Evaluating services for older adults with multi-morbidity across health and social care

Petronella Natasha Chitalu

UCL

A thesis submitted for the degree of Doctor of Philosophy

Supervisors

Professor Elena Pizzo

Professor Daniel Davis

Declaration

I, Petronella Chitalu, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Acknowledgements

This PhD was funded by the National Institute for Health Research (NIHR) Applied Research Collaboration (ARC) North Thames.

This thesis stands as a testament to the collective support and unwavering encouragement I have received over the last three years. I extend my deepest gratitude to my supervisors, Professors Daniel Davis and Elena Pizzo, whose expertise and insightful guidance were indispensable. I am also profoundly thankful to my peers for their camaraderie and support, and to my family for their endless love and encouragement. This journey was made possible by their belief in me.

Abstract

Background

Increasing life expectancy is associated with a higher prevalence of living with multiple chronic conditions (multimorbidity). Multimorbidity and age-related functional decline are components of frailty, an independent predictor of adverse health outcomes. While chronic disease management increasingly accounts for multimorbidity, such strategies do not always also consider frailty. This thesis explores the consequences of multimorbidity on health, frailty and functional outcomes, including quality of life, service use and costs. It uses cohort data and linked datasets to assess the impact of multimorbidity on chronic disease management for complex older adults.

Methods and Results

I conducted a systematic review evaluating the literature on the efficacy and cost-effectiveness of multimorbidity interventions for older adults. I found that the effectiveness of multimorbidity interventions was generally inconsistent, with many studies giving varied results. However, one theme suggested that comprehensive assessments from an interdisciplinary team were beneficial. A more striking descriptive finding was that most multimorbidity interventions were often designed or evaluated without considering frailty.

I then used cohort data to understand the simultaneous impact of multimorbidity and frailty on (arguably) the highest-order function: quality of life. I undertook a cross-sectional analysis of a population-representative cohort, using linear regression models to estimate quality of life scores using multimorbidity measures, life-space assessment, and a frailty index. Frailty measures were much more informative than multimorbidity, with quality of life being associated with both frailty and life space scores. Interactions suggested the strongest associations between functional mobility and quality of life was evident in those with higher frailty. Overall, this indicated that over and above

multimorbidity, mobility interventions could have the biggest impact on quality of life in individuals living with frailty.

Using datasets linked across primary, secondary, community, mental health and social care, I examined the longitudinal relationship between multimorbidity, unscheduled (acute) inpatient admission and long-term service use. I found that acute admissions were associated with increased service use across primary, secondary and social care settings. Though this attenuated over time, there was evidence of increased service utilisation well beyond the acute illness period. This was worse where there was more multimorbidity. Costs were greater across all settings, but particularly for social care after an acute admission.

Conclusion

For older adults, services for multimorbidity could be more effective if frailty is simultaneously evaluated and managed. This is apparent in cohort data describing relationships between variables not usually available in routine health and social care records. However, using linked datasets provides opportunities to understand service use patterns in a more complete ecosystem. Together, these findings may help with integrated and coordinated service design, both in whole populations, and in subgroups.

Impact Statement

The findings of this thesis have implications for managing multimorbidity in older adults, emphasising a need to look beyond and include considerations of frailty. This research should guide healthcare policy, improve clinical practice, and shape future research for older people living with multimorbidity and frailty.

The thesis underscores the need for healthcare policies to recognise the intersection between multimorbidity and frailty. My findings highlight that interventions focusing solely on multimorbidity without considering frailty may be ineffective. This insight is relevant for policymakers and healthcare providers in designing more holistic and patient-centred care models. By advocating for the simultaneous evaluation and management of frailty in multimorbidity care, the thesis provides a foundation for developing integrated health services better tailored to older adults' complex needs. This approach can potentially lead to more effective allocation of resources and improved health outcomes, especially in reducing the long-term costs associated with acute admissions and increased service use.

Clinically, this thesis offers insights for practitioners working with older adults. The emphasis on comprehensive assessments by interdisciplinary teams as beneficial in managing multimorbidity is particularly noteworthy. This recommendation should prompt clinical practice to foster a more collaborative and multidisciplinary approach to care. The findings also suggest that interventions improving functional mobility could enhance the quality of life in older individuals with higher levels of frailty. This could shift focus towards mobility interventions in clinical settings, offering a new direction in managing frailty and multimorbidity.

The research opens new avenues for further investigation. While it establishes a strong link between multimorbidity, frailty, and quality of life, it also highlights the variability and inconsistencies in current multimorbidity interventions. Future research could explore more deeply the mechanisms through which

frailty influences the effectiveness of these interventions and develop more targeted, evidence-based strategies for managing complex health conditions in older adults. Additionally, the use of linked datasets in this thesis sets a precedent for future studies to adopt a more comprehensive approach to understanding older adults' healthcare utilisation patterns.

This thesis contributes to the academic understanding of multimorbidity and frailty in healthcare policy, clinical practice, and future research directions. By highlighting the interconnectedness of these two critical aspects of older people’s health, it paves the way for more integrated, efficient, and patient-centred healthcare services.

UCL Research Paper Declaration Form

referencing the doctoral candidate's own published work(s)

Please use this form to declare if parts of your thesis are already available in another format, e.g. if data, text, or figures:

- *have been uploaded to a preprint server*
- *are in submission to a peer-reviewed publication*
- *have been published in a peer-reviewed publication, e.g. journal, textbook.*

This form should be completed as many times as necessary. For instance, if you have seven thesis chapters, two of which containing material that has already been published, you would complete this form twice.

1. **For a research manuscript that has already been published** (if not yet published, please skip to section 2)

   a) **What is the title of the manuscript?**

Life-space, frailty, and health-related quality of life

   b) **Please include a link to or doi for the work**

10.1186/s12877-022-03355-2

   c) **Where was the work published?**

BMC Geriatrics

   d) **Who published the work?** (e.g. OUP)

BioMed Central

e) **When was the work published?**

August 2022

f) **List the manuscript's authors in the order they appear on the publication**

Chitalu, Petronella

Tsui, Alex

Searle, Samuel D.

Davis, Daniel

g) **Was the work peer reviewed?**

Yes

h) **Have you retained the copyright?**

Yes

i) **Was an earlier form of the manuscript uploaded to a preprint server?** (e.g. medRxiv). If 'Yes', please give a link or doi)

Yes https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3949364

If 'No', please seek permission from the relevant publisher and check the box next to the below statement:

☐

*I acknowledge permission of the publisher named under **1d** to include in this thesis portions of the publication named as included in **1c**.*

2. **For a research manuscript prepared for publication but that has not yet been published** (if already published, please skip to section 3)

    a) **What is the current title of the manuscript?**

Click or tap here to enter text.

    b) **Has the manuscript been uploaded to a preprint server?** (e.g. medRxiv; if 'Yes', please give a link or doi)

Click or tap here to enter text.

    c) **Where is the work intended to be published?** (e.g. journal names)

Click or tap here to enter text.

    d) **List the manuscript's authors in the intended authorship order**

Click or tap here to enter text.

    e) **Stage of publication** (e.g. in submission)

Click or tap here to enter text.

3. **For multi-authored work, please give a statement of contribution covering all authors** (if single-author, please skip to section 4)

PC, AT, SDS, DD contributed to data curation and methodology. DD contributed to the conception, funding acquisition, resources, and supervision. Formal analysis and investigation were done by PC and DD. Project administration was done by AT and DD. PC wrote the original

draft and all authors reviewed and edited the article. The authors read and approved the final manuscript.

4. **In which chapter(s) of your thesis can this material be found?**

   Chapter 6

5. **e-Signatures confirming that the information above is accurate** (this form should be co-signed by the supervisor/ senior author unless this is not appropriate, e.g. if the paper was a single-author work)

   Candidate

   Petronella Chitalu

   Date:

   26/02/2024

   Supervisor/ Senior Author (where appropriate)

   Daniel Davis

   Date

   26/02/2024

Table of Contents

Table of tables

Table of figures

Abbreviations

A&E	Accident And Emergency
BHR	Dagenham, Havering and Redbridge
CAN	Care Assessment Need
CASP	Critical Appraisals Skills Programme
CCG	Clinical Commissioning Group
CGA	Comprehensive Geriatric Assessment
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CHI	Community Health Index
CI	Confidence Interval
CKD	Chronic Kidney Disease
CPRD	Clinical Practice Research Datalink
CVD	Cardiovascular Disease
DELPHIC	Delirium and Population Health Informatics Cohort
GP	General Practitioner
H&C	Health and Care
HCP	Healthcare Professional
HES	Hospital Episode Statistics
HIC	High-Income Country
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HRG	Healthcare Resource Group
HRQoL	Health-related Quality of Life

ICD	International Classification of Diseases
ICER	Incremental Cost-Effectiveness Ratio
ICS	Integrated Care System
IMD	Index of Multiple Deprivation
LBBD	London Borough of Barking and Dagenham
LDL	Low-Density Lipoprotein
LSA	Life-Space Assessment
LSOA	Lower Layer Super Output Area
LTCF	Long-Term Care Facilities
MAI	Medication Appropriateness Index
MD	Mean Difference
MESH	Medical Subject Headings
MI	Multiple Imputation
NCD	Non-Communicable Disease
NELFT	North-East London NHS Foundation Trust
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
ONS	Office for National Statistics
OOP	Out-of-Pocket
OR	Odds Ratio
PCI	Pharmaceutical Care Issues
PCS	Physical Component Summary
PICOS	Population, Intervention, Comparison, Outcome, and Study Type

PRISMA	Preferred Reporting of Items for Systematic Review and Meta-Analysis
QALY	Quality Adjusted Life Years
QoL	Quality of Life
RCT	Randomised Control Trial
RR	Risk Ratio
RWD	Real-World Data
UK	United Kingdom
UPRN	Unique Property Reference Number
USA	United States of America
VAS	Visual Analogue Scale
WHO	World Health Organisation
YLD	Years Lost to Disability
YLL	Years of Life Lost

Chapter 1 Introduction

The global rise in life expectancy, particularly in high-income countries, indicates improving health and living standards. Population ageing, however, introduces challenges to the health and well-being of nations. Increasing age comes with a decline in physiological function, resulting in chronic illness and frailty (Le Reste *et al.*, 2013; World Health Organization, 2016). Multiple chronic conditions or the coexistence of two or more physical and/or mental health conditions of any individual body system is now widely known as multimorbidity (World Health Organization, 2016). In 1970, *comorbidity* was initially proposed to define an additional condition alongside an index condition. Multimorbidity was introduced much later to describe several co-existing conditions where none receives primary focus over another (The Academy of Medical Sciences, 2018). Thus, comorbidity and multimorbidity are related but not synonymous. Multimorbidity is associated with older age and lower socio-economic position; it is increasingly the norm rather than the exception in these groups. Therefore, the prevalence of multimorbidity is highest in disadvantaged areas, where it also occurs earlier in life (Barnett *et al.*, 2012).

Health settings have historically been designed and have operated with a single disease focus; understanding the challenges presented by multimorbidity for how services are configured and then used by older adults, and the resulting outcomes provides opportunities to generate knowledge for service design. One approach to understanding the complex patterns of service use among older adults with multimorbidity is to analyse population-representative cohorts and examine service use at the individual level. However, the lack of a universal definition for multimorbidity presents a crucial challenge, with clinicians and researchers having inconsistent approaches on what diseases to consider within their definition of multimorbidity; this results in a lack of a comprehensive approach across health and social care. This thesis explores the evidence that multimorbidity adds to our understanding of health for older adults, and how it relates to service use and health and social care expenditure, through exploring

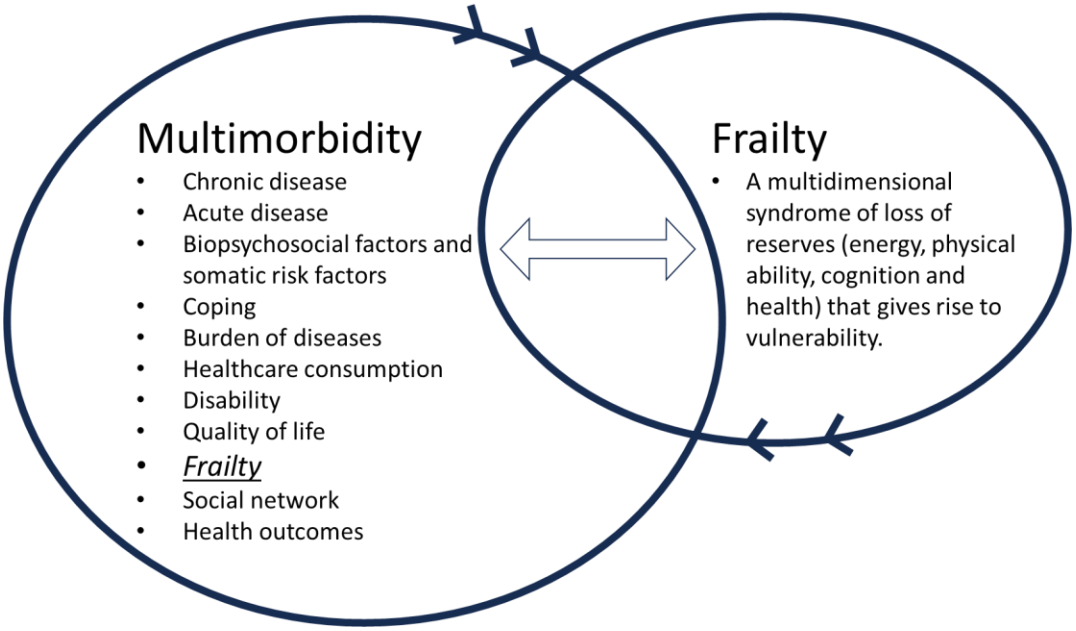
determinants and consequences of multimorbidity; including the dimensions of health that may determine service use. In this chapter, I introduce existing literature on multimorbidity and summarise other crucial challenges in older age that relate to multimorbidity. In the following Chapter 2 I describe the aims and objectives of the thesis, including an outline of the remaining chapters.

1.1 Evolving Definitions of Multimorbidity

As previously touched on, although generally described as multiple chronic conditions, how multimorbidity is defined varies within research and clinical practice. Each definition, however, centres around the co-existence of long-term conditions or diseases. Generally, multimorbidity refers to multiple chronic conditions in the same individual where none is the index. Several publications have sought to clarify and resolve inconsistencies in operational definitions over the last decade. In 2013, Le Reste and colleagues proposed that multimorbidity management encompasses not only chronic *diseases*, but health problems, symptoms, and biopsychosocial and somatic risk factors in clinical practice (Figure 1-1). In this way, each should contribute to multimorbidity counts rather than solely disease entities (Le Reste *et al.*, 2013). In 2016, the World Health Organization (WHO) reviewed published evidence, educational curricula and advice from field experts, as recommended by the Safer Primary Care Expert Working Group. They defined it as multiple chronic conditions or the coexistence of two or more physical and/or mental health conditions of any body system; this can include cognitive conditions such as dementia or long-term non-communicable conditions such as cancer (World Health Organization, 2016). Subsequently, in 2018, the Academy of Medical Science detailed the challenges of establishing a universal definition and reporting framework for multimorbidity. This report adapted the WHO's definition of multimorbidity by adding long-term infectious diseases such as human immunodeficiency virus (HIV) or hepatitis (The Academy of Medical Sciences, 2018). These definitions have provided clarity for some researchers with Le Reste and colleagues' definition perhaps being more orientated to clinicians (Johnston *et al.*, 2019). Despite the variations in definitions and approaches to its management, the

problem of multimorbidity continues to become the norm rather than the exception.

Figure 1-1: Themes and subthemes identified for multimorbidity conditions, adapted from Le Reste et al (2013)



1.2 Epidemiology of Multimorbidity

Due to varied definitions and the lack of consensus on a reporting framework, prevalence data on multimorbidity are imprecise. Nonetheless, multimorbidity is currently and will continue to be one of health and social care services' greatest challenges. By 2035, the prevalence of multimorbidity in the United Kingdom (UK) is projected to almost double from 17% (Kingston *et al.*, 2018). Over half of those aged ≥ 65 in the UK live with two or more chronic conditions (Barnett *et al.*, 2012; Kingston *et al.*, 2018). Chronic disease surveillance data from Scotland estimates that one in four adults has two or more chronic conditions (Barnett *et al.*, 2012). As populations age, we expect these challenges to increase; predictions from the Office for National Statistics (ONS) show that the proportion of pensionable-age adults by mid-2045 will rise to 15.2 million, increasing by 28% compared with 2020 (Office for National Statistics, 2022). Common conditions contributing to multimorbidity include hypertension, musculoskeletal problems and

depression or anxiety (Nicholson *et al.*, 2019). This overlap between physical and mental health conditions adds to the heterogeneous complexity of multimorbidity.

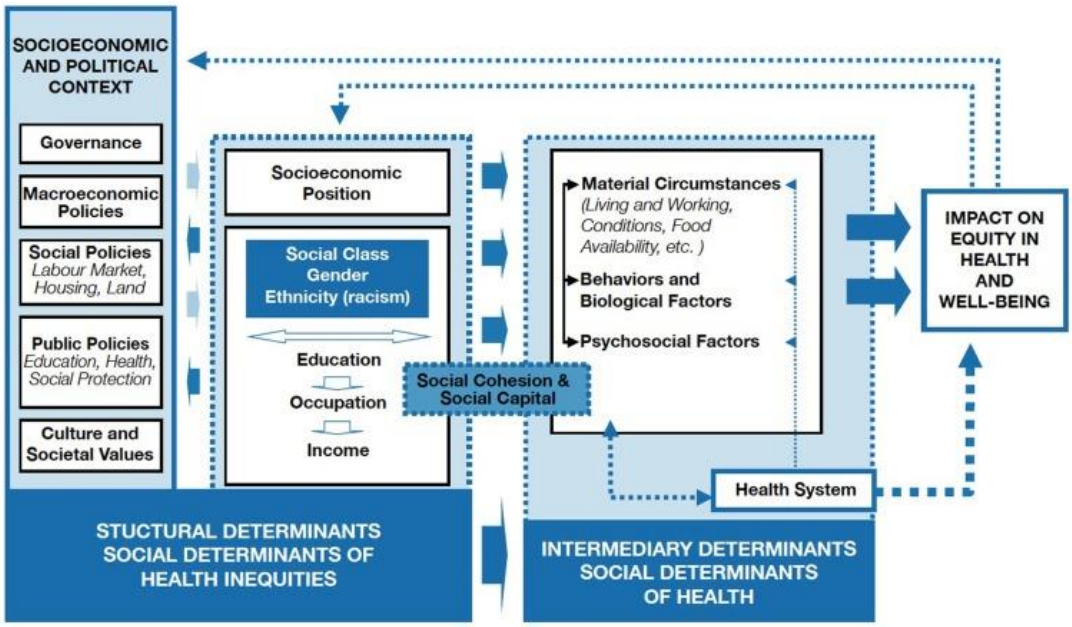
How increased longevity translates into multimorbidity, associated functional decline, and increased health and social care needs, by how much and in whom, remains a major individual and public health question (Singer *et al.*, 2019). These interacting influences predict and determine service utilisation in relation to multimorbidity, from demographic characteristics to increases in the likelihood of referrals between a variety of health providers who experience poor integration between services that focus on single diseases and offer fragmented care (World Health Organization, 2016). Understanding and tackling these determinants of health, health and social care service utilisation, and expenditure in relation to multimorbidity, provides clarity in health policy design and in understanding the implications of multimorbidity in older adults to establish services with the potential to be applied more widely.

1.3 Determinants and Consequences of Multimorbidity

Rather than a simple number of conditions, we can view multimorbidity as a series of non-random disease clusters (Pearson-Stuttard *et al.*, 2019). Some biological mechanisms underlie multimorbidity, for example, the link between chronic kidney disease (CKD) and cardiovascular disease (CVD), in part mediated by CVD risk factors such as hypertension and diabetes (The Academy of Medical Sciences, 2018). Lifestyle risk factors have also long been associated with individual conditions such as smoking and lung cancer, and so the same risky health behaviours increase the chance of developing multiple conditions. As older age and socio-economic position are key determinants of multimorbidity, health inequalities between different socio-economic positions may point to mediating factors. The ultimate impact of these determinants is seen in equity in health and well-being, indicating that disparities in these determinants can lead to health inequalities across different populations. This dynamic process with feedback loops highlights the complexity of the relationship between social determinants and health outcomes. (Figure 1-2). These determinants may include poor nutrition,

reduced physical activity, environmental risk factors such as pollution and risky health-related behaviours such as excess alcohol consumption and smoking (The Academy of Medical Sciences, 2018). Whether in high-income or low-income countries, the risk factors for multimorbidity remain the same. However, the context around how these risk factors arise is what differs; for example, individuals living in poverty and low-income countries may increase their risk of multimorbidity through consuming more alcohol, whereas alcohol consumption is higher in older birth cohorts in high-income countries (Stewart *et al.*, 2019). Additional factors contribute to the development or progression of multimorbidity, such as the coexistence of a mental health condition. This occurs in one in three patients with multimorbidity (Pearson-Stuttard *et al.*, 2019). Understanding this bidirectional relationship between mental and physical health remains a research priority. Other factors associated with multimorbidity include lacking social support, being a woman, and having a low income or low educational attainment (Northwood *et al.*, 2018; Gontijo Guerra *et al.*, 2019).

Figure 1-2: World Health Organization's Commission on Social Determinants of Health (CSDH) Framework



The presence of frailty is associated with the progression of multimorbidity, just as multimorbidity is related to adverse health and functional outcomes from frailty (The Academy of Medical Sciences, 2018). The concepts of frailty and multimorbidity are intricately related in older adults, with frailty being a major public health concern that is in part determined by multimorbidity (World Health Organization, 2017). Understanding the determinants of multimorbidity and their role in further influencing the long-term development of frailty would have clear policy implications. The continuum between fitness and frailty is widely distributed in older age; frailty can determine and predict dimensions of health that impact service use. Exploring the concepts of frailty and multimorbidity, including how they co-relate, would be beneficial for improving the effectiveness of multimorbidity interventions through robust and efficient surveillance for planning and tailoring interventions. To contribute to existing interventions for older adults with multimorbidity, we need to understand the implications and outcomes, not only determinants, of multimorbidity in old age, including how it relates to key problems such as frailty. The outcomes that relate to multimorbidity are varied and complex and can include but are not limited to:

- Functional dependence.
- Reduced health-related quality of life.
- Frailty - the cumulative decline across multiple physiological systems, causing decreased resistance to stressors and vulnerability to adverse outcomes.
- Hospitalisation (e.g., emergency admissions, adverse drug reactions).
- Increase in health and social care service use and expenditure.
- Mortality.

1.4 Implications and Outcomes For Older Adults With Multimorbidity

1.4.1 Effects on health-related quality of life

The intricate relationship between frailty and multimorbidity in older adults has significant implications for their health and quality of life. These

interactions not only contribute to functional dependence, increased healthcare utilisation, and mortality, but also lead to a cumulative decline in physiological resilience. Certain investigations measure disease impact in isolation using metrics like years of life lost (YLL) and years lost to disability (YLD) without considering multimorbidity (Hilderink *et al.*, 2016), but it is clear having multiple health conditions is linked to greater disability, functional decline, and a higher likelihood of death, even after considering age (Fried *et al.*, 1999; Bayliss *et al.*, 2004; Marengoni *et al.*, 2009, 2011; Ryan *et al.*, 2015). This evidence suggests that people with multimorbidity often report lower overall health and quality of life. Most of this data originates from high-income countries, notably in Europe and the United States of America (USA) (Fortin *et al.*, 2004; Lawson *et al.*, 2013; Mavaddat *et al.*, 2014; Walker *et al.*, 2016). However, findings from the WHO's Global AGEing and Adult Health (SAGE) Wave 1 survey highlight a similar correlation between multimorbidity and diminished health perception and quality of life in numerous low- and middle-income countries (Arokiasamy *et al.*, 2015).

1.4.1.1 Conceptualisation and Measurement of Quality of Life

Quality of life (QoL) is a broad and multi-dimensional concept that typically includes subjective evaluations of both positive and negative aspects of life. It is not only a reflection of an individual's health status but also encompasses psychological, social, and environmental domains. The World Health Organization defines QoL as:

> *"an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns."* (World Health Organization, 2012)

Several instruments have been developed to measure QoL, each with its own conceptual foundation and domains of interest. Among the most commonly used are the Short Form Health Survey (SF-36), the WHO Quality of Life-BREF (WHOQOL-BREF), and the EuroQol-5 Dimension (EQ-5D).

- SF-36: This instrument includes 36 items covering eight domains: physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning,

pain, and general health perceptions. It is widely used in clinical practice and research to assess general health and well-being (Brazier *et al.*, 1992).

- WHOQOL-BREF: Developed by the WHO, this questionnaire assesses QoL across four domains: physical health, psychological health, social relationships, and environment. It is culturally sensitive and can be used across different settings and populations (World Health Organization, 2012).
- EQ-5D: The EQ-5D is a standardised instrument used as a measure of health outcome. It provides a simple descriptive profile and a single index value for health status. The EQ-5D covers five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It is known for its simplicity and ease of use, which makes it a popular choice in both clinical settings and large-scale health surveys (Herdman *et al.*, 2011).

1.4.1.1.1 Variation Between Different Measures

The choice of QoL measurement tool can significantly affect the outcomes and interpretations of a study. For instance, while the SF-36 provides a comprehensive assessment across multiple domains, its length can be burdensome for older adults or those with severe health conditions. The WHOQOL-BREF, on the other hand, offers a more culturally nuanced perspective but may lack the specificity needed in clinical trials focused on specific health interventions.

The EQ-5D, with its focus on five essential dimensions of health, strikes a balance between comprehensiveness and simplicity. Its design allows for the generation of a single index value that can be used in economic evaluations of health interventions. This makes it particularly useful in health services research where the economic impact of interventions is a key consideration.

In this thesis, the EQ-5D was employed to measure health-related quality of life (HRQoL) among older adults with multimorbidity and frailty. The choice of EQ-5D is driven by its validated use in diverse populations, its ability to generate a single summary index for health status, and its practicality in large cohort studies. By using the EQ-5D, this research aims to provide clear and comparable measures of HRQoL that can inform health policy and clinical practice. In this context, the EQ-5D's comprehensive approach to measuring

HRQoL becomes particularly relevant, as it can effectively capture the broad impacts of various health conditions and their combinations.

The array of health conditions can have varying impacts on quality of life, with the gravity of these conditions directly affecting it. Some studies even suggest that certain condition combinations can reduce life quality more than what might be anticipated from examining each ailment individually (Fortin *et al.*, 2007). However, many of these investigations only focus on specific conditions or categorise them based on their respective organ systems. It is also important to note that factors like age, gender, and socio-economic position might influence quality of life along with multimorbidity. Current research is mixed as to the extent to which these factors explain the connection between multimorbidity and quality of life or the role of frailty in this relationship. A noticeable gap exists in longitudinal studies in this area, making it hard to determine how multimorbidity influences quality of life. Further research is necessary to truly understand the effect of multimorbidity on quality of life and the role of potential confounding elements.

Health-related quality of life depends in part on multimorbidity and associated adverse outcomes (Gu *et al.*, 2018; Makovski *et al.*, 2019). Quality of life is a core outcome measure and is a meaningful metric when evaluating multimorbidity services (Smith *et al.*, 2018). Many studies have identified a positive association between high-burden multimorbidity and mortality, in addition to many other outcomes such as hospitalisation and poor function (Tisminetzky *et al.*, 2016, 2020; Jones *et al.*, 2017; Olaya *et al.*, 2017). Moreover, a positive association has also been identified between multimorbidity and increased demand for healthcare services (Violán *et al.*, 2014). Studies investigating a specific range of conditions have shown that quality of life varies according to the conditions present, with physical and mental health conditions impacting different component measures of quality of life (Walker *et al.*, 2016). One study found vascular, upper gastrointestinal and musculoskeletal conditions had the strongest negative impact on quality of life (Fortin *et al.*, 2007). There remains uncertainty about confounding factors such as socio-economic position, age, physical functioning, and social networks in the association between multimorbidity and quality of life

(Lawson *et al.*, 2013). Accounting for these factors could indicate potential avenues for treatment management interventions to improve quality of life in people living with multimorbidity.

1.5 Challenges in Treatment Management

1.5.1 Definition and Implications

The term *treatment burden* refers to the strain and demands placed on patients (and their caregivers) due to navigating care from various providers, adhering to intricate medication regimens, and managing multiple aspects of their healthcare (Mair *et al.*, 2014; Wallace *et al.*, 2015; Rosbach *et al.*, 2017). Studies focusing on individuals with singular health issues like diabetes, heart failure, or cancer underscore the significance of this burden. Such challenges can lead to patients feeling overwhelmed, making them less likely to stick to their medication routines and manage their health actively. This can also influence their perception of the quality of care they receive. For instance, some UK-based findings suggest that individuals with multiple chronic ailments may not have as favourable an experience in primary care settings as those with fewer or no chronic issues (Paddison *et al.*, 2015; Weston *et al.*, 2016).

While the concept of treatment burden is recognised, there is a shortage of detailed research on its magnitude and ramifications, especially among patients grappling with multiple conditions simultaneously. One challenge is the absence of standardised tools to assess treatment burden beyond the side effects of medications quantitatively. Despite initial efforts to develop such instruments for those with multiple chronic conditions (Tran *et al.*, 2012; Eton *et al.*, 2015), a clearer understanding of how patients perceive and cope with this burden and its influence on clinical results is urgently needed.

1.5.2 Consequences of multimorbidity for caregivers

Carers often face significant strain when assisting individuals with chronic conditions. Evidence has shown that those who provide care for persons with chronic issues tend to experience elevated risks of mental and physical health problems, even leading to increased mortality rates (Schulz *et al.*,

2008; Adelman *et al.*, 2014). Research focusing on patients with multiple conditions in their last year of life showed that both the patient and caregiver grapple with medication management and continuity of care issues (Mason *et al.*, 2016). A similar sentiment was echoed in a Canadian study, where caregivers frequently expressed dissatisfaction due to poor communication among medical professionals (Gill *et al.*, 2014). Yet, research specifically targeting caregivers of those with multiple conditions remains limited, leaving questions regarding whether their challenges are heightened due to the intricacies of managing several ailments.

1.5.3 Challenges for healthcare professionals in managing multimorbidity

Healthcare professionals (HCPs) often face obstacles when attending to patients with multiple conditions, primarily due to limited time, resources, and complexities in implementing various clinical guidelines for one individual (O'Brien *et al.*, 2011). Specialist HCPs might also find it challenging to manage conditions beyond their expertise or adjust treatments considering multiple conditions. A systematic review encompassing multiple high-income countries revealed that HCPs encounter a myriad of issues, ranging from fragmented healthcare systems to the challenges of providing patient-centric care and promoting shared decision-making (Sinnott *et al.*, 2013). General practitioners, in particular, often feel professionally isolated when managing such patients. Evidence suggests that these challenges can compromise the quality of care provided (Zulman *et al.*, 2014).

1.6 Economic Burden of Multimorbidity

1.6.1 Patterns and dynamics of healthcare utilisation in multimorbidity

Patients with multiple health conditions significantly impact healthcare demand, often visiting primary care more and having higher hospital admission rates, regardless of age, gender, or socio-economic position (Payne *et al.*, 2013). An increase in chronic conditions correlates with higher healthcare usage even in low- and middle-income countries, though these data are less comprehensive than that from more affluent nations (Lehnert *et*

al., 2011; The Academy of Medical Sciences, 2018). Additional evidence indicates that social care costs associated with both professional care providers and informal caregivers increase substantially when multimorbidity is present (König *et al.*, 2013; Kasteridis *et al.*, 2015; Picco *et al.*, 2016).

As health services have historically operated with a single disease focus, there are few multimorbidity guidelines, with the 2015 National Institute for Health and Care Excellence (NICE) guideline being one of the first. Poor transitions between services for older people increase the risk of adverse outcomes, influencing service utilisation. A critical research priority should be addressing the increased vulnerability to these outcomes, including death or functional decline (Walsh *et al.*, 2020), hospitalisation (Tisminetzky *et al.*, 2020), adverse drug reactions (Stevenson *et al.*, 2019), and rapid increases in healthcare expenditure (Kuo *et al.*, 2013; Orueta *et al.*, 2014; Chen *et al.*, 2018; Caballer-Tarazona *et al.*, 2019).

Individuals often bear a significant portion of expenses, particularly when covering out-of-pocket (OOP) costs. In the US, it is clear that the average OOP expenditure escalates with an increasing number of chronic conditions (Crystal *et al.*, 2000; Schoenberg *et al.*, 2007). This trend is consistent across various nations where individuals must bear a part of their healthcare bills. Moreover, findings from the WHO's SAGE study highlighted that outpatient OOP costs rose in tandem with the number of non-communicable diseases (NCDs), with medication often being the biggest expense (Lee *et al.*, 2015).

Multimorbidity also brings about indirect costs, such as transportation and lodging for medical appointments or the loss of earnings for both the patients and their carers. The available financial data on multimorbidity primarily stems from HICs and predominantly pertains to older people.

To aid in decision-making and resource allocation further research is needed to understand healthcare use patterns in individuals with multimorbidity, focusing on identifying barriers and facilitators to efficient service use. Key areas include analysing differences in healthcare utilisation based on disease burden, frailty, overall usage, and socio-demographic characteristics. This has implications for both individuals and society, not least in terms of cost.

While the high use of primary and specialist ambulatory care may be appropriate for long-term multimorbidity management, frequent unscheduled care is an equally common outcome that services must address (Purdy, 2010). High-burden multimorbidity, even if small in absolute terms, accounts for the largest proportion of unscheduled care use (Payne *et al.*, 2013; Stokes *et al.*, 2021). There are relatively few studies examining the relationship between multimorbidity and unscheduled care and how this relates to long-term service use. The high rate of unscheduled hospital admissions may be attributed to many factors. These can include using basic diagnostic testing or treatments that take little account of the complexity of an individual's health, disease progression requiring acute care, a delay by patients in seeking care, medical errors and the inability to access urgent home care services (Reed *et al.*, 2015).

Service use following an episode of unscheduled care often involves inpatient readmission (Coatsworth-Puspoky *et al.*, 2021) and increased primary and social care use (Williams *et al.*, 1991; Stafford *et al.*, 2018). Health and function before and following an unscheduled admission are likely to influence service use after discharge, though they have not been comprehensively quantified (McPeake *et al.*, 2021).

Navigating the complex landscape of multimorbidity requires a multifaceted and systematic approach that integrates various services and prevention strategies at different levels of healthcare management. Understanding the complex patterns in service utilisation is necessary to achieve this dynamic integration, which is fundamental to establishing services that adequately address multimorbidity at the individual level (e.g. personalised self-management plans) and at the service and organisational level (Harvey *et al.*, 2018). In England, the concept of integrated care varies in meaning to people and has taken on numerous forms in health policy. One such policy introduction is the Health and Care Bill from 2022, introduced to foster closer ties between services and legally establish Integrated Care Systems (comprising Integrated Care Boards and Partnerships), in particular within the NHS and social care sectors (UK Government, 2022).

Since its inception in 1948, the NHS (in England and Wales) has not been responsible for delivering social care—a sector dedicated to offering sustained support for individuals living with long-term challenges due to ageing, economic hardships, chronic illness, or disabilities. Rather, this duty has remained with local governmental entities, resulting in a distinct separation in how health and social care services are provided and financed (Briggs *et al.*, 2020). Consequently, this delineation of duties has produced persistent barriers to achieving seamless integration between these two critical sectors.

Despite these challenges, the government has actively implemented initiatives to dismantle these barriers. It has sought ways to promote and facilitate collaboration among health and care establishments in the conceptualisation and roll-out of services (Maniatopoulos *et al.*, 2019; Lewis *et al.*, 2021). Such endeavours stem from the understanding that the current complex and segmented system creates challenges for patients navigating the system and possibly engenders conflicting organisational motivations, which could be at odds with the overarching goal of enhancing the health outcomes of the wider population.

1.7 Prevention of Multimorbidity as a Strategy

With multimorbidity increasing worldwide, proactive measures to counteract the onset of multimorbidity are crucial. A primary prevention approach involves employing established techniques that curb individual conditions that typically group together. For instance, smoking cessation reduces cardiovascular, respiratory, and specific cancer risks, leading to reduced mortality (Doll *et al.*, 2004). Likewise, managing blood pressure can prevent coronary disease, heart failure, and kidney disease. Also, managing LDL-cholesterol can counteract coronary heart diseases. Understanding that these conditions often converge means interventions can curtail the likelihood of associated multimorbidity. For example, integrating smoking cessation, blood pressure reduction, and cholesterol management can cut down incidences of heart diseases and related conditions.

Besides personal-level benefits, broader community changes, like taxing unhealthy products, can cut down multimorbidity at a population scale. Evidence suggests that levies on tobacco can curb smoking and associated illnesses (Jha *et al.*, 2014). Similarly, taxing sugar-rich products can potentially diminish chronic cardiometabolic diseases by controlling obesity, a known precursor to hypertension and type 2 diabetes. However, understanding the feasibility and effectiveness of these strategies is vital, especially considering their economic implications. Regarding conditions like depression, back pain, or cognitive issues, definitive prevention methods remain elusive. Some studies suggest blood pressure management might reduce dementia risks (The Lancet Neurology, 2017).

A holistic approach to preventing multimorbidity may necessitate the integration of non-communicable and infectious disease insights. Some cancers, like cervical cancer from HPV, and chronic ailments like heart disease from bacterial infections, underscore the interplay of infectious agents in chronic disease development. Enhancing infectious disease control via vaccines and treatments might reduce the onset of multimorbidity in terms of both infectious and chronic diseases.

Improving multimorbidity prevention requires discerning which conditions cluster and carry the most disease burden, aiding in tailoring diagnosis and preventative measures. Challenges persist in synchronising multiple preventative interventions and handling cases where one condition might trigger another. However, blending insights from individual condition prevention with knowledge about condition clusters can pave the way for integrated prevention methods, possibly more effective than focusing on individual conditions in isolation.

1.8 Modern Approaches to Multimorbidity Management

Addressing the needs of patients with multiple ailments does not always necessitate a specialised multimorbidity-focused approach. However, as the intricacy of the conditions or the associated treatments intensifies, there is a heightened demand for tailored strategies that consider the multifaceted nature of multimorbidity (Farmer *et al.*, 2016; National Institute for Health and

Care Excellence, 2016). Furthermore, care for older adults in secondary care settings is reactive to acute health crises such as falls, immobility and delirium (Turner *et al.*, 2014). The resulting pressure on acute services from emergency admissions has resulted in a shift in how care is delivered, from primary care settings towards specialist hospital-based care (Turner *et al.*, 2014). An example of this includes decisions about how a frail older adult should be cared for being made by non-specialist health and social care staff in community settings without support from specialists (Turner *et al.*, 2014; Harvey *et al.*, 2018). Yet, determining the best care approach for these patients, especially those with intricate healthcare requirements, remains a challenge for several reasons.

1.9 Modern Management Challenges in Multimorbidity

1.9.1 Clinical trials and multimorbidity considerations

A foundational aspect of treating patients with multiple conditions is using proven safe and effective techniques for individual conditions. However, these treatments are typically validated through clinical trials that may exclude patients with multimorbidity (Fortin *et al.*, 2006; Buffel du Vaure *et al.*, 2016). This exclusion often stems from concerns that having other conditions might overshadow the treatment's intended effects or magnify its side effects. Despite these concerns, it is unclear whether excluding such patients from trials is an equitable approach to those patients most likely to need evidence-based care. Due to stringent eligibility criteria, many trials might not encapsulate the broader patient population affected by the condition under study. Consequently, extrapolating results from these trials to a larger demographic, especially those with other co-existing conditions, becomes problematic. Although the criteria differ across trials, comprehensive analyses can still gauge treatment effects within multimorbidity-defined subgroups. For instance, blood pressure and cholesterol level reduction studies indicate similar cardiovascular risk reduction regardless of major comorbidities (Kearney *et al.*, 2008; Blood Pressure Lowering Treatment Trialists' Collaboration, 2014). However, due to their elevated risk, the net benefit may be higher in those with certain

comorbidities, like pre-existing heart issues. Moreover, the adverse effects might disproportionately affect patients based on their unique health profiles. For instance, a diabetes medication might increase fall risk by a modest percentage, translating to minor concerns for a young individual but posing significant dangers to an older post-stroke patient. One approach to navigate this disparity is by combining relative treatment effects from trials with real-world risk data, providing a more personalised treatment perspective.

1.9.2 Single disease model and multimorbidity

Contemporary healthcare models and guidelines primarily focus on treating specific ailments, often sidelining the integrated care needed for multiple conditions. This single-condition focus is evident in advanced healthcare sectors, structured around particular medical specialisations. Patients with multiple ailments often express dissatisfaction with this fragmented approach, lamenting the need to interact with several health professionals and wade through intricate healthcare systems (Sinnott *et al.*, 2013). This dissatisfaction can amplify treatment-related burdens and negatively influence their perception of care quality. Health professionals echo these sentiments, frequently feeling constrained by brief consultations and inadequately equipped to tackle patients with conditions outside their main expertise (Stokes *et al.*, 2017). Current single-condition guidelines rarely address concurrent conditions and can overwhelm health professionals. To deliver comprehensive care, they must be conversant with all guidelines for common conditions and meld this knowledge to tailor a patient's care plan (Wyatt *et al.*, 2014). Given the complex nature of these guidelines, their constant updates, and potential inconsistencies, this becomes a Herculean task. With healthcare pivoting around individual-condition specialties and directives, there is a looming threat of polypharmacy for patients dealing with multimorbidity. As the drug count escalates, so does the possibility of adverse effects, accentuating risks for multimorbid individuals, particularly when they get prescriptions from across healthcare sectors. This becomes even more precarious for older people.

1.9.3 Addressing multimorbidity in modern healthcare

There is substantial evidence linking multimorbidity, especially in those with co-existing physical and mental conditions, to increased instances of adverse drug reactions (Moffat *et al.*, 2015). Moreover, as the number of chronic conditions increases, so does the likelihood of patients reporting safety incidents. It is particularly alarming for the older population where treatment from multiple physicians correlates with increased adverse drug reactions.

Many healthcare professionals express reservations about applying single-condition guidelines to multimorbid patients, fearing potentially inappropriate care. Addressing this could involve creating guidelines centred on frequently occurring condition clusters. Still, this necessitates more data from trials evaluating treatments targeting multiple conditions either simultaneously or sequentially.

Overall, the current fragmented approach for multimorbidity care might result in inadequate management. The division between mental and physical healthcare in several nations puts those with both conditions at risk, despite their heightened healthcare interaction. It is vital to prioritise research into treatment plans tailored for prevalent multimorbidity patterns.

1.9.4 Rethinking healthcare models for multimorbidity

Three key healthcare levels that could be revamped to cater to multimorbidity are the patient, provider, and organisational levels. The success of any model depends on its context. It is imperative to test innovative interventions empirically across varied settings and demographics. Both designing and assessing multimorbidity interventions might be complex, emphasising the need for a standardised framework for developing and reporting care models (Moore *et al.*, 2015).

Personalised interventions aim to empower patients by promoting self-management and facilitating meaningful conversations with HCPs about individual preferences and concerns. This might encompass non-medical considerations crucial to patients, like their social and environmental backgrounds.

Healthcare provider interventions primarily focus on enhancing the capabilities of HCPs when catering to patients with multiple conditions. However, current research does not provide conclusive evidence about these interventions leading to enhanced care or better patient outcomes. Nevertheless, it is plausible that offering support to HCPs at the provider level might elevate the quality of care for those with multiple illnesses. A key challenge for providers is reconciling multiple and potentially conflicting treatment guidelines for individual ailments.

Personalised care planning is a cornerstone in coordinating the treatment and management of multimorbidity. This involves consciously developing tailored strategies sensitive to each patient’s unique needs and circumstances. A crucial element in this process is the adoption of a preventative approach, which can be delineated into primary (preventing the onset of disease by managing risk factors), secondary (preventing the exacerbation of existing diseases), and tertiary prevention strategies (aimed at reducing symptoms and enhancing the quality of life) (Lorig, 1996; Gordis, 2014). Moreover, the management of multimorbidity has now emerged to include quaternary prevention. This level of prevention scrutinises the individual's overall health state and conditions, to discern which treatments or investigations are essential, moving beyond rigid adherence to guidelines. It involves judicious appraisal of the clinical picture and critically evaluating the potential benefits and drawbacks of various treatment modalities (The Academy of Medical Sciences, 2018). Digital tools supporting clinical decisions about treatment measures might be useful in this regard, although these methods addressing multiple conditions have yet to be adequately evaluated.

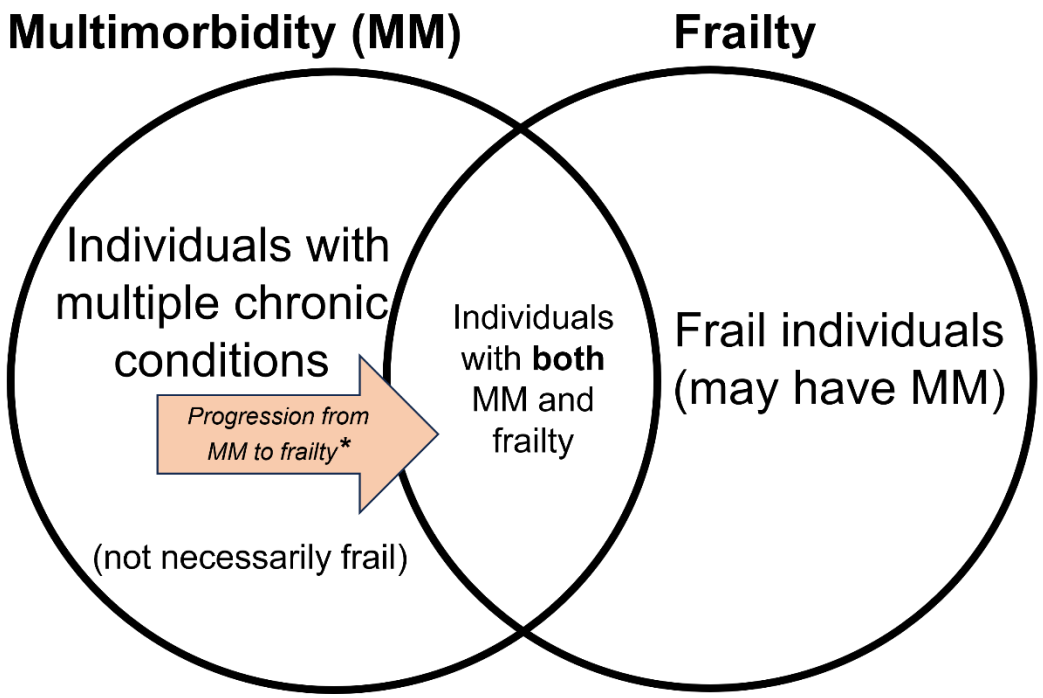
In addition to these preventive strategies, an emphasis on an individualised assessment of the health state and facilitating the establishment of realistic treatment objectives firmly grounded in the patient’s priorities and preferences is termed the *Ariadne principles* (Mangin *et al.*, 2016). Although few tools exist for measuring patient priorities and preferences regarding their treatment plan, implementing such an approach fosters a patient-centred care environment, where the individual's values and desires are seamlessly

integrated into the treatment paradigm, fostering better health outcomes and enhanced quality of life.

1.10 The Relationship Between Multimorbidity and Frailty

Along with multimorbidity, the complex needs of older adults are commonly also related to frailty (Clegg *et al.*, 2013), determining where an individual sits on the health continuum (Ensrud *et al.*, 2018; Zucchelli *et al.*, 2018). Frailty is the cumulative decline across multiple physiological systems, causing decreased resistance to stressors and vulnerability to adverse outcomes (Fried *et al.*, 2001). Frailty is associated with multimorbidity, although not synonymous. Nonetheless, it is common in individuals with multimorbidity, with evidence of a bidirectional association (Figure 1-3) (The Academy of Medical Sciences, 2018).

Figure 1-3: Relationship between multimorbidity and frailty in older adults



***** Typical progression, but not always the case.

Note: This figure illustrates that while there is a significant overlap between multimorbidity and frailty, the two are distinct conditions. Most frail individuals have multimorbidity, but not all individuals with multimorbidity become frail.

1.10.1 Competing models of frailty

Frailty can be conceptualised through various models, each providing a unique perspective on its assessment and management:

1. The Phenotype Model: Proposed by Fried et al., this model identifies frailty based on the presence of specific clinical criteria such as weight loss, exhaustion, weakness, slowness, and low physical activity. Individuals meeting three or more of these criteria are classified as frail (Fried *et al.*, 2001).
2. The Cumulative Deficit Model: This model, developed by Rockwood et al., views frailty as the accumulation of deficits across multiple domains, including physical, cognitive, and social aspects. The frailty index is calculated by counting the number of deficits present in an individual (Rockwood *et al.*, 2007).
3. The Biopsychosocial Model: This comprehensive approach incorporates biological, psychological, and social factors to understand frailty. It emphasises the interaction between these domains and how they collectively influence an individual's frailty status (Cohen *et al.*, 2023).
4. The Multidimensional Model: This model considers frailty as a multidimensional syndrome that includes physical, cognitive, emotional, and social components. It highlights the need for integrated assessments and interventions that address all these aspects simultaneously (Dent *et al.*, 2016).

There is a wealth of evidence on the management of frailty. Beneficial interventions include physical activity (De Labra *et al.*, 2015; Negm *et al.*, 2019), de-prescribing (Ibrahim *et al.*, 2021) and multifactorial nutritional changes (Khor *et al.*, 2021). In comparison to frailty, the evidence around multimorbidity, while emerging, remains limited and inconsistent. Part of the reason is the difficulty in selecting appropriate outcome measures in trials (disease-specific measures may have limited applicability) or identifying

subgroups for targeted treatment in such a heterogeneous patient population (Xu *et al.*, 2017; Smith *et al.*, 2021). In contrast, frailty interventions are more likely to focus on functional measures such as independence with activities of daily living. In older adults, multimorbidity and frailty are independently associated with high service use, with a multiplicative rise in costs (Villacampa-Fernández *et al.*, 2017; Cheung *et al.*, 2018; Ensrud *et al.*, 2018; Shand *et al.*, 2021). However, how multimorbidity alone influences service use and cost and how the presence of frailty then modifies this requires additional investigation.

Identifying frailty in multimorbidity management could be useful in establishing interventions that consistently improve outcomes (Le Reste *et al.*, 2013; Yarnall *et al.*, 2017; Hanlon *et al.*, 2018). Because frailty also accounts for functional abilities in older people with multimorbidity, the construct might capture those especially vulnerable to adverse outcomes (Yarnall *et al.*, 2017). Given the existing evidence-based interventions for frailty, identifying frailty in multimorbidity management could improve the accuracy of targeted interventions (Le Reste *et al.*, 2013; Yarnall *et al.*, 2017; Hanlon *et al.*, 2018; The Academy of Medical Sciences, 2018). Yet frailty is not consistently used to inform the management of multimorbidity. Evidence emphasising the imperative of incorporating the assessment of frailty when measuring and designing interventions when addressing multimorbidity is required.

Conceptually, frailty incorporates multimorbidity in how it is measured but multimorbidity is not often measured with frailty being among the counts of conditions. These two conditions are intricately related, and evidence has shown that one should be consistently considered when measuring the other (Farmer *et al.*, 2016; National Institute for Health and Care Excellence, 2016).

As touched on above (tertiary and quaternary prevention, Ariadne principles) good health in old age is not just the absence of disease (Wang *et al.*, 2017). The potential role of enhancing one's intrinsic capacity as a strategy to decelerate the progression of frailty has been an area of focus in the existing

literature. However, there is a complex relationship whereby frailty emerges due to the cumulative burden associated with managing multimorbidity and undergoing numerous treatments. Despite health promotion efforts, multiple illnesses and their treatments may eventually lead to frailty. In contrast, it is also possible for an individual, with up to five concurrent diseases, to maintain a well-managed health regime and functional independence, averting the onset of frailty. Alternatively, frailty might develop, but any subsequent incident disease beyond the third does not exacerbate the frailty progression in a significant manner. This suggests a nuanced interplay between multimorbidity and frailty, indicating the need for a deeper exploration and understanding of these dynamics *(Wang et al., 2017).* As previously touched on, frailty can be considered in relation to deficit accumulation with a frailty index being a measure of this condition; a frailty index counts deficits in health which may include symptoms, disabilities and diseases (Rockwood *et al.*, 2007; Searle *et al.*, 2008). Thus, by design frailty considers multimorbidity in how it is measured, this is not often the case for considering frailty within how multimorbidity is measured despite recommendations from organisations such as NICE.

1.10.2 Management of multimorbidity and frailty

Care models that reconcile differences between disease-specific recommendations are crucial for managing multimorbidity (Valentijn *et al.*, 2013). Integration, a model of care across services including hospitals, community and social care, facilitates collaboration without barriers between healthcare partners (Shaw *et al.*, 2011). Far-reaching benefits for older adults with frailty and multimorbidity can be achieved from coordination or integration of care (Nolte *et al.*, 2014; Turner *et al.*, 2014). In early 2021, the English Department of Health and Social Care published legislative proposals for a Health and Care Bill: *Integration and Innovation: working together to improve health and social care for all* (Department of Health and Social Care, 2021) indicating this as a post-pandemic policy priority. The Health and Care act of 2022 put integrated care systems (ICSs) on a statutory footing in contributing toward this priority.

Acute care for older adults, essentially reactive to acute health crises such as falls, immobility and delirium, is mainly based in secondary care settings (Turner *et al.*, 2014). Specialist Geriatrician input is now delivered in hospital-based settings rather than community settings (Turner *et al.*, 2014). Integrated care models seek to resolve separations such as this. Measuring how individuals navigate between services would provide valuable insights into how integrating care systems affects multimorbidity outcomes (Briggs *et al.*, 2020). Conversely, any adverse outcomes and opportunity costs from integration must be evaluated as part of any implementation. Establishing the determinants and implications of multimorbidity to be addressed through care integration requires whole-population data. Additionally, linking data from across health and social care settings facilitates the analysis of outcomes within a single health economy. Valuable evidence from cohort analyses of linked data can inform the long-term integrated management of multimorbidity in complex older adults.

Interventions for older adults should address multimorbidity and frailty compared to targeting only one aspect. As individuals age, they traverse a spectrum that ranges from a state of robustness to a phase characterised by frailty and increased dependence on care. Determining the appropriate interventions at various stages can benefit greatly from establishing clear markers that signify the transition from one phase to another, such as the shift from robustness to a state of frailty.

Moreover, it is essential to foster a proactive approach to maintaining health among older adults and their caregivers. Often, the trajectory involves a frail older adult experiencing an emergency room visit due to an incident or rapid deterioration in health, followed by a transfer to a geriatric unit for further diagnostic procedures and care. This hospitalisation period frequently exacerbates functional impairments, which might not be addressed adequately before discharge. If returning home is not feasible due to clinical or social issues, the individual might be placed in a care facility, heightening their dependence on care.

A pivotal strategy in realigning services to meet the needs of these individuals involves the active identification of grades of frailty. In this scenario, equipping physicians, healthcare personnel, and policymakers with the necessary knowledge on detecting frailty is fundamental, particularly when managing multimorbidity has been the primary focus.

1.11 Cohort Methods for Health Services Research

Multimorbidity can be complicated because the clinical manifestations of the same conditions can vary across individuals. A useful method of investigating multimorbidity is analysing prospective data, particularly for adverse outcomes, independent of and concerning frailty. Data from longitudinal cohort studies gather information on demographic characteristics, clinical features or presentations that may change with time and outcome data relevant to multimorbidity. Such studies describe disease manifestations and their long-term implications. Cohort studies provide useful evidence to plan trials, such as multimorbidity management interventions.

A key feature of a longitudinal cohort is the degree to which it has been internally and externally validated. This refers to the representativeness of participants for the population from which they were drawn. A random sample meeting this requirement aims to minimise selection bias. Additionally, tools measuring variables must be valid and reliable, with effort made to maximise follow-up to avoid attrition bias. The design and analysis of a dataset can account for confounders, including temporal or baseline characteristics. Analysis of electronic data linked across health and social care, including service use and cost, is another method for informing service design.

Despite the benefits, cohort studies have methodological limitations that need emphasis. Relationships between exposure and outcomes are subject to confounding between variables. Addressing this involves adjusting for the individual effects of each variable on the outcome. Longitudinal analyses link observations from one individual over time and consider time-varying aspects to quantify exposures and outcomes. These aspects can be addressed statistically. Proportions of participants showing multimorbidity patterns, alone or together with frailty, can then be identified. Associations identified in

cohorts can then inform the development of interventions, including randomised control trials (RCT). These relationships additionally inform service design, such as integrated care systems for multimorbidity. Frailty, which encapsulates the essence of old age, is a key predictor of health-related factors influencing service usage or treatment response to management interventions. Investigating this relationship in a cohort, and the role of multimorbidity, would yield crucial insights for designing healthcare services.

1.12 Data Linkage and Health and Social Care Service Use

As healthcare systems strive to evolve in a manner that maximises both efficiency and patient-centred approaches, better integration of care across settings is required to understand the patient journey and deliver effective and efficient care. Health and social care data linkage at the individual level offers a quantifiable view of a person's interaction with services across health settings. This facility has the potential to understand actual service use within health economies more comprehensively. Since the late 1980s, UK primary medical care has transitioned to almost exclusively electronic records. This shift enabled the creation of major research databases, including the Clinical Practice Research Datalink (CPRD) and Hospital Episode Statistics (HES), and expanded the use of Electronic Health Records for diverse epidemiological studies and clinical trials (Edwards *et al.*, 2023). Available data might start with routinely collected health data from the primary care setting, including demographic characteristics and information on chronic illness. To this, local authority data collected as a statutory requirement, such as housing, education and social care can be linked. Other data sources that may be linked include data from the acute care setting, showing how an individual navigates and uses services. However, the main challenge in achieving this is that individual health and care organisations store and process their data separately, including collecting, further highlighting the separation between the health and social care settings and barriers to integration.

Using and sharing real-world data (RWD) presents particular challenges, especially around data protection and associated data governance. Public benefit is potentially forfeited by the underutilisation of RWD for secondary uses, in part due to risk aversion. Risk aversion refers to the tendency of individuals or organisations to avoid taking risks, even if the potential benefits outweigh the potential costs (Jones *et al.*, 2023). Risk aversion can lead to underutilisation due to concerns around data protection and governance in the context of using real-world data for public benefit. The use of RWD for research purposes raises ethical challenges, such as ensuring the confidentiality and security of patient information, obtaining appropriate approvals, demonstrating research merit, and adhering to strict data security and privacy standards. Additionally, research involving human subjects must comply with ethical standards, and independent research ethics committees review and approve research proposals to ensure that they meet ethical guidelines (Jones *et al.*, 2023). Despite this challenge, it is possible to link data from different settings and utilise the benefits that data linkage offers to achieve care integration.

In England and Wales, every individual is assigned a unique identifier the first time they receive NHS care or treatment (commonly at birth), the NHS number. In Scotland, this is the Community Health Index (CHI) number and in Northern Ireland, a Health and Care (H&C) number. This unique identifier can be used to identify patient records across settings and link health data accurately. However, other sources of data, such as the local authority who would hold data on social care for example, are unlikely to use these unique identifiers used in the NHS as their own individual identifiers have been established. This can be resolved by using the sensitive data of individuals such as first and last name, address, and date of birth, though as previously discussed, this does introduce a different set of ethical challenges for research.

1.12.1 Benefits of data linkage

1.12.1.1 A Comprehensive View of Individual Health

Data linkage allows the amalgamation of information from different sectors and provides a 360-degree view of an individual's health and social needs. This comprehensive data repository can allow researchers to investigate how individuals navigate a health system and the relative impact of problems such as multimorbidity on this journey, in part understanding any limitations in service provision at different points. In addition, the resulting findings can guide healthcare professionals in crafting personalised treatment and intervention strategies, grounded in a well-rounded understanding of the individual's circumstances.

1.12.1.2 Resource Allocation and Strategic Planning

By mapping the patterns of service use, data linkage assists in the discerning allocation of resources, helping identify areas where services are either under or over-utilised. Consequently, it enables strategic planning that aligns with the real-time needs of the population, fostering a health economy that is both responsive and sustainable.

1.12.1.3 Research and Policy Development

Aggregated data derived from individual-level linkage serves as a rich resource for researchers and policymakers. It facilitates analysing trends, identifying gaps in service provision, and crafting policies that cater to specific community needs, thus fostering an environment of informed decision-making and policy development.

Data linkage, with its potential to enhance our understanding of how individuals navigate health and social care services is vital for improving how services are integrated to achieve better outcomes. By embracing the integration of health and social care data at the individual level, healthcare systems can transition towards a model that is more responsive, coordinated, and attuned to the unique needs in a time when the population is ageing and health needs are becoming increasingly complex. Employing data linkage methods allows for an in-depth analysis of how demographic characteristics, health states and specific dimensions of health that predict service utilisation

are reflected in actual service use. It is also possible to explore this relationship in the context of multimorbidity and ageing to predict health and social care service utilisation and expenditure.

From the topics discussed in this Chapter, some research priorities emerge. The first emphasises the importance of identifying optimal strategies to enhance treatment outcomes for patients with multimorbidity. For this purpose, it is vital to consider how tools can be developed to aid healthcare professionals in offering holistic, guideline-compliant care. Furthermore, exploring methods that ensure the maximum benefits and minimal risks from the array of treatments often prescribed to these patients is crucial. A significant component of this focus is exploring multimorbidity with consideration for related conditions such as frailty to determine approaches that can better address the needs of older adults.

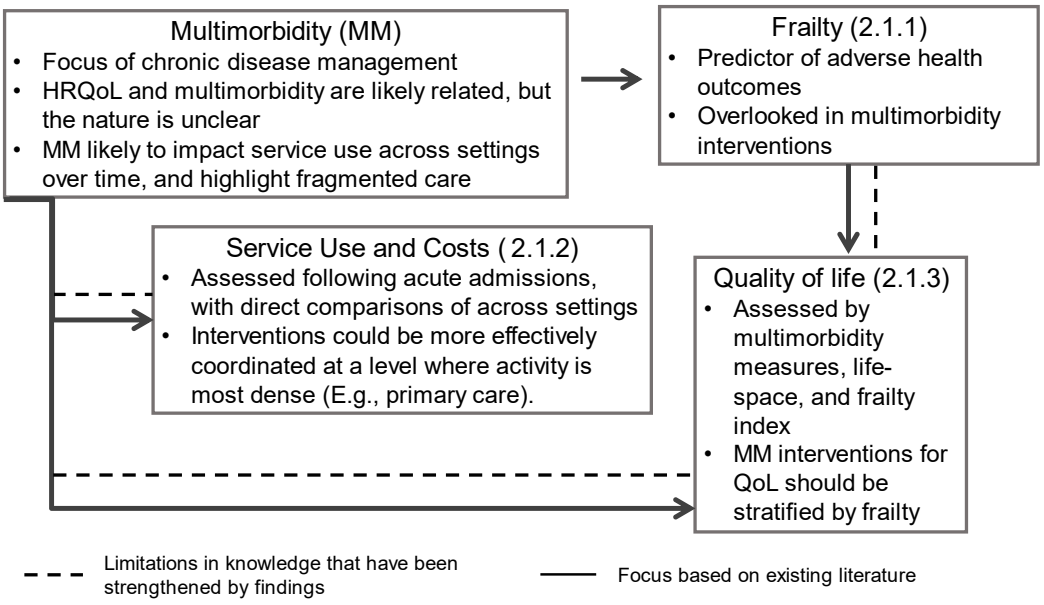
Similarly, the second is centred on the need to optimise healthcare structures to best serve patients with multimorbidity. This involves identifying effective methods to seamlessly integrate services for such patients, by understanding the patient journey and service utilisation patterns. Enhancing clinical outcomes, increasing patient satisfaction, and improving cost efficiency is essential.

This thesis explores the management of multimorbidity and frailty in older adults, focusing on the effectiveness of interventions (Chapter 3), the economic burden (Chapter 5), and potentiel intervention targets by understanding the relationship between life-space mobility, frailty, and quality of life (Chapter 6).

Chapter 2 Research aims and questions

By exploring the consequences of multimorbidity on health and functional outcomes, including quality of life, service use and cost, in older adults with multimorbidity, this PhD will contribute to the evidence base for multimorbidity management (Figure 2-1).

Figure 2-1: Conceptual framework of this thesis



2.1 Research questions

2.1.1 How effective are multimorbidity interventions for older people?

I conducted a systematic review to explore the effectiveness of multimorbidity interventions for older people. The systematic review also described the economic impact of these interventions. Given the overlap between frailty and multimorbidity, I recorded whether multimorbidity-focused studies also accounted for co-existing frailty.

2.1.2 How does unscheduled care impact long-term service use and costs?

Acute admissions reflect not just immediate health crises but also critical changes in patients' functional mobility and the burden of multimorbidity. I

wanted to understand the total health and social care use that might result following such a significant event. Within a single health economy (London Borough of Barking and Dagenham), I explored how unscheduled care impacted long-term service use and costs using data linked across health and social care settings. I explored how demographic characteristics and health states are linked to actual health and social care service use and expenditure.

2.1.3 How do multimorbidity, frailty and mobility relate to health-related quality of life*?*

Poorer quality of life can result from multimorbidity, and a cohort study can quantify the association, particularly to identify sub-groups who might benefit from interventions. I used population-representative data to establish how frailty, multimorbidity, and mobility relate to each other in older age and how they influence quality of life. By seeing how multimorbidity and frailty predicted dimensions of health, measured through health-related quality of life, I considered likely patterns of service need through impairments in functional mobility.

Chapter 3 Which interventions for older people living with multimorbidity are efficacious and cost-effective? A systematic review.

3.1 Summary

In Chapter 1, I described multimorbidity as a public health challenge as populations age and how the physiological decline that occurs results in frailty. Chronic disease management interventions increasingly focus on multimorbidity, though evidence of their effectiveness and economic value remains limited. In section 1.10, I described evidence of an overlap between frailty and multimorbidity in older adults. I also highlighted limitations of existing evidence: despite the overlap between frailty and multimorbidity in older adults, how comprehensively and consistently frailty is used to inform multimorbidity management research is unclear.

This chapter presents a systematic review to determine the efficacy and cost-effectiveness of multimorbidity interventions in older people, and whether focusing solely on multimorbidity enhances our understanding of the health of older people, even without explicitly considering frailty.

I conducted a systematic search across various databases including the Cost-Effectiveness Analysis (CEA) Registry, PubMed, CINAHL, PsycINFO, and Embase, to identify randomised controlled trials assessing multimorbidity interventions in older individuals with an average age of 65 years or older, and with two or more chronic conditions. Key outcomes included quality of life, adverse drug reactions, physical functioning, and prevention of further morbidity. The studies were appraised for quality by two reviewers, and a narrative synthesis was performed, recording data on effect size, homogeneity, and bias. For interventions and outcomes that were the same across different studies, three effect estimates were combined.

This chapter presents findings from 21 studies involving 10,734 participants. It was observed that patient-professional collaborations or integrated care interventions reduced acute admissions and mortality but did not significantly impact quality of life, self-management, or functional disability. Technology

interventions showed positive effects on the quality of care and decreased the incidence of depression, but they did not significantly affect adverse drug reactions or hospitalisations. Although results varied, interventions involving comprehensive assessments by interdisciplinary teams showed clear benefits. However, despite the noted overlap between frailty and multimorbidity, I concluded that interventions for older people with multimorbidity often do not consider frailty and are not apparently cost-effective. Identifying frailty in multimorbidity is likely to be a more useful approach to developing more targeted and effective interventions in older adults.

3.2 Introduction

With greater longevity comes the prospect of living with multiple long-term health conditions (multimorbidity) (Aiden, 2018). Most people living with a long-term disorder will have multimorbidity (The Academy of Medical Sciences, 2018). There is a socio-economic gradient, with disadvantaged populations experiencing multimorbidity 10 to 15 years earlier than in advantaged areas (Barnett *et al.*, 2012). Cumulatively, multimorbidity is associated with poor outcomes such as mortality, hospitalisation, functional dependence, inefficient care, and poor patient experience (Tisminetzky *et al.*, 2016, 2020; Jones *et al.*, 2017; Olaya *et al.*, 2017). Healthcare expenditure also increases along with multimorbidity burden (Caballer-Tarazona *et al.*, 2019). Consequently, understanding the health service inefficiencies in managing multimorbidity in older adults could lead to better care models and economic benefits (Harvey *et al.*, 2018).

The complex health needs that develop with age are also related to frailty, an independent predictor of outcomes including death, hospitalisation, and disability (Turner *et al.*, 2014). Frailty is defined as *a physiological syndrome characterised by decreased reserve and diminished resistance to stressors, resulting from cumulative decline across multiple physiological systems, and causing vulnerability to adverse outcomes* (Fried *et al.*, 2004). There is a clear overlap between multimorbidity and frailty (Figure 1-3) (Vetrano *et al.*,

2019), though many research funding initiatives are orientated to the former. Nonetheless, a wealth of evidence supports the management of frailty (Ellis et al., 2017). Recognising any limitations that might arise if research only focuses on multimorbidity in older people without incorporating the frailty construct is necessary.

Previous systematic reviews in older people have examined interventions for specific disease combinations (e.g., diabetes and depression) (Kastner *et al.*, 2018), polypharmacy management (Hasan Ibrahim *et al.*, 2021; Laberge *et al.*, 2021), or general lifestyle interventions (Crowe *et al.*, 2016). I sought to expand this work by considering all multimorbidity interventions for any older person living with multimorbidity. In frail older people, comprehensive geriatric assessments (CGAs) and complex interventions are beneficial for maintaining living at home and reducing nursing home or hospital admission (Beswick *et al.*, 2008; Ellis *et al.*, 2017). In this chapter, my review contributes to these findings, in addition to the systematic reviews cited above, by investigating the impact of interventions when they are designed and targeted at multimorbidity in older adults. I also aimed to describe studies reporting the economic effectiveness of these interventions. A broader objective was to assess if multimorbidity studies added to our understanding of older people's health even without explicitly considering frailty. During the review process, how crucial frailty was in multimorbidity research for older adults became evident. This led to an important shift in my approach, prompting me to expand the scope of the review to include frailty as a key consideration.

This systematic review sets the foundation for understanding the critical role of frailty in managing multimorbidity. The findings will be further explored in Chapter 6, which examines the relationship between life-space mobility, quality of life, and frailty, and in Chapter 5, which analyses the economic burden of multimorbidity following acute admissions.

3.3 Research aims

In older adults with multimorbidity, I set out to systematically review evidence on: (i) types of interventions for older adults with multimorbidity; (ii) the efficacy of these interventions; and (iii) establish the economic impact of targeted interventions.

3.4 Methods

3.4.1 Protocol and registration

This review follows the Preferred Reporting of Items for Systematic Review and Meta-analysis (PRISMA) guidelines (Page *et al.*, 2021). The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO CRD42021243419). Initially, the review was designed to focus solely on multimorbidity interventions. However, as the review process progressed, how crucial frailty was in multimorbidity research for older adults became evident. Compared to multimorbidity, there is a wealth of evidence on frailty management because frailty is a strong predictor of health and functional outcomes in older adults, as discussed in Chapter 1. Expanding the original protocol and search strategy to cover frailty would have resulted in an overwhelming shift in the evidence gathered. The existing evidence on chronic disease management of multimorbidity would have been overshadowed by the focus on frailty. To avoid this, I maintained the original search strategy but investigated the results for whether published evidence followed guidance to consider frailty in multimorbidity management. This adaptation was guided by emerging evidence and expert recommendations, underscoring the relevance of frailty in multimorbidity research for older adults.

3.4.2 Search strategy and selection criteria

I searched the following databases from inception to 28 June 2021: CEA Registry, PubMed, CINAHL, PsycINFO, and Embase. The search strategy was initially developed in PubMed and adapted for each database used (Appendix Table 1). I also searched the following trial registries: World Health Organization International Clinical Trials Registry Platform and

ClinicalTrials.gov. The search was updated in November 2023, prior to the submission of this thesis.

3.4.3 Study selection

3.4.3.1 Study type

I considered only randomised controlled trials (RCTs). Studies on single conditions with multiple symptoms or medications rather than two or more chronic conditions were excluded. To establish an intervention effect, I excluded studies that assessed only the education or training of healthcare professionals without actual delivery of interventions on older people with multimorbidity (Appendix Table 2).

3.4.3.2 Participants

I included studies of adults where the mean age of the study population was ≥65 years. In line with the WHO (World Health Organization, 2016) and The Academy of Medical Sciences (The Academy of Medical Sciences, 2018), multimorbidity was defined as two or more long-term physical and/or mental health conditions of any body system. This may include cognitive disorders such as dementia or long-term non-communicable conditions such as cancer, or long-term infectious diseases such as hepatitis. *Multimorbidity* became a MeSH term in 2018, updating the previous *comorbidity* term; both were included in the search.

3.4.3.3 Interventions

All interventions specifically designed to address health or functional outcomes in older adults with multimorbidity were considered. Included interventions could involve health and social care professionals such as doctors, nurses, link workers and other care professionals, or health and information technology interventions.

3.4.3.4 Outcome measures

I included studies reporting changes in health state and functional state or ability. Such outcomes could be quality of life, health status or self-management of chronic conditions, activities of daily living, and disability. Economic outcomes included measuring cost-effectiveness, cost-benefit or utility of the intervention.

3.4.4 Data collection and analysis

After de-duplication, two reviewers undertook the eligibility screening of all titles and abstracts for consistency. For studies with multiple publications, I used the most complete data. Studies of potential relevance that I could not confirm for full inclusion by title or abstract were read in full. Each article selected for inclusion was quality assessed in full by the first and second reviewer. I used the Rayyan app to manage this process (Ouzzani *et al.*, 2016).

3.4.4.1 Quality assessment

I used both the Critical Appraisals Skills Programme (CASP) (Appendix Table 3) (Critical Appraisal Skills Programme (CASP), 2013) and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (Appendix Table 4) (Husereau *et al.*, 2013). These tools assess bias, choice of outcome measure, statistical issues, quality of reporting and generalisability. I contacted study authors for additional information where necessary. Quality assessment was not used to exclude studies.

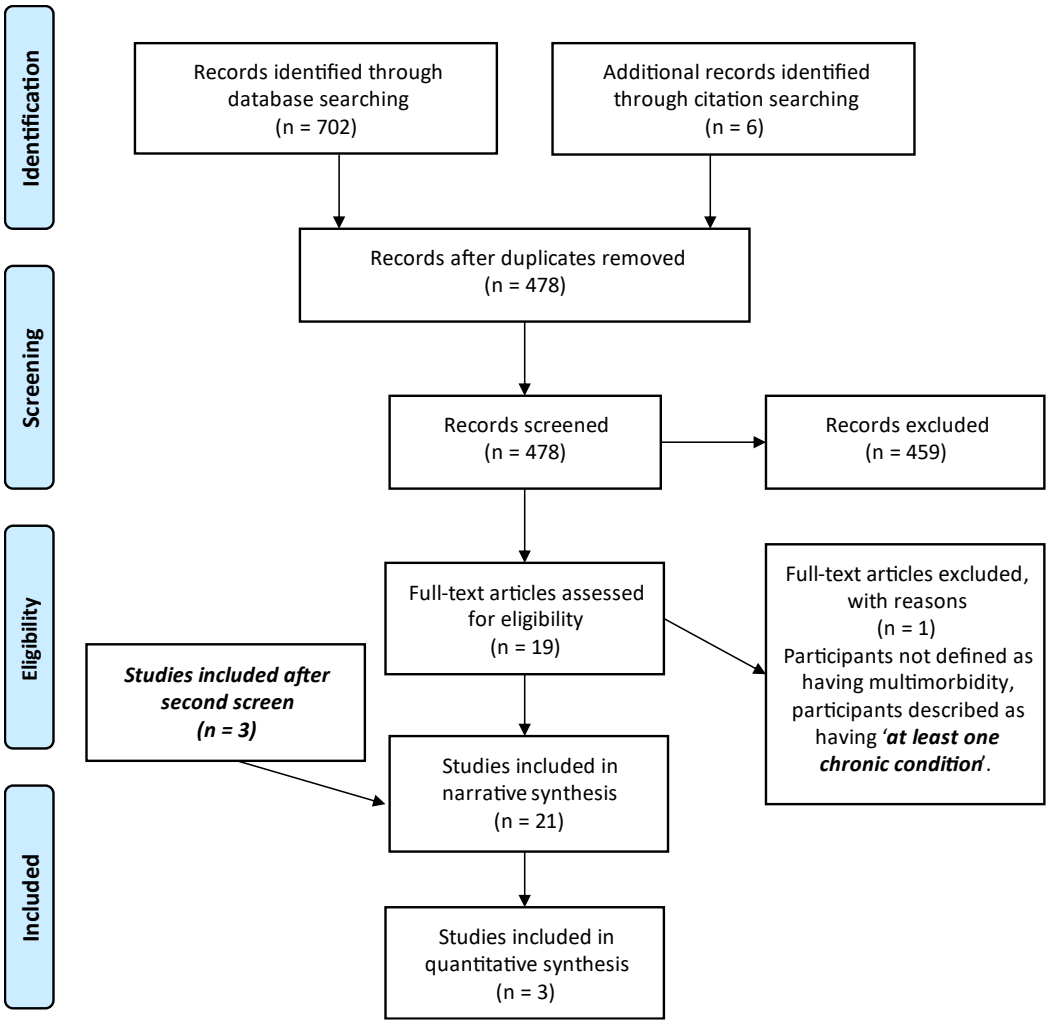
3.4.4.2 Data extraction

Data on setting, participants' clinical and demographic details, operationalisation of multimorbidity, intervention type and outcomes were extracted using a *pro forma*. I used these data for narrative synthesis, recording effect size, homogeneity, and bias. I grouped studies according to the type of intervention. Where appropriate, I combined estimates from studies using random-effects meta-analysis, quantifying statistical heterogeneity using the I2 statistic. All analyses used Stata 16.0 (StataCorp LLC, College Station, Texas).

3.5 Results

I initially identified 478 publications, after removal of duplicates, with 21 randomised controlled trials included (Figure 3-1). Characteristics of these studies are summarised in Table 3-1, describing a total of 10,734 individuals, across varied settings in high-income countries.

Figure 3-1: PRISMA flow diagram



Note: Numbers in ***bolded italics*** show the results from a second screen conducted in November 2023 to update the results of this review prior to submission of this thesis.

Table 3-1: Characteristics of included studies (n=21)

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator
Schäfer (2018)	Germany	GP practices	65 years to 84 years; at least 3 diagnosed conditions. Mean age Control: 74 Intervention: 73	Not well known to their GP (new GP registration or rare appointments); patients lacking mental capacity to consent; psychiatric illness, deafness, or insufficient	650	At least 3 out of 42 ICD-10-based conditions.	Based on chronic care model and narrative based medicine; GPs trained complete narrative-based doctor–patient dialogues regarding treatment targets, priorities, and	Usual GP care

				German language skills; life expectancy of 3 months or less; nursing home residents.			medication reviews. Three separate (30 minute) doctor–patient conversations completed during study period.	
Berntsen (2019)	Norway	Community and hospital	≥60 years; identified for the PAtient Centred Team referral. Mean age Control:79	< 60 years; Wrong home municipality; declined PAtient Centred Team referral.	439	No clear definition provided, suggested as being more than one chronic disease.	A combination of person-centred care, integrated care, and pro-active care delivered through a medical doctor and a team of	Usual care

			Intervention: 80				pharmacists, nurse coordinators, physio- and occupational therapists, geriatric nurses, and medical secretaries.	
Muth (2018)	Germany	GP practices	≥60 years; three or more chronic conditions under pharmacological treatment;	Cognitively impaired; life expectancy less than 12 months at recruitment; alcohol and drug abuse;	505	Multiple chronic or acute diseases and medical conditions co-occurring and in one person.	GP review of all medications (involving use of a computerised decision support system),	Usual care and GP practice team given guidelines for ambulatory geriatric

five or more long-term prescriptions of drugs with systemic effects. Mean age Control: 72 Intervention: 73	participant in another clinical trial in 30 days prior to inclusion.		checklist-based interview with patient regarding medication problems and GP consultation with patient to optimise and prioritise medications.	care to harmonise usual care in both groups.

Table 3-1 Continued

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator
Hastings (2021)	USA	Community	≥65 years and medically complex (defined as having a Care Assessment Need (CAN) score of 90 or greater).	Cognitive impairment or lacking decision making capacity; no available care partner; serious mental illness; high suicide risk; active substance abuse; current	40	Multiple chronic conditions.	Video-enhanced care management involving monthly video calls between patient and study nurse.	Telephone based care management involving monthly phone calls with study nurse.

			Mean age: 65	hospitalisation; nursing home resident; eligible for hospice eligible; unable to communicate by telephone; no email or unwilling to obtain one.				
Ekdahl (2015)	Sweden	Ambulatory care	≥75 years and received inpatient hospital care three	In institutional care	844	Three or more concomitant medical diagnoses.	Comprehensive geriatric assessment team of nurses, doctors, and allied health	Usual care

	or more times in the 12 months prior to recruitment; three or more co-occurring medical diagnoses. Mean age Control: 83 Intervention: 82	professionals. Intervention group supported by team as and when required. Contact could be a few times in a year or daily or weekly. Support given via telephone, home, ambulatory visit.

Noel (2004)	USA	Community	Older patients; high users of healthcare services with complex co-morbidities. Mean age: 71	None stated	104	Chronic complex co-morbidities.	Home telehealth and nurse case manager, intervention delivered through video call and regular telephone reminders).	Usual home healthcare and nurse case management.

Table 3-1 Continued

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator
Kim (2020)	South Korea	Nursing homes	≥65 years; resident of nursing home for at least one week prior to recruitment; neither in a terminal condition nor comatose. Mean age	Transferred out of nursing home.	525	Complex chronic conditions.	Use of an Information and Communication Technology (ICT) system to support nursing staff in a nursing home to conduct standardised comprehensive geriatric assessments, develop care	Usual nursing home care.

			Control:83 Intervention: 83				plans and monitor care.	
Panagioti (2018)	England	Community	≥65 years with two or more self-reported long-term conditions. Mean age: 75	Palliative care patients or patients with reduced capacity to consent.	1,306	Co-existence of two or more chronic condition, where one is not necessarily more central than the other.	Telephone health coaching (promoting healthy behaviours), social prescribing (linking participants to community resources), low-intensity support for low mood (assessing common mental	Usual NHS care

							health problems and offering simple lifestyle advice and behavioural techniques).	
Miklavcic (2020)	Canada	Community	≥65 years English speaker; type 2 Diabetic with at least two other chronic conditions; passed cognitive screening	Living in long-term care facility or living with someone who is already enrolled in study.	132	Two or more chronic conditions.	Up to three in-home visits by nurse, dietician, or both; group session at community site every 6 months; monthly conferences for intervention team; care coordination led by nurse	Usual care

	assessment; referral to chronic disease management program in 24 months prior to recruitment. Mean age not stated.	working collaboratively with others on intervention team and client linked to other relevant health or social services.

Table 3-1 Continued

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator
Markle-Reid (2018)	Canada	Community	≥65 years; English speaker or able to use available interpreter; not planning to leave community for six months study period;	Referred more than two years ago to chronic disease management program team; living with another participant; less than two chronic conditions (in	159	Multiple (two or more) chronic conditions.	Interprofessional team of registered nurses and registered dietitians, a program coordinator, and peer volunteers delivering three in-home visits, having monthly group wellness sessions, monthly case conferences	Usual care

			cognitively intact. Mean age not stated.	addition to diabetes) and planning to leave community in 6 months study period.			and ongoing nurse-led care coordination.	
O'Mahony (2020)	Ireland, Scotland, Spain, Italy, Belgium, and Iceland	Hospital (inpatient)	≥65 years; hospitalised with acute unselected medical or surgical illness.	Under care of specialist or due to undergo specialist consultation.	1,537	Three or more active co-morbidities (conditions requiring ongoing medical therapy).	SENATOR software that produces advice reports to be used in preventing inappropriate prescribing.	Usual care

			Mean age: 78					
Fisher (2020)	Canada	Community	≥65 years; receiving home care services with at least three chronic conditions; English speaking or have access to a translator; mentally competent.	Palliative; no longer receiving home care; planning to move from study community.	59	Three plus conditions.	Interprofessional team of care coordinator, nurse, physiotherapist, occupational therapist, and personal support worker who delivered at least one in-home visit for assessment. In-home visit followed by monthly case conferences to	Usual care

	Mean age not stated.	discuss and follow up care. Case coordinator monitored changes in health or managed concerns about participants health.

Table 3-1 Continued

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator
Read (2020)	Australia	Community	≥65 years with two or more chronic physical conditions and with access to a tablet or computer and proficient in English.	Minor or major depression and dysthymia; consumption of illicit drugs; more than five alcoholic units consumed per day; history of bipolar or schizophrenia; previously	302	Two or more chronic physical conditions.	Digital wellbeing course delivered by clinical psychologist, involving five lessons delivered over eight weeks (including weekly or email contact with psychologist)	Usual care, control group had access to wellbeing course resources after 2 year follow up period.

			Mean age: 73	undergone psychological therapy in 12 months prior to recruitment.				
Chow and Wong (2014)	Hong Kong	Community (initially inpatient)	≥65 years; admitted to hospital with medical diagnosis related to chronic respiratory, cardiac, type 2 diabetes or renal diseases; able to	Cognitive problems; discharged from hospital before assessment; being monitored by a designated disease management team after discharge;	281	Primary and secondary diagnoses of specified chronic diseases.	Pre-discharge assessment completed by nurse case manager, followed by post-discharge weekly assessments involving self-management discussions.	No specialised pre- or post-discharge assessments, followed by research assistant calling control group twice over four weeks to discuss non-

communicate in Cantonese; able to be contacted by telephone after discharge. Median age: 76	unable to communicate; terminally ill.	specific topics such as the weather.

Table 3-1 Continued

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator
Lundqvist (2018)	Sweden	Community (with a visit to ambulatory geriatric unit (AGU) scheduled during the study.	≥75 years with three or more concomitant diagnoses and with three or more inpatient hospital admissions in the past 12 months.	In institutional care.	844	Three or more concomitant diagnoses.	Comprehensive geriatric assessment team of nurses, doctors, and allied health professionals. Intervention group supported by team as and when required. Contact could be a few times in a year or daily or	Usual care.

			Mean age Control: 83 Intervention: 83				weekly. Support given via telephone, home or ambulatory visit.	
Krska (2001)	Scotland	GP practices	≥65 years with regular requests for at least four repeat prescription medicines and diagnosed with at least	Diagnosed dementia and considered by the GP as unable to cope with the study.	332	Not defined but referred to as having at least two chronic diseases.	Individualised patient profiles completed by clinically trained pharmacist using medical notes and patient records. This is followed by a medication review within the	Usual care but also including a medication review, however no additional specialist care plan implementation.

	two chronic diseases. Mean age Control: 75 Intervention: 75	home which also includes assessing for any pharmaceutical care issues. The care plan that is created from this is inserted into medical notes and shared with GP, with pharmacist implementing all agreed actions with assistance from other staff.

Table 3-1 Continued

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator
Salisbury (2018)	England and Scotland	GP practices	18 years or older, with at least three types of chronic conditions. Mean age Control: 71 Intervention: 71	A life expectancy of less than 12 months; at serious suicidal risk; known to be leaving the practice within 12 months; unable to complete questionnaires in English;	1,546	At least 3 out of 17 major chronic conditions from those included in the UK Quality and Outcomes Framework (QOF) pay-for-performance programme.	Two appointments with a nurse who identifies the health problems most important to the patient such as pain or disease management.	Usual care.

taking part in another healthcare research project; lacking capacity to give consent; deemed unsuitable to be invited by their general practitioner.

Followed by an appointment with a named responsible physician in the practice and then a records-based medication review by a pharmacist. Findings are printed as a patient-held agenda to inform subsequent

							consultations with the doctor.	
Reed (2018)	Australia	Community	≥60 years; diagnosed with two or more chronic diseases; ambulatory and English speaking. Mean age not reported.	A terminal Illness; significant cognitive impairment, or severe hearing Loss; self-rated health is “very good” or “excellent”, or residing in a long term care facility.	231	Multiple chronic conditions.	Chronic disease self-management support program involves cue and response interviews, problems and goals assessment, and allows clinicians and patients to collaboratively	Usual care and health information relevant to participants’ conditions also given as well as scheduled contact with a clinician who provides positive attention.

							assess self-management behaviour, identify problems, set goals, and develop individual care plans.	

Table 3-1 Continued

Study	Country	Setting	Sample	Exclusion criteria	N	Multimorbidity definition	Description of intervention	Comparator

Lee (2022)	Taiwan	Community	≥65 years; diagnosed with three or more chronic medical conditions, as defined by Taiwan National Health Insurance. Mean age: 72	Terminal illness; Severe disability; inability to communicate adequately with study staff. Having malignancy and undergoing active chemotherapy. Having a life expectancy of less than 12 months. Being currently institutionalised	340	The presence of multiple chronic medical conditions in an individual	Integrated geriatric care plus a multidomain intervention; 16 structured 2-hour training sessions (sessions included various components such as physical exercise, cognitive training, diet education,	Usual care

							and chronic condition management)	
Yang (2022)	China	GP practices	≥60 years; diagnosed with at least three chronic conditions Mean age Control: 73 Intervention: 71	Life expectancy of less than 12 months; institutionalised in a nursing home or a long-term care facility; plan to move away in the next 6 months; cognitive impairment; participating in another study involving chronic	136	The existence of multiple medical diseases in a single individual	6-week nurse-led medication self-management program consisting of three 30-40 minute face-to-face educational sessions and two follow-up phone calls to enhance	Usual care

				disease management			medication adherence.	
McCarthy (2022)	Republic of Ireland	GP practices	≥ 65 years; prescribed 15 or more repeat medicines	Unable to attend the practice for a face-to-face medication review (e.g., nursing home residents or housebound patients); judged by their GP as unable to give informed consent.	422	The presence of two or more chronic conditions	A structured, patient-centred medication review conducted by a pharmacist and a GP	Usual care

Interventions were of three types: (i) patient-professional collaboration interventions; (ii) new service or integrated care interventions; and (iii) technology interventions. Reported outcomes were: quality of life, hospitalisation, self-management, self-rated health, adverse drug reactions, medication management, incidence of depression, and physical functioning (Table 3-2). Eight studies included a cost analysis (Table 3-3) and six studies considered frailty in their assessment (Appendix 6).

3.5.1 Patient-professional collaborations

I identified five studies assessing the impact of collaborations between patients and health professionals or providers (Chow *et al.*, 2014; Panagioti *et al.*, 2018; Reed *et al.*, 2018; Schäfer *et al.*, 2018). One found pre-discharge nurse assessment combined with a post-discharge supported self-management model reduced readmission at 84 days, though not at 28 days (Chow *et al.*, 2014). Another study showed that a chronic disease self-management support program improved self-rated health at six months follow-up (Reed *et al.*, 2018). A six-week medication self-management intervention resulted in significant improvements in medication adherence immediately after the intervention (Yang *et al.*, 2022). In the other studies, there was no evidence that similar interventions reduced the total number of medications taken by a patient or improved quality of life and self-management of long-term conditions.

3.5.2 New services or integrated care

Ten studies investigated interdisciplinary or integrated care interventions (Krska *et al.*, 2001; Ekdahl *et al.*, 2015; Lundqvist *et al.*, 2018; Markle-Reid *et al.*, 2018; Salisbury *et al.*, 2018; Berntsen *et al.*, 2019; Fisher *et al.*, 2020; Miklavcic *et al.*, 2020; McCarthy *et al.*, 2022; Yang *et al.*, 2022). I combined three estimates for in-home support and assessment from an interprofessional team with a common outcome (physical function), showing no effect (effect size -0.79 (CI -3.35 to 1.77). Two other studies separately found a reduction in total emergency in-patient days (Berntsen *et al.*, 2019) and improved pharmacy care (Krska *et al.*, 2001). An integrated multidomain lifestyle intervention significantly improved cognitive function, and enhanced

quality of life (Lee *et al.*, 2022) and another patient-centred medication review intervention resulted in a reduction in the number of medicines but no evidence of a clear effect on potentially inappropriate prescribing (McCarthy *et al.*, 2022). However, the other new interventions did not show fewer total hospitalisations or improved quality of life and physical functioning.

3.5.3 New technologies

Of six studies introducing technology interventions, four demonstrated feasibility and acceptability (Hastings *et al.*, 2021) and benefits on cognition (Noel *et al.*, 2004), increased quality of care indicators (H. Kim *et al.*, 2020) and reduced incidence of depression (Read *et al.*, 2020). These interventions included routine home-based virtual assessments, use of a specialised software system to guide comprehensive geriatric assessments, and a clinician-supported digital wellbeing course. No benefits were observed for medication appropriateness index or adverse drug reactions (Muth *et al.*, 2018; O'Mahony *et al.*, 2020).

Table 3-2: Effect size of intervention for primary outcomes (grouped by intervention type)

Study	Type of Intervention	Duration	Primary outcome(s)	Effect size (intervention vs control), 95% CI or SD
Schäfer (2018)	Patient-professional collaboration	14 months	Total number of medications and health related quality of life measured using EQ-5D questionnaire.	Number of medications (linear regression coefficient) 0.43 (-0.07 to 0.93) Health-related quality of life (linear regression coefficient) 0.34 (-0.05 to 0.74)
Panagioti (2018)	Patient-professional collaboration	20 months	Self-management of long-term conditions measured using Patient Activation Measure and quality of life measured	Self-management MD: 1.44 (−0.46 to 3.33) Quality of Life MD: 1.62 (−0.32 to 3.56)

			using the World Health Organization Quality of Life brief measure.	
Chow and Wong (2014)	Patient-professional collaboration	3 months	Reduction in hospital readmission.	The two intervention groups had lower readmission rates at 28 days post discharge, (15.4%) and (16.0%) compared with control group (22.9%). At 84 days post discharge the control group readmission rate was 45.4%, whereas the two intervention groups were 33.0% and 28.3%. *****
Reed (2018)	Patient-professional collaboration	6 months	Self-rated health measured with scales provided by the Stanford Patient	Self-rated health OR: 2.50 (1.13 to 5.50) *****

			Education Research Centre.	
Yang (2022)	Patient-professional collaboration	3 months	Medication adherence measured using the MARS-5.	Medication adherence Time 1 (linear regression coefficient): 1.67 (0.47 to 2.86) Time 2 (linear regression coefficient): 1.42 (0.54 to 2.30)

MD: mean difference, RR: risk ratio, OR: odds ratio

+ primary outcome was not defined

* Significance at 95%

Table 3-2 Continued

Study	Type of Intervention	Duration	Primary outcome(s)	Effect size (intervention vs control), 95% CI or SD
Berntsen (2019)	New service or integrated care	6 months	Emergency admission count (care required within 24 hours), total emergency inpatient bed days and count of re-admissions within 30 days.	Emergency admissions count RR: 0.90 (0.82 to 0.99) Total emergency bed days RR: 0.68 (0.52 to 0.79) ***** 30-days readmissions count RR: 0.72 (0.41 to 1.24)
Ekdahl (2015)	New service or integrated care	24 months	Hospitalisation during 2-year study period.	Hospitalisations MD: 0.3 (SD 0.1)

Miklavcic (2020)	New service or integrated care	6 months	Physical Component Summary (PCS) score measured using the 12- item Medical Outcomes Study Short Form-12v1 Health Survey (SF-12).	PCS MD: 0.74 (− 3.22 to 1.74)
Markle-Reid (2018)	New service or integrated care	6 months	Health-Related Quality of Life measured according to the PCS which measures physical functioning.	PCS MD: 0.04 (–2.22 to 2.30)

Fisher (2020)	New service or integrated care	6 months	Physical functioning measured using PCS from SF-12.	PCS MD: -3.93 (-8.52 to 0.67)
Lundqvist (2018)	New service or integrated care	24 months	Incremental cost-effectiveness ratio (ICER) of CGA compared with usual care and Quality Adjusted Life Years (QALY).	ICER 45,987; Life year gain of 1.05; QALY of 0.54
Krska (2001)	New service or integrated care	3 months	Pharmaceutical care issues (PCIs).	Resolved PCIs- Intervention: 950 (78.8%), control: 542 (39.3%), absolute difference 39.5%*****

Salisbury (2018)	New service or integrated care	15 months	Health-related quality of life measured using the EQ-5D-5L.	Health-related quality of life MD: 0·00 (–0·02 to 0·02)
Lee (2022)	New service or integrated care	12 months	Cognitive performance measured by Montreal Cognitive Assessment (MoCA).	MoCA (linear regression coefficient): 1.1 (0.4 to 1.8)
			Physical frailty evaluated using the Cardiovascular Health Study (CHS) frailty scores.	Frailty (linear regression coefficient): -0.3 (-0.5 to -0.1)
McCarthy (2022)	New service or integrated care	6 months	Number of repeat medicines and the proportion of patients	Number of medicines IRR from multilevel Poisson regression: 0.95 (0.899 to 0.999)

		with any potentially inappropriate prescribing (PIP)	PIP OR from multilevel logistic regression0.39 (0.140 to 1.064)

MD: mean difference, RR: risk ratio, OR: odds ratio, IRR: Intracluster correlation coefficient

+ primary outcome was not defined

* Significance at 95%

Table 3-2 Continued

Study	Type of Intervention	Duration	Primary outcome(s)	Effect size (intervention vs control), 95% CI or SD
Hastings (2021)	Technology	3.5 months	Feasibility, acceptability, usability, and perceived value of the intervention.	Intervention was feasible and acceptable to most medically complex veterans with suspected cognitive impairment and their care partners.
Muth (2018)	Technology	6 months	Difference in medication appropriateness index (MAI) score at 6 months.	MAI score MD: 0.7 (−0.2 to 1.6)

Noel (2004)	Technology	12 months	Reduction in healthcare costs and improvement in quality of life. **+**	Diabetic A1C MD (at 6 months only): -0.53; cognitive status MD (at 12 months): 0.57***;** functional level MD (at 12 months): -0.66; satisfaction MD (at 12 months): 14.18; self-rated health MD (at 12 months): 5.79
Kim (2020)	Technology	6 months	Quality of care reported via a composite score of quality indicators using the interRAI Long-Term Care Facilities (LTCF) assessment.	Quality of care (linear regression coefficient) -0.025 *****
O'Mahony (2020)	Technology	3 months	Reduction in adverse drug reaction.	Adverse drug reaction OR: 0.98 (0.77 to 1.24)

Read (2020)	Technology	6 months	Incidence of depressive disorder measured using the PRIME-MD diagnostic interview.	Intervention n=5 (3.3%), Control n=15 (9.8%), Absolute difference: 6.5% *****

MD: mean difference, RR: risk ratio, OR: odds ratio

+ primary outcome was not defined

* Significance at 95%

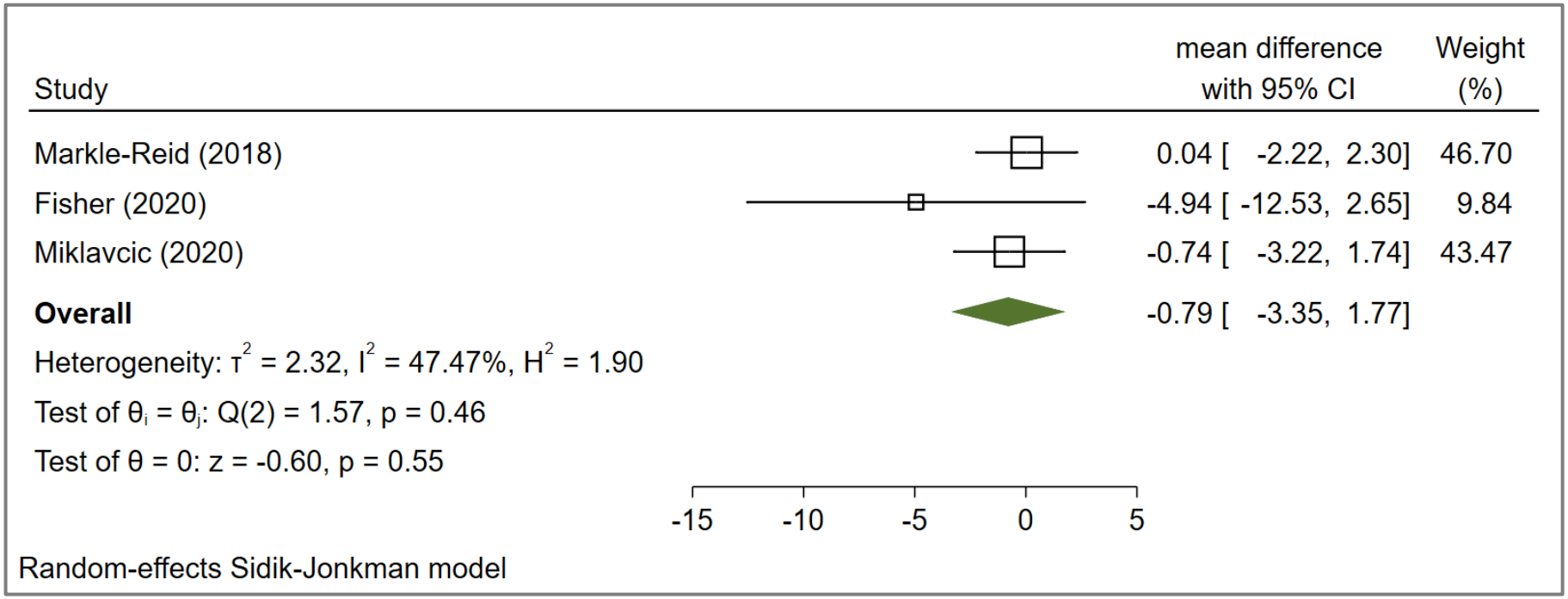
Table 3-3: Costs

Study	Type of intervention	Duration	Perspective	Effect size (intervention vs control)
Panagioti (2018)	Patient-professional collaboration	20 months	NHS England	Mean total cost (£): Intervention 4007.88; Control 3424.16; Incremental cost 150.583; Incremental QALYs 0.019; ICER 8049.96.
Ekdahl (2015)	New service or integrated care	24 months	Not stated	Total cost of health and social care (£/ patient [SD]: Intervention 33,371 [39,947]; Control 30,490 [31,568]).
Miklavcic (2020)	New service or integrated care	6 months	Societal (Canada)	Total costs including acute care ($): Intervention 2528.01 (CI 678.25 to 3769.45); Control 2084.60 (CI 465.32 to 3865.82).

Markle-Reid (2018)	New service or integrated care	6 months	Societal (Canada)	Median cost at 6 months ($): Intervention 3175.06; Control 2906.11.
Fisher (2020)	New service or integrated care	6 months	Societal (Canada)	Median cost ($CAD): Intervention 2998.23; Control 1914.33; Absolute difference 1083.90.
Noel (2004)	Technology	12 months	Not stated	Total cost ($): Intervention 4,849; Control 5,832; Absolute difference 983.
Lundqvist (2018)	New service or integrated care	24 months	Public healthcare sector (Sweden)	Total cost (EUR): Intervention 113,327; Control 88649; Incremental cost 25,000; ICER 45,987
Krska (2001)	New service or integrated care	3 months	Not stated	Mean cost (£ per month): Intervention 38.83; Control 42.61

*significance at 95%

Figure 3-2: Mean difference in Physical Component Summary (PCS) score, a comparison of new service or integrated care versus usual care



3.5.4 Costs

I identified eight reports quantifying the economic impact of the intervention (Krska *et al.*, 2001; Noel *et al.*, 2004; Ekdahl *et al.*, 2015; Lundqvist *et al.*, 2018; Markle-Reid *et al.*, 2018; Panagioti *et al.*, 2018; Fisher *et al.*, 2020; Miklavcic *et al.*, 2020). Mostly, interventions resulted in higher costs, except one using home-based virtual assessments in high-resource users was cheaper (Noel *et al.*, 2004) and another involving creating a medication management care plan to reduce polypharmacy (Krska *et al.*, 2001). In one study of a telephone health coaching programme designed to reduce polypharmacy, the associated incremental cost per QALY was £8,050 representing a cost-effective intervention though it did not yield the anticipated clinical improvement (Panagioti *et al.*, 2018). Another study introduced a geriatric assessment team with a QALY gain of 0.54 and an incremental cost per QALY of €46,000 which may be considered cost-effective in a Swedish healthcare context (Lundqvist *et al.*, 2018).

3.6 Discussion

This systematic review showed interventions of patient-professional collaborations or integrated care had some benefit on acute admissions and mortality, but not on quality of life, self-management, or functional disability. Interventions involving complex comprehensive assessments by a multidisciplinary team showed improvements in healthcare utilisation. Technology interventions appeared to improve quality of care and reduced incidence of depression. However, they did not reduce adverse drug reactions or hospitalisations. Taken together, these findings suggest certain strategies may improve multimorbidity outcomes, though the strength of evidence is small in proportion to the prevalence of older patients living with multimorbidity.

3.6.1 Strength and limitations

Although I performed a systematic search of multiple databases, it is possible I did not identify every relevant study. I only included randomised trials to

determine the efficacy of a given intervention. However, broader evidence from observational designs may add to our understanding, even though individual studies might be subject to effects such as residual confounding. The available data on cost-effectiveness were limited. These results are only generalisable to the small range of patient groups and settings identified. Nonetheless, I have been able to synthesise a diversity of studies to define precisely where gaps in knowledge exist.

The quality of the RCTs included in this review was assessed using the CASP (Appendix 3). Key findings indicate that most studies addressed clearly focused research questions and utilised randomisation effectively. Methodological soundness was high, with comprehensive reporting of intervention effects and precision estimates. While the benefits of interventions generally outweighed harms and costs, the applicability to local contexts varied.

The economic evaluations were assessed using the CHEERS checklist (Appendix 4). Findings revealed that most studies clearly identified themselves as economic evaluations and provided structured summaries. There was consistency in describing the study context, base case populations, and decision-making perspectives. Results were generally well-reported, including costs, outcomes, and incremental cost-effectiveness ratios.

Overall, the quality of the included studies profoundly influences the findings of this thesis. High-quality studies provide more reliable, valid, and generalisable results. Conversely, studies with methodological weaknesses or incomplete reporting can introduce biases, reduce the applicability of findings, and obscure the true impact of interventions. Therefore, careful consideration of study quality was essential for interpreting the results and drawing meaningful conclusions.

This chapter highlights a notable observation: adopting a perspective focused solely on multimorbidity in older adults, without explicitly considering frailty, yields a surprisingly limited evidence base. This raises a critical question: is it worthwhile to target multimorbidity independently of frailty? Revisiting the

foundational definitions, it is clear that while multimorbidity and frailty often coexist and overlap, they are distinct entities. The relationship between them is not symmetrical; most individuals with frailty have multimorbidity, but not all with multimorbidity are frail. This nuanced asymmetry, where multimorbidity is more likely to precipitate frailty than frailty is to lead to multimorbidity, is illustrated in the proposed Figure 1-3. Typically, multimorbidity precedes frailty, however, the findings from this review challenge the notion suggesting that there might be a practical period where multimorbidity can be effectively addressed before the onset of frailty, in this specific age group.

Among the studies reviewed, only six considered or measured frailty. These studies incorporated elements of comprehensive geriatric assessment, with five out of six demonstrating benefits from such an approach. This indicates the potential value of integrating frailty assessment in the management of multimorbidity in older populations. Notably, the National Institute for Health and Care Excellence (NICE) recommends that frailty be assessed in the management of multimorbidity in complex older adults (National Institute for Health and Care Excellence, 2016).

My review highlights that although a sole focus on multimorbidity may add value to younger populations, the same may not apply to older adults because of the predominating influence of frailty. We know that multimorbidity is highly prevalent in frail people and this relationship is bidirectional (Hanlon *et al.*, 2018; Vetrano *et al.*, 2019). The existing evidence base for frailty management includes studies in a wealth of settings: primary, secondary, and community care (Chin A Paw *et al.*, 2008; Giné-Garriga *et al.*, 2014; Negm *et al.*, 2019; Travers *et al.*, 2019; King *et al.*, 2021). Comprehensive geriatric assessments (CGA) for frailty benefit long-term management and support living at home (Ellis *et al.*, 2017), even if they do not reduce mortality risk and functional dependence. Given the limited body of work I identified on multimorbidity interventions alone, it would not appear to be useful as a concept separate from frailty management.

The increased healthcare utilisation seen with multimorbidity highlights the fragmentation of health and care systems, which often focus narrowly on

individual diseases and specific interventions. This fragmentation becomes particularly problematic for older adults, whose care for acute health crises—such as falls, immobility, and delirium—tends to be reactive and poorly integrated with chronic disease management strategies (Yarnall *et al.*, 2017). The need for complex assessments and interventions to manage these needs of older people, aimed at preventing hospital admissions and reducing mortality and dependency, is clear. Integrating care for chronic conditions with proactive consideration of frailty can address these challenges, emphasising the importance of a holistic approach to care (Ellis *et al.*, 2014).

3.7 Conclusion

There is a clear need to establish specific interventions for multimorbidity that can be widely implemented in routine practice. In older people, identifying frailty as part of interventions and the core involvement of a multidisciplinary team to carry out complex assessments from the outset is likely to be critical for multimorbidity management. Yes, of the small number of multimorbidity interventions in older people, only six identified frailty directly. Additionally, many multimorbidity-specific interventions appear to experience low engagement from patients and professionals, ultimately limiting effectiveness.

In taking this striking descriptive finding – that most multimorbidity interventions were often designed or evaluated without considering frailty – I wanted to consider data from cohort studies simultaneously ascertaining multimorbidity and frailty. This would quantify how these two conditions, together and separately, affect health and functional outcomes, service use and cost. Triangulating these findings would allow me to uncover new relationships not identified in randomised trials regarding frailty's role in managing multimorbidity.

Chapter 4 Research methods and data sources

In Chapter 1, I described the challenges of understanding multimorbidity, outlining the methodological issues, its relationship with frailty, and summarising the population challenges and costs of service provision. This chapter presents the primary data sources and methods I have used in my research.

The data for this research are from the Delirium and Population Health Informatics Cohort (DELPHIC) and the Care City Cohort (Table 4-1). Data linkage is the common feature and strength of these datasets. Both include population-based cohorts with linked data across health and social care settings. DELPHIC is a longitudinal study with ascertainment across primary, secondary and community care. In contrast, the Care City Cohort is formed through data linkage from administrative health and social care sources.

This chapter provides a comprehensive overview of the research methods and data sources utilised in this thesis. The research context, settings, populations and study designs are explored in detail in Chapters 5 (section 5.3) and 6 (section 6.3). To ensure clarity and precision in my methodological approach, I have distinctly defined the study designs I have used for the two primary datasets used:

- DELPHIC: A cross-sectional study design was used to analyse data at a single point in time, providing a snapshot of the population and its characteristics, including the prevalence of multimorbidity and frailty.
- Care City Cohort: A cohort study design was used, which involves following a group of individuals over time to observe changes and developments in their health status, service use, and outcomes related to multimorbidity and frailty.

4.1 Systematic Review

Prior to the quantitative analyses presented in Chapters 5 and 6, a systematic review was conducted, as detailed in Chapter 3. This review was undertaken to address a key knowledge gap and to lay the groundwork for the subsequent analyses. I undertook a systematic review to address a key

knowledge gap highlighted in Chapter 1: what interventions for multimorbidity are effective? A critical aspect to understanding this is whether its close relationship with frailty makes multimorbidity difficult to consider separately as a direct intervention target. Considering the dual challenges of multimorbidity and frailty, the aim was twofold. First, to critically assess the effectiveness of multimorbidity interventions in improving health outcomes, and second, to evaluate their cost-effectiveness. This contributes to a more complete understanding of multimorbidity management, considering both health and economic perspectives.

In addressing these objectives, the review seeks to quantify the current state of research and identify potential areas for future study. By systematically collating and evaluating existing studies, the review aims to discern whether there is evidence to focus solely on multimorbidity or if incorporating considerations of frailty could lead to more effective management strategies.

The systematic review method was chosen for its structured and comprehensive approach to research synthesis, ensuring that the evaluation of interventions is valid and methodological biases are made explicit (Mulrow, 1994; Owens, 2021). I formulated a specific approach using the PICOS criteria framework: Population, Intervention, Comparison, Outcome, and Study type (Mulrow, 1994). These questions guided the entire review process, and I prospectively registered it on PROSPERO, to ensure enhanced transparency and prevent research duplication. I developed a comprehensive search across multiple databases using predetermined keywords, refined by searching the study references already identified.

Systematic reviews, while robust, are subject to various forms of bias and errors, such as selection bias, attrition bias, and the risk of Type I and Type II errors, and publication bias, where results demonstrating statistical significance are more likely to be published. I tried to limit these by using an electronic data management tool, and I involved a second assessor to improve reliability.

Table 4-1: A comparison of DELPHIC and Care City Cohort datasets

				Settings				
Dataset	**Time period**	**Prospective or Routine**	**Sample and geography**	**Primary**	**Hospital**	**Social Care**	**Community**	**Mental Health**
DELPHIC	2018	Prospective data that incorporates routinely collected data from EHR	1,500 individuals aged ≥70 years residing in the London Borough of Camden (London, UK)	X	X	X	X	X
Care City Cohort	2011 onwards	Routinely collected data from EHR and local authority	Approx. 250,000 residents of the London Borough of Barking and Dagenham (London, UK). 9% of this population is ≥ 65 (19,807)	X	X	X	X	X

4.2 DELPHIC

DELPHIC is a population-based prospective longitudinal study of people aged ≥70 years residing in the London Borough of Camden (London, UK) (Davis *et al.*, 2018). This region has over 270,000 residents and recent population estimates show approximately 43,600 people aged over 65 years reside in Camden (Office for National Statistics, 2021). My analysis is of the baseline data collected from the first 1,510 individuals recruited into the study and is a cross-sectional analysis of the baseline assessment. The aim of DELPHIC was to assess baseline cognition and delirium and how that relates to follow-up cognitive impairment.

4.2.1 Covariates

4.2.1.1 Socio-demographic characteristics

In my analysis I included data on age, sex, ethnicity, education, occupation and IMD for all individuals. The sample measured socio-economic position using IMD, educational attainment, and occupational class. The IMD is an ecological measure of relative deprivation for small areas in England. It is calculated by ranking every small area in England (LSOA) from 1 (most deprived area) to 32844 (least deprived area). Information from seven domains is combined to produce a relative measure of deprivation. The index combines information from seven domains to produce an overall relative measure of deprivation. The domains are Income Deprivation (22.5%), Employment Deprivation (22.5%), Health Deprivation and Disability (13.5%), Education Skills and Training Deprivation (13.5%), Barriers to Housing and Services (9.3%), Crime (9.3%) and Living Environment Deprivation (9.3%).

Participants selected one of 14 categories during their assessment to indicate their highest educational attainment. In the dataset, I combined this into three levels: *up to primary*, *up to secondary*, and *degree level*. Occupational class was derived from the Office for National Statistics UK Occupational Skill Classification. Participants indicated their current occupation or last occupation before retirement during data collection. Levels 1 and 2 refer to skills gained from compulsory and post-compulsory education. Level 3 and 4 refer to skills gained from additional work-related

training (normally without a bachelor's degree) and professional skills with a degree or equivalent, respectively. Sex was categorised as *male* or *female* from self-report and GP records. For ethnicity, individuals identified their ethnic origin from a list of 17 categories. The sample was majority White British; other ethnicities were combined into one category *non-White*. An additional category *missing* was generated for all variables to account for any missing data.

4.2.1.2 Health and function variables

Once data were collected, multimorbidity burden was quantified as a count of diagnosed conditions, with two or more long-term conditions being defined as multimorbidity. Frailty was quantified using a Frailty Index, representing the proportion of accumulated health deficits, including co-morbidities (0 to 1). This was derived using 35 items drawn from the baseline assessment covering general health, co-morbidities, medications, health behaviours, hearing, vision, dental health, continence, falls, depression, personal and instrumental activities of daily living, and calculated according to standard procedures (Searle *et al.*, 2008). The inclusion of co-morbidities in calculating a Frailty Index resulted in multicollinearity between frailty and multimorbidity variables, an individual multimorbidity variable was not included in the final models.

The life-space assessment (LSA) is a self-reported measure which asks respondents to quantify how far and how often they have mobilised, with or without assistance, in the last four weeks. By considering an individual's mobility in various settings, from their room to outside their town or city, the LSA gathers information on functional mobility. The instrument operates at multiple levels (see Chapter 6, section 6.2 and section 6.3.2), scoring for functional abilities at each level. I generated a total score for LSA, a multiplication of these dimension scores.

Quality of life was operationalised from five health domains comprising the EuroQol EQ-5D-5L questionnaire (Herdman *et al.*, 2011). These domains include mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain is scored out of five levels: having no

problems (Level 1), slight problems (Level 2), moderate problems (Level 3), severe problems (Level 4) to completely unable or extreme problems (Level 5). Using empirical value sets for an English population, these input score are used to calculate an EQ-5D index value, reflecting how good or bad a health state is. Values range from 0 to 1, where 1 indicates a health utility showing *full health* and a negative value equals *worse than dead*. The EuroQol Health Index tool also includes a visual analogue scale (VAS), which is a self-rating for quality of life and ranges from 0 to 100 (100 = best health).

4.3 The Care City Cohort

With a population of approximately 214,000, Barking and Dagenham is characterised by a younger demographic, increased ethnic diversity, and greater social disadvantage than the rest of the UK (London Borough of Barking and Dagenham, 2021). The population registered with a GP is 187,000. The Care City Cohort that informed this research comprises residents of the London Borough of Barking and Dagenham, integrates data from local government, health providers, and commissioners, and includes data from 2011 onwards. Sociodemographic, health, care and household data are linked at the individual level. My sample was defined as adults aged ≥ 60 years residing in Barking and Dagenham between 1 April 2014 to 31 March 2017. This population is relatively young but more disadvantaged, justifying the age cut-off. This dataset comprised details including patient demographics, residential address, mortality data, and records of service usage across various health and social care settings (detailed in Table 5-1).

4.3.1 Covariates

The association between multimorbidity, service use, costs, and variables described in Chapter 1 is well-established, informing the inclusion of covariates in the final dataset. Four categories describe the included covariates: socio-demographic characteristics, health variables, service use variables and cost variables.

4.3.1.1 Socio-demographic characteristics

For all individuals, the socio-demographic characteristics I included were age, gender, ethnicity, education, and index of multiple deprivation (IMD).

Each year's linked dataset included the maximum age a person could be that year was grouped into five age categories (19–49, 50–64, 65–74, 75–85, 85+). Care City only had access to the year of birth rather than the date or month of birth for pseudonymisation purposes, so individuals' ages were calculated based on the difference between the year of birth and the relevant year. My analysis was restricted to those over 60. I focused on adults, starting at age 60 years because LBBD is relatively disadvantaged and where multimorbidity occurs earlier in life. For my final linked datasets, I removed all individuals whose maximum age would be under 60 each in year (e.g., in 2015/2016, all individuals born after 1956 were excluded).

Data on sex were categorised as in primary care records, female, male or other. For ethnicity, the codes were extracted from primary care records. These codes were grouped into five categories: White, Mixed/Multiple ethnic groups, Asian, Black and Other. Any missing data was coded as *unknown*.

4.3.1.2 Health variables

Markers of health and health status predict a decline in health or functioning. I included BMI, smoking and multimorbidity. Data on BMI are routinely collected and Care City extracted the most recently recorded BMI from primary care records for each year. These values were categorised into five categories defined by the NHS: underweight (below 18.5), healthy (between 18.5 and 24.9), overweight (between 25 and 29.9), obese (between 30 and 39.9) and morbidly obese (over 40). Individuals with impossible BMI values were re-coded as missing, with a corresponding category of *unknown*. Data on smoking are also routinely collected; individuals were assigned into one of four categories: non-smoker, ex-smoker, smoker or unknown, *unknown* referred to individuals with missing data or those who preferred not to say. As previously discussed, Care City contains a list of 16 chronic conditions with data gathered for every year. These data are extracted from primary care records. A count of the number of long-term conditions an individual has was

included under a multimorbidity flag; this was then also categorised as the sum of conditions under none, one condition, and two or more conditions.

4.3.1.3 Outcome measure: Service use and cost implications after an inpatient emergency admission.

Cost-weighted service utilisation was measured by setting and as the outcome measurement in the analysis. Unscheduled care was described using the incidence of inpatient admission for non-elective care (excluding attendances discharged directly from the emergency department). Care City estimates cost from activity data in each care setting. This is calculated using the Healthcare Resource Group (HRG) national tariff. I also calculated the total cost for each financial year, which is the outcome being measured alongside service use, by aggregating costs within and across the care settings: hospital, primary care and social care. Linked data on service use within these settings was used to quantify total health and social care use in the year following an unscheduled inpatient admission. Additionally, the cost of this contact with services was calculated and connected with the different contact frequencies. This contact with health and social care services was included as a baseline exposure in a subsequent analysis for the next year as part of a descriptive analysis.

4.4 Advanced Statistical Techniques

In data analysis, particularly within the context of examining the intricate dynamics between multimorbidity, frailty, and their consequences on health outcomes and healthcare utilisation, advanced statistical techniques play a crucial role in addressing complex data structures and inherent uncertainties. Among these methods, multiple imputation and random-effects models stand out for their ability to manage missing data and account for variability within clustered or hierarchical data structures, respectively. This section delves into the intricacies of these techniques, elucidating their methodology, applications, and the value they add to statistical analysis. This research employed multiple imputation and random-effects models to navigate the challenges posed by missing data and the inherent variability within the data,

derived from a population-based cohort and linked health and social care datasets.

4.4.1 Multiple Imputation for Missing Data

Multiple imputation (MI) has emerged as a powerful solution to the pervasive problem of missing data in research. Missing data can introduce bias, reduce statistical power, and compromise the validity of conclusions. MI addresses these issues by creating several (typically three to five) complete datasets, where the missing values are imputed using a statistical model that captures the relationships observed in the data. Each of these datasets is then analysed using standard statistical methods, and the results are combined to produce estimates that reflect the uncertainty due to the missing data.

The process of MI involves three main steps:

1. Imputation: Missing values are filled in multiple times to create several complete datasets. The imputation model incorporates randomness, ensuring that the imputed values reflect the uncertainty about what the true values might have been.
2. Analysis: Each complete dataset is analysed separately using the same statistical method.
3. Pooling: The results from these analyses are combined, using rules developed by Rubin (Rubin, 1987), to produce a single set of estimates that account for the variability both within and across the imputed datasets.

MI is particularly advantageous because it uses all available data, preserves sample size, and acknowledges the uncertainty introduced by missing data, thereby providing more valid and reliable results than traditional single-imputation methods.

4.4.2 Random-Effects Models for Hierarchical Data

Random-effects models, also known as mixed-effects models, are employed to analyse data that arise from hierarchical or clustered structures. Such data structures are common in health sciences research, where measurements

might be nested within individuals, and individuals nested within larger units (like hospitals or communities). These models are crucial for acknowledging the non-independence of observations within clusters and for capturing both fixed effects (consistent across all units) and random effects (varying across units).

Random-effects models incorporate random terms to account for the variability at different levels of the data hierarchy. This approach provides several key benefits:

- Flexibility: They can model variability at each level of the data structure, providing a nuanced understanding of the data.
- Efficiency: By accounting for the clustered nature of data, these models can lead to more precise estimates of the fixed effects.
- Generalisability: Random-effects models allow for the extrapolation of conclusions to a broader population, beyond the specific study sample.

In practice, specifying a random-effects model involves determining which effects are fixed and which are random, often based on the study design and the research questions of interest. The analysis yields estimates of the fixed effects (average effects) and the variance components associated with the random effects, offering insights into the variability within and across clusters.

Employing advanced statistical methods like MI and Random-Effects Models has allowed us to rigorously analyse complex relationships in health services research. These techniques have been instrumental in my investigation into multimorbidity and frailty, facilitating a deeper understanding of their influences and the implications for healthcare practices.

Chapter 5 Service use and cost implications after emergency admission in older adults: a longitudinal analysis of the Care City Cohort

This chapter analyses service use and cost implications following emergency admissions in older adults, highlighting the burden of multimorbidity. By examining data from the Care City Cohort, this study identifies patterns in healthcare utilisation and the associated economic impact. The findings underscore the fragmented nature of current health and social care systems and emphasise the need for integrated care approaches to manage multimorbidity more effectively. The analysis sets the stage for understanding how multimorbidity contributes to increased service use and healthcare costs. It lays the groundwork for exploring health-related quality of life, arguably the most important outcome of all, and the relationship between life space, quality of life, and frailty in the subsequent chapter.

5.1 Summary

This study describes patterns of service use after acute hospital admissions over four years in a population of older adults within the London Borough of Barking and Dagenham. Leveraging the rich, integrated dataset of the Care City Cohort, I identified the service usage patterns and cost implications across primary, secondary, and social care settings post-acute admissions, taking into account confounding variables such as gender, age, ethnicity, deprivation, and multimorbidity.

The results show that acute admissions are associated with increased service use and costs, particularly in social care settings. This trend persists in the long term, even after accounting for multimorbidity. In primary care, acute admissions correlate with a higher frequency of contacts, which is highest in those living with multimorbidity. Emergency Department (ED) services see a decrease in use post-admission, suggesting improved care management or a shift in the point of care. Elective inpatient and outpatient care usage also increased with acute admissions, with outpatient care showing a sustained rise

over time. Survival analysis demonstrated a significant increase in mortality risk linked to acute admissions.

By comparing healthcare usage and costs between patients with and without acute admissions over several years, I identified that acute admissions had knock-on effects throughout the health and social care ecosystem. It may be that improving care coordination can address the sustained demand on healthcare resources after acute hospitalisation. The findings advocate for a transition towards community-based care models to manage better the long-term impacts of acute admissions on the healthcare system in this patient group.

5.2 Introduction

Emergency hospital admissions pose a significant challenge for global healthcare systems, especially among older adults, where higher hospitalisation and readmission rates are expected. Such admissions, while necessary at times, can escalate service use and associated costs across a spectrum of health and social care settings. Although earlier research has shed light on factors leading to increased service use post-acute admissions (Denholm *et al.*, 2020; Elkjær *et al.*, 2021) and determinants of such admissions (Condelius *et al.*, 2008; Payne *et al.*, 2013; Baré *et al.*, 2021), a more comprehensive understanding is essential. Specifically, there is a need to quantify the repercussions of acute admissions across the whole care ecosystem. Furthermore, recognising strategies to enhance care coordination and reduce the negative outcomes from acute admissions would have individual and public health impact.

While prior studies have pinpointed contributors to elevated service use following acute admissions and the precursors of these admissions (Surate Solaligue *et al.*, 2014; Xia *et al.*, 2020), a gap remains concerning the long-term implications of acute hospitalisation on health and social care consumption and expenditure. This study seeks to bridge this gap, focusing on the cascading effects of emergency hospital admissions on the utilisation and costs of primary, secondary, and social care services over a three-year

period. I aimed to detail how acute admissions influence subsequent service use longitudinally and whether specific patient factors — including age, gender, multimorbidity, and socio-economic position — affect these associations. The findings will show if acute admissions present an opportunity to formulate better healthcare policies and strategies around care coordination.

By identifying patient groups predisposed to higher service use post-acute admission, health and social care stakeholders can refine their approaches to improve care quality (Kremers *et al.*, 2019; Juul-Larsen *et al.*, 2020). It is unclear which post-acute services are most impacted by hospitalisation, the magnitude and duration of this increase across settings, and the relationship with mortality. Examining the economic aspects and the evolution of costs following an acute admission is equally paramount.

This chapter analyses the economic burden of multimorbidity following acute admissions, it also provides critical context for understanding the broader impacts of multimorbidity on healthcare systems.

5.3 Methods

5.3.1 Context, population, setting and study design

Care City is a Community Interest Company founded by the North East London NHS Foundation Trust (NELFT) and the London Borough of Barking and Dagenham (LBBD). Their aim is to deliver health and social care by bringing together partners from health, social care, research, technology settings and many more. Care City has worked with UCLPartners, NIHR ARC North Thames, the Dagenham, Havering and Redbridge (BHR) Clinical Commissioning Group (CCG), LBBD and NELFT to create a unique dataset, known as the Care City Cohort. This cohort comprises residents of Barking and Dagenham, an English local authority, and includes data from 2011 onwards. The Care City Cohort is a linked dataset that combines data from local government, health providers and commissioners. It links sociodemographic, health, care and household data at the individual level.

LBBD is a densely populated London Borough in North East London (UK). Barking and Dagenham's population is younger than other areas in the region and is ethnically diverse. The 2020 population estimate from ONS for Barking and Dagenham was 214,107, with 9% of this population aged ≥65 years, 19,807 people (London borough of Barking and Dagenham, 2020). The Care City Cohort is the Local Authority's major resource for understanding health and social care needs, and whether service provisions meet those needs.

Ten different datasets make up the Care City Cohort, and access is requested for relevant data according to the context of the proposed research. Of these datasets, those from the NHS are initially linked at the individual level using unique NHS numbers. BHR CCG follows this process with accuracy checks on variables using address, age, and sex. The remaining datasets are from the council and contribute variables such as education and household data. To link NHS and council data, fuzzy logic matching was initially applied to full names, dates of birth and postcodes, allowing NHS numbers to be added. Fuzzy logic matching is a method that allows for the identification and connection of patient records across different databases without requiring exact matches, accommodating variations and inaccuracies in data. It employs algorithms to assess similarity between records, enabling more accurate and comprehensive patient information management despite the inherent challenges of data discrepancies and errors. Records that could not be successfully linked with full confidence were still retained. De-identification was carried out with all patient-identifiable data such as names and addresses removed, and two new identification codes were introduced to replace NHS numbers and Unique Property Reference Numbers (UPRN). Additional steps to ensure data integrity included replacing the full date of birth and date of death with the year and month of birth and year of death only.

Individuals could opt out of data sharing through the BHR CCG website, those who did so would have their data removed at the source. Relevant ethical reviews were carried out and other legal requirements were met through oversight by the BHR Information Governance group. The dataset is

processed, stored, and managed in the BHR CCG Data Safe Haven where it is hosted, researchers can access only de-identified data. New identification codes were generated to replace UPRNs and NHS numbers to carry out data linkage as required (e.g., in cases where sociodemographic data are recorded in two different datasets). A research proposal was required before gaining access to the BHR Data Safe Haven. This included a summary of variables I requested, and a literature review informing this selection of variables. Consideration was given to data completeness and quality as influencing factors in variable selection and planning the analysis. I was given an honorary contract with BHR CCG to access and analyse the datasets through the BHR-accredited Data Safe Haven.

I proposed a longitudinal analysis of older adults aged ≥ 60 years in Barking and Dagenham from 2014 to 2019. Though the list of available chronic conditions in 2018/2019 and 2019/2020 was more extensive than previously, I only considered the same 16 conditions recorded in all years. Primary care data was complete until 2017/2018; 2018/2019 primary care data is currently being collated and cleaned. To ensure quality, accuracy, and comparability, I focused only on the four years with complete data required for my analysis (2014 to 2017).

5.3.2 Creating a linked longitudinal dataset

Initially, service use and cost datasets were recorded in long form, separately indicating each time an individual was in contact with Accident & Emergency, outpatients, elective and non-elective care, and social care services each year and the associated cost per contact (one line per event). The council, individual and primary care datasets were in wide form (one line per individual). First, I reshaped the long datasets to wide. Second, I merged these datasets with the individual and primary care datasets to create a linked dataset in wide form. Third, I repeated this process for the other years and had a linked dataset for 2014/2015, 2015/2016 and 2016/2017, which would be year 1, year 2 and year 3, respectively. The three datasets I created were linked at the individual level across primary, secondary, community and social care using unique IDs. Fourth, I renamed the variables

in each dataset to be uniquely identifiable as being from a predefined year (1 to 3) and merged these three datasets into one. Fifth, I reshaped this final dataset into long form to be able to carry out longitudinal analysis. This linkage was carried out using R programming software using the *merge* and *reshape* functions from the R base package.

Care City carried out extensive data cleaning at inception. Where necessary, I conducted further re-coded and labelled variables to help interpret outputs, with particular attention to missing data.

Data from 2019/2020 contained an extensive list of 38 conditions with flags to indicate whether a chronic condition was absent or present (0 or 1). The datasets from prior years only gave 16 chronic conditions with a date to indicate when the condition was first recorded in primary care. If a condition had not been diagnosed the field was empty. I generated new variables which would contain flags to indicate “yes” or “no” for each chronic condition, if a date of diagnosis was present, I coded this as 1 and if the date was missing, I coded this as 0. Due to how data were recorded, it was impossible to separate missing data from ‘not diagnosed with a condition’ which introduces the risk of information bias. Despite this, having a date as reference is beneficial as it becomes possible to examine service use considering the length of time since diagnosis.

The 16 chronic conditions that are recorded in the years 2014/2015, 2015/2016, and 2016/2017 were identified through consultation with clinical experts in conjunction with literature review. Eight of these conditions were initially identified due to good quality data collection in primary care records in Barking and Dagenham and Havering. The high standards of data quality result from Barking and Dagenham CCG’s involvement in the testing and implementation of *Health 100*, a new model of care for people with multiple long-term conditions, as part of The Prime Minister’s Challenge Fund (NHS England, 2015).

In summary, Care City includes baseline characteristics such as age, sex, ethnicity, socioeconomic position, health-related behaviours, and general health sourced from GP and local authority records. Service use includes

emergency and elective services, primary care, mental health services, and associated costs from health providers and commissioners. Costs are already included in the datasets and were calculated using the Healthcare Resource Group (HRG) national tariff.

5.3.3 Data on expenditure

Costs for each activity varied according to the setting. For primary care, the Personal Social Services Research Unit reference manual was used (PSSRU) (Personal Social Services Research Unit, 2022) and, for each respective year, every GP consultation and other healthcare professional appointments had a corresponding cost attributed. Each prescription was costed based on the average expenses per prescription according to the PSSRU. NHS National Reference Costs (NHS Digital, 2017) provided the framework for secondary care unit costs, essential for NHS hospital payments. For social care funded by the local authority, costs were sourced from the weekly invoiced amounts for every care package. These costs were subject to alterations based on weekly revisions. Cost adjustments for inflation within the study period were made (Personal Social Services Research Unit, 2022).

5.3.4 Confounders

Potential confounders considered in the study were variables anticipated to correlate with predicting healthcare use and expenditure, and mortality risk; principally gender, age, ethnicity, local deprivation, and morbidity (Napoli *et al.*, 2014; Shoff *et al.*, 2019). Deprivation levels were defined from the 2015 English Index of Multiple Deprivation, based on patient postcode (specifically the Lower Layer Super Output Area, an average of 1500 residents). Multimorbidity was quantified based on the presence of up to 16 chronic conditions documented in primary care (Appendix 11). Prescription volume was also considered, with each single item written on a prescription form counted as a separate prescription item, reflecting the medication burden.

5.3.5 Analysis

I used random-effects models to estimate service contacts (outcome) for each care setting, delineating between primary care (e.g., general practitioner visits), secondary care (e.g., hospital admissions, outpatients specialist consultations, emergency department visits), and social care (e.g., home care package) (Table 5-1). Models were adjusted by time, demographic characteristics, general health and health-related behaviours. A strength of random effects models is their ability to handle missing data from unequal follow-up times. I also performed a survival analysis using a Cox proportional hazards model. To visualise temporal patterns in relation to acute admission, I plotted the marginal effects from the interaction between follow-up time and acute admission status for each setting. I used a Kaplan-Meier plot to show the survival probability according to acute admission status. For costs, I calculated the mean differences by setting for individuals with an acute admission in the previous year and those without, assessing differences with paired t-tests. I also stratified mean and percentage differences by demographic characteristics, which included age, multimorbidity burden—defined as the simple count of diagnosed conditions and further categorised as 'simple multimorbidity' for conditions within the same body system and 'complex multimorbidity' for two or more diagnosed conditions from differing body systems—and ethnicity, in relation to acute admission status in the previous year. All analyses and data processing were conducted using R version 3.5.1.

Table 5-1: Definition of care settings in Care City Cohort

Setting	Definition
Unplanned Hospital Care	Unscheduled inpatient hospital care (non-elective)

Accident and emergency **with an admission**	Accident and emergency (**acute inpatient admission via ED**)
Accident and emergency **attendance only**	Accident and emergency (**visit only with no inpatient admission**)
Planned Hospital Care	Scheduled inpatient hospital care (elective)
Social Care	Care delivered in home or residence (including institutional care) to support activities of daily living
Primary Care	Care delivered by both general practitioners (GPs) and other healthcare professionals in general practice settings
Outpatient Care	Specialist outpatient care

5.4 Results

The demographic characteristics of the Care City Cohort were stable over four years (Table 5-2). The sample size was 30,470 in 2014/2015, 31,248 in 2015/2016, and 31,746 in 2016/2017. The average age of individuals with acute admission ranged from 71.3 to 78.1 years, while those without acute admissions were younger (range 71.5 and 74.8 years). Women consistently comprised around 55% of the sample across years and admission statuses. The data indicated higher multimorbidity counts for those with acute admissions, with values spanning from 2.5 to 2.6, compared to 1.5 to 1.6 ($p<0.01$) for those without acute admissions. Complex multimorbidity was more prevalent among the acute admission group (33%). The average IMD score across years was 2.7, suggesting a consistent level of moderate deprivation (1 indicates the most deprived and 5 indicates the least deprived). In terms of ethnicity, White individuals predominated, making up 78% to 88% of the sample. Prescription counts varied considerably between acute (94.7 to 95.6) and non-acute admissions (42.4 to 42.9). The BMI score

was similar between groups, with an average range of 27.3 to 28.5. A majority were non-smokers (51%), followed by ex-smokers (27-34%) and then smokers (14-16%). Over these four years, 4012 (10.3%) died. Individuals with an acute admission in the previous year had higher mean service use across all settings (detailed below) (Table 5-3).

Table 5-2: Descriptive characteristics of the Care City Cohort sample

	Year 1 (2014/2015)				Year 2 (2015/2016)				Year 3 (2016/2017)			
	Acute admission (n=4263)	**No** acute admission (n=26207)	P	Missing/ Unknown	Acute admission (n=4478)	**No** acute admission (n=26770)	P	Missing/ Unknown	Acute admission (n=4345)	**No** acute admission (n=27419)	P	Missing/ Unknown
Age (years (SD))	78.1 (10.1)	71.5 (8.9)	<0.01	-	77.5 (10.3)	71.4 (8.9)	<0.01	-	77.5 (10.4)	71.3 (9.1)	<0.01	-
Women	2338 (55%)	14487 (55%)	0.6	-	2433 (54%)	14731 (55%)	0.4	-	2408 (55%)	14936 (54%)	0.3	-
Multimorbidity (count (SD))	2.6 (1.6)	1.5 (1.3)	<0.01	-	2.6 (1.6)	1.5 (1.3)	<0.01	-	2.5 (1.6)	1.5 (1.3)	<0.01	-
Complex multimorbidity	1403 (33%)	3205 (12%)	<0.01	-	1460 (33%)	3432 (13%)	<0.01	-	1372 (32%)	3533 (13%)	<0.01	-
IMD (score (SD))	2.6 (1.0)	2.7 (1.1)	4.9	-	2.6 (1.0)	2.7 (1.1)	<0.01	-	2.7 (1.0)	2.7 (1.1)	<0.01	-

Ethnicity												
	White	3284 (86%)	18238 (79%)	<0.01	243 (2%)	3422 (84%)	18483 (78%)	<0.01	269 (2%)	3294 (83%)	18809 (76%)	<0.01	270 (2%)
	Asian	260 (7%)	2031 (9%)			301 (7%)	2294 (10%)			339 (9%)	2502 (10%)		
	Black	152 (4%)	1809 (8%)			200 (5%)	2244 (9%)			220 (6%)	2499 (10%)		
	Mixed	57 (1%)	419 (2%)			48 (1%)	283 (1%)			44 (1%)	318 (1%)		
	Other	36 (1%)	282 (1%)			42 (1%)	293 (1%)			27 (1%)	327 (1 %)		
Prescriptions (count mean (SD))		94.7 (94)	42.9 (54.4)	<0.01	-	91.84 (91.9)	41.47 (54.4)	<0.01	-	95.6 (104.2)	42.4 (60.7)	<0.01	-
BMI (score mean (SD))		27.3 (6.4)	28.4 (5.9)	<0.01	1298	27.5 (6.6)	28.48 (5.9)	<0.01	1287	27.6 (6.7)	28.5 (5.9)	<0.01	1253
Smoking Status													
	Non-smoker	2171 (51%)	14271 (55%)	<0.01	528 (3%)	2228 (50%)	14677 (55%)	<0.01	604 (3%)	2215 (51%)	15291 (56%)	<0.01	429 (2%)

Ex-smoker	1430 (34%)	7156 (27%)		1541 (34%)	7233 (27%)	1474 (34%)	7344 (27%)
Smoker	615 (14%)	4299 (16%)		658 (15%)	4307 (16%)	618 (14%)	4393 (16%)

Data are mean (SD) or n (%). BMI=Body Mass Index.

Table 5-3: Service use by setting, with and without an acute admission in the previous year

Setting	Year 1 (2014/2015)					Year 2 (2015/2016)					Year 3 (2016/2017)				
	Acute admission in 2013/2014		**No** acute admission in 2013/2014		P	Acute admission in 2014/2015		**No** acute admission in 2014/2015		P	Acute admission in 2015/2016		**No** acute admission in 2015/2016		P
	mean	SD	mean	SD		mean	SD	mean	SD		mean	SD	mean	SD	
Accident & Emergency [a]	1.0	2.1	0.9	1.0	0.1	1.2	2.1	1.0	1.0	<0.01	1.5	2.8	1.1	1.1	<0.01
Hospital (elective)	1.8	1.4	1.5	1.2	<0.01	1.8	1.5	1.5	1.0	<0.01	1.6	1.4	1.5	1.1	<0.01
Social care	3.5	3.9	2.1	2.3	<0.01	3.5	3.8	2.1	2.4	<0.01	3.2	3.1	2.2	2.1	<0.01
Outpatients	7.6	7.3	5.3	5.3	<0.01	7.7	7.5	5.2	5.2	<0.01	7.4	7.2	5.2	5.2	<0.01
Primary care	10.8	7.7	7.2	5.8	<0.01	10.2	8.0	7.2	5.4	<0.01	9.0	7.9	6.0	5.5	<0.01

a - Not including people who went on to be admitted for acute care through A&E.

5.4.1 Social Care

There was a baseline increase in social care use over time: 0.9 contacts/year (95% CI -0.017 to 0.190). Individuals with one or two acute admissions compared with none had higher social care use of 1.3 contacts/year (95% CI: 0.9 to 1.7), rising further by 4.1 more contacts (95% CI: 3.7 to 4.5) in those with three or more admissions. Social care use declined slightly over time,(-0.02 contacts, 95% CI -0.3 to -0.2), but there was a net sustained increase throughout follow-up (Table 5-4) (Figure 5-1). After adjusting for confounding factors, increasing age, deprivation, higher prescription counts, as well as mortality, were significantly associated with higher social care use while multimorbidity did not show significant independent effects over and above these factors (Table 5-4).

Table 5-4: Null and adjusted linear random-effects models for social care utilisation over a 3-year period

	Unadjusted Coef (95% CI)	**Multivariable** Coef (95% CI)
Wave (year)	-0.009 (-0.043,0.026)	0.086* (-0.017,0.190)
Acute admissions		
None	[ref]	[ref]
One or two	1.300*** (1.200,1.400)	1.300*** (0.970,1.700)
Three or more	4.000*** (3.900,4.100)	4.100*** (3.700,4.500)
Multimorbidity		
None	[ref]	[ref]
One condition	0.240*** (0.094,0.390)	-0.041 (-0.290,0.200)
Two or three conditions	0.630*** (0.490,0.760)	0.003 (-0.220,0.230)
Four or more conditions	1.100*** (1.000,1.300)	-0.075 (-0.330,0.180)
Age (years)	0.059*** (0.055,0.063)	0.026*** (0.023,0.030)
IMD (score)	-0.053*** (-0.093,-0.014)	-0.046*** (-0.081,-0.011)
Men cf. women	-0.061 (-0.140,0.021)	-0.034 (-0.110,0.038)
Smoking status		

Non-smoker	[ref]	[ref]
Ex-smoker	-0.037	-0.120***
	(-0.120,0.052)	(-0.200,-0.041)
Smoker	-0.210***	-0.002
	(-0.330,-0.095)	(-0.110,0.100)
Unknown	0.870***	0.13
	(0.470,1.300)	(-0.400,0.660)
BMI		
Normal	[ref]	[ref]
Morbidly obese	-0.590***	-0.049
	(-0.780,-0.410)	(-0.210,0.120)
Obese	-0.470***	-0.073
	(-0.580,-0.370)	(-0.170,0.019)
Overweight	-0.400***	-0.120***
	(-0.500,-0.300)	(-0.210,-0.037)
Underweight	0.480***	0.13
	(0.280,0.670)	(-0.036,0.290)
Ethnicity		
White	[ref]	[ref]
Asian	-0.390***	-0.086
	(-0.550,-0.230)	(-0.220,0.052)
Black	-0.380***	0.044
	(-0.570,-0.190)	(-0.120,0.210)
Mixed	-0.18	0.075
	(-0.580,0.230)	(-0.260,0.410)
Other	-0.440*	-0.039
	(-0.920,0.029)	(-0.430,0.350)
Unknown	0.12	-0.15
	(-0.250,0.480)	(-0.460,0.170)
Total prescriptions (count)	0.006***	0.002***
	(0.005,0.006)	(0.002,0.003)
Died [a]	1.100***	-0.130**
	(0.940,1.200)	(-0.240,-0.026)
1-2 acute admissions # 1 condition		-0.047
		(-0.420,0.320)
≥3 acute admissions # 1 condition		-0.097
		(-0.560,0.360)
1-2 acute admissions # 2-3 conditions		-0.16
		(-0.510,0.180)
≥3 acute admissions # 2-3 conditions		0.095
		(-0.330,0.520)
1-2 acute admissions # ≥4 more conditions		-0.18
		(-0.550,0.180)
≥3 acute admissions # ≥4 conditions		0.11
		(-0.320,0.550)
Wave (year) # 1-2 acute admissions		-0.022
		(-0.097,0.053)
Wave (year) # ≥3 acute admissions		-0.230***

	(-0.320,-0.150)
Wave (year) # 1 condition	-0.026
	(-0.150,0.096)
Wave (year) # 2-3 conditions	-0.072
	(-0.180,0.040)
Wave (year) # ≥4 conditions	-0.097
	(-0.220,0.025)

Note: *p<0.1; **p<0.05; ***p<0.01
a Died during study period
cf: compared with
BMI: Body mass index

5.4.2 Primary Care

With primary care, after adjusting for confounding variables, having one or two and three or more acute admissions in comparison to none was associated with a rise of 1.6 (95% CI: 1.3 to 2.0) and 2.3 more contacts (95% CI: 1.6 to 2.9) respectively. This rise in primary care use continues to rise by 0.1 contacts over time for those who had three or more acute admissions (95% CI -0.01 to 0.2) (Table 5-5) (Figure 5-1). There is a linear increase in primary care use as the multimorbidity burden increases, after adjusting for confounding variables (Table 5-5).

Table 5-5: Null and adjusted linear random-effects models for primary care utilisation over a 3-year period

	Unadjusted Coef (95% CI)	**Multivariable** Coef (95% CI)
Wave (year)	-0.180***	-0.039
	(-0.210,-0.160)	(-0.092,0.015)
Acute admissions		
None	[ref]	[ref]
One or two	1.800***	1.600***
	(1.700,1.900)	(1.300,2.000)
Three or more	3.300***	2.300***
	(3.200,3.500)	(1.600,2.900)
Multimorbidity		
None	[ref]	[ref]
One condition	2.500***	2.100***
	(2.400,2.600)	(1.900,2.300)
Two or three conditions	4.700***	3.800***

	(4.600,4.800)	(3.600,4.000)
Four or more conditions	7.100***	6.000***
	(7.000,7.300)	(5.700,6.300)
Age (years)	0.083***	0.001
	(0.078,0.088)	(-0.004,0.006)
IMD (score)	-0.180***	-0.040*
	(-0.220,-0.130)	(-0.082,0.003)
Men cf. women	-0.530***	-0.290***
	(-0.630,-0.430)	(-0.380,-0.200)
Smoking status		
Non-smoker	[ref]	[ref]
Ex-smoker	0.850***	0.330***
	(0.760,0.950)	(0.230,0.420)
Smoker	-0.250***	-0.150**
	(-0.380,-0.130)	(-0.270,-0.027)
Unknown	-3.600***	-0.490*
	(-3.900,-3.300)	(-0.980,0.006)
BMI		
Normal	[ref]	[ref]
Morbidly obese	0.990***	0.12
	(0.770,1.200)	(-0.091,0.330)
Obese	0.440***	0.087
	(0.320,0.560)	(-0.024,0.200)
Overweight	0.085	0.068
	(-0.017,0.190)	(-0.030,0.160)
Underweight	0.820***	0.330***
	(0.570,1.100)	(0.081,0.570)
Ethnicity		
White	[ref]	[ref]
Asian	0.270***	0.580***
	(0.096,0.450)	(0.420,0.740)
Black	-1.300***	-0.320***
	(-1.500,-1.100)	(-0.480,-0.160)
Mixed	-0.28	0.350**
	(-0.650,0.083)	(0.020,0.690)
Other	-1.400***	-0.590***
	(-1.800,-0.960)	(-0.960,-0.220)
Unknown	0.008	-0.12
	(-0.380,0.400)	(-0.480,0.230)
Total prescriptions (count)	0.035***	0.023***
	(0.035,0.036)	(0.022,0.024)
Died [a]	-1.900***	-2.900***
	(-2.100,-1.800)	(-3.100,-2.800)
1-2 acute admissions # 1 condition		-0.28
		(-0.640,0.089)
≥3 acute admissions # 1 condition		-0.26
		(-0.930,0.400)
1-2 acute admissions # 2-3 conditions		-0.28

	(-0.620,0.060)
≥3 acute admissions # 2-3 conditions	-0.12
	(-0.740,0.490)
1-2 acute admissions # ≥4 more conditions	-0.880***
	(-1.300,-0.500)
≥3 acute admissions # ≥4 conditions	0.01
	(-0.620,0.640)
Wave (year) # 1-2 acute admissions	0.043
	(-0.043,0.130)
Wave (year) # ≥3 acute admissions	0.110*
	(-0.010,0.230)
Wave (year) # 1 condition	-0.180***
	(-0.250,-0.110)
Wave (year) # 2-3 conditions	-0.340***
	(-0.400,-0.270)
Wave (year) # ≥4 conditions	-0.590***
	(-0.690,-0.500)

Note: *p<0.1; **p<0.05; ***p<0.01
a Died during study period
cf: compared with
BMI: Body mass index

5.4.3 Emergency presentations

ED use, where there was no resulting inpatient admission, fell by -0.9 (95% CI -1.1 to -0.8) for those with one or two acute admissions and -0.4 (95% CI -0.6 to -0.2) for those with three or more acute admissions. With each increasing year, this was higher for both groups compared to those who had no acute admissions, a rise of 0.1 (95% CI 0.1 to 0.2) and 0.3 (95% CI 0.2 to 0.3), respectively (Table 5-6) (Figure 5-1)). Increasing age, affluence, and mortality were associated with decreasing emergency department visits after adjusting for confounding factors. However, in contrast, being male and having a BMI above normal was significantly associated with higher emergency department visits. When these factors were considered, multimorbidity showed no significant independent effect on emergency department visits. (Table 5-6).

Table 5-6: Null and adjusted linear random-effects models for A&E utilisation (no inpatient admission) over a 3-year period

	Unadjusted Coef (95% CI)	**Multivariable** Coef (95% CI)
Wave (year)	0.120*** (0.100,0.130)	0.004 (-0.044,0.053)
Acute admissions		
None	[ref]	[ref]
One or two	-0.700*** (-0.740,-0.670)	-0.930*** (-1.100,-0.790)
Three or more	-0.280*** (-0.320,-0.230)	-0.430*** (-0.640,-0.220)
Multimorbidity		
None	[ref]	[ref]
One condition	-0.076** (-0.140,-0.016)	-0.016 (-0.180,0.140)
Two or three conditions	-0.087*** (-0.140,-0.031)	0.042 (-0.110,0.190)
Four or more conditions	-0.078** (-0.140,-0.015)	0.022 (-0.150,0.200)
Age (years)	-0.013*** (-0.015,-0.012)	-0.009*** (-0.011,-0.006)
IMD (score)	-0.015* (-0.032,0.002)	-0.021** (-0.039,-0.002)
Men cf. women	0.053*** (0.018,0.089)	0.051** (0.012,0.089)
Smoking status		
Non-smoker	[ref]	[ref]
Ex-smoker	-0.038* (-0.076,0.001)	-0.024 (-0.066,0.019)
Smoker	-0.026 (-0.076,0.025)	-0.054* (-0.110,0.003)
Unknown	-0.220** (-0.390,-0.053)	-0.027 (-0.270,0.220)
BMI		
Normal	[ref]	[ref]
Morbidly obese	0.006 (-0.085,0.097)	-0.130*** (-0.230,-0.033)
Obese	0.074*** (0.027,0.120)	-0.054** (-0.100,-0.003)
Overweight	0.02 (-0.024,0.063)	-0.049** (-0.095,-0.004)
Underweight	-0.170*** (-0.260,-0.083)	-0.035 (-0.130,0.059)
Ethnicity		

White	[ref]	[ref]
Asian	0.140***	0.006
	(0.073,0.210)	(-0.065,0.076)
Black	0.190***	0.037
	(0.110,0.270)	(-0.044,0.120)
Mixed	0.190**	0.12
	(0.013,0.360)	(-0.055,0.290)
Other	0.069	0.042
	(-0.120,0.260)	(-0.140,0.220)
Unknown	-0.14	-0.1
	(-0.310,0.032)	(-0.270,0.066)
Total prescriptions (count)	0.001***	0.001***
	(0.001,0.001)	(0.001,0.001)
Died [a]	-0.400***	-0.270***
	(-0.460,-0.350)	(-0.330,-0.210)
1-2 acute admissions # 1 condition		-0.022
		(-0.160,0.120)
≥3 acute admissions # 1 condition		-0.430***
		(-0.640,-0.220)
1-2 acute admissions # 2-3 conditions		-0.002
		(-0.130,0.130)
≥3 acute admissions # 2-3 conditions		-0.410***
		(-0.610,-0.220)
1-2 acute admissions # ≥4 more conditions		-0.019
		(-0.170,0.130)
≥3 acute admissions # ≥4 conditions		-0.310***
		(-0.520,-0.100)
Wave (year) # 1-2 acute admissions		0.120***
		(0.089,0.160)
Wave (year) # ≥3 acute admissions		0.260***
		(0.210,0.300)
Wave (year) # 1 condition		0.011
		(-0.046,0.068)
Wave (year) # 2-3 conditions		-0.005
		(-0.057,0.048)
Wave (year) # ≥4 conditions		0.008
		(-0.051,0.067)

Note: *p<0.1; **p<0.05; ***p<0.01
a Died during study period
cf: compared with
BMI: Body mass index

5.4.4 Elective Hospital Care

Elective inpatient hospital use increased in individuals who had an acute admission, by 0.2 (95% CI -0.01 to 0.4) for those with one or two admissions and 0.6 (95% CI 0.3 to 0.9) for those with three or more acute admissions. With each increasing year, the rise in elective inpatient hospital contact starts to fall by -0.07 (95% CI -0.1 to -0.02) (Table 5-7) (Figure 5-1). There is a linear increase in elective inpatient hospital use as the multimorbidity burden increases after adjusting for confounding variables (Table 5-7).

Table 5-7: Null and adjusted linear random-effects models for elective inpatient care utilisation over a 3-year period

	Unadjusted Coef (95% CI)	**Multivariable** Coef (95% CI)
Wave (year)	-0.022*** (-0.038,-0.007)	0.009 (-0.032,0.050)
Acute admissions		
None	[ref]	[ref]
One or two	0.210*** (0.160,0.260)	0.170* (-0.011,0.350)
Three or more	0.380*** (0.320,0.430)	0.610*** (0.340,0.890)
Multimorbidity		
None	[ref]	[ref]
One condition	0.085*** (0.026,0.140)	0.130* (-0.006,0.270)
Two or three conditions	0.140*** (0.082,0.190)	0.140** (0.008,0.270)
Four or more conditions	0.240*** (0.170,0.310)	0.230*** (0.074,0.400)
Age (years)	0.003*** (0.001,0.005)	-0.001 (-0.004,0.001)
IMD (score)	-0.009 (-0.026,0.008)	-0.007 (-0.025,0.011)
Men cf. women	0.140*** (0.098,0.170)	0.110*** (0.070,0.150)
Smoking status		
Non-smoker	[ref]	[ref]
Ex-smoker	0.084*** (0.044,0.120)	0.052** (0.010,0.094)
Smoker	-0.017 (-0.071,0.037)	-0.039 (-0.096,0.017)

Unknown	0.003 (-0.230,0.240)	0.063 (-0.190,0.320)
BMI		
Normal	[ref]	[ref]
Morbidly obese	-0.094** (-0.190,-0.001)	-0.084* (-0.180,0.013)
Obese	-0.055** (-0.100,-0.007)	-0.046* (-0.096,0.004)
Overweight	-0.048** (-0.093,-0.004)	-0.036 (-0.082,0.009)
Underweight	-0.036 (-0.150,0.083)	-0.051 (-0.170,0.070)
Ethnicity		
White	[ref]	[ref]
Asian	-0.060* (-0.130,0.010)	-0.054 (-0.130,0.017)
Black	-0.059 (-0.140,0.021)	-0.019 (-0.099,0.061)
Mixed	-0.06 (-0.240,0.120)	-0.059 (-0.240,0.120)
Other	-0.095 (-0.280,0.088)	-0.072 (-0.250,0.100)
Unknown	-0.067 (-0.240,0.100)	-0.087 (-0.250,0.076)
Total prescriptions (count)	0.001*** (0.001,0.001)	0.0003* (-0.00002,0.001)
Died [a]	0.095* (-0.003,0.190)	-0.057 (-0.160,0.046)
1-2 acute admissions # 1 condition		0.180** (0.001,0.350)
≥3 acute admissions # 1 condition		0.23 (-0.054,0.510)
1-2 acute admissions # 2-3 conditions		0.064 (-0.099,0.230)
≥3 acute admissions # 2-3 conditions		-0.092 (-0.350,0.170)
1-2 acute admissions # ≥4 more conditions		0.061 (-0.120,0.240)
≥3 acute admissions # ≥4 conditions		-0.340** (-0.610,-0.074)
Wave (year) # 1-2 acute admissions		-0.028 (-0.070,0.015)
Wave (year) # ≥3 acute admissions		-0.071*** (-0.120,-0.017)
Wave (year) # 1 condition		-0.047* (-0.098,0.003)
Wave (year) # 2-3 conditions		-0.019

	(-0.066,0.028)
Wave (year) # ≥4 conditions	-0.016
	(-0.073,0.042)

Note: *p<0.1; **p<0.05; ***p<0.01
a Died during study period
cf: compared with
BMI: Body mass index

5.4.5 Outpatient Care

Outpatient contact increased in those who had an acute admission, by 1.9 (95% CI 1.4 to 2.4) for those with one or two admissions and 3.3 (95% CI 2.5 to 4.1) for those with three or more acute admissions. Per each increase in year, the rise in the use of outpatient services increases by 0.2 (95% CI 0.1 to 0.3) for those who had three or more acute admissions (Table 5-8) (Figure 5-1). There is a linear increase in outpatient care utilisation as the multimorbidity burden increases after adjusting for confounding variables (Table 5-8).

Table 5-8: Null and adjusted linear random-effects models for outpatient care utilisation over a 3-year period

	Unadjusted Coef (95% CI)	**Multivariable** Coef (95% CI)
Wave (year)	0.048***	0.056
	(0.013,0.083)	(-0.040,0.150)
Acute admissions		
None	[ref]	[ref]
One or two	1.700***	1.900***
	(1.600,1.900)	(1.400,2.400)
Three or more	3.500***	3.300***
	(3.300,3.600)	(2.500,4.100)
Multimorbidity		
None	[ref]	[ref]
One condition	0.560***	0.360**
	(0.410,0.720)	(0.018,0.710)
Two or three conditions	1.600***	1.100***
	(1.400,1.700)	(0.720,1.400)
Four or more conditions	3.400***	2.800***
	(3.200,3.600)	(2.400,3.300)
Age (years)	0.015***	-0.044***

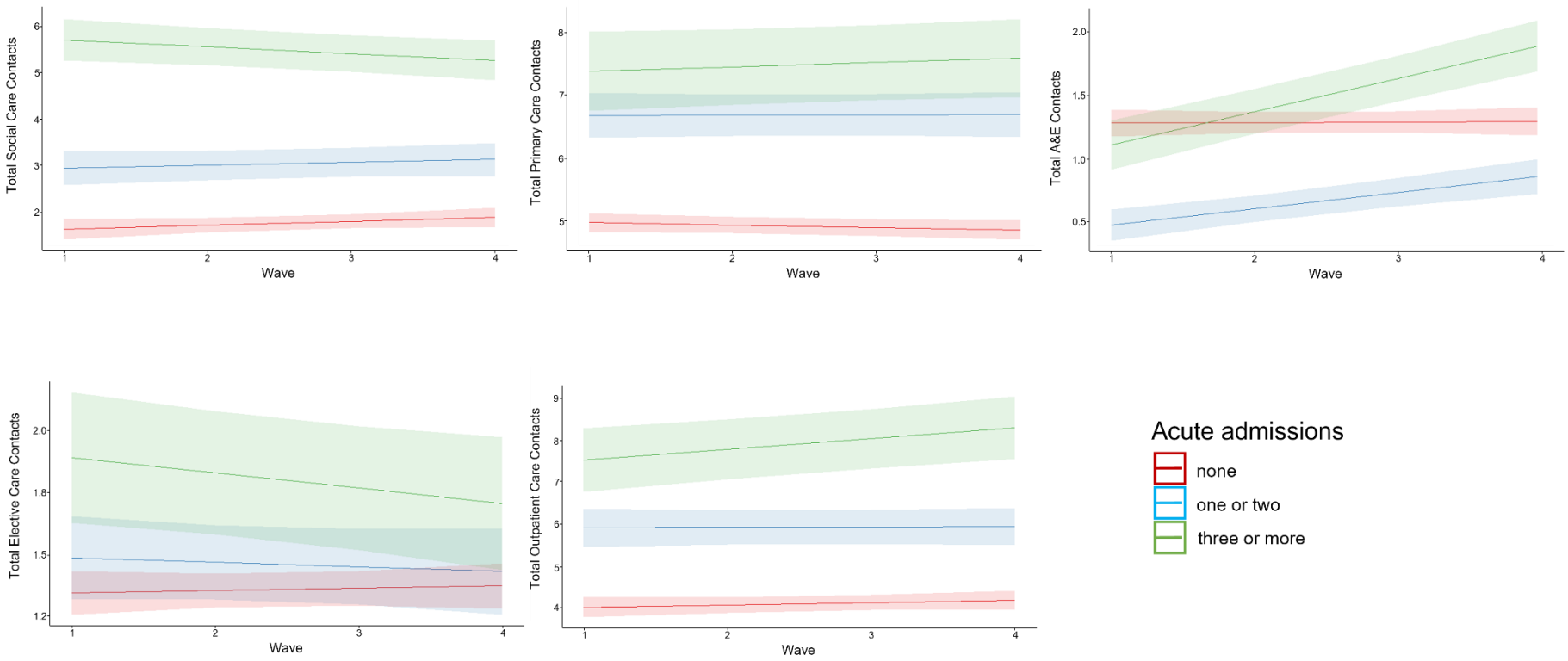
	(0.009,0.020)	(-0.050,-0.037)
IMD (score)	0.064**	0.170***
	(0.014,0.110)	(0.120,0.230)
Men cf. women	0.130**	0.027
	(0.023,0.240)	(-0.086,0.140)
Smoking status		
Non-smoker	[ref]	[ref]
Ex-smoker	0.480***	0.170***
	(0.370,0.590)	(0.051,0.290)
Smoker	-0.190**	-0.400***
	(-0.340,-0.045)	(-0.550,-0.240)
Unknown	-0.34	0.650*
	(-0.890,0.200)	(-0.034,1.300)
BMI		
Normal	[ref]	[ref]
Morbidly obese	0.300**	-0.300**
	(0.045,0.560)	(-0.570,-0.037)
Obese	0.160**	-0.120*
	(0.022,0.290)	(-0.260,0.022)
Overweight	-0.031	-0.071
	(-0.150,0.093)	(-0.200,0.055)
Underweight	0.048	-0.320**
	(-0.260,0.360)	(-0.630,-0.0003)
Ethnicity		
White	[ref]	[ref]
Asian	-0.045	-0.370***
	(-0.240,0.150)	(-0.570,-0.170)
Black	-0.380***	-0.11
	(-0.600,-0.170)	(-0.330,0.100)
Mixed	0.12	0.081
	(-0.340,0.590)	(-0.380,0.540)
Other	-0.15	-0.15
	(-0.680,0.380)	(-0.660,0.360)
Unknown	0.056	-0.036
	(-0.420,0.540)	(-0.500,0.430)
Total prescriptions (count)	0.016***	0.010***
	(0.015,0.016)	(0.009,0.010)
Died [a]	-0.480***	-1.800***
	(-0.680,-0.280)	(-2.000,-1.600)
1-2 acute admissions # 1 condition		-0.19
		(-0.650,0.270)
≥3 acute admissions # 1 condition		-0.44
		(-1.200,0.350)
1-2 acute admissions # 2-3 conditions		-0.068
		(-0.490,0.360)
≥3 acute admissions # 2-3 conditions		-0.48
		(-1.200,0.260)

1-2 acute admissions # ≥4 more conditions	-0.23 (-0.700,0.240)
≥3 acute admissions # ≥4 conditions	-0.46 (-1.200,0.300)
Wave (year) # 1-2 acute admissions	-0.045 (-0.150,0.061)
Wave (year) # ≥3 acute admissions	0.200*** (0.063,0.340)
Wave (year) # 1 condition	0.019 (-0.098,0.140)
Wave (year) # 2-3 conditions	-0.013 (-0.120,0.097)
Wave (year) # ≥4 conditions	-0.260*** (-0.400,-0.120)

Note: *p<0.1; **p<0.05; ***p<0.01
a Died during study period
cf: compared with
BMI: Body mass index

Figure 5-1 illustrates the interaction between time and acute admissions in their association with service use across different settings. Notably, individuals with three or more acute admissions most commonly have the highest levels of service use, those with one or two admissions begin with moderate use and individuals with no acute admissions consistently show the lowest level of service use. Although service utilisation may converge downward over time in most settings, the persisting influence of acute admissions on the demand for services across settings is still evident.

Figure 5-1: Interaction between time and acute admission, and their association with service use across settings



5.4.6 Costs

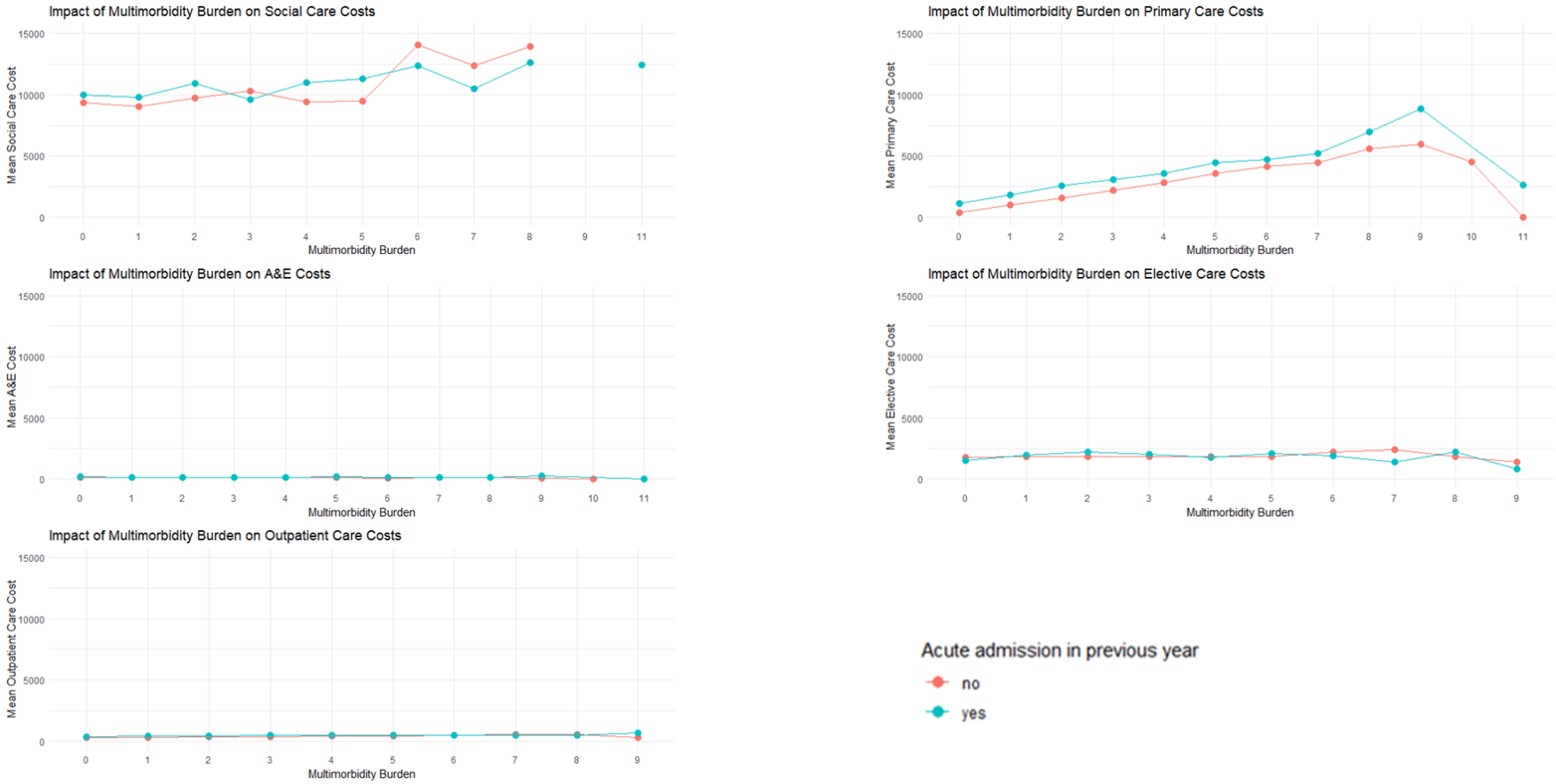
Associated service costs across healthcare settings showed that individuals with acute admissions in the prior year consistently incurred higher mean service costs in all settings (Table 5-9). Both social care and primary care costs escalate in conjunction with the rise in multimorbidity burden, even more pronounced among patients who had an acute admission in the preceding year (Figure 5-2). Conversely, ED costs remain largely consistent for patients without prior acute admissions, while those with such admissions experience a marginal cost increase. Outpatient care costs present a more complex pattern: they initially increase with the multimorbidity burden but subsequently taper off, reaching a peak before declining. This downward trend manifests sooner for patients with a history of acute admission. Meanwhile, elective care costs maintain a steady line across varying levels of multimorbidity burden, showing only a minor increase in expenses for patients with acute admissions.

Table 5-9: Service cost (£) by setting, with and without an acute admission in the previous year

Setting	Year 1 (2014/2015)					Year 2 (2015/2016)					Year 3 (2016/2017)				
	Acute admission in 2013/2014		**No** acute admission in 2013/2014		P	Acute admission in 2014/2015		**No** acute admission in 2014/2015		P	Acute admission in 2016/2016		**No** acute admission in 2015/2016		P
	mean	SD	mean	SD		mean	SD	mean	SD		mean	SD	mean	SD	
Accident & Emergency [a]	117.6	224.6	104.4	110.9	0.02	166.2	280.3	131.4	136.3	<0.01	224.9	390	152.5	161	<0.01
Outpatients	418.3	514.8	323.4	384	<0.01	454.2	518.1	346.2	377.1	<0.01	511.9	595	394.1	436.9	<0.01
Hospital (elective)	2064	2881	1896	2410	0.1	2149	3134	1764	2349	<0.01	1794	2145	1911	2423	0.1
Social care	11153	11229	9252	9720	0.002	10407	10460	11379	10808	0.3	9791	10738	9194	12264	0.5
Primary care	2548	2246	1237	1373	0.003	2934	2765	1368	1544	<0.01	3077	3107	1416	1799	<0.01

a - Not including people who went on to be admitted for acute care through A&E.

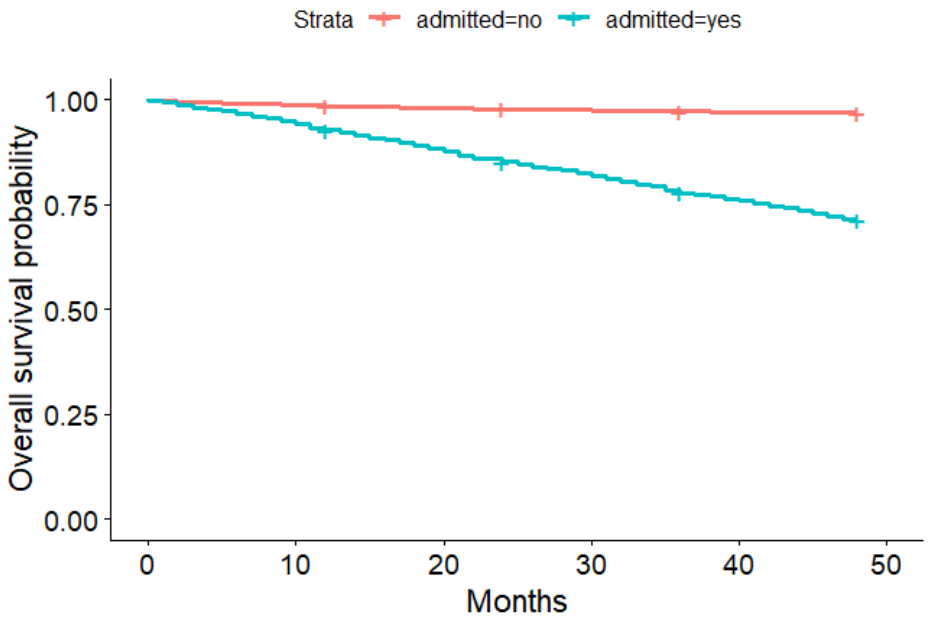
Figure 5-2: Costs associated with multimorbidity across care settings



5.4.7 Mortality

Over this three-year period, 4012 (10.3%) in total died and survival analysis at wave 1 showed that having one or two admissions at wave 1 was associated with a near five-fold increase in mortality risk (HR=4.7, 95% CI 3.1 to 7.1) and, also compared with no admission, those with three or more acute admissions showed a 10 fold increase in mortality risk (HR=10.1, 95% CI 6.3 to 16.1) (Appendix 12). This mortality risk is consistent in the following years (Appendix 13) (Appendix 14). A Kaplan-Meier plot shows the survival probabilities over time for two strata: individuals who had been admitted and those who had not been admitted (Figure 5-3). It shows that for those who were not admitted during the study period, their survival probability starts at 1.0 and remains relatively flat, indicating that this group's survival rate does not change much over time. In contrast, the curve for those who were admitted, their survival probability decreases more steeply over time, suggesting a lower survival rate as time progresses.

Figure 5-3: Kaplan-Meier survival analysis: comparison of admitted vs. non-admitted individuals



5.5 Discussion

This study sought to elucidate the implications of acute hospital admissions on mortality, primary, secondary, and social care service use, and associated costs over four years. The findings demonstrate that in a population of older adults in Barking and Dagenham, acute hospitalisation led to pronounced increases in service usage and costs. Importantly, the surge in service use post-acute admission persisted over time, never reverting to baseline levels. Moreover, survival rates were worse in patients with the highest frequency of acute admissions, illustrating the range of health and social care encounters occurring in the last few years of life. The high service use and costs associated with multimorbidity, as revealed in this chapter, align with the systematic review findings in Chapter 3 that emphasised the need for integrated care strategies.

While prior research has explored how to reduce acute admissions (Credé *et al.*, 2017), factors that predict service use preceding an acute admission (Feldblum *et al.*, 2009; Smulowitz *et al.*, 2023), and affirmed the escalation in service utilisation and expenditure post-admission, this study provides novel insights by uniquely quantifying these elevations and their persistence over time across multiple health and social care settings. This research further adds value through being able to assess use over several years.

Numerous studies have explored interventions to reduce acute admissions (Rosenberg, 2012; Credé *et al.*, 2017), and one particular study shows the surge in primary and secondary care use 30 days post-hospitalisation (Säfström *et al.*, 2018). Additional intervention strategies, like intensive transitional care by clinical social workers, has shown promise in reducing hospital readmissions and emergency visits (Xiang *et al.*, 2019). Yet, the question remains: how can we directly make service use ensuing from acute admissions across diverse healthcare settings more integrated and efficient? This study augments previous findings by detailing which services are most often used, by whom, and for how long.

It is clear that acute admissions may indicate worsening health in the longer-term (Godden *et al.*, 2001; García-Peña *et al.*, 2018; Patel *et al.*, 2021). The

relationship between acute admissions, multimorbidity, and long-term service use underscores the complexities of older people's health and social care needs. A consistent uptick in social care use was evident throughout the study, emphasising the enduring effects of acute hospitalisations. Similarly, for primary care, the number of acute admissions was proportional to an increase in contacts, and even worse in those with pre-existing multimorbidity.

Furthermore, when delving into ED use without subsequent inpatient admission, the study observed a decline in utilisation for those with one or more acute admissions. This trend may suggest that acute admissions potentially mitigate the need for ED visits, or perhaps reflect an improved care pathway after an acute admission. Conversely, elective inpatient hospital use and outpatient contacts both manifested an upward trajectory for individuals with acute admissions, highlighting the profound impact of acute episodes on healthcare resource consumption. As the multimorbidity burden escalates, there is a consistent linear growth in both elective inpatient hospital and outpatient care utilisation. This may be indicative of the complex needs of multimorbid patients necessitating frequent specialist consultations and planned interventions. Moreover, survival analysis reveals a dramatic escalation in mortality risk associated with the number of conditions in all four years, emphasising the critical implications of acute admissions and multimorbidity on patient outcomes.

The 2012 Health and Social Care Act in England aspired to transition patient care from hospital-centric models to community-based paradigms (Lopez Bernal *et al.*, 2017). However, the outcomes from its enactment suggested gaps in care coordination and acute admission risk management. This underscores the significance of comprehending the ripple effects of acute admissions across diverse health and social care settings. Improved coordination, underpinned by a community-centric model, might provide better outcomes when optimising patient journeys post-acute admissions.

The strength of this study lies in its utilisation of the Care City Cohort's comprehensive, linked dataset, which facilitated a detailed examination of

service use patterns across multiple care settings in an older adult population. The longitudinal nature of the data allowed me to observe trends over a four-year period, providing robust evidence on the sustained impact of acute admissions on service utilisation and costs. However, the study is not without limitations. One potential issue is reverse causality; it is possible that the higher service use observed post-acute admission could be a result of the admission event itself, which may lead to new diagnoses and an apparent increase in multimorbidity. This could suggest that the multimorbidity observed is partly an object of increased healthcare contact rather than a true reflection of the patient's baseline health status. Even with this limitation, examining what an acute admission means for an individual's long-term health and care needs is still valuable by quantifying and contextualising the implications. This evidence can be applied towards preventing acute admissions by targeting resources toward primary and social care services, which were shown to experience the highest burden in this study. Furthermore, the study is confined to a single borough within London, which may limit the generalisability of the findings to other populations. Future research should consider these factors and aim to replicate the findings in a broader demographic to affirm the implications of acute admissions on long-term health and social care use.

This study shows that while service utilisation generally decreases over time, those with multiple acute admissions maintain a comparatively higher usage. This persistent demand raises the question of necessity and highlights potential areas for reducing service fragmentation. My systematic review identified that patient-professional collaborations and integrated care interventions, which were effective in reducing readmissions and inpatient days, could be pivotal in streamlining these services. Moreover, the trend towards increased contacts in primary care for those with multimorbidity suggests that interventions could be more effectively coordinated at this level. This is where the activity is most dense, indicating a potential focal point for developing coordination services. Technology interventions, also noted for improving quality of care, could be leveraged to minimise unnecessary contacts and enhance care coordination, particularly within

primary care settings, to address the complex needs of this population efficiently. By integrating these approaches, fragmentation in service delivery may be reduced and cost-effectiveness of interventions for older adults with multimorbidity can be improved.

5.6 Conclusion

To conclude, this study shines a light on the profound influence of acute admissions on healthcare systems and outcomes. The findings underscore the imperative for holistic interventions, especially targeting at-risk subgroups, to mitigate the ramifications of acute admissions and the ensuing prolonged service dependence. This study highlights that although the rise in service use after acute admission attenuates over time, there is evidence of increased service utilisation well beyond the acute illness period. Services experiencing the highest burden were primary care and social care, emphasising the need for focused and tailored interventions where services are designed around proactive community-based frameworks rather than reactive hospital-centric care.

The analysis in this chapter reveals the significant burden that multimorbidity places on healthcare systems, as evidenced by the high rates of service use and associated costs following emergency admissions. These findings highlight the need for more integrated and proactive care strategies to manage the complex needs of older adults with multimorbidity. This chapter's insights provide a critical context for the following chapter, which will explore how health-related quality of life, arguably the most important outcome in chronic disease management, relates to frailty and life-space mobility. By examining the interplay between functional mobility, multimorbidity, frailty, and HRQoL, I aimed to identify potential intervention targets for multimorbidity management. This approach could lead to the identification of subgroups and the development of tailored interventions that address the broader goals of improving overall well-being and functionality in patients with multimorbidity.

Chapter 6 Life-space, frailty, and health-related quality of life in DELPHIC

Building on the findings from the previous chapter on service use and cost implications, this chapter explores the relationship between life space, quality of life, and frailty in older adults. Frailty was assessed using a cumulative deficit model, which incorporates multimorbidity. Health-related quality of life emerges as a crucial endpoint in multimorbidity management, reflecting the holistic impact of multiple chronic conditions on overall well-being. Using data from the DELPHIC study, this analysis investigates the interplay between functional mobility, multimorbidity, frailty, and HRQoL. I sought to understand if particular subgroups might be better targets for multimorbidity management, where the goal extends beyond treating diseases. This complements the service use findings discussed in the previous chapter.

6.1 Summary

Functional mobility and frailty are closely linked to health-related quality of life. Understanding their inter-relationship could indicate potential intervention targets for improving quality of life. I set out to quantify the relationship between multimorbidity, frailty and life-space (a functional mobility , and their relative impact on quality of life measures.

Using cross-sectional data from a population-representative cohort of people aged ≥70 years, I used the EuroQol Health Index tool (5-levels) (EQ-5D-5L) as a quality of life measure. I also used the life-space assessment, derived a frailty index and a multimorbidity count. Linear regression models estimated EQ-5D-5L scores (dependent variable) using life-space assessment, frailty index and interactions between them. All models were adjusted by age, sex, lifestyle, and social care factors.

Frailty was more strongly associated with EQ-5D-5L than multimorbidity and dominated most model estimates. A higher EQ-5D Index was associated with higher life-space (0.02 per life-space assessment score, 95%CI: 0.01 to 0.03, $p<0.01$) and decreasing frailty (-0.01 per SD, 95%CI: -0.01 to -0.01, $p<0.01$). There was evidence of an interaction between life-space and frailty, where

the steepest gradient for life-space and EQ-5D was in those classified as most frail (interaction term = 0.02 per SD of frailty, 95%CI: 0.01 to 0.03, p<0.01).

Individuals who were frail were twice as likely to have higher quality of life in association with a larger life-space. Interventions designed to improve quality of life in frail older people could focus on increasing a person's life-space, this supports identifying frailty as a useful method of targeting interventions.

6.2 Introduction

Maintaining health-related quality of life into older age is a key ambition for multidisciplinary healthcare teams (Vanleerberghe *et al.*, 2017, 2019). Quality of life has several dimensions, covering the physical, psychological, and social aspects of an individual's well-being and function (Karimi *et al.*, 2016). Other multidimensional quantities relevant to older people include frailty and life-space (Clegg *et al.*, 2013; Taylor *et al.*, 2019). Frailty results from cumulative decline across multiple physiological systems. Life-space assessments integrate several aspects of functional mobility. As such, each measure is closely linked, and understanding their inter-relationship could indicate potential intervention targets for improving quality of life (Bentley *et al.*, 2013; Vanleerberghe *et al.*, 2019).

Life-space is a rich and informative assessment with good construct validity, yet it is not well-established as a clinical tool (Johnson *et al.*, 2020). It quantifies three dimensions of functional mobility: distance travelled (up to 5 points), frequency (up to 4 points), and need for mobility assistance (up to 2 points). Higher scores reflect greater degrees of function, and these scores can be multiplied to give a single measure (Baker *et al.*, 2003). An individual's total life-space is dynamic and may change as a result of acute (e.g., after stroke or surgery) and chronic (e.g., dementia or osteoarthritis) health conditions (Lo *et al.*, 2014; Miyashita *et al.*, 2021). Smaller life-space is associated with a lower quality of life (Rantanen *et al.*, 2021), though how changes in life-space impact quality of life across the spectrum of frailty has not been described (Rantakokko *et al.*, 2016). Frailty is an important

contextual factor given that frail and pre-frail individuals have greater decline in life-space compared with non-frail individuals (Portegijs *et al.*, 2016). It is possible that life-space mediates some of the relationship between frailty and quality of life, and so could prove to be a tractable target for physical and occupational therapy interventions.

I sought to quantify the relationship between life-space, frailty, and their relative impact on overall quality of life in a population-representative cohort. I set out to investigate variables associated with quality of life and life-space, hypothesising that these would have interactions that might indicate how these relationships varied with frailty. This analysis contributes to evidence on identifying frailty as a method of targeting interventions in complex older people. It focuses on understanding how life-space, frailty, and health-related quality of life interact and influence each other within the studied population.

6.3 Methods

6.3.1 Population, setting and study design

Eligible participants of DELPHIC were invited to enrol by letter from their Camden-based general practice lists. To include a wider range of health states, this list was supplemented with patients who were directly recruited from memory clinics and those recently discharged from secondary care. The ratio for this recruitment method was 8:1:1. In accordance with the Mental Capacity Act 2005, all individuals or their named proxies gave consent or agreement to participate. Individuals not eligible for inclusion included those with severe hearing impairments, aphasia, those unable to speak sufficient English to take part in a basic cognitive assessment or individuals with a terminal illness. The exclusion process was carried out using codes available in primary care records. DELPHIC received approval from an NHS Research Ethics Committee (16/LO/1217) and the Health Research Authority (IRAS 164446).

6.3.2 Clinical assessments and procedures

Data including demographic, health, social and lifestyle factors, frequency of contact with next of kin, and care package input were collected through a

standard interview by trained interviewers or were self-reported. Data on these variables were collected at baseline through community assessments mainly by telephone, with some participants being assessed face to face. Graduate researchers performed baseline community assessments in pairs, and registered healthcare professionals performed hospital assessments. The baseline assessment interview gathered and recorded data on sociodemographic factors, general health, comorbidities, medications, health behaviours, hearing, vision, quality of life, dental health, continence, falls, depression, activities of daily living, and socio-economic position which was measured through index of multiple deprivation (IMD), occupation, and education.

6.3.2.1 Outcome

Quality of life was defined by EuroQol Health Index tool (5-levels) (EQ-5D-5L), which includes a visual analogue scale (VAS) summarising a self-rating for quality of life from 0 to 100 (100= 'best health'). EQ-5D-5L also has domains on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Using empirical value sets for an English population, a score in each domain generates an overall EQ-5D index where 0 is equivalent to dead (negative values mean 'worse than dead') and 1 refers to 'full health' (values above 1 indicate even higher health utility).

6.3.2.2 Exposure

The life-space assessment is a self-reported measure of an individual's independent mobility. It relates to the dimensions of geographical space where a person's life occurs. Life-space has three components: distance travelled (5 levels, from bedroom only to beyond the neighbourhood); frequency of travel (4 levels, from daily to <1/week); need for assistance (3 levels, none / with equipment / with personal assistance). Responses refer to the previous four weeks' activity. Multiplying these scores indicates an individual's functional mobility (range 0 to 120).

6.3.2.3 Covariates

I included health, social and lifestyle factors, such as frailty, frequency of contact with next of kin, and care package input. Contact with next of kin was

a self-reported measure, the highest frequency of in person and by phone contact was recorded as daily, weekly, monthly, yearly, or less. Receipt of a care package was recorded as frequency of social carer support, including hired cleaners only. Social care support was recorded as none, weekly, daily, or multiple times daily. Frailty was quantified using a Frailty Index, representing the proportion of accumulated health deficits, including co-morbidities (0 to 1). This was derived using 35 items drawn from the baseline assessment covering general health, co-morbidities, medications, health behaviours, hearing, vision, dental health, continence, falls, depression, personal and instrumental activities of daily living, and calculated according to standard procedures (Appendix 8) (Searle *et al.*, 2008). Socio-economic position (SEP) was operationalised using highest educational attainment (primary/secondary/tertiary), the Office for National Statistics occupational skill classification (4 levels) and Index of Multiple Deprivation (IMD) score, an ecological measure where higher scores indicate neighbourhood disadvantage (Ministry of Housing Communities & Local Government, 2019; Office for National Statistics, 2020).

6.3.3 Statistical analysis

I used a series of linear regression models to estimate the associations between the continuous outcomes (EQ-5D index, visual analogue scale) and covariates. These models allowed me to explore the relationships between these variables while adjusting for potential confounders. I used median imputation for any data missing within the life-space assessment dimensions and multiple imputation (20 imputations) for other missing covariate data. I assessed multiplicative interactions between life-space and frailty index scores. To improve comparability and ease of interpretation, I transformed these into standardised z-scores (score-mean)/standard deviation). I used Stata version 16.1 for all analyses (StataCorp LLC, College Station, Texas).

6.4 Results

The mean age of the full sample was 78 (SD 6.2), and 41% were men, and most individuals were educated to degree or postgraduate level and had high skill occupations (Table 6-1). On average, in this older population, the individuals in the total sample had a multimorbidity count of 1.4 conditions, with a standard deviation (SD) of 1.2 suggesting a moderate level of variability in the number of conditions per individual in the sample. Looking at the multimorbidity data across the different EQ-5D-5L Index categories, there were no significant differences in multimorbidity count across the three groups (EQ-5D-5L Index <0.70, 0.70 to 0.80, >0.80), with means of around 1.4 and similar standard deviations. The P-values across these groups (0.447, 0.488, 0.488, respectively) suggest that there is no statistically significant difference in the number of comorbid conditions among the different health-related quality of life scores measured by the EQ-5D-5L Index. At least one outcome score was missing in 24% of participants, though only 5% were missing both EQ-5D Index and the Visual Analogue Scale score. Missing outcome scores were more likely in people with higher frailty (FI 0.19 versus 0.15) and with more comorbidities (1.3 versus 1.6 diseases) (Table 6-1). The remainder of the analyses were on participants with available EQ-5D Index and Visual Analogue Scale data (n=1152). Individuals in the middle tertile of EQ-5D Index (between 0.7 and 0.8) had a Visual Analogue Scale score of 79/100. Participants reported an average life-space of 66/120, broadly equivalent to someone who is able to leave their neighbourhood several times a week with the assistance of equipment. The average frailty index was 0.15 (Table 6-1). Table 6-2 describes typical clinical presentations of different levels of life-space by degree of frailty and Table 6-3 describes multimorbidity burden by the degree of frailty.

Table 6-1: Descriptive characteristics of the DELPHIC sample (n = 1510, missing EQ-5D-5L Index = 358 (24%))

		Missing quality of life		EQ-5D-5L Index			
	Total sample (n=1510)	(Both measures)	*P*	<0.70 (n=324)	0.70 to 0.80 (n=428)	>0.80 (n=400)	*P*
	n or mean	n or mean		n or mean	n or mean	n or mean	
Men	625 (41%)	27 (2%)	0.305	133 (43%)	178 (43%)	172 (44%)	0.875
EQ-Visual Analogue Scale (SD)	78.6 (15.6)			78.6 (16.4)	79.1 (15.5)	78.7 (15.4)	0.928
Life-space (score, SD)	65.7 (17.5)	82 (53.7)	0.186	64.7 (18.5)	66.3 (17.4)	65.5 (17.6)	0.585
Frailty index (SD)	0.15 (0.13)	0.19 (0.15)	0.005	0.15 (0.12)	0.14 (0.12)	0.16 (0.14)	0.447
Age (years, SD)	78 (6.2)	78 (6.0)	0.488	78 (6.4)	78 (5.9)	78 (6.2)	0.774
Multimorbidity (count, SD)	1.4 (1.2)	1.6 (1.3)	0.039	1.3 (1.1)	1.4 (1.3)	1.4 (1.1)	0.488
IMD (deprivation score, SD)	16.6 (9.1)	17.9 (8.9)	0.226	15.8 (8.5)	17.1 (9.6)	17.0 (9.1)	0.125
Education							
Up to primary	213 (14%)	12 (1%)	0.44	50 (16%)	52 (12%)	58 (15%)	0.679
Up to secondary	313 (21%)	21 (1%)		62 (19%)	89 (21%)	83 (21%)	
Degree level	968 (64%)	47 (3%)		210 (65%)	285 (67%)	251 (64%)	
Occupational skill level							

Level 1	81 (5%)	6 (0.4%)	0.068	21 (7%)	21 (5%)	22 (6%)	0.446
Level 2	237 (16%)	13 (1%)		46 (14%)	59 (14%)	68 (17%)	
Level 3	246 (16%)	20 (1%)		41 (13%)	70 (16%)	67 (17%)	
Level 4	935 (62%)	39 (3%)		215 (67%)	276 (65%)	242 (61%)	
NOK contact (in person)							
Daily or weekly	1099 (73%)	63 (4%)	0.411	237 (75%)	325 (76%)	286 (72%)	0.485
Monthly	211 (14%)	8 (1%)		44 (14%)	57 (14%)	61 (15%)	
Yearly or less	167 (11%)	7 (0.5%)		35 (11%)	37 (9%)	48 (12%)	
NOK contact (by phone)							
Daily or weekly	1026 (68%)	53 (5%)	0.231	222 (88%)	299 (91%)	267 (86%)	0.372
Monthly	97 (6%)	3 (0.3%)		21 (8%)	22 (7%)	34 (11%)	
Yearly or less	40 (3%)	0 (0%)		9 (4%)	9 (3%)	11 (4%)	
Care package							
None	1413 (94%)	73 (5%)	0.632	303 (94%)	405 (95%)	370 (93%)	0.706
Weekly	26 (2%)	2 (0.1%)		4 (1%)	7 (2%)	8 (2%)	
Daily or more	68 (5%)	5 (0.3%)		16 (5%)	16 (4%)	22 (6%)	
Smoking status							
Never	640 (42%)	30 (2%)	0.447	144 (45%)	179 (42%)	170 (43%)	0.907
Ex-smoker	774 (51%)	43 (3%)		160 (50%)	226 (53%)	203 (51%)	

Current	91 (6%)	7 (0.5%)		19 (6%)	23 (5%)	25 (6%)	
Alcohol intake							
Daily	534 (35%)	30 (2%)	0.12	110 (39%)	140 (41%)	149 (44%)	0.754
Weekly	458 (30%)	16 (1%)		112 (40%)	134 (39%)	120 (35%)	
Monthly or less	267 (18%)	18 (1%)		60 (21%)	71 (21%)	71 (21%)	
Distance from NOK (miles, SD)	201.9 (1299.2)	299 (1242.9)	0.507	120.2 (595.3)	151.1 (1088.2)	207.1 (1074.2)	0.478

Items assessed by interview or self-reported.

Table 6-2: Life-space scores and profiles according to frailty

	Low	Medium	High
Life-space: mean (SD)	74.3 (11.5)	66.9 (14.0)	41.4 (20.0)
Description of typical individual	Independently travels outside city on a weekly basis.	Mobilises outdoors independently but rarely beyond their neighbourhood.	Leaves house daily or able to but needs rollator frame; leaves neighbourhood rarely and would need personal assistance to do so.

Table 6-3: Multimorbidity count in relation to frailty

	Low	Medium	High
Multimorbidity burden: mean (SD)	0.4 (0.6)	1.6 (3.5)	2.9 (6.3)

A higher EQ-5D Index was associated with older age (0.01 per year, 95%CI: 0.005 to 0.02, p<0.01), higher life-space (0.02 per life-space assessment score, 95%CI: 0.01 to 0.03, p<0.01) and decreasing frailty (-0.1 per SD, 95%CI: -0.1 to -0.1, p<0.01) (Table 6-4, Figure 6-1). Women had a lower EQ-5D Index (-0.02, 95%CI: -0.04 to 0.01, p<0.01). Similar patterns were evident for the Visual Analogue Scale scores. Neither self-reported loneliness, frequency of contact, nor distance from next of kin were associated with quality of life.

Figure 6-1: Variables associated with HRQoL

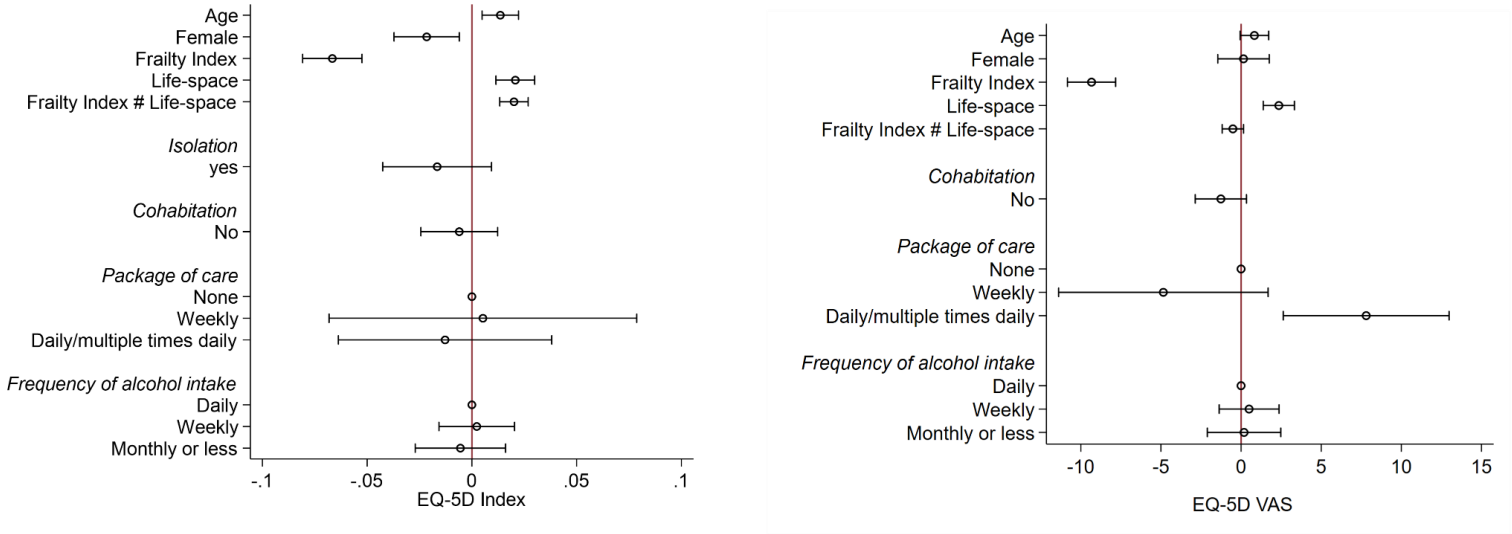


Table 6-4: Null and adjusted linear model for variables that have an association with quality of life (**EQ-5D Index**)

	Unadjusted		**Multivariable** (n = 943)	
	Coef. (95% CI)	*P*	Coef. (95% CI)	*P*
Age	-0.03 (-0.04,0.02)	<0.001	0.01 (0.005,0.02)	0.002
Women (cf.) Men	-0.03 (-0.04,-0.01)	0.003	-0.02 (-0.04,-0.01)	0.007
Frailty index	-0.1 (-0.1,-0.1)	<0.001	-0.1 (-0.1,-0.1)	<0.001
Life-space	0.1 (0.1,0.1)	<0.001	0.02 (0.01,0.03)	<0.001
Frailty Index # Life-space			0.02 (0.01,0.03)	<0.001
NOK contact (in person)				
Daily/weekly	[ref]	0.047		
Monthly	-0.01 (-0.03,0.02)			
Yearly or less	-0.04 (-0.1,-0.01)			
NOK contact (by phone)				
Daily/weekly	[ref]	0.051		
Monthly	-0.04 (-0.1,-0.005)			
Yearly or less	-0.03 (-0.1,0.02)			
Loneliness	-0.04 (-0.1,-0.01)	0.010	-0.02 (-0.04,0.01)	0.210
Lives alone	-0.03 (-0.05,-0.01)	0.001	-0.01 (-0.02,0.01)	0.518
Distance from NOK (miles)	-0.001 (-0.01,0.01)	0.809		
Care package				
None	[ref]	<0.001		0.853
Weekly	-0.2 (-0.2,-0.1)		0.01 (-0.1,0.1)	
Daily/multiple times daily	-0.3 (-0.4,-0.3)		-0.01 (-0.1,0.04)	
Smoking status				
Never	[ref]	0.533		
Ex-smoker	-0.01 (-0.02,0.01)			
Current	-0.02 (-0.1,0.02)			
Alcohol intake				
Daily	[ref]	<0.001		0.769

Weekly	-0.004 (-0.03,0.02)	0.002 (-0.02,0.02)
Monthly or less	-0.06 (-0.08,-0.04)	-0.01 (-0.03,0.02)

Table 6-4 Continued: Null and adjusted linear model for variables that have an association with quality of life (**Visual Analogue Scale**)

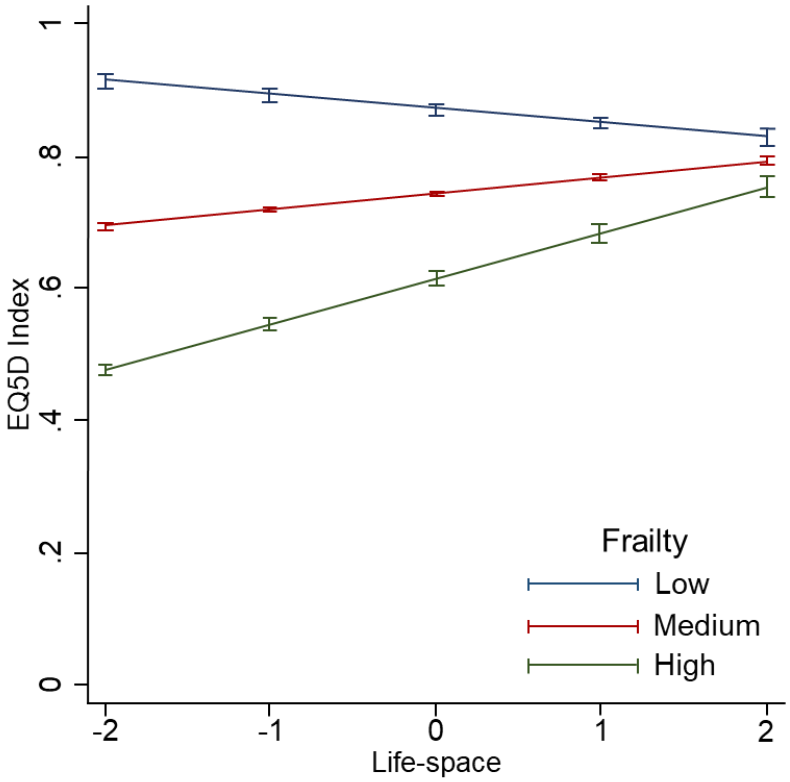
	Unadjusted		**Multivariable** (n=1,152)	
	Coef. (95% CI)	*P*	Coef. (95% CI)	*P*
Age	-3.6 (-4.5,-2.7)	<0.001	0.8 (-0.1,1.7)	0.068
Women (cf.) Men	0.1 (-1.7,2.0)	0.873	0.2 (-1.5,1.8)	0.851
Frailty index	-9.5 (-10.4,-8.6)	<0.001	-9.3 (-10.8,-7.8)	<0.001
Life-space	6.0 (5.2,6.7)	<0.001	2.4 (1.4,3.3)	<0.001
Frailty Index # Life-space			-0.5 (-1.2,0.2)	0.134
NOK contact (in person)				
Daily/weekly	[ref]	0.174		
Monthly	-0.9 (-3.5,1.7)			
Yearly or less	-2.6 (-5.4,0.2)			
NOK contact (by phone)				
Daily/weekly	[ref]	0.219		
Monthly	0.2 (-3.3,3.8)			
Yearly or less	-4.6 (-9.8,0.6)			
Loneliness	-1.8 (-4.8,1.3)	0.252		
Lives alone	-3.0 (-4.8,-1.2)	0.001	-1.3 (-2.9,0.3)	0.123
Distance from NOK (miles)	0.001 (-0.9,0.9)	0.999		
Care package				
None	[ref]	<0.001		0.001
Weekly	-23.8 (-30.8,-16.8)		-4.9 (-11.4,1.7)	
Daily/multiple times daily	-15.6 (-20.2,-11.1)		7.8 (2.6,13.0)	
Smoking status				
Never	[ref]	0.168		
Ex-smoker	-0.8 (-2.7,1.0)			

Current	-3.7 (-7.6,0.3)			
Alcohol intake				
Daily	[ref]	<0.001		0.886
Weekly	0.1 (-2.1,2.3)		0.5 (-1.4,2.4)	
Monthly or less	-4.7 (-7.3,-2.2)		0.2 (-2.1,2.5)	

Lower life-space was associated with older age (-2.5 per year (95%CI: -3.2 to -1.7, p<0.01) and frailty (-6.6 per SD, 95%CI: -7.4 to -5.7, p<0.01) (Appendix Table 9, Appendix Figure 7). Women had lower life-space (-2.0, 95%CI: -3.4 to -0.5, p<0.01). There was a graded association between educational attainment and life-space such that those with no qualifications had the lowest life-space (-3.5, 95%CI: -6.3 to -0.7, p=0.03).

I found evidence of an interaction between life-space and frailty and associated EQ-5D (Figure 6-2). EQ-5D in people who were not frail was broadly similar regardless of life-space, but the steepest gradient for life-space and EQ-5D was in those classified as most frail (interaction term = 0.02 per SD of frailty, 95%CI: 0.01 to 0.03, p<0.01). This coefficient was the same as the association between life-space and EQ-5D, which translates to doubling the effect size for each SD of increasing frailty. In terms of the patterns described in Table 6-3, the model suggests improving indoor and outdoor mobility (and frequency of being outdoors) to the extent independent outdoor mobility were possible (-1SD to +1SD), would be associated with a 0.1 point (one tertile) improvement in quality of life – comparable to the differences expected in an individual 10 years younger. Conversely, additional gains in life-space were not associated with better quality of life for those not frail

Figure 6-2: Interaction between life-space and frailty and their association with EQ-5D



6.5 Discussion

Health-related quality of life appears to depend on both life-space and frailty, even after adjustment for multimorbidity, domestic contact, isolation and need for social care. While life-space and frailty are closely related, their associations with quality of life vary depending on the underlying level of frailty. Life-space and quality of life have a stronger association in those with high frailty. Taken together, these findings suggest that targeted improvements in life-space mobility may be most beneficial for quality of life in older adults with high frailty compared to those with a low and medium level of frailty. The interplay between life-space mobility and quality of life, as discussed in this chapter, supports the systematic review's conclusions in Chapter 3 about the necessity of integrating frailty assessments in multimorbidity interventions.

These results are consistent with studies separately demonstrating the two associations between frailty and quality of life (Hewston *et al.*, 2020; M. J.

Kim *et al.*, 2020) and life-space and quality of life (Saraiva *et al.*, 2021). However, showing how changes in life-space could impact quality of life across the spectrum of frailty is novel. My findings emphasise the importance of understanding the determinants of life-space and how interventions in this domain could improve quality of life. The nature of this interaction would suggest that interventions to improve life-space could have the largest impact in those already living with frailty. The degree to which life-space could be modified has not been extensively studied. In a study of post-acute patients recently discharged, inpatient rehabilitation did not appear to improve life-space (Brown *et al.*, 2016). Similarly, although a resistance and balance training programme decreased falls risk, it did not increase life-space in care home residents (Hewitt *et al.*, 2018). After knee arthroplasty, patients who were less frail (by selection) and receiving an extended walking intervention showed improved life-space (Hiyama *et al.*, 2019). However, a multidisciplinary team community rehabilitation intervention demonstrated greater life-space in frail patients, even after 12 months (Fairhall *et al.*, 2012). In this respect, it might be expected that such interventions could also lead to improvements in quality of life. Overall, I interpret the interaction between life-space and frailty as identifying a subpopulation of individuals, those with most frailty, for whom mobility-related goals might make the biggest difference to their quality of life.

The cross-sectional nature of the data limits my findings, so I cannot establish any temporal relationships. I had some missing quality of life data for one quarter of the sample, with the likely effect that this under-estimated the associations with life-space and frailty. Simultaneously comparing data on life-space, frailty and quality of life required me to standardise and transform the independent variables. Though I could establish overall relationships, it is difficult to link the estimated models directly to absolute levels of frailty. I also could only report the observed relationships between the variables at a single point in time. Therefore, any interpretations is made with caution, acknowledging that I cannot determine the direction or causative nature of these associations. As with other observational studies, these results are subject to residual confounding. It is also not possible to

generalise the findings outside the sample's predominantly white, well-educated urban setting. Nonetheless, population cohorts have the advantage of offering data on the full range of life-space and frailty states.

In a population-representative cohort of older people, I demonstrate that life-space has the strongest relationship with quality of life in frail older adults. Frail individuals were twice as likely to have higher quality of life in association with a larger life-space. Interventions designed to improve quality of life in frail older adults could focus on increasing a person's life-space. These findings support the identification of frailty as a method of offering targeted resources and interventions in complex older people. It is important to recognise that these findings are associative rather than causative, nonethelessthere are indications for this to be further explored regarding multimorbidity management.

Chapter 7 Discussion

7.1 Key contributions of this thesis to the wider field

My systematic review in Chapter 3 found that certain strategies may improve multimorbidity outcomes, though the strength of evidence was low in proportion to the prevalence of older adults living with multimorbidity. The small amount of data initially indicated that the interventions were not cost-effective during the early stages, potentially the first few months or the first year; these being the study period. Potential reasons may be due to high initial costs, such as setup expenses and training, coupled with lower initial efficiencies. However, it is important to note that as the interventions progressed, they may gradually become more cost-effective, offsetting the early expenses over time. This observation is based on a limited dataset, and a more comprehensive analysis in these studies might reveal a more nuanced picture of the interventions' cost-effectiveness over their entire lifecycle. The review identified how, in addition to multimorbidity, frailty is an overlapping or complementary construct that needs consideration in the management of this complex patient population.

My study in Chapter 6 explored whether interventions targeting multimorbidity in this particular age group could achieve more consistent and positive outcomes when tailored to specific degrees of frailty. The findings lend support to this approach, aligning with existing suggestions and guidelines that advocate for such tailored interventions. However, the unique contribution of my research lies in providing concrete evidence that supports the effectiveness of tailoring multimorbidity interventions based on frailty profiles. This evidence corroborates the proposed direction of healthcare guidelines and offers a practical framework for implementing more effective treatment strategies in managing multimorbidity among older adults.

The systematic review (Chapter 3) underscored the critical role of frailty in managing multimorbidity. It found that interventions targeting multimorbidity have potential to be more effective when frailty is also considered. This

chapter highlighted the need for a comprehensive approach that integrates frailty assessments in multimorbidity interventions.

The analysis of service use and costs following acute admissions (Chapter 5) revealed the substantial burden multimorbidity places on healthcare systems. The findings emphasised the need for integrated care strategies to manage the complex needs of older adults with multimorbidity and the associated economic implications.

Chapter 6 explored the intricate relationships between life-space mobility, quality of life, and frailty. It demonstrated that enhancing functional mobility and addressing frailty can significantly improve HRQoL in older adults with multimorbidity.

This thesis makes significant contributions to the understanding and management of multimorbidity and frailty in older adults by examining the effectiveness of interventions, the economic burden of multimorbidity, and potential intervention targets by understanding the relationship between life-space mobility, frailty, and quality of life.

7.2 Identifying factors to improve health-related quality of life in older people with multimorbidity

The cross-sectional analysis I conducted of a population-representative cohort in the London Borough of Camden sought to provide evidence and insight into the limitations in evidence found in the systematic review. Central to a research need to identify strategies that maximise the benefits of treatment among older patients with multimorbidity, I examined the utility of frailty as a potential prism for enhancing outcomes in multimorbid patients. Using linear regression, I found that HRQoL, which encompasses dimensions of health critical for determining and predicting health and social care service usage, is evidently influenced by both life-space mobility and frailty. In this analysis, life-space mobility refers to the extent to which an individual moves within their environment, and frailty is considered as a measure of decreased physiological reserve. The data indicated a significant relationship, suggesting that individuals with restricted mobility and higher

levels of frailty are likely to experience a lower HRQoL. This relationship is crucial for healthcare planning, as it underscores the need for targeted interventions to improve functional mobility and manage frailty to enhance HRQoL and reduce the demand for health and social care services. However, it is important to note that these findings are preliminary and further research is needed to fully understand the complexities of these relationships.

Even when controlled for variables like domestic contact, feelings of loneliness, and the requisite need for social care, the intricate relationship between life-space and frailty is evident. While both are intrinsically linked, their relationship with HRQoL varies depending on the inherent frailty level. It emerges that life-space and HRQoL share a heightened relationship among frail individuals, underscoring the potential that multimorbidity interventions targeting an outcome such as HRQoL could be tailored to frailty subgroups or levels. It is important to reiterate that the associations reported in Chapter 6 are based on cross-sectional data, which precludes causal inferences. The observed relationships between frailty, life-space, and HRQoL highlight significant associations, but we cannot determine causality or influence from this study design. Future research should consider longitudinal approaches to better understand the causal pathways and dynamics over time.

Such insights support the potential to utilise frailty as a strategic tool, tailoring resources and interventions to manage the nuanced needs of older, complex patients with multimorbidity. The intersection of frailty and life-space mobility offers a fresh perspective, with potential evidence that could influence multimorbidity management. Further investigations into the role of frailty in multimorbidity management in older adults for other outcomes could pave the way for more targeted, effective interventions, enhancing the lives of those in this complex patient population. For example, my model would predict that mobility-based interventions (or at least ways of increasing life-space) would help in highly frail subgroups amongst older adults.

7.3 Enhancing healthcare systems for older adults with multimorbidity

The findings from these chapters collectively provide a comprehensive understanding of multimorbidity management in older adults:

1. Interplay Between Frailty and Multimorbidity:

The systematic review in Chapter 3 highlighted the importance of considering frailty in multimorbidity interventions. This finding aligns with the service use and cost implications observed in Chapter 5, suggesting that addressing frailty could mitigate some of these burdens.

2. Impact on Service Use and Cost:

The economic and service use implications detailed in Chapter 5 provide context for the economic burden of multimorbidity. Addressing both medical and functional aspects of care, as highlighted in Chapter 6, could reduce healthcare utilisation and costs, enhancing patient outcomes through targeted interventions.

3. Quality of Life and Functional Mobility:

Chapter 6's exploration of life-space mobility and quality of life complements the systematic review findings from Chapter 3 and explores potential intervention targets. Integrating frailty assessments, as suggested in Chapter 3, can improve life-space mobility and overall quality of life, offering a more comprehensive approach to multimorbidity management.

In Chapter 5, I provided novel insights into how the increased service use across primary, secondary and social care settings that results following an acute admission, slowly declines but remains elevated above normal over time. This is exacerbated by the presence of multimorbidity. Additionally, survival is shown to be lowest in those with the highest level of acute admissions. Associated costs across settings also reflect this increase, with social care costs remaining highest in all settings in both individuals who had an acute admission and those who did not. The necessity for acute hospital care often parallels changes in a patient’s functional mobility. Interventions

for the period of time immediately prior to and post-hospital discharge following an acute admission that are designed to improve the transition between services, care coordination and support professionals in social care, primary care and secondary care settings could improve the rate at which service use following an acute admission stabilises over time.

The data from this study indicates that ED and elective care services may not experience significant cost variations due to multimorbidity, suggesting that resource allocation could be optimised by focusing more on social and primary care services, where the cost impact is more pronounced.

These findings suggest utilising linked datasets provides opportunities to describe disease manifestations and their long-term implications. This is in addition to the influence of outcomes such as acute hospitalisations on a patient's trajectory within and across various healthcare and social care environments leading to valuable evidence for the long-term management of multimorbidity in complex older adults and improving the coordination or integration of services.

7.4 Strengths and limitations of this thesis

In earlier chapters of this thesis, each of my studies' respective chapters details their strengths and limitations. Here, I have described the strengths and limitations of this thesis overall. The strengths of the research methodology and findings are manifold, reflecting a comprehensive approach to understanding the multifaceted impact of multimorbidity and frailty in older adults.

Firstly, the systematic review conducted is a significant strength. It thoroughly examines existing literature, offering insights into the efficacy and cost-effectiveness of multimorbidity interventions for older adults. The finding that comprehensive assessments by interdisciplinary teams are beneficial is particularly noteworthy. This suggests a need for more holistic and collaborative approaches in chronic disease management, which is a valuable recommendation for healthcare policy and practice.

Another major strength of the thesis is the use of cohort data to analyse the simultaneous impact of multimorbidity and frailty on quality of life. The cross-sectional analysis utilising linear regression models enables a nuanced understanding of how these factors affect older adults' health-related quality of life. The revelation that frailty measures are informative in predicting quality of life underscores the importance of considering frailty in healthcare interventions. Moreover, the discovery of a strong association between functional mobility and quality of life in those with higher frailty levels is a crucial finding, highlighting the potential of mobility interventions in enhancing the health-related quality of life of this population.

Another strength is utilising linked datasets across multiple healthcare settings to examine the longitudinal relationship between multimorbidity, acute inpatient admission, and long-term service use. This approach allows for a comprehensive evaluation of service utilisation patterns, revealing that acute admissions are associated with increased service use across various care settings. The study's ability to track these patterns over time provides valuable insights into the long-term effects of acute illnesses, particularly in multimorbidity.

Moreover, the thesis highlights the increased costs associated with multimorbidity, especially in social care following acute admissions. This finding is pivotal for healthcare planning and resource allocation, emphasising the need for strategies to manage multimorbidity more effectively to reduce long-term care costs.

Additionally, the strengths of this thesis lie in its comprehensive methodology, spanning a systematic literature review, cross-sectional analysis, and the use of linked datasets. Collectively, these approaches provide a rich and multi-dimensional understanding of the subject matter, offering valuable insights for healthcare policy, practice, and future research directions. The findings underscore the necessity of integrating frailty evaluations into multimorbidity management, paving the way for more effective and targeted healthcare interventions.

While the research in this thesis presents several strengths, it is also essential to acknowledge its limitations. These limitations offer insights into areas for future research and potential improvements in study design and methodology. One of the primary limitations is the reliance on existing literature in the systematic review. While this approach provides a broad overview of the field, it is confined to the scope and quality of the existing studies. The variability in the methodologies, populations, and interventions studied across the reviewed literature may have introduced biases or inconsistencies in the findings. This limitation underscores the need for more standardised research in the field of multimorbidity interventions.

The cross-sectional design of the study analysing the impact of multimorbidity and frailty on health-related quality of life is another limitation. While this design is effective for exploring associations at a single point in time, it does not allow for examining causal relationships or changes over time. Longitudinal studies would be more informative in understanding the progression of multimorbidity and frailty and their long-term impacts on health-related quality of life. Though statistically robust, the use of linear regression models in the analysis may not fully capture the complex and non-linear relationships between multimorbidity, frailty, and quality of life. Additionally, the reliance on self-reported measures for some variables might have introduced response bias, affecting the accuracy of the findings. Another limitation is the generalisability of the findings. The DELPHIC cohort used in the study may not be fully representative of the wider population of older adults, especially those from diverse socio-economic and cultural backgrounds.

Using linked datasets, while a strength in providing a comprehensive view of service utilisation, also comes with limitations. The quality and completeness of the data in these datasets can vary, potentially affecting the accuracy and reliability of the findings; community and mental health settings were two additional settings that could be explored in the Care City Cohort, but this was not possible due to limitations in data completeness in the years analysed. Moreover, these datasets might not have captured all relevant

variables, leading to potential confounding factors not accounted for in the analysis.

This PhD provides valuable insights into managing multimorbidity and frailty in older adults. However, the limitations highlighted above must be considered when interpreting the findings. Future research should address these limitations, perhaps through longitudinal studies, more diverse population samples, and more advanced statistical methods. Acknowledging these limitations does not diminish the research's value but adds to its credibility and provides context for the interpretation and application of the findings.

7.4.1 Reflections on Research Development and Critical Reflections

7.4.1.1 Personal development as a researcher

Throughout the course of this research, I have grown significantly as a researcher. Conducting the systematic review in Chapter 3 sharpened my skills in critically appraising literature and synthesising complex information. This foundational work informed my understanding of the intricate relationship between frailty and multimorbidity, guiding the subsequent analyses.

Chapter 5 presented the challenge of linking clinical outcomes with economic data. Analysing service use and cost implications honed my ability to work with large datasets and complex variables, highlighting the economic impact of multimorbidity and the necessity for cost-effective interventions.

Working on Chapter 6, which examined the relationship between life-space mobility, quality of life, and frailty, deepened my understanding of statistical analyses and the importance of considering multiple dimensions of health in older adults. This chapter also underscored the value of interdisciplinary approaches, integrating insights from gerontology, public health, and clinical medicine.

7.4.1.2 Critical reflections on the data and research process

One of the critical reflections on the data is the variability and quality of studies included in the systematic review. While the review provided valuable

insights, the heterogeneity in study designs and outcome measures posed challenges in synthesising the findings. Future research would benefit from standardized methodologies to enhance comparability.

In Chapter 6, the data on life-space mobility and quality of life revealed significant associations, yet the cross-sectional nature of the data limits causal inferences. Longitudinal studies are needed to establish the directionality of these relationships and to understand the long-term impact of interventions.

Chapter 5 highlighted the substantial healthcare costs associated with multimorbidity, but the data also underscored the fragmentation in health service delivery. This fragmentation complicates the analysis and interpretation of cost data, suggesting a need for more integrated data systems that capture comprehensive patient journeys across different care settings.

7.5 Policy and research implications for multimorbidity care

7.5.1 Tailoring multimorbidity interventions in practice

Insights from chapter 6 underscore the viability of tailoring multimorbidity interventions for outcomes such as HRQoL, factoring in varying degrees of frailty. Notably, while most older adults with frailty exhibit multimorbidity, the converse isn't necessarily true: many with multimorbidity aren't necessarily frail, even though they face heightened health risks compared to peers of a similar age (Zazzara *et al.*, 2020). Both frailty and multimorbidity often coexist, as acknowledged in recent NICE guidelines. Singular illnesses may evolve into broader multimorbidity patterns, with the coexistence of numerous long-term conditions potentially culminating in frailty. This makes the affected population particularly susceptible to detrimental outcomes like hospitalisations, falls, and increased mortality.

Distinctly, prominent frailty models emphasise functional components, like mobility restrictions, that multimorbidity models typically overlook (St John *et al.*, 2014). This distinction is pivotal since interventions targeting functional issues have shown to benefit frail elders, as seen in methods like the

Comprehensive Geriatric Assessment. Moreover, multimorbidity's connection to mortality becomes inconspicuous when accounting for functional issues, emphasising the importance of recognising frailty in multimorbid elderly populations (St John *et al.*, 2014). My findings in chapter 6 demonstrate the value that can be gained from tailoring multimorbidity interventions in this way.

The pathophysiology of frailty is characterised by a prominent decline in physiological resilience, more than is expected in chronological ageing. Given the overlap of frailty and multimorbidity, NICE guidelines advocate recognising frailty as a means to pinpoint multimorbid individuals who might benefit from personalised care. In outpatient settings, several tools like the 'Timed Up and Go' test (Avers, 2020) and PRISMA-7 questionnaire (Hoffmann *et al.*, 2020) have been proposed for frailty detection. However, implementing these tools in acute environments poses challenges as physical performance measures of frailty are not advocated in these settings (National Institute for Health and Care Excellence, 2016). Furthermore, the NICE guidelines emphasise the relevance of frailty in determining intervention strategies for multimorbid individuals, marking it as pivotal for clinical evaluations and suggesting its potential for treatment adjustments in people with high multimorbidity levels.

7.5.2 Utilising linked datasets and improving integrated care

Results from the study in chapter 5 demonstrate the advantage of using linked datasets to show disease presentations and their long-term implications. Such findings contribute to crucial insights beneficial for the prolonged management of multimorbidity in complex elderly populations, enhancing service coordination and integration.

My findings suggest that an increase in service use across primary, secondary and social care settings following acute admissions remains elevated, even if attenuated over time. To address this, it would be beneficial to improve the coordination of care between services. In working toward integrating services, initiatives like the 'Vanguard' sites through the Vanguard

'New Care Models' programme, were launched in England in 2015 and aimed to design and test prototypes for integrating health and social care services (Morciano *et al.*, 2020). The programme swiftly segued into endeavours like 'social prescribing' and care navigation services, culminating in the Integrated Care Systems programme (The King's Fund, 2016).

In 2022, there was the formal establishment of Integrated Care Systems. These systems represent collaborative efforts that unite NHS organisations, local authority bodies, and various other stakeholders. Their core objective is to jointly deliver services, enhance public health, and diminish disparities within specific regions (The King's Fund, 2022). Notably, comprehensive evaluations of these initiatives is often elusive prior to their expansive deployment (National Audit Office, 2017; Husk *et al.*, 2019). Integration efforts also compete with the cyclical introduction of fresh policy programs, changing leadership approaches, organisational structures, and funding. These events highlight the balancing act policymakers face: fostering innovation while simultaneously allotting sufficient time for new integrated care models to stabilise and mature before any evaluations.

Evidence coming from research such as the study described in chapter 5 is valuable for guiding these initiatives or policies that enhance or develop new care models. Comparing not only the impact of acute admissions on various settings, but also comparing these differences between settings offers particular value for efficient resource allocation and innovative planning.

7.6 Conclusion

This thesis underscores the importance of a holistic approach to managing multimorbidity in older adults. The combined insights from the systematic review, service use analysis, and exploration of life-space mobility and quality of life provide a roadmap for improving care and outcomes in this population. By integrating frailty assessments and focusing on both medical and functional interventions, healthcare systems can better address the complex needs of older adults with multimorbidity, ultimately leading to more effective and sustainable care strategies.

In conclusion, this thesis makes novel contributions toward services for older adults with multimorbidity and frailty. It highlights the importance of tailored interventions based on specific frailty profiles, providing a practical framework for improving treatment strategies. The systematic review, cross-sectional analysis, and utilisation of linked datasets collectively offer a comprehensive understanding of how multimorbidity, frailty, and acute hospital admissions, a key multimorbidity outcome and indicator of changes in functional mobility, impact service use, costs, and patient outcomes. This work underscores the need for more holistic and integrated approaches in managing complex health conditions among older adults.

The thesis also sheds light on the potential of using frailty as a strategic tool in tailoring care for older adults with multimorbidity, suggesting that interventions targeting outcomes like health-related quality of life could be more effective when tailored to different levels of frailty. Furthermore, it points to the need for optimising resource allocation in healthcare, focusing more on social and primary care services where the cost impact of acute admissions is more pronounced.

However, the thesis acknowledges its limitations, including the reliance on existing literature and the cross-sectional study design, suggesting future research directions to address these gaps. These limitations notwithstanding, the thesis provides valuable insights and recommendations for policy and practice in the care of older adults with multimorbidity, emphasising the significance of integrated care models, tailored interventions and the use of linked datasets for developing long-term management strategies.

Overall, this thesis contributes to a better understanding of multimorbidity and frailty in older adults and offers evidence-based recommendations for improving healthcare systems, ultimately enhancing the quality of life and care coordination for this complex patient population.

Current Publications

Krogseth, M., Davis, D., Jackson, T. A., Zetterberg, H., Watne, L. O., Lindberg, M., **Chitalu, P**., Tsui, A., Selbæk, G. and Wyller, T. B. (2023). 'Delirium, neurofilament light chain, and progressive cognitive impairment: analysis of a prospective Norwegian population-based cohort'. *The Lancet Healthy Longevity*, 4 (8), pp. e399–e408. doi: 10.1016/S2666-7568(23)00098-3.

Chitalu, P., Tsui, A., Searle, S. D. and Davis, D. (2022). 'Life-space, frailty, and health-related quality of life'. *BMC Geriatrics*. BioMed Central, 22 (1), p. 646. doi: 10.1186/s12877-022-03355-2.

Tsui, A., Searle, S. D., Bowden, H., Hoffmann, K., Hornby, J., Goslett, A., Weston-Clarke, M., Hamill Howes, L., Street, R., Perera, R., Taee, K., Kustermann, C., **Chitalu, P**., Razavi, B., Magni, F., Das, D., Kim, S., Chaturvedi, N., Sampson, E. L., Rockwood, K., Cunningham, C., Ely, E. W., Richardson, S. J., Brayne, C., Muniz Terrera, G., Tieges, Z., MacLullich, A. and Davis, D. (2022). 'The effect of baseline cognition and delirium on long-term cognitive impairment and mortality: a prospective population-based study'. *The Lancet Healthy Longevity*. Elsevier, 3 (4), pp. e232–e241. doi: 10.1016/S2666-7568(22)00013-7.

Goodyer, E., Mah, J. C., Rangan, A., **Chitalu, P**., Andrew, M. K., Searle, S. D., Davis, D. and Tsui, A. (2022). 'The relative impact of socioeconomic position and frailty varies by population setting'. *AGING MEDICINE*. John Wiley & Sons, Ltd, 5 (1), pp. 10–16. doi: 10.1002/agm2.12200.

Bibliography

Adelman, R. D., Tmanova, L. L., Delgado, D., Dion, S. and Lachs, M. S. (2014). 'Caregiver burden: a clinical review.' *JAMA*. American Medical Association, 311 (10), pp. 1052–60. doi: 10.1001/jama.2014.304.

Aiden, H. (2018). *Multimorbidity- Understanding the challenge*. Available at: https://richmondgroupofcharities.org.uk/sites/default/files/multimorbidity_-_understanding_the_challenge.pdf.

Arokiasamy, P., Uttamacharya, U., Jain, K., Biritwum, R. B., Yawson, A. E., Wu, F., Guo, Y., Maximova, T., Espinoza, B. M., Rodríguez, A. S., Afshar, S., Pati, S., Ice, G., Banerjee, S., Liebert, M. A., Snodgrass, J. J., Naidoo, N., Chatterji, S. and Kowal, P. (2015). 'The impact of multimorbidity on adult physical and mental health in low- and middle-income countries: what does the study on global ageing and adult health (SAGE) reveal?' *BMC medicine*. BioMed Central Ltd., 13 (1), p. 178. doi: 10.1186/s12916-015-0402-8.

Avers, D. (2020). 'Functional Performance Measures and Assessment for Older Adults'. in *Guccione's Geriatric Physical Therapy*. Elsevier, pp. 137–165. doi: 10.1016/B978-0-323-60912-8.00007-5.

Baker, P. S., Bodner, E. V. and Allman, R. M. (2003). 'Measuring Life-Space Mobility in Community-Dwelling Older Adults'. *Journal of the American Geriatrics Society*. John Wiley & Sons, Ltd, 51 (11), pp. 1610–1614. doi: 10.1046/J.1532-5415.2003.51512.X.

Baré, M., Herranz, S., Roso-Llorach, A., Jordana, R., Violán, C., Lleal, M., Roura-Poch, P., Arellano, M., Estrada, R. and Nazco, G. J. (2021). 'Multimorbidity patterns of chronic conditions and geriatric syndromes in older patients from the MoPIM multicentre cohort study'. *BMJ Open*, 11 (11), p. e049334. doi: 10.1136/bmjopen-2021-049334.

Barnett, K., Mercer, S. W., Norbury, M., Watt, G., Wyke, S. and Guthrie, B. (2012). 'Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study.' *Lancet (London, England)*. Lancet Publishing Group, 380 (9836), pp. 37–43. doi:

10.1016/S0140-6736(12)60240-2.

Bayliss, E. A., Bayliss, M. S., Ware, J. E. and Steiner, J. F. (2004). 'Predicting declines in physical function in persons with multiple chronic medical conditions: What we can learn from the medical problem list'. *Health and Quality of Life Outcomes*, 2 (1), p. 47. doi: 10.1186/1477-7525-2-47.

Bentley, J. P., Brown, C. J., McGwin, G., Sawyer, P., Allman, R. M. and Roth, D. L. (2013). 'Functional status, life-space mobility, and quality of life: A longitudinal mediation analysis'. *Quality of Life Research*. Qual Life Res, 22 (7), pp. 1621–1632. doi: 10.1007/s11136-012-0315-3.

Berntsen, G. K. R., Dalbakk, M., Hurley, J. S., Bergmo, T., Solbakken, B., Spansvoll, L., Bellika, J. G., Skrøvseth, S. O., Brattland, T. and Rumpsfeld, M. (2019). 'Person-centred, integrated and pro-active care for multi-morbid elderly with advanced care needs: A propensity score-matched controlled trial'. *BMC Health Services Research*. BioMed Central Ltd., 19 (1). doi: 10.1186/s12913-019-4397-2.

Beswick, A. D., Rees, K., Dieppe, P., Ayis, S., Gooberman-Hill, R., Horwood, J. and Ebrahim, S. (2008). 'Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis'. *The Lancet*. Elsevier B.V., 371 (9614), pp. 725–735. doi: 10.1016/S0140-6736(08)60342-6.

Blood Pressure Lowering Treatment Trialists' Collaboration. (2014). 'Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data'. *The Lancet*. Elsevier B.V., 384 (9943), pp. 591–598. doi: 10.1016/S0140-6736(14)61212-5.

Brazier, J. E., Harper, R., Jones, N. M. B., O'Cathain, A., Thomas, K. J., Usherwood, T. and Westlake, L. (1992). 'Validating the SF-36 health survey questionnaire: new outcome measure for primary care'. *BMJ (Clinical research ed.)*. BMJ, 305 (6846), pp. 160–164. doi: 10.1136/BMJ.305.6846.160.

Briggs, A. D. M., Göpfert, A., Thorlby, R., Allwood, D. and Alderwick, H. (2020). 'Integrated health and care systems in England: can they help prevent disease?Integrated health and care systems in England: can they help prevent

disease?' *Integrated Healthcare Journal*. BMJ, 22 (11), p. e000013. doi: 10.1136/ihj-2019-000013.

Brown, C. J., Foley, K. T., Lowman, J. D., MacLennan, P. A., Razjouyan, J., Najafi, B., Locher, J. and Allman, R. M. (2016). 'Comparison of posthospitalization function and community mobility in hospital mobility program and usual care patients a randomized clinical trial'. *JAMA Internal Medicine*. JAMA Intern Med, 176 (7), pp. 921–927. doi: 10.1001/jamainternmed.2016.1870.

Buffel du Vaure, C., Dechartres, A., Battin, C., Ravaud, P. and Boutron, I. (2016). 'Exclusion of patients with concomitant chronic conditions in ongoing randomised controlled trials targeting 10 common chronic conditions and registered at ClinicalTrials.gov: a systematic review of registration details.' *BMJ open*. British Medical Journal Publishing Group, 6 (9), p. e012265. doi: 10.1136/bmjopen-2016-012265.

Caballer-Tarazona, V., Guadalajara-Olmeda, N. and Vivas-Consuelo, D. (2019). 'Predicting healthcare expenditure by multimorbidity groups'. *Health Policy*. Elsevier Ireland Ltd, 123 (4), pp. 427–434. doi: 10.1016/j.healthpol.2019.02.002.

Chen, H., Chen, Y. and Cui, B. (2018). 'The association of multimorbidity with healthcare expenditure among the elderly patients in Beijing, China'. *Archives of Gerontology and Geriatrics*. Elsevier Ireland Ltd, 79, pp. 32–38. doi: 10.1016/j.archger.2018.07.008.

Cheung, J. T. K., Yu, R., Wu, Z., Wong, S. Y. S. and Woo, J. (2018). 'Geriatric syndromes, multimorbidity, and disability overlap and increase healthcare use among older Chinese'. *BMC Geriatrics*. BioMed Central, 18 (1). doi: 10.1186/S12877-018-0840-1.

Chin A Paw, M. J. M., Van Uffelen, J. G. Z., Riphagen, I. and Van Mechelen, W. (2008). 'The functional effects of physical exercise training in frail older people : a systematic review'. *Sports medicine (Auckland, N.Z.)*. Sports Med, 38 (9), pp. 781–793. doi: 10.2165/00007256-200838090-00006.

Chow, S. K. Y. and Wong, F. K. Y. (2014). 'A randomized controlled trial of a

nurse-led case management programme for hospital-discharged older adults with co-morbidities'. *Journal of Advanced Nursing*. Blackwell Publishing Ltd, 70 (10), pp. 2257–2271. doi: 10.1111/jan.12375.

Clegg, A., Young, J., Iliffe, S., Rikkert, M. O. and Rockwood, K. (2013). 'Frailty in elderly people'. *The Lancet*. Lancet Publishing Group, 381 (9868), pp. 752–762. doi: 10.1016/S0140-6736(12)62167-9.

Coatsworth-Puspoky, R., Duggleby, W., Dahlke, S. and Hunter, K. (2021). 'Unplanned readmission for older persons: A concept analysis'. *Journal of Advanced Nursing*. John Wiley and Sons Inc, 77 (11), pp. 4291–4305. doi: 10.1111/jan.14893.

Cohen, C. I., Benyaminov, R., Rahman, M., Ngu, D. and Reinhardt, M. (2023). 'Frailty: A Multidimensional Biopsychosocial Syndrome'. *Medical Clinics of North America*. Elsevier, 107 (1), pp. 183–197. doi: 10.1016/J.MCNA.2022.04.006.

Condelius, A., Edberg, A.-K., Jakobsson, U. and Hallberg, I. R. (2008). 'Hospital admissions among people 65+ related to multimorbidity, municipal and outpatient care'. *Archives of Gerontology and Geriatrics*, 46 (1), pp. 41–55. doi: 10.1016/j.archger.2007.02.005.

Credé, S. H., O'Keeffe, C., Mason, S., Sutton, A., Howe, E., Croft, S. J. and Whiteside, M. (2017). 'What is the evidence for the management of patients along the pathway from the emergency department to acute admission to reduce unplanned attendance and admission? An evidence synthesis'. *BMC Health Services Research*. BMC, 17 (1), p. 355. doi: 10.1186/s12913-017-2299-8.

Critical Appraisal Skills Programme (CASP). (2013). *Randomised Controlled Trials Checklist*. *CASP checklists Oxford*. Available at: http://www.casp-uk.net (Accessed: 20 May 2021).

Crowe, M., Jordan, J., Burrell, B., Jones, V., Gillon, D., Harris, S. and Wilkinson, A. (2016). 'Clinical effectiveness of transdiagnostic health management interventions for older people with multimorbidity: a quantitative systematic review'. *Journal of Advanced Nursing*. John Wiley & Sons, Ltd, 72

(10), pp. 2315–2329. doi: 10.1111/jan.13011.

Crystal, S., Johnson, R. W., Harman, J., Sambamoorthi, U. and Kumar, R. (2000). 'Out-of-pocket health care costs among older Americans.' *The journals of gerontology. Series B, Psychological sciences and social sciences*. J Gerontol B Psychol Sci Soc Sci, 55 (1), pp. S51-62. doi: 10.1093/geronb/55.1.s51.

Davis, D., Richardson, S., Hornby, J., Bowden, H., Hoffmann, K., Weston-Clarke, M., Green, F., Chaturvedi, N., Hughes, A., Kuh, D., Sampson, E., Mizoguchi, R., Cheah, K. L., Romain, M., Sinha, A., Jenkin, R., Brayne, C. and MacLullich, A. (2018). 'The delirium and population health informatics cohort study protocol: ascertaining the determinants and outcomes from delirium in a whole population'. *BMC Geriatrics*. BioMed Central, 18 (1), p. 45. doi: 10.1186/s12877-018-0742-2.

Denholm, R., Morris, R., Purdy, S. and Payne, R. (2020). 'Impact of emergency hospital admissions on patterns of primary care prescribing: a retrospective cohort analysis of electronic records in England'. *British Journal of General Practice*, 70 (695), pp. e399–e405. doi: 10.3399/bjgp20X709385.

Dent, E., Kowal, P. and Hoogendijk, E. O. (2016). 'Frailty measurement in research and clinical practice: A review'. *European Journal of Internal Medicine*. Elsevier, 31, pp. 3–10. doi: 10.1016/J.EJIM.2016.03.007.

Department of Health and Social Care. (2021). *Integration and Innovation: working together to improve health and social care for all*.

Doll, R., Peto, R., Boreham, J. and Sutherland, I. (2004). 'Mortality in relation to smoking: 50 years' observations on male British doctors.' *BMJ (Clinical research ed.)*. British Medical Journal Publishing Group, 328 (7455), p. 1519. doi: 10.1136/bmj.38142.554479.AE.

Edwards, L., Pickett, J., Ashcroft, D. M., Dambha-Miller, H., Majeed, A., Mallen, C., Petersen, I., Qureshi, N., van Staa, T., Abel, G., Carvalho, C., Denholm, R., Kontopantelis, E., Macaulay, A. and Macleod, J. (2023). 'UK research data resources based on primary care electronic health records: review and summary for potential users'. *BJGP Open*. Royal College of

General Practitioners, 7 (3), p. BJGPO.2023.0057. doi: 10.3399/BJGPO.2023.0057.

Ekdahl, A. W., Wirehn, A. B., Alwin, J., Jaarsma, T., Unosson, M., Husberg, M., Eckerblad, J., Milberg, A., Krevers, B. and Carlsson, P. (2015). 'Costs and Effects of an Ambulatory Geriatric Unit (the AGe-FIT Study): A Randomized Controlled Trial'. *Journal of the American Medical Directors Association*. Elsevier Inc., 16 (6), pp. 497–503. doi: 10.1016/j.jamda.2015.01.074.

Elkjær, M., Wolff, D. L., Primdahl, J., Mogensen, C. B., Brabrand, M. and Gram, B. (2021). 'Older adults who receive homecare are at increased risk of readmission and mortality following a short ED admission: a nationally register-based cohort study'. *BMC Geriatrics*, 21 (1), p. 696. doi: 10.1186/s12877-021-02644-6.

Ellis, G., Gardner, M., Tsiachristas, A., Langhorne, P., Burke, O., Harwood, R. H., Conroy, S. P., Kircher, T., Somme, D., Saltvedt, I., Wald, H., O'Neill, D., Robinson, D. and Shepperd, S. (2017). 'Comprehensive geriatric assessment for older adults admitted to hospital'. *Cochrane Database of Systematic Reviews*. Cochrane Database Syst Rev, 2017 (9). doi: 10.1002/14651858.CD006211.pub3.

Ellis, G., Marshall, T. and Ritchie, C. (2014). 'Comprehensive geriatric assessment in the emergency department'. *Clinical Interventions in Aging*. Dove Medical Press Ltd., pp. 2033–2044. doi: 10.2147/CIA.S29662.

Ensrud, K. E., Kats, A. M., Schousboe, J. T., Taylor, B. C., Cawthon, P. M., Hillier, T. A., Yaffe, K., Cummings, S. R., Cauley, J. A. and Langsetmo, L. (2018). 'Frailty Phenotype and Healthcare Costs and Utilization in Older Women'. *Journal of the American Geriatrics Society*. Blackwell Publishing Inc., 66 (7), pp. 1276–1283. doi: 10.1111/jgs.15381.

Eton, D., Ridgeway, J., Egginton, J., Tiedje, K., Linzer, M., Boehm, D., Poplau, S., Oliveira, D., Odell, L., Montori, V. M., May, C. and Anderson, R. (2015). 'Finalizing a measurement framework for the burden of treatment in complex patients with chronic conditions'. *Patient Related Outcome Measures*. Patient Relat Outcome Meas, 6, p. 117. doi: 10.2147/PROM.S78955.

Fairhall, N., Sherrington, C., Kurrle, S. E., Lord, S. R., Lockwood, K. and Cameron, I. D. (2012). 'Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people: randomised controlled trial'. *BMC Medicine*. BMC Med, 10 (1), p. 120. doi: 10.1186/1741-7015-10-120.

Farmer, C., Fenu, E., O'Flynn, N. and Guthrie, B. (2016). 'Clinical assessment and management of multimorbidity: summary of NICE guidance.' *BMJ (Clinical research ed.)*. British Medical Journal Publishing Group, 354, p. i4843. doi: 10.1136/bmj.i4843.

Feldblum, I., German, L., Bilenko, N., Shahar, A., Enten, R., Greenberg, D., Harman, I., Castel, H. and Shahar, D. R. (2009). 'Nutritional risk and health care use before and after an acute hospitalization among the elderly'. *Nutrition*. Nutrition, 25 (4), pp. 415–420. doi: 10.1016/j.nut.2008.10.016.

Fisher, K., Markle-Reid, M., Ploeg, J., Bartholomew, A., Griffith, L. E., Gafni, A., Thabane, L. and Yous, M.-L. (2020). 'Self-management program versus usual care for community-dwelling older adults with multimorbidity: A pragmatic randomized controlled trial in Ontario, Canada'. *Journal of Comorbidity*. SAGE Publications, 10, p. 2235042X2096339. doi: 10.1177/2235042x20963390.

Fortin, M., Dionne, J., Pinho, G., Gignac, J., Almirall, J. and Lapointe, L. (2006). 'Randomized controlled trials: do they have external validity for patients with multiple comorbidities?' *Annals of family medicine*. Ann Fam Med, 4 (2), pp. 104–8. doi: 10.1370/afm.516.

Fortin, M., Dubois, M. F., Hudon, C., Soubhi, H. and Almirall, J. (2007). 'Multimorbidity and quality of life: A closer look'. *Health and Quality of Life Outcomes*. BioMed Central, 5 (1), pp. 1–8. doi: 10.1186/1477-7525-5-52/FIGURES/3.

Fortin, M., Lapointe, L., Hudon, C., Vanasse, A., Ntetu, A. L. and Maltais, D. (2004). 'Multimorbidity and quality of life in primary care: a systematic review.' *Health and quality of life outcomes*, 2, p. 51. doi: 10.1186/1477-7525-2-51.

Fried, L. P., Bandeen-Roche, K., Kasper, J. D. and Guralnik, J. M. (1999). 'Association of comorbidity with disability in older women: the Women's Health

and Aging Study.' *Journal of clinical epidemiology*, 52 (1), pp. 27–37. doi: 10.1016/s0895-4356(98)00124-3.

Fried, L. P., Ferrucci, L., Darer, J., Williamson, J. D. and Anderson, G. (2004). 'Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care'. *Journal of Gerontology*, 59 (3), pp. 255–263.

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W. J., Burke, G. and McBurnie, M. A. (2001). 'Frailty in older adults: Evidence for a phenotype'. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*. Gerontological Society of America, 56 (3), pp. 146–156. doi: 10.1093/gerona/56.3.m146.

García-Peña, C., Pérez-Zepeda, M. U., Robles-Jiménez, L. V., Sánchez-García, S., Ramírez-Aldana, R. and Tella-Vega, P. (2018). 'Mortality and associated risk factors for older adults admitted to the emergency department: a hospital cohort'. *BMC Geriatrics*. BMC Geriatr, 18 (1), p. 144. doi: 10.1186/s12877-018-0833-0.

Gill, A., Kuluski, K., Jaakkimainen, L., Naganathan, G., Upshur, R. and Wodchis, W. (2014). '"Where Do We Go from Here?" Health System Frustrations Expressed by Patients with Multimorbidity, Their Caregivers and Family Physicians'. *Healthcare Policy | Politiques de Santé*. Longwoods Publishing, 9 (4), pp. 73–89. doi: 10.12927/hcpol.2014.23811.

Giné-Garriga, M., Roqué-Fíguls, M., Coll-Planas, L., Sitjà-Rabert, M. and Salvà, A. (2014). 'Physical exercise interventions for improving performance-based measures of physical function in community-dwelling, frail older adults: a systematic review and meta-analysis'. *Archives of physical medicine and rehabilitation*. Arch Phys Med Rehabil, 95 (4). doi: 10.1016/J.APMR.2013.11.007.

Godden, S. and Pollock, A. M. (2001). 'The use of acute hospital services by elderly residents of nursing and residential care homes'. *Health & Social Care in the Community*. John Wiley & Sons, Ltd, 9 (6), pp. 367–374. doi: 10.1046/j.1365-2524.2001.00314.x.

Gontijo Guerra, S., Berbiche, D. and Vasiliadis, H.-M. (2019). 'Measuring multimorbidity in older adults: comparing different data sources'. *BMC Geriatrics*. BMC Geriatr, 19 (1), p. 166. doi: 10.1186/s12877-019-1173-4.

Gordis, L. (2014). *Epidemiology*. Fifth edit. *Epidemiology*. Fifth edit. Philadelphia: Elsevier Saunders.

Gu, J., Chao, J., Chen, W., Xu, H., Zhang, R., He, T. and Deng, L. (2018). 'Multimorbidity and health-related quality of life among the community-dwelling elderly: A longitudinal study'. *Archives of Gerontology and Geriatrics*. Arch Gerontol Geriatr, 74, pp. 133–140. doi: 10.1016/j.archger.2017.10.019.

Hanlon, P., Nicholl, B. I., Jani, B. D., Lee, D., McQueenie, R. and Mair, F. S. (2018). 'Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants'. *The Lancet Public Health*. Elsevier Ltd, 3 (7), pp. e323–e332. doi: 10.1016/S2468-2667(18)30091-4.

Harvey, G., Dollard, J., Marshall, A. and Mittinty, M. M. (2018). 'Achieving integrated care for older people: Shuffling the deckchairs or making the system watertight for the future?' *International Journal of Health Policy and Management*. Kerman University of Medical Sciences, pp. 290–293. doi: 10.15171/ijhpm.2017.144.

Hasan Ibrahim, A. S., Barry, H. E. and Hughes, C. M. (2021). 'A systematic review of general practice-based pharmacists' services to optimize medicines management in older people with multimorbidity and polypharmacy'. *Family Practice*, 38 (4), pp. 509–523. doi: 10.1093/fampra/cmaa146.

Hastings, S. N., Mahanna, E. P., Berkowitz, T. S. Z., Smith, V. A., Choate, A. L., Hughes, J. M., Pavon, J., Robinson, K., Hendrix, C., Van Houtven, C., Gentry, P., Rose, C., Plassman, B. L., Potter, G. and Oddone, E. (2021). 'Video-Enhanced Care Management for Medically Complex Older Adults with Cognitive Impairment'. *Journal of the American Geriatrics Society*. Blackwell Publishing Inc., 69 (1), pp. 77–84. doi: 10.1111/jgs.16819.

Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., Bonsel, G. and Badia, X. (2011). 'Development and preliminary testing of the new five-

level version of EQ-5D (EQ-5D-5L).' *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation*. Qual Life Res, 20 (10), pp. 1727–36. doi: 10.1007/s11136-011-9903-x.

Hewitt, J., Goodall, S., Clemson, L., Henwood, T. and Refshauge, K. (2018). 'Progressive Resistance and Balance Training for Falls Prevention in Long-Term Residential Aged Care: A Cluster Randomized Trial of the Sunbeam Program'. *Journal of the American Medical Directors Association*. J Am Med Dir Assoc, 19 (4), pp. 361–369. doi: 10.1016/j.jamda.2017.12.014.

Hewston, P., Grenier, A., Burke, E., Kennedy, C. C. and Papaioannou, A. (2020). 'Frailty and Life-Space Mobility: Implications for Clinical Practice and Research'. *Occupational Therapy In Health Care*, 35 (1), pp. 16–24. doi: 10.1080/07380577.2020.1846235.

Hilderink, H. B. M., Plasmans, M. H. D., Snijders, B. E. P., Boshuizen, H. C., Poos, M. J. J. C. and van Gool, C. H. (2016). 'Accounting for multimorbidity can affect the estimation of the Burden of Disease: a comparison of approaches'. *Archives of Public Health*, 74 (1), p. 37. doi: 10.1186/s13690-016-0147-7.

Hiyama, Y., Kamitani, T. and Mori, K. (2019). 'Effects of an Intervention to Improve Life-Space Mobility and Self-Efficacy in Patients following Total Knee Arthroplasty'. *The Journal of Knee Surgery*. J Knee Surg, 32 (10), pp. 966–971. doi: 10.1055/s-0038-1672199.

Hoffmann, S., Wiben, A., Kruse, M., Jacobsen, K. K., Lembeck, M. A. and Holm, E. A. (2020). 'Predictive validity of PRISMA-7 as a screening instrument for frailty in a hospital setting'. *BMJ Open*. British Medical Journal Publishing Group, 10 (10), p. e038768. doi: 10.1136/bmjopen-2020-038768.

Husereau, D., Drummond, M., Petrou, S., Carswell, C., Moher, D., Greenberg, D., Augustovski, F., Briggs, A. H., Mauskopf, J. and Loder, E. (2013). 'Consolidated health economic evaluation reporting standards (CHEERS)-explanation and elaboration: A report of the ISPOR health economic evaluation publication guidelines good reporting practices task force'. *Value in Health*. Value Health, 16 (2), pp. 231–250. doi: 10.1016/j.jval.2013.02.002.

Husk, K., Elston, J., Gradinger, F., Callaghan, L. and Asthana, S. (2019). 'Social prescribing: where is the evidence?' *British Journal of General Practice*. British Journal of General Practice, 69 (678), pp. 6–7. doi: 10.3399/bjgp19X700325.

Ibrahim, K., Cox, N. J., Stevenson, J. M., Lim, S., Fraser, S. D. S. and Roberts, H. C. (2021). 'A systematic review of the evidence for deprescribing interventions among older people living with frailty'. *BMC geriatrics*. BMC Geriatr, 21 (1). doi: 10.1186/S12877-021-02208-8.

Jha, P. and Peto, R. (2014). 'Global effects of smoking, of quitting, and of taxing tobacco.' *The New England journal of medicine*. N Engl J Med, 370 (1), pp. 60–8. doi: 10.1056/NEJMra1308383.

Johnson, J., Rodriguez, M. A. and Snih, S. Al. (2020). 'Life-space mobility in the elderly: Current perspectives'. *Clinical Interventions in Aging*. Dove Medical Press Ltd, 15, pp. 1665–1674. doi: 10.2147/CIA.S196944.

Johnston, M. C., Crilly, M., Black, C., Prescott, G. J. and Mercer, S. W. (2019). 'Defining and measuring multimorbidity: A systematic review of systematic reviews'. *European Journal of Public Health*. Oxford University Press, 29 (1), pp. 182–189. doi: 10.1093/eurpub/cky098.

Jones, J., Jones, G. D., Thacker, M. and Faithfull, S. (2017). 'Physical activity interventions are delivered consistently across hospitalized older adults but multimorbidity is associated with poorer rehabilitation outcomes: A population-based cohort study'. *Journal of Evaluation in Clinical Practice*. Blackwell Publishing Ltd, 23 (6), pp. 1469–1477. doi: 10.1111/jep.12833.

Jones, M. C., Stone, T., Mason, S. M., Eames, A. and Franklin, M. (2023). 'Navigating data governance associated with real-world data for public benefit: an overview in the UK and future considerations'. *BMJ Open*, 13 (10), p. e069925. doi: 10.1136/bmjopen-2022-069925.

Juul-Larsen, H. G., Andersen, O., Bandholm, T., Bodilsen, A. C., Kallemose, T., Jørgensen, L. M., Klausen, H. H., Gilkes, H. and Petersen, J. (2020). 'Differences in function and recovery profiles between patterns of multimorbidity among older medical patients the first year after an acute

admission—An exploratory latent class analysis'. *Archives of Gerontology and Geriatrics*, 86, p. 103956. doi: 10.1016/j.archger.2019.103956.

Karimi, M. and Brazier, J. (2016). 'Health, Health-Related Quality of Life, and Quality of Life: What is the Difference?' *PharmacoEconomics*. Springer International Publishing, 34 (7), pp. 645–649. doi: 10.1007/s40273-016-0389-9.

Kasteridis, P., Street, A., Dolman, M., Gallier, L., Hudson, K., Martin, J. and Wyer, I. (2015). 'Who would most benefit from improved integrated care? Implementing an analytical strategy in South Somerset.' *International journal of integrated care*. Ubiquity Press, 15 (January-March 2015), p. e001. doi: 10.5334/ijic.1594.

Kastner, M., Cardoso, R., Lai, Y., Treister, V., Hamid, J. S., Hayden, L., Wong, G., Ivers, N. M., Liu, B., Marr, S., Holroyd-Leduc, J. and Straus, S. E. (2018). 'effectiveness of interventions for managing multiple high-burden chronic diseases in older adults: A systematic review and meta-analysis'. *Cmaj*. Canadian Medical Association, 190 (34), pp. E1004–E1012. doi: 10.1503/cmaj.171391.

Kearney, P., Blackwell, L., Collins, R., Keech, A., Simes, J., Peto, R., Armitage, J. and Baigent, C. (2008). 'Efficacy of cholesterol-lowering therapy in 18 686 people with diabetes in 14 randomised trials of statins: a meta-analysis'. *The Lancet*. Lancet, 371 (9607), pp. 117–125. doi: 10.1016/S0140-6736(08)60104-X.

Khor, P. Y., Vearing, R. M. and Charlton, K. E. (2021). 'The effectiveness of nutrition interventions in improving frailty and its associated constructs related to malnutrition and functional decline among community-dwelling older adults: A systematic review'. *Journal of Human Nutrition and Dietetics*. John Wiley & Sons, Ltd. doi: 10.1111/jhn.12943.

Kim, H., Jung, Y. Il, Kim, G. S., Choi, H. and Park, Y. H. (2020). 'Effectiveness of a Technology-Enhanced Integrated Care Model for Frail Older People: A Stepped-Wedge Cluster Randomized Trial in Nursing Homes'. *Gerontologist*. Oxford University Press (OUP), 61 (3), pp. 460–469. doi:

10.1093/geront/gnaa090.

Kim, M. J., Park, S., Jung, Y.-I., Kim, S.-H. and Oh, I.-H. (2020). 'Exploring health-related quality of life and frailty in older adults based on the Korean Frailty and Aging Cohort Study'. *Quality of Life Research*, 29 (11), pp. 2911–2919. doi: 10.1007/s11136-020-02568-5.

King, S. J., Raine, K. A., Peel, N. M. and Hubbard, R. E. (2021). 'Interventions for frail older inpatients: A systematic review of frailty measures and reported outcomes in randomised controlled trials'. *Australasian Journal on Ageing*. Blackwell Publishing, 40 (2), pp. 129–144. doi: 10.1111/AJAG.12951.

Kingston, A., Robinson, L., Booth, H., Knapp, M. and Jagger, C. (2018). 'Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model'. *Age and Ageing*. Oxford Academic, 47 (3), pp. 374–380. doi: 10.1093/ageing/afx201.

König, H. H., Leicht, H., Bickel, H., Fuchs, A., Gensichen, J., Maier, W., Mergenthal, K., Riedel-Heller, S., Schäfer, I., Schön, G., Weyerer, S., Wiese, B., Bussche, H. Van Den, Scherer, M. and Eckardt, M. (2013). 'Effects of multiple chronic conditions on health care costs: An analysis based on an advanced tree-based regression model'. *BMC Health Services Research*. BioMed Central, 13 (1), pp. 1–13. doi: 10.1186/1472-6963-13-219/TABLES/4.

Kremers, M. N. T., Nanayakkara, P. W. B., Levi, M., Bell, D. and Haak, H. R. (2019). 'Strengths and weaknesses of the acute care systems in the United Kingdom and the Netherlands: what can we learn from each other?' *BMC Emergency Medicine*, 19 (1), p. 40. doi: 10.1186/s12873-019-0257-y.

Krska, J., Cromarty, J. A., Arris, F., Jamieson, D., Hansford, D., Duffus, P. R. S., Downie, G. and Seymour, D. G. (2001). 'Pharmacist-led medication review in patients over 65: A randomized, controlled trial in primary care'. *Age and Ageing*. Oxford Academic, 30 (3), pp. 205–211. doi: 10.1093/ageing/30.3.205.

Kuo, R. N. and Lai, M. S. (2013). 'The influence of socio-economic status and multimorbidity patterns on healthcare costs: A six-year follow-up under a universal healthcare system'. *International Journal for Equity in Health*.

BioMed Central, 12 (1), p. 69. doi: 10.1186/1475-9276-12-69.

Laberge, M., Sirois, C., Lunghi, C., Gaudreault, M., Nakamura, Y., Bolduc, C. and Laroche, M.-L. (2021). 'Economic Evaluations of Interventions to Optimize Medication Use in Older Adults with Polypharmacy and Multimorbidity: A Systematic Review'. *Clinical Interventions in Aging*. Clin Interv Aging, 16, pp. 767–779. doi: 10.2147/CIA.S304074.

De Labra, C., Guimaraes-Pinheiro, C., Maseda, A., Lorenzo, T. and Millán-Calenti, J. C. (2015). 'Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials'. *BMC geriatrics*. BMC Geriatr, 15 (1). doi: 10.1186/S12877-015-0155-4.

Lawson, K. D., Mercer, S. W., Wyke, S., Grieve, E., Guthrie, B., Watt, G. C. and Fenwick, E. A. (2013). 'Double trouble: the impact of multimorbidity and deprivation on preference-weighted health related quality of life a cross sectional analysis of the Scottish Health Survey'. *International Journal for Equity in Health*. BioMed Central, 12 (1), p. 67. doi: 10.1186/1475-9276-12-67.

Lee, J. T., Hamid, F., Pati, S., Atun, R. and Millett, C. (2015). 'Impact of Noncommunicable Disease Multimorbidity on Healthcare Utilisation and Out-Of-Pocket Expenditures in Middle-Income Countries: Cross Sectional Analysis.' *PloS one*. PLoS One, 10 (7), p. e0127199. doi: 10.1371/journal.pone.0127199.

Lee, W.-J., Peng, L.-N., Lin, M.-H., Lin, C.-H. and Chen, L.-K. (2022). 'Clinical Efficacy of Multidomain Interventions among Multimorbid Older People Stratified by the Status of Physio-Cognitive Declines: A Secondary Analysis from the Randomized Controlled Trial for Healthy Aging'. *The journal of nutrition, health & aging*, 26 (10), pp. 909–917. doi: 10.1007/s12603-022-1843-3.

Lehnert, T., Heider, D., Leicht, H., Heinrich, S., Corrieri, S., Luppa, M., Riedel-Heller, S. and König, H. H. (2011). 'Review: Health care utilization and costs of elderly persons with multiple chronic conditions'. *Medical Care Research and Review*. SAGE PublicationsSage CA: Los Angeles, CA, 68 (4), pp. 387–420. doi: 10.1177/1077558711399580.

Lewis, R. Q., Checkland, K., Durand, M. A., Ling, T., Mays, N., Roland, M. and Smith, J. A. (2021). 'Integrated Care in England – what can we Learn from a Decade of National Pilot Programmes?' *International Journal of Integrated Care*. Int J Integr Care, 21 (4). doi: 10.5334/ijic.5631.

Lo, A. X., Brown, C. J., Sawyer, P., Kennedy, R. E. and Allman, R. M. (2014). 'Life-space mobility declines associated with incident falls and fractures'. *Journal of the American Geriatrics Society*. Blackwell Publishing Inc., 62 (5), pp. 919–923. doi: 10.1111/jgs.12787.

London borough of Barking and Dagenham. (2020). *Population and demographic data | LBBD*. Available at: https://www.lbbd.gov.uk/population-and-demographic-data (Accessed: 25 April 2022).

London Borough of Barking and Dagenham. (2021). *Joint strategic needs assessment (JSNA)*. London.

Lopez Bernal, J. A., Lu, C. Y., Gasparrini, A., Cummins, S., Wharham, J. F. and Soumerai, S. B. (2017). 'Association between the 2012 Health and Social Care Act and specialist visits and hospitalisations in England: A controlled interrupted time series analysis'. *PLOS Medicine*. Edited by A. Sheikh. PLoS Med, 14 (11), p. e1002427. doi: 10.1371/journal.pmed.1002427.

Lorig, K. (1996). 'Chronic Disease Self-Management'. *American Behavioral Scientist*. Sage PublicationsThousand Oaks, 39 (6), pp. 676–683. doi: 10.1177/0002764296039006005.

Lundqvist, M., Alwin, J., Henriksson, M., Husberg, M., Carlsson, P. and Ekdahl, A. W. (2018). 'Cost-effectiveness of comprehensive geriatric assessment at an ambulatory geriatric unit based on the AGe-FIT trial'. *BMC Geriatrics*. BioMed Central Ltd., 18 (1). doi: 10.1186/s12877-017-0703-1.

Mair, F. S. and May, C. R. (2014). 'Thinking about the burden of treatment'. *BMJ*. British Medical Journal Publishing Group, 349 (nov10 4), pp. g6680–g6680. doi: 10.1136/bmj.g6680.

Makovski, T. T., Schmitz, S., Zeegers, M. P., Stranges, S. and van den Akker, M. (2019). 'Multimorbidity and quality of life: Systematic literature review and meta-analysis'. *Ageing Research Reviews*. Elsevier, 53, p. 100903. doi:

10.1016/j.arr.2019.04.005.

Mangin, D., Stephen, G., Bismah, V. and Risdon, C. (2016). ‘Making patient values visible in healthcare: a systematic review of tools to assess patient treatment priorities and preferences in the context of multimorbidity’. *BMJ Open*. BMJ Publishing Group, 6 (6), p. e010903. doi: 10.1136/bmjopen-2015-010903.

Maniatopoulos, G., Hunter, D. J., Erskine, J. and Hudson, B. (2019). ‘Lessons learnt from the implementation of new care models in the NHS: a qualitative study of the North East Vanguards programme’. *BMJ Open*. BMJ Open, 9 (11), p. e032107. doi: 10.1136/bmjopen-2019-032107.

Marengoni, A., Angleman, S., Melis, R., Mangialasche, F., Karp, A., Garmen, A., Meinow, B. and Fratiglioni, L. (2011). ‘Aging with multimorbidity: A systematic review of the literature’. *Ageing Research Reviews*. Elsevier, 10 (4), pp. 430–439. doi: 10.1016/j.arr.2011.03.003.

Marengoni, A., Von Strauss, E., Rizzuto, D., Winblad, B. and Fratiglioni, L. (2009). ‘The impact of chronic multimorbidity and disability on functional decline and survival in elderly persons. A community-based, longitudinal study’. *Journal of Internal Medicine*, 265 (2), pp. 288–295. doi: 10.1111/j.1365-2796.2008.02017.x.

Markle-Reid, M., Ploeg, J., Fraser, K. D., Fisher, K. A., Bartholomew, A., Griffith, L. E., Miklavcic, J., Gafni, A., Thabane, L. and Upshur, R. (2018). ‘Community Program Improves Quality of Life and Self-Management in Older Adults with Diabetes Mellitus and Comorbidity’. *Journal of the American Geriatrics Society*. Blackwell Publishing Inc., 66 (2), pp. 263–273. doi: 10.1111/jgs.15173.

Mason, B., Nanton, V., Epiphaniou, E., Murray, S. A., Donaldson, A., Shipman, C., Daveson, B. A., Harding, R., Higginson, I. J., Munday, D., Barclay, S., Dale, J., Kendall, M., Worth, A. and Boyd, K. (2016). ‘“My body’s falling apart.” Understanding the experiences of patients with advanced multimorbidity to improve care: serial interviews with patients and carers.’ *BMJ supportive & palliative care*. BMJ Support Palliat Care, 6 (1), pp. 60–5. doi:

10.1136/bmjspcare-2013-000639.

Mavaddat, N., Valderas, J. M., van der Linde, R., Khaw, K. T. and Kinmonth, A. L. (2014). 'Association of self-rated health with multimorbidity, chronic disease and psychosocial factors in a large middle-aged and older cohort from general practice: a cross-sectional study'. *BMC Family Practice*, 15 (1), p. 185. doi: 10.1186/s12875-014-0185-6.

McCarthy, C., Clyne, B., Boland, F., Moriarty, F., Flood, M., Wallace, E. and Smith, S. M. (2022). 'GP-delivered medication review of polypharmacy, deprescribing, and patient priorities in older people with multimorbidity in Irish primary care (SPPiRE Study): A cluster randomised controlled trial'. *PLOS Medicine*. Edited by I. Scott, 19 (1), p. e1003862. doi: 10.1371/journal.pmed.1003862.

McPeake, J., Quasim, T., Henderson, P., Leyland, A. H., Lone, N. I., Walters, M., Iwashyna, T. J. and Shaw, M. (2021). 'Multimorbidity and Its Relationship With Long-Term Outcomes After Critical Care Discharge'. *Chest*. Elsevier Inc., 160 (5), pp. 1681–1692. doi: 10.1016/j.chest.2021.05.069.

Miklavcic, J. J., Fraser, K. D., Ploeg, J., Markle-Reid, M., Fisher, K., Gafni, A., Griffith, L. E., Hirst, S., Sadowski, C. A., Thabane, L., Triscott, J. A. C. and Upshur, R. (2020). 'Effectiveness of a community program for older adults with type 2 diabetes and multimorbidity: A pragmatic randomized controlled trial'. *BMC Geriatrics*. BioMed Central Ltd., 20 (1). doi: 10.1186/s12877-020-01557-0.

Ministry of Housing Communities & Local Government. (2019). *The English Indices of Deprivation 2019 (IoD2019)*. Available at: https://www.gov.uk/government/publications/english-indices-of-deprivation-2019-technical-report%0Ahttps://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/833959/IoD2019_Infographic.pdf (Accessed: 21 October 2021).

Miyashita, T., Tadaka, E. and Arimoto, A. (2021). 'Cross-sectional study of individual and environmental factors associated with life-space mobility among

community-dwelling independent older people'. *Environmental Health and Preventive Medicine*. BioMed Central Ltd, 26 (1), p. 9. doi: 10.1186/s12199-021-00936-2.

Moffat, K. and Mercer, S. W. (2015). 'Challenges of managing people with multimorbidity in today's healthcare systems.' *BMC family practice*. BioMed Central Ltd., 16 (1), p. 129. doi: 10.1186/s12875-015-0344-4.

Moore, G. F., Audrey, S., Barker, M., Bond, L., Bonell, C., Hardeman, W., Moore, L., O'Cathain, A., Tinati, T., Wight, D. and Baird, J. (2015). 'Process evaluation of complex interventions: Medical Research Council guidance.' *BMJ (Clinical research ed.)*. British Medical Journal Publishing Group, 350, p. h1258. doi: 10.1136/bmj.h1258.

Morciano, M., Checkland, K., Billings, J., Coleman, A., Stokes, J., Tallack, C. and Sutton, M. (2020). 'New integrated care models in England associated with small reduction in hospital admissions in longer-term: A difference-in-differences analysis'. *Health Policy*. Elsevier, 124 (8), pp. 826–833. doi: 10.1016/j.healthpol.2020.06.004.

Mulrow, C. D. (1994). 'Systematic Reviews: Rationale for systematic reviews'. *BMJ*. British Medical Journal Publishing Group, 309 (6954), pp. 597–599. doi: 10.1136/bmj.309.6954.597.

Muth, C., Uhlmann, L., Haefeli, W. E., Rochon, J., Van Den Akker, M., Perera, R., Güthlin, C., Beyer, M., Oswald, F., Valderas, J. M., Knottnerus, J. A., Gerlach, F. M. and Harder, S. (2018). 'Effectiveness of a complex intervention on Prioritising Multimedication in Multimorbidity (PRIMUM) in primary care: Results of a pragmatic cluster randomised controlled trial'. *BMJ Open*. BMJ Publishing Group, 8 (2). doi: 10.1136/bmjopen-2017-017740.

Napoli, A. M., Mullins, P. M. and Pines, J. M. (2014). 'Predictors of hospital admission after ED observation unit care'. *The American Journal of Emergency Medicine*. W.B. Saunders, 32 (11), pp. 1405–1407. doi: 10.1016/J.AJEM.2014.08.039.

National Audit Office. (2017). *Health and Social Care Integration*.

National Institute for Health and Care Excellence. (2016). *Multimorbidity:*

clinical assessment and management.

Negm, A. M., Kennedy, C. C., Thabane, L., Veroniki, A. A., Adachi, J. D., Richardson, J., Cameron, I. D., Giangregorio, A., Petropoulou, M., Alsaad, S. M., Alzahrani, J., Maaz, M., Ahmed, M. M., Kim, E., Tehfe, H., Dima, R., Sabanayagam, K., Hewston, P., Abu Alrob, H. and Papaioannou, A. (2019). 'Management of Frailty: A Systematic Review and Network Meta-analysis of Randomized Controlled Trials'. *Journal of the American Medical Directors Association*. Elsevier, 20 (10), pp. 1190–1198. doi: 10.1016/J.JAMDA.2019.08.009.

NHS Digital. (2017). *Archive: Costing - Reference Costs Grouper*. Available at: https://webarchive.nationalarchives.gov.uk/ukgwa/20171011071739/http:/content.digital.nhs.uk/article/2062/Archive-costing (Accessed: 31 October 2023).

Nicholson, K., Terry, A. L., Fortin, M., Williamson, T., Bauer, M. and Thind, A. (2019). 'Prevalence, characteristics, and patterns of patients with multimorbidity in primary care: A retrospective cohort analysis in Canada'. *British Journal of General Practice*. Royal College of General Practitioners, 69 (686), pp. E647–E656. doi: 10.3399/bjgp19X704657.

Noel, H. C., Vogel, D. C., Erdos, J. J., Cornwall, D. and Levin, F. (2004). 'Home Telehealth Reduces Healthcare Costs'. *Telemedicine Journal and e-Health*, 10 (2), pp. 170–183. doi: 10.1089/tmj.2004.10.170.

Nolte, E. and Pitchforth, E. (2014). *What is the evidence on the economic impacts of integrated care? POLICY SUMMARY*.

Northwood, M., Ploeg, J., Markle-Reid, M. and Sherifali, D. (2018). 'Integrative review of the social determinants of health in older adults with multimorbidity'. *Journal of Advanced Nursing*. John Wiley & Sons, Ltd, 74 (1), pp. 45–60. doi: 10.1111/jan.13408.

O'Brien, R., Wyke, S., Guthrie, B., Watt, G. and Mercer, S. (2011). 'An "endless struggle": a qualitative study of general practitioners' and practice nurses' experiences of managing multimorbidity in socio-economically deprived areas of Scotland.' *Chronic illness*. SAGE PublicationsSage UK: London, England, 7 (1), pp. 45–59. doi: 10.1177/1742395310382461.

O'Mahony, D., Gudmundsson, A., Soiza, R. L., Petrovic, M., Jose Cruz-Jentoft, A., Cherubini, A., Fordham, R., Byrne, S., Dahly, D., Gallagher, P., Lavan, A., Curtin, D., Dalton, K., Cullinan, S., Flanagan, E., Shiely, F., Samuelsson, O., Sverrisdottir, A., Subbarayan, S., Vandaele, L., Meireson, E., Montero-Errasquin, B., Rexach-Cano, A., Correa Perez, A., Lozano-Montoya, I., Vélez-Díaz-Pallarés, M., Cerenzia, A., Corradi, S., Soledad Cotorruelo Ferreiro, M., Dimitri, F., Marinelli, P., Martelli, G., Fong Soe Khioe, R. and Eustace, J. (2020). 'Prevention of adverse drug reactions in hospitalized older patients with multi-morbidity and polypharmacy: the SENATOR* randomized controlled clinical trial.' *Age and ageing*. Oxford University Press, 49 (4), pp. 605–614. doi: 10.1093/ageing/afaa072.

Office for National Statistics. (2020). *SOC 2020 Volume 1: structure and descriptions of unit groups* .

Office for National Statistics. (2021). *Population Estimates for UK, England and Wales, Scotland and Northern Ireland*.

Office for National Statistics. (2022). *National population projections: 2020-based interim*.

Olaya, B., Moneta, M. V., Caballero, F. F., Tyrovolas, S., Bayes, I., Ayuso-Mateos, J. L. and Haro, J. M. (2017). 'Latent class analysis of multimorbidity patterns and associated outcomes in Spanish older adults: a prospective cohort study'. *BMC Geriatrics*. BioMed Central Ltd., 17 (1), p. 186. doi: 10.1186/s12877-017-0586-1.

Orueta, J. F., García-Álvarez, A., García-Goñi, M., Paolucci, F. and Nuño-Solinís, R. (2014). 'Prevalence and costs of multimorbidity by deprivation levels in the Basque Country: A population based study using health administrative databases'. *PLoS ONE*. Public Library of Science, 9 (2). doi: 10.1371/journal.pone.0089787.

Ouzzani, M., Hammady, H., Fedorowicz, Z. and Elmagarmid, A. (2016). 'Rayyan-a web and mobile app for systematic reviews'. *Systematic Reviews*, 5 (1), p. 210. doi: 10.1186/s13643-016-0384-4.

Owens, J. K. (2021). 'Systematic reviews: Brief overview of methods,

limitations, and resources'. *Nurse Author & Editor*. John Wiley & Sons, Ltd, 31 (3–4), pp. 69–72. doi: 10.1111/nae2.28.

Paddison, C. A. M., Saunders, C. L., Abel, G. A., Payne, R. A., Campbell, J. L. and Roland, M. (2015). 'Why do patients with multimorbidity in England report worse experiences in primary care? Evidence from the General Practice Patient Survey'. *BMJ Open*, 5 (3), pp. e006172–e006172. doi: 10.1136/bmjopen-2014-006172.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., Stewart, L. A., Thomas, J., Tricco, A. C., Welch, V. A., Whiting, P. and Moher, D. (2021). 'The PRISMA 2020 statement: An updated guideline for reporting systematic reviews'. *The BMJ*. BMJ Publishing Group, 372. doi: 10.1136/bmj.n71.

Panagioti, M., Reeves, D., Meacock, R., Parkinson, B., Lovell, K., Hann, M., Howells, K., Blakemore, A., Riste, L., Coventry, P., Blakeman, T., Sidaway, M. and Bower, P. (2018). 'Is telephone health coaching a useful population health strategy for supporting older people with multimorbidity? An evaluation of reach, effectiveness and cost-effectiveness using a "trial within a cohort"'. *BMC Medicine*. BioMed Central Ltd., 16 (1). doi: 10.1186/s12916-018-1051-5.

Patel, R., Bhimjiyani, A., Ben-Shlomo, Y. and Gregson, C. L. (2021). 'Social deprivation predicts adverse health outcomes after hospital admission with hip fracture in England'. *Osteoporosis International*. Springer Science and Business Media Deutschland GmbH, 32 (6), pp. 1129–1141. doi: 10.1007/s00198-020-05768-4.

Payne, R., Abel, G. A., Guthrie, B. and Mercer, S. W. (2013). 'The effect of physical multimorbidity, mental health conditions and socioeconomic deprivation on unplanned admissions to hospital: a retrospective cohort study'. *Canadian Medical Association Journal*, 185 (5), pp. E221–E228. doi: 10.1503/cmaj.121349.

Pearson-Stuttard, J., Ezzati, M. and Gregg, E. W. (2019). 'Multimorbidity—a

defining challenge for health systems'. *The Lancet Public Health*. Elsevier, 4 (12), pp. e599–e600. doi: 10.1016/S2468-2667(19)30222-1.

Personal Social Services Research Unit. (2022). *Unit Costs of Health and Social Care | PSSRU*. Kent. Available at: https://www.pssru.ac.uk/project-pages/unit-costs/ (Accessed: 31 October 2023).

Picco, L., Achilla, E., Abdin, E., Chong, S. A., Vaingankar, J. A., McCrone, P., Chua, H. C., Heng, D., Magadi, H., Ng, L. L., Prince, M. and Subramaniam, M. (2016). 'Economic burden of multimorbidity among older adults: impact on healthcare and societal costs'. *BMC Health Services Research*. BioMed Central, 16 (1). doi: 10.1186/S12913-016-1421-7.

Portegijs, E., Rantakokko, M., Viljanen, A., Sipilä, S. and Rantanen, T. (2016). 'Is frailty associated with life-space mobility and perceived autonomy in participation outdoors? A longitudinal study'. *Age and Ageing*. Oxford University Press, 45 (4), pp. 550–553. doi: 10.1093/ageing/afw072.

Purdy, S. (2010). *Avoiding hospital admissions: What does the research evidence say?* London.

Rantakokko, M., Portegijs, E., Viljanen, A., Iwarsson, S., Kauppinen, M. and Rantanen, T. (2016). 'Changes in life-space mobility and quality of life among community-dwelling older people: a 2-year follow-up study'. *Quality of Life Research*. Springer International Publishing, 25 (5), pp. 1189–1197. doi: 10.1007/s11136-015-1137-x.

Rantanen, T., Eronen, J., Kauppinen, M., Kokko, K., Sanaslahti, S., Kajan, N. and Portegijs, E. (2021). 'Life-Space Mobility and Active Aging as Factors Underlying Quality of Life among Older People before and during COVID-19 Lockdown in Finland - A Longitudinal Study'. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*. Oxford University Press (OUP), 76 (3), pp. E60–E67. doi: 10.1093/gerona/glaa274.

Read, J., Sharpe, L., Burton, A. L., Arean, P. A., Raue, P. J., McDonald, S., Titov, N., Gandy, M. and Dear, B. F. (2020). 'A randomized controlled trial of internet-delivered cognitive behaviour therapy to prevent the development of depressive disorders in older adults with multimorbidity.' *Journal of affective*

disorders. Elsevier B.V., 264, pp. 464–473. doi: 10.1016/j.jad.2019.11.077.

Reed, R., Isherwood, L. and Ben-Tovim, D. (2015). 'Why do older people with multi-morbidity experience unplanned hospital admissions from the community: a root cause analysis'. *BMC Health Services Research*. BioMed Central Ltd., 15 (1), p. 525. doi: 10.1186/s12913-015-1170-z.

Reed, R. L., Roeger, L., Howard, S., Oliver-Baxter, J. M., Battersby, M. W., Bond, M. and Osborne, R. H. (2018). 'A self-management support program for older Australians with multiple chronic conditions: A randomised controlled trial'. *Medical Journal of Australia*. Australasian Medical Publishing Co. Ltd, 208 (2), pp. 69–74. doi: 10.5694/mja17.00127.

Le Reste, J. Y., Nabbe, P., Manceau, B., Lygidakis, C., Doerr, C., Lingner, H., Czachowski, S., Munoz, M., Argyriadou, S., Claveria, A., Le Floch, B., Barais, M., Bower, P., Van Marwijk, H., Van Royen, P. and Lietard, C. (2013). 'The European General Practice Research Network Presents a Comprehensive Definition of Multimorbidity in Family Medicine and Long Term Care, Following a Systematic Review of Relevant Literature'. *Journal of the American Medical Directors Association*. Elsevier, 14 (5), pp. 319–325. doi: 10.1016/j.jamda.2013.01.001.

Rockwood, K. and Mitnitski, A. (2007). 'Frailty in Relation to the Accumulation of Deficits'. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. J Gerontol A Biol Sci Med Sci, 62 (7), pp. 722–727. doi: 10.1093/gerona/62.7.722.

Rosbach, M. and Andersen, J. S. (2017). 'Patient-experienced burden of treatment in patients with multimorbidity – A systematic review of qualitative data'. *PLOS ONE*. Edited by J. P. van Wouwe, 12 (6), p. e0179916. doi: 10.1371/journal.pone.0179916.

Rosenberg, T. (2012). 'Acute Hospital Use, Nursing Home Placement, and Mortality in a Frail Community-Dwelling Cohort Managed with Primary Integrated Interdisciplinary Elder Care at Home'. *Journal of the American Geriatrics Society*. J Am Geriatr Soc, 60 (7), pp. 1340–1346. doi: 10.1111/j.1532-5415.2012.03965.x.

Rubin, D. B. (1987). *Multiple Imputation for Nonresponse in Surveys*. Wiley (Wiley Series in Probability and Statistics). doi: 10.1002/9780470316696.

Ryan, A., Wallace, E., O'Hara, P. and Smith, S. M. (2015). 'Multimorbidity and functional decline in community-dwelling adults: a systematic review'. *Health and Quality of Life Outcomes*, 13 (1), p. 168. doi: 10.1186/s12955-015-0355-9.

Säfström, E., Jaarsma, T. and Strömberg, A. (2018). 'Continuity and utilization of health and community care in elderly patients with heart failure before and after hospitalization'. *BMC Geriatrics*. BMC Geriatr, 18 (1), p. 177. doi: 10.1186/s12877-018-0861-9.

Salisbury, C., Man, M.-S., Bower, P., Guthrie, B., Chaplin, K., Gaunt, D. M., Brookes, S., Fitzpatrick, B., Gardner, C., Hollinghurst, S., Lee, V., McLeod, J., Mann, C., Moffat, K. R. and Mercer, S. W. (2018). 'Management of multimorbidity using a patient-centred care model: a pragmatic cluster-randomised trial of the 3D approach'. *The Lancet*. Lancet Publishing Group, 392 (10141), pp. 41–50. doi: 10.1016/S0140-6736(18)31308-4.

Saraiva, M. D., Apolinario, D., Avelino-Silva, T. J., De Assis Moura Tavares, C., Gattás-Vernaglia, I. F., Marques Fernandes, C., Rabelo, L. M., Tavares Fernandes Yamaguti, S., Karnakis, T., Kalil-Filho, R., Jacob-Filho, W. and Romero Aliberti, M. J. (2021). 'The Impact of Frailty on the Relationship between Life-Space Mobility and Quality of Life in Older Adults during the COVID-19 Pandemic'. *The journal of nutrition, health & aging*, 25 (4), pp. 440–447. doi: 10.1007/s12603-020-1532-z.

Schäfer, I., Kaduszkiewicz, H., Mellert, C., Löffler, C., Mortsiefer, A., Ernst, A., Stolzenbach, C. O., Wiese, B., Abholz, H. H., Scherer, M., Van Den Bussche, H. and Altiner, A. (2018). 'Narrative medicine-based intervention in primary care to reduce polypharmacy: Results from the cluster-randomised controlled trial MultiCare AGENDA'. *BMJ Open*. BMJ Publishing Group, 8 (1). doi: 10.1136/bmjopen-2017-017653.

Schoenberg, N. E., Kim, H., Edwards, W. and Fleming, S. T. (2007). 'Burden of common multiple-morbidity constellations on out-of-pocket medical

expenditures among older adults.' *The Gerontologist*. Gerontologist, 47 (4), pp. 423–37. doi: 10.1093/geront/47.4.423.

Schulz, R. and Sherwood, P. R. (2008). 'Physical and mental health effects of family caregiving.' *The American journal of nursing*. NIH Public Access, 108 (9 Suppl), pp. 23–7; quiz 27. doi: 10.1097/01.NAJ.0000336406.45248.4c.

Searle, S. D., Mitnitski, A., Gahbauer, E. A., Gill, T. M. and Rockwood, K. (2008). 'A standard procedure for creating a frailty index'. *BMC Geriatrics*. BioMed Central, 8 (1), pp. 1–10. doi: 10.1186/1471-2318-8-24.

Shand, J., Morris, S. and Gomes, M. (2021). 'Understanding health and care expenditure by setting – who matters to whom?' *Journal of Health Services Research and Policy*. SAGE Publications Ltd, 26 (2), pp. 77–84. doi: 10.1177/1355819620936721.

Shaw, S., Rosen, R. and Rumbold, B. (2011). *What is integrated care?* . London.

Shoff, C., Caines, K. and Pines, J. M. (2019). 'Geographic variation in predictors of ED admission rates in U.S. Medicare fee-for-service beneficiaries'. *The American Journal of Emergency Medicine*. W.B. Saunders, 37 (6), pp. 1078–1084. doi: 10.1016/J.AJEM.2018.08.060.

Singer, L., Green, M., Rowe, F., Ben-Shlomo, Y. and Morrissey, K. (2019). 'Social determinants of multimorbidity and multiple functional limitations among the ageing population of England, 2002–2015'. *SSM - Population Health*. SSM Popul Health, 8, p. 100413. doi: 10.1016/j.ssmph.2019.100413.

Sinnott, C., Mc Hugh, S., Browne, J. and Bradley, C. (2013). 'GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research.' *BMJ open*. BMJ Open, 3 (9), p. e003610. doi: 10.1136/bmjopen-2013-003610.

Smith, S. M., Wallace, E., O'Dowd, T. and Fortin, M. (2021). 'Interventions for improving outcomes in patients with multimorbidity in primary care and community settings'. *Cochrane Database of Systematic Reviews*, 2021 (5). doi: 10.1002/14651858.CD006560.pub4.

Smith, S. M., Wallace, E., Salisbury, C., Sasseville, M., Bayliss, E. and Fortin, M. (2018). 'A Core Outcome Set for Multimorbidity Research (COSmm)'. *Annals of family medicine*. Ann Fam Med, 16 (2), pp. 132–138. doi: 10.1370/AFM.2178.

Smulowitz, P. B., Weinreb, G., McWilliams, J. M., O'Malley, A. J. and Landon, B. E. (2023). 'Association of Functional Status, Cognition, Social Support, and Geriatric Syndrome With Admission From the Emergency Department'. *JAMA Internal Medicine*. American Medical Association, 183 (8), p. 784. doi: 10.1001/jamainternmed.2023.2149.

St John, P. D., Tyas, S. L., Menec, V. and Tate, R. (2014). 'Multimorbidity, disability, and mortality in community-dwelling older adults.' *Canadian family physician Medecin de famille canadien*. College of Family Physicians of Canada, 60 (5), pp. e272-80.

Stafford, M., Steventon, A., Thorlby, R., Fisher, R., Turton, C. and Deeny, S. (2018). *Briefing: Understanding the health care needs of people with multiple health conditions*. London.

Stevenson, J. M., Davies, J. G. and Martin, F. C. (2019). 'Medication-related harm: A geriatric syndrome'. *Age and Ageing*. England, 49 (1), pp. 7–11. doi: 10.1093/ageing/afz121.

Stewart, D. and Mccambridge, J. (2019). 'Alcohol complicates multimorbidity in older adults'. *The BMJ*. British Medical Journal Publishing Group, 365. doi: 10.1136/bmj.l4304.

Stokes, J., Guthrie, B., Mercer, S. W., Rice, N. and Sutton, M. (2021). 'Multimorbidity combinations, costs of hospital care and potentially preventable emergency admissions in England: A cohort study'. *PLOS Medicine*. Edited by L. C. Rosella. Public Library of Science, 18 (1), p. e1003514. doi: 10.1371/journal.pmed.1003514.

Stokes, T., Tumilty, E., Doolan-Noble, F. and Gauld, R. (2017). 'Multimorbidity, clinical decision making and health care delivery in New Zealand Primary care: a qualitative study.' *BMC family practice*. BioMed Central Ltd., 18 (1), p. 51. doi: 10.1186/s12875-017-0622-4.

Surate Solaligue, D. E., Hederman, L. and Martin, C. M. (2014). 'What weekday? How acute? An analysis of reported planned and unplanned GP visits by older multi-morbid patients in the Patient Journey Record System database'. *Journal of Evaluation in Clinical Practice*, 20 (4), pp. 522–526. doi: 10.1111/jep.12171.

Taylor, J. K., Buchan, I. E. and van der Veer, S. N. (2019). 'Assessing life-space mobility for a more holistic view on wellbeing in geriatric research and clinical practice'. *Aging Clinical and Experimental Research*. Springer International Publishing, pp. 439–445. doi: 10.1007/s40520-018-0999-5.

The Academy of Medical Sciences. (2018). *Multimorbidity: a priority for global health research*. London.

The King's Fund. (2016). *New care models Emerging innovations in governance and organisational form*. London.

The King's Fund. (2022). *The first days of statutory integrated care systems: born into a storm*.

The Lancet Neurology. (2017). 'Pointing the way to primary prevention of dementia'. *The Lancet Neurology*. Lancet Publishing Group, 16 (9), p. 677. doi: 10.1016/S1474-4422(17)30256-9.

Tisminetzky, M., Goldberg, R. and Gurwitz, J. H. (2016). 'Magnitude and Impact of Multimorbidity on Clinical Outcomes in Older Adults with Cardiovascular Disease. A Literature Review.' *Clinics in Geriatric Medicine*. W.B. Saunders, pp. 227–246. doi: 10.1016/j.cger.2016.01.014.

Tisminetzky, M., Gurwitz, J. H., Fan, D., Reynolds, K., Smith, D. H., Fouayzi, H., Sung, S. H., Goldberg, R. and Go, A. S. (2020). 'Noncardiac-related morbidity, mobility limitation, and outcomes in older adults with heart failure'. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*. Oxford University Press (OUP), 75 (10), pp. 1981–1988. doi: 10.1093/gerona/glz285.

Tran, V.-T., Montori, V. M., Eton, D. T., Baruch, D., Falissard, B. and Ravaud, P. (2012). 'Development and description of measurement properties of an instrument to assess treatment burden among patients with multiple chronic

conditions'. *BMC Medicine*. BioMed Central, 10 (1), p. 68. doi: 10.1186/1741-7015-10-68.

Travers, J., Romero-Ortuno, R., Bailey, J. and Cooney, M. T. (2019). 'Delaying and reversing frailty: a systematic review of primary care interventions'. *The British journal of general practice : the journal of the Royal College of General Practitioners*. Br J Gen Pract, 69 (678), pp. E61–E69. doi: 10.3399/BJGP18X700241.

Turner, G. and Clegg, A. (2014). 'Best practice guidelines for the management of frailty: A British Geriatrics Society, Age UK and Royal College of General Practitioners report'. *Age and Ageing*. Oxford University Press, 43 (6), pp. 744–747. doi: 10.1093/ageing/afu138.

UK Government. (2022). *Health and Care Act 2022*.

Valentijn, P. P., Schepman, S. M., Opheij, W. and Bruijnzeels, M. A. (2013). 'Understanding integrated care: a comprehensive conceptual framework based on the integrative functions of primary care'. *International journal of integrated care*. Int J Integr Care, 13 (JANUARY-MARCH 2). doi: 10.5334/IJIC.886.

Vanleerberghe, P., De Witte, N., Claes, C., Schalock, R. L. and Verté, D. (2017). 'The quality of life of older people aging in place: a literature review'. *Quality of Life Research*. Springer International Publishing, pp. 2899–2907. doi: 10.1007/s11136-017-1651-0.

Vanleerberghe, P., De Witte, N., Claes, C. and Verté, D. (2019). 'The association between frailty and quality of life when aging in place'. *Archives of Gerontology and Geriatrics*. Elsevier Ireland Ltd, 85, p. 103915. doi: 10.1016/j.archger.2019.103915.

Vetrano, D. L., Palmer, K., Marengoni, A., Marzetti, E., Lattanzio, F., Roller-Wirnsberger, R., Samaniego, L. L., Rodríguez-Mañas, L., Bernabei, R. and Onder, G. (2019). 'Frailty and multimorbidity: A systematic review and meta-analysis'. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 74 (5), pp. 659–666. doi: 10.1093/gerona/gly110.

Villacampa-Fernández, P., Navarro-Pardo, E., Tarín, J. J. and Cano, A.

(2017). ‘Frailty and multimorbidity: Two related yet different concepts’. *Maturitas*. Elsevier Ireland Ltd., 95, pp. 31–35. doi: 10.1016/j.maturitas.2016.10.008.

Violán, C., Foguet-Boreu, Q., Roso-Llorach, A., Rodriguez-Blanco, T., Pons-Vigués, M., Pujol-Ribera, E., Muñoz-Pérez, M. Á. and Valderas, J. M. (2014). ‘Burden of multimorbidity, socioeconomic status and use of health services across stages of life in urban areas: a cross-sectional study’. *BMC Public Health*, 14 (1), p. 530. doi: 10.1186/1471-2458-14-530.

Walker, V., Perret-Guillaume, C., Kesse-Guyot, E., Agrinier, N., Hercberg, S., Galan, P., Assmann, K. E., Briançon, S. and Rotonda, C. (2016). ‘Effect of Multimorbidity on Health-Related Quality of Life in Adults Aged 55 Years or Older: Results from the SU.VI.MAX 2 Cohort’. *PLOS ONE*. Edited by A. Montazeri. Public Library of Science, 11 (12), p. e0169282. doi: 10.1371/journal.pone.0169282.

Wallace, E., Salisbury, C., Guthrie, B., Lewis, C., Fahey, T. and Smith, S. M. (2015). ‘Managing patients with multimorbidity in primary care.’ *BMJ (Clinical research ed.)*. British Medical Journal Publishing Group, 350, p. h176. doi: 10.1136/bmj.h176.

Walsh, C. A., Bennett, K. E., Wallace, E. and Cahir, C. (2020). ‘Identifying Adherence Patterns Across Multiple Medications and Their Association With Health Outcomes in Older Community-Dwelling Adults With Multimorbidity’. *Value in Health*. Elsevier Ltd, 23 (8), pp. 1063–1071. doi: 10.1016/j.jval.2020.03.016.

Wang, J., Boehm, L. and Mion, L. C. (2017). ‘Intrinsic capacity in older hospitalized adults: Implications for nursing practice’. *Geriatric Nursing*. Mosby Inc., 38 (4), pp. 359–361. doi: 10.1016/j.gerinurse.2017.06.008.

Weston, C., Gilkes, A., Durbaba, S., Schofield, P., White, P. and Ashworth, M. (2016). ‘Long term condition morbidity in English general practice: a cross-sectional study using three composite morbidity measures.’ *BMC family practice*. BioMed Central, 17 (1), p. 166. doi: 10.1186/s12875-016-0563-3.

Williams, E. I. and Fitton, F. (1991). ‘Use of nursing and social services by

elderly patients discharged from hospital.' *The British Journal of General Practice*, 41 (343), pp. 72–5.

World Health Organization. (2012). *WHOQOL: Measuring Quality of Life*.

World Health Organization. (2016). *Multimorbidity*. World Health Organization (Technical Series on Safer Primary Care). Available at: https://apps.who.int/iris/handle/10665/252275.

World Health Organization. (2017). *WHO Clinical Consortium on Healthy Ageing Topic focus: frailty and intrinsic capacity*. Geneva.

Wyatt, K. D., Stuart, L. M., Brito, J. P., Carranza Leon, B., Domecq, J. P., Prutsky, G. J., Egginton, J. S., Calvin, A. D., Shah, N. D., Murad, M. H. and Montori, V. M. (2014). 'Out of context: clinical practice guidelines and patients with multiple chronic conditions: a systematic review.' *Medical care*, 52 Suppl 3 (3 SUPPL. 2), pp. S92–S100. doi: 10.1097/MLR.0b013e3182a51b3d.

Xia, T., Enticott, J., Pearce, C., Mazza, D. and Turner, L. R. (2020). 'Predictors of ED attendance in older patients with chronic disease: a data linkage study'. *Australian Health Review*, 44 (4), pp. 550–556. doi: 10.1071/AH19169.

Xiang, X., Zuverink, A., Rosenberg, W. and Mahmoudi, E. (2019). 'Social work-based transitional care intervention for super utilizers of medical care: a retrospective analysis of the bridge model for super utilizers'. *Social Work in Health Care*. Routledge, 58 (1), pp. 126–141. doi: 10.1080/00981389.2018.1547345.

Xu, X., Mishra, G. D. and Jones, M. (2017). 'Evidence on multimorbidity from definition to intervention: An overview of systematic reviews'. *Ageing Research Reviews*, 37, pp. 53–68. doi: 10.1016/j.arr.2017.05.003.

Yang, C., Lee, D. T. F., Wang, X. and Chair, S. Y. (2022). 'Effects of a nurse-led medication self-management intervention on medication adherence and health outcomes in older people with multimorbidity: A randomised controlled trial'. *International Journal of Nursing Studies*. Elsevier Ltd, 134, p. 104314. doi: 10.1016/j.ijnurstu.2022.104314.

Yarnall, A. J., Sayer, A. A., Clegg, A., Rockwood, K., Parker, S. and Hindle, J.

V. (2017). ‘New horizons in multimorbidity in older adults’. *Age and Ageing*. Age Ageing, 46 (6), pp. 882–888. doi: 10.1093/ageing/afx150.

Zazzara, M. B., Vetrano, D. L., Carfì, A. and Onder, G. (2020). ‘Frailty and chronic disease’. *Panminerva Medica*. Panminerva Med, 61 (4), pp. 486–492. doi: 10.23736/S0031-0808.19.03731-5.

Zucchelli, A., Vetrano, D. L., Marengoni, A., Grande, G., Romanelli, G., Calderón-Larrañaga, A., Fratiglioni, L. and Rizzuto, D. (2018). ‘Frailty predicts short-term survival even in older adults without multimorbidity’. *European Journal of Internal Medicine*. Elsevier, 56, pp. 53–56. doi: 10.1016/j.ejim.2018.06.012.

Zulman, D. M., Asch, S. M., Martins, S. B., Kerr, E. A., Hoffman, B. B. and Goldstein, M. K. (2014). ‘Quality of Care for Patients with Multiple Chronic Conditions: The Role of Comorbidity Interrelatedness’. *Journal of General Internal Medicine*. Springer, 29 (3), pp. 529–537. doi: 10.1007/s11606-013-2616-9.

Appendix 1: Systematic review search strategy

“aged”[MeSH Terms] OR "older adult"[Title/Abstract] OR "older people"[Title/Abstract] OR "geriatric"[Title/Abstract] OR "elderly"[Title/Abstract]
AND
“multimorbidity”[MeSH Terms] OR "multimorbidit*"[Title/Abstract] OR "multi morbidit*"[Title/Abstract] OR "comorbidit*"[Title/Abstract] OR "co morbidit*"[Title/Abstract]
AND
("economical"[All Fields] OR "economics"[MeSH Terms] OR "economics"[All Fields] OR "economic"[All Fields] OR "economically"[All Fields] OR "economics"[MeSH Subheading] OR "economization"[All Fields] OR "economize"[All Fields] OR "economized"[All Fields] OR "economizes"[All Fields] OR "economizing"[All Fields]) AND ("analysis"[MeSH Subheading] OR "analysis"[All Fields]) OR ("economics"[MeSH Subheading] OR "economics"[All Fields] OR "cost"[All Fields] OR "costs and cost analysis"[MeSH Terms] OR ("costs"[All Fields] AND "cost"[All Fields] AND "analysis"[All Fields]) OR "costs and cost analysis"[All Fields]) AND ("statistics and numerical data"[MeSH Subheading] OR ("statistics"[All Fields] AND "numerical"[All Fields] AND "data"[All Fields]) OR "statistics and numerical data"[All Fields] OR "utilization"[All Fields] OR "utilisation"[All Fields] OR "utilisations"[All Fields] OR "utilise"[All Fields] OR "utilised"[All Fields] OR "utilises"[All Fields] OR "utilising"[All Fields] OR "utilities"[All Fields] OR "utility"[All Fields] OR "utilizations"[All Fields] OR "utilize"[All Fields] OR "utilized"[All Fields] OR

"utilizer"[All Fields] OR "utilizers"[All Fields] OR "utilizes"[All Fields] OR "utilizing"[All Fields])

OR

"cost-utility"[All Fields]

OR

"cost benefit analysis"[MeSH Terms] OR ("cost benefit"[All Fields] AND "analysis"[All Fields]) OR "cost benefit analysis"[All Fields] OR ("cost"[All Fields] AND "benefit"[All Fields]) OR "cost benefit"[All Fields]

OR

"cost benefit analysis"[MeSH Terms] OR ("cost benefit"[All Fields] AND "analysis"[All Fields]) OR "cost benefit analysis"[All Fields] OR ("cost"[All Fields] AND "benefit"[All Fields]) OR "cost benefit"[All Fields]

OR

"cost effectiv*"[All Fields]

OR

("economics"[MeSH Subheading] OR "economics"[All Fields] OR "cost"[All Fields] OR "costs and cost analysis"[MeSH Terms] OR ("costs"[All Fields] AND "cost"[All Fields] AND "analysis"[All Fields]) OR "costs and cost analysis"[All Fields]) AND "effectiv*"[All Fields]

OR

("economics"[MeSH Subheading] OR "economics"[All Fields] OR "cost"[All Fields] OR "costs and cost analysis"[MeSH Terms] OR ("costs"[All Fields] AND "cost"[All Fields] AND "analysis"[All Fields]) OR "costs and cost

analysis"[All Fields]) AND ("minimal"[All Fields] OR "minimisation"[All Fields] OR "minimisations"[All Fields] OR "minimise"[All Fields] OR "minimised"[All Fields] OR "minimises"[All Fields] OR "minimising"[All Fields] OR "minimization"[All Fields] OR "minimizations"[All Fields] OR "minimize"[All Fields] OR "minimized"[All Fields] OR "minimizer"[All Fields] OR "minimizers"[All Fields] OR "minimizes"[All Fields] OR "minimizing"[All Fields])

OR

"cost-minimisation"[All Fields]

AND

(("ambulatory care facilities"[MeSH Terms] OR ("ambulatory"[All Fields] AND "care"[All Fields] AND "facilities"[All Fields]) OR "ambulatory care facilities"[All Fields] OR "clinic"[All Fields] OR "clinic s"[All Fields] OR "clinical"[All Fields] OR "clinically"[All Fields] OR "clinicals"[All Fields] OR "clinics"[All Fields]) AND "outcom*"[All Fields])

OR

(("health"[MeSH Terms] OR "health"[All Fields] OR "health s"[All Fields] OR "healthful"[All Fields] OR "healthfulness"[All Fields] OR "healths"[All Fields]) AND "outcom*"[All Fields])

OR

(("functional"[All Fields] OR "functional s"[All Fields] OR "functionalities"[All Fields] OR "functionality"[All Fields] OR "functionalization"[All Fields] OR "functionalizations"[All Fields] OR "functionalize"[All Fields] OR "functionalized"[All Fields] OR "functionalizes"[All Fields] OR "functionalizing"[All Fields] OR "functionally"[All Fields] OR "functionals"[All Fields] OR "functioned"[All Fields] OR "functioning"[All Fields] OR

"functionings"[All Fields] OR "functions"[All Fields] OR "physiology"[MeSH Subheading] OR "physiology"[All Fields] OR "function"[All Fields] OR "physiology"[MeSH Terms]) AND "outcom*"[All Fields])

Appendix 2: Systematic review inclusion and exclusion criteria

INCLUDED	EXCLUDED
Study design • Randomised controlled trials (RCTs) **Population** • Older adults with a mean age of ≥65 with multimorbidity (may be defined as comorbidity). Multimorbidity is defined as two or more long term physical and/or mental health conditions of any body system. **Intervention** • All interventions that are specifically designed and directed towards addressing health or functional outcomes in older adults with multimorbidity. This may include health and social care professionals as the intervention such as doctors, nurses, link workers and other care professionals. **Comparator** • Usual care or alternative care. **Outcome**	• Non-English publication • Participants' mean age <65 • Studies on single conditions with multiple symptoms or medications rather than multimorbidity. • Studies that include no direct delivery of an intervention and only involve education of professionals who deliver multimorbidity interventions.

• Outcomes may be measured by quality of life or clinical parameters such as hospitalisation rates, death (including all causes), blood pressure and blood glucose control. • functional outcomes may be measured by level of self-management of activities of daily living or functional disability. • Economic outcomes should include economic analysis, including measuring cost-effectiveness, cost benefit or utility of the intervention being delivered.	

Appendix 3: Summary of Critical Appraisal Skills Programme (CASP) Randomised Controlled Trial Checklist

Study	**Section A:** Is the basic study design valid for an RCT?			**Section B:** Was the study methodologically sound?			**Section C:** What are the results?			**Section D:** Will the results help locally?	
	1. Did the study address a clearly focused research question?	2. Was the assignment of participants to interventions randomised?	3. Were all participants who entered the study accounted for at its conclusion?	4. Were the participants/ investigators/ assessors 'blind' to intervention given to participants?	5. Were the study groups similar at the start?	6. Apart from the experimental intervention, did each study group receive the same level of care?	7. Were the effects of intervention reported comprehensively?	8. Was the precision of the estimate of the intervention or treatment effect reported?	9. Do the benefits of the experimental intervention outweigh the harms and costs?	10. Can the results be applied to your local population or in your context?	11. Would the experimental intervention provide greater value in current practice than any of the existing interventions?

Schäfer (2018)	✓	✓	✓	X	✓	✓	✓	✓	✓	?	X
Panagioti (2018)	✓	✓	✓	X	✓	✓	✓	✓	?	X	X
Chow and Wong (2014)	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	?
Berntsen (2019)	?	✓	✓	X	✓	✓	✓	✓	✓	✓	✓
Ekdahl (2015)	✓	✓	✓	X	✓	✓	✓	X	✓	✓	✓
Miklavcic (2020)	✓	✓	✓	X	?	✓	✓	✓	X	X	X

Markle-Reid (2018)	✓	✓	✓	X	✓	✓	✓	✓	?	✓	?
Fisher (2020)	✓	✓	✓	✓	✓	✓	✓	✓	X	X	X
Hastings (2021)	✓	✓	✓	X	X	✓	?	X	✓	?	✓
Muth (2018)	✓	✓	✓	X	✓	✓	✓	✓	X	X	X
Noel (2004)	✓	?	X	X	X	✓	✓	X	✓	✓	?
Kim (2020)	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓
O'Mahony (2020)	✓	✓	✓	✓	✓	✓	✓	✓	X	?	X
Read (2020)	✓	✓	✓	X	X	✓	✓	X	✓	X	X

Lundqvist (2018)	✓	✓	✓	X	✓	✓	✓	X	✓	✓	✓
Reed (2018)	✓	✓	✓	?	✓	✓	✓	X	✓	✓	✓
Krska (2001)	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓
Salisbury (2018)	✓	✓	✓	X	✓	✓	✓	✓	X	X	X
Lee (2022)	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓
Yang (2022)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
McCarthy (2022)	✓	✓	✓	✓	✓	✓	✓	✓	✓	?	X

✓ Yes

X No

? Can't tell

Appendix 4: Summary of Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist

Item No.	Section/Item	Panagioti (2018)	Ekdahl (2015)	Miklavcic (2020)	Markle-Reid (2018)	Fisher (2020)	Noel (2004)	Lundqvist (2018)	Krska (2001)
	Title and abstract								
1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	Yes	Yes	Not clear	Not clear	Not clear	Not clear	Yes	No
2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	(including base case and uncertainty analyses), and conclusions.								
	Introduction								
3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Yes	Yes	Yes	Yes	Not clear	Not clear	Yes	Yes
	Methods								
4	Describe characteristics of the base case population	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	and subgroups analysed, including why they were chosen.								
5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Describe the perspective of the study and relate this to the costs being evaluated.	Yes	Not clear	Yes	Yes	Yes	No	Yes	No
7	Describe the interventions or strategies being compared and state why they were chosen.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Not clear	Yes	Not clear	Not clear	Not clear	Not clear	Yes	No
9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Yes	No	No	No	No	No	Yes	No
10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Yes	Yes	Yes	Yes	Yes	Not clear	Yes	Yes

11a	Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Yes	Not clear	Not clear	Not clear	Yes	No	Yes	Yes
11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
13b	Model-based economic evaluation: Describe approaches and data	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.								
14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes

	necessary. Describe methods for converting costs into a common currency base and the exchange rate.								
15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	No	No	No	No	No	No	Yes	No
16	Describe all structural or other assumptions underpinning the decision-analytical model.	No	No	No	No	No	No	Yes	No

17	Describe all analytical methods supporting the evaluation, including methods for dealing with skewed, missing, or censored data; extrapolation methods; pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Yes	Yes	Yes	Yes	Yes	Not clear	Yes	No
	Results								

18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. A table to show the input values is strongly recommended.	Yes	Not clear	Yes	Yes	Yes	Not clear	Yes	Yes
19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	report incremental cost-effectiveness ratios.								
20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Yes	No	No	No	No	No	Yes	No
20b	Model-based economic evaluation: Describe the effects on the results of	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.									
21	If applicable, report differences in costs, outcomes, or cost-effectiveness explained by variations between subgroups of patients with different baseline characteristics or other observed variability not reducible by more information.	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	

	Discussions								
22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Other								
23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	the analysis. Describe other non-monetary sources of support.								
24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Yes	Yes	Yes	Yes	Yes	No	Yes	No

Appendix 5: PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	52
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.	53
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	55
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	56
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.	655

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.	56-57
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.	57-59
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
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).	56-57
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.	57
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	58
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.	58
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	91-101
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.	91-104

Section/topic	#	Checklist item	Reported on page #
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).	58
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	104
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.	58 and figure 3-1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	58-88
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).	Appendix 3
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.	91-103
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	90

Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Appendix 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	94
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 providers, users, and policy makers).	104
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).	105
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	107
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.	53

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

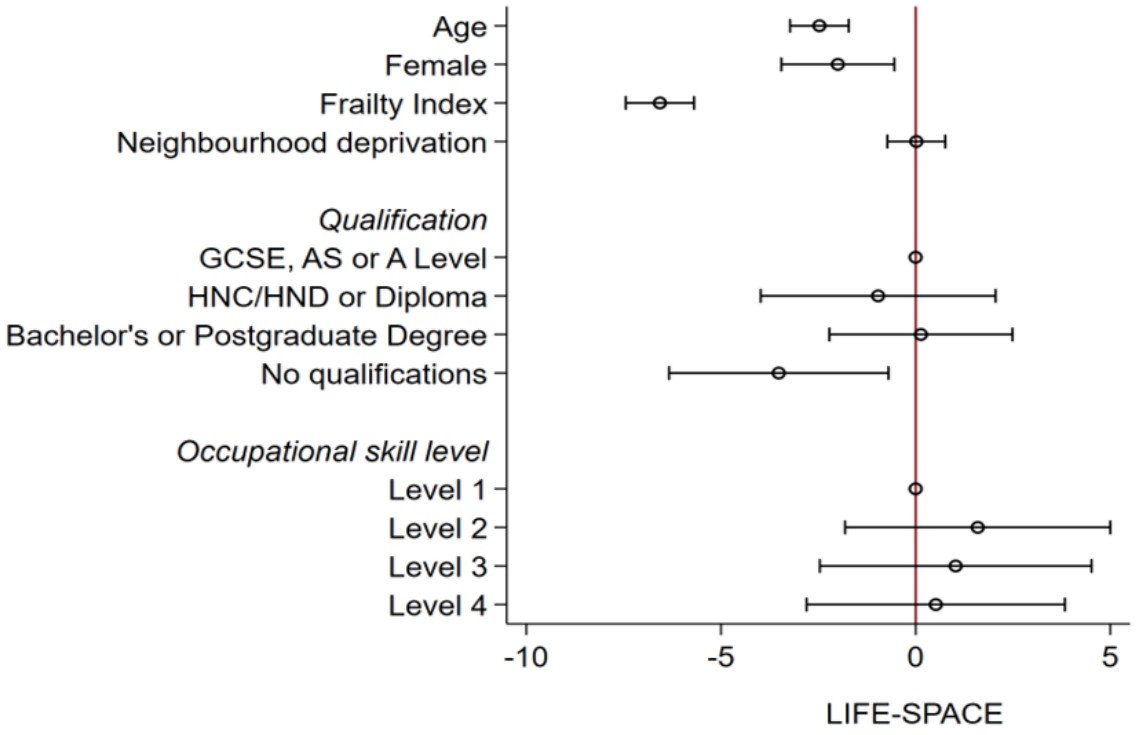
Appendix 6: Selected systematic review studies designed with some consideration of frailty

Study	Intervention	Result
Berntsen (2019)	A combination of person-centred care, integrated care, and pro-active care delivered through a medical doctor and a team of pharmacists, nurse coordinators, physio- and occupational therapists, geriatric nurses, and medical secretaries.	Beneficial for total emergency bed days but not for emergency admissions or 30-days readmissions count.
Ekdahl (2015)	Comprehensive geriatric assessment team of nurses, doctors, and allied health professionals. Intervention group supported by team as and when required. Contact could be a few times in a year or daily or weekly. Support given via telephone, home, ambulatory visit.	No improvement in total hospitalisations

Lundqvist (2018)	Comprehensive geriatric assessment team of nurses, doctors, and allied health professionals. Intervention group supported by team as and when required. Contact could be a few times in a year or daily or weekly. Support given via telephone, home, ambulatory visit.	0.54 (half a year) QALYs gained resulting in a cost per QALY of 46,000 EUR which is suggested as reasonable in a Swedish healthcare context.
Kim (2020)	Use of an Information and Communication Technology (ICT) system to support nursing staff in a nursing home to conduct standardised comprehensive geriatric assessments, develop care plans and monitor care.	Beneficial for quality of care
Noel (2004)	Home telehealth and nurse case manager, intervention delivered through video call and regular telephone reminders).	Beneficial for cognition, patient satisfaction but not on health care use, physical function, self-rated health and diabetes management.
Lee (2022)	Integrated geriatric care plus a multidomain intervention; 16 structured 2-hour training sessions (sessions included various components such as	Improved cognitive function and enhanced quality of life

physical exercise, cognitive training, diet education,
and chronic condition management)

Appendix 7: Variables associated with life-space



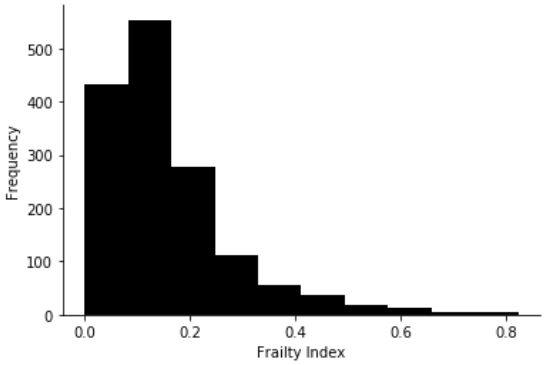
Appendix 8: Creation of Frailty Index in DELPHIC cohort

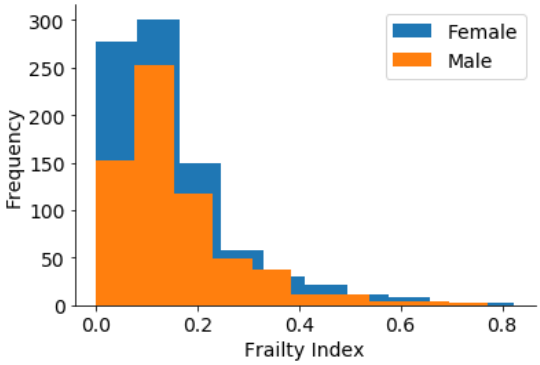
Item	Type	Scoring:	Prevalence (%)	
General Health “baseline_generalhealth_fi”	Self rated	Excellent, Very good, good (1,2,3) = 0 Fair/Poor (4,5) = 1	0 = 82.0 1 = 17.0 Missing = 1	1
Myocardial Infarction 'mi_fi'	Comorbidity	Yes = 1 No =0	0 = 78.6 1 = 20.8 Missing = 0	2
Hypertension 'htn_fi'	Comorbidity	Yes = 1 No =0	0=49.6 1=49.4 Missing =0	3
Diabetes 'dm_fi'	Comorbidity	Yes = 1 No =0	0=87.4 1=12.1 Missing =0	4
Stroke 'stroke_fi'	Comorbidity	Yes = 1 No =0	0=90.5 1=8.9 Missing =0	5
Cancer 'cancer_fi'	Comorbidity	Yes = 1 No =0	0=75.9 1=23.6 Missing=0.0	6
COPD 'copd_fi'	Comorbidity	Yes = 1 No =0	0=85.7 1=13.7 Missing=0.6	7
Read Newspaper 'baseline_readingpaper (problemvisionhearing)_fi'	Sensory	No or Little Difficulty (1,2) = 0 Some or Great Deal Difficulty (3,4) = 1	0=96.6 1=2.8 Missing=5.9	8
Read Signs 'baseline_readingsigns (problemvisionhearing)_fi'	Sensory	No or Little Difficulty (1,2) = 0 Some or Great Deal Difficulty (3,4) = 1	0=91.1 1=8.2 Missing=0.7	9

Hear Converstations ' baseline_hearingconversation (problemvisionhearing)_fi'	Sensory	No or Little Difficulty (1,2) = 0 Some or Great Deal Difficulty (3,4) = 1	0=97.1 1=2.5 Missing=0.4	10
Hear Noisy Room 'baseline_hearinginnoisyroom (problemvisionhearing)_fi'	Sensory	No or Little Difficulty (1,2) = 0 Some or Great Deal Difficulty (3,4) = 1	0=72.8 1=26.5 Missing=0.6	11
Urinary Incontinence 'baseline_urineleak_fi'		Less than once a week (0,1,2) = 0 At least once a day (3,4,5) = 1	0=88.9 1=10.5 Missing=0.6	12
Fall by accident 'baseline_fallenbyaccident_fi'	Function	No (2) = 0 Yes (1) = 1	1=64.3 0=34.6 Missing=1.0	13
Weight loss 'baseline_weightloss_fi'		Loss >3kg (0) = 1 Anything less than 3kg (1,2,3) = 0	0=97.1 1=2.4 Missing=0.4	14
Mobility 'baseline_mobility.1_fi'		Immobile or requires 1 person (0,1,2) = 1 Independent with or w/o aid (3) = 0	0=96.8 1=2.7 Missing=0.5	15
Feed 'baseline_kitchen-kfeed_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1 Alone easily (4) = 0	0=98.4 1=1.2 Missing=0.3	16
Make hot drink baseline_kitchen-khotdrink_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1 Alone easily (4) = 0	0=95.6 1=4.0 Missing=0.3	17
Wash up in kitchen 'baseline_kitchen- kwashingup_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1	0=94.3 1=5.3 Missing=0.4	18

		Alone easily (4) = 0		
Finances 'baseline_domestic-dmoney_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1 Alone easily (4) = 0	0=93.5 1=5.9 Missing=0.6	19
Laundry 'baseline_domestic-dsmallclothes_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1 Alone easily (4) = 0	0=89.5 1=9.8 Missing=0.6	20
Shopping 'baseline_domestic-dshopping_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1 Alone easily (4) = 0	0=82.1 1=17.4 Missing=0.5	21
Social activities 'baseline_leisure-lsocial_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1 Alone easily (4) = 0	0=87.4 1=11.8 Missing=0.8	22
Garden 'baseline_leisure-lgarden_fi'	Function	Not at all, with help or alone with difficulty (1,2,3) = 1 Alone easily (4) = 0	0=54.2 1=38.2 Missing=7.6	23
Polypharmacy 'poly_fi'		$\geq$ 5 Meds = 1 <5 Meds = 0	0=62.9 1=33.4 Missing=3.6	24
Past Delirium 'baseline_delirium_fi'		No = 0 Yes = 1	0=87.3 1=10.7 Missing=2.0	25
Immediate Racall 'immediate_fi'	Cognitive	$\geq$4 words = 0 <4 words = 1 *25th percentile	0=64.4 1=35.6	26
Delayed Recall 'delayed_fi'	Cognitive	$\geq$2 words = 0 <2 words = 1 *25th percentile	0=66.2 1=33.8	27

Groom 'groom_fi'	Function	Independent (5) = 0 Needs help (0) = 1	0=96.8 1=1.6 Missing=1.6	28
Stairs 'stairs_fi'	Function	Independent (10,15) = 0 Unable to needs help (0,5) = 1	0=93.6 1=5.8 Missing=0.6	29
Transfer 'transfer_fi'	Function	Independent (15) = 0 Any help or unable (0, 5,10) = 1	0=93.6 1=5.8 Missing=0.4	30
Bath 'bath_fi'	Function	Independent, unsupervised (0) = 0 Dependent (5) = 1	0=95.8 1=3.7 Missing=0.5	31
Dress 'dress_fi'	Function	10 = 0 0,5 = 1	0=96.0 1=3.6 Missing=0.5	32
Toilet 'toilet_fi'	Function	10 = 0 0,5 = 1	0=98.0 1=1.6 Missing=0.4	33
Verbal fluency (animals) 'animals_fluency_fi'	Cognitive	≥10 words = 0 <10 words = 1	0=86.9 1=8.8 Missing=4.3	34
Verbal fluency (letter words) 'letters_fluency_fi'	Cognitive	≥10 words = 0 <10 words = 1	0=79.8 1=16.1 Missing=4.2	35





Cross Sectional Slope = 3.3%

Appendix 9: Variables associated with life-space (n=1,510)

Life-space	Unadjusted				Multivariate Linear Regression of 1,493 individuals			
	Coef.	[95% Conf. Interval]		*P*	Coef.	[95% Conf. Interval]		*P*
Age	-5.3	-6.0	-4.6	<0.001	-2.5	-3.2	-1.7	<0.001
Women (cf.) men	-1.4	-3.0	0.3	0.102	-2.0	-3.4	-0.5	0.007
Frailty Index	-8.2	-8.9	-7.4	<0.001	-6.6	-7.4	-5.7	<0.001
IMD	-1.4	-2.2	-0.5	0.001	0.02	-0.7	0.8	0.962
Qualification								
GCSE, AS or A levels	[ref]				[ref]			
HNC/HND or Diploma	-0.4	-3.8	3.0		-1.0	-4.0	2.1	
Bachelor's or Postgraduate	3.0	0.5	5.4	<0.001	0.1	-2.2	2.5	0.027
No qualifications	-8.9	-12.0	-5.9		-3.5	-6.3	-0.7	
Occupational skill								
Level 1	[ref]			<0.001				0.704
Level 2	4.8	0.9	8.7		1.6	-1.8	5.0	

Level 3	7.3	3.4	11.2	1.0	-2.5	4.5
Level 4	9.3	5.8	12.8	0.5	-2.8	3.8

Cf. = compared with.

IMD = Index of Multiple Deprivation

Appendix 10: Variables associated with HRQoL (with frailty in levels)

	EQ-5D Index			
	Multivariate Linear Regression of 943 individuals			
	Coef.	[95% conf. interval]		*P*
Age	0.01	0.0002	0.02	0.045
Female (cf.) Men	-0.02	-0.04	-0.003	0.020
Frailty				
Low	[ref]			
Medium	-0.04	-0.06	-0.02	<0.001
High	-0.1	-0.1	-0.1	
Life-space	0.01	-0.01	0.03	0.319
Frailty#Life-space				
Low	[ref]			
Medium	0.02	-0.002	0.04	<0.001
High	0.06	0.03	0.08	
Loneliness	-0.01	-0.04	0.01	0.304
Lives alone	-0.01	-0.03	0.01	0.544
Care package				
None	[ref]			
Weekly	-0.9	-0.2	-0.01	<0.001
Daily/multiple times daily	-0.1	-0.2	-0.1	
Alcohol intake				
Daily	[ref]			
Weekly	-0.001	-0.02	0.02	0.674
Monthly or less	-0.01	-0.03	0.01	

Cf. = compared with.

Appendix 11: Long term conditions used to define multimorbidity in the Care City Dataset

Atrial Fibrillation
Asthma
Cancer
Coronary Heart Disease
Chronic Obstructive Pulmonary Disease
Dementia
Depression
Diabetes
Epilepsy
Heart Failure
Hypertension
Hypothyroidism
Mental Health
Palliative Care
Stroke
Learning Difficulty

Appendix 12: Year 1 survival analysis adjusted for acute admissions, demographic, general health and health-related behaviour variables

	Coef.	lower 95%	upper 95%	P
Acute admissions				
None	[ref]			
One or two	4.7	3.1	7.1	***
Three or more	10.1	6.3	16.1	***
Multimorbidity				
None	[ref]			
One condition	1.3	1.0	1.6	*
Two or three conditions	2.2	1.8	2.7	***
Four or more conditions	4.2	3.4	5.3	***
Age (years)	1.1	1.1	1.1	***
IMD (score)	1.0	0.9	1.0	
Men cf. women	1.4	1.3	1.5	***
Smoking status				
Non-smoker	[ref]			
Ex-smoker	1.2	1.1	1.3	***
Smoker	1.6	1.4	1.8	***
Unknown	1.3	0.7	2.2	
BMI				
Normal	[ref]			
Morbidly obese	0.9	0.7	1.2	
Obese	0.6	0.6	0.7	***
Overweight	0.7	0.7	0.8	***
Underweight	1.9	1.6	2.2	***
Ethnicity				
White	[ref]			
Asian	0.8	0.7	1.0	*
Black	0.8	0.6	1.0	.
Mixed	0.9	0.6	1.4	

Other	0.7	0.4	1.1	
Unknown	1.4	1.0	1.9	.
Total prescription (count)	1.0	1.0	1.0	*
One or two acute admissions # One condition	0.9	0.5	1.4	
Three or more acute admissions # One condition	0.7	0.4	1.2	
One or two acute admissions # Two or three conditions	0.7	0.4	1.0	.
Three or more acute admissions # Two or three conditions	0.6	0.3	0.9	*
One or two acute admissions # Four or more conditions	0.5	0.3	0.8	**
Three or more acute admissions # Four or more conditions	0.3	0.2	0.5	***

Note: *p<0.1; **p 0.05; ***p<0.01

cf: compared with

BMI: Body Mass Index

IMD: Index of Multiple Deprivation

Appendix 13: Year 2 survival analysis adjusted for acute admissions, demographic, general health and health-related behaviour variables

	Coef.	lower 95%	upper 95%	P
Acute admissions				
None	[ref]			
One or two	5.5	3.2	9.4	***
Three or more	20.9	12.9	34.1	***
Multimorbidity				
None	[ref]			
One condition	1.3	1.0	1.8	.
Two or three conditions	2.6	2.0	3.5	***
Four or more conditions	5.6	4.1	7.6	***
Age (years)	1.1	1.1	1.1	***
IMD (score)	1.0	0.9	1.0	.
Men cf. women	1.3	1.2	1.5	***
Smoking status				
Non-smoker	[ref]			
Ex-smoker	1.2	1.1	1.4	***
Smoker	1.4	1.2	1.6	***
Unknown	1.3	0.7	2.5	
BMI				
Normal	[ref]			
Morbidly obese	0.8	0.6	1.0	.
Obese	0.6	0.5	0.7	***
Overweight	0.7	0.6	0.8	***
Underweight	1.9	1.6	2.2	***
Ethnicity				
White	[ref]			
Asian	1.0	0.8	1.2	
Black	0.9	0.7	1.2	
Mixed	0.6	0.3	1.2	
Other	0.4	0.2	0.9	*

Unknown	1.3	0.9	1.9	
Total prescription (count)	1.0	1.0	1.0	***
One or two acute admissions # One condition	1.2	0.7	2.2	
Three or more acute admissions # One condition	0.7	0.4	1.2	
One or two acute admissions # Two or three conditions	0.9	0.5	1.6	
Three or more acute admissions # Two or three conditions	0.4	0.2	0.7	***
One or two acute admissions # Four or more conditions	0.6	0.3	1.1	.
Three or more acute admissions # Four or more conditions	0.3	0.2	0.5	***

Note: *p<0.1; **p 0.05; ***p<0.01

cf: compared with

BMI: Body Mass Index

IMD: Index of Multiple Deprivation

Appendix 14: Year 3 survival analysis adjusted for acute admissions, demographic, general health and health-related behaviour variables

	Coef.	lower 95%	upper 95%	P
Acute admissions				
None	[ref]			
One or two	13.9	6.9	27.9	***
Three or more	28.0	12.7	61.6	***
Multimorbidity				
None	[ref]			
One condition	1.6	0.9	2.7	.
Two or three conditions	3.6	2.2	5.8	***
Four or more conditions	12.0	7.3	19.7	***
Age (years)	1.0	1.0	1.1	***
IMD (score)	1.0	0.9	1.0	
Men cf. women	1.3	1.1	1.5	***
Smoking status				
Non-smoker	[ref]			
Ex-smoker	1.1	0.9	1.3	
Smoker	1.3	1.0	1.6	*
Unknown	18.3	5.8	58.2	***
BMI				
Normal	[ref]			
Morbidly obese	0.9	0.6	1.3	
Obese	0.5	0.4	0.7	***
Overweight	0.7	0.6	0.8	***
Underweight	1.7	1.4	2.2	***
Ethnicity				
White	[ref]			
Asian	1.1	0.8	1.4	
Black	0.9	0.6	1.3	
Mixed	0.3	0.1	1.4	
Other	0.1	0.02	1.0	*

Unknown	1.8	1.2	2.8	**
Total prescription (count)	1.0	1.0	1.0	***
One or two acute admissions # One condition	1.0	0.4	2.2	
Three or more acute admissions # One condition	0.9	0.4	2.3	
One or two acute admissions # Two or three conditions	0.7	0.4	1.6	
Three or more acute admissions # Two or three conditions	0.7	0.3	1.5	
One or two acute admissions # Four or more conditions	0.4	0.2	0.8	*
Three or more acute admissions # Four or more conditions	0.3	0.1	0.7	**

Note: *p<0.1; **p 0.05; ***p<0.01

cf: compared with

BMI: Body Mass Index

IMD: Index of Multiple Deprivation