However, the

usefulness of specialist input was limited by a lack of timely access to and communication from specialists, or by their single disease rather than generalist approach to the patient:

> "*in fairness to them, all their letters were bang on ... for COPD: do the sputum, give him the azithromycin, he has the home oxygen- tell him to use that. Everything was according to guidelines. Renal the same, trial this - if this doesn't work this is what we're doing - push this as far as we can, nephro-protection and all this, and it's all bang on target. The same for cardiology. But when you put it in the clinical setting it isn't working…*" (gp2 discussing a 51 year old man with eight chronic diseases on thirteen medications)

Broadening the loop to fellow GPs

When faced with difficult decisions, many GPs elected to "*have a practice discussion about it I think, it won't take very long*" (gp18). They found that "*to bounce [ideas] off your colleagues just helps, even if it is just something like 'what in the name of God am I going to do about this', it's really important*" (gp8). Single handed GPs struggled in this regard, although some used continuing medical education, especially small group meetings, as a forum for discussing complicated cases with other GPs.

Time over multiple consultations

Return consultations were an opportunity to re-evaluate the patient, thereby reassuring the GP and patient, giving clarity on the best approach to take, and facilitating the management of multiple competing demands:

> "*We checked her blood pressure; upped her medications; had a chat about her knees; I encouraged her to go back to the weight watchers. I'm going to follow*

her up in a month's time; she hasn't had her bloods done for a bit, so she'll have that done before she gets back. I chatted to her about the antidepressant - she was keen on cutting it down but I've known her for years and winter is her bad time… so, I said 'Look Mary how about waiting until the spring again we can have a chat about it then and just see?' and maybe if she loses a bit of weight, she might find that she is feeling a little bit better in herself and it might be a more appropriate time to do it" (gp11 discussing a 52 year old woman with depression, anxiety, hypertension, ANA positive arthritis, prior cauda equine syndrome, osteoarthritis, obesity and acne on six medications)

A lack of relational continuity of care adversely affected management, especially in some of the larger practices where "*you have different people making a clinical judgement on him based on how he is from week to week which is difficult*" (gp2).

Time within the consultation

GPs reported that rationalising medications "*is time consuming, you definitely want to have your wits about you, and without it (extra time) the potential for making mistakes is very much increased*" (gp14). Thus, lack of time pushed GPs towards "*maintaining the status quo*" rather than active attempts to change management, especially if considering changing "*something that you have been giving them for the last fifteen years -and now you're suddenly saying the evidence is saying that we shouldn't be giving you aspirin anymore - it takes time, time to explain that to them*" (gp6).

6.4. Discussion

This qualitative study demonstrates the range of influences on GPs' prescribing decisions in multimorbid patients. When conflicts arise between these factors, GPs take an approach of satisficing – providing care they feel is satisfactory and sufficient for a particular patient. With changing chronic disease trajectories, satisficing means accepting trade-offs between drugs, diseases and best practice recommendations. In stable multimorbidity and in the absence of nuanced communication techniques, GPs act to preserve the doctor-patient relationship ahead of medication rationalization.

Strengths and limitations

The credibility of our findings was enhanced by using chart stimulated recall (CSR), which has been shown to be a valid way of assessing clinical decision-making through improving recall of actual rather than perceived behaviour. CSR also facilitated probing of why certain decisions were made which was necessary for our purpose of identifying targets for a professional intervention (228, 229, 231). By combining CSR and grounded theory, substantive issues for GPs emerged from our data which are additive to existing qualitative research with GPs on multimorbidity, much of which is based on case vignettes or focus groups (202, 208, 209, 211). Although we recruited a sample that was representative of the national GP profile, those who participated may have had a greater interest in, or a particular agenda relating to the study question (232). The sample size was likely sufficient given data saturation was achieved (233). Clinician researchers have been shown to get richer data from GP participants than non-clinical researchers, but can introduce clinical biases into data collection and interpretation (234). In this study, the risk of professional bias was addressed by including researchers with diverse professional backgrounds on the research team (235).

Main findings and comparisons with other studies

Satisficing, a portmanteau of the words satisfy and suffice, was initially described by Simon in 1956 as human decision-making that is limited by "uncertainty about the consequences that would follow from each alternative, incomplete information about the set of alternatives and complexity that prevents necessary computations from being carried out" (236). Satisficing involves evaluation of the options available only until an acceptable one is found. It was evident in this study in situations where GPs were unable to evaluate the risk-benefit of all potential options for a multimorbid patient, because of deficiencies in the evidence base and a lack of time available for making decisions.

In a focus group study, Smith et al. described GPs' and pharmacists' views that polypharmacy in multimorbid patients resulted from the appropriate prescribing of risk-reducing medications indicated by single-disease guidelines (202). The current study moves beyond this concept to describe the strategies used by GPs to manage multiple medications where conflicting guidance exists.

Some of the approaches to satisficing, such as relaxing targets for disease control, may have arisen due to the relative clinical independence of GPs in the Irish healthcare system. This contrasts with the findings of Bower et al. who found greater tensions between disease-focused and patient-centred care in English general practice, where GPs strive to meet the demands of the Quality Outcomes Framework (208).

Processes similar to satisficing are also evident in large quantitative studies in multimorbidity. For example, studies from the US show that patients with discordant multimorbidity are less likely to have guideline-consistent hyperlipidaemia management (85, 237). In Switzerland, trends for preventative care are lower in

multimorbid patients with dementia (238). However, there is increasing recognition that improving adherence to guidelines may not be the best management strategy for patients with multiple medical problems (225, 239).

Implications for research and practice

Although prescribing in multimorbidity is challenging, the potential negative outcomes associated with both polypharmacy and suboptimal disease management must be remembered (116). Approaches to support GPs' prescribing in multimorbidity are required to mitigate these negative effects. In hospital specialities, there is an increasing trend towards multidisciplinary team (MDT) meetings, which operationalize collaborative decision-making to deliver evidence-based yet patient-centred care. The potential for multidisciplinary review in primary care has also been evaluated in trials such as PINCER, a pharmacist-led information technology intervention that reduced medication errors in general practice (152). However, the qualitative findings from PINCER showed that some 'prescribing errors' were over-ruled by GPs on the basis of their superior knowledge of the patient and there were concerns about the long-term feasibility of pharmacists working in a general practice (153). Participants in our study undertook informal case reviews of complicated multimorbid patients with their fellow GPs. Even without the rigorous processes of the MDT, participants benefitted from the close proximity, ready availability and generalist perspective of their colleagues. Collaborative decision-making between GPs deserves further exploration as a potential intervention strategy in this field (240).

Regarding shared decision-making, previous research has shown that although patients like to hear about the management options available to them, many still seek and accept their GP's advice on the best option to take (241). This implies that GPs must

have the knowledge and confidence to offer patients specific recommendations (242, 243). Although attempts are underway to improve the attentiveness of guidelines to multimorbidity, they will not be able to cover all eventualities in multimorbidity and some professional judgement will always be required (121, 142). Relational continuity of care was an essential feature of how such judgements were made in this study, and should be prioritized in interventions that aim to promote shared decision-making with multimorbid patients.

Lastly, in consultations with patients with multimorbidity, there are often multiple competing demands on a GP's time, which can distract the GP from proactive management of medications. A number of trials are already addressing the issue of time as part of a multifaceted intervention in multimorbidity and the results of these studies are keenly awaited (244, 245).

6.5. Conclusions

The Cochrane review group suggested that future multimorbidity interventions should be embedded with inter-professional collaboration and integrated into existing healthcare systems (145). Our results suggest that interventions to support prescribing in multimorbidity should also prioritize relational continuity of care, facilitate communication with patients on available and preferred options, and provide GPs with a means of collaborative decision-making and treatment planning. These findings will help inform the development of interventions that aim to improve medication management and patient-centred care in multimorbidity.

CHAPTER 8. PSYCHOSOCIAL COMPLEXITY IN MULTIMORBIDITY: THE LEGACY OF ADVERSE CHILDHOOD EXPERIENCES

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8.1. Abstract

Background

To effectively meet the healthcare needs of multimorbid patients, the most important psychosocial factors associated with multimorbidity must be discerned. Our aim was to examine the association between self-reported adverse childhood experiences (ACE) and multimorbidity, and the contribution of other social, behavioural and psychological factors to this relationship.

Methods

We analysed cross-sectional data from the Mitchelstown study, a population based cohort recruited from a large primary care centre. ACE was measured by self-report using the Centre for Disease Control ACE questionnaire. Multimorbidity status was categorized as no, one or two or more chronic conditions, which were ascertained by self-report of doctor diagnosis. Ordinal logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for multimorbidity, using ACE as the independent variable with adjustment for social (education, public health cover through the GMS scheme), behavioural (smoking, exercise, diet, body mass index), and psychological factors (anxiety/depression scores).

Results

Of 2047 participants, 45.3% (n=927, 95% CI 43.1-47.4%) reported multimorbidity. ACE was reported by 28.4% (n=248, 95% CI 25.3-31.3%) of multimorbid participants, 21% (n=113, 95% CI 18.0-25.1%) of participants with a single chronic condition, and 16% (n=83, 95% CI 13.2-19.7%) of those with no chronic conditions. The OR for multimorbidity with any history of ACE was 1.6 (95% CI 1.4-2.0, $p<0.001$). Adjusting for

social, behavioural and psychological factors only marginally ameliorated this association, OR 1.4 (95% CI 1.1-1.7, p=0.002).

Conclusions

Multimorbidity is independently associated with a history of adverse childhood experiences. These findings demonstrate the psychosocial complexity associated with multimorbidity, and should be used to inform healthcare provision in this patient cohort.

8.2. Introduction

Multimorbidity, the co-occurrence of two or more chronic conditions, affects over 50% of patients with chronic disease in primary care (33, 51). However, the management of chronic disease tends to be aligned to individual rather than co-occurring conditions (66). This mismatch in patients' manifestations of disease and healthcare provision leads to problems in the co-ordination of care, excessive treatment burdens and high levels of healthcare utilisation (3, 226). As the prevalence of multimorbidity continues to rise, there are calls for re-configuration of how we deliver chronic disease care, to better meet the needs of our aging multimorbid populations (51, 276, 277).

To date, efforts have focused on increasing the applicability of guidelines to multimorbidity and integrating guidelines to limit duplication and waste (121, 276). However, it is increasingly evident that multimorbidity represents more than just the sum of single diseases. Recently, a large population based study revealed a strong social gradient in multimorbidity, with an average age of onset ten years earlier in areas of deprivation compared to more affluent areas (51). Health behaviours such as smoking (278, 279), physical inactivity (278, 280), and obesity (278, 281), as well as poor educational attainment (279), are also all more common among multimorbid patient cohorts. This new information will help guide the development of patient-centred interventions to improve health outcomes in multimorbidity. Yet, the relationship between multimorbidity and other psychosocial factors, especially those relating to early life and childhood, remains to be discerned (66, 277). For instance, there is strong evidence that adverse childhood experiences (ACE) are associated with the development of individual chronic conditions (e.g. ischaemic heart disease, chronic lung disease etc.), mediated by the adoption of unhealthy behaviours in later life

(Figure 10) (168, 169, 282). However, the association between ACE and multimorbidity has not been examined.

A history of adverse childhood experiences would represent a potentially important psychological burden in multimorbid patients, in addition to being a potential aetiological factor in the development of multiple rather than single chronic conditions. Our aim in this study was to examine the association between ACE and multimorbidity, and to determine the contributing role of other social, behavioural and psychological risk factors in this relationship.

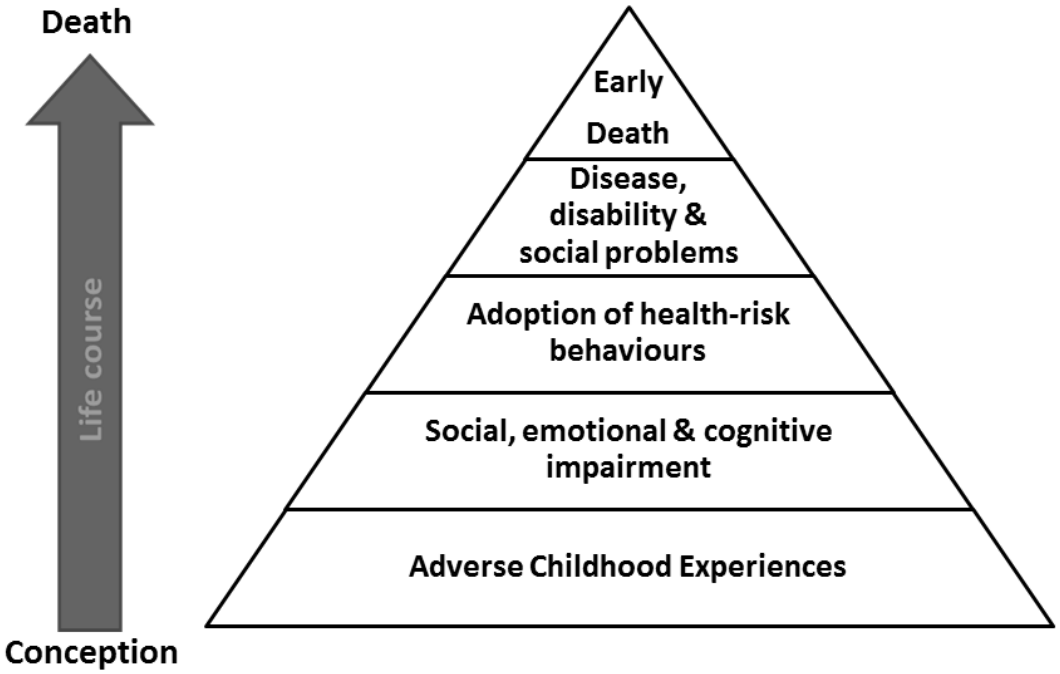

Figure 10. The Center for Disease Control and Prevention Framework for adverse childhood experiences, chronic disease and premature mortality (168)

8.3. Methods

Study design and subjects

We used cross-sectional baseline data from the Mitchelstown Cohort, a study of 50 to 69 year old adults randomly selected from a single large primary care centre in Mitchelstown, Ireland in 2010-11. Participants were invited to complete a detailed health and lifestyle questionnaire, and attend for a physical examination by research nurses using standardised measurements and validated instruments. The study methods have been reported in detail previously (283), but an overview is provided here. Ethical approval for the original study was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals.

Predictor: Adverse childhood experiences

Adverse childhood experiences were measured using the ACE questionnaire, a validated instrument used to assess associations between ACE and health and well-being in later life (282, 284). This ten-item questionnaire categorizes ACE into three groups which relate to: abuse (emotional, physical or sexual), neglect (emotional or physical), and household dysfunction (domestic abuse, parents divorced, parents in prison, parental addiction or parental mental illness). Responses were dichotomized into any history of ACE (yes/no), and were also categorized by type of ACE (abuse, neglect, household dysfunction). During data collection, participants were offered separate sealed envelopes in which to submit their responses to the ACE questionnaire.

Outcome: Multimorbidity status

The presence of a chronic condition was determined by the question “Has a doctor ever told you that you have xx?” referring to twenty common chronic conditions (which

are listed in Figure 11). Multimorbidity status was determined by categorizing responses into three ordered groups: no chronic condition, one chronic condition or multimorbidity (two or more chronic conditions) (28). Participants who answered no, don't know or did not answer a chronic condition question were categorized as not having the condition in question.

Covariates

Education: Educational attainment was ascertained by the question "What is the highest level of education you have completed?" and responses were dichotomized into primary level or secondary level and above.

Social class: Social class was defined using the European socio-economic occupation-based classification scheme, validated for use in the Irish population (285). Participants were asked "What job have you done for the longest period of time?" The ten class model was collapsed to four classes: salariat, intermediate, working class and never worked/long-term unemployed.

General Medical Services (GMS) cover: Participants were asked whether they had public health cover through the GMS scheme, which entitles those covered to free medical care at the point of access. Responses were categorized as GMS patient (yes/no). Eligibility for the GMS scheme is based on low income thresholds.

Dietary habits: A standardised food frequency questionnaire, validated for use in the Irish population (286), was used to assess dietary habits. For this analysis, fruit and vegetable intake was collapsed to a binary variable, with participants consuming five or

more servings daily categorized as having a healthy diet, and those consuming less than five servings daily as having an unhealthy diet.

Physical Activity: Physical activity was measured as metabolic equivalents (METs) minutes per week using the short form International Physical Activity Questionnaire (287), and was dichotomized into two groups (low or moderate-high) based on MET minutes per week in all activity types.

Smoking: Smoking status was dichotomized as never smoked or current/former smoker in response to the questions “have you smoked at least 100 cigarettes in your entire life?” and “are you a current smoker?”

Alcohol: Alcohol consumption was derived from the question “During the past seven days how many standard drinks of any alcoholic beverage did you have each day?” and was categorized as within or above the gender specific recommended weekly allowance (≤21units for men and ≤14units for women) (288).

Body mass index: Height and weight were measured using standardised methods by study personnel and used to calculate body mass index (BMI, kg/m2).

Psychological health: Psychological health was measured by the Centre for Epidemiologic Studies Depression Scale (CES-D) (289) and Hospital Anxiety and Depression Scale (HADS) (290) anxiety questions. These instruments measure point-in-time psychological health, in contrast to the prior doctor–diagnosis of depression and anxiety used in the outcome variable. In the CES-D, answers are scored from one to

four over twenty questions. Depression is considered likely in scores of sixteen and above. In the HADS-A, answers are scored zero to three over seven questions. Anxiety is considered likely in scores of eight or above.

Statistical Analysis

Stata statistical software IC 12.0 was used for all analyses. Descriptive analysis was stratified by multimorbidity status. Categorical variables were expressed as frequencies (percentage) and continuous variables as means with standard deviations (SD) or medians with interquartile range (IQR). Differences between groups were tested using chi square, ANOVA or Kruskal Wallis tests as appropriate. We used the Center for Disease Control and Prevention framework of ACE and subsequent chronic disease, shown in Figure 10 (168), to inform multivariable modelling. We included covariates to the regression model by forward stepwise selection, including only variables that had a $p<0.05$ level of significance with multimorbidity on univariate analysis. Ordinal logistic regression was used to calculate the odds of a higher ordinal category (multimorbidity) versus the middle and lower categories (one or no chronic conditions). The proportional odds assumption for multimorbidity status as an ordinal variable was satisfied using the Stata omodel and Brant tests. We calculated the adjusted odds ratios (OR) and 95% confidence intervals (95% CI) for multimorbidity by inclusion of ACE, age, gender, GMS status, educational attainment, dietary habits, smoking status, physical activity, BMI, depression score and anxiety score in the models. Statistical interactions were sought between ACE and age, gender, and GMS cover.

Subgroup analysis

Subtypes of ACE

Multivariable ordinal logistic regression was used to examine the relationship between each of the subtypes of ACE (abuse, neglect, household dysfunction) and multimorbidity.

Subtypes of multimorbidity

Within the group with multimorbidity, we categorized participants according to whether they had a psychiatric condition as a component of their multimorbidity or not. The mean number of physical conditions for those with and without a psychiatric condition as a component of their multimorbidity was calculated. Multivariable logistic regression was used to determine odds ratios for the associations between ACE/ACE subtypes and a multimorbid patient having a psychiatric condition.

Sensitivity analysis

We first repeated the analysis after excluding doctor-diagnosed anxiety or depression from the outcome variable, to assess whether the observed association was attributable to psychiatric sequelae of ACE. Secondly, we used logistic regression to examine the association between ACE and multimorbidity defined with increasing numbers of conditions (three or more, four or more etc.).

Missing data

In multivariable analysis, missing data in predictor and included co-variates were replaced using Stata chained multiple imputation functions. Complete case sensitivity

analysis was performed. The STROBE statement was used to inform the study report (provided in Supplementary material 15).

8.4. Results

Baseline characteristics

Of 3051 people invited to participate in the Mitchelstown Cohort study, 2047 completed the baseline assessment (response rate 67%) and were included in the current analysis. The mean age at baseline was 55.8 years and 51% (n= 1,039) were female. Overall, 45.3% (n= 927, 95% CI 43.1-47.4) of participants reported multimorbidity and 23.4 % (n= 444, 95% CI 21.5-25.3) reported any ACE.

ACE was reported by significantly more multimorbid participants at 28.4% (n= 248, 95% CI 25.3- 31.3%) than participants with a single chronic condition, 21% (n=113, 95% CI 18.0-25.1%) or participants without any chronic condition, 16% (n=83, 95% CI 13.2-19.7%) ($p<0.001$), as shown in Table 7.

Table 7. Baseline characteristics of participants in the Mitchelstown Cohort Study stratified by multimorbidity status

	No chronic condition N=564 N (%)	One chronic condition N=556 N (%)	Multimorbidity N=927 N (%)	P value	Missing data N (%)
Age -mean (SD)	55.6 (14.7)	55.4 (15.7)	56.2 (16.5)	0.55	0
Gender					
Female	242 (42.9)	273 (49.1)	524 (56.5)	<0.001	0
Male	322 (57.1)	283 (50.9)	403 (43.5)		
Early life factors					
Any history of ACE	83 (16.5)	113 (21.6)	248 (28.4)	<0.001	146 (7.1)
Education Attainment					
Primary	128 (24.8)	118 (22.7)	291 (33.5)	<0.001	139 (6.8)
Secondary or above	389 (75.2)	403 (77.3)	579 (66.5)		
Later life social factors					
Occupational class					
Salariat	71 (15.9)	80 (17.1)	110 (13.6)	0.11	324 (15.8)
Intermediate	127 (28.4)	125 (26.7)	187 (23.1)		
Working class	193(43.2)	199 (42.5)	387 (47.9)		
Long-term unemployed	56 (12.5)	64 (13.7)	124 (15.4)		
GMS status					
GMS cover	134 (29.6)	156 (31.5)	445 (53.2)	<0.001	262 (12.8)
Later life behavioural factors					
Alcohol					
Within RWA	317 (90.6)	340 (91.2)	546 (90.7)	0.95	722 (35.3)
Dietary habits					
Unhealthy diet	226 (42.0)	212 (39.0)	316 (34.8)	0.02	58 (2.8)
Physical Activity					
Low	218 (42.9)	253 (48.1)	461 (52.2)	0.004	129 (6.3)
Moderate/high	290 (57.1)	273 (51.9)	423 (47.8)		
Smoking					
Never	271 (51.9)	299 (55.7)	432 (47.7)	<0.012	82 (4.0)
Current /former	251 (48.1)	238 (44.3)	474 (52.3)		
BMI					
BMI- median (IQR)	27.4 (25.0, 29.9)	28.0 (25.0, 30.7)	28.7 (25.8, 31.9)	<0.001	7 (0.3)
Later life mental health					
CES-D, median (IQR)	6 (3, 11)	7 (3, 12)	10 (5, 15)	<0.001	173 (8.5)
HADS-A, median (IQR)	3 (1, 5)	3 (2, 5)	4 (2, 7)	<0.001	210 (10.3)

Participants with multimorbidity were more likely to be female, to have GMS cover, and to have only attained primary level education. Multimorbid patients also had higher BMIs, lower levels of physical activity, and were more likely to be current/former smokers. Depression and anxiety scores were significantly higher in multimorbid patients. Figure 11 shows the prevalence of each individual chronic condition in participants with or without ACE (numerical data for this figure is provided in Supplementary material 16).

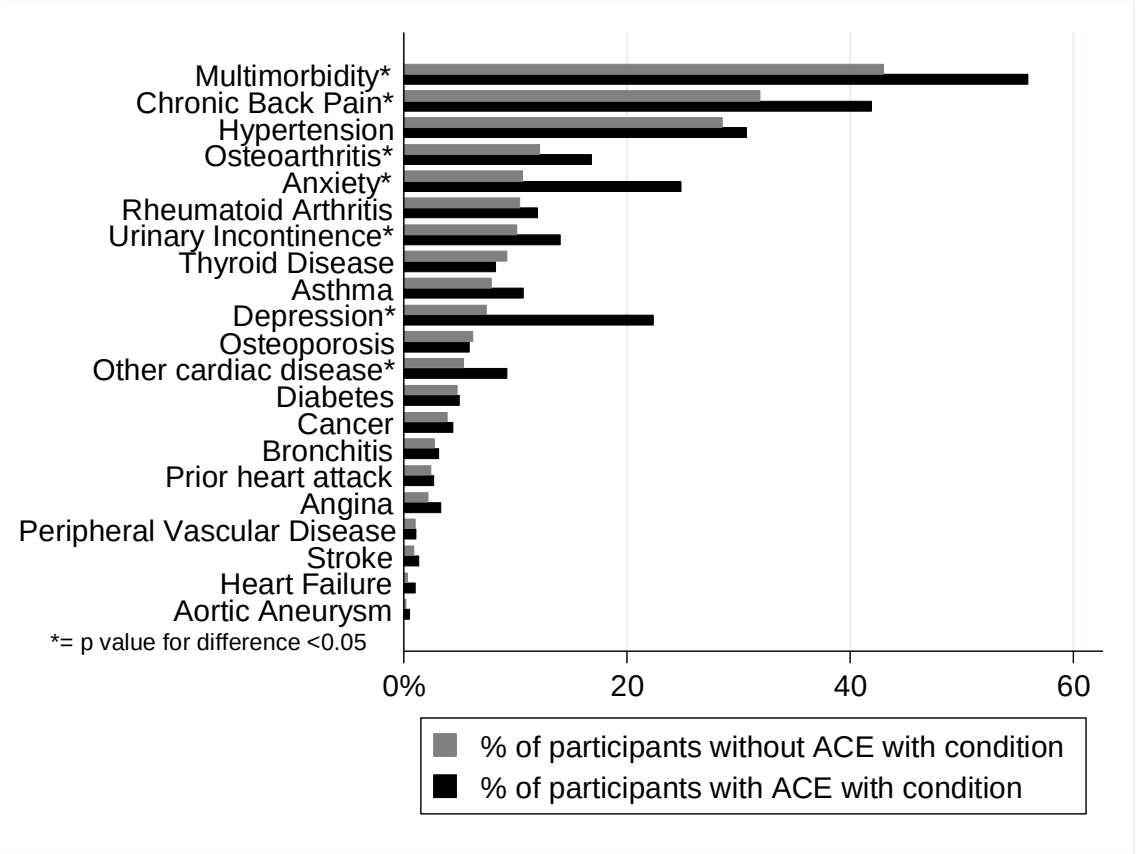

Figure 11. Prevalence of chronic conditions and multimorbidity in participants in the Mitchelstown cohort study, stratified by history of adverse childhood experiences

Ordinal logistic regression analysis

In the unadjusted model, participants who reported a history of ACE had an odds ratio for multimorbidity of 1.6 (95% CI 1.4-2.0), shown in Table 8. After including age, gender, and the social and behavioural co-variates that were significantly associated with multimorbidity in univariate analysis, the relationship between ACE and multimorbidity remained of similar magnitude, OR 1.6 (95% CI 1.3-1.9). However, including current psychological status in the model partially attenuated the relationship, OR 1.4 (95% CI 1.1 – 1.7). Other covariates significantly related to multimorbidity in the fully adjusted model included female gender, OR 1.4 (95% CI 1.2-1.7) and GMS cover, OR 1.7 (95% CI 1.3-2.1). Educational attainment was inversely associated with multimorbidity, OR 0.8 (95% CI 0.6-0.9). BMI, depression and anxiety scores were marginally but significantly associated with multimorbidity. No significant statistical interactions between ACE and age, gender or GMS cover were observed.

Subgroup analysis

Subtypes of ACE

The subtypes of ACE (abuse, neglect, household dysfunction) were examined for their independent association with multimorbidity: ACE relating to abuse and household dysfunction were significantly associated with multimorbidity in the fully adjusted model but ACE relating to neglect was not (shown in table 25 in Supplementary material 17).

Subtypes of multimorbidity

In the subgroup of patients with multimorbidity (n=927), 66% (n=615, 95% CI 63.2 – 69.4%) reported only physical multimorbidity while 34% (n=312, 95% CI 30.6 – 36.7%)

had a psychiatric condition as a component of their multimorbidity. Those with a psychiatric condition had a mean of 2.1 (SD 1.5) physical conditions, compared to 2.7 (SD 1.0) in those with only physical conditions ($p<0.001$). ACE was associated with higher odds of a multimorbid patient having a psychiatric condition, adjusted OR 1.5 (95% CI 1.1-2.1). Each subtype of ACE was independently associated with a multimorbid patient having a psychiatric condition (shown in figure 15 in Supplementary material 18).

Sensitivity analysis

Sensitivity analyses showed similar results. When we excluded doctor-diagnosed anxiety or depression from the outcome variable, the adjusted odds ratio between ACE and multimorbidity was 1.3 (95% CI 1.0-1.5, $p=0.019$). ACE was more strongly associated with multimorbidity defined by higher numbers of conditions (Figure 12).

Missing data

In complete case sensitivity analysis (n= 1335), the association between ACE and multimorbidity remained of similar magnitude, OR 1.6 (95% CI 1.2-2.0).

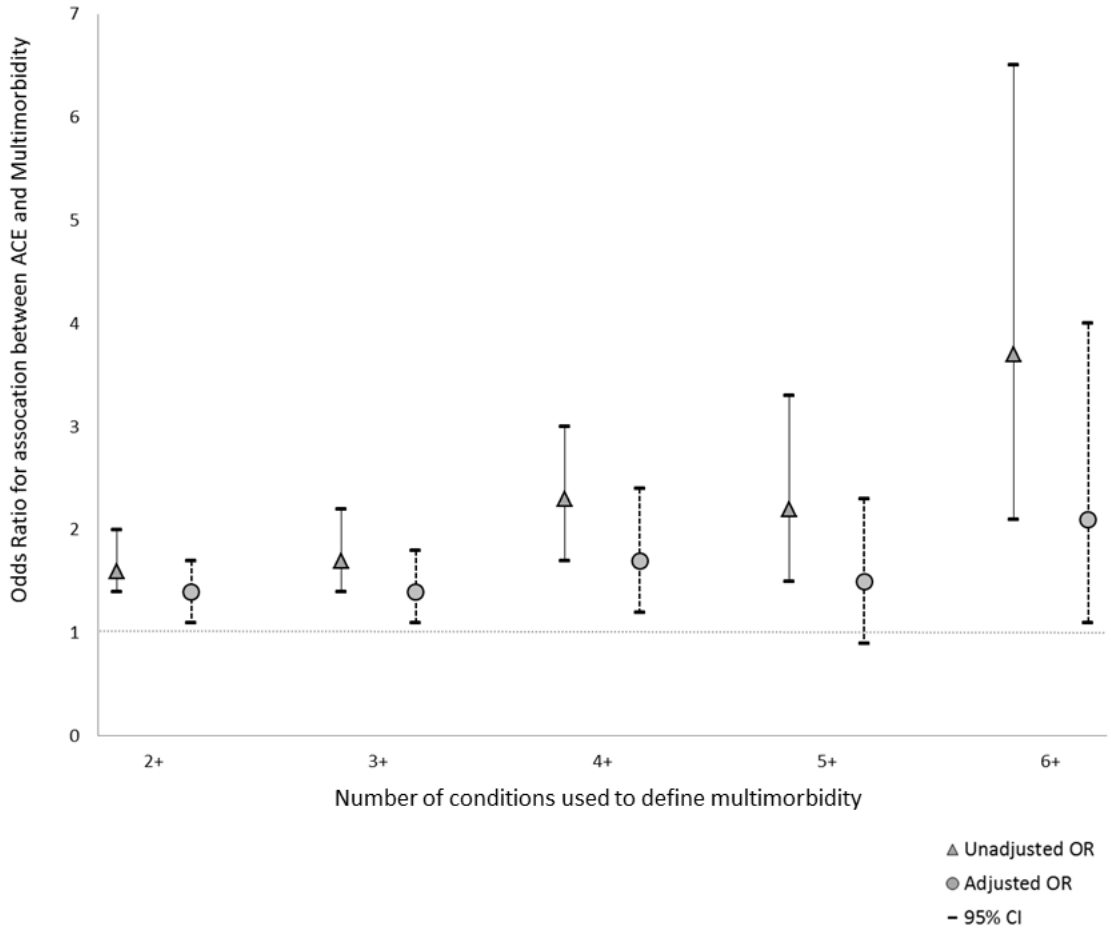

Figure 12. Unadjusted and adjusted* odds ratios and 95% confidence intervals for the association between adverse childhood experiences and multimorbidity, using increasing numbers of conditions to define multimorbidity in baseline data from the Mitchelstown cohort study.

*The adjusted models include age, gender, education, GMS status, behavioural factors (BMI, diet, physical activity, smoking), depression and anxiety scores.

Table 8. Odds ratios and 95% CIs for multimorbidity in multivariable ordinal logistic regression models in participants at baseline in the Mitchelstown cohort study

	Unadjusted OR (95% CI)	Age & Gender OR (95% CI)	+ Early life factors OR (95% CI)	+ Social factors OR (95% CI)	+ Behavioural OR (95% CI)	+ Mental health OR (95% CI)
ACE	1.6 (1.4 – 2.0)**	1.7 (1.4-2.1)**	1.7(1.4 – 2.1)**	1.6 (1.3 – 2.0)**	1.6 (1.3 – 1.9)**	1.4 (1.1 – 1.7)*
Age		1.0 (0.9-1.0)	1.0 (1.0-1.0)	1.0 (1.0– 1.0)	1.0 (1.0– 1.0)	1.0 (1.0– 1.0)
Female gender		1.6 (1.3 – 1.8)**	1.6 (1.4 – 1.9)**	1.5 (1.3-1.8)**	1.6 (1.3-1.9)**	1.4 (1.2 – 1.7)**
Early Life:						
Higher educational attainment			.6 (0.5 - 0.7)**	0.8 (0.7– 0.9)*	0.8 (0.6 – 1.0)*	0.8 (0.6- 0.9)*
Later life social factors:						
GMS cover				1.9 (1.6 – 2.4)**	1.8 (1.5 – 2.2)**	1.7 (1.3 – 2.1)**
Behavioural factors:						
BMI (kg/m2)					1.1 (1.0-1.1)**	1.1 (1.0 – 1.1)**
Healthy diet					1.3 (1.1-1.6)*	1.3 (1.1 – 1.6)*
Mod-high physical activity					.9 (0.7-1.0)	0.9 (0.8 – 1.1)
Current/former smoker					1.2 (0.9 -1.4)	1.1 (0.9 – 1.3)
Mental health:						
CES-Depression score						1.0 (1.0 - 1.1)**
HADS-Anxiety score						1.1 (1.0 - 1.1)*

The reference categories for the multivariable model are: ACE, no ACE as reference; gender, male as reference; GMS cover, no GMS cover as reference; educational attainment, primary level as reference; smoking, never smoked as reference; physical activity, low activity as reference; diet, unhealthy diet as reference. The bold values indicate co-variates that are significantly associated with multimorbidity.
*P < 0.05; **P < 0.001

8.5. Discussion

In this population based study, adverse childhood experiences were reported by approximately one third of multimorbid participants, a significantly higher proportion than in those without multimorbidity. This association persisted even after adjusting for related social, behavioural and psychological factors. While other studies have reported an association between ACE and individual chronic conditions, ours is the first study to show that adverse childhood experiences are a specific concern in multimorbid patients. These findings have implications for both disease prevention activities for survivors of childhood adversity and for the development of patient-centred interventions that aim to improve health outcomes in multimorbidity.

Comparison with existing literature

Almost half of our participants reported multimorbidity. This is slightly lower than previous national estimates which were of the order of 66% (3). The difference may relate to the method of determining multimorbidity status: Glynn et al. (3) extracted data on 147 chronic conditions from patient records, rather than using self-report on twenty conditions. In addition, the age profile of patients in the Mitchelstown cohort was younger than that in the study by Glynn et al. We found similar relationships between female gender, public health (GMS) cover and educational attainment with multimorbidity as other international studies (33, 291).

Overall, the prevalence of ACE in the Mitchelstown study was 23%. In the Irish Longitudinal Study on Ageing (TILDA), the prevalence of self-reported childhood adversity was marginally higher at 34% (292). In contrast to the specific ten-item questionnaire used in the Mitchelstown study, TILDA used a compound measure of adversity in childhood which included five questions relating to physical abuse, sexual

abuse and parental addiction, and a self-rating of being “poor” in childhood. However, the authors found similar associations between childhood adversity and health outcomes, with increases in the risk of individual chronic diseases of the order of 19% to 69% (292).

Notwithstanding the cross-sectional nature of our data, the temporality between ACE and multimorbidity in later life suggests that ACE may play an aetiological role in the development of multimorbidity in some patients. A number of theories exist to explain this relationship. Adverse childhood experiences have been linked with individual chronic conditions via the adoption of hazardous lifestyle behaviours, such as smoking, unhealthy diet or problem alcohol consumption (169). While we found multimorbidity was associated with lower levels of physical activity, higher rates of smoking and higher BMI, the relationship between ACE and multimorbidity was independent of these risk factors. Biological theories purport that early manifestations of childhood adversity, such as failure to thrive or neurodevelopmental stress, may initiate pathophysiological processes that manifest as chronic disease in later life (282). An alternative theory holds that traumatic issues relating to one’s childhood may go unaddressed within conventional medical care. Patients who attend primary care physicians with vague symptoms or somatic manifestations of distress are at risk of higher numbers of screening and diagnostic tests. The consequent diagnostic labelling may compound the patient’s list of morbidities, without getting to the source of their problems (282). The latter explanation is supported by our subgroup analysis which showed that ACE was associated with an incremental risk of having a psychiatric condition as a component of one’s multimorbidity.

Implications for research and practice

The true nature of the relationship between ACE and multimorbidity is likely to be complex and multifactorial, so may be best tackled at multiple levels. From a public health perspective, efforts to reduce childhood abuse and neglect are on-going (282). Interventions that target the coping strategies of survivors of child abuse may yield future benefits in chronic disease prevention (169). For general practice, it is important that the challenge of multimorbidity is not reduced to the simple aggregation of multiple sets of guidelines. Our findings reinforce the need for comprehensive, patient-centred care in multimorbidity, which goes 'beyond protocols' and gives consideration to the psychosocial causes and consequences of multiple chronic diseases (51, 276, 277). Prospective cohort studies of multimorbidity are underway which will also help to inform healthcare delivery to this complex group (293).

Strengths and limitations

The Mitchelstown cohort study is underpinned by validated standardised instruments and objective measures of health and well-being (283). Although the sample is a relatively homogenous 50 to 69 year old Caucasian population taken from a single primary care centre, it is representative of the profile of the source population reported in national census data (283). Nevertheless, care is required when interpreting the results. ACE was measured by retrospective self-report of events that happened approximately thirty years previously. While most questions concerned specific events such as abuse, or parental incarceration, questions on neglect concerned less objective events, such as whether the participant felt unloved. These questions may be subject to greater recall bias, which may explain the weaker association between multimorbidity overall and neglect in this study. Despite the risk of

recall bias, the questionnaire has been previously shown to have good test-retest reliability (294). The sensitive nature of the ACE questions was acknowledged during data collection by offering patients a separate sealed envelope in which to submit their responses.

Multimorbidity status was also ascertained by self-report. Although also subject to response bias, this method has high sensitivity and specificity for identifying chronic disease compared with available administrative data collection. Moreover, as patients are more likely to report conditions that have a material impact on their health related quality of life, self-report may be more patient focused than alternative methods (295). As we were limited to the twenty conditions included in the original Mitchelstown study questionnaire, the true burden of multimorbidity in this cohort may have been underestimated. Other influential papers in this field have included from five to over 300 conditions in their indices (33, 51). Debate on the most appropriate definition of multimorbidity continues; we chose the most commonly used definition, two or more conditions, for reasons of comparability (28).

8.6. Conclusion

This population based observational study of middle-aged adults found a significant association between multimorbidity and self-report of adverse childhood experiences, even after accounting for other social, behavioural and psychological factors. These findings have implications for disease prevention activities for victims of childhood maltreatment, and highlight the importance of psychosocial dimensions to interventions that aim to meet the healthcare needs of, and improve health outcomes in, people with multimorbidity.

CHAPTER 9. IMPROVING MEDICATION MANAGEMENT IN MULTIMORBIDITY: DEVELOPMENT OF THE MULTIMORBIDITY COLLABORATIVE MEDICATION REVIEW AND DECISION MAKING (MY COMRADE) INTERVENTION USING THE BEHAVIOUR CHANGE WHEEL.

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9.1. Abstract

Background

Multimorbidity, the presence of two or more chronic conditions, affects over 50% of patients in primary care. Due to its association with polypharmacy, the development of interventions to optimize medication management in patients with multimorbidity is a priority. The Behaviour Change Wheel is a new approach for applying behavioural theory to intervention development. Here, we describe how we have used results from a review of previous research, original research of our own and the Behaviour Change Wheel to develop an intervention to improve medication management in multimorbidity by GPs, within the overarching UK Medical Research Council guidance on complex interventions.

Methods

Following the steps of the Behaviour Change Wheel, we identified behaviours associated with medication management in multimorbidity by conducting a systematic review and qualitative study with GPs. From the modifiable GP behaviours identified, we selected one and conducted a focused behavioural analysis to explain why GPs were or were not engaging in this behaviour. We used the behavioural analysis to determine the intervention functions, behaviour change techniques and implementation plan most likely to effect behaviour change.

Results

We identified numerous modifiable GP behaviours in the systematic review and qualitative study, from which active medication review (rather than passively maintaining the status quo) was chosen as the target behaviour. Behavioural analysis

revealed GPs' capabilities, opportunities and motivations relating to active medication review. We combined the three intervention functions deemed most likely to effect behaviour change (enablement, environmental restructuring and incentivisation) to form the Multimorbidity Collaborative Medication Review And Decision-making (MY COMRADE) intervention. MY COMRADE primarily involves the behaviour change technique of social support: two GPs review the medications prescribed to a complex multimorbid patient together. Four other behaviour change techniques are incorporated: restructuring the social environment, prompts/cues, action planning, and self-incentives.

Conclusions

This study is the first to use the Behaviour Change Wheel to develop an intervention targeting multimorbidity, and confirms the usability and usefulness of the approach in a complex area of clinical care. The systematic development of the MY COMRADE intervention will facilitate a thorough evaluation of its effectiveness in the next phase of this work.

9.2. Introduction

Multimorbidity, the co-occurrence of two or more chronic conditions, affects over 50% of patients with chronic disease in primary care (33, 51). In a healthcare system that has evolved around the management of single chronic diseases, this presents major challenges to healthcare provision, research and medical education (51). In 2014, the US Department of Health and Human Services recognised these challenges by stating the need to better equip clinicians in the management of multimorbidity, making specific reference to medication management (66). Multimorbidity frequently leads to the prescription of multiple long-term medications (222). The resulting polypharmacy is an independent risk factor for negative health outcomes such as adverse effects and drug interactions (6). For prescribers, this creates a tension between keeping the number of medicines to a minimum while still prescribing what evidence-based guidelines advocate as being in the patient's best interest (126). This is especially the case for GPs, who must co-ordinate and oversee the medications prescribed by numerous doctors involved in the care of a multimorbid patient (202).

Despite the prevalence of multimorbidity, few interventions have been developed to improve medication management in this field to date. A recent systematic review, which focussed on interventions to optimize outcomes in patients with multimorbidity in primary care, found only two studies that specifically addressed medication management. However, both interventions related to enhanced involvement of pharmacists, rather than the prescribing actions of GPs (145). Thus the development of interventions to GPs' contribution to medication management in patients with multimorbidity is a priority.

In the past, interventions that aimed to change healthcare professionals' behaviour have resulted in suboptimal effects, due to a lack of theoretical consideration at the

development stage (296). The UK Medical Research Council (MRC) guidance for the development of complex interventions in healthcare emphasizes the importance of using theory in intervention design (8). However, the MRC document does not put forth any specific suggestions on how to do this which leaves intervention designers, many of whom are interested in theory only to the extent that it can help them achieve improvements in clinical care, with an array of dilemmas (297). The large pool of available theoretical models means that critical theories may be missed, and there is little clarity on how to choose the most appropriate theory for the behaviour in question (227). In addition, intervention developers have traditionally had little to guide them on the specification of intervention content (298).

Over the last few years, this gap has been addressed by an approach known as the Behaviour Change Wheel (BCW), which explicitly integrates behavioural theory with the development and description of behaviour change interventions (171). A core feature of the BCW is a theoretical model, known as the COM-B, which is used to conduct an analysis of the behaviour in question. The COM-B model is based on the hypothesis that the interaction between one's capability (C), opportunity (O) and motivation (M) can provide explanations for why a particular behaviour (B) is or is not performed. Each of these components can be further subdivided (Figure 13). Capability may be physical (the physical skill, strength and stamina) or psychological (the knowledge or psychological skills, strength or stamina to engage in the necessary mental processes). Opportunity may be physical (afforded by the environment, including resources, locations, time etc.) or social (afforded by interpersonal influences, social cues, and cultural norms that influence the way we think about things). Motivation may be reflective (plans, self-conscious intentions or evaluations) or automatic (reflex responses, impulses, drive states). The COM-B behavioural analysis

guides the choice of intervention functions (or strategies) most likely to achieve behaviour change. Additionally, the intervention functions have been linked to a taxonomy of 93 replicable behaviour change techniques (299), and the techniques particularly suitable for each intervention function have been highlighted (171). Following this structured approach lends transparency to the process of intervention development, and facilitates its subsequent implementation and evaluation [12].

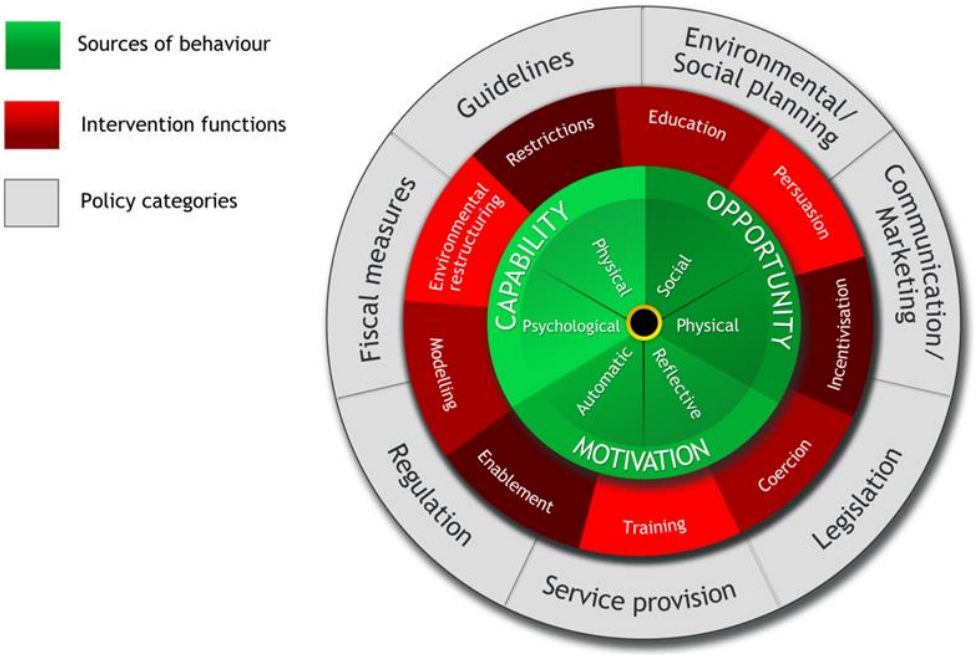

Figure 13. The Behaviour Change Wheel

Since its original publication in 2011, the BCW has received a lot of academic interest, and a number of groups have already used it to develop or study the implementation

of interventions by healthcare professionals (300-303). To our knowledge, there are no published examples using the BCW to develop a de-novo intervention targeted at healthcare professionals in the complex field of multimorbidity. As the application of the BCW may vary according to the setting and target behaviour, examples of the generalisability of the approach are required. Furthermore, published examples of its use will contribute to the on-going development and refinement of the approach.

In this paper, we describe the development of an intervention to improve medication management in multimorbidity by GPs, in which we applied the steps of the BCW to enable a more transparent implementation of the MRC framework for design and evaluation of complex interventions.

9.3. Methods

In the MRC framework, intervention development comprises three stages: identifying the evidence base, identifying and applying appropriate theory to the available (and if necessary, new) evidence, and modelling processes and outcomes (8). Like the MRC framework, the BCW (171) also has three broad stages but they involve different tasks (i.e. understanding the behaviour; identifying intervention options; and identifying content and implementation options) and are subdivided into a further eight steps (i.e. defining the problem in behavioural terms; selecting the target behaviour; specifying the target behaviour; identifying what needs to change; identifying appropriate intervention functions; identifying policy categories; identifying behaviour change techniques; and determining the mode of delivery) (171). As we were using the BCW within the overarching framework of the MRC, we mapped the eight BCW steps directly on to the three development stages of the MRC to enhance the clarity and generalisability of our approach (see Table 9).

Table 9. Mapping steps of Behaviour Change Wheel to the three stages of intervention development in the UK Medical Research Council guide

MRC Development Stage(8)	BCW Steps(171)	BCW Stages
1. Identify the evidence base	1. Define the problem in behavioural terms	1. Understand the behaviour
	2. Select the target behaviour	
	3. Specify the target behaviour	
2. Identify/develop theory	4. Identify what needs to change	
	5. Identify appropriate intervention functions	2. Identify intervention options
	6. Identifying policy categories	
3. Model process and outcomes	7. Identifying behaviour change techniques	3. Identify content and implementation options
	8. Determine the mode of delivery	

MRC Stage 1: Identifying the evidence base

To begin, we reviewed the existing evidence on medication management in multimorbidity and supplemented this with new evidence in order to clearly define our problem of interest and then select and specify the behavioural target for intervention.

BCW Step 1. Define the problem in behavioural terms.

We searched for relevant published literature, in particular existing systematic reviews, to help us understand the problems associated with medication management in multimorbidity in primary care. While we identified two relevant quantitative reviews (103, 145), we also found a number of pertinent qualitative studies. Therefore, we conducted a systematic review and synthesis of the relevant qualitative evidence

(Chapter 5) (226). We addressed the gaps identified from the qualitative synthesis by conducting a qualitative interview study, specifically to generate further information on their approaches to prescribing in multimorbidity. The methods for the interview study are described elsewhere (Chapter 6) (257). A cross-sectional study was conducted to examine the psychosocial factors that add additional complexity to the management of patients with multimorbidity (Chapter 8) (304).

BCW Step 2: Select the target behaviour.

From the aggregated qualitative synthesis and interview data, we (CS & CB) identified the modifiable GP behaviours relating to medication management in multimorbidity, and selected one key behaviour to target in our intervention. This judgement was informed by criteria set out in the BCW guide which are: the likelihood that behaviour change would be implemented, the likely impact of changing the behaviour, the spill-over or knock on effect of change on other behaviours, and the ease with which each behaviour could be measured (171).

BCW Step 3: Specify the target behaviour*.*

Once the target behaviour was decided, we specified in greater detail what and who needed to change, and where and when this change should happen.

MRC Stage 2: Identifying/developing theory

In the next stage, we used the COM-B (capability, opportunity, motivation - behaviour) model to develop a theoretical understanding of the target behaviour and guide our choice of intervention functions.

BCW Step 4: Identify what needs to change to achieve the desired behaviour.

We used the COM-B model to frame our qualitative behavioural analysis of the qualitative synthesis and interview data. We (CS & CB) coded empirical data relevant to GPs' psychological and physical capabilities (C), social and physical opportunities (O) and reflective and automatic motivations (M) to highlight why GPs were or were not engaging in the target behaviour, and what needed to change for the target behaviour to be achieved. Where multiple COM-B components were potentially relevant to one section of the data, the component whose definition (as set out in the BCW guide (171)) best fit the context of our data was chosen. The results of this analysis was presented to the other authors at a consensus meeting and refined accordingly.

BCW Step 5: Identify intervention functions to achieve the desired behaviour

The BCW incorporates a comprehensive panel of nine intervention functions, shown in red in Figure 13, which were drawn from a synthesis of 19 frameworks of behavioural-intervention strategies (171). We determined which intervention functions would be most likely to effect behaviour change in our intervention by mapping the individual components of the COM-B behavioural analysis onto the published BCW linkage matrices (171). Each intervention function that was potentially relevant to our data was considered in detail. We used the APEASE criteria (affordability, practicability, effectiveness and cost effectiveness, acceptability, side effects/safety and equity), another component of the BCW approach, to grade the potentially relevant intervention functions into first and second line options (171).

BCW Step 6: Policy categories

The BCW also includes matrices which sign post seven broad policy-level interventions for achieving behaviour change, shown in grey in Figure 13. As we were not primarily concerned with changing policy in this study, we did not undertake this step in detail, other than listing the options that may be relevant to levering our intervention in the future.

MRC Stage 3: Modelling process and outcomes

In this third stage, we specified our intervention content in more detail and identified an appropriate way of implementing the intervention within our context.

BCW Step 7: Identify behaviour change techniques

The selected intervention functions represented our broad approach to achieving behaviour change, but we required fine-grained techniques to operationalize these functions. We used the links previously drawn between the BCW and the taxonomy of 93 behaviour change techniques (171, 305) to list those techniques most frequently used with our selected intervention functions. We held an expert panel consensus meeting to review the suitability of each of these techniques, in light of our previously collected qualitative data, the context of the intervention, and by referring to the APEASE criteria. Each member of the panel had expertise in one or more areas of relevance (clinical pharmacology and prescribing (CB, MD, RP), general practice (CB, CS, MD, RP, SM), behavioural science and intervention design (MB), and multimorbidity (CS, RP, SM)).

BCW Step 8: Identify mode of delivery

As we were developing an intervention to be implemented by individual GPs, this step (mode of delivery) required explicit consideration of implementation in the heterogeneous setting of general practice. We used the expert panel consensus to specifically address modelling questions posed in the MRC framework which were: would it be possible to use this; what subgroup of patients should it be used for; what outcomes should be sought; and what are the facilitators/obstacles at practice level (8). If multiple implementation options existed, agreement was reached by discussing each option, with reference to the APEASE criteria (171).

9.4. Results

MRC Stage 1: identifying the evidence base

BCW Step 1. Define the problem in behavioural terms.

We identified two existing systematic reviews which were relevant. Patterson et al. reviewed existing interventions to improve prescribing and polypharmacy in older patients (103). Only one of the included studies involved GPs and showed that computer decision-support reduced inappropriate drug initiation in primary care (306). The authors suggested that future polypharmacy interventions must address the complexity of clinical situations and the individuality of prescribers. Smith et al. reviewed interventions to improve patient outcomes in multimorbidity in primary care. Two included studies addressed medication management but these involved pharmacists rather than GPs. Here, the authors suggested that future interventions should target specific problems relating to multimorbidity, be integrated into existing healthcare systems, and be embedded with inter-professional collaboration (145).

Our qualitative synthesis included ten studies from seven countries involving a total of 275 GPs (see Chapter 5)(226). A key theme was GPs' sense of professional isolation in the management of multimorbid patients. This emanated from the interplay between four aspects of the management of patients with multimorbidity: i) the disorganization and fragmentation of healthcare between primary and secondary care; (ii) the inadequacy of guidelines and evidence-based medicine for multimorbidity; (iii) challenges in delivering patient-centred, rather than disease-focused, care; and (iv) barriers to shared decision-making.

In the qualitative interview study, we found that GPs responded to clinical dilemmas in multimorbidity by 'satisficing', i.e. accepting care that they deemed satisfactory and sufficient for a particular patient, yet acknowledging that aspects of that care may not

be optimal (see Chapter 6)(257). In patients with changing disease trajectories, satisficing was manifest as relaxing targets for disease control, negotiating compromise with the patient, or making 'best guesses' about the most appropriate course of action to take. In multimorbid patients perceived as stable, GPs' default approach was to 'maintain the status quo' rather than actively rationalize medications. The cross-sectional study demonstrated the negative psychosocial factors that can introduce additional complexity into the management of patients with multimorbidity; these findings emphasized the need for patient-centred interventions that prioritize a view of the whole patient in context (304).

BCW Step 2: Select the target behaviour.

The modifiable GP behaviours relating to medication management in multimorbidity are shown in Figure 14. "Maintaining the status quo" was observed in all of the qualitative interviews despite best practice guidelines which state that patients receiving long-term medicines need medication reviews at regular intervals. Targeting this behaviour would likely result in behaviour change as the qualitative study showed GPs' extant discomfort with it (discussed in Chapter 6). Furthermore, it would be desirable to see GPs adopt a less passive approach to medication management even if it did not always lead to downstream changes to medications. There was a high possibility of "spill over" from the actions of medication review for multimorbidity to other prescribing activities. Lastly, changing this behaviour would be relatively easy to measure. We judged that the other modifiable behaviours were not as attractive. Adopting practice protocols would have a big impact and high spill over, but given current financial and staffing pressure on practices, would be a difficult organisational change to achieve. Relaxing targets for disease control is likely appropriate in some

patients in multimorbidity, and enforcing strict adherence to guideline targets is not patient-centred and may be resisted by GPs. Addressing shared decision-making has merit but requires interventions targeting GPs' communication skills (rather than prescribing) which was not our specific focus.

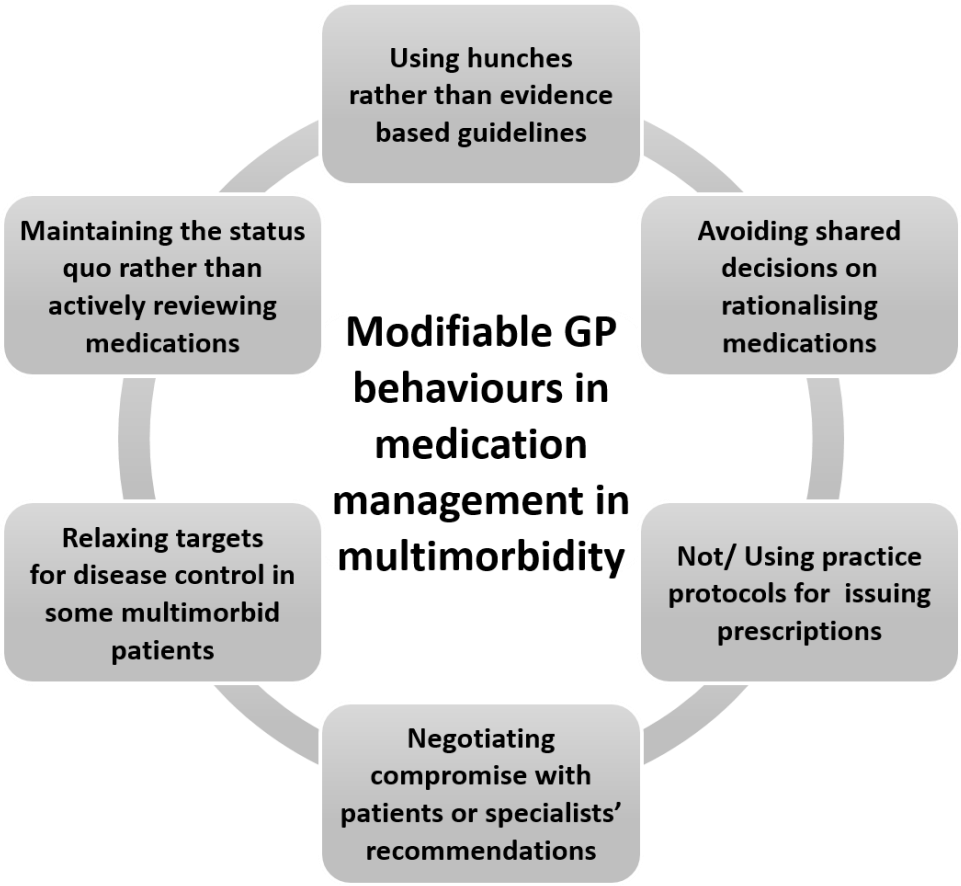

Figure 14. Modifiable GP behaviours in medication management in multimorbidity identified in qualitative synthesis (Chapter 5) and interview study (Chapter 6)

***BCW Step 3: Specify the target behaviour*.**

The target behaviour was specified as active, purposeful medication review instead of passive "maintaining the status quo" for patients with multimorbidity, to be conducted by GPs, in routine general practice, on a regular basis.

MRC Stage 2: Identifying/developing theory

BCW Step 4: Identify what needs to change to achieve the desired behaviour

We used COM-B to identify GPs' capabilities (C), opportunities (O) and motivations (M) for engaging, or not engaging, in active medication review. The themes that emerged from this analysis are shown in Table 10, with illustrative quotes from the qualitative synthesis and the interview study. For example, GPs adopted a passive approach to medication management due to their uncertainty (lack of psychological capability) about which medications were most valuable in patients with multimorbidity, especially given the absence of satisfactory guidelines in this field. Insufficient consultation time led to a lack of physical opportunity to review medications. GPs also found medication review difficult because of a cultural milieu which holds that treatment for chronic disease is lifelong (lack of social opportunity). This was particularly the case if the patient had been compliant with their medications for many years. Many GPs had developed a habitual response to "not rock the boat" in patients with multimorbidity, an approach which involved not making changes to medications unless there was a pressing reason to do so. This response was reinforced by their experiences of the negative consequences of stopping or changing medications for patients with multimorbidity in the past (automatic motivation). GPs' reflective motivations against medication review included the opportunity cost of using their professional time for this purpose, and a fear of negative consequences from

rationalising medications. GPs also had motivations to review medications which included improving patient outcomes, reassuring themselves that they were delivering best care, and guarding against medico-legal repercussions.

BCW Step 5: Identify intervention functions

We found that all nine intervention functions listed in the BCW were relevant to our behavioural analysis. Supplementary material 19 shows our assessment and grading of each intervention function into first and second line options using the APEASE criteria. The three intervention functions most relevant for our intervention were enablement, environmental re-structuring, and incentivisation. The relationships between the components of the COM-B behavioural analysis and these three intervention functions are shown in Table 10.

BCW Step 6: Policy categories

The broad policy options, signposted by the BCW matrices as being potentially useful for achieving behaviour change, were communication/marketing, service-provision policy, legislation, guidelines and regulation.

Table 10. Behavioural analysis, selected intervention functions and behaviour change techniques, referencing empirical data from the qualitative synthesis (QS) and the interview study (IS)

Behavioural Analysis using COM-B: Why does medication review not happen in multimorbidity? (Step 4)		**Intervention functions** (Step 5)	**Selected behaviour change techniques (labelled in bold) and empirical data to support their selection** (Step 7)	
Uncertainty about what medications were most valuable IS gp2 "she is not fitting in to either box for us so we are not using any guidelines, we're not using anything you know - we're just using our clinical acumen on a daily basis with her" IS gp14 "Well, in some instances there is no evidence at all, because most clinical trials don't include, you know, 80 something year olds.." IS gp5 "Well the difficulty is, with evidence-based medicine, there is no place in one sense for the opinions of the family physician or any doctor, because they don't fit, there's no place for them (patients with multimorbidity) in guidelines… so if people are going on about evidence-based medicine- it is all about you know, what's the cholesterol, what's this, what's the FEV1s, so if it's down below that you put them on this, you put them on that, you know. There is nowhere in guidelines where they say, you know, you don't put them on warfarin if they are living on their own and they are seventy odd years of age, so that's the difficulty"	Capability: Psychological	Enablement	**Social support (practical)** Advise on, or provide practical help (e.g. colleagues) for performance of behaviour	Two GPs support each other to review medications, tapping into professional convention to discuss cases anecdotally. QS: "GPs feel isolated in the management of patients with multimorbidity, a group that they are specifically tasked with caring for." IS: "it helps sometimes to talk it over with the lads and say 'how will we handle this'."
Perceptions that social norms make patients unwilling to stop long-term medications IS gp13"some of the stuff she is on, like the domperidone and the betahistine and stuff, I'm not really convinced that she needs it. I have talked to her a little bit about it - about whether or not it might be useful to take things off but she's reluctant to take them out and as far as she is concerned they've been started at some point over the years for her for the dizziness - as she sees it, and so she wants to try and keep them"	Opportunity: Social			

Lack of time to properly review medications IS gp1"if you just had a 30-minute consultation with a patient while you don't have the waiting room building up… you could actually get to the bottom of some of the stuff they're on"	Opportunity: Physical	Environmental restructuring	**Restructuring social environment** Change, or advise to change the social environment in order to facilitate performance of the wanted behaviour **Action planning** Prompt detailed planning of performance of behaviour (must include at least one of frequency, context, duration, intensity.	Planning and agreeing on protected time for the two GPs to come together to conduct the review is necessary. QS: "Insufficient consultation time seen as reason for suboptimal approach to multimorbidity care." IS: "I'll have to do some of this another day... in a different structure or format"
An instinct not to 'rock the boat' IS gp11"she's been doing better than she has in a long time- I'm not going to rock the boat at all" IS gp14 "there is that aspect of not rocking the boat, you know and being straight up about it as well, sometimes as well you can get into the routine 'oh are you just in for the prescription?', you just print it off automatically without giving due consideration to can we shorten this, can we do this that and the other." IS gp18 "Take the line of least resistance! Here's another 3 months prescription for it!!" IS gp19 "anything that complex I really didn't entertain changing because why stir things up?" QS "avoidance of decision-making"	Motivation: Automatic	Environmental restructuring Enablement	**Prompts/cues** Introduce environmental or social stimulus for the purpose of prompting or cueing behaviour	GPs will use a list of generic prompts prompt the medication reviews. QS: "Most GPs felt that guidelines were less useful in multimorbidity and that they actually added to the complexity in some case."
Opportunity cost of using time to conduct medication reviews IS gp11"she has had multiple other things going on as well, so the consultation time is all taken up" **Fear of negative consequences** QS "would be loath to stop it, it's probably medico-legal"	Motivation: Reflective	Incentives	**Self-incentives** Plan to reward self in future if and only if there has been effort and/or progress in performing the behaviours.	GPs can award themselves professional development points for conducting the reviews. Some GP's were already meeting to discuss troublesome cases for this purpose although without a focus on medications.

MRC Stage 3: Modelling process and outcomes

BCW Step 7: Identify behaviour change techniques

From the taxonomy of 93 behaviour change techniques, we listed the techniques most frequently used to deliver the three intervention functions we had selected (171, 305). The resulting 32 potentially relevant techniques are listed in Supplementary material 20. We reviewed, with the expert panel, how each of these techniques could be applied to the context of medication management in multimorbidity. The panel's choice of techniques was influenced principally by the key findings of the qualitative studies: GPs' sense of isolation in the management of multimorbid patients revealed in the qualitative synthesis (Chapter 5), and GPs' lack of certainty and efforts to "share the onus of responsibility" seen in the interview study (Chapter 6). Thus, we focused on options that would enhance GPs' means of professional support. Although enhanced communication between GPs and pharmacists is being investigated in other healthcare systems, it was felt not to be an option for our intervention due to the lack of community pharmacists available in Ireland. Similarly, communication between GPs and specialists involved in the care of patients with multimorbidity was seen in both qualitative studies to be fraught by poor access and a single-disease approach. However, GPs considered their GP colleagues to be a useful source of support (Chapter 6). These interactions occurred on an informal basis within practices, and were notable for their ready accessibility and generalist nature. We were unaware of any work exploring collaborative decision-making between GPs in multimorbidity, so focused on this as a new approach. From the list of 32 techniques, we considered which techniques would pragmatically facilitate collaborative decision-making between GPs. Many techniques were quickly eliminated as they were irrelevant to the context or

purpose of the intervention (described in Supplementary material 20). The five techniques eventually selected as "active ingredients" were: social support (practical), restructuring the social environment, use of prompts/cues, action planning, and self-incentives. The definition of each technique, and qualitative data to support their selection, are shown in Table 10. The combination and integration of each technique into the overall intervention, named Multimorbidity Collaborative Medication Review And Decision-making (MY COMRADE), is shown in Table 11.

Table 11. Description of final intervention

The Multimorbidity Collaborative Medication Review And Decision-making (MY COMRADE) intervention
GPs will be asked to schedule protected time for themselves and one of their GP colleagues to conduct the collaborative medication review, and enter this time into the practice appointment book. They will be asked to choose a day/time/office that suits them best, and decide how many patient cases to review in one sitting (action planning)*. The GPs will choose multimorbid patients from their caseload, and in the scheduled review time will review medications, supported by their GP colleague (social support and restructuring social environment). The medication review will be prompted by the seven prompts described in the NO TEARS (307) medication checklist (prompts and cues). GPs will be asked to record recommendations for medication change that arise from the review in the patient's notes, to allow them to discuss these with the patient during their next consultation. After completing the review, GPs will award themselves continuing professional development points: one point for each cumulative hour of the activity completed (self-incentives). *behaviour change techniques indicated in brackets

BCW Step 8: Identify mode of delivery

In the expert panel meeting, we then formulated an intervention implementation plan. Four specific aspects of implementation were reviewed, and the various options considered for each aspect are fully described in Supplementary material 21. In summary, the following implementation plan was formulated:

What prompts should be used to guide medication review in MY COMRADE?

After reviewing eight different prescribing tools and checklists (listed in Supplementary material 21), it was agreed that a modified version of the seven prompts in the NOTEARS (307) checklist for medication review would be used to prompt the review.

How should GPs choose which patients to review using MY COMRADE?

After reviewing multiple options (listed in Supplementary material 21), it was agreed that GPs should choose patients prescribed ten or more regular medicines or five or more medicines with at least one other complicating factor (i.e. meets criteria for potentially inappropriate prescribing, at risk of a well-recognised drug-drug interaction, has poor adherence or receiving end-of-life or palliative care), in line with recommendations from the Kings Fund report on Polypharmacy and Medication Optimisation (99).

How should the behaviour change technique "action planning" be operationalized?

One of the behaviour change techniques, action planning, specifically relates to implementation and was selected to account for the wide variety of structures and systems that occur in general practice. Each GP will be given clear guidance on how to tailor MY COMRADE to suit their practice. This will involve asking them to choose a

particular day, time of the day, and office in which to do the review. They will decide on the number of cases to review in one sitting, and the GP pairs that will conduct reviews within a practice. In advance of trialling MY COMRADE, GPs will be asked to consider what they envision as problematic for its implementation, and how these problems could be tackled, knowing their own practice.

How should the intervention be evaluated?

The initial evaluation will focus on intervention implementation (i.e. did medication review take place?). The behaviour change techniques and other causal or contextual mechanisms associated with behaviour change will be determined using qualitative methods. If MY COMRADE is shown to be acceptable and implementable, future evaluations will assess effectiveness using health outcomes such as the number of/type of medication changes made and changes in rates of healthcare utilisation.

9.5. Discussion

This paper describes the systematic, structured development of an intervention to improve medication management for multimorbid patients by GPs. The intervention is called Multimorbidity Collaborative Medication Review And Decision-making (MY COMRADE). It is, to our knowledge, the first intervention directed at the management of multimorbidity in primary care, developed by using the Behaviour Change Wheel to clearly implement the framework of the MRC guide on complex interventions.

MY COMRADE involves collaborative decision-making by two GPs who support each other in the review of medications prescribed to a complex multimorbid patient, guided by prompts which relate to safe prescribing. The broad functions of the intervention (enablement, environmental restructuring and incentivisation) are theoretically based. These functions will be achieved using five specific behaviour change techniques: social support (practical), restructuring the social environment, use of prompts/cues, action planning, and self-incentives. The technique of peer support is a crucial feature of our intervention, which we expect will greatly enable GPs' capabilities in conducting active medication reviews. Peer support may be particularly important in deprescribing medications or prioritising patient-centred rather than disease-focused care in multimorbidity; these aspects of medication management are challenging for GPs due to fear of litigation which the MY COMRADE intervention may now help ameliorate.

Comparison with other work

Since its publication in 2011, the BCW has been used in the development of interventions targeting healthcare professionals in a variety of ways. For example, Alexander et al. used COM-B to understand barriers and enablers to preventative

health examinations for young children in Australian general practice, with a view to designing an implementation intervention to increase the conduct of these examinations (300). They did not describe later steps of the BCW, such as choice of intervention functions, and did not provide any detail on the format of their implementation intervention. In contrast, we used the BCW to highlight areas for improvement in professional practice and then develop an intervention targeted to these areas, rather than simply increasing the implementation of a pre-existing intervention.

Murphy et al. used COM-B to develop a capacity-building programme to enhance pharmacists' roles in mental healthcare (303). This group felt that implementation processes must be prioritised during the early stages of intervention development, and they wove theories of behaviour change and implementation together in an iterative way. While we agree that implementation should be considered at all stages of development work, we did not find it necessary to use a specific implementation framework. The initial steps of the BCW revealed multiple behaviours that could be targeted to improve GPs' professional practice. Once one behaviour had been chosen, the remaining steps of the BCW involved developing an implementation intervention to enhance the performance of this desired behaviour. Additionally, by incorporating the behaviour change technique of action planning, implementation was explicitly integrated into our intervention. Action planning requires an individual GP to plan the frequency, duration and intensity of the planned intervention activity (171). Thus, rather than a prescriptive implementation strategy, action planning will allow each GP to adapt the intervention for use within their own practice. The variation in implementation, as well as fidelity to other behaviour change techniques, will be

evaluated in the next phase of this work and will help to inform the debate on optimal approaches to implementation planning in intervention development.

Strengths and weaknesses

We began this work with the broad aim of developing an intervention to improve medication management in multimorbidity, but we did not have a predefined idea of what the intervention would be at the outset. Adhering to the guidance of the MRC by using a theoretical approach, which was chosen a priori, gave direction, structure and transparency to this process in multiple ways.

First, the MRC states the need to identify the evidence base, and supplement this with new evidence if necessary. In doing this, we generated much needed data on the management of medications in multimorbidity, increased our understanding of the problematic areas experienced by GPs, and revealed how they currently respond to these difficulties. Second, we then used this empirical data to directly influence the development of the intervention. Following the steps of the BCW allowed us to develop a list of options for behaviour change and to clarify what we were, and what we were not, trying to achieve. Third, we benefitted from using the links between the BCW model and the taxonomy of behaviour change techniques. The taxonomy highlighted novel strategies for behaviour change, many of which we would heretofore not have considered. Although only five techniques are ultimately included in the final intervention, many of the other techniques influenced our thinking during the development of the intervention and the implementation strategy.

Despite the highly systematic and structured approach of the BCW, there are challenges associated with its use and it is not a magic bullet for intervention development. For example, the researcher must make a series of subjective and pragmatic decisions throughout the process. These ‘real life’ decisions can seem at

odds with the scientific approach. To counter this and to improve the transparency and generalisability of our methods, we recorded in detail the multiple options available to us at each step of the BCW and expanded on why options were or were not taken Furthermore, the multiple steps of intervention development involved a lengthy process: from the beginning of our systematic review to final refinements of the intervention spanned almost three years. Such a prolonged course must be factored in by those pursuing and funding evidence-based intervention development.

Other intervention developers have used a 'top-down' approach of applying classical behavioural theories such as social cognitive (308) or control theory (309) to inform their choice of intervention functions and behaviour change techniques. In contrast, we employed a 'bottom-up' approach to theory development in which the framework of the BCW guided our use of existing evidence and our own qualitative explorations. This led to an intervention which was logical and practical yet still theoretically based.

In addition to the COM-B, the BCW also includes an optional, more detailed framework for behavioural analysis known as the Theoretical Domains Framework (171). After completing our intervention development as described above, an additional exercise was conducted in which the qualitative data were assessed using the Theoretical Domains Framework. This process is described in detail in Supplementary material 22, and reassuringly demonstrated the same associations between the qualitative data, and the intervention functions and behaviour change techniques that were incorporated into the MY COMRADE intervention.

Implications for future research

We used the BCW as a lens for viewing GP behaviour, understanding what needed to shift, and determining how this shift could be achieved. Our experience confirms the

usefulness and generalisability of this approach. Multimorbidity presents many challenges to GPs, particularly relating to the conflicts between patient-centred and disease-focused care but the BCW approach was not hampered by these complexities. Based on our experience, the method is potentially useful for intervention developers across disciplines as long as sufficient contextual and empirical data exists or can be generated.

Throughout this study, we adhered to the "less is more" maxim of intervention design (171). We could have taken a more complex multi-faceted approach, such as incorporating other stakeholders i.e. pharmacists or specialists. Instead, we adopted the recommendations from the systematic review by Smith et al. that changes targeting specific problems are more likely to be effective (145). Smaller changes can be achieved, sustained and built upon in future interventions, and substantial behaviour change is more likely to result from the aggregation of these smaller changes (171). We applied the same tenets to our assessment of outcomes – rather than initially looking at downstream effects such as changes in prescribing, we will concentrate first on proximal changes such as implementation of the intervention. Once we are assured that it is acceptable, feasible, and leads to behaviour change, then we can assess the impact on patient-related outcomes, prescribing safety and polypharmacy.

To date there is limited evidence available on which behaviour change techniques are most effective in specific settings. We expect that characterizing the active components in the MY COMRADE intervention using the taxonomy of behaviour change techniques (299) will aid implementation and replication of the intervention. The clear specification of the intervention will also facilitate a thorough evaluation of the impact

of the selected behaviour change techniques and will help to inform evidence-based strategies for intervention development in the future.

In this study, we did not undertake the sixth step of the BCW relating to policy options in detail. However, if the intervention is shown to be effective in our on-going feasibility and pilot work, scaling-up of the intervention will require greater consideration of the external context of healthcare policy and widespread implementation.

9.6. Conclusions

This paper describes the development of an intervention to improve medication management in multimorbidity by GPs. The intervention, which is called Multimorbidity Collaborative Medication Review And Decision-making (MY COMRADE), is based on purposively collected data on behaviour in context and a novel approach to intervention design, the Behaviour Change Wheel. While the Behaviour Change Wheel is not a magic bullet for intervention design, this paper confirms the usability and usefulness of this approach in a complex area of clinical care. The systematic, transparent approach used in the development of the MY COMRADE intervention will facilitate its thorough evaluation in the next phase of this work.

CHAPTER 11. DISCUSSION

11.1. Main findings

The overarching aim of this thesis was to develop an intervention to support patient-centred prescribing for patients with multimorbidity. Previous interventions have had limited impact because they were not integrated into clinical practice, did not focus on specific issues that physicians and patients have difficulty with, or did not involve sufficient interaction between clinical decision-makers (95, 145). By following the guidance for intervention development set out by the MRC, the consecutive pieces of work in this thesis have transparently and systematically addressed these limitations. The product is a promising intervention which uses a new approach to support patient-centred prescribing for patients with multimorbidity: collaborative medication review by two GPs.

Although the guidance from the MRC states that intervention development is not necessarily a linear process, it was useful to conduct the phases of work in sequence, with each study iteratively informing the next. First, the existing qualitative literature on GPs' perceptions of the management of multimorbidity was synthesized using a meta-ethnographic approach (Chapter 5). The review showed that GPs experience challenges in four domains of clinical practice (disorganization and fragmentation of health care; the inadequacy of guidelines and evidence based medicine; challenges in delivering patient-centred care; and barriers to shared decision-making), which can in turn lead them to feel unsupported and professionally isolated in the management of patients with multimorbidity. The study was published in the BMJ Open in 2013, and has already been cited by over twenty peer-reviewed papers.

As none of the papers included in the review provided detailed information on how GPs deal with difficulties in medication management in multimorbidity, a qualitative study

was conducted with GPs to explore this issue in depth (Chapter 6). The key finding was that GPs' default approach was to "maintain the status quo" rather than actively review medication for their multimorbid patients. This study was published, and editorialised, in the British Journal of General Practice in March 2015.

In the qualitative interview study, chart-stimulated recall was found to be a useful and efficient technique for gaining insights into clinical decision-making. Therefore, a scoping review of the application of chart-stimulated recall to clinical research was performed, to serve as a guide for other researchers interested in using the technique (Chapter 7). A manuscript of this paper is currently under peer-review.

One of the challenges which emerged from the qualitative study was the influence of psychosocial complexity on the clinical management of multimorbid patients. To explore this issue further, a cross-sectional study using baseline data from a regional cohort study was conducted (Chapter 8). A significant association between multimorbidity and adverse childhood experiences, as well as other negative psychosocial factors such as lower socioeconomic class, poor diet and high body mass index was found. This study highlighted the complex health needs and psychosocial problems that often co-occur in patients with multimorbidity. The findings emphasize the need for interventions that promote consideration of the whole-person in context, and allow prioritization of non-physical issues or deviation from clinical practice guidelines if necessary. The study was published in Family Practice in April 2015 and received attention in the national press (e.g. Irish Examiner, Irish Herald), medical press (e.g. Irish Medical News, Medical Independent) and in social media (Twitter).

To inform the development of a prescribing intervention, the new qualitative data were applied to the Capability-Opportunity-Motivation-Behaviour (COM-B) model, the Behaviour Change Wheel framework of intervention strategies and the Behaviour

Change Technique Taxonomy (Chapter 9). A panel of experts was convened to guide intervention development and enhance the transparency and rigour of our approach. The result was the Multimorbidity Collaborative Medication Review And Decision-making (MY COMRADE) intervention, which incorporates five components, principal of which is collaborative medication review between two GPs. One of other features of the intervention was a simple prescribing checklist. This checklist was chosen ahead of more complicated prescribing tools, and was prefaced with an instruction to the GP to share details of the patient including their social situation (Supplementary material 25). In line with the conclusion of Chapter 8, this put the "whole person" view of the patient up-front of the medication review, and aimed to avoid reducing the patient to a series of biomedical issues.

The feasibility study of the intervention was described in Chapter 10. The focus here was on implementation rather than effect, and the implementation outcome framework published by Proctor et al. (178) was a key resource. The intervention was well received by GPs, who deemed it acceptable and appropriate to the context of multimorbidity in general practice, and reported that recommendations for medication optimisation emerged from all reviews.

At the end of this series of studies, the main product is a carefully developed intervention that is ready to undergo larger scale evaluation. The systematic review, qualitative study and cross-sectional study were conducted to inform the development of a specific intervention. However, the publication of these studies in international journals means they may also inform and benefit the work of other research groups aiming to improve healthcare for patients with multimorbidity.

11.2. Medical decision-making

A better understanding of GPs' decision-making processes in multimorbidity was needed to underpin intervention development, and gaining this understanding was a key focus in this work. Broadly, there are two approaches to decision-making. Optimal decision-making involves collecting and evaluating every single option before choosing the best one. Satisficing, the human response to decision-making when optimization is out of reach, involves using a limited range of options until an option that is 'good enough' is found (236). In multimorbidity, optimization is certainly out of reach due to the difficulties revealed in the systematic review in Chapter 5. Satisficing is a pragmatic and iterative approach to decision-making and it should not be perceived as wrong. However, interventions that incorporate peer support (like MY COMRADE) may help GPs to satisfice "better".

At its origins, evidence-based medicine involved integrating patient preference, clinical expertise and the best available external evidence (135). Since then, external evidence has gained primacy, and as illustrated in Chapter 3, this can lead to harmful consequences for patients with multimorbidity. Physicians may feel insecure if not practicing in adherence with "the evidence", therefore they need support and reassurance in order to tip the balance back in favour of patient preference and clinical expertise (84). Peer support, as it is used in the MY COMRADE intervention, allows sharing of tacit and explicit medical knowledge and informed reflection on alternative options (240). It can help to maintain professional standards while simultaneously giving consideration to the broader context of the patient. Other decision-making support such as information technology, computer decision support systems, or explicit prescribing tools do not allow the same level of individualisation or generalist approach.

11.2.1. Inter-professional peer supported decision-making

Evidence on the usefulness of professional collaboration is emerging, although it tends to focus on collaboration between different professions. In the review of models of comprehensive healthcare for older persons with chronic conditions conducted by Boult et al. (158), nine out of the fifteen successful models involved interdisciplinary primary care, or models that supplemented primary care. In 2015, Bleich et al. updated this review with new studies that focused specifically on multimorbidity (321). Of the twenty seven studies included, sixteen were based in primary care and incorporated some element of multidisciplinary care (i.e. appointing a nurse or social worker to help patients navigate the healthcare system, provide them with information about their chronic conditions or engage them in actively managing their chronic conditions). These interventions led to improvements in healthcare use and clinical outcomes, but not in patient-reported outcomes.

The Collaborative Interventions for Circulation and Depression (COINCIDE) trial, described in Chapter 3, integrated the healthcare provided by psychological well-being practitioners and nurses, and led to reductions in patients' depression scores. However, the qualitative evaluation of the study generated interesting insights (161). Healthcare professionals found that collaborating with each other allowed them to offer an expanded range of services to the patients. However, some of the professionals highlighted the boundaries of their responsibility which may have hampered true sharing of information and therapeutic integration. Patients were positive about enhanced communication between professionals, but they did not feel that this needed to happen when they were present. Some patients volunteered that they preferred treatment spaces that separated out management for different conditions.

Therefore, multidisciplinary care holds promise but future work in this field must be sensitive to patients' preferences, and optimize interactions between professionals to effect sustained improvements in patient-reported outcomes.

11.2.2. Intra-professional peer supported decision-making

Grass-root approaches to collaborative decision-making between GPs, such as quality circles or practice-based small group learning programmes, have emerged in recent years and mirror the intra-disciplinary nature of our intervention (322). Quality circles and related groups provide an opportunity for reflective practice and discussion of troubling or challenging patient cases between GPs. They have been shown to improve medication costs (323), the prescribing of generic medications (324), and healthcare utilisation (325). Additionally, participants report that practice-based learning groups are places of social support and provide protection against burnout (326). In an exploration of cases brought by GPs to such a programme, many of the cases related to complexities in the management of patients with multimorbidity (310).

11.2.3. Sharing decision-making with patients

The MY COMRADE intervention upholds the importance of shared decision-making with patients although it does not directly incorporate shared decision-making. Charles et al. suggested that shared decision-making had three stages: bidirectional exchange of information, relaying of options, and choice of one option. For patients, feeling involved in decision-making can be more important than actually making the decision (327, 328). Patients are often guided by physician recommendations (243), and physician uncertainty can inhibit shared decision-making (242). By removing medication review from the competing demands of the consultation (on average, three

issues are addressed in every consultation in general practice (253)), physicians can focus on medications and clarify what changes should be made. This clarity should facilitate more meaningful communication with patients, which in turn, should lead to higher patient satisfaction and improved outcomes (329, 330).

11.4. Strengths and limitations

This section provides a synopsis of the overall strengths and limitations of this thesis. The strengths and limitations of the individual papers have been addressed in the previous chapters.

By starting this work with a synthesis of the existing qualitative literature, the subsequent qualitative research was tailored to answer new questions, address knowledge gaps and prevent research waste.

Obtaining rich, case-based data during the qualitative interviews helped to reveal the day-to-day challenges experienced by GPs, and their responses to those challenges; this information was crucial for developing an intervention that would be useful to and used by GPs. The dependability of the study findings was further enhanced by gaining thematic data saturation.

GPs reported the psychosocial influences on decision-making in the qualitative study; these findings were explored further in the cross-sectional study. Triangulating the findings from the qualitative interviews and the quantitative analysis gives weight to the clinical and statistical importance of the association.

There is debate on the value of theory in intervention development (164, 170, 312). We found the theoretically informed approach was useful. It lent transparency and structure to the process of intervention development, and led to the development of a

novel intervention that we had not conceived of before the thesis began. By using the taxonomy of behaviour change techniques, the final intervention was highly specified thus easier to implement, replicate and evaluate.

As with all clinical research, there are also limitations in this work. The qualitative interviews and the feasibility study of the new intervention involved GPs working in the South West of Ireland. Although potential benefits were seen in this limited geographical area, the intervention remains untested elsewhere. Participants were purposively sampled to represent the spectrum of Irish general practice, which improves the transferability of the findings within Ireland. Furthermore, the likelihood of the intervention's wider applicability is enhanced because it addresses many of the challenges found in the systematic review (Chapter 5) which represented GPs from seven different countries.

The search for the published systematic review was conducted in September 2012. An update of the search in November 2015 shows that there are nine new qualitative studies relevant to the review (Supplementary data 28). The qualitative findings of these nine studies map onto the domains outlined in the original systematic review with one exception: the newer studies show a greater emphasis on the need for education and training for GPs in the management of patients with multimorbidity. This interesting development shows the evolution of the qualitative literature on multimorbidity from focusing on problems to moving towards solutions.

Many different health professionals are involved in the management of medications in patients with multimorbidity. As explained in Chapter 3, interventions incorporating different professionals (i.e. pharmacists, geriatricians) have not demonstrated consistent success in improving patient outcomes, suggesting a need for alternative

new approaches. Although the focus in this thesis came to lie on a new approach involving collaboration between two GPs, strategies to enhance better inter-disciplinary collaboration in the management of patients with multimorbidity are also needed.

Patients were not directly involved in the intervention, although it was emphasized that any changes to medications must first be discussed with the patient. Developing communication techniques to enhance patient involvement in decision-making, especially when it comes to deprescribing, are also required.

The MY COMRADE intervention will assist GPs working in group practices. However, a significant proportion of Irish GPs continue to work single-handedly (232). For these GPs, local continuing medical education groups or e-communication may allow collaborative case reviews with GP colleagues.

There is a risk that my medical background influenced my interpretation of findings throughout all of this work. To counter this and improve the neutrality of study findings, I engaged researchers who were not GPs to double code interview data, check interpretation of statistical findings, assess implementation outcomes etc.

This thesis did not deal directly with the contribution of overdiagnosis and excessive disease labelling to multimorbidity. Recently, groups of researchers and clinicians have formed to raise and address these issues and help avoid unwanted and unhelpful medicine (331, 332).

11.5. Policy implications

Since 2001, Irish healthcare policy has recognised the potential for primary care to improve patient outcomes and reduce healthcare costs in chronic disease (10). More recent policy documents, such as Future Health and the National Service Plan for 2016,

prioritize the reform of current services to promote integrated person-centred approaches to chronic disease management, especially in older more complex patients (333, 334). One of the pillars of the proposed reforms is to move away from the current hospital-centric model of care towards a new model of integrated care which treats patients at the lowest level of complexity that is safe, timely, efficient, and as close to home as possible. Such efforts are expected to reduce costs, improve access and move from the existing emphasis on episodic reactive care towards preventative, planned and co-ordinated care. The novel approach to medication review developed in this thesis will be a useful tool to support the delivery of co-ordinated, community based comprehensive care.

However, the budgetary allocations for healthcare present significant challenges for the development and even the maintenance of existing services. The MY COMRADE intervention has the potential to meet many of the current health policy objectives and is not resource intensive. Furthermore, unbiased syntheses of existing information and research on behaviour change are two of the most important contributions researchers can offer to policy makers (335), both of which were incorporated into the development of the intervention.

In Chapter 9, a range of policy options were signposted as being potentially useful for achieving behaviour change associated with the MY COMRADE intervention. These policy options merit consideration for the up-scaling of the intervention if its effectiveness is demonstrated in a larger scale study.

In 2015, the first pay for performance initiative for chronic disease care was introduced in Ireland. It involves a new cycle of care for diabetes, and because it provides additional resources to primary care, was broadly welcomed by GPs. However, caution is required with single-disease pay for performance schemes if patient-centred care in

patients with multimorbidity is to be protected. The MY COMRADE intervention is an example of a performance initiative that could be used to channel resources to complex patients. Furthermore, the aforementioned Future Health document proposes the introduction of a new Money Follows the Patient (MFTP) funding model, which will create incentives that encourage safe, timely, and efficient care at the lowest level of complexity. This funding model will facilitate GPs' engagement in activities such as collaborative medication review. Morbidity-adjusted capitation payments or morbidity-based bonuses are an alternative option for directing limited financial resources to care for the patients who need it most.

Lastly, the complexity of management of multimorbidity revealed in Chapters 5, 6 and 8 highlights the need for greater representation of primary care physicians at a national policy level. Their presence is needed so that multimorbidity is accounted for in the planning and implementation of all future chronic disease initiatives and guidelines (130).

11.6. Future research

The most important next step in this project is to move on to a larger scale evaluation of the MY COMRADE intervention. This step is justified by our results to date and is consistent with the overall approach advocated by the MRC. Up-scaling the intervention to the level of a cluster-randomised control trial will allow definitive assessment of effectiveness and an economic evaluation. Outcomes will include those of interest to policy makers (i.e. healthcare utilisation rates, hospital referral rates, medication costs and overall healthcare costs) and patients (i.e. measures of satisfaction with care or patient-centredness (329)). To optimize the relevance of future research on the MY COMRADE intervention for patient-centred care, public and

patient involvement will be sought in the governance, priority setting, and conduct of the research. Patient representatives will be invited to sit on the project advisory group for the trial, asked to help identify outcome priorities, and contribute to the development of patient information leaflets.

The range of methodological and theoretical approaches used here warrant greater consideration by other researchers interested in quality improvement and intervention development. We have shown that the Behaviour Change Wheel is useful for operationalising the guidance of the MRC for intervention development. However, the time required to adhere to each step of the MRC process is considerable and works against the urgency with which many healthcare interventions are required (335). As experience with these models grows, more pragmatic approaches to intervention development may emerge.

The applicability of clinical evidence to the management of patients with multimorbidity must be improved. As discussed in Chapter 3, reanalysis of trial data and preferential enrolment of patients with common combinations of chronic diseases into trials will help (336). Focusing future trials on the impact and outcomes associated with multimorbidity (i.e. health utilisation, treatment burden, patient illness perceptions etc.) may lead to more clinically and economically meaningful research outputs (143).

Undergraduate and post-graduate medical curricula lack content and skills training on the clinical management of multimorbidity (27). The checklist and collaborative approach to decision-making incorporated in the MY COMRADE intervention could be easily adapted for educational use, either with data from vignettes or patients seen in practice. Educational research is warranted to determine if such an adaption provides

an effective learning experience for students and GP trainees in the management of medications for patients with multimorbidity.

11.7. Conclusion

This thesis responds to the call for interventions to improve patient-centred medication management in multimorbidity. The choice of intervention option was not clear at the outset. However, taking the time to explore the difficulties encountered by GPs in clinical practice helped to reveal pragmatic solutions. Careful application of existing and new evidence to models of behaviour and behaviour change have led to the development of a novel intervention which fits well into clinical practice. Thus, this work has made a meaningful contribution to our understanding of chronic disease care in general practice; the process of intervention development in areas of clinical complexity; and hopefully, the improvement of healthcare delivered to and experienced by patients with multimorbidity.

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Appendix I. Supplementary material for Chapter 5. Systematic review

The materials in this appendix are online supplements to the published version of the systematic review.

Supplementary material 1. Review protocol

Study protocol for a systematic search, appraisal and synthesis of qualitative research on GPs experience of patients with multimorbidity.

Objectives (defining the focus)

1. To search the medical and grey literature in a systematic way to retrieve qualitative research studies addressing difficult decisions encountered by GPs in the medical management/prescribing for patients with multimorbidity.

2. To appraise the quality of studies retrieved using the CASP criteria (198) for appraising qualitative research.

3. To conduct a synthesis of retrieved studies using the meta-ethnographic method (192).

4. To interpret the synthesized literature in a way which will define what is known on this topic in a generalisable way.

5. To develop and refine future research questions using this synthesized literature, and address clinical needs in this area.

Design

Systematic appraisal and synthesis of qualitative research.

Sampling

As purposive/theoretical sampling of qualitative research studies has not been validated, a comprehensive search of relevant databases, grey literature, hand searching of relevant journal and references of included studies will be completed to retrieve all relevant studies in this area. This approach will reduce the risk that any relevant data is excluded.

Search Strategy

- Electronic searches of specialist databases: EMBASE, Medline, CINAHL, PsychInfo, ASC, Social Science Citation Index using both database specific search terms and validated methods for retrieving qualitative studies.
- Supplemented by searches of databases of grey literature, contacting other qualitative health researchers in relevant areas, searching reference lists of studies retrieved

Inclusion criteria

Papers involving all of the following will be included

1. Studies using recognised qualitative research methods
2. Participants are general practitioners (or any practitioner who fulfils the role of a GP/ primary care physician/ family physician etc.)
3. Papers that concern multi-morbidity or multiple chronic conditions where there is no index condition, or one condition is not considered more important than the others.

The primary focus is to review the literature on medications management in multi-morbidity, but papers with a broader focus are included in the search to increase the number of relevant papers retrieved.

Making decisions on inclusion: Citations that are returned from our search strategy will be title scanned. The abstracts will be read for papers with relevant titles. Full papers will be retrieved for papers with relevant abstracts or potentially relevant or ambiguous abstracts (197). Full papers will be reviewed by two researchers.

Quality assessment

Quality assessment will performed using the CASP tool (198). The quality assessment will be used when evaluating the contribution of different papers to the synthesis findings, and to describe the range of quality that exists for the papers included. Quality appraisal will not be used to exclude studies that otherwise meet the inclusion criteria.

Data Extraction

The source material are the included texts. Data on the study design and settings, research methods, and main themes (participants' quotes and authors' interpretations) will be extracted. One researcher will extract data from all studies and to assess the reliability of this data extraction, and a second researcher will extract data from a selection of studies. The data (participants' quotes and authors' interpretations) will be recorded as verbatim extraction where possible to limit the loss of important detail. Data will be extracted from findings that are relevant to our research question rather than from the paper as a whole (i.e. difficult decision making/prescribing in patients with multi-morbidity rather than experience of multimorbidity overall).

Synthesis strategy

The synthesis will be undertaken using the seven step meta-ethnographic method (details below) (192). An interpretive approach rather than an integrative approach will be used (337). Interpretative synthesis involves techniques to identify related concepts in the original studies, which are then reworked and reformulated to extend theory and develop new constructs. Integrative approaches on the other hand involve quantification and systemic integration of data. In this review, concepts will not be specified *a priori*, and will not be rigidly defined. As per Estabrooks et al. the review question is focused on similar populations (GPs) or general themes (management of multimorbidity) (338). Other than this, the key concepts and themes will be sought inductively.

Data analysis/synthesis

<u>Meta-ethnography – the seven steps</u>

1. Getting started. This will involve stating the specific research question we aim to answer, and the contribution that it will make to current debates in this field.

2. Deciding what is relevant to the initial interest. Noblit and Hare stated that the scope of a meta-ethnography is more restricted than that of a narrative review, to avoid making gross generalisations across disparate fields (192). It includes several distinct processes such as i) defining the focus; ii) locating relevant studies; iii) making decisions on inclusion; and iv) quality assessment. Sampling may be conducted theoretically until saturation is reached, but it is not possible to establish the population of studies from which to sample without first identifying all relevant studies.

3. Reading the studies. Included studies will be carefully read to identify the nature of the study, the type of scenarios discussed, the study setting, study participants, and the main findings. Studies may be grouped together according to shared perspectives, settings or contexts, guided by the research question. The different contributions of each study to the review will be examined to determine if some appear to have more important findings than others (in narrative synthesis this would be termed weighting). Quality assessment will be conducted at this stage, and the contribution of each study will be considered with reference to its quality, validity and trustworthiness.

4. Determining how studies are related. The major themes from each study will be recorded in a grid. These themes will initially be generated from first order interpretations (FOIs) or participants' views. Second order interpretations (SOIs) will be extracted as author interpretations. Comparisons will be made between studies for recurring concepts (which may include similar or disparate findings) and absences of these concepts. Overarching themes that encompass the major findings from all studies will be constructed. Each cell of the grid will be considered in turn to ensure that the main themes from each paper are encompassed in overarching themes.

5. Translating the studies into each other (i.e. constructing a common rubric across studies). This involves identifying the same themes that are expressed differently across studies, and viewing these in relation to each other.

6. Synthesizing translations. This step is not mechanistic: it involves interpreting the translated contributions from each study to the overarching themes, and assessing how these contributions relate to each other. The two types of translation described by Noblit and Hare (192) will be performed: reciprocal translation (accounts are directly comparable) and refutational translation (the accounts are oppositional). Third order

interpretations (TOIs) will be generated by combining the FOIs and SOIs across studies. The combination of TOIs will allow a line of argument to be constructed. The line of argument describes all the concepts in a paragraph; breakdown of the principal features of the line of argument are reflected in the third order interpretations (TOIs). TOIs are generally expressed as a testable hypothesis. TOIs are consistent with the original study results while also extending beyond them; they justify the claim the meta-ethnography achieves more than a traditional review, in relation to a focused research question.

7. Expressing the synthesis. This depends on who we are targeting: clinicians, researchers or policy makers. We will take the additional step suggested by Britten et al. (339): to consult with the authors of included primary studies to test the validity of the interpretations developed during the synthesis and the extent to which they are supported by the primary data. This is most likely to be useful where the number of primary studies is small but the authors of the primary studies may have useful insights into the possible accuracy and generalisability of the synthesis.

Expected output of research

1. Interpretation and synthesis of qualitative research to be published in peer reviewed journals

2. Comprehensive description of work that has been conducted in this area

3. New interpretation across studies to highlight generalisable and outlying findings

4. Direction for the next steps or the research required to improve the quality of medicines management in patients with multi-morbidity, and inform the next stage of a PhD research project.

5. Presentations of the synthesis findings to different audiences.

Supplementary material 2. Search terms for systematic review

Locating relevant studies

The following databases were searched using database specific search terms and validated methods for retrieving qualitative studies (194-196): EMBASE (Elsevier), Medline (Ovid), CINAHL, PsycInfo, Academic Search Complete, SocIndex, Social Science Full Text (all Ebsco). For the published review, this search was last updated on 21st September 2012. (An updated search is available in supplementary material 27.)

Supplementary search

The database search was supplemented by searching through the references of included articles (this yielded one relevant article). The following grey literature databases were searched: WORLDCAT via the Online Computer Library Center (OCLC), Proquest, and PapersFirst via OCLC, ASSIA (Applied Social Sciences Index and Abstracts), Directory of Open Access Books (DOAB) and Ebrary.

1. Search Terms for Database Embase, Platform: Elsevier

(Qualitative search terms were taken from Walters et al. (195).)

#1.1: interview*:ab,ti
#1.2: 'health care organization'/exp
#1.3:experiences:ab,ti
#1.4:'qualitative research'/exp
#1: #1.1 OR #1.2 OR #1.3 OR #1.4
#2.1: comorbid*:ab,ti
#2.2: morbid*:ab,ti
#2.3: (multi* NEXT/3 (disease* OR ill* OR condition*)):ab,ti
#2.4: pluripathology:ab,ti
#2.5: (chronic NEXT/3 (disease* OR ill* OR condition* OR disorder* OR health OR medication* OR syndrome* OR symptom*)):ab,ti
#2.6: multimorbid*:ab,ti
#2.1 OR #2.2 OR #2.3 OR #2.4 OR #2.5 OR #2.6
#2: #2.1 OR #2.2 OR #2.3 OR #2.4 OR #2.5 OR #2.6
#3: 'prescription'/exp OR 'inappropriate prescribing'/exp OR 'clinical decision

making'/exp OR 'medical decision making'/exp OR 'polypharmacy'/exp OR 'clinical practice'/exp OR 'medical practice'/exp
#4.1:'general practice'/exp
#4.2:'general practitioner'/exp OR 'general practitioners'/exp
#4.3:'family medicine'/exp
#4.4:'family health'/exp
#4.5:'primary health care'/exp
#4.6: 'primary medical care'/exp
#4.7:'ambulatory care'/exp
#4.8:'community care'/exp
#4.1 OR #4.2 OR #4.3 OR #4.4 OR #4.5 OR #4.6 OR #4.7 OR #4.8
#4: #4.1 OR #4.2 OR #4.3 OR #4.4 OR #4.5 OR #4.6 OR #4.7 OR #4.8
#5: #1 AND #2 AND #3 AND #4
#6: #5 AND ('clinical trial'/de OR 'cohort analysis'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'cross-sectional study'/de OR 'randomised controlled trial'/de OR 'retrospective study'/de OR 'case control study'/de OR and 'statistical model'/de)
#7: #5 NOT #6

2. Search Terms for Database CINAHL, Platform: EBSCO

(Qualitative terms taken from Wilczynski NL, Marks S, Haynes RB.(194).)

S1	SU multimorbidity OR TI multimorbidity OR AB multimorbidity
S2	SU multimorbid* OR TI multimorbid* OR AB multimorbid*
S3	SU multi# morbid* OR TI multi# morbid* OR AB multi# morbid*
S4	SU (multiple chronic N3 (disease* OR illness* OR condition*)) OR TI (multiple chronic N3 (disease*OR illness* OR condition*)) OR AB (multiple chronic N3 (disease*OR illness* OR condition*))
S5	SU (chronic N3 (disease* OR illness* OR condition*)) OR TI (chronic N3 (disease*OR illness* OR condition*)) OR AB (chronic N3 (disease*OR illness* OR condition*))
S6	SU pluripathology OR TI pluripathology OR AB pluripathology
S7	SU comorbidity OR TI comorbidity OR AB comorbidity
S8	SU comorbid* OR TI comorbid* OR AB comorbid
S9	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
S10	SU 'family medicine' OR TI 'family medicine' OR AB 'family medicine'
S11	SU 'family practice' OR TI 'family practice' OR AB 'family practice'
S12	SU general practice' OR TI 'general practice' OR AB 'general practice'
S13	SU general practitioner*' OR TI 'general practitioner*' OR AB 'general practitioner*'
S14	SU family physician* OR TI family physician* OR AB family physician*
S15	SU primary care OR TI primary care OR AB primary care
S16	SU primary health care OR TI primary health care OR AB primary health care
S17	SU primary medical care OR TI primary medical care OR AB primary health care
S18	SU ambulatory care OR TI ambulatory care OR AB ambulatory care
S19	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18
S20	SU Decision making OR TI Decision making OR AB Decision making
S21	SU health care delivery OR TI health care delivery OR AB health care delivery
S22	SU Prescribing OR TI Prescribing OR AB Prescribing

S23	SU polypharmacy OR TI polypharmacy OR AB polypharmacy
S24	SU ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*)) OR TI ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*)) OR AB ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*))
S25	SU (multi* N3 (drug* OR medication* OR prescription*)) OR TI (multi* N3 (drug* OR medication* OR prescription*)) OR AB (multi* N3 (drug* OR medication* OR prescription*))
S26	SU clinical practice OR TI clinical practice OR AB clinical practice
S27	S20 or S21 or S22 or S23 or S24 or S25 or S26
S28	TI interview OR AB interview
S29	SU audiorecording OR MW audiorecording
S30	MW qualitative stud* OR TI qualitative stud* OR AB qualitative stud*
S31	S28 or S29 or S30
S32	TI morbidity OR AB morbidity OR MW morbidity
S33	S9 or S32
S34	S19 and S27 and S31 and S33

3. Search terms for Database Medline, Platform OVID.

(Qualitative search terms taken from Wong et al. (193).)

1. interview:.mp.
2. experience:.mp.
3. qualitative.tw.
4. exp Qualitative Research/
5. 1 or 2 or 3 or 4
6. exp Family Practice/or exp General Practice/
7. exp General Practitioners/
8. exp Family Practice/or family medicine.mp.
9. exp Primary Health Care/
10. exp Physicians, Family/
11. exp Physicians, Primary Care/
12. exp Ambulatory Care/
13. 6 or 7 or 8 or 9 or 10 or 11 or 12
14. co-morbid:.ti. or co-morbid:.ab. or comorbid:.ti. or comorbid:.ab. or co morbid:.ab. or co morbid:.ti.
15. morbid:.ti. or morbid:.ab.
16. (multi: adj3 (ill: or disease: or condition:)).ab,ti.
17. pluripathology.ab,ti.
18. (chronic adj3 (disease: or ill: or condition: or disorder: or health or medication: or syndrome: or symptom:)).ab,ti.
19. (multimorbid: or multi morbid: or multi-morbid:).ab,ti.
20. 14 or 15 or 16 or 17 or 18 or 19
21. exp Decision Making/
22. exp Professional Practice/
23. exp Physician's Practice Patterns/

24. exp Inappropriate Prescribing/
25. exp Drug Prescriptions/
26. exp Polypharmacy/
27. 21 or 22 or 23 or 24 or 25 or 26
28. 5 AND 13 AND 20 AND 27

4. Search terms for Database PsycInfo, Platform EBSCO

(Qualitative search terms taken from McKibbon et al. (196).)

S1	SU multimorbidity OR TI multimorbidity OR AB multimorbidity
S2	SU multimorbid* OR TI multimorbid* OR AB multimorbid*
S3	SU multi# morbid* OR TI multi# morbid* OR AB multi# morbid*
S4	SU (multiple chronic N3 (disease* OR illness* OR condition*)) OR TI (multiple chronic N3 (disease*OR illness* OR condition*)) OR AB (multiple chronic N3 (disease*OR illness* OR condition*))
S5	SU (chronic N3 (disease* OR illness* OR condition*)) OR TI (chronic N3 (disease*OR illness* OR condition*)) OR AB (chronic N3 (disease*OR illness* OR condition*))
S6	SU pluripathology OR TI pluripathology OR AB pluripathology
S7	SU comorbidity OR TI comorbidity OR AB comorbidity
S8	SU comorbid* OR TI comorbid* OR AB comorbid
S9	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
S10	SU 'family medicine' OR TI 'family medicine' OR AB 'family medicine'
S11	SU 'family practice' OR TI 'family practice' OR AB 'family practice'
S12	SU general practice' OR TI 'general practice' OR AB 'general practice'
S13	SU general practitioner*' OR TI 'general practitioner*' OR AB 'general practitioner*'
S14	SU family physician* OR TI family physician* OR AB family physician*
S15	SU primary care OR TI primary care OR AB primary care
S16	SU primary health care OR TI primary health care OR AB primary health care
S17	SU primary medical care OR TI primary medical care OR AB primary health care
S18	SU ambulatory care OR TI ambulatory care OR AB ambulatory care
S19	S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18
S20	SU Decision making OR TI Decision making OR AB Decision making
S21	SU health care delivery OR TI health care delivery OR AB health care delivery
S22	SU Prescribing OR TI Prescribing OR AB Prescribing
S23	SU polypharmacy OR TI polypharmacy OR AB polypharmacy
S24	SU ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*)) OR TI ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*)) OR AB ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*))
S25	SU (multi* N3 (drug* OR medication* OR prescription*)) OR TI (multi* N3 (drug* OR medication* OR prescription*)) OR AB (multi* N3 (drug* OR medication* OR prescription*))
S26	SU clinical practice OR TI clinical practice OR AB clinical practice
S27	SU experience level OR TI experience level OR AB experience level

S28 SU morbidity OR TI morbidity OR AB morbidity
S29 S9 or S28
S30 S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27
S31 S19 and S29 and S30
S32 TI experiences OR AB experiences
S33 TI interview* OR AB interview*
S34 TI qualitative OR AB qualitative
S35 S32 or S33 or S34
S36 S31 and S35
S37 CC 3410 (Professional Education & Training)
S38 CC 3430 (Professional Personnel Attitudes & Characteristics)
S39 CC 3400 (Professional Psychological & Health Personnel Issues)
S40 S37 or S38 or S39
S41 S30 or S40
S42 S19 and S29 and S41
S43 S35 and S42

5. Search terms used for Academic Search Complete; Social Sciences Full Text (H.W. Wilson);SocINDEX with Full Text, Platform EBSCO

S1 Qualitative research OR AB qualitative OR TI Qualitative
S2 SU attitude* of health personnel
S3 SU questionnaire* or AB questionnaire* OR TI questionnaire*
S4 'nursing methodology research'
S5 AB interview* OR TI interview* OR SU interview*
S6 AB focus group* OR TI focus group* OR SU focus group*
S7 SU multimorbidity OR TI multimorbidity OR AB multimorbidity
S8 SU multimorbid* OR TI multimorbid* OR AB multimorbid*
S9 SU multi# morbid* OR TI multi# morbid* OR AB multi# morbid*
S10 SU (multiple chronic N3 (disease* OR illness* OR condition*)) OR TI (multiple chronic N3 (disease*OR illness* OR condition*)) OR AB (multiple chronic N3 (disease*OR illness* OR condition*))
S11 SU (chronic N3 (disease* OR illness* OR condition*)) OR TI (chronic N3 (disease*OR illness* OR condition*)) OR AB (chronic N3 (disease*OR illness* OR condition*))
S12 SU pluripathology OR TI pluripathology OR AB pluripathology
S13 SU comorbidity OR TI comorbidity OR AB comorbidity
S14 SU comorbid* OR TI comorbid* OR AB comorbid
S15 S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14
S16 S1 or S2 or S3 or S4 or S5 or S6
S17 SU 'family medicine' OR TI 'family medicine' OR AB 'family medicine'
S18 SU 'family practice' OR TI 'family practice' OR AB 'family practice'
S19 SU general practice' OR TI 'general practice' OR AB 'general practice'
S20 SU general practitioner*' OR TI 'general practitioner*' OR AB 'general practitioner*'
S21 SU family physician* OR TI family physician* OR AB family physician*
S22 SU primary care OR TI primary care OR AB primary care

S23 SU primary health care OR TI primary health care OR AB primary health care
S24 SU primary medical care OR TI primary medical care OR AB primary health care
S25 SU ambulatory care OR TI ambulatory care OR AB ambulatory care
S26 S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25
S27 S15 and S16 and S26
S28 SU Decision making OR TI Decision making OR AB Decision making
S29 SU health care delivery OR TI health care delivery OR AB health care delivery
S30 SU Prescribing OR TI Prescribing OR AB Prescribing
S31 SU polypharmacy OR TI polypharmacy OR AB polypharmacy
S32 SU ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*)) OR TI ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*)) OR AB ((inappropriate OR appropriate OR suboptimal OR under OR over OR optimal) N3 (prescribing OR prescription OR medication* or drug*))
S33 SU (multi* N3 (drug* OR medication* OR prescription*)) OR TI (multi* N3 (drug* OR medication* OR prescription*)) OR AB (multi* N3 (drug* OR medication* OR prescription*))
S34 SU clinical practice OR TI clinical practice OR AB clinical practice
S35 S28 or S29 or S30 or S31 or S32 or S33 or S34
S36 S27 and S35
S37 morbidity OR TI morbidity OR AB morbidity
S38 S15 or S37
S39 S16 and S26 and S35 and S38

Supplementary material 3. Data extraction form for systematic review

Author	
Background of authors	
Country of study	
Year of publication	
Setting of study	
Aims (Phenomena of Interest)	
Participants GPs (n) Others (profession, n)	
Professional Orientation/Focus of GPs	
Methodology	
Methods Data collection Data analysis	
Main findings	

Adapted from the Joanne Briggs data extraction form (199).

Supplementary material 4. Table 15. ENTREQ statement

Table 15. Enhancing transparency in reporting the synthesis of qualitative research (ENTREQ) statement

No	Item	Guide and description
1	Aim	To synthesize the existing published literature on the perceptions of GPs or their equivalent on the clinical management of multimorbidity and determine targets for future research that aims to improve clinical care in multimorbidity
2	Synthesis methodology	Meta-ethnography
3	Approach to searching	Pre-planned comprehensive search strategies to seek all available studies
4	Inclusion criteria	Qualitative research methods (i.e. data collection and analysis) Population: General practitioners or their equivalent Topic: Clinical management of multimorbidity No language or year limits
5	Data sources	Electronic databases (EMBASE, Medline, CINAHL, PsychInfo, ASC, Social Science Citation Index). Grey literature databases included WORLDCAT via the Online Computer Library Center (OCLC), Proquest, PapersFirst via OCLC, ASSIA (Applied Social Sciences Index and Abstracts), Directory of Open Access Books (DOAB) and Ebrary. Last search update for published paper was on 21st September 2012.
6	Electronic Search strategy	Literature search terms are described in detail in Supplementary material 1.
7	Study screening methods	The titles and abstracts of retrieved citations were scanned by one reviewer (CS). Full papers were ordered for all potentially relevant abstracts. Full papers were reviewed by two researchers (CS, CB) and were included if they met our inclusion criteria.
8	Study characteristics	The characteristics of the included studies are presented in Table 1.
9	Study selection results	The studies screened are described in brief in Figure 4 (Flow diagram) and in greater detail in Supplementary material 5.
10	Rationale for appraisal	One researcher (CS) formally assessed quality. Decisions on inclusion and relevance of studies to our research question was independently conducted by two reviewers (CS, CB)
11	Appraisal items	The CASP tool was used to appraise all included studies
12	Appraisal process	Quality assessment was formerly conducted by one reviewer (CS)
13	Appraisal results	The overall quality of the ten included studies was high, with all articles meeting the majority of CASP criteria. The most common weaknesses were related to data saturation (not reported in six studies) and reflexivity (not discussed in five studies). GPs with

		academic/research affiliations were over-represented as research subjects in five studies, representing a potential source of bias. An overview of the quality appraisal is available in Supplementary material 6 and the quality assessments for each included paper is available here: https://drive.google.com/file/d/0BxJS5MOWiRUtQWo0ek4zaXlSaXc/view?usp=sharing
14	Data extraction	A data extraction form was derived from the Johanna Briggs data extraction form (Supplementary material 3). All text under the headings "results /conclusions" was considered data from the primary studies unless it was stated to be given by a healthcare professional that was not a GP. This data was extracted electronically and entered into a computer software package to facilitate data management.
15	Software	NVivo 9
16	Number of reviewers	Three reviewers – CS, SMH, CB.
17	Coding	The meta-ethnographic approach described by Noblit & Hare informed coding of data. Relevant data was initially open coded, with in vivo coding used where possible. Axial coding was informed by steps 4-6 of the meta-ethnographic approach.
18	Study comparison	Overarching concepts that represented the entire dataset were formulated after initial readings of the included papers. The specific contribution of each paper to each key concept was then determined.
19	Derivation of themes	Themes were derived initially as key concepts representing the entire dataset. The contribution of each paper to each key concept was determined and the meaning of the key concept was modified based on the comparisons and synthesis of contributions to the key concept.
20	Quotations	Quotations from the primary studies are provided in Table 2 to illustrate themes/constructs.
21	Synthesis output	A line of argument was derived which represents a statement of GPs' perception of multimorbidity. The key concepts demonstrate key areas that have arisen from existing qualitative work, in a variety of health care settings, and as such gives direction to on-going research and intervention development in this field.

Supplementary material 5. Excluded studies

Exclusions were made by applying the following criteria in this order: not qualitative research; not dealing with multimorbidity/focus is on index diseases; not primary care/GP. Once one reason for exclusion was found, no other reasons were sought. For foreign language titles, Google translate was used to ascertain if the title was applicable. Table 15 shows the number of citations returned from each database, the number that remained after removal of duplicates, and the number excluded on the basis of title or abstracts. Full text papers were retrieved for all remaining citations. These were read, and decisions made regarding their inclusion by two reviewers. The reasons for exclusion of full text papers are provided below.

Table 16. Reasons for excluded papers stratified by database

	Citations	Duplicates between databases*	After removal of duplicates	Excluded by title/abstract	Not Primary Care	Not Qualitative Research	Not Multimorbidity	Not Doctor's perspective	Full text read	Not Primary Care	Not Qualitative Research	Not Multimorbidity	Not Doctor's perspective	Included	Abstract only - no full text paper	Excluded by Full text
EMBASE	1121	16	1105	1082	34	577	447	24	23	0	11	7	0	4	1	19
CINAHL	65	6	59	55	0	14	32	9	4	0	0	3	0	1	0	3
PsycInfo	184	47	137	134	0	48	72	14	3	0	0	2	0	1	0	2
Academic Search Complete	198	58	140	137	2	67	65	3	3	0	0	2	0	1	0	2
Medline (Ovid)	437	73	364	360	12	185	153	10	4	0	0	2	0	2	0	2
Total	2005	200	1805	1768	48	891	769	60	37	0	11	16	0	9	1	28

*Duplicates searched for in order of EMBASE/CINAHL/Medline/PsycInfo/ASS)

Detail on excluded full-texts

EMBASE

Full texts retrieved for 23 citations; 18 were excluded, one was only available in abstract form, and four were included.

1. Ampt AJ, et al. Attitudes, norms and controls influencing lifestyle risk factor management in general practice. BMC Family Practice 2009,10:59. Concerns lifestyle modification in the management of chronic disease, but does not incorporate multimorbidity.
2. Balla J, et al. Clinical decision making in a high-risk primary care environment: A qualitative study in the UK. BMJ Open 2012;2(1). Concerns decision making in out of hours care, not multimorbidity.
3. Boyd CM, et al. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA. 2005 Aug 10;294(6):716-24. Review of one case vignette, and application of guidelines.
4. Davidson W, et al. Physician characteristics and prescribing for elderly people in New Brunswick: Relation to patient outcomes Canadian Medical Association Journal. 1995. 152. 8. Quantitative analysis only.
5. Demirkol A, et al. Providing healthcare for people with chronic illness: the views of Australian GPs. Med J Aust. 2003 Sep 1;179(5):269.Does not focus on multimorbidity.
6. Fortin M, et al. Multimorbidity's many challenges. BMJ. 2007 334(7602):1016-7. Editorial.
7. Horne R, et al. Shared care: a qualitative study of GPs' and hospital doctors' views on prescribing specialist medicines. Br J Gen Pract. 2001 Mar;51(464):187-93.

Relates to GPs perceptions of shared care between primary and secondary care, not multimorbidity.

8. Hudon C, et al. Patient-centered care in chronic disease management: A thematic analysis of the literature in family medicine. Patient Educ Couns. 2012 Aug;88(2):170-6. Analysis of existing literature rather than primary data.
9. Kadam U. Redesigning the general practice consultation to improve care for patients with multimorbidity. BMJ.2012;345:e6202. Editorial
10. Loeb DF, et al. Primary care physician perceptions on caring for complex patients with medical and mental illness. J Gen Intern Med. 2012 Aug;27(8):945-52. Epub 2012 Feb 28. Focuses on the interaction between mental and physical illness, using mental illness an index illness.
11. Mangin D, et al.Beyond diagnosis: rising to the multimorbidity challenge. BMJ. 2012 Jun 13;344:e3526. Editorial.
12. Martin C, Rohan BG. Chronic illness care as a balancing act. A qualitative study. Australian family physician. 2002. Concerns models of care rather than delivery of care or multimorbidity.
13. May C, et al. Framing the doctor-patient relationship in chronic illness: a comparative study of general practitioners' accounts. Sociol Health Illn. 2004 Mar;26(2):135-58. Re-analysis of previously gathered qualitative data to examine the doctor-patient relationship.
14. Salisbury, 2012. Editorial.
15. Saltman, 2004. Editorial.
16. Shepherd, 2012. Letter in response to Mercer article.
17. Webster, 2000. Letter.

18. Weiner M, et al. Perspectives of general practitioners towards evaluation and treatment of cardiovascular diseases among older people. J Prim Health Care. 2009 Sep;1(3):198-206. Although reported as mixed methods, the qualitative component was just 'narrative comments' at the end of a quantitative/likert questionnaire.
19. Abstract only: Limm B, Hughes TB, Boyd C, Rand C. Primary care providers' experiences of assessing and minimizing treatment burden of multimorbid older adults. J Am Geriatr Soc. 2012;60. Abstract from AGS 2012 annual meeting. Study authors contacted – Dr C Boyd – and full account not yet published.
20. Bower, 2011: included.
21. Smith, 2010: included.
22. O'Brien, 2011: included.
23. Marx, 2009: included.

CINAHL

Full texts retrieved for four citations, and three were excluded.

1. Rashidian A, et al. Falling on stony ground? A qualitative study of implementation of clinical guidelines' prescribing recommendations in primary care. Health Policy, 2008 Feb; 85 (2): 148-61. Focused on the implementation of guidelines' prescribing recommendations- not multimorbidity.
2. Kupka NJ. Interactions between practitioners and patients with chronic illnesses. Rush University, College of Nursing, 2003; Doctoral dissertation – research. Focuses on the use of motivational techniques by GPs in managing chronic disease – not multimorbidity.
3. Lown BA, et al. Mutual influence in shared decision making: a collaborative study of patients and physicians. Health Expectations. Jun 2009, Vol. 12 Issue 2, p160-174.

Concerns characteristics of the doctor-patient relationship and decision making- not multimorbidity.

4. Fried: included.

Medline

Full texts retrieved for four citations, and two were excluded.

1. Müller-Engelmann M, et al. Shared decision making in medicine: the influence of situational treatment factors. Patient Educ Couns. 2011 Feb;82(2):240-6. Concerns situations where shared decision making is an appropriate approach- not multimorbidity.
2. Harries C, et al. Which doctors are influenced by a patient's age? A multi-method study of angina treatment in general practice, cardiology and gerontology.Qual Saf Health Care. 2007 Feb;16(1):23-7. Focuses on management of angina and has only one line on multimorbidity in qualitative section.
3. Solomon: included.
4. Luijks: included.

PsycInfo

Full texts retrieved for three citations, and two were excluded.

1. Peters-Klimm et al. Physicians' view of primary care-based case management for patients with heart failure: A qualitative study. International Journal for Quality in Health Care, Vol 21(5), Oct, 2009. pp. 363-371.Concerns the evaluation of the implementation of a case management programme for heart failure- not multimorbidity.

2. Chew-Graham CA, Hogg T. Patients with chronic physical illness and co-existing psychological morbidity: GPs' views on their role in detection and management. Primary Care Psychiatry 2002, 2:35-39. Focuses on the management and diagnosis of an index condition (depression) in patients with chronic physical disease.
3. Steinman: included.

Academic Search Complete / Social Science Full Text

Full texts were retrieved for three citations, and two were excluded.

1. Malin A, et al. GPs' decision-making--perceiving the patient as a person or a disease. BMC Family Practice. 2012, Vol. 13 Issue 1, p38-43. 6p. Quantitative analysis.
2. Hunt LM, et al. The Changing Face of Chronic Illness Management in Primary Care: A Qualitative Study of Underlying Influences and Unintended Outcomes. Ann Fam Med. 2012. Addresses individual chronic diseases (diabetes and hypertension) but not the presentation of these in tandem.
3. Schuling: included.

Supplementary material 6. Table 17. Quality assessments for systematic review

This table provides a summary of the CASP quality analysis for each paper included in the systematic review.

Table 17. Quality assessments for systematic review

	Smith	Bower	O'Brien	Fried	Marx	Steinman	Solomon	Schuling	Luijks	Anthierens
Was there a clear statement of the aims of the research?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Is a qualitative methodology appropriate?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the research design appropriate to address the aims of the research?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the recruitment strategy appropriate to the aims of the research?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the data collected in a way that addressed the research issue?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Has the relationship between researcher and participants been adequately considered?	Y	N	Y	N	Y	N	N	Y	Y	N
Have ethical issues been taken into consideration?	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the data analysis sufficiently rigorous?	Y	Y	Y	Y	Y	Y	N	N	Y	~
Is there a clear statement of the findings?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
How valuable is the research?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

- Studies by Smith et al., Fried et al., Marx et al. and Schuling et al. involved participants that were strongly involved with academia or medical education rather than full time GPs. GPs in the study by Bower et al. were in a research network.
- Data saturation not discussed by Smith, O'Brien, Steinman, Fried, Solomon or Anthierens.
- Reflexivity not discussed by Bower, Schuling, Steinman, Fried, Solomon, Anthierens.
- How qualitative quotes were chosen was not described in the studies by Luijks, Bower, Schuling.
- Description of analysis in Schuling lacked detail.
- Location for interview not given in Fried, Smith, Schuling, Luijks,
- Deviant cases not discussed in Anthierens.

Supplementary material 7. Table 18. Key concepts and subthemes

Table 18. Key concepts from the included papers and subthemes that occurred with each key concept

Key concept (number of studies this related to)	Sub-themes in each key concept (number of studies this related to)
Disorganisation and fragmentation of care (8)	Structure of primary care (6) Inadequate time (5) Fragmented care and involvement of secondary care (8)
The inadequacy of guidelines and evidence based medicine (10)	Single disease focus (5) Doubts on the evidence underpinning guidelines (5) Guidelines add to complexity (7) Queries on the relevance of disease specific outcomes (6) The use of guidelines for primary prevention (5) Using modified approaches to guidelines (5) Linking guidelines to physician reimbursement (3)
Challenges in delivering patient-centred care (10)	Individualising management (7) Taking a generalist approach (10) Importance of a longitudinal patient-GP relationship(7) The impact of multimorbidity and treatment burden (6) Specific complicating patient characteristics (6)
Challenges in shared decision-making (10)	Discussing risks and outcomes associated with treatment options (8) Using alternative models of decision-making (7) Lack of appropriate communication skills (3) Approaches to changing or deprescribing medications (6)

Appendix II. Supplementary data for Chapter 6. Qualitative interview study.

The materials in this appendix are supplements to the published version of the qualitative interview study.

Supplementary material 8. Topic guides for interviews 1, 10 and 20 showing iterative refinement of interview probes.

Topic Guide Interview 1

Introduction: Data shows that the management of multimorbidity can be difficult for GPs. I want to understand the issues that GPs experience in multimorbidity to see if we can target anything to make the management of these patients easier.

- Describe my background (GP trainee and PhD student).
- Permission to record interview.
- No patient identifying information required.
- Ethics approval gained from ICGP and UCC. Full confidentiality ensured, data will be password protected and stored only in UCC.

Opening questions

- Participant's job title, role, qualifications.
- Length of time in practice, how long in this practice, how many sessions per week.
- Describe practice: size, no of GPs, practice population.
- Any practice protocols on multiple chronic diseases? Do they work?
- What does the term multimorbidity mean?

Description of patients chosen for chart-stimulated recall

- Patient's gender, age, social background, diseases and current medications.
- Describe last four consultations with this patient, beginning with fourth last.

Probes

- Organisation of care
- Role of specialists

- Guidelines
- Polypharmacy
- Adverse drug effects
- Goals of care
- Patient-centredness
- Shared decision making
- What hindered/helped/would have helped

Topic Guide Interview 10

No change in introduction, opening questions and case descriptors.

Probes

- Fragmentation
    - Communication with other healthcare professionals
    - Good experiences and bad experiences
- Goals of care
    - What has influenced these?
- Managing medications
    - What do you do when you look at a list of meds and question their usefulness – how do you respond to that thought?
    - Reasons to change them?
    - Stopping medications?
    - Inherited medications?
    - Other GPs have told me that they stay away from messing with these patients' medicines - do you ever feel like that? Why? What would make it easier for you?
    - Polypharmacy – issues for the patient and/or the doctor
    - Conflicts: ideally patients would not be on these two meds, but patients are far from ideal….. When you were deciding to start this med, how did you decide to use it?
- Are guidelines useful in multimorbidity?

    - What ones do you use? Why?
    - What do guidelines say regarding options?
    - What makes you comfortable in not using them?
- Shared decision-making
    - Approaching this with the patient
- Longitudinal care
- Negative cases: This case seems to be going well for you. Can you think of any cases where you found it hard to decide what to do with the medications?
- Support for patient. Support for doctor.

Topic Guide Interview 20

No change in introduction, opening questions and case descriptors.

Probes

- Communication with other healthcare professionals
- Patient-centred care and goals of care
- Managing medications
    - Not rocking the boat
    - Polypharmacy –What stops you from stopping meds?
    - Who has control of prescribing for these patients?
    - Where does the balance in prescribing decisions lie? How does this balance change with time (years of doctor- patient relationship)? When doctor and patient disagree, how is course of action decided on?
- What helps you decide what is best practice in medical management?
- Shared decision-making
    - Communication strategies around multiple options.
    - Patient attachment to meds
- Longitudinal care and trust. How does this change things?
- What combinations of conditions are challenging?
- Informing patients of adverse drug effects: how much information should we give about options /interactions?

- Next of kin: useful or unwanted input- what would you have done if they were not involved?
- Chronic disease programmes – will this change prescribing for multimorbid patients?
- Any practice processes that help manage medications/safety?

Supplementary material 9. Table 19. COREQ statement

Consolidated criteria for reporting qualitative research (COREQ) statement (340)

Table 19. Consolidated criteria for reporting qualitative research (COREQ) statement

Domain 1: Research team and reflexivity			
Personal Characteristics			
1.	Interviewer/ Facilitator	Which author conducted the interviews?	CS conduced the interviews.
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD*	CS is a medical doctor, has the medical and GP memberships, and is a senior registrar in general practice and a PhD candidate as part of an academic/clinical fellowship programme.
3.	Occupation	What was their occupation at the time of the study?	Academic/clinical research fellow in general practice, with three days per week in research and two days per week in general practice.
4.	Gender	Was the researcher male or female?	Female
5.	Experience and training	What experience or training did the researcher have?	CS received training at the Health Experience Research Group, Oxford University; completed training in NVivo computer assisted qualitative data management; and achieved first class honours in Qualitative Research Methods in University College Cork, Ireland.
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement?	6/20 of the GPs that participated were tutors for the Department of General Practice, University College Cork but there was no other relationship established between the participants and the research team prior to commencing the study.
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e*.g. personal goals, reasons for doing the research*	Participants were aware that CS was a senior registrar in GP and a PhD candidate in General Practice.
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. *Bias, assumptions, reasons and interests in the research topic*	As a fellow member of the profession of General Practice, it is likely that GPs may have opened up more to CS than a non-clinical researcher. However, as an early career GP, CS is also less likely to have conceptual blindness to many of the issues in the day to day

			management of patients in multimorbidity than an established GP.
Domain 2: study design			
Theoretical framework			
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? *e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis*	Grounded Theory as described by Charmaz (166)
Participant selection			
10.	Sampling	How were participants selected? *e.g. purposive, convenience, consecutive, snowball*	20 GPs were interviewed. GP participants were initially purposively sampled from CPD meetings. This method was complemented with snow ball sampling to achieve adequate representation of our sampling frame. Of 21 GPs that signed up from CPD groups, 14 were interviewed. The remaining six participants were snowball sampled to give representation of pre-determined criteria of rural/urban, single/group practice and length of time qualified.
11.	Method of approach	How were participants approached? e*.g. face-to-face, telephone, mail, email*	At CPD meetings for purposive and by contacting individual GPs for snowball sampling based on recommendations from GPs already enrolled and participating.
12.	Sample size	How many participants were in the study?	20
13.	Non-participation	How many people refused to participate or dropped out? Reasons?	Of 21 GPs that signed up from CPD groups, 14 responded to further contact and all 14 were interviewed. The remaining six participants were snowball sampled to give representation of pre-determined criteria of rural/urban, single/group practice and length of time qualified.
Setting			
14.	Setting of data collection	Where was the data collected? e*.g. home, clinic, workplace*	In the GP participants' surgeries or clinics.
15.	Presence of non-	Was anyone else present besides the participants and	No

	participants	researchers?	
16.	Description of sample	What are the important characteristics of the sample? *e.g. demographic data, date*	See Table 3: Almost have were in rural practice; 70% were in group practices and 70% were qualified as GPs for longer than ten years.
Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Early interviews (gp1-3) were reviewed by MB for questions and interview technique. Topic guides were used and reviewed after every interview.
18.	Repeat interviews	Were repeat interviews carried out?	No
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?	All interviews were audio recorded.
20.	Field notes	Were field notes made during and/or after the interview or focus group?	Field notes were made during and immediately after the interviews, and were referred to during the early stages of analysis, and during refinement of the topic guides.
21.	Duration	What was the duration of the interviews or focus group?	GPs were asked to give approximately 30 minutes for each interview. The average length was 42 minutes, range 32-65mins.
22.	Data saturation	Was data saturation discussed?	Yes, conceptual data saturation was achieved at interview 18, as subsequent interviews did not lead to further categories in coding.
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction?	No.
Domain 3: analysis and findings			
Data analysis			
24.	Number of data coders	How many data coders coded the data?	Four data coders coded the data.
25.	Description of the coding tree	Did authors provide a description of the coding tree?	No coding tree was developed but all members of the research team discussed and agreed on the grounded theory approach to analysis a priori.
26.	Derivation of themes	Were themes identified in advance or derived from the data?	Coding was data driven. The first stage involved open coding for GPs' actions in multimorbidity, and the causes, conditions and consequences of these actions. Divergent or disconfirming cases were actively sought. The second stage of coding involved

			categorization of the coded data based on thematic or conceptual similarity.
27.	Software	What software, if applicable, was used to manage the data?	NVivo 10 was used to facilitate data management.
28.	Participant checking	Did participants provide feedback on the findings?	No
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes /findings? Was each quotation identified? e.*g. participant number*	Yes, the source GP for each quote is provided.
30.	Data and findings consistent	Was there consistency between the data presented and the findings?	Quotes are embedded in text so are used to illustrate our findings in participants own language as much as possible.
31.	Clarity of major themes	Were major themes clearly presented in the findings?	Major themes are presented in the results section.
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Subthemes are presented within the major headings. Further details are provided on the cases discussed in Supplementary material 10.

Supplementary material 10. Overview of cases discussed by GPs in chart-stimulated recall

Age (years)	Gender (m/f)	List of chronic diseases provided by GP
60	f	Hypertension, hypothyroidism, type 2 diabetes mellitus, asthma, hiatus hernia and gastro-oesophageal reflux.
78	m	Type 2 diabetes mellitus, multiple PEs /DVTs, osteoarthritis (right total knee replacement), hypothyroidism, BPH, hypertension, glaucoma, depression, irritable bowel syndrome, deafness, dyspepsia, gallstones, haemorrhoids
61	m	Ischaemic heart disease (MI, recent bypass), COAD, right heart failure, recent PE, delirium recurrent /agitation at night, type 2 diabetes mellitus, BPH, hyperlipidaemia
51	f	Hyperlipidaemia, hypertension, carpal tunnel syndrome, benign positional /recurrent vertigo, migraine, cerebrovascular disease, depression, medically unexplained symptoms /chronic pain query cause, chronic Lyme disease, hypothyroidism, dyspepsia.
78	f	Hypertension, atrial fibrillation, hyperlipidaemia, hearing loss, schizophrenia, depression
50	m	IHD, hypothyroidism, haemochromatosis, obesity, hypertension, hyperlipidaemia
50	f	Depression, anxiety, alcoholism, recurrent deliberate self-harm, bipolar affective disorder, seizure disorder, menorrhagia, hypothyroidism, diarrhoea under investigation, cerebrovascular disease
60	m	Type 2 diabetes mellitus, multiple sclerosis, cognitive impairment, lumbar disc issues with leg pain, high PSA, anaemia query cause, depression, hypertension
76	f	Hypertension, CKD, hyperlipidaemia, cervical cancer, chronic lower back pain, recent PE, schizophrenia
84	f	Recurrent DVT, IHD: recent angina, COAD, osteoarthritis with bilateral total hip replacements, practically blind, hypertension, recurrent falls with fractured distal radius, osteoporosis, glaucoma, constipation
84	f	Ischaemic heart disease: MI 1998, hypertension, hyperlipidaemia, chronic back pain due to osteoarthritis and disc disease, squamous cell carcinoma of skin, DVT last year, prostate cancer, metastatic bone disease, osteoporosis, constipation
72	f	Anxiety, depression, obesity, osteoarthritis with prior total knee replacement, GORD, urinary frequency, urgency & incontinence, recurrent UTIs, hyperlipidaemia, hypertension, gout, IHD: angina,

		fibroids, COAD/asthma, cardiac failure, type 2diabetes mellitus, cognitive impairment
77	m	Polymyalgia rheumatica, multiple PEs, iron deficiency anaemia, Crohn's disease, left lung lobectomy for lung cancer, type 2 diabetes, left ventricular failure, asthma/COAD, obesity
67	f	Depression, anxiety, type 2 diabetes, non-ischaemic dilated cardiomyopathy with cardiac failure, alcohol abuse
39	f	Recurrent depression, chronic back pain, bilateral PEs, psychoactive substance abuse, post-traumatic stress disorder/neurosis
43	m	Hepatitis C, HIV, COAD /asthma, depression with psychotic features, anxiety, addiction /substance abuse, dyspepsia
81	f	COAD and asthma, peripheral vascular disease: left external iliac artery stenosis, macular degeneration with disciform scar on left side and visual impairment, osteoarthritis & hip replacement, chronic sinusitis, shortness of breath under investigation (being treated as IHD), stage 2 CKD, glaucoma
86	f	Anxiety, osteoporosis, stage 3 CKD, hypothyroidism, facial squamous cell carcinoma requiring zygoma excision, IHD: single vessel coronary disease with a stent in 2009, atrial fibrillation, cardiac failure, musculoskeletal pain: prior shoulder dislocation, left knee replacement, right thumb fracture, fracture left side, stress urinary incontinence, COAD, diverticulosis, aortic stenosis with valvuloplasty 2012, constipation
75	m	Cerebrovascular disease/stroke: history of a right occipital lobe haemorrhage with a residual left homonymous hemianopia, IHD: minor coronary disease, hypertension, aortic stenosis moderate, anxiety, irritable bowel syndrome, dyspepsia with prior duodenal ulcer, seizure disorder.
75	m	Morbid obesity, haemochromatosis, hypertension, dyspepsia, autoimmune lichen planus, type 2 diabetes mellitus, gout, osteoarthritis: right and left hip replacement, transitional cell carcinoma of the bladder in 2012 - currently in remission, CKD, peripheral vascular disease: prior aortic aneurysm repair, awaiting a femoral popliteal bypass, colonisation with MRSA undergoing treatment, cardiac failure, COAD, constipation.
39	m	Gender reassignment with hormonal feminization, dyspepsia, anaemia query cause, high risk for thromboembolic disease.
71	m	BPH, depression, IHD, hyperparathyroidism with hypercalcaemia
79	f	Type 2 diabetes mellitus, hypertension, hyperlipidaemia, hypothyroidism, urge incontinence/irritable bladder, cerebrovascular disease – prior amaurosis fugax and transient ischaemic attacks, psoriatic arthritis, temporal arthritis, cataracts

		from steroids, glaucoma, osteopenia, recurrent UTIs, vulval lichen sclerosis
52	f	Depression, anxiety/panic, hypertension, mucinous ovarian cyst with recent hysterectomy, Anti –nuclear antibody positive arthritis, chronic lower back pain with prior cauda equine syndrome, obesity, acne.
83	f	Malignant melanoma, hypertension, atrial fibrillation, cerebrovascular disease – transient ischaemic attacks, breast cancer with double mastectomy, type 2 diabetes mellitus, dementia, pernicious anaemia, urinary incontinence, CKD, depression.
75	f	IHD (MIs and stents), depression, cerebrovascular disease: stroke, vascular Parkinson's, dementia, type 2 diabetes mellitus, osteoarthritis, fibromyalgia, temporal arteritis, osteoporosis, recurrent UTIs, irritable bladder, cataracts with decreased vision, glaucoma
62	m	Ischaemic heart disease (MI with cardiac arrest in 2011, now post bypass surgery), recent PE, hypothyroidism, hyperlipidaemia, depression, type 2 diabetes mellitus
85	f	Recurrent DVTs and PEs with greenfield filter, hypothyroidism, hyperlipidaemia, shoulder problems and sacroiliac joint pain, chronic cough likely COAD, tinnitus, diverticulosis, hypertension
60	m	Anxiety, depression, urinary incontinence, COAD/asthma-mild, impaired glucose tolerance, hypertension, hyperlipidaemia, constipation, dyspepsia, learning disability
84	f	IHD, cardiac failure, hyperlipidaemia, asthma, osteoporosis, dizziness/vertigo, arrhythmia 2:1 heart block
66	m	Hypertension, hyperlipidaemia, hiatus hernia, CKD, anaemia of chronic disease, cardiac failure, IHD, obesity, type 2 diabetes mellitus, atrial fibrillation
80	m	Dementia, cerebrovascular disease, rheumatoid arthritis, osteoarthritis, postural hypotension, recurrent falls, prostatic cancer on chemotherapy, osteopaenia
81	m	Rheumatoid arthritis, IHD, hypertension, osteoarthritis with cervical spondylosis and shoulder impingement, recurrent falls.
92	m	Ischaemic heart disease, congestive cardiac failure, osteoarthritis – neck, hips, shoulders- with neuropathic pain from neck, Parkinson's disease , stage 3 CKD, hypertension, anaemia of chronic disease, falls with prior fracture humerus, actinic Keratosis, possible squamous cell carcinoma on face, eczema
62	f	Type 2 diabetes mellitus, asthma, hypertension, osteoarthritis – prior knee replacement, osteoporosis, diverticular disease, breast

		cancer (2011), hiatus hernia with Barrett's oesophagus
61	f	Ulcerative colitis with prior subtotal colectomy, retinal occlusion secondary to recent endocarditis – sustained visual impairment, mitral valve prolapse and repair, atrial fibrillation, recurrent lentigo maligna, renal Calculi requiring recurrent lithotripsy, osteoporosis, dyspepsia and prior duodenal ulcer
77	f	Rheumatoid arthritis, osteoporosis, hyperlipidaemia, anaemia of chronic disease, IHD (non-obstructive coronary artery disease)
58	f	Systemic lupus, chronic pain, chronic anaemia, hyperhidrosis, diverticular disease, GORD, osteoporosis, benign essential tremor, IHD, high prolactin query cause.
76	m	CKD, heart failure, osteoarthritis with prior hip replacement, cerebrovascular disease-prior stroke, hypercholesterolemia, COAD, bowel carcinoma with right hemi colectomy, atrial fibrillation, alcohol abuse
69	m	Gout, atrial fibrillation, alcohol abuse, type 2 diabetes mellitus, hypertension, hyperlipidaemia, IHD.
40	m	Peptic ulcer disease, depression, chronic pain, chronic headache, constipation, alcoholism, mitochondrial disorder ("never fully nailed down")
80	f	Hypertension, atrial fibrillation, recurrent UTIs, chronic pain query cause, chronic sinusitis
64	m	Type 2 diabetes mellitus, erectile dysfunction, ischaemic heart disease, morbid obesity, stage 3 CKD, BPH, hypertension, hyperlipidaemia, recurrent UTIs and prior urinary calculus, recurrent GI bleeds
59	f	Breast cancer currently on chemotherapy, hyperlipidaemia, osteoporosis
87	f	Atrial fibrillation, lipid disorder, hypertension, osteopaenia
79	f	Type 2 diabetes mellitus, hypertension, migraine, temporal arteritis
75	m	Atrial fibrillation, PEs, prostate carcinoma, lung cancer undergoing radiotherapy, unclear psychiatric diagnosis
78	m	Cerebrovascular disease with prior stroke and marked spasticity, urolithiasis, recurrent UTIs, oesophageal cancer, dyspepsia, hypertension, depression, constipation, chronic pain, anaemia query cause.
82	m	Cerebrovascular disease, multi-infarct dementia, parkinsonism, bilateral subdural haematomas with bilateral frontal shunts, rheumatoid arthritis, right upper lobe neoplasm not for intervention or radiotherapy, COAD, polycythaemia rubra vera, gout, fragility and mobility problems, constipation
71	f	Osteoporosis with fractured right neck of femur, heart failure with

		biventricular defibrillator, orthostatic hypotension, atrial fibrillation, hyperlipidaemia, irritable bowel, cerebrovascular disease, cognitive impairment, recurrent UTIs
82	f	Adenocarcinoma caecum- right hemi-colectomy, asthma which is steroid dependant, COAD in addition to asthma, glaucoma, hypothyroidism, chronic pain from neuralgia and osteoarthritis, osteoporosis with Colles fracture and fractured ankle, hyperlipidaemia, GORD with an oesophageal web, steroid induced myopathy, MI in 2005, severe diverticular disease, chronic iron deficiency anaemia, PE.

Abbreviations:

BPH: Benign prostatic hypertrophy

CKD: Chronic kidney disease

COAD: Chronic obstructive airways disease

DVT: Deep venous thrombosis

GORD: Gastro-oesophageal disease

IHD: Ischaemic heart disease

MI: Myocardial infarction

PE: pulmonary embolism

PSA: Prostate specific antigen

UTI: Urinary tract infection

Appendix III. Supplementary data for Chapter 7. Scoping review

The materials in this appendix are supplements to the manuscript of the scoping review that was submitted for publication.

Supplementary material 11. Table 20. Search terms for scoping review

Table 20. Example of search terms for scoping review

#	Query	Limiters/Expanders	Last Run Via
S1	TX chart-stimulated recall OR TX chart stimulated recall OR TX case-based discussion OR TX case-based oral	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text
S2	TX general practice AND TX general practitioner AND TX family practice AND TX family physician AND TX family medicine AND TX primary care AND TX primary health care AND TX primary medical care AND TX primary care physician AND TX family practitioner	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text
S3	TX general practice OR TX general practitioner OR TX family practice OR TX family physician OR TX family medicine OR TX primary care OR TX primary health care OR TX primary medical care OR TX primary care physician OR TX family practitioner	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text
S4	S1 AND S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text

Supplementary material 12. Data extraction form for scoping review of chart-stimulated recall

Author	
Year of publication	
Aims (Phenomena of Interest)	
Setting of study	
Participants: how sampled • GPs (n) • Others (profession, n)	
How were charts chosen	
How was topic guide developed and used	
Method of data analysis	
Main findings	
How was CSR useful in generating these findings	
Duration of interviews	
Professional background and training of interviewer	
Other issues of note (especially potential pitfalls and how to avoid them)	

Supplementary material 13. Table 21. PRISMA checklist

Table 21. PRISMA checklist for scoping review (341)

Item			Page#
Title	1	Identify the report as a systematic review, meta-analysis, or both.	118
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	119
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	121
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	123-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	123-4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	282
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	124
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	125
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	125 & 283

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	125 & 287
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	125
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	125
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	124 & 287
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	126
Study characteristic	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	136-6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	287
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	287
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	128-34
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g.,healthcare professionals, users, and policy makers).	137
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	137
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	138-9

Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	27

Supplementary material 14. Table 22. Quality appraisal of included studies

Table 22. Quality appraisal of studies included in scoping review of chart-stimulated recall

Critical Appraisal Skills Programme (CASP) tool for qualitative research	Ab	Dee	Guerra	Guerra	Lockyer	Jennett	Rochefort	Sinnott
1. Was there a clear statement of the aims of the research?	y	y	y	y	y	y	y	y
2. Is a qualitative methodology appropriate?	y	y	y	y	y	y	y	y
Detailed Questions:								
3. Was the research design appropriate to address the aims of the research?	y	y	y	y	~(i)	y	y	y
4. Was the recruitment strategy appropriate to the aims of the research?	y	y (ii)	y	y	y	y	y	y
5. Were the data collected in a way that addressed the research issue?	y	~(iii)	y	y	~(iv)	y	y	y
6. Has the relationship between researcher and participants been adequately considered? (v)	n	n	n	n	y	n	n	y
7. Have ethical issues been taken into consideration?								
-Research ethics committee approval	y	n	y	y	n	n	y	y
-Ethical concerns (vi)	n	n	n	n	n	n	n	n
8. Was the data analysis sufficiently rigorous?	y	n(vii)	y	y	~ (viii)	~ (viii)	~(viii)	y
9. Is there a clear statement of findings?	y	y	y	y	y	y	y	y
10. How valuable is the research?	y	y	y	y	y	y	y	y

Footnotes to quality appraisal of studies included in scoping review of chart-stimulated recall:

i. The interviews in Lockyer et al. used survey type questions rather than open-ended or exploratory questions. It was difficult to see what the charts added here.

ii. Participation rates in these studies were low. In Dee et al. it took an “extensive search…considerable effort, patience and accommodation”, 6% agreed in Jennett et al., 20% in Guerra et al., 36% Rochefort et al.

iii. Information was collected by Dee et al. to show what clinical questions arose on reflection. They did not demonstrate if these questions interfered with care, or if the doctors would have actually gone on to seek answers to them. So the findings could have been an artefact of the study rather than a clinical reality.

iv. In Lockyer et al. it wasn’t clear if the physicians answered questions based on the chart of the baby that led to the interview being triggered, or whether their answers to the Likert scale type questions were more rhetorical or free-floating.

v. Although the professional background of the researcher was given in the studies by Dee, Jennett, Guerra, Lockyer, Sinnott; it was only the Sinnott paper where there was a discussion on how this may have impacted on the interviewee and on the data. Training of the interviewer was discussed in Lockyer et al. Ab et al. said that interviews were non-confrontational and open-ended questions used.

vi. While most of the studies, especially the more recent ones described ethical approval, none discussed ethical concerns specific to CSR.

vii. Qualitative data analysis only briefly mentioned or not discussed.

viii. The qualitative findings were not related back to the charts discussed in Rochefort et al. (i.e. quotes do not concern cases) and there are no qualitative findings (i.e. quotes) in Dee et al. or Lockyer et al. Overall sense that Dee were not conducted as a rigorous piece of qualitative research. Lockyer was evaluation of dissemination strategy using qualitative means.

Appendix IV. Supplementary data for Chapter 8. Cross-sectional study

The materials in this appendix are online supplements to the published version of the cross-sectional study.

Supplementary material 15. Table 23. STROBE statement

Table 23. STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement

Item		Recommendation	Page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	141
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	142
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	144
Objectives	3	State specific objectives, including any pre-specified hypotheses	145
Methods			
Study design	4	Present key elements of study design early in the paper	146
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	146
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	146
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	146-9
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	146-9
Bias	9	Describe any efforts to address potential sources of bias (Response & recall bias addressed in methods & discussion section]=)	146
Study size	10	Explain how the study size was arrived at (Baseline data for primary care cohort study)	146

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	146-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	149
		(*b*) Describe any methods used to examine subgroups and interactions	150
		(*c*) Explain how missing data were addressed	150
		(*d*) If applicable, describe analytical methods taking account of sampling strategy.	NA
		(*e*) Describe any sensitivity analyses	150
Results			
Participants	13	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	151
		(b) Give reasons for non-participation at each stage- discussed in prior publication, referenced in manuscript.	Prior paper (283)
		(c) Consider use of a flow diagram.	
Descriptive data	14	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Table 7
		(b) Indicate number of participants with missing data for each variable of interest	Table 7
Outcome data	15	Report numbers of outcome events or summary measures	Table 7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	151-2
		(*b*) Report category boundaries when continuous variables were categorized	151-2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	154
Discussion			
Key results	18	Summarise key results with reference to study objectives	158

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	160
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	160
Generalisability	21	Discuss the generalisability (external validity) of the study results	160
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	27

Supplementary material 16. Table 24. Prevalence of chronic conditions in the Mitchelstown Cohort Study overall and stratified into those with or without adverse childhood experiences

Table 24. Prevalence of individual chronic conditions in the overall Mitchelstown Cohort Study, and stratified into those with or without ACE.

Self-reported chronic condtion	Patients who report condition n=2047 n (%)	Patients without ACE with condition n=1457 n (%)	Patients with ACE with condition n=444 n (%)	P
Low back pain	656 (33.9)	445 (32.0)	177 (42.0)	<0.000
Hypertension	567 (29.0)	401 (28.6)	131 (30.7)	0.41
Anxiety	264 (13.9)	145 (10.6)	101 (24.9)	<0.000
Osteoarthritis	247 (13.2)	165 (12.2)	68 (16.8)	0.02
Urinary incontinence	209 (11.0)	138 (10.1)	58 (14.0)	0.03
Depression	205 (10.9)	101 (7.4)	90 (22.4)	<0.000
Rheumatoid arthritis	204 (10.7)	143 (10.4)	49 (12.0)	0.35
Thyroid disease	173 (9.3)	124 (9.3)	34 (8.3)	0.544
Asthma	165 (8.4)	111 (7.8)	46 (10.7)	0.06
Other cardiac	115 (6.2)	73 (5.4)	38 (9.3)	0.005
Osteoporosis	111 (5.9)	83 (6.2)	24 (5.9)	0.84
Diabetes	101 (5.0)	69 (4.8)	22 (5.0)	0.84
Cancer	80 (4.0)	55 (3.9)	19 (4.4)	0.65
Bronchitis	55 (2.8)	39 (2.8)	13 (3.1)	0.74
Angina	47 (2.4)	31 (2.2)	14 (3.3)	0.19
Prior heart attack	49 (2.4)	36 (2.5)	12 (2.7)	0.77
PVD	21 (1.0)	14 (1.0)	5 (1.1)	0.74
Stroke	22 (1.1)	13 (0.9)	6 (1.4)	0.37
Heart failure	8 (0.4)	4 (0.3)	4 (1.0)	0.07
Aortic Aneurysm	5 (0.3)	3 (0.2)	2 (0.5)	0.37
Any chronic condition	1483 (72.5)	1036 (71.1)	361 (81.3)	<0.000
Multimorbidity	927 (45.3)	626 (43.0)	248 (55.9)	<0.000

Supplementary material 17. Table 25. The association between subtypes of adverse childhood experience and multimorbidity at baseline in participants in the Mitchelstown Cohort Study

Table 25. Adjusted odd ratios and 95% confidence intervals for the association between subtypes of adverse childhood experience and multimorbidity at baseline in participants in the Mitchelstown Cohort Study

Subtypes of ACE	Prevalence n (%)	Odd ratios (95% CI) for multimorbidity in fully adjusted model
Abuse: emotional, physical or sexual	256 (12.5)	1.4 (1.1, 1.8)*
Neglect: emotional or physical	136 (6.6)	1.1 (0.7, 1.5)
Household dysfunction: domestic abuse, parents divorced, parents in prison, parental addiction or mental illness	295 (14.4)	1.4 (1.1, 1.7)*

*p<0.05

The models shown here are adjusted for age, gender, education, GMS status, behavioural factors (body mass index, diet, physical activity, smoking), depression and anxiety scores.

Supplementary material 18. Figure 15. The association between a history of any adverse childhood experience or subtype of adverse childhood experience, and psychiatric conditions in participants with multimorbidity in the Mitchelstown Cohort Study.

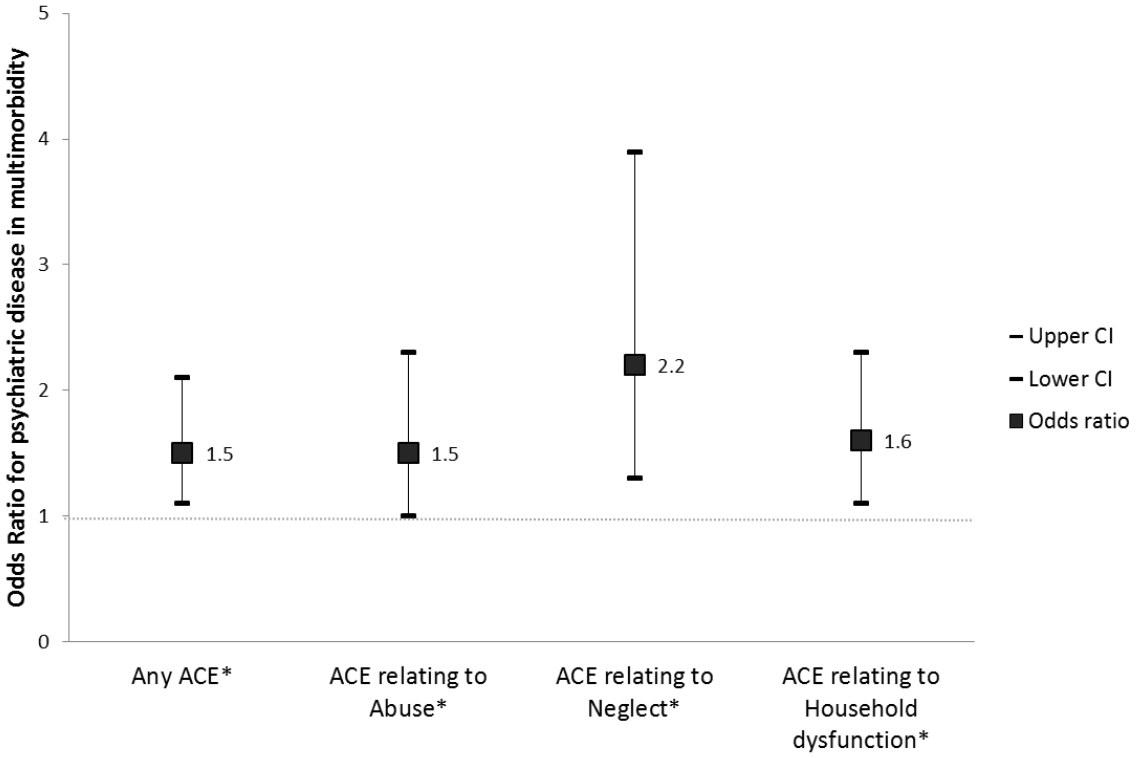

Figure 15. Adjusted odds ratios and 95% confidence intervals for the association between a history of any ACE or subtype of ACE, and psychiatric conditions in participants with multimorbidity in the Mitchelstown Cohort Study.

*p<0.05.

The models shown here are adjusted for age, gender, education, GMS status, behavioural factors (body mass index, diet, physical activity, smoking), depression and anxiety scores.

Appendix V. Supplementary data for Chapter 9. Intervention development paper.

The materials in this appendix are online supplements to the published version of the Intervention Development study.

Supplementary material 19. Table 26. Behaviour Change Wheel Step 5: Identify intervention functions

We found that all nine intervention functions listed in the BCW were potentially relevant to our behavioural analysis. Therefore, we used the APEASE criteria (171) to assess and grade each intervention function into first and second line options. The APEASE acronym stands for affordability, practicability, effectiveness and cost effectiveness, acceptability, side effects/safety and equity. The first line approaches were chosen for the intervention.

Table 26. BCW Step 5: Identify intervention functions using APEASE criteria

BCW Intervention Functions	Affordability	Practicability	Effectiveness & cost effectiveness	Acceptability	Side effects/unwanted consequences	Equity	Comments	Decision: First line Second Line Not appropriate
Incentives	✓	✓	✓	✓	×	✓	Creating an expectation of award is a crucial characteristic for the intervention, given the competing demands on GPs time, and the lack of remuneration for chronic disease management. Financial incentives are effective in changing healthcare professional practice (342), but care must be taken that the incentive chosen is affordable and widely available (equitable). As the incentive is for the behaviour of reviewing medications, not the outcome of stopping or reducing medications, unintended consequences on prescribing are unlikely.	First line

Environmental Restructuring	✓	✓	✓	✓	×	✓	Changing the existing social environment will be required if medication review is to be conducted in a safe and systematic way. Adding low cost, generalisable paper-based prompts to the environment is affordable, and likely to be effective if appropriate prompts are chosen.	First line
Enablement	✓	✓	✓	✓	×	✓	Increasing GPs' capability is acceptable, affordable and will be effective if existing barriers are addressed.	First line
Education	×/-	✓	×	✓	✓	×	Increasing GPs' knowledge through educational programmes is practicable and acceptable: numerous such programmes already exist. However, delivering information on medication review would unlikely be implemented directly without further interventional support; for example, prior educational interventions on prescribing were only effective if consideration was given to local context (162). Also, putting excessive educational focus on the rationalisation of medications may lead to unintended consequences in prescribing. Access to educational programmes may be inequitable/unaffordable. Educational meetings alone are unlikely to effectively change complex behaviours (343).	Second line
Training	×/-	×	×	×	✓	×/-	The myriad combinations of drugs and diseases that can occur in multimorbidity make it difficult to develop and deliver training programmes. Similar to education, equitable access and affordability cannot be guaranteed. Training in other aspects of medication management in multimorbidity, i.e. communication skills on deprescribing, may be useful for other interventions but we are focusing on the conduct of medication reviews.	Second line
Restriction	×	×	×	×	✓	×/-	This function concerns using rules to increase the target behaviour (medication review)	Not

							by reducing the opportunity to engage in competing behaviours. Thus, this is not practicable as we are trying to encourage a behaviour that does have a direct competing behaviour.	appropriate
Coercion	✓	×	×	×	✓	✓	In Ireland, chronic disease care is currently not remunerated under GPs contract of service, so it would not be possible to withhold payments *etc.* for it. Creating an expectation of punishment or limiting access to certain categories of drugs without evidence of medication review would not be acceptable to GPs.	Not appropriate
Persuasion	✓	×	×	×	×	✓	As most GPs in the qualitative study already agreed with the need for medication reviews, trying to further persuade them of the benefits would be unlikely to stimulate any sustained behaviour change.	Not appropriate
Modelling	✓	×	×	×	✓	✓	Using local opinion leaders as an example for GPs to aspire to is inappropriate in this context (344), particularly considering the need for patient-centred decision-making in multimorbidity.	Not appropriate

Supplementary material 20. Table 27. Behaviour Change Wheel Step 7: Identify behaviour change techniques

This table shows the behaviour change techniques (n=32) that are associated with the three chosen intervention functions (incentivisation, enablement and environmental re-structuring) and were deemed potentially relevant to our intervention. The possible operationalization of each technique and reasons for choosing/ not choosing it are described in column three.

Table 27. BCW Step 7: Identify behaviour change techniques

Intervention functions	**Behaviour change techniques associated with this intervention function**	**Possible operationalization of the technique based on the standard definition of the technique from Michie et al. (171) (in italics) and reasons for choosing it (indicated by ✓) or not choosing it.**
Incentivisation	Self-monitoring of behaviour/outcome of behaviour	*Establish a method for the GP to monitor and record their conduct of medication reviews /outcomes of medication reviews as part of a behaviour change strategy.* In itself and in the current climate in general practice where medication review is not a priority for GPs, this behaviour change technique is unlikely to motivate GPs without associated initiative or reward.
	Feedback on the behaviour/outcome(s) of the behaviour	*Monitor and provide informative or evaluative feedback on medication review /outcome of medication review.* May be successful, as monitoring of GPs prescribing of benzodiazepines is already utilised and accepted by GPs. Unless there was imminent reward or punishment associated with the behaviour, it may be capturing information to feed back to GPs.
	Monitoring of behaviour/outcome of behaviour by others with feedback	*Observe or record medication review/outcomes of medication review with the GP's knowledge as part of a behaviour change strategy.* In current climate, unlikely to motivate GPs unless there was associated reward or a threat of punishment for failing to conduct medication reviews.
	Material incentive or reward	*Inform that payment of money, or other valued objects will be delivered if and only if there has been effort and/or progress in performing medication reviews*. This would likely be very successful in changing GP behaviour (e.g. QOF initiatives in UK) but is outside the scope of our resources.

	Self- incentives or rewards ✓	*Plan to reward self in future if there has been effort in performing medication review*. This is deliverable in the form of continuing medical education points for engaging in medication review.
	Discrepancy between current behaviour and goal	*Draw attention to the discrepancies between a GP's current behaviour regarding medication review and their previously set action plans, outcome or behavioural goals*. Most GPs want to do the best by their patients regarding medications, and many believe in regular medication reviews for the purpose of minimizing treatment burdens as seen in the qualitative study. Given the current pressures on time being experienced by GP, highlighting their shortcomings in the area of medication review is a negative approach. In the short-term, it may dissuade GPs from becoming involved in the feasibility study of the intervention.
Enablement	Social support (unspecified/practical) ✓	*Advise or provide practical help for GP for the performance of medication review (e.g. GP colleagues).* From our date, many GPs were already engaging in informal conversation with their GP colleagues on how to manage challenging or complex patients, so this avenue is worth exploring as useful.
	Reduce negative emotions	*Advise GPs on ways of reducing negative emotions (i.e. frustrations/stress/uncertainty) to facilitate performance of medication review.* Current behaviour (maintaining the status quo) occurs to some extent because GPs are avoiding these negative emotions. Tackling the status quo will involve additional work for the GP which may further add to their negative emotions. Rather than targeting the GP's negative emotions it would be more professionally appropriate to target the source of those emotions i.e. rather than targeting GPs' fear of medico legal consequences, target reducing the risk of medico legal consequences.
	Conserve mental resources	*To advise GP on ways of minimising demands on mental resources to facilitate medication review.* This behaviour change technique could be applied by encouraging GPs to use guidelines to help them remember the role for certain drugs. However, in multimorbidity, mental resources are required to compute the possible interactions between drugs and diseases, and what potential changes are of value. As no one guideline is available for the myriad combinations of diseases in multimorbidity, facilitating use of mental resources, rather than conservation of mental resources is required.
	Generalisation of a target behaviour	*Advise GP to use their approach to medication review in non-multimorbid patients, in a situation involving multimorbidity*. Given the particular difficulties relating to polypharmacy, drug-drug and drug-disease interactions reported by

		GPs in multimorbid patients, the solution will require more than extrapolation of prescribing skills from straight forward ones to multimorbid ones.
	Action planning (implementation strategy) ✓	*Prompt detailed planning of the medication review (must include at least one of time of week, number done together, time of day, with or without patient presentation, triggers for).* This is important to give GPs some control over how the intervention is implemented in their practice. As the flexibility of implementation should be seen as an asset in our intervention, this behaviour change technique should be incorporated as an active component.
	Problem solving	*Analyse, or prompt the GP to analyse factors influencing their ability to conduct medication reviews and generate or select strategies that include overcoming barriers and/or increasing facilitators.* While GPs trying to conduct more medication reviews will have to tailor their approach for their own practice, they are unlikely to have the time or interest in formulating and developing the change strategy themselves. It may work better to develop an intervention and then ask GPs to tailor it for their practice, which is more implementation strategy than problem solving.
	Pros and cons	*Advise the person to identify and compare reasons for wanting and not wanting to change their behaviour regarding medication reviews.* The qualitative study has already identified that GPs already respect the need to do medication reviews (pros). It has also showed some of the down sides (cons) to medication reviews in patients with multimorbidity/polypharmacy which lead them to maintaining the status quo instead. The need here is to facilitate medication reviews, rather than just highlight its importance.
	Valued self-identity	*Advise the GP to write or complete grading scales about a cherished value or personal strength as a means of affirming their identity as part of a behaviour change strategy.* It is important to empower GPs and improve their sense of self-esteem as professionals in the management of chronic disease, and that may be a useful side effect of any intervention that we undertake. However using this as an active component of the intervention may be perceived by GPs as condescending and viewed with scepticism.
	Graded tasks	*Set the GP easy to perform tasks, making them increasingly difficult, but achievable until medication review is performed.* This may be useful in an educational setting but in routine practice it is not appropriate to stagger the tasks required in medication review: it is important that all medications are reviewed in the context of each other, and

		the wider bio-psychosocial context of the patient.
	Focus on past success	*Advise GPs to think about situations in which they previously conducted successful medication reviews*. In many cases, these successes may have occurred in an ad hoc fashion; therefore emphasizing their success detracts from the need for systematic, planned medication reviews that we are trying to encourage. This approach may be useful once the medication reviews are underway, to consolidate on-going behaviour change.
	Goal setting: behaviour	*Set or agree on a goal defined in terms of the conduct of medication review to be achieved.* Unsure how much this will achieve, as intention is already there, but competing demands and opportunity cost too great.
	Goal setting: outcome	*Set or agree on a goal defined in terms of a positive outcome of the conduct of medication review*. In some patients, there may be no change in medications required. If focus is on outcomes, and there are no specific outcomes apparent, this could de-motivate GPs to continue doing medication review. The focus should instead be on the practice of doing medication reviews, regardless of whether changes are made to medications.
	Commitment	*Ask the GP to affirm or reaffirm statements indicating commitment to conduct medication reviews.* Although GPs may affirm this, they face many competing demands for their time, so alone, this behaviour change technique will not be effective, and may in fact cause a sense of failure if they do not enact their commitment.
	Self-monitoring	*Establish a method for the GP to monitor and record their medication review as part of a behaviour change strategy*. This alone is unlikely to strongly motivate GPs. If it was coupled with some incentive, especially financial incentives, it may be useful.
	Review behavioural goals	*GP to review their goals for medication review jointly and consider modifying them in light of current achievement of these goals.* It is unlikely that GPs will have set goals for medication review prior to this intervention.
	Review outcome goals	*Review the outcome of medication reviews to date jointly with another person and consider modifying goals in light of current achievement*. This may be useful behaviour change techniques once the medication reviews are underway, but it is unlikely that GPs will have set goals for medication review prior to this intervention.
	Comparative imaginings of future outcomes	*Prompt or advise the imagining and comparing of future outcomes of changed (regular or structured reviews of medications) versus unchanged behaviour (non-systematic reviews of medications.* Using data from the qualitative study, future outcomes here include the long-term time-saving nature of regular

		medication reviews, the lessening of patients risk of adverse effects and less medico-legal risk. While these points would highlight the benefits of doing medication reviews, the imaginings would not be sustainable, and given the competing priorities for GPs in practice, would be unlikely to produce behaviour change.
Environmental re-structuring	Prompts/cue ✓	*Introduce a stimulus with the purpose of cueing medication review, which would be used at the time of performance of medication review* This could be easily implemented in the form of a checklist of things to consider. Could be written or computerised.
	Adding objects to the environment	*Add objects to the general practice environment in order to facilitate performance of medication reviews, involving more than verbal, visual, or written information*. The use of Information Technology and Computer Assisted Decision Support Systems is relevant here, and is being researched as an intervention by other groups.
	Restructuring the social environment ✓	*Change, or advise to change the social environment in order to facilitate performance of the medication review*. If medication review was scheduled, and accepted within the practice as a reasonable activity for the GP to spend time on, this could potentially impact on number of medication reviews conducted in major way – as indicated by qualitative study.
	Restructuring the physical environment	*Change, or advise to change the physical environment in order to facilitate performance of medication review*. May not be acceptable to alter GPs working environment physically, and as medication review is a cognitive task, not likely to yield great benefit.
	Associative learning	*Present a neutral stimulus jointly with a stimulus that already elicits the behaviour repeatedly until the neutral stimulus elicits that behaviour*. No stimulus to prompt medication review already exists, so could not operationalize this.

Supplementary material 21. Behaviour Change Wheel Step 8: Identify mode of delivery using expert panel

The expert panel critically reviewed the format of the emerging intervention strategy, the behaviour change techniques chosen, and the implementation plan. The panel focused on the following aspects of the intervention:

1. What prompts should be used to guide medication review in MY COMRADE??

Many instruments are available to assess prescribing (112). The expert panel explicitly considered the following:

- RCGP Prescribing Indicators (345)
- Medication Appropriateness Index (346)
- Welsh Medicines Support Centre questions (347)
- Use of medicine framework: Australia tool (348)
- Polypharmacy Guidance, NHS Scotland (349)
- STOPP START (114)
- NO TEARS (307)

The purpose is to prompt discussion between GPs rather than prompt prolonged pharmacological assessment. The panel felt that a broad, generic, pragmatic checklist was most appropriate. Such approaches have been found to improve quality of care in other fields of medicine (350). The last option, NO TEARS (307), was originally designed as a generic checklist to underpin *doctor-patient* communication about medications. The seven letters in the acronym prompt the doctor to: review the **N**eed and indication for the medication, ask **O**pen questions to the gain the patient's views on their medication, ensure appropriate **T**ests and monitoring have been conducted, ensure no changes have occurred in recent **E**vidence and guidelines, ensure that the patient is not

experiencing **A**dverse effects, ensure that medications are optimized for **R**isk reduction or prevention, and consider **S**implification of medication to improve adherence. We felt this short list, which was not bound by drug or disease would allow consideration of the individual context of each patient, including the psychosocial issues that were shown to be of a greater burden in multimorbid patients in Chapter 8. To transform this checklist to make it fit for discussion between two GPs, rather than a GP and patient, the second prompt was modified. We used **O** to prompt GPs to review whether a patients need for a medication **O**n-going. The need to discuss changes with the patient is not removed; it will just occur downstream from the activities targeted in this intervention.

2. How should GPs choose which patients to review using MY COMRADE?

As GPs cannot be expected to review all patients using the format set out in our intervention, they should be informed which type of patients to choose. The expert panel considered the following options for patient selection:

- Patient age (i.e. >65 years)
- Number of prescribed medications (i.e. >5 or >10)
- Number of comorbidities (i.e. >3, >4, etc.)
- Level of patient disability or functional impairment, including care home residence
- Use of high risk medications such as warfarin, non-steroidal anti-inflammatories, diuretics etc.
- GP choice as indicated by GPs discomfort with current medication regimen

With specific reference to the Kings Fund report (99) co-authored by two of the expert panel (MD &RP), it was agreed that GPs choose patients that were prescribed ten or more regular medicines, or five or more medicines with another complicating factor.

Complicating factors include medications that are a well-recognised source of interactions or risk, poor adherence, impaired cognition, psychosocial complexity, or end-of-life or palliative care.

3. How should the behaviour change technique of "action planning" be operationalized?

The behaviour change technique action planning (which includes implementation planning) was incorporated into the intervention to allow tailoring to individual general practices. The expert panel concluded that while the best people to tailor the intervention would be the GPs themselves they must be given clear guidance on how to do this. Thus in order to address barriers to implementation up front, each practice will be asked to consider the following prior to adopting the intervention:

1. What will make this intervention difficult?
2. How should these difficulties be tackled, *knowing your practice*?
3. What is your plan for rolling out this intervention?
    - What day? What time of day? Which office? How many at one session? Which GP will you involve? Anything else, specific to how your practice runs?

This process will enhance GPs' engagement with the intervention, give them autonomy over how it is rolled out, and highlight potential stumbling blocks before they occur. The practice specific implementation plans will be examined in the evaluation process.

4. How should the intervention be evaluated?

As the goal of the intervention was to change GPs behaviour from "maintaining the status quo" to actively reviewing medications, the expert panel agreed the primary

outcome for the initial evaluation would be whether medication reviews were performed using this approach. The evaluation will provide information on the implementation process, reasons for why the intervention succeeds, fails, or has unexpected consequences, and will identify other causal and contextual mechanisms associated with achieving behaviour change.

As per the MRC framework, a single primary outcome may not make the best use of the data: a range of measures will be needed and unintended consequences picked up where possible. Therefore, secondary outcomes that will be evaluated in the future include:

- Medication related
    - the number of changes recommended in each collaborative medication review
    - the number of changes that are subsequently made to the patients medications
    - the medication appropriateness scores/number of potentially inappropriate medications before and after the collaborative medication review
- Process of care related
    - number of consultations that directly result from the review
    - the amount of time taken per review
    - additional workload generated by review i.e. investigations, referrals etc.

Supplementary material 22. Validation of the chosen intervention functions and behaviour change techniques using the theoretical domains framework

The theoretical domains framework (TDF) is a set of domains that each contain multiple theoretical constructs relating to theory of behaviour change (171, 351). It has been developed in conjunction with the COM-B and the Behaviour Change Wheel, and may also be used in intervention development. We applied the TDF to our empirical data to see if it led to a similar set of intervention strategies and behaviour change techniques as the original COM-B based approach.

Table 28 shows the TDF domains relevant to our qualitative data.

Table 29 shows the intervention functions related to these TDF domains: all of the intervention functions in the Behaviour Change Wheel (BCW) were indicated as potentially relevant for our intervention. This was also found in the COM-B behavioural analysis (described in Chapter 9).

Table 30 shows the behaviour change techniques (BCTs) that were included in the MY COMRADE intervention (Chapter 9). We mapped these techniques to the TDF domains associated with them in a paper by Cane et al.(352) and on page 156 of the Guide to Designing Interventions (171). The TDF domains associated with the behaviour change techniques in MY COMRADE were amongst the TDF domains relevant to our qualitative data (shown in Table 28).

Table 28. Determination of intervention functions relevant to the empirical qualitative date using the theoretical domains framework

COM-B component	Behavioural description and interview source	Potentially relevant TDF domains (constructs)
Capability-Psychological	**Pharmacological knowledge, an inadequate evidence base, conflicting practice by others, lack of information relevant to general practice reduces GPs capability to do medication reviews** In some cases, GPs feel there is no available evidence for what is best in multimorbidity *gp5 "so can we honestly say that this tablet that she has been on X number of years, that by stopping it that she'll be any better? No we can't, can we say that by stopping it that it won't speed up her death? No we can't"* *gp7 "It is very hard to justify getting rid of any of his meds, although polypharmacy is a big problem for him."* Existing tools/guidelines are not helpful to GPs when conducting medication reviews, and sometimes make things more difficult: *gp16 "I've yet to see any really decent guidelines, I don't know if they are that useful to be honest in day-to-day decision-making, we prefer to kind of tailor (management) ourselves do you know"* *gp7 "with this guy, the guidelines tend to go out the window, because I think if you try to be too strict, if you try to completely adhere to the guidelines with any of his problems then it is going to, adversely affect his other morbidities."* Insufficient knowledge on new drugs *gp3 "we are getting these pieces of information from the drug companies that are nearly impossible to digest, they don't seem to have any relevance for what I am doing, I find them very hard to read them"* Information relevant to general practice required *gp17 "GP led education is what we will do, none of us have any interest in sitting down to a lecture by a nephrologist and more, you know, you don't have to tell us they are clever"*	Knowledge (knowledge) Skills (skills, practice, competence) Memory/attention/decision making processes (attention, decision making, cognitive overload)

	Involvement of hospital prescribers can complicate matters in multimorbidity and confuses GPs further *gp6 " our consultant hospital colleagues, they are giving the statins out - the Prosper trial seems to be totally ignored, the evidence from it does not seem to be taken on board."* *gp6 "(patients)are never strictly in the right boxes; there are always the complicating factors; there's always the, you know, diabetes with the gout - and you send them up to a rheumatologist they come back with a huge dose of steroid then, you say 'well I could have done that'"* *gp10 "when Dr XX put her on a big whack of steroids, this women is a diabetic, and there was no reference to the fact that she was diabetic - the adjustments that would need to be made, you know?"*	
Opportunity-Physical	**GPs feel they do not have adequate time resources to conduct medication reviews** Lack of time for renewing scripts within the consultation. *gp13 "there are times when you kind of have to say to someone when they come in 'I'll have to do some of this another day, or you'll have to come back to me, we'll do it in a different structure in a different format"* *gp1 "if I just had time to have a 30 -45 minute consultation with a patient while you don't have the waiting room building up, you could actually get to the bottom of some of the stuff they're on"* Lack of systems within the practice that allocate time to the activity of medication review *gp9 "it's one of the old chestnuts is that you are so busy when you are working that to take the time to look at these things in proper, I mean if you are going to do it, you have to do it obviously properly"* *gp12 "sometimes it would be nice to start afresh and I could ask the patient to come into me instead of them coming to me with some big long thing or whatever they had wrong with them today; instead me saying to them 'now this is what I want to talk about (sorting out medications)'"*	Environmental context and resources (organisational culture, resources/material resources, barriers and facilitators) Goals (action planning)
Opportunity-Social	**GPs feel that conducting medication reviews is complicated by the lack of social convention or acceptability, from a patient's perspective, of having medications removed or rationalized.** Patient attachment to medications *gp11 "She's attached to them, so I haven't, I haven't had the heart to broach it"* *gp7 "She wasn't keen to change her Risperdal because she had been on it for years"* *gp5- " they say 'oh god, doc, I want to stay on that' even if you feel it's doing feck all good you'll just*	Social influences (social pressures, social norms)

	prescribe it out again, you know- who are we to say 'no, no we need to stop that' do you know" *gp9 "she would be the type of patient, I would think, where you'd maybe get a phone call the following week saying 'I don't feel as well off that tablet as I did on it' in a lot of cases you'd end up putting her back on it."* Patients' misconceptions about longstanding medications *gp13 – "some of the stuff she is on like the domperidone and the betahistine and stuff I'm not really convinced that she needs it. I have talked to her about it - about whether or not it might be useful to take things off but she's reluctant to take them out and as far as she is concerned they've been started at some point over the years for her for some reason, so she wants to try and keep them"*	
Motivation-Automatic	**Reflex responses to polypharmacy in multimorbid patients, who demonstrate no obvious adverse drug effects, was to "maintain the status quo" in almost all interviews. This occurred due to lack of time in the consultation, lack of consistency in hospital prescribers, lack of convention for stopping medications, and lack of confidence in own prescribing.** gp11 "she has been doing better than she has been in a long time so I'm not going to rock the boat at all" gp12 "'look she's on it, she's fine, it doesn't bother her, it's suiting her fine" gp13 "largely for her I'd let it sit, I think if she is stable I don't try and change too much" gp14 "there is that aspect of not rocking the boat, you know and being straight up about it as well, sometimes as well you can get into the routine 'oh are you just in for the prescription?', you just print it off automatically without giving due consideration to can we shorten this, can we do this that and the other." gp18 "take the line of least resistance! Here's another 3 months prescription!" gp19 "anything that complex I didn't entertain changing because why stir up?"	Reinforcement (rewards, incentives)
Motivation-Reflective	**MOTIVATIONS AGAINST MEDICATION REVIEW** **GPs have beliefs about negative consequences of medication rationalisation such as potential medico-legal repercussions, negative responses from patient/next of kin, and harming the doctor-patient relationship due to risk of patient perception of medication rationalization as withdrawal of care.**	Social/professional role and identity (Professional role & identity) Beliefs about capabilities (self-efficacy, empowerment, professional confidence)

gp9 “would be loath to stop it, again probably in that situation it’s probably medico-legal, if you stop it and they do get a thrombosis the next week, you will feel a bit guilty” gp6 “his wife or he will say ‘hang on a second I want to go on as long as I can, why are you risking me getting a heart attack?’ Why stop my aspirin and my statin, if there is a small risk I’ll get a heart attack, why not leave me on it, why are you taking me off’” Leaving decisions to other clinicians: gp16 “I'd prefer to have them (specialists) say yes or no, because that way at least if I get sued I've covered myself.”	Beliefs about consequences (anticipated regret or consequences)
Some GPs have negative beliefs about their capabilities relative to other prescribers, and find it difficult to stop what others have started (low self-efficacy /empowerment) gp6 “I find that in some of the situations that the patient comes to you, they’ve been in hospital, something happens they end up in hospital but when they come out, they come out on medications that I would not have necessarily have started” gp9 “I suppose it’s deference to consultant opinion as usual, I suppose I should probably read up about it again and see whether I can think of reducing it.” and “the problem is, I suppose, in terms of cardiac stuff and in particular anti-angina stuff you have to be very brave to stop that I think, in a lot of ways.” gp13 “I’m absolutely in fear of changing these medications at all (shakily laughing)”	
The opportunity cost of medications reviews is using that time for other purposes, some of which are associated with greater gains (financial /time efficiency /delivering patient determined rather than doctor determined care) Lack of remuneration for changing medications: *gp17 “at some point I have invested as much time as I can, in to them, and don’t forget this is all pro bono, and you know, sometime you say ‘will I keep doing it?”* *gp11 “she has had multiple other things going on as well, so the consultation time would be taken up (if medications were also reviewed)”* *gp6 “to really get him on the amount of medication he needs, we’d be seeing him almost every few weeks - we’d be seeing him very frequently and that has huge implications because you have so many*	

patients and you can't, if you saw everybody every few weeks, you can't do it"

MOTIVATIONS TO REVIEW MEDICATIONS:

GPs also have beliefs about <u>the consequences of not reviewing medications</u> that could be used to motivate them to do reviews:

Demonstrating that medications have been reviewed is important medico-legally:

gp19 "It is your signature on the GMS prescription so if you haven't weighed up the pros and cons, and made a decision yourself, even though someone else started it, if they end up addicted to such and such a thing, you're responsible"

gp10 "What is important in theory and what is actually important in practice, on the ground, are often two entirely different things; but medico-legally the problem is that if this guy dies of renal failure they are going to be looking at his medication list and you will be thinking 'oh, crap'"

It is good defensible practice to do and document medication reviews:

gp10 "the longer I am in practice the longer my clinical notes are getting and the more I am documenting; aware of interaction, need to watch renal function but that must balance benefits versus risks."

Important to review medications in order to discuss implications of polypharmacy with patients:

gp10"Everything interacts with everything these days and you explain to them 'look, technically you are not supposed to be on that but look it's working for you'"

Negative emotions about not reviewing medications, could be alleviated by reviewing them:

gp11 "it would make you feel nervous, because obviously you wouldn't like anything happening somebody, and she probably was on it too long, it would have been difficult for me to probably stand over it... I could have probably been in trouble myself if something had happened her"

gp8 "He was on something else, I think it was a PPI and it was interfering with his HIV and I felt very bad about that after, because when he came out of hospital, i thought, oh my god"

Increasing comfort with prescribing if reviewed systematically:

gp17 "we try and do a three month chart review on diabetics to make sure that we have pulled all of them in and they are as up to date as we can get them, so the plan is that everybody has all the boxes ticked, so now I'm quite comfortable with diabetes, I'm quite comfortable with hypertension"

Table 29. Mapping the TDF domains relevant to the empirical qualitative date (Table 28) to their related intervention functions

	Intervention Functions								
Relevant TDF domains and constructs	Education	Training	Environmental restructuring	Restriction	Incentivisation	Enablement	Persuasion	Coercion	Modelling
Knowledge	+								
Skills		+							
Memory/attention/decision-making processes		+	+			+			
Environmental context and resources		+	+	+		+			
Goals	+				+	+	+	+	+
Social influences			+	+		+			+
Reinforcement		+	+		+			+	
Social/professional role and identity	+						+		+
Beliefs about capabilities	+					+	+		+
Beliefs about consequences	+						+		+

Table 30. Mapping the behaviour change techniques in the final MY COMRADE intervention to the TDF domains associated with them

Chosen intervention function	Behaviour change techniques in MY COMRADE	Related TDF domains (352)
Environmental Restructuring	Restructuring the social environment✓	Environmental context & resources
	Prompts/cue✓	Environmental context & resources
Enablement	Social support (practical)-✓	Social influences
	Action planning (implementation intentions)✓	Goals
Incentivisation	Self-reward or incentive – CME✓	Reinforcement

The links between the TDF domains and the behaviour change techniques are taken from the Guide to Designing Interventions (171) and the paper by Cane et al. (352)

Appendix VI. Supplementary data for Chapter 10. Feasibility study

Supplementary material 23. GP information sheet

GP participant information leaflet on a feasibility study on collaborative medication review for multimorbidity in primary care.

Why is this study being done?

Many patients attending GPs have multimorbidity (multiple chronic diseases). However, clinical guidelines generally do not take multimorbidity into account. This can lead to a situation where the guidelines for one condition suggest medications that may adversely affect a co-existing disease, or can lead to high numbers of medications or problematic polypharmacy. We have studied how GPs make decisions in these challenging multimorbid patients, and found that they often speak to their GP colleagues. In this study, we would like to formalize this interaction – that is examine what happens when two GPs review a patient's notes together, with a view to making recommendations on the patient's medication regimen.

Who is organising and funding the study?

The project is sponsored by the Health Research Board and the Health Service Executive. The research team is based in University College Cork. The principal researcher, Dr Carol Sinnott, is a trainee in general practice. The principal investigator and supervisor is Professor Colin Bradley.

Why am I being asked to take part?

We are asking you to take part because in the course of your everyday work, you are likely to be faced long and complicated prescriptions for patients with multiple morbidities. We want to explore how useful a new approach to medication review would be for these cases. This new approach involves two GPs reviewing the medications together with the help of a list of prompts/checklist.

How will the study be carried out?

This is a feasibility study. If you agree to participate, Carol will attend your practice at a time that suits and explain how the case review should take place- this meeting will only take 15 minutes.

You will be given the checklist (includes only 7 prompting questions), which you and your GP colleague can refer to when you are systematically reviewing your patient's medications. For the purposes of case review, we will ask you to choose 3 -5 cases from your practice, each with multiple chronic diseases that require 10+ medications or 5+

medications with another complicating factor. The case reviews, which can take place at a time that suits you and your GP colleague, will take approximately ten minutes per case. You can make a note of any potential changes to medications on the checklist page, and scan it into the patient's notes. This will make the next review easier and is important medico-legally. Any potential changes to medications should be discussed with the patient before making the change. After you have completed the case reviews, Carol will re-attend your practice to explore how the process went, if any changes were made to the patient's medications and if you have any recommendations on how it could be improved. We will not ask for any patient identifying information. However we will take details of the patient's age, gender, diagnoses and list of medications. With your permission, we will record this second meeting, and the recorded data will be analysed for recurrent issues that arise for GPs in this area.

What about confidentiality?

All information obtained during the study will be strictly confidential. All identifiable information will be removed from recorded data. A study ID number will be assigned to any data relating to your practice, to maintain anonymity. Only investigators named on this information sheet will have access to the data, which will be stored securely in UCC.

What will happen with the results of this study?

The findings of this study will be written up for the HRB report and subsequent publications. The results will also be compiled and submitted as part of a PhD thesis. In all cases only anonymous extracts or quotes will be reported. Copies of the findings will be made available to participants.

Who has reviewed this study?

This research gained approval from the ethics committee of the CREC, UCC. If you decide to take part you will be asked to sign a consent form. You are free to withdraw at any time. If you have any questions or concerns, please do not hesitate to contact the research team detailed below.

Dr Carol Sinnott	Professor Colin Bradley
GP Trainee, South East Training Scheme	Professor and Head of Department
Research Fellow, University College Cork	Department of General Practice, University College Cork.
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Supplementary material 24. GP instruction sheet for feasibility study

What to do

1. Choose three patients each on which to do the medication review. Try to choose patients prescribed 10+ medications or 5+ medications with another complicating factor.
2. Schedule a time to discuss these patients with another GP in your practice
3. Use the attached checklist as a guide for the discussion. Make a note of any potential changes to medications on the page, and scan into the patient's notes.
4. Please try to complete the cases reviews within the next month – they take approximately 10mins each, but may take longer initially.

Before starting, Consider

4. What benefits would you see in this format for medication review? What might make it difficult?
5. What plan would suit *your practice*, for trying this out?
    - What day of the week?
    - What time of day?
    - Which office?
    - How many case reviews will you do at one sitting?
    - Which GP will you involve?
    - Anything else, specific to how your practice runs?

Additional points

- Document the medication review in the patient's notes - it will make the next review easier and is important medico-legally.

- Highlight any potential options for medication changes -these options should be discussed with the patient at their next consultation, prior to making any changes.

- Internal CME points apply.

- For further information, please contact: Dr Carol Sinnott, Research fellow in General Practice, UCC. csinnott@ucc.ie

Supplementary material 25. Prescribing checklist

Collaborative Medication Review

Review by: Dr. _____ & Dr. _____

Date of review:

Patient name & DOB:

- Give your GP colleague a brief description of the case (e.g. 75 year old lady, lives alone, history of diabetes and arthritis).
- Discuss each medication (or groups of medications, such as anti-hypertensives) using the points below.
- Not all points will be relevant.

N	What is the **need** or indication for this medication?
O	Is this need **on-going**? Has the patient's condition or life expectancy changed since this medication was started? Was long term treatment intended?
T	Is the patient getting appropriate **tests** and monitoring associated with this medication?
E	Has the **evidence** or guidelines changed in relation to this medication/condition since it was commenced? (*think of big messages*)
A	Are there any **adverse** effects with this medication? Check for interactions, duplications, contraindications.
R	**Risk reduction** and prevention: Are doses/medications optimised to lower the patient's risk?
S	Can treatment be **simplified** to a safer /easier to use alternative?

List the medications where there is potential to change /further action required:

Additional points

- The medication review should be documented in the patient's notes (e.g. scan in this page). It will make the next review easier.
- Any options for medication changes should be discussed with the patient at their next consultation, prior to making any changes.
- The 'NO TEARS' checklist is adapted from the BMJ 2004;329:434

Supplementary material 26. Topic guide for evaluation interviews

1. Acceptability: what was your initial impression of this approach to MR? Were you optimistic that it would work?* Is it credible, does it have any advantages to existing approaches.
2. Adoption: what was your initial plan on how to bring this into your practice?* What were your goals and intentions with relation to it?*
3. Appropriateness: how fitting is this intervention to the setting of multimorbidity? How fitting is it to the setting of GP? Did you think it would be useful? For what?* How was making decisions in this format (easier or more complicated)?* What about discussing your practice with another GP – comfortable /uncomfortable?
4. Feasibility: how feasible is it for you right now, to continue doing this? Is it practical /trialable? Were you confident that you could conduct it? Any concerns about being able to do it? * what are the main barriers (need link to meds info for example?)
5. Fidelity: how did you do it? What happened in the review? Especially specific BCTs: social support, checklist, action planning, changing social environment, awarded CME points? Which features were most related to success/failure of intervention?
6. Implementation cost: were there opportunity costs? Were there other things that you could not do as a result of this intervention? (i.e. house visits /seeing patients /going home)
7. Coverage: how widely applicable is this to your patients on multiple meds? Are there many that you find this not appropriate in?
8. Sustainability: do you think it could become routine. Incorporated in to regular practice? What are the incentives for you to continue (CME/safety/time saver)?*

*=question adopted from the theoretical domains framework (351)

Supplementary material 27. Table 31. Template for Intervention Description and Replication (TIDIER) Checklist

Table 31. Template for Intervention Description and Replication (TIDIER) Checklist

Item no.	Item	Where located (page #)
Title		
1	Multimorbidity Collaborative Medication Review And Decision-making (MY COMRADE)	197-8
Why		
2	We used the results of a systematic review and qualitative interview together with the Capability-Opportunity-Motivation-Behaviour (COM-B) model of behaviour, the Behaviour Change Wheel approach to intervention development and the Behaviour Change Technique taxonomy to develop this intervention specifically to facilitate the conduct of active medication review.	197-8
What		
3	Participants were provided with an information leaflet, and instructions on how to implement the intervention, which detailed the five behaviour change techniques included in the intervention. They were also provided with copies of the prescribing checklist that was used as one of the behaviour change techniques. This checklist was a modified version of the NO TEARS tool for medication review.	Provided in supplementary material 23, 24 and 25.
4	Each pair of GPs was asked to conduct six medication reviews using the MY COMRADE approach (or three medications reviews per GP). GPs were asked to choose patients with multimorbidity who were prescribed 10 or more medications or 5 or more medications with another complicating factor (i.e. impaired cognition, psychosocial complexity, poor life expectancy etc.).	Page 198
Who		
5	Only practicing GPs implemented the intervention	Page 198
How		
6	GPs implemented the intervention in pairs.	Page 198
Where		
7	The intervention was implemented in the GP practice. The participating GPs were asked to come up with an action plan in which they would specify when and where (i.e. which office within the practice) they would conduct the reviews.	Page 198

When and how much		
8	Each pair of GPs was asked to conduct six medication reviews using the MY COMRADE approach (or three medications reviews per GP). GPs were asked to choose patients with multimorbidity who were prescribed 10 or more medications or 5 or more medications with another complicating factor (i.e. impaired cognition, psychosocial complexity, poor life expectancy etc.). They were asked to complete the reviews within a one month interval.	Page 198
Tailoring		
9	Participating GPs were advised that could adapt the action plan (when, where, how many patients to review in one sitting etc.) to suit their own practice. This adaption was captured in evaluation interviews.	Page 198, and supplementary material 23 and 24.
Modifications		
10	The only modification from the researcher perspective was that instead of leaving the date for follow-up interviews for the GPs to organize, the research team started to set follow-up dates from the third practice on.	Page 201
How well		
11	Intervention adherence and fidelity were assessed in evaluation interviews with CS, using self-report by participants.	Page 206
12	Observation or recording of implementation of the intervention was not performed.	

Appendix VII. Supplementary data for Chapter 11.

Supplementary material 28. Results of updated search for systematic review.

Introduction

Given the increasing interest in the management of multimorbidity, there was a need to ascertain if there had been important developments in the qualitative literature since the systematic review and synthesis, conducted in September 2012.

Aim

- To identify qualitative literature on GPs perceptions and experiences of managing patients with multimorbidity published since September 2012.
- To interpret any relevant new literature using the domains derived in the original review (Chapter 5).
- To highlight new domains of importance (if any) in this field.

Methods

The original search was repeated: EMBASE, MEDLINE, CINAHL, PsycInfo, Academic Search Complete, SocIndex, Social Science Full Text were search from September 2012 to November 2015 to identify literature using qualitative methods on GPs perceptions and experiences of managing patients with multimorbidity. Citations were screened by a single reviewer (CS). Full texts were read and interpreted using the lens of the four domains that emerged in the original systematic review. The four domains were i) disorganisation and fragmentation of healthcare ii) inadequacy of guidelines and evidence-based medicine iii) challenges in delivering patient-centred care and iv) challenges in shared decision-making.

Results

The search results are shown in the table 32. In total, there were 858 citations, which led to nine relevant papers. The characteristics of the nine papers are shown in Table 33. The contribution of the nine papers to each of the four domains in the original review, and any notable new findings are shown in Table 34.

Discussion

While the nine new papers show much overlap with the four domains that arose in our original review, there are also consistent new findings. The most striking of these is the call for greater training and education on how to deal with challenges in patients with multimorbidity, suggesting that physicians are now accepting that the challenges at health system level and in the medical evidence base will not be addressed in the short term. In particular, approaches to shared decision-making are called for. The need for enhanced communication was a strong finding in all studies: between GPs and specialists, GPs and allied healthcare professionals and in one case, between the multiple lay carers for the patient. This brief synthesis shows the evolution of the qualitative literature on multimorbidity from focusing on problems to moving towards solutions. This change is encouraging and if the momentum continues, promises improvements in the provision of care to patients with multimorbidity.

Table 32. Results of updated search

Database	Number of citations	Number of relevant papers
Embase	562	4
CINAHL	53	2
PsychInfo, Social Sciences Full Text, SocIndex, Academic Search Complete	131	1
Medline	112	1
Reference searching		1
Total	858	9

Table 33. Characteristics of new papers relevant to qualitative systematic review

First author (reference)	Title of study	Participants and setting	Data collection	Data analysis
Sondergaard et al. (353)	Problems and challenges in relation to the treatment of patients with multimorbidity: GPs' views and attitudes	180 GPs attending a workshop on multimorbidity in Tampere, Finland.	Audio recorded workshop and 76 questionnaires	Framework analysis
Loffler et al. (354)	Approaches of GPs and patients to multimorbidity: A qualitative study	9 GPs and 19 multimorbid patients in Nordrhein-Westfalen, Germany.	Narrative interviews with GPs and patients	Content analysis Written in German – English abstract & google translate used here.
Herrmann et al. (355)	GP medication prioritisation in older patients with multiple comorbidities recently discharged from hospital: a case-based bottom-up approach	44 GPs in Sachsen-Anhalt, Germany.	Focus group discussions and semi-standardised interviews. Vignettes related to drug optimisation were discussed in the interviews/focus groups.	Grounded theory Written in German – English abstract & google translate used here.
Junius-Walker et al. (356)	What is important, what needs treating? How GPs perceive older patients' multiple health problems: a mixed method research study	9 GPs and 35 patients in Hannover, Germany.	Interviews with GPs, based on how they prioritised the multiple issues facing their multimorbid patients. The lists of problems were provided to the GPs from a geriatric assessment.	Content analysis
Nuno-Solinis et al. (357)	Multiple comorbidities from the perspective of primary care health professionals	Fourteen health professionals: 6 specialists in family medicine, 3 hospital specialists, 4 nurses, and 1 community pharmacist. Basque region, Spain.	A co-creation workshop (12 participants) and 10 interviews with health professionals	Thematic analysis Written in Spanish – English abstract & google translate used here.
Sellappans et al. (358)	Challenges faced by primary care physicians when prescribing for patients with chronic diseases in a teaching hospital in Malaysia: a qualitative study	14 family medicine trainees and 5 service medical officers. Teaching primary care clinic, Malaysia.	3 focus group discussions	Thematic analysis
Schoenborn et al. (359)	Current Practices and Opportunities in a Resident Clinic Regarding the Care of Older Adults with Multimorbidity	21 internal medicine residents and 30 of their primary care patients. Johns Hopkins Bayview General	Audio-recording of 30 clinic visits	Content analysis of consultations

		Medical Clinic.		
Gill, et al. (360)	"Where do we go from here?" Health system frustrations expressed by patients with multimorbidity, their caregivers and family physicians	27 triads involving patients, their informal caregivers and family physicians. Family Health Team, Ontario, Canada.	Semi-structured interviews	Qualitative descriptive
Kuluski et al. (361)	A qualitative descriptive study on the alignment of care goals between older persons with multimorbidities, their family physicians and informal caregivers.	27 triads involving patients, their informal caregivers and family physicians. Family Health Team, Ontario, Canada.	Semi-structured interviews	Qualitative descriptive

Table 34. Contribution of new papers to the original domains and new findings

Study author	Domains arising from original review				Other findings
	Disorganisation and fragmentation of health care	Inadequacy of guidelines and evidence-based medicine	Challenges in delivering patient-centred care	Challenges in shared decision-making	
Sondergaard et al.	Complex care pathways and insufficient cooperation between professionals involved in the care of multimorbid patients underlined the GPs' impression of a fragmented healthcare system especially: • Difficulties with inter- and cross-sectoral cooperation • Lack of communication • Lack of mutual recognition	Guidelines developed for single diseases were identified as very challenging when handling patients with multimorbidity, especially in relation to: • Medical complexity • Emerging new symptoms • Polypharmacy	Current payment systems were criticized for not matching the treatment patterns of patients with multimorbidity • Mismatch between patients' wishes and resources • Uncertainty about the GP's role • Fits poorly with existing payment	GPs found it challenging to establish a good dialogue and prioritize problems with patients within the timeframe of a normal consultation, especially if: • they lacked contextual knowledge • trying to prioritize between diseases • there were complicating	Important role for GPs in diminishing health inequality was highlighted.

			systems in some countries	Psychosocial factors • they lacked time	
Loffler et al.			GPs and multimorbid patients often had relatively different priorities. Whereas GPs mostly focused on the management of diseases, patients put an emphasis on maintaining autonomy and a social life.		
Herrmann at al.	Influences on prioritisation included: their own abilities with in the health system, communication between secondary and primary care and their respective influences on each other.	Influences on prioritisation included: the evidence base.		Influences on prioritisation included: patient health literacy, patient safety, patient wishes, and quality of life.	Focused on the influences on GPs as they prioritise medications in multimorbid elderly patients at the transition between inpatient and home care
Junius-Walker at al.	GPs tended to view problems that they could not help with (i.e. social issues) as less important – and tried to direct responsibility for these matters to other agencies (family members or social care organisations)	GP viewed problems directly linked with aging as less important than actively treatable medical conditions –the evidence base dictated what GPs prioritised for care. The provision of care is undermined by a lack of available treatment approaches for complex chronic illnesses and disabilities.	GPs tend to prioritise treatable clinical conditions, that require active treatment or monitoring, or that induce empathy or awareness but cannot be assisted further.	Patient empowerment strategies need to be developed to improve their input into the prioritisation of their illnesses.	Relates multimorbidity to ageing and disability, and suggests that GPs' perception of this overlap inhibits some aspects of how they care for multimorbidity. Highlights the need for multidisciplinary approach.
Nuno-Solinis et al.	Multimorbidity poses challenges that related to working in a "disease-centered" health system. This leads to daily issues in the co-ordination of care between healthcare settings.	The management of polypharmacy is a challenge. There is a lack of decision-making tools appropriate for multimorbidity.	The health system presents barriers to getting appropriate care for these patients.	The patient-health professional relationship and clinical decision-making are frustrated in multimorbidity due to health system structures.	Highlights the need for agreement on what the most appropriate professional competencies in multimorbidity are, and training in these competencies.
Sellappans et al.	A lack of continuity of care and difficulties in prescribing for	Difficulties in managing side effects caused by the patients'	-	Patients were less likely to follow primary care	Focused on challenges in medication management

	patients with multimorbidity due to a lack of communication among different healthcare professionals. Exacerbated in the Malaysian context due to rotations among family members of carer responsibilities.	complex medication regimen, and identifying what the cause of side effects may be.		physician's advice on medications than specialist advice. Large variation in patients' preferences and adherence made decision-making difficult.	(i.e. adherence, lack of knowledge) and lack of communication within families that alternate caring for older patients.
Schoenborn et al.	Patients reacted to fragmented care by not attending for diagnostic tests or clinic visits. No mention was made of physician perceptions of fragmentation on the patients' care.	While medical evidence was occasionally discussed in consultations, no reference was made to the applicability of evidence to older patients with multimorbidity. Patients took the lead on stopping therapies from which they experienced no benefit.	Physicians did not respond to patient comments on prognosis or life expectancy. Some efforts to enhance the clinical feasibility or reduce treatment burden were made.	Patient preferences, if discussed, were mostly incorporated into the care plan.	Found missed opportunities to address the guiding principles for the care of older adults with multimorbidity set out by the American Geriatrics Society Expert Panel.
Gill et al.	Frustrations expressed by family physicians included lack of access to appropriate care, poor communication, long wait times and lack of care co-ordination.	-	Physicians were unsure how to prioritize patient needs and felt that they lacked the appropriate resources to do so.	Challenges included difficult symptoms, the inability to prevent crises, or diagnose conditions rapidly when these were confounded by other diseases, and lack of adherence.	Not all physicians were frustrated in providing patient care, particularly if the patient was stable, or if the patient–caregiver unit organised their own care.
Kuluski et al.	Mobilising services for declining patients was a primary concern for physicians.	-	-	Goals were often the same but discrepancies occurred in attempts to achieving those goals. Divergence of goals most likely when patients were less stable.	Focused on goal-setting between patient, physician and carer

Appendix VIII. Research and clinical training undertaken during doctoral research

Research training

Sept 2015	Certificate in Professional Skills for Research Leaders University College Cork and the Irish Management Institute.
June 2015	Fellow on the 47th Ten Day International Teaching Seminar in Cardiovascular Disease and Prevention, June 2015. Hosted by Fiji National University and University of Cambridge
Apr 2015	Postgraduate Certificate in Teaching & Learning for Higher Education University College Cork. NFQ Level 9, 30 credits.
March 2015	Development of Behavioural Change Interventions Workshop, Centre for Behavioural Change, University College London
Nov 2014	Health Economic Evaluation Workshop, Department of Economics, University College Cork
Jan 2014	Certificate in Behavioural Economics in Action, Rotman School of Management, University of Toronto (on-line programme)
Jan 2013	Certificate in Health in Numbers: Quantitative Methods in Clinical & Public Health Research, Harvard School of Public Health, Harvard University (on-line programme)
Nov 2013	Certificate in Clinical Research & Good Clinical Practice for Investigational Medicinal Products, Irish Clinical Research Infrastructure Network (ICRIN)
Feb 2013	Introduction to Qualitative Interviewing, Health Experiences Research Group,

	Department of Primary Care Health Sciences, University of Oxford
2012	Postgraduate research training modules, University College Cork: PG6001 Scientific Training for Enhanced Postgraduate Studies PG7016 Systematic Reviews for the Health Sciences PG6024 Qualitative Research Inquiry EH6031 Advanced Epidemiology
June 2012	Certificate in Cochrane Systematic Reviews, Cochrane Review Training Course, Cork

Clinical training and professional development

Nov 2015	Conferred with Membership of Irish College of General Practitioners
July 2015	Certificate in Promoting Alcohol Reduction Irish College of General Practitioners, Dublin
Dec 2014	Certificate in Long-Acting Reversible Contraception (LARC) Irish College of General Practitioners, Dublin
Sept 2013	Certificate in Family Planning & Contraception Irish College of General Practitioners, Dublin
June 2013	Certificate in Methadone Treatment & the Management of Drug Users in General Practice Irish College of General Practitioners, Dublin
June 2012	Completion of Membership of the Irish College of General Practitioner Examinations (MICGP)

Appendix IX. Prizes and awards relating to doctoral research

May 2015	Prize winner in Irish Times essay competition to celebrate International Clinical Trials Day 2015. Title: Clinical Trials Matter in General Practice. https://www.hrb-tmrn.ie/news/competition-winners/
March 2015	Winner of the Professor William Shannon Prize, Association of University Departments of General Practice Annual Meeting for research presentation on "The association between adverse childhood experiences and multimorbidity"
Dec 2014	Winner of the Sheppard Memorial Prize, awarded by the Royal College of Practitioners in Ireland for essay on "What to give the patient who has everything? A qualitative study of prescribing for multimorbidity in primary care"
Nov 2014	Winner of Jacqueline Horgan Medal. Royal Academy of Medicine in Ireland, Section of Epidemiology & Public Health Medicine for research presentation on "The association between adverse childhood experiences and multimorbidity"
Sept 2014	Early Career Researcher Award, Society for Social Medicine, Annual Scientific Meeting 2014, Keble College, University of Oxford.
May 2014	Second prize winner (poster), European General Practice Research Network Scientific Meeting, Barcelona, 2014.
June 2013	First prize winner, Irish College of General Practitioners Research & Audit Day, 2013.
June 2012	Finalist in the Doctoral Showcase, University College Cork presenting thesis proposal and protocol

Appendix X. Dissemination of doctoral research

Peer-reviewed publications

Sinnott C, Mercer S, Payne R, Duerden M, Bradley C, Byrne M. Development of the Multimorbidit Collaborative Medication Review And Decision-making (MY COMRADE) intervention using the Behaviour Change Wheel. *Implementation Science* 2015, **10**:132

Sinnott C, Bradley CP. Multimorbidity or polypharmacy: two sides of the same coin? Journal of Comorbidity 2015;5:29–31

Sinnott C, McHugh S, Fitzgerald AP, Bradley CP, Kearney PM. Psychosocial complexity in multimorbidity: the legacy of adverse childhood experiences. Family Practice (2015) 32 (3): 269-275

Sinnott C, McHugh SM, Boyce MB, Bradley CP. What to give the patient who has everything? A qualitative study of prescribing for multimorbidity in primary care. Br J Gen Pract. Mar 2015;65(632):e184-191.

Sinnott C, McHugh S, Browne J, Bradley C. GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. BMJ Open. 2013;3(9):e003610.

Peer-reviewed abstract publications

Mellon L, McHugh SM, Sinnott C, Kearney PM. Adverse childhood experience and health service utilisation: findings from a primary care-based study. J Epidemiol Community Health 2015;69:A46

Sinnott C, Mc Hugh S, Boyce M, Bradley C. PL02 Resolving conflicts in the multimorbid consultation: how do general practitioners balance diseases, drugs and the views of other doctors? Journal of Epidemiology and Community Health. September 1, 2014 2014;68(Suppl 1):A3.

Sinnott C, McHugh S, Bradley C. Informing intervention design in multimorbidity: An exploration of difficult decision making using chart stimulated recall. European Journal of General Practice. 2014;20(3):226.

Sinnott C, Hugh SM, Browne J, Bradley CP. OP89 Challenges in Managing Multimorbid Patients: A Meta-Ethnography of the GPS Perspective. Journal of Epidemiology and Community Health. September 1, 2013 2013;67(Suppl 1):A41-A42**.**

Conference proceedings: oral presentations

July 2015	Development of a prescribing intervention for multimorbidity. Society of Academic Primary Care Annual Scientific Meeting, University of Oxford, UK.
June 2015	Research-led Teaching in Multimorbidity: The Power of Two. European Conference on the Scholarship of Teaching and Learning, University College Cork.
May 2015	Implementing medication review for multimorbid patients. Global Implementation Conference (GIC) 2015, Conference Centre, Dublin, Ireland.
March 2015	Psychosocial complexity in multimorbidity: the legacy of adverse childhood experiences. Association of University Departments of General Practice of Ireland. **Winner**, Professor William Shannon Prize
March 2015	Chart-stimulated recall. A method for investigating complex care in primary care. Association of University Departments of General Practice of Ireland.
Nov 2014	More than the sum of single diseases: The association between multimorbidity and adverse childhood experiences **Winner** Jacqueline Horgan Medal meeting, Royal Academy of Medicine in Ireland.
Sept 2014	Resolving conflicts in the multimorbid consultation: How do GPs balance diseases, drugs and the views of other doctors? Society for Social Medicine Annual Meeting, Oxford. **Plenary presentation and high scoring abstract**

July 2014	Resolving conflicts in the multimorbid consultation: How do GPs balance diseases, drugs and the views of other doctors? Society of Academic Primary Care Annual Meeting, Edinburgh, Scotland.
July 2014	Engaging GPs in clinical trials: Barriers and facilitators encountered in the Thyroid Hormone Replacement for Subclinical Hypothyroidism (TRUST) study. Society of Academic Primary Care Annual Meeting, Edinburgh, Scotland.
March 2014	A qualitative exploration of difficult decision-making in multimorbidity: Getting the pieces to fit. Association of University Departments of General Practice of Ireland, Annual Scientific Meeting, Cork.
Sept 2013	GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. Society for Social Medicine, Brighton, UK
July 2013	GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. Society of Academic Primary Care Annual Meeting, Nottingham, UK
June 2013	GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. **First Prize Winner**. Irish College of General Practitioners Research and Audit Conference.

Conference proceedings: poster presentations

July 2015	Collaborative medication review: an approach for teaching multimorbid medication review in GP training. Society of Academic Primary Care Annual Scientific Meeting, University of Oxford, UK
March 2015	Using Behavioral Theory To Develop A Prescribing Intervention for Multimorbidity. Association of University Departments of General Practice of Ireland, Belfast, Northern Ireland
May 2014	Informing intervention design in multimorbidity: An exploration of difficult decision-making using chart stimulated recall. European General Practice Research Network, Barcelona.
Sept 2013	GPs' perspectives on the management of patients with multimorbidity The International Training Programme on Ageing, Trinity College, Dublin.
Dec 2012	Challenges in managing multimorbidity: A meta-ethnography of the GPs' experience. North American Primary Care Research Group Annual Meeting, New Orleans, US.

Appendix XI. Additional academic activity during the conduct of this research

Workshop presentations

Nov 2015	"Why…How.. and Gim'me the Money!! Facilitating Research in Primary Care." ICGP Winter Meeting, Athlone.
Oct 2015	Developing behaviour change interventions for primary care. Annual Early Career meeting, Association of University Departments of Primary Care in Ireland, National University of Ireland, Galway.
Oct 2015	Designing Behavioural Interventions in Chronic Disease, Irish Nephrology Society Annual Winter Meeting. Waterford Health Park, Waterford.

Invited presentations

Oct 2015	Invited Speaker, Irish Nephrology Society Annual Winter Meeting. Multimorbidity; What is it and why does it matter in nephrology? Waterford Health Park, Waterford.
Sept 2015	Invited Speaker. The importance of ICD-10 coding in research and practice. SENATOR 4th General Assembly and Steering Committee Meeting, Ancona, Italy.
Oct 2013	Invited speaker. Network of Establishing GPs – Cork Faculty. "Opportunities and funding for research in General Practice."
Oct 2013	Invited Speaker. National Association of GP Trainees Annual Meeting, Lyrath, Kilkenny. "How to get your abstract accepted into a research conference."

Book Chapters

Chapter 3.13 Qualitative Interviewing Healthcare Research at a Glance. Wiley & Sons (in press)

Research letters

Sinnott C. Drug-disease and drug-drug interactions in "concordant" combinations. Response to Drug-disease and drug-drug interactions: systematic examination of recommendations in 12 UK national clinical guidelines.
http://www.bmj.com/content/350/bmj.h949/rr-0

Sinnott C. Clinical inertia and the role of continuity of care. Response to Depression and Clinical Inertia in Patients With Uncontrolled Hypertension
JAMA Intern Med. 2014;174(5):818-819. doi:10.1001/jamainternmed.2014.115

Sinnott C. Response to: Facilitated physical activity as a treatment for depressed adults: randomised controlled trial. http://www.bmj.com/content/344/bmj.e2758/rr/589073

Sinnott C. Complexity rising? Response to Multimorbidity of chronic diseases and healthcare utilization in general practice. BMC Family Practice 2014, 15:61
http://www.biomedcentral.com/1471-2296/15/61/comments

Research Funding Awards

Sept 2015	Strategic Fund Award, University College Cork Awarded €980 to attend the International Training Fellowship in Cardiovascular Epidemiology and Prevention.
Feb 2015	Irish Research Council New Foundations Award for Collaboration and Knowledge Exchange. Awarded €2513.
May 2014	Irish College of General Practitioners' Research Travel Bursary
Fund	Awarded €500

Dec 2013	Irish Research Council New Foundations Award for Collaboration and Knowledge Exchange. Awarded €3868 euro.
Dec 2012	College of Medicine and Health Student Doctoral Travel Bursary, Graduate School, University College Cork. Awarded €1000
Apr 2011	Health Research Board Ireland. Research funding for PhD project. Awarded €30,685 and three years of salary support.

Conference organisation

Conference title: Medication Optimisation for Multimorbidity.

In September 2014, I hosted a conference in University College Cork, September 2014 for the purposes of inter-disciplinary knowledge exchange on research on medication optimisation in multimorbidity. Researchers from the fields of pharmacy, general practice, health psychology and geriatric medicine were invited. The conference was attended by over thirty national and international researchers. I gained funding to support the conference from the Irish Research Council New Foundations Award.

Appendix XII. Links to published papers

1. Sinnott C, McHugh S, Browne J, Bradley C. GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. BMJ Open. 2013;3(9):e003610. http://bmjopen.bmj.com/content/3/9/e003610.long
2. Sinnott C, McHugh SM, Boyce MB, Bradley CP. What to give the patient who has everything? A qualitative study of prescribing for multimorbidity in primary care. Br J Gen Pract. Mar 2015;65(632):e184-191. http://bjgp.org/content/65/632/e184.long
3. Sinnott C, McHugh S, Fitzgerald AP, Bradley CP, Kearney PM. Psychosocial complexity in multimorbidity: the legacy of adverse childhood experiences. Family Practice (2015) 32 (3): 269-275 http://fampra.oxfordjournals.org/content/32/3/269.long
4. Sinnott C, Mercer S, Payne R, Duerden M, Bradley C, Byrne M. Development of the MultimorbiditY COllaborative Medication Review And DEcision Making (MY COMRADE) intervention using the Behaviour Change Wheel. Implementation Science 2015, 10:132 http://implementationscience.biomedcentral.com/articles/10.1186/s13012-015-0322-1