Measuring multimorbidity using Australian linked administrative health data sources

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Measuring multimorbidity using Australian linked administrative data sources

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Measuring multimorbidity using Australian linked administrative data sources

Thesis submission for the degree of Doctor of Philosophy

Thesis Title and Abstract | Declarations | Inclusion of Publications Statement | Corrected Thesis and Responses

Thesis Title

Measuring multimorbidity using Australian linked administrative health data sources

Thesis Abstract

The growing number of individuals living with multimorbidity – the presence of two or more chronic conditions – is a challenge facing many healthcare systems internationally. Multimorbidity has been hailed a priority for research and practice, but Australian studies of multimorbidity are impeded by the lack of national primary care data, data silos, researcher access to data, and limited information contained within the data that are available.

This thesis demonstrates how data linkage can be used to enhance the understanding of multimorbidity and its outcomes via a series of studies using Australian linked data sources, including claims-based, cohort study and clinical registry datasets for residents of NSW, Australia's most populous state.

Thesis studies found variations in the recording of common health conditions between hospitals, under ascertainment of multimorbidity in administrative data, and differences in the estimates of multimorbidity dependent on the data used. Thesis studies also showed we can enhance our understanding of multimorbidity by exploring related concepts of patient risk and complexity. Within administrative hospital inpatient data, one-third of hospitalised patients had both multimorbidity and elevated risks of frailty – and these patients had worse outcomes than those with one or neither factor. The addition of clinical registry data also improved risk adjustment for hospital readmission performance indicators for total knee and hip replacement over and above models including multimorbidity measured using administrative hospital inpatient data.

The research presented here highlights the benefits of the use of linked data in Australian multimorbidity research in three ways. Firstly, it underlines the need for incorporation of chronic disease information from multiple databases, including self-reported, inpatient, and claims-based data to accurately capture the extent of chronic disease and to identify people with multimorbidity. Secondly, it emphasises the need to examine complexities in the interplay between drivers of adverse outcomes – including multimorbidity, frailty and clinical assessment of a patient's overall health – in identifying patients with increased risk of complications and informing future hospital resource planning. And thirdly, it demonstrates the value of integrating new data sources, such as clinical registries with linked administrative data for improving risk-adjustment of hospital performance measures.

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Publication Details #1

Full Title:	Variation in the recording of common health conditions in routine hospital data: study using linked survey and administrative data in New South Wales, Australia
Authors:	Lujic S, Watson DE, Randall DA, Simpson JM, Jorm LR
Journal or Book Name:	BMJ Open
Volume/Page Numbers:	4:e005768
Date Accepted/Published:	First published September 3, 2014
Status:	published
The Candidate's Contribution to the Work:	I had the overall responsibility for the design of this study, data management, carrying out the statistical analysis, interpreting results, drafting the initial manuscript, and reviewing and revising the manuscript in response to co-authors and reviewers. Co-authors Diane Watson and Louisa Jorm contributed to the conception and design of the study. Louisa Jorm helped with data acquisition and provided oversight for all analyses. Deborah Randall and Judy Simpson provided oversight and advice for the design and interpretation of the statistical analyses. All authors read and approved the final version as published.
Location of the work in the thesis and/or how the work is incorporated in the thesis:	Published paper is included in lieu of thesis chapter, and is presented in Chapter 4 of the thesis.

Publication Details #2

Full Title:	Multimorbidity in Australia: Comparing estimates derived using administrative data sources and survey data
Authors:	Lujic S, Simpson JM, Zwar N, Hosseinzadeh H, Jorm LJ
Journal or Book Name:	PLoS ONE
Volume/Page Numbers:	12(8)
Date Accepted/Published:	Published 29 August 29, 2017
Status:	published
The Candidate's Contribution to the Work:	I conceptualised and designed the study with the help from co-authors. I carried out data curation and management, performed statistical analysis and visualisations, drafted the initial manuscript, and reviewed and revised the manuscript following co-authors' and reviewers' comments. Louisa Jorm acquired the data. Supervisors (Louisa Jorm and Judy Simpson) provided oversight of the analysis and contributed to the study result interpretations. Co-authors Nicholas Zwar and Hassan Hosseinzadeh provided advice on the study interpretation.
Location of the work in the thesis and/or how the work is incorporated in the thesis:	Published paper is included in lieu of thesis chapter, and is presented in Chapter 5 of the thesis.

Publication Details #3

Full Title:	Interaction effects of multimorbidity and frailty on adverse health outcomes in elderly hospitalised patients
Authors:	Lujic S, Randall DA, Simpson JM, Falster OM, Jorm LJ
Journal or Book Name:	Scientific Reports
Volume/Page Numbers:	
Date Accepted/Published:	
Status:	submitted
The Candidate's Contribution to the Work:	I conceived and designed the study with oversight from all other authors. I performed the statistical analyses, interpreted results, drafted the initial manuscript and reviewed and revised the manuscript following advice from co-authors. Louisa Jorm acquired the data. Deborah Randall, Judy Simpson and Michael Falster supervised the statistical analyses and reviewed the manuscript. Deborah Randall performed the initial data cleaning of the IHOPE dataset. All authors read and approved the submitted version, as presented in the thesis.
Location of the work in the thesis and/or how the work is incorporated in the thesis:	Submitted paper is included in lieu of thesis chapter, and is presented in Chapter 6 of the thesis.

Candidate's Declaration

I confirm that where I have used a publication in lieu of a chapter, the listed publication(s) above meet(s) the requirements to be included in the thesis. I also declare that I have complied with the Thesis Examination Procedure.

Author Contribution

I undertook this thesis as a part-time student during 30 April 2012 – 28 May 2021, with maternity leave and pandemic disruption in between.

The work contained in the body of this thesis is result of my own ideas. Co-author contributions are listed below, with further details in Chapters 4 – 7.

Chapter 4 is published in *BMJ Open*. I had the overall responsibility for the design of this study, data management, statistical analysis, drafting the initial manuscript, and reviewing and revising it. Co-authors Diane E Watson (DEW) and Louisa R Jorm (LRJ) contributed to the conception and design of the study. LRJ helped with data acquisition and provided oversight for all analyses. Deborah R Randall (DAR) and Judy M Simpson (JMS) provided oversight and advice for the design and interpretation of the statistical analyses.

Chapter 5 is published in *PLoS One*. I conceptualised and designed the study with the help from co-authors. I curated and analysed the data, drafted initial manuscript, and reviewed and revised it following co-authors' and reviewers' comments. Co-authors of the study, JMS, LJ, Nicholas Zwar and Hassan Hosseinzadeh helped with conceptualisation, methodology, supervision and reviewing and editing of the manuscript.

Chapter 6 is under review in *Scientific Reports*. I conceived and designed the study, performed the statistical analyses, interpreted results, drafted the initial manuscript and reviewed and revised the manuscript following input from other co-authors. Co-authors DAR, JMS, LRJ and Michael O Falster (MOF) contributed to the design and methodology, supervision, interpretation of findings, reviewing and editing of the manuscript.

Chapter 7 is being prepared for submission to the *Medical Journal of Australia*. I conceived and designed the study with oversight from my supervisors. Data management, statistical analyses and full draft of the paper were also done by me. Ian Harris provided clinical advice and contributed to the result interpretation. Michelle Lorimer prepared the AOANJRR data extraction and edited the draft manuscript.

Abstract

The growing number of individuals living with multimorbidity – the presence of two or more chronic conditions – is a challenge facing many healthcare systems internationally. Multimorbidity has been hailed a priority for research, medical practice, and health policy reform, but Australian studies of multimorbidity are impeded by the lack of national primary care data, data silos, researcher access to data, and limited information contained within the data that are available.

This thesis demonstrates how data linkage can be used to enhance the understanding of multimorbidity and its outcomes via a series of studies using Australian linked data sources, including claims-based, cohort study and clinical registry datasets for residents of NSW, Australia's most populous state.

Thesis studies found variations in the recording of common health conditions between hospitals, under ascertainment of multimorbidity in administrative data, and differences in the estimates of multimorbidity dependent on the data used. Thesis studies also showed we can enhance our understanding of multimorbidity by exploring related concepts of patient risk and complexity. Within administrative hospital inpatient data, one-third of hospitalised patients had both multimorbidity and elevated risks of frailty – and these patients had worse outcomes than those with one or neither factor. The addition of clinical registry data also improved risk adjustment for hospital readmission performance indicators for total knee and hip replacement over and above models including multimorbidity measured using administrative hospital inpatient data.

The research presented here highlights the benefits of the use of linked data in Australian multimorbidity research in three ways. Firstly, it underlines the need for incorporation of chronic disease information from multiple databases, including self-reported, inpatient, and claims-based data to accurately capture the extent of chronic disease and to identify people with multimorbidity. Secondly, it emphasises the need to examine complexities in the interplay between drivers of adverse outcomes – including multimorbidity, frailty and clinical assessment of a patient's overall health – in identifying patients with increased risk of complications and informing future hospital resource planning. And thirdly, it demonstrates the value of integrating new data sources, such as clinical registries with linked administrative data for improving risk-adjustment of hospital performance measures,

with potentially much wider applications in health outcomes research and program evaluation.

With a policy focus on patient-centred care, and burgeoning new sources of clinical data including registries and electronic health records, the importance of cross sectoral and cross jurisdictional data linkage has never been greater. Availability and use of these data will be crucial for bettering patient outcomes and experience and providing an evidence base to support service providers and health system planners in (re)designing care to benefit the Australian population.

Acknowledgements

I would like to express my gratitude to a variety of individuals involved in my scholarly journey.

My first and deepest gratitude is to my supervisors – Louisa Jorm, Judy Simpson and Michael Falster – for their expertise, encouragement and generosity. Louisa planted the PhD seed, and has been nothing short of an inspiring boss, mentor, and supervisor, providing opportunities novice researchers can only dream of. Judy guided and mentored me since my days as a trainee biostatistician and has instilled the importance of rigour and sound statistical practice in both my work and study. I am deeply grateful to Michael for his support, advice, encouragement, and guidance, particularly during the latter parts of the candidature. It has been a privilege to be guided and supported by such incredible supervisors.

This research would not have been possible without linked data. I am grateful to the NSW Ministry of Health, the Sax Institute, Department of Human Services, Australian Orthopaedic Association National Joint Replacement Registry for data provision, the NSW Centre for Health Record Linkage for data linkage, and thousands of participants in the 45 and Up Study.

I would like to thank my co-authors of the papers included in this thesis for their thoughtful comments, valuable insights, and contributions. I am particularly immensely grateful to Deborah Randall for her help, support and advice and exemplary work on the IHOPE data and project management.

Studying and working with researchers from multiple disciplines at the Centre for Big Data Research in Health at UNSW, and the Centre for Health Research at the Western Sydney University has been gratifying. I would like to thank my colleagues, Duong Tran, Alys Havard, Louise Francis, Melisa Litchfield, Oscar Perez Concha and Mark Hanly, for their ongoing support, encouragement and advice.

My final thanks are to my friends and family for their continued and unwavering support. My husband Dragan and daughter Lana have been my biggest fans and sources of moral and emotional support. I started my PhD journey solo and finished it with two incredible humans by my side. My great sources of inspiration have been my parents and my brother, who have taught me the value of kindness, resilience, and hard work. Thank you for your strength and belief. This one is for you.

Contents

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List of Abbreviations

ACG	Adjusted Clinical Groups
ACS	Australian Coding Standards
ACSQHC	Australian Commission on Safety and Quality in Health Care
AH&MRC	Aboriginal Health and Medical Research Council
AIHW	Australian Institute of Health and Welfare
ALSWH	Australian Longitudinal Study on Women's Health
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
APDC	Admitted Patient Data Collection
APHID	Assessing Preventable Hospitalisation InDicators
aRR	Adjusted relative risk
ASA	American Society of Anaesthesiologists
ATC	Anatomical Therapeutic Chemical
AUC	Area under the receiver operating characteristic curve
BEACH	Bettering the Evaluation and Care of Health
CHeReL	Centre for Health Record Linkage
CCI	Charlson Comorbidity Index
CDS	Chronic Disease Score
CI	Confidence Interval
CIRS	Cumulative Illness Rating Scale
COSmm	Core Outcome Set for Multimorbidity Research
CQR	Clinical quality registries
DRG	Diagnosis Related Group

eFI	Electronic Frailty Index
EHR	Electronic health record
EOC	Episode of care
GP	General practitioner
HFRS	Hospital Frailty Risk Score
HREC	Human Research Ethics Committees
ICC	Intraclass correlation coefficient
ICD-10	International Statistical Classification of Diseases and Health Related Problems, 10th Revision
ICD-10-AM	International Statistical Classification of Diseases and Health Related Problems, 10th Revision, Australian Modification
ICED	Index of Coexistent Disease
IHOPE	Indigenous Health Outcomes Patient Evaluation
IQR	Interquartile range
MBS	Medicare Benefits Schedule
MLK	Master Linkage Key
MOR	Median odds ratio
NHMD	National Hospital Morbidity Database
NHMRC	National Health and Medical Research Council
NICE	National Institute for Health and Care Excellence
NIHSI	National Integrated Health Services Infrastructure
NSW	New South Wales
OR	Odds Ratio
PBS	Pharmaceutical Benefits Schedule
PHSREC	NSW Population and Health Services Research Ethics Committee

POS	Period of stay
RR	Relative Risk
RBDM	Registry of Births, Deaths and Marriages
SLA	Statistical Local Area
THA	Total hip arthroplasty
TKA	Total knee arthroplasty
UK	United Kingdom
US	United States
VPC	Variance partitioning coefficient
WHO	World Health Organisation

Publications, presentations

Publications

Published

Paper 1 **Lujic S**, Watson DE, Randall DA, Simpson JM, Jorm LR. Variation in the recording of common health conditions in routine hospital data: study using linked survey and administrative data in New South Wales, Australia. *BMJ Open*. 2014;4(9):e005768.

Paper2 **Lujic S**, Simpson JM, Zwar N, Hosseinzadeh H, Jorm LJ. Multimorbidity in Australia: Comparing estimates derived using administrative data sources and survey data. *PLoS ONE*. 2017;12(8).

Under review

Paper 3 **Lujic S,** Randall DA, Simpson JM, Falster OM, Jorm LJ. Interaction effects of multimorbidity and frailty on adverse health outcomes in elderly hospitalised patients (*Scientific Reports*)

Preparing for submission

Paper 4 **Lujic S,** Falster MO, Simpson JM, Jorm LJ. Complementing administrative data with clinical registries: an example using total hip (THA) and total knee arthroplasty (TKA) readmission rates for performance measurement. (*Medical Journal of Australia*)

Related co-authored publications

- Aitken SJ, **Lujic S**, Randall DA, Noguchi N, Naganathan V, Blyth FM. Predicting outcomes in older patients undergoing vascular surgery using the Hospital Frailty Risk Score. *Br J Surg*. 2020; Oct 9
- Havard A, Straka P, Sara G, **Lujic S**, Tran DT, Jorm LR. Identifying patients using antidepressants for the treatment of depression: A predictive algorithm for use in pharmaceutical and medical claims data. *Pharmacoepidemiol Drug Saf*. 2019;28(3):354-61

- Randall DA, **Lujic S**, Havard A, Eades SJ, Jorm L. Multimorbidity among Aboriginal people in New South Wales contributes significantly to their higher mortality. *MJA*. 2018;209(1):19-23.

Related co-authored reports

- **Lujic, S.**, Raichand, S., Jorm, L. (2015) Rapid literature review of readmission indicators for CHBOI 4: developments since 2010. Commissioned by the Australian Commission on Safety and Quality in Health Care. UNSW Centre for Big Data Research in Health, Sydney.
- **Lujic, S**., Liu, A., Jorm, L. (2015) Rapid literature review of hospital-based mortality outcome indicators: developments since 2013. Commissioned by the Australian Commission on Safety and Quality in Health Care. UNSW Centre for Big Data Research in Health, Sydney.

Presentations (conference)

- **Lujic S**, Watson D, Jorm L: Validation of morbidity, smoking and obesity codes in the NSW hospitalisation data. *45 and Up Collaborators meeting*, Sydney, 2012
- **Lujic S,** Jorm L: Multimorbidity in older Australians: patterning by age, sex and socioeconomic status. *Health Services and Policy Research conference*, Wellington, New Zealand 2013.
- **Lujic S,** Jorm L: Multimorbidity in older Australian. *45 and Up Collaborators meeting* Sydney, 2013.
- **Lujic S**, Jorm L, Randall D: Variations in the level of recording of common health conditions and risk factors in hospital morbidity data. *Health Services and Policy Research conference*, Wellington, New Zealand 2013.
- **Lujic S**, Jorm L, Randall D: Using hospital data to identify comorbidity and multimorbidity in Australia. *Scottish Health Informatics Program (SHIP) conference*, St Andrews, Scotland 2013.
- **Lujic S**, Jorm L: Variations in the level of recording of common health conditions and risk factors in hospital morbidity data. *International Health Data Linkage conference*, Vancouver, Canada 2014.

Presentations (invited talks and seminars)

- **Lujic S**, Havard A. The accuracy of identifying smoking and obesity from hospital data: Can smokers and obese patients be correctly identified through hospital admission histories? *NSW Ministry of Health* (invited talk), October 2012
- **Lujic S.** Using hospital data to identify comorbidity and multimorbidity in older NSW residents. *Centre for Positive Psychology and Education* (invited talk), University of Western Sydney, November 2013
- **Lujic S.** Identifying multimorbidity using administrative data in NSW. *Capital Markets cooperative research centre* (invited talk), April 2015
- **Lujic S**. Variations in the level of recording of common health conditions and risk factors in hospital morbidity data. *School of Mathematics and Statistics* (invited talk), UNSW, September 2015
- **Lujic S**. Variations in the recording of common health conditions and risk factors in hospital morbidity data. *National Centre for Classification in Health* (invited talk), University of Sydney, November 2015
- **Lujic S.** Multimorbidity in NSW: comparing estimates derived using administrative data sources and survey data, *Centre For Big Data Research in Health PhD presentations*, November 2016
- **Lujic S**, Multimorbidity and frailty as drivers of adverse health outcomes in elderly hospitalised patients. *The Kolling Institute* (invited talk), July 2019
- **Lujic S**. Contributions of multimorbidity and frailty to adverse health outcomes in elderly hospitalised patients. *Centre for Big Data Research in Health Surgical Outcomes teams meeting*, September 2020
- **Lujic S.** Synergistic effects of multimorbidity and frailty to adverse health outcomes in elderly hospitalised patients, *Centre for Big Data Research in Health PhD seminar*, October 2020
- **Lujic S.** Complementing administrative data with clinical registries: an example using THA/TKA readmission rates for hospital performance measurement. *Enhancing Joint Replacement Outcomes through National Data Linkage research meeting*, March 2021

CHAPTER 1

Background and Overview

1.1 Background

Ageing populations and increases in longevity due to advances in medical care and prevention contribute to the growing proportion of people with multiple concurrent chronic diseases ('multimorbidity'). These people have demonstrably worse health outcomes than others. The increasing prevalence of multimorbidity has been accompanied by a shift in the way health care professionals and researchers conceptualise the interplay between personal, social and health characteristics, met and unmet needs for health care and health outcomes. A move from a disease-centric concept of comorbidity, where one condition is the principal focus and other conditions are considered as additional to this, to a person-centric concept of multimorbidity, has been gaining momentum over the past decade.

Initial research into multimorbidity centred on its epidemiology – incidence, prevalence and associated risk factors – gradually moving to examining outcomes and exploring disease clustering and disease trajectories. Studies of the relationships between multimorbidity, acuity and frailty have also started to appear in recent years. However, most international studies of multimorbidity focus on community and primary care settings and studies in acute care settings are scarce. [1]

Australian research on multimorbidity and its impacts on health outcomes is hampered by gaps in routine data collections. Australian primary care claims data lack information on diagnoses or reasons for service encounter, restricting Australian research on multimorbidity in primary care settings. Representative national surveys of general practitioners (GPs) and their patient encounters conducted under the Bettering the Evaluation and Care of Health (BEACH)[2] program helped fill the gap in primary care data, but BEACH ceased in 2016.[3] Also, although BEACH collected data about an extensive list

of morbidities, it did not ascertain patient outcomes post visit. Australian inpatient data, on the other hand, provide means of examining patient and care outcomes, but only capture diagnoses recorded during the inpatient encounter.

Furthermore, Australian's health system is a complex mix of public and private hospitals, primary health care services and referred medical services, with multiple sources of funding and multiple legislative and contractual frameworks. Data collection and stewardship is distributed across state, territory and Commonwealth agencies, limiting data sharing between sectors. This siloing has created an imperative for linkage of health data collections over time and across sectors, in order to understand longitudinal patterns of morbidity and outcomes for the Australian population.

Australia has a potential treasure trove of health data, which is becoming more readily available for research and policy guidance purposes. The availability of linked health data, encompassing routinely collected administrative data, clinical registries and survey data, provides an avenue for multifaceted multimorbidity research spanning incidence and prevalence of multimorbidity and exploration of patient outcomes. Studies in this thesis provide examples of ways in which big data can be used to measure and explore multimorbidity, and point to new avenues for policy-relevant research using these data.

1.2 Thesis aims and research questions

The overall aim of this thesis is to explore measurement of multimorbidity, its interplay with frailty, and associations with outcomes via a series of studies using Australian linked health data sources. More specifically, the thesis addresses the following questions:

1. What is the agreement between self-reported health conditions and coded diagnoses in routine hospital inpatient data? What patient- and hospital-factors explain this agreement?
2. Do multimorbidity prevalence estimates vary according to data source? Are different individuals identified as multimorbid using different data sources?
3. What effects do the different measures of multimorbidity and frailty have on adverse patient outcomes? How do multimorbidity and frailty interact?
4. How does multimorbidity contribute to variations in hospital-level outcome indicators used for performance measurement? Does the addition of variables from

clinical registries improve predictive ability (discriminative performance) of models used to monitor health performance metrics?

1.3 Thesis outline

This thesis presents two published scientific papers, one manuscript under review and one manuscript being prepared for submission. These make up the four main analytical chapters of the thesis, each presenting original research. The remaining chapters introduce the work, give details of the methods used within each of the four studies, and discuss the main findings and their implications for practice, and further research.

The main datasets used, and outputs, for the analytic chapters are summarised in Table 1.1. Each of the analytic chapters is prefaced by preamble describing aims and key findings.

1.4 Candidate contribution

I developed the research questions and designed the analysis plans for each of the four studies, under the guidance of my supervisors. I performed all data management and curation, variable checking and construction, carried out statistical analyses, drafted each of the manuscripts, incorporated feedback from co-authors, and managed the processes of article submission and responding to reviewers' comments.

Table 1.1 Thesis structure

Chapter 1 Overview

- Provides a brief background to the thesis and outlines its structure

Chapter 2 Introduction

- Overview of the existing literature on multimorbidity and the use of administrative data in health research

Chapter 3 Methods

- Key methods used in the thesis, including statistical methods and key concept measures.

Chapter 4 Variation in recording of health conditions

- Study 1 - published in *BMJ Open*
- Data sources used: Survey + hospital data

Chapter 5 Measuring multimorbidity in administrative data

- Study 2 - published in *PLoS ONE*
- Data sources used: Survey + hospital data + medication dispensing data

Chapter 6 Interaction of multimorbidity and frailty

- Study 3 - under review in *Scientific Reports*
- Data sources used: Hospital data + deaths

Chapter 7 Supplementing administrative data with clinical registry

- Study 4 - in preparation for submission to *Medical Journal of Austrlia*
- Data sources used: Hospital data + deaths + national joint replacement registry

Chapter 8 Discussion

- Discusses the main findings, outlines their implications for policy and practice, and provides suggestions for future research direction

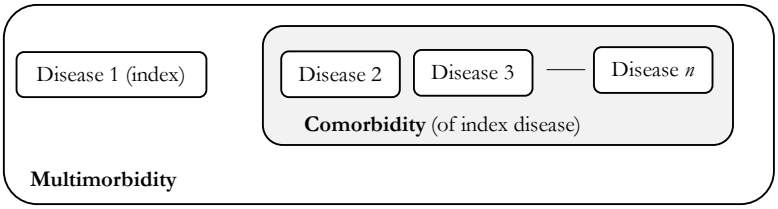
CHAPTER 2

Introduction

2.1 What is multimorbidity?

Ageing populations, coupled with advances in medical care and prevention, are contributing to a growing proportion of people with multiple concurrent health conditions – multimorbidity. The term multimorbidity was coined in the late 1990s by van den Akker et al.,[4] to distinguish between an index disease with comorbidities (additional entities that co-exist with an index disease under study) and examination of all morbidities within an individual (Figure 2.1). In this definition, multimorbidity was deemed as "the co-occurrence of multiple chronic or acute diseases and medical conditions within one person".[4] In 2010, Boyd and Fortin further simplified the definition to "co-occurrence of two or more chronic conditions, where one is not necessarily more central than the others".[5] This delineation marked the move from disease-centric to person-centric exploration of morbidities, recognising the growing number of patients with complex care needs, which should not be treated in isolation.

Figure 2.1 Multimorbidity and comorbidity distinction

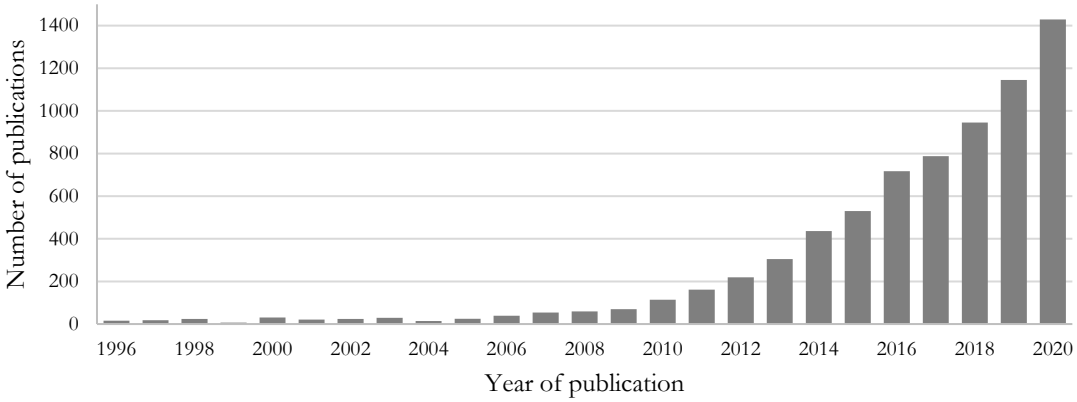


Adapted from Valderas et al.[6]

In recognition of the growing issues faced by patients with multimorbidity and their care providers, research on multimorbidity has increased rapidly over the past decade. Over 80% of articles listing multimorbidity as a keyword are published from 2010 onwards (Figure 2.2). The introduction of a Medical Subject Heading (MeSH) 'multimorbidity' ("the complex interactions of several coexisting diseases") in 2018 has helped distinguish it from comorbidity, a distinct MeSH, described as "the presence of coexisting or additional

diagnoses with reference to an initial diagnosis or with reference to index condition that is the subject of the study".[7]

Figure 2.2 Rise in the number of publications with multimorbidity as keyword



Source: PubMed search: (multimorbidity) OR (multi-morbidity) OR (multimorbid), March 2021

2.1.1. How is multimorbidity measured?

Multimorbidity has been hailed by the editors of the Lancet as "the next major health priority".[8] However there is no clear consensus on how it should be defined and measured, which has hampered both research and actions to improve care for patients with multimorbidity.[9,10]

The measurement of multimorbidity is subject to considerable confusion. This is in part due to the variations in the reasons for measuring and capturing multimorbidity. The most common purposes for multimorbidity measurement, identified by Nicholson et al.[11] and Suls et al.[12] include: 1) tracking population health, 2) identifying associations between multimorbidity and health outcomes, 3) predicting outcomes for individual patients or health facilities, 4) understanding patterns of co-occurrence of conditions and interactions between them, 5) adjusting for confounding effects of multimorbidity in studies exploring the impact of other factors on health outcomes and 6) predicting multimorbidity as an outcome. The method for measuring multimorbidity will vary based on the purpose for which it is being used, which has prompted recent guidance for aligning the choice of the measure with the measurement purpose.[12]

Variations in the existing measures of multimorbidity are multifaceted. Several systematic reviews[10, 13, 14] focusing on the definitions and measurement of multimorbidity (Table 2.1)

found that, while there is consensus in the literature on the definition of multimorbidity as the presence of multiple chronic conditions, there are inconsistencies in what constitutes a chronic condition, what number of conditions should be used, and how these conditions are measured. Lack of consensus on these elements of multimorbidity has prompted suggestions for its operationalisation via a standardised list of chronic conditions.[15, 16]

Table 2.1. Systematic reviews of multimorbidity definition and measurement

Author	Time period	Keywords	Objective	Findings	Conclusions
Definition of multimorbidity					
Willadsen *et al.* 2016[13]	Inception – 2013	Comorbidity AND multimorbidity	Definition and role of disease, risk factors and symptoms	163 articles on conditions commonly studied (diseases, risk factors and symptoms)	Between 4 and 137 conditions studied, including diseases, risk factors and symptoms. 71% of articles used individually constructed definition of multimorbidity, 18% used morbidity indices (not specifically for multimorbidity). Risk factors such as hypertension, osteoporosis, hypercholesterolemia, obesity, and overweight included in 85% of the studies. (Elixhauser Index not included)
Johnston *et al.* 2018[10]	Inception – 2017	Multimorbidity AND review	Definition and measurement of multimorbidity	Systematic review of reviews on definitions and measurement	The choice of the measure and its definition should be specified, with the choice of the measure based on outcome studied. If no validated measure available, disease count use is appropriate

Table 2.1. Systematic reviews of multimorbidity definition and measurement, *cont.*

Author	Time period	Keywords	Objective	Findings	Conclusions
Measurement of multimorbidity					
De Groot *et al.* 2003[17]	1966 – 2000	Comorbidity, multimorbidity, coexistent disease	Comorbidity measurement for use in RCTs and prognostic trials	13 measures: 1 disease count and 12 indices; 9/13 generic measures (multimorbidity), 4 measures for comorbidity	Charlson Index (CCI), Cumulative Illness Rating Scale (CIRS), Index of Co-Existent Disease (ICED) and Kaplan Index found to be reliable measures of comorbidity
Diederichs *et al.* 2011[14]	1960 – 2009	Comorbidity, multimorbidity	Multimorbidity measurement	39 indices: - 21 associated with outcome - 18 weighted indices	150 different conditions identified across studies (ranging from 4 to 102 diseases). Selection of diseases based on high prevalence in the population with severe impact on affected people
Huntley *et al.* 2012[18]	Inception – 2009	Multimorbidity or comorbidity AND measures or indices AND ambulatory, outpatient, primary or community care or general, community population	Identify measures of multimorbidity and morbidity for use in research in primary and community populations	17 measures identified for use in primary and community setting	Diagnoses (n=13) and medication-based (n=4) measures identified. Disease counts, CCI, Adjusted Clinical Groups (ACG) System, CIRS, Chronic Disease Score (CDS) most used. Evidence for predictive ability differs by outcomes of interest: • Care utilisation – CCI, disease count, ACG • Costs – ACG • Mortality – CCI • Quality of life – CCI, disease counts
Sharabiani *et al.* 2012[19]	1987 – 2011	CCI, Elixhauser, comorbidity, casemix, mortality and morbidity	Comparison of comorbidity measures in use with administrative data	Measures/indices for use with administrative data, including adaptations of CCI and Elixhauser Index	Predictive ability of index/measure dependent on the patient group and outcome of interest, with indices better able to predict longer term outcome than short term. Elixhauser index performs better than CCI adaptations.

2.1.1.1 How are chronic conditions defined?

People with multimorbidity have multiple health problems. However, there are differences in the terminology used to describe these, with the terms *chronic disease* and *chronic condition* often used interchangeably, although each captures a different range of health problems.

The term *chronic disease* refers to the pathological process with underlying signs and symptoms,[20] with variations in the list of diseases included under the broad term of 'chronic disease' across studies and settings, as well as differences in how chronicity is measured.[21] Examples of the commonly used chronic diseases used for surveillance reporting include cardiovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes and cancer, to name a few.

Chronic conditions cover a broader spectrum of health issues, including physical medical conditions, mental health conditions, and substance and cognitive impairment disorders.[21, 22] The World Health Organisation uses the term chronic condition in its definition of multimorbidity,[23] in line with the definitions of van den Akker et al.[4] and Boyd & Fortin.[5] Furthermore, a recent systematic review of the role of disease, risk-factors and symptoms in the definition of multimorbidity found that the majority (85%) of 163 articles reviewed included at least one chronic condition, such as hypertension, osteoporosis, hypercholesterolemia, overweight and obesity, in defining multimorbidity.[13]

In this thesis I consider multimorbidity to include a broader spectrum of health issues. The term *chronic condition* is therefore used in the thesis.

2.1.1.2 What data sources are used?

A variety of data sources can be used to capture multimorbidity. These can broadly be grouped into electronic health records (EHRs), administrative data, health surveys, with differences in the capture of conditions within each data source.

EHRs are the underlying data stored in the clinical information system for shared use by authorised providers in health care settings and are an electronic equivalent of the patient's history.[24] EHRs are a rich source of clinical information which may include demographics, health conditions, prescriptions, radiology images, and test results.[25] Health conditions can be abstracted from diagnoses selected from a structured medical dictionary,[24] coded by a range of healthcare providers, or by constructing algorithms including information from

diagnoses, medications and test results. However, they can be prone to misclassification and missing data leading to measurement errors or selection bias,[12, 24] and access, extraction, and analysis of EHRs can be time consuming and challenging. EHR data include information collected by both acute care and primary care services. Unless otherwise specified, the term EHR in this thesis is used to represent primary care EHR.

Administrative data are generated as a by-product of operating health services, and include hospital inpatient data, medical and pharmaceutical claims data, and pharmaceutical dispensing data. As these data provide comprehensive, and sometimes complete, coverage of real-world patient populations, they are increasingly being used for health research.[26] However, administrative data have limitations. Inpatient data contain limited information about illness severity, and are restricted in the number of diagnosed conditions recorded, potentially resulting in undercoding.[27-29] Furthermore, variations in coding systems, such as the version of the ICD used, maximum allowable coding fields and differences in how conditions are defined,[30] pose challenges for between-country comparisons. Medical claims data differ between countries and may not include the clinical information needed to ascertain morbidities. Pharmaceutical claims and dispensing data generally lack information about indication for which medication is prescribed,[31] posing challenges to identifying health conditions using medications that can be prescribed for differing uses.

Health surveys are used internationally for chronic disease monitoring and reporting. This information is generally collected via self-reported answers to a survey question along the lines "Have you ever been told by a doctor or other health professional that you have *(specific health condition)*?"[12] The list of conditions is usually short, capturing most prevalent diseases, sometimes of weak clinical specificity,[12] with responses prone to recall bias. These can lead to underestimation of chronic conditions and multimorbidity.

Bringing together information from multiple data sources can help enhance capture of multimorbidity and help overcome the disadvantages of single data sources outlined above. Administrative data sources have increasingly been linked together and with other data sources to provide a unique opportunity for research to generate evidence for complete population groups and track their outcomes over long time periods. This thesis leverages the power of linked data sources to explore the effects of multimorbidity and aspects of patient complexity on patient outcomes.

2.1.1.3 How many conditions are measured?

The lists of conditions used to define multimorbidity vary between studies,[32] due not only to the broader or narrower range of chronic diseases, that are formally diagnosed, but also to the variable inclusion of risk factors for developing disease and symptoms experienced by patients.[13] The lists of conditions used in multimorbidity literature comprise between four[33, 34] and 147[35] conditions. A systematic review of 21 prevalence studies of multimorbidity in primary care or the general population by Fortin et al.[32] reported that a minimum of 5 conditions in primary care and 7 in the general population were used. The authors[32] suggested that a minimum of 12 conditions be used for the estimation of multimorbidity as more homogeneity in the prevalence estimates was observed in studies that used at least 12 conditions.

A systematic review by Diederichs et al.[14] of 39 weighted multimorbidity indices using self-reported, physician reports, medical records and administrative data, reported that these included a median number of 14 conditions, with the majority of indices (87%) including between 6 and 25 chronic conditions. The authors concluded that at least 11 diagnoses (cancer, diabetes, depression, hypertension, myocardial infarction, chronic ischaemic heart disease, hart arrhythmias, heart insufficiency, stroke, COPD and arthritis) should be used in studies based on administrative data relying on International Classification of Disease (ICD) coded diagnoses, due to their high prevalence in inpatient and outpatient settings.[14]

The lack of uniformity in the list of conditions used has made comparisons between studies and populations difficult, resulting in calls to standardise methods to allow valid intra-study comparisons.[36] Comparison of multimorbidity prevalence estimates generated from different data collections for the same sample of individuals and the same set of chronic conditions is lacking, and this knowledge gap is addressed in **Chapter 5**.

2.1.1.4 How are multimorbidity measures constructed?

A variety of measures are used to identify multimorbidity. Simple counts of conditions are often presented as just the number of a select set of conditions, or dichotomised into patients being classified as multimorbid (e.g. two or more conditions) or not. Indices usually have conditions selected based on their impact on outcomes such as mortality, quality of life and resource utilisation, and can be presented in different formats (e.g. counts, individual conditions, a weighted score).[37] The choice of the measure is largely

guided by availability of data,[10, 12] the purpose for measurement and the outcomes of interest.

Indices used for measurement of multimorbidity in community and primary care settings are many, varied and growing over time. A 2012 systematic review[18] of 194 articles identified 17 different measures of multimorbidity for use in these settings, with measures performing differently for different outcomes. A 2020 systematic review,[38] in the same setting, identified 35 multimorbidity indices based on the index components of chronic conditions, medications, physiological measures, and outcomes encompassing information beyond simple counts of conditions. Both reviews highlight the need to select the measure based on the study purpose, outcome and setting in mind.

Measurement of multimorbidity using administrative data that include coded diagnoses is also varied and dependent on the outcome of interest. The most-used and best-known indices are the Charlson Index[39] and Elixhauser index,[40] developed to account for morbidities for specific purposes and within specific clinical populations. The Charlson Index was developed using data from *medical records* to classify comorbid conditions for use in longitudinal studies investigating prognostic burden of chronic diseases on mortality, and later adapted for use with administrative data.[41] The index originally contained 19 conditions selected as significant predictors of mortality. The Elixhauser Index was developed for use with *administrative inpatient data*, containing 30 conditions associated with mortality, increased length of stay and costs.[40]

The conditions included in the Charlson and Elixhauser indices differ. The Charlson Index does not contain any mental health comorbidities, which are found to be prevalent in multimorbid patients,[42] leading to underestimation of multimorbidity. And while there is partial overlap between the two indices (Table 2.2), there are diseases that are not covered by either,[19] leaving scope for the inclusion of other chronic conditions based on the relevance to the setting in which the research is carried out.

Systematic reviews of indices using administrative data[18, 19, 41] conclude that the choice of an index should be based on the population and outcome of interest. But the choice can also be driven the purpose of the study – be it prediction or explanation.[43] The drive to find the best morbidity index to predict adverse patient outcomes has seen myriad papers comparing the performance of Charlson and Elixhauser indices, as well as the development of new ones. However, the choice of the multimorbidity measure used when examining associations with outcomes should be based on the measure's purpose as suggested in the

systematic reviews.[19, 41] When no validated measure exists, or if multiple outcomes are considered within the same study, simple disease counts could be used.[10, 18]

Measurement of multimorbidity using medication prescription data is possible using medication-based indices, such as the Rx-Risk-V.[44] The index consists of 46 comorbidity categories, with Pratt et al.[45] providing mappings to WHO's Anatomical Therapeutic Chemical (ATC) Classification System for 42 morbidities for which medications can be prescribed. Although the Rx-Risk-V was shown to be a valid measure of comorbidity,[46] its use for measurement of individual chronic conditions is uncommon,[47] as medications can be prescribed for different indications.

In this thesis, a combination of simple counts and use of individual or combined indices was used to measure multimorbidity, driven by the data sources, study objectives and outcomes explored. Briefly, Chapters 4 and 5 use counts of patient reported chronic conditions, and Chapter 6 and 7 use a combination of Elixhauser and Charlson indices as they use administrative data sources. Further details on the measurement of multimorbidity are provided in **Chapter 3**.

Table 2.2. Comparison of Charlson and Elixhauser Index conditions

Condition[a]	Elixhauser Index	Charlson Index
Cancer		
Lymphoma	✓	
Malignancy	✓	✓
Metastatic cancer	✓	✓
Cardiovascular/blood		
Anticoagulation/coagulopathy	✓	
Cardiac arrhythmia	✓	
Cerebrovascular disease		✓
Congestive heart failure	✓	✓
Hypertension	✓	
Myocardial infarction		✓
Peripheral vascular disease	✓	✓
Pulmonary circulation disorders	✓	
Valvular disease	✓	

Table 2.2 Comparison of Charlson and Elixhauser Index conditions, *cont.*

Condition[a]	Elixhauser Index	Charlson Index
Endocrine		
Diabetes	✓	✓
Hyperthyroidism	✓	
Gastrointestinal		
Liver disease (mild)	✓	✓
Liver disease (severe) or failure		✓
Peptic ulcer disease	✓	✓
Musculoskeletal/pain related		
RA/collagen vascular disorder	✓	✓
Neurologic		
Dementia		✓
Epilepsy	✓	
Paralysis	✓	✓
Parkinson's	✓	
Other neurological disorders	✓	
Nutrition/obesity		
Anaemia	✓	
Fluid and electrolyte disorders	✓	
Obesity	✓	
Weight loss	✓	
Psychological/behavioural		
Alcohol abuse/dependence	✓	
Depression	✓	
Drug abuse	✓	
Psychotic illness/psychoses	✓	
Renal/urologic		
Renal disease/failure	✓	✓
Respiratory		
Chronic pulmonary disease	✓	✓
Miscellaneous		
HIV/AIDS	✓	✓

[a] adapted from Inacio *et al.*[48] ✓ - included in the index

2.1.1.5 Summary of measures of multimorbidity

The measurement of multimorbidity should be driven by the purpose of the measurement, outcomes of interest, study setting and availably of data sources.[12] Table below outlines examples of multimorbidity measurement approaches and selection of instruments, adapted from Suls et al.[12]

Table Examples of instruments used for multimorbidity measurement

Purpose	Setting	Example measurement options
Prevalence	Population	National health surveys National claims-based databases
	Primary care	GP questionnaires (e.g. BEACH[1] in Australia) Patient-based questionnaires (e.g. Fortin et al[49])
	Acute care	CIRS[50] CCI or adaptations Elixhauser Index – binary or weighted score
	Ambulatory care	ACG system
Predictor (covariate) of outcomes	Guidance on the instrument choice can be driven by comparisons of discriminative performance of the models[51] (e.g., AUC for binary outcomes) when more than one measure is considered.	
	Acute care	CCI Elixhauser Index
	Setting with prescription medication information available	Rx-Risk
	System-wide	Combination of diagnoses-based (CCI, EI) and medication-based indices (Rx-Risk)
Comparison of cumulative predictive ability of multimorbidity and other measures of patient complexity/severity	Examine interaction effects of covariates or use machine learning approaches such as regression and classification trees	
	System wide	Diagnoses-based (CCI, EI) or medication-based indices (Rx-Risk), or their combination, for multimorbidity ascertainment

Table Examples of instruments used for multimorbidity measurement, *cont.*

Purpose	Setting	Example measurement options
Patient prognosis	Use machine level approaches and examine prediction model performance[52] (e.g., c-statistic) when choosing the optimal prediction model.	
	System wide	Diagnoses-based (CCI, EI) or medication-based indices (Rx-Risk), or their combination, for multimorbidity ascertainment. Binary or continuous forms of measurements can be used, with choice of function form and interactions with other variables decided by machine learning algorithm, rather than an individual.

ACG – Adjusted Clinical Groups, CCI – Charlson Comorbidity Index, CIRS – Cumulative Illness Rating Scale, EI – Elixhauser Index

2.1.2 How is multimorbidity related to health outcomes?

Despite the variation in its definition, multimorbidity is consistently found to be associated with a range of adverse health outcomes, including higher mortality,[53-55] prolonged length of stay,[56, 57] increased potentially preventable hospitalisations,[58, 59] higher hospital readmission rates,[60] poorer quality of life,[61-63] increased disability,[54, 64-66] higher health care utilisation and costs[67-71] and increased patient safety incidents.[72] A range of other outcomes have also been studied in the literature, including functional decline, out-of-pocket medical costs and quality of care.[11]

Five meta-analyses[55, 72-75] of associations between multimorbidity and health outcomes have been published since 2015 (Table 2.3). These meta-analyses further highlight positive associations between multimorbidity and mortality,[55] frailty,[74] patient safety incidents,[72] and risks of depressive disorder.[73] Inverse association was found with quality of life.[75] Collective comparison of the pooled estimates from meta-analyses (Table 2.3) indicates that the strongest relationship with adverse outcomes is for active patient safety incidents,[72] including adverse drug events and medical complications. This is perhaps unsurprising given that multimorbidity is strongly associated with increased polypharmacy (the concurrent use of multiple medicines),[76] which can lead to adverse drug events.[77]

A Delphi consensus process involving an international panel of experts[78] identified 17 outcomes for inclusion in a Core Outcome Set for Multimorbidity Research (COSmm), with health-related quality of life, mental health outcomes and mortality regarded as essential core outcomes. Other identified outcomes include patient-reported outcome

measures (PROMs), such as self-rated health, self-management behaviour, treatment burden, self-efficacy, and adherence.[78] Notably, routine collection of PROMs is still in its infancy in most health systems, limiting the current potential to explore their relationships with multimorbidity

Table 2.3 Meta-analyses of multimorbidity associations with outcomes

Author (number of studies)	Multimorbidity in association with	Meta-analysis pooled estimates
Nunes *et al.*[55] (n=26)	Mortality	HR: 1.44 (95%CI 1.34 – 1.55) Multimorbidity was associated with higher mortality rates
Read *et al.*[73] (n=40)	Depressive disorder	RR: 2.13 (95%CI 1.62 – 2.80) Risk of depressive disorder higher in multimorbid patients
Vetrano *et al.*[74] (n=25)	Frailty	OR: 2.27 (95% CI 1.97 – 2.62) Multimorbidity associated with frailty
Makovski *et al.*[75] (n=39)	Quality of life	Physical health: −3.27% (95%CI: −4.79%, −1.74%) Mental health: −1.55% (95%CI: −2.97%, −0.13%) Decreases in the measured quality of life between -3.27% and -1.55% per individual condition added
Panagioti *et al.*[72] (n=75)	Patient safety incidents	Active patient safety incidents (adverse drug events, medical complications): OR 2.36 (95% CI 1.40-3.38) Precursors of safety incidents (prescription errors, medication non-adherence, poor quality of care, diagnostic errors): OR 1.69 (95%CI 1.36 – 2.03) Associations with both events for physical-mental morbidity, and only for active incidents in physical morbidity

OR – odds ratio, RR – relative risk, HR – hazard ratio

2.1.3 What is the relationship between multimorbidity and frailty?

Frailty is a condition that is characterised by a decline in functioning, accompanied by increased vulnerability to stressors from the accumulated consequences of morbidities or their treatments.[79, 80] As for multimorbidity, standardised measurement of frailty is lacking in research and clinical practice. At least 65 frailty measurement instruments exist,[81] the two most commonly used being the frailty phenotype developed by Fried et al.[82] and the frailty

index developed by Rookwood and Mitnitksi et al.[83] Most of the instruments are based on clinical assessments requiring functional measurements, supplemented with patient questionnaires,[81] which are not routinely recorded in EHRs.[84] Regardless of the measure used, frail individuals have been shown to have an increased risk of adverse outcomes such as falls and fractures, hospitalisation and mortality.[84]

Population-based studies of frailty have been lacking due to the time- and resource-intensive nature of measuring frailty. However, five new frailty measurement tools using administrative data have been developed since 2016.[85] Two of these have been validated independently – the electronic Frailty Index (eFI) by Clegg et al.[86] and the hospital frailty risk score (HFRS) by Gilbert et al.[87] The eFI was developed using routine primary care electronic health record data, while HFRS was developed in an inpatient setting. Validation studies found fair agreement between the Fried Index and HFRS (correlation 0.41, 95% CI 0.38 – 0.47),[87] and moderate agreement between the Fried Index and eFI (correlation 0.51, 95% CI 0.42 – 0.59).[88] The eFI is currently used in UK primary care to screen for frailty, but deficiencies in the capture of GP patient diagnoses using standardised software in other countries restrict its use internationally.[89] HFRS, on the other hand, uses ICD-10 codes to measure patients' risk of frailty, and has seen a larger uptake in the literature, with 214 citations since its publication in 2018 (source: PubMed search). Two recent systematic reviews of the claims-based frailty indices using administrative data, by Shashikumar et al.[81] and Nghiem et al.[85], show association between frailty and outcomes including mortality, hospitalisation, prolonged lengths of stay, readmissions and daily self-care activities independent of multimorbidity.

Multimorbidity and frailty are sometimes used interchangeably,[9, 90] but they are recognised as two distinct entities.[91] A recent systematic review by Vetrano et al.[74] indicated that the two concepts are related, with most frail individuals being multimorbid, but fewer multimorbid individuals being frail. Patients with co-occurring multimorbidity and frailty are likely to have complex care needs,[9] resulting in the recommendation for assessing frailty in people with multimorbidity.[92] The National Institute for Health and Care Excellence (NICE) *Multimorbidity: Clinical assessment and management* guideline suggestions for frailty assessment in primary and outpatient settings include physical assessments of gait speed, or screening tools such as Program of Research to Integrate Services for the Maintenance of Autonomy (PRISMA-7).[92, 93] In tertiary settings, however, frailty assessments are not

frequently carried out,[85] potentially failing to identify at-risk patients in need of further targeted health services.

Co-occurring frailty and multimorbidity is shown to have additive or synergistic effects on health outcomes in studies[90, 94-96] using the Fried definition for assessing frailty, gathered using patient questionnaires. However, studies examining interactions between frailty and multimorbidity in acute care settings, independent of patient-report, are lacking. The gap in knowledge about the interaction effects of frailty and multimorbidity in acute settings using population-level data is addressed in **Chapter 6.**

2.2 Multimorbidity in Australia

2.2.1 Overview of the Australian health system

Australia's health system is complex, including a mix of public and private hospitals, primary health care services (including GPs in private practice and allied health care services) and referred medical services (including specialist services).[97] These services are paid for and delivered by the Australian or state and territory governments, private health insurers, not-for-profit organisations and patient out-of-pocket costs.[97] The cost of health services amounts to 10% of the Australian gross domestic product, totalling $195.7 billion in 2018-19.[98]

Australia's universal health insurance scheme, Medicare, pays rebates for primary health services and some hospital services for privately insured patients through the Medicare Benefits Schedule (MBS), and provides access to free hospital services for public patients in public hospitals.[99] MBS records claims of subsidised services by GPs, specialists, allied health professionals and dental professionals.[100] To be eligible for a subsidy, consultations with allied health and dental professionals are generally coordinated by GPs as part of multidisciplinary team care arrangement for people with chronic conditions, with a limited number of claims allowed per year. Services not covered by Medicare, such as ambulance services, most dental and optical services, and accommodation and theatre costs for private hospitals, are covered by private health insurers and patient out-of-pocket costs, with cover options including hospital and/or general treatment services. In December 2019, 44% of Australians had some form of private hospital cover and 53% had general treatment cover.[101] Australia's universal health care also subsidises a variety of prescription medications under the Pharmaceutical Benefits Scheme (PBS).

Primary health care

Australian primary health care consists of a variety of providers across public, private and non-government sectors[102] with a total of 609,021 registered practitioners, including 101,841 medical practitioners, 344,941 nurses and midwives, 21,307 dental practitioners, 25,845 pharmacists and 549 Aboriginal health workers.[103] Australian patients can choose their own general practitioners (GPs), who are primarily paid on a fee-for-service basis through the MBS.[104] Primary Health Care networks (independent primary health care organisations) were established in 2015 with an aim to increase efficiency and effectiveness of medical services and improve care coordination.[105]

Information about chronic disease in Australian primary care data is varied. Capture of chronic disease is lacking in claims-based datasets such as the MBS, which primarily record billing information (e.g. type of service provided) with no information about the patient reason for encounter documented in the dataset. This information is present in the EHRs, which are used by most GPs.[106] However there is no current integration between MBS and EHR data, hindering Australian research into multimorbidity using primary health care data sets.

Other examples of Australian general practice datasets include data held in the NPS MedicineInsight program,[106] Primary Health Networks, and academic departments of general practice.[107] These data are not linked between service providers, or with other datasets, and are restricted to specific geographic areas or GP practices, limiting their use for longitudinal studies of multimorbidity.

Hospital services

Australian hospitals play an important role in the health system, providing services to admitted (hospitalised) and non-admitted patients (emergency department presentations and outpatient clinic attendance). Australia has 1350 public and private hospitals, with 11.5 million hospitalisations and $74 billion in expenditure in 2018-19.[108] New South Wales (NSW) is Australia's most populous state with 8 million residents in 2018[109] served by 221 public and 210 private hospitals.[110]

A formal admission to a hospital is deemed an admitted patient service, or hospitalisation, and includes both same-day admissions and stays of one or more nights. Hospitalisations

are classified as acute (medical, surgical, other), subacute (e.g. rehabilitation, palliative care), or non-acute (e.g. maintenance for a person suffering limitations due to a health condition),[97] and can be classified by the urgency status – emergency/unplanned, elective/planned or not assigned.

2.2.2 Australian health data collections

Australia has a plethora of health data, collected routinely through contacts with numerous health services, which can be used for health monitoring and research purposes. Each of these can play a role in filling the evidence gaps around development and progression of multimorbidity. Examples of the currently available Australian data can be summarised into categories of the common sources of health data – administrative data, clinical registries, population surveys and longitudinal cohorts (Table 2.4). Data features and their advantages and disadvantages are described in separate sections that follow.

Table 2.4 Examples of Australian health data sources for chronic disease monitoring and research

Source	Description	Conditions	Coverage
Administrative data sources			
State/territory-based hospital datasets**	Census of all inpatient separations from NSW public and private hospitals, multipurpose services, and day procedure centres.	ICD-10-AM diagnoses	State/territory, collected by health departments in each state/territory
National Hospital Morbidity Database (NHMD)	Compilation of inpatient records from state/territory-based hospital datasets	ICD-10-AM diagnoses	National, supplied based on National Minimum Data Set for admitted patient care, supplied by states and territories
PBS**	Data captured after a prescribed medicine has been dispensed and subsidised by the PBS	Contains information on the medicines dispensed (e.g. item and anatomic therapeutic chemical [ATC] codes), but does not contain indication for which medication is prescribed	National

Table 2.4. Examples of Australian health data sources for chronic disease monitoring and research, *cont.*

Source	Description	Conditions	Coverage
MBS	Records claims for subsidised services by GPs, specialists, pathology clinics etc	Clinical information (diagnoses, test results) not provided in the dataset	National
Registries			
Australian Cancer Database[111]	Data collection of all primary, malignant cancers diagnosed in Australia	No chronic disease information collected, but detailed tumour information present	National (from 1982)
Australian and New Zealand Dialysis and Transplant Registry[112]	Clinical quality registry collecting information relating to the outcomes of treatment of patients with end stage renal failure	Chronic lung disease, coronary artery disease, peripheral vascular disease, cerebrovascular disease, diabetes, cancer, hepatitis, other comorbid disease (coded using ICD-10)	Australia and New Zealand (from 1977)
Australian Orthopaedic Association National Joint Replacement **Registry**[113]	Clinical quality registry collecting information for individuals receiving joint replacement surgery	No chronic disease information collected. ASA and BMI collected since 2015.	National (since 2002)
National (insulin treated) Diabetes register[114]	Collects information about people who use insulin as part of their treatment for diabetes	Thalassaemia, hypothyroidism, hyperthyroidism, wolfram syndrome, Addison disease, ovarian failure, polycystic ovarian syndrome, cystic fibrosis, depression, anxiety, anorexia, bulimia, other eating disorder, autism, epilepsy, angina, acute myocardial infarction, heart failure, stroke, peripheral vascular disease, Down syndrome, Turner Syndrome, Klinefelter syndrome	National (since 2013)

Table 2.4. Examples of Australian health data sources for chronic disease monitoring and research, *cont.*

Source	Description	Conditions	Coverage
Australasian Cardiac outcomes registry[115]	Clinical Quality Registry that records information on cardiac procedures and devices	Stoke, transient ischaemic attack, peripheral arterial disease, chronic lunch disease, hypertension, diabetes, chronic kidney disease, smoking, as well as clinical frailty score and range of clinical data	Australia and New Zealand
Surveys			
National Health Survey (ABS)	Collects information about health of Australians including health conditions, risk factors	Arthritis, asthma, back problems, cancer, chronic obstructive pulmonary disease, cardiovascular disease, diabetes and mental health conditions + kidney disease and osteoporosis from 2017	National 1989-90, 1995, 2004-05, 2007-08, 2011-12, 2014-15, 2017-18
NSW Adult population health survey (NSW Health)	Provides ongoing information on self-reported health status, health risk factors, health service use, and satisfaction with health services	Asthma, cardiovascular disease, diabetes, mental health	State, yearly from 1996
BEACH	National study of GP clinical activity	Up to 4 problems managed by the GP recorded per patient, classified using ICPC-2 classification	National, yearly, 1996 – 2016
Longitudinal studies			
45 and Up Study**	Cohort study of NSW patients aged 45 and over, with consent to link to health care datasets	Cancer, heart disease, hypertension, stroke, diabetes, asthma, depression, anxiety, Parkinson's, thrombosis	State, NSW (n=267,000) recruited between 2006 – 2009
ALSWH	Examines health and wellbeing of Australian women across the life course. Data linkage to other health datasets available	Diabetes, heart disease, hypertension, stroke, thrombosis, asthma, cancer, osteoporosis, depression, anxiety, other psychiatric disorder, arthritis, osteoarthritis, bronchitis, rheumatoid arthritis	National (n=58,000) women, recruited from 1996

Table 2.4. Examples of Australian health data sources for chronic disease monitoring and research, *cont.*

Source	Description	Conditions	Coverage
HILDA	Nationally representative household survey focusing on social and economic information. Chronic conditions reported in some waves	Arthritis/osteoporosis, asthma, cancer, chronic bronchitis emphysema, diabetes, depression, anxiety, other mental illness, heart disease, hypertension, other serious circulatory condition	National (n=17,000 yearly) recruited since 2001
ALSA	Studies how social, biomedical and environmental factors are associated with ageing in persons aged 40 and over	Asthma, angina, arthritis, 11 cancers, chronic bronchitis, diabetes, gastrointestinal ulcer, heart attack, heart condition, hypertension, hiatus hernia, mental disorder, osteoporosis stroke	State, South Australia (n=2,087) recruited from 1992

** Used in the thesis, ALSA – Australian longitudinal study of ageing, ALSWH – Australian Longitudinal Study on Women's Health, ASA – American Society of Anaesthesiologists, BEACH - Bettering the Evaluation and Care of Health, BMI – Body Mass index, HILDA – Household, Income and Labour Dynamics in Australia, ICPC-2 – International Classification of Primary Care Second edition, MBS – Medicare Benefits Scheme, PBS – Pharmaceutical Benefits Scheme

Administrative data

Inpatient data

Episode-level information from admitted patient encounters in public and private hospitals is collected by each Australian state and territory. This data is also compiled into the National Hospital Morbidity Database (NHMD), based on a National Minimum Data Set. Hospital inpatient data usually includes patient demographics, administrative data, diagnoses, procedures and external causes of injury and poisoning.[116] Diagnoses and external causes are coded using ICD-10 Australian modification (ICD-10-AM) by trained medical coders using medical records, at patient discharge. The Australian Coding Standards (ACS) support the coding conventions of ICD-10-AM,[117] and govern when and how a diagnosis is recorded for a particular patient episode.

Administrative data provide an objective way of examining multimorbidity and how it relates to health outcomes at the person-level and health-service provider level. The

advantage of these data is their size, coverage, cost effectiveness and ability to support longitudinal studies.[12, 118] However, they do not capture conditions not significantly affecting patient management, leaving these data prone to underestimating disease[119] particularly due to their reliance on clinician notes with varying levels of documentation.[120] Exploration of variability in the recording of single and multiple chronic conditions between Australian hospitals is lacking, and this issue is addressed in **Chapter 4**.

Under-ascertainment of chronic disease using ICD-10-AM codes can potentially be improved with the inclusion of supplementary codes for chronic conditions ('U' codes), which has been implemented in Australia through their inclusion in the ACS since July 2015. A list of 29 clinically important conditions (Table 2.5), which had not previously met the criteria for coding additional diagnoses,[121] are now being coded when documented as being present during an episode of admitted care.[122] These 'U' codes are sequenced after all other ICD-10-AM codes and are not included in the Diagnosis Related Group (DRG) allocation. The impact of the inclusions of these supplementary codes on the ascertainment of multimorbidity is investigated in **Chapter 7**.

Table 2.5 Australian supplementary codes for chronic conditions

Diseases of the nervous system	**Diseases of the respiratory system**
Parkinson's disease	Emphysema
Multiple sclerosis	Chronic obstructive pulmonary disease
Epilepsy	Asthma
Cerebral palsy	Bronchiectasis
Tetraplegia, paraplegia, diplegia, monoplegia, hemiplegia	Chronic respiratory failure
Disorders of musculoskeletal system and connective tissue	**Mental and behavioural disorders**
Rheumatoid arthritis	Dementia
Arthritis and osteoarthritis	Schizophrenia
Systemic lupus erythematosus	Depression
Osteoporosis	Disorders of intellectual development
Diseases of the respiratory system	**Diseases of the digestive system**
Ischaemic heart disease	Crohn's disease
Chronic heart failure	Ulcerative colitis
Hypertension	Chronic liver failure

Table 2.5 Australian supplementary codes for chronic conditions, *cont.*

Endocrine, nutritional and metabolic disease	**Congenital malformations, deformities and chromosomal abnormalities**
Obesity	Spina bifida
Cystic fibrosis	Down's syndrome
Diseases of genitourinary system	
Chronic kidney disease, stage 3-5	

Claims-based data

As discussed in section 2.2.1, MBS data record claims for subsidised medical care delivered by GPs, specialists, allied health professionals and dental professionals.[100] MBS only captures services that attract a subsidy, leaving uncaptured other services such as those provided by community-controlled health centres, most dental services, those rendered free-of-charge by hospitals and services qualifying for a benefit under Department of Veterans' Affairs.[123]

MBS data items include information about dates of services provision, fees and subsidies paid, service provider information and type of service claimed, identified by item description, grouping similar professional services together. MBS includes specific chronic disease management items (such as diabetes cycle of care) for measuring service use,[124] but in general they cannot be used for estimating the prevalence of health conditions due to the lack of clinical information in the database.

PBS data contain information about subsidised claims for prescribed medicines. Before 2012, the data captured claims for which a full government subsidy was paid, leaving medicines falling below a co-payment threshold uncaptured. From 1 April 2012, claims for medicines under the co-payment threshold were recorded in the PBS data collection.[125] PBS data include medicine details (including PBS item code and Anatomical Therapeutic Chemical (ATC) codes), dates of dispensing, quantity supplied, costs, and prescriber information (e.g. scrambled identifier; speciality). Reasons for prescribing are not captured, leaving patient diagnosis uncertain for drugs with multiple indications for prescribing.

Clinical registries

Registry-based collections refer to a central repository of information that is collected when certain diseases or conditions of interests are diagnosed, or certain procedures are performed. Clinical quality registries (CQR) monitor quality of care, by collecting and analysing clinical data and patient outcomes within specific clinical domains,[126, 127] with 40 CQRs currently operating in Australia.[128] CQR differ in patient capture, reliability of coding conditions and interventions, completeness of data and reliability and validation of captured information,[128] potentially limiting their use for broader multimorbidity research. Integration of CQR data into national and jurisdictional datasets is a vision for the first Australian National Clinical Quality Registry and Virtual Registry Strategy 2020-2030,[127] although to date access to and integration of CQR data has been limited. An example of the potential impact of supplementing multimorbidity measured using administrative data with CQR data is presented in **Chapter 7**.

Surveys and longitudinal studies

In the Australian setting, national and state-based surveys are currently used to monitor the prevalence of selected conditions in the general population. The data for monitoring are gathered via the Australian Bureau of Statistics (ABS) National Health Survey using patient self-report. Conditions monitored include arthritis, asthma, back problems, cancer, chronic obstructive pulmonary disease, cardiovascular disease, diabetes, mental health conditions,[124] and from 2018 chronic kidney disease and osteoporosis.[129] These data have an advantage of providing national estimates of chronic disease prevalence, and can be used to examine trends over time to provide evidence of impacts of health policy changes[130] or interventions. However, they capture only a small subset of most prevalent chronic diseases, leading to underestimation of multimorbidity.[12]

BEACH was a continuous national study of GP activity between 1996 and 2016, sampling 1000 GPs per year, and recording information about GP practice and patient encounters, including reasons for encounter, problems managed, and management provided.[3] These data provided a rich source of patient encounters, and were used to derive prevalence of multimorbidity in the Australian primary care setting. However, the data were cross-sectional in nature and did not provide information about longitudinal patient outcomes.[131] BEACH closed in June 2016.[3]

Longitudinal studies provide a means of investigating disease trajectories, clusters, and their associated outcomes, especially if such data are linked to administrative data bases, which is the case for two major Australian cohort studies: the 45 and Up study[132] and the Australian Longitudinal Study on Women's Health (ALSWH).[133, 134] These also allow for the exploration of the role of behavioural risk factors and social determinants of health in the development of chronic conditions and multimorbidity. However, longitudinal studies generally only capture information on a limited number of chronic conditions, and they may not be representative of the general population.

Linkage across data collections

Data linkage brings together information from multiple data sources on the same individual or event and provides a rich source of the information about the population. Linkage across data collections enables health services and policy research, which can contribute to health improvements.[135] The linkage is performed by accredited bodies, using best practice protocols[136] for preservation of individual privacy and protection of data confidentiality.

In Australia, the capacity for data linkage has increased dramatically in recent years, with State and Commonwealth government investment in data linkage capacity, establishment of the Population Health Research Network (PHRN), building of nationwide data linkage infrastructure – including six State/Territory data linkage units and the national data linkage unit at the Australian institute of Health and Welfare (AIHW). State-based linkage units use probabilistic matching and clerical review to create master linkage keys,[137] which are continuously updated links of a variety of datasets including births, deaths, inpatient hospitalisation, emergency department presentations, cancer registrations and a variety of other datasets. Additional datasets, not routinely contained in the master linkage keys, can be linked for research and policy purposes, with approvals from data custodians and Human Research Ethics Committees (HRECs).

The use of linked data in multimorbidity research has its advantages. While administrative data collections, clinical registries, and health surveys each provide some context on multimorbidity, linking these data together provides a way of broadening our knowledge about multimorbidity even further, allowing us to fill existing information gaps across epidemiology and the healthcare utilisation spectrum as well as examine longitudinal assessment of outcomes.

This thesis harnesses the power of linked administrative, longitudinal and registry data to explore multimorbidity in Australia from an administrative data perspective, given the gap in availability of primary health care data.

2.2.3 Chronic conditions and multimorbidity in Australia

Chronic conditions account for the majority of total burden of disease in Australia (measured using disability adjusted life years), with coronary heart disease, back pain and problems, chronic obstructive pulmonary disease (COPD), dementia and lung cancer causing the most burden.[138]

Chronic conditions are the major cause of death and disability, accounting for 9 in 10 deaths in 2018, and contributing to around 61% of the total burden of disease in Australia in 2015.[124, 139] In 2015-16 the management of cardiovascular, musculoskeletal, mental and substance use disorders, and cancer cost the health system $40 billion, a third of the total health expenditure.[140] The Australian Burden of Disease 2015 study[138] estimated that 38% of the burden of disease is attributable to modifiable risk factors: smoking, overweight and obesity, alcohol and physical inactivity.

There is longstanding history of tracking the prevalence of chronic conditions in the community. Monitoring and reporting on chronic conditions, risk factors and health outcomes in the Australian population has been ongoing since 1996, with individual states and territories undertaking population health surveys since early 1990.[141] The ABS National Health Survey estimates that just under half (47%) of the Australian general population had at least one health condition in 2017-18, rising to 80% in those aged 65 and over.[139]

General population estimates of multimorbidity prevalence have only recently started to be reported by the AIHW. These are based on the ten conditions reported in the ABS National Health Survey. A 2020 report estimated that 20% of Australians had two or more chronic conditions, with females of all ages and older people having higher prevalence of multimorbidity.[139] This estimate is even higher when more conditions are included in the morbidity list, with population-weighted BEACH study results estimating 30.6% of the general population experience multimorbidity.[142]

Most care for chronic conditions is managed in the primary care setting. Australian estimates of prevalence of multimorbidity in primary care settings derived from the BEACH data show that close to half (47%) patients attending general practice have

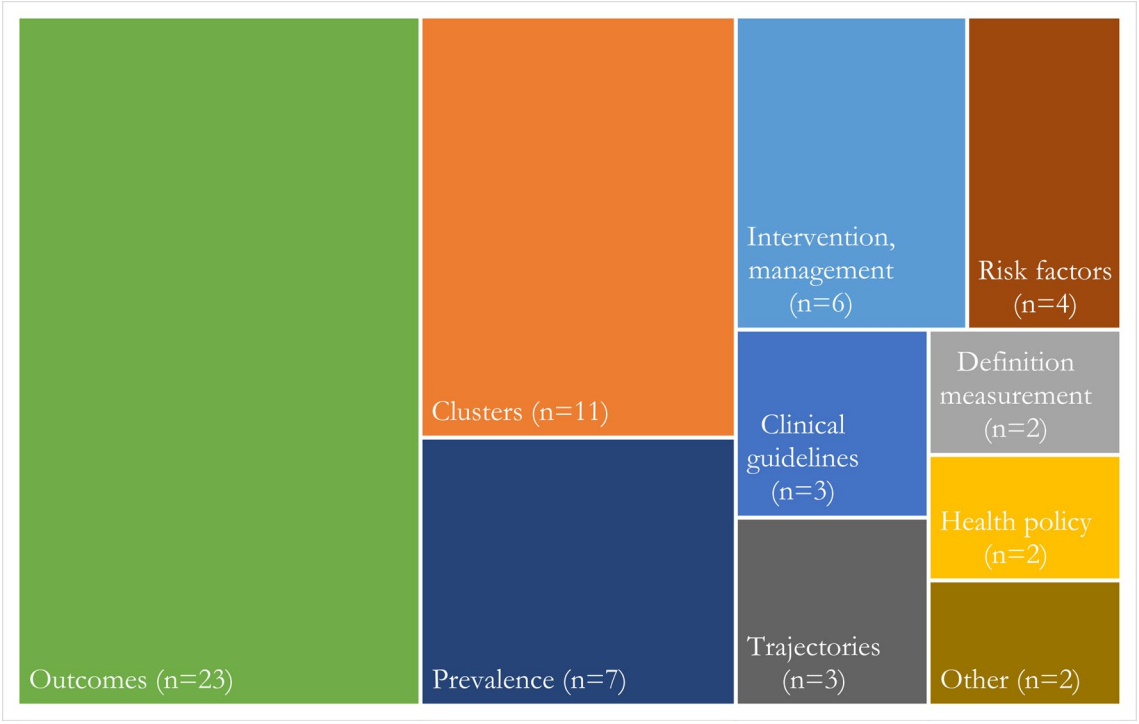
multimorbidity and 27% have complex multimorbidity (three or more conditions affecting three or more body systems[143]),[142] further highlighting the growing importance multiple chronic diseases have on individuals and health services.

2.2.4 Australian studies of multimorbidity

A literature search of the Australian studies on multimorbidity (search terms (Multimorbid*(Title/Abstract)) AND (Australia*(Title/Abstract)) from 1996 to January 2021 via PubMed found 164 articles, with 55 specifically examining multimorbidity (Appendix 1, Table 1), 29 studies on multimorbidity with index disease focus (comorbidity) (Appendix 1, Table 2), and the remaining studies referring to the concept without a specific focus on multimorbidity. Studies that I authored were not included in the summary of findings below.

Of the 55 studies on multimorbidity, 41 (75%) were quantitative, 4 qualitative and 10 were review studies, with topics including outcomes (n=23), disease clusters/patterns (n=11), prevalence (n=7), intervention/management (n=6) and other topics (Figure 2.3). Only a small proportion of studies (n=6, 15%) used linked data sources.[144-149]

Figure 2.3 Summary of research topics in 55 Australian studies of multimorbidity, 1996 – 2021



The most frequently used data sources for the Australian studies on multimorbidity are shown in Table 2.6. The studies varied in terms of sample demographics, setting and size. Half of the 41 qualitative studies on multimorbidity were done among people aged 45 years and over. The most common setting was the general population (n=25, 61% studies), followed by primary health practices (n=12, 29%) and tertiary settings (n=5, 13%). Heterogeneity in sample sizes was observed, with sizes ranging from 17[146] to 351,471[145] patients, the median number of participants being 6,776 across studies. Most studies (90%) included fewer than 50,000 participants, with largest studies using administrative data sources internally linked (i.e., within the same dataset) or linked with at least one other data set.

Table 2.6 Data sources used in 41 quantitative Australian studies on multimorbidity, 1996 – 2021 PubMed search

Data source	Sample size	Number of publications reference
Trial, RCT	351 – 1,281	5 [150-154]
Surveys		
Australian National Survey of Mental Health and Wellbeing	8,841	1 [155]
BEACH	8,707 – 43,501	4 [142, 143, 156, 157]
GP attendee survey	7,620	1 [158]
National Seniors	2,540 – 4,574	3 [159-162]
South Australian Omnibus Survey	2,912	1 [163]
South Australian Monitoring and Surveillance System	36,663	1[164]
WORC	78,000	1 [165]
Longitudinal studies		
45 Up Study	53,867 – 229,964	2 [144, 146]
ALSWH	8,865 – 10,334	5 [147, 166-169]
CHAMP	1,464	1 [170]
FAMAS	2,039	1 [171]
HILDA	5,532 – 17,529	4 [172-176]
NWAHS	696 – 1,854	2 [176, 177]

Table 2.6 Data sources used in 41 quantitative Australian studies on multimorbidity, 1996 – 2021 PubMed search

Data source	Sample size	Number of publications reference
Administrative data		
Hospital data (emergency department, inpatient)	38,156 – 229,964	3 [144, 148, 149]
MBS	2,039 – 229,964	3 [144, 146, 171]
Medical records	17 – 64,474	6 [149, 178-182]
PBS	10,334 – 351,471	4 [144, 146, 147, 183]

ALSWH – Australian Longitudinal Study on Women's Health, BEACH – Bettering the Evaluation and Care of Health, CHAMP – Concord Health and Ageing in Men Project, FAMAS – Florey Adelaide Male Ageing Study, HILDA – Household, Income and Labour Dynamics in Australia, PBS – Pharmaceutical Benefits Scheme, MBS – Medicare Benefits Schedule, NWAHS - North West Adelaide Longitudinal Health Study, WORC – Australian Work Outcomes Research Cost-benefit

Longitudinal studies were commonly used, with ALSWH and Household, Income and Labour Dynamics in Australia (HILDA) used most frequently. Administrative data were predominantly used in longitudinal studies involving data linkage, apart from two studies which used a 10% sample of national PBS data[183] or hospitalisation data,[148] without linkage to other data sources. None of the studies was conducted using whole of population data for Australia or an Australian state or territory.

The studies varied in terms of sample demographics, setting and size. Half of the 41 qualitative studies on multimorbidity were done among people aged 45 years and over. The most common setting was the general population (n=25, 61% studies), followed by primary health practices (n=12, 29%) and tertiary settings (n=5, 13%). Heterogeneity in sample sizes was observed, with sizes ranging from 17[179] to 351,471[183] patients, the median number of participants being 6,776 across studies. Most studies (90%) included fewer than 50,000 participants, with largest studies using administrative data sources internally linked (i.e., within the same dataset) or linked with at least one other data set.

The measures of multimorbidity used varied among the Australian studies, as with the international literature. Chronic disease ascertainment in Australian studies was usually done via patient self-report (n=26, 63% studies), with a third of the studies using

classification systems of either diagnoses (n=9) or medications (n=4) (Appendix 1, Table 1) using information from electronic medical records[149] or administrative datasets. [144, 146, 148] The number of recorded chronic diseases ranged between 3 and 60, the median number of chronic conditions being 13 (IQR: 11 – 21), including chronic diseases and risk factors.

Australian multimorbidity studies have examined a variety of outcomes, most frequently health-related quality of life, health service utilisation and functional status (Appendix 1, Table 3). Outcomes measures were mainly ascertained using patient self-report, except in seven studies[144, 146-149, 169, 171] that used linked data. Despite mortality being regarded as one of the three core outcomes for studies in multimorbidity (COSmm)[78], it was reported in only one Australian study[169] found in the literature review.

Australian literature gaps around the lack of information using population-level datasets and examination of mortality, and other adverse patient outcomes are addressed in **Chapters 6 and 7**.

2.2.5 Use of multimorbidity within Australian policy settings

The rising prevalence of chronic disease around the world has led to development of a variety of strategies to guide policy reform. Internationally, the World Health Organisation (WHO) Global Action Plan for the Prevention and Control of Noncommunicable Diseases (NCDs) 2013–2020[184] aims to reduce the NCD burden by 2025, via a set of nine global targets and 25 indicators.[185] Internationally, specific guidelines on multimorbidity are rare, except for the UK[9] NICE *Multimorbidity: Clinical assessment and management*[92] clinical guidelines for optimising care for adults with multimorbidity.[9]

In the Australian setting, prevention and better management of chronic conditions to improve health outcomes is supported by the National Strategic Framework for Chronic Conditions[186] in conjunction with chronic disease policies on the national, state and territory levels, and other international and national policies and programs.[186] Australia lacks specific guidelines on multimorbidity,[187] but comorbidity is often discussed in the context of disease-specific guidelines.[188]

Multimorbidity is on the Australian national health policy agenda and is increasingly being monitored for healthcare planning and evaluation. The concept is embedded into the National Strategic Framework for Chronic Conditions within its approach to move away from a disease-specific focus to a broader focus on shared health determinants, risk factors

and multimorbidity across chronic conditions.[186] One of the three broad objectives of the Framework is the 'Provision of efficient, effective and appropriate care to support people with chronic conditions to optimise quality of life', with the aim of people experiencing fewer complications, multimorbidity or disabilities with chronic conditions.[186] Example indicators of success include tracking the prevalence of chronic condition multimorbidity and reducing unplanned hospital readmissions for chronic conditions, both of which are discussed below.

Measurement of chronic conditions for national-level monitoring in Australia is currently being reviewed. Definitions of chronic conditions and their measurement for collective monitoring using Australian data are being evaluated by the newly established National Centre for Monitoring Chronic Conditions at AIHW. As mentioned previously, current estimates of the prevalence of chronic conditions and multimorbidity are derived using a list of ten chronic conditions captured from the ABS National Health Survey, which can underestimate the true burden of multimorbidity. A recent AIHW report[124] highlights the possibilities of enhancing chronic condition monitoring via linkage of information from multiple data sources, including administrative health data. This thesis highlights the capabilities of administrative data in **Chapters 4-7**.

Measuring multimorbidity is also critical for broader evaluation of the Australian health system. A variety of indicators are used for public reporting and performance monitoring, which require some form of adjustment for patient's risk of adverse outcomes. For example, the national core, hospital-based indicator specification by the Australian Commission on Safety and Quality in Health Care (ACSQHC)[189] includes specifications for mortality and readmissions, with state-based agencies (such as the NSW Bureau of Health Information and the Victorian Agency for Health Information) using their own set of indicators. All indicators are risk-adjusted for patient mix, usually adjusting for patient-level factors known to influence outcomes, such as age, sex and medical morbidities, with mental health and functional status sometimes included as well.[190]

Morbidity measures are usually derived using inpatient administrative data sources and use either specific conditions or indices to correct for confounding. However, this adjustment may not always sufficiently control for patient complexity, for example with medical morbidities being better able to predict mortality than in predicting readmissions.[184] There may be additional patient characteristics and markers of patient complexity that also contribute to patient outcomes such as readmissions, which complement and refine the

way we consider multimorbidity. This concept is explored in **Chapter 6** via the inclusion of frailty, and in **Chapter 7** through the inclusion of clinical registry data.

2.3 Thesis contribution

The Australian health data landscape is changing. Increasing access to the national linked data sources and methods to improve capture of chronic disease information are paving the way to utilising the power of big data to explore multimorbidity and its outcomes. This will provide crucial information to inform health system policy responses and monitor the effectiveness of these.

In this thesis, I will demonstrate how linked administrative health databases can be used to measure multimorbidity, how multimorbidity relates to the associated measure of frailty, and the impact of these on patients' health outcomes. In doing so, I will highlight how the power of big data can be used to address gaps in what we understand about patients with multimorbidity in Australia, broadening the scope of knowledge from small-sample community to population-level research, and illustrating how measurement of multimorbidity can be supplemented with other measures of patient complexity.

CHAPTER 3

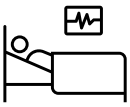
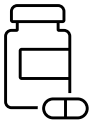
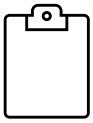
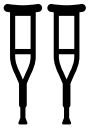
Methods

This thesis presents a series of analytical studies using administrative data exploring the measurement of multimorbidity and outcomes in older patients. This chapter provides the rationale for quantitative methods used in these studies. Specifically, it covers the use of routinely collected linked health data, followed by an overview of the construction of the key variables and outcomes used in statistical modelling, and details of the main types of analyses used in the studies. Whilst each of the studies (Chapters 4 – 7) includes a full description of the methods used, this chapter supplements those descriptions by giving an overview of the different datasets and methods, and provides more comprehensive information about the data sources, data management and cleaning, and definitions of exposure and outcome variables. Rather than replicating the information included in the methods within each published study, this chapter aims to consolidate and extend the information already presented in Chapters 4 – 7.

3.1 Datasets

This thesis uses multiple data sources to address the main study objectives, including administrative data, registry data and survey datasets. These datasets were sourced within several projects, each using different data, study populations and periods of availability. An outline of the key datasets used in each of the Studies is presented in Table 3.1. Full details of each of the datasets and details of the broad projects within which this work is embedded are given in the sections below.

Table 3.1. Datasets used in the thesis

Study	NHMRC project	Administrative data			Survey data	Registry data
		APDC	RBDM	PBS	45 Up Study	AOANJRR
						
Study 1	APHID	✓	✓		✓	
Study 2	APHID	✓	✓	✓	✓	
Study 3	IHOPE	✓	✓			
Study 4	Surgical	✓	✓			✓

AOANJRR – Australian Orthopaedic Association National Joint Replacement Registry APDC – Admitted Patient Data Collection, APHID – Assessing Preventable Hospitalisation Indicators, IHOPE – Indigenous Health Outcomes Patient Evaluation, RBDM – Registry of Births, Deaths and Marriages, PBS – Pharmaceutical Benefits Schedule

3.1.1 Administrative data

Admitted Patient Data Collection (APDC)

The APDC is an administrative data collection of inpatient separations (discharges, transfers, type-changes and deaths) covering all admitted patient services provided by the NSW public and private hospitals, public psychiatric hospitals, multipurpose services and private day procedure centres. Records for all admissions in NSW hospitals are included, including those from other Australian states and territories. Records for NSW residents admitted to other non-NSW hospitals are not recorded in the dataset.

Each record represents one episode of care (EOC), with contiguous periods of stay (POS) able to be constructed from dates and a variable denoting separation mode (details are given in Section 3.2.2). APDC contains multiple patient demographic, diagnosis and procedure variables. Hospital diagnoses for each EOC are coded using International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian modification (ICD-10-AM) and procedures using the Australian Classification of Health Interventions (ACHI).[191]

Registry of Births, Deaths and Marriages (RBDM) deaths data

RBDM captures all deaths registered in NSW, and it contains person demographic variables and date of death only. RBDM data was used for censoring purposes in studies 1 (Chapter 4), 2 (Chapter 5) and 4 (Chapter 7) and for outcome construction in study 3 (Chapter 6).

Pharmaceutical Benefits Schedule (PBS)

The PBS database contains information on Commonwealth government subsidised claims for prescribed medicines listed on the Schedule of Pharmaceutical Benefits.[125] PBS data included date of dispensing, beneficiary status, and medicines coded using both PBS item code and Anatomical Therapeutic Chemical (ATC) code.

3.1.2 Survey data

The 45 and Up Study

This study is the largest ongoing cohort study of healthy ageing in Australia, with over 265,000 men and women aged 45 and over across NSW enrolled during 2005 – 2009. About 18% of those invited participated and participants included about 11% of the NSW population aged 45 years and over.[132] Participants completed a baseline questionnaire and consented to be followed up with regular surveys and linkage to other health data.[132] In this thesis, only the baseline questionnaire was used (Appendix 2), and data were linked to administrative data as shown in Table 3.1.

The baseline questionnaire contains sections about participant sociodemographic factors (age, sex, country of birth, ancestry, work and relationship status, highest qualification, household income), health status (psychological distress, functional capacity, self-rated health), health behaviours (smoking, alcohol, physical activity, fruit and vegetable intake), and general health data (including disease and surgical history, medication use, family history of disease, incontinence) (full data dictionary available at https://www.saxinstitute.org.au/our-work/45-up-study/questionnaires/).

For this thesis, the key questions of interest are:

- Self-reported health conditions, ascertained from the question "Has a doctor EVER told you that you have (health condition)?";
- Self-reported smoking ascertained using the question "Are you a regular smoker now?"; and
- Obesity calculated from self-reported height ("How tall are you without shoes?) and weight ("About how much do you weigh?).

3.1.3 Registry data

Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR)

The AOANJRR collects data on individuals receiving primary and revision joint arthroplasty surgery at both public and private hospitals in Australia, with almost complete coverage (>99%).[192] Data are collected via forms filled out at the time of surgery, including information on patient details (including body mass index [BMI] and American Society of Anesthesiologists [ASA] score), diagnoses, type of and reason for arthroplasty, surgical technique and components inserted.

3.1.4 NHMRC projects

This thesis uses data from three National Health and Medical Research Council (NHMRC) funded projects, with different data sources, study populations and data availability. A brief outline of the projects and the way they are used in the Thesis is presented in Table 3.2.

Table 3.2. List of NHMRC projects

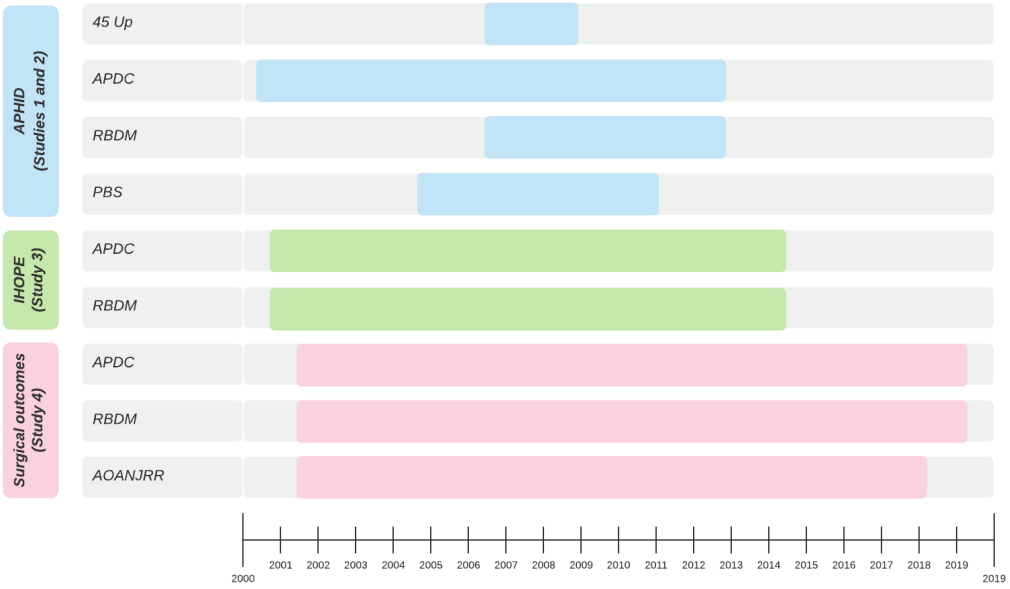
Project title	Project description	Student role in the project, and thesis use
Assessing Preventable Hospitalisation InDicators (APHID) study	The APHID Study is a partnership project with partner organisations the Australian Commission on Safety and Quality in Health Care (ACSQHC), the Agency for Clinical Innovation (ACI), and the Bureau of Health Information (BHI) to validate preventable hospitalisations as a measure of health system performance in Australia[188]	Associate investigator APHID study used in studies 1 and 2 to investigate variation in the measurement of common chronic conditions in the hospital data

Table 3.2 List of NHMRC projects, *cont.*

Project title	Project description	Student role in the project, and thesis use
Indigenous Health Outcomes Patient Evaluation (IHOPE) study	The IHOPE project aims to disentangle the contributions of the individual, the neighbourhood and the hospital of admission to risk of hospitalisation and risk of poor outcomes after hospital admission, for Aboriginal people in NSW compared with non-Aboriginal people.	Chief investigator (CIF) IHOPE study used in study 3 to investigate interactions between multimorbidity and frailty and their impacts on health outcomes.
Post-surgery care fragmentation: impacts and implications	The study uses linked administrative data for patients who had common surgical procedures to investigate whether outcomes are worse for patients who are readmitted to a different hospital from where their surgery was done.	Collaborator Used in study 4 to investigate value-add of complementing administrative data with clinical registry data when examining hospital performance

The timeline of data availability for each thesis study is shown in Figure 3.1, stratified by NHRMC project. In each study, the core dataset used is the APDC, with RBDM used to censor individuals' times or construct outcomes. Survey and registry data are used to complement information provided in the APDC, and to allow comparisons of multimorbidity estimates between data sources.

Figure 3.1. Data availability timeline



AOANJRR – Australian Orthopaedic Association National Joint Replacement Registry APDC – Admitted Patient Data Collection, RBDM – Registry of Births, Deaths and Marriages, PBS – Pharmaceutical Benefits Schedule

3.2 Data linkage

3.2.1 Data linkage process

All Studies in this thesis use linked data, which were obtained through three separate data linkage processes, one for each of the three NHMRC projects. In each case, data linkage was performed by the NSW Centre for Health Record Linkage (CHeReL) (https://www.cherel.org.au/), a trusted third party which carries out health linked data in accordance with ethical, legal and privacy protection requirements.

The CHeReL links identifying information (names, sex, addresses, date of birth) from each dataset using a probabilistic linkage algorithm via ChoiceMaker software.[194] The process of linking includes the calculation of a linkage likelihood or probability weight adjusting for data entry errors, spelling mistakes, incomplete and missing data using a mixture of machine learning, processing (standardising parsing, blocking), and clerical review steps. Linkage weights can be separated into links, non-links and possible links based on upper

and lower probability cut-offs. The CHeReL adjusts the cut-offs for each linkage to ensure the numbers of false positive and false negative links are minimised, with any pairs of records with linkage weights between the upper and lower cut-off points manually reviewed. The CHeReL estimate false-positive and false-negative rates of < 0.5%.[195]

Following linkage, the CHeReL creates anonymous linkage keys that are passed to the data custodians, who attach the keys to the approved clinical and service data and forward the data to the researchers. All projects in this thesis were supplied with linkage keys attached, which provided the means of creating person-level data used in the analyses.

Details about the data sources, their date ranges and number of records within each of the datasets are given in Table 3.3.

Table 3.3. Data sources, number of records per dataset and number of subjects per study

Data source	APHID project		IHOPE project		Surgical outcomes project	
	Date range	N Records	Date range	N Records	Date range	N Records
45 Up	Feb 2006 – Dec 2009	267,079				
APDC	Jul 2000 – Dec 2013	1,761,178	Jul 2000 – Mar 2014	32,920,055	Jul 2001 – Jun 2019	39,980,770
RBDM	Feb 2006 – Dec 2013	18,430	Jul 2000 – Mar 2014	643,136	Jul 2001 – Jun 2019	641,615
PBS	Jun 2004 – Dec 2011	35,453,776				
AOANJRR					Jul 2001 – Dec 2018	491,817
N subjects in Thesis	study 1 study 2	32,832 90,352	study 3	257,535	study 4	16,038

3.2.2 Cleaning of linked data

Working with linked data requires considerable data cleaning and preparation prior to the construction of analysis datasets. In each of the Studies, I undertook data cleaning to check possible erroneous or implausible values, incorrect links, and inconsistent entries. Data cleaning steps varied between data sources and studies, with hospital data cleaning being the most common and complex of the data steps, as outlined below.

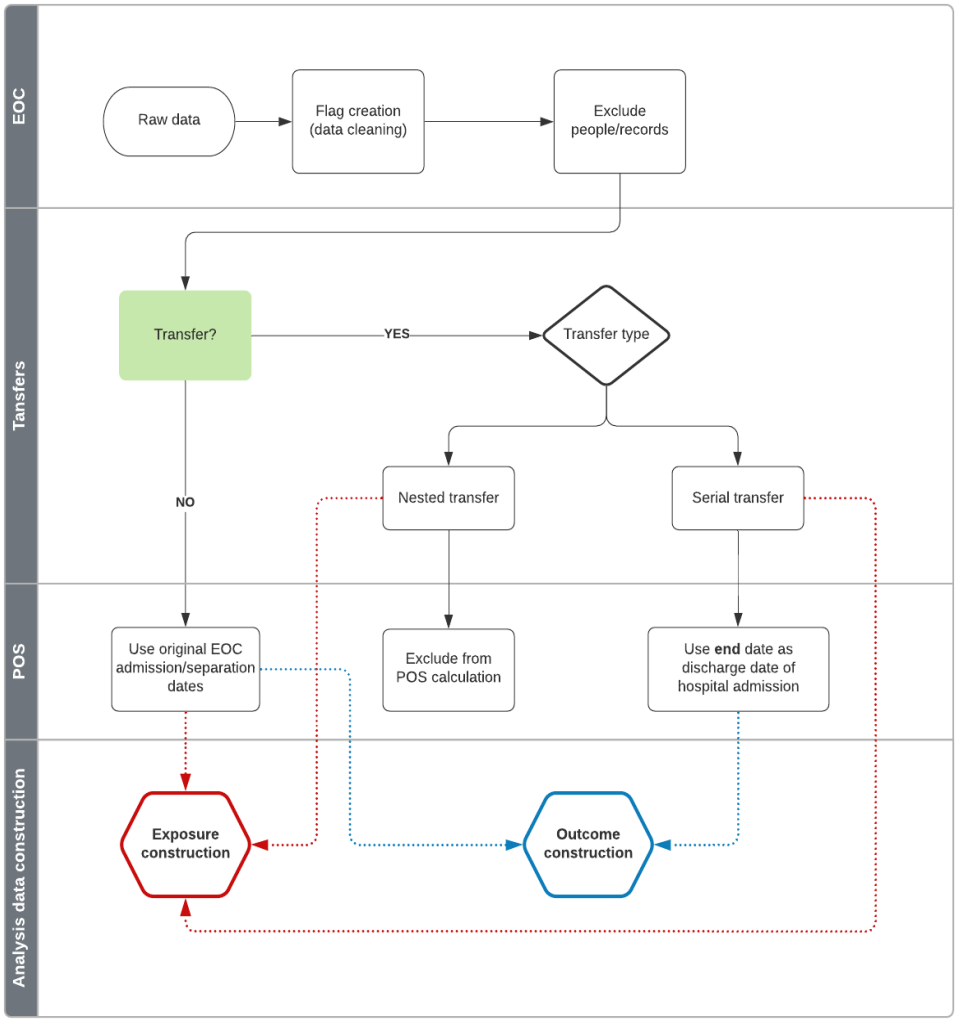
Hospital data cleaning

Potentially erroneous episode of care (EOC) records are initially flagged and then decisions were made about whether to exclude them from the analyses. The exclusions included removing persons with missing sex, admissions after date of death or death separation mode, and non-NSW residents.

More extensive cleaning and checking of APDC data was carried out in studies 3 (Chapter 6) and 4 (Chapter 7) in which APDC data was used for measurement and outcome construction (Appendix 7, Tables 7.1.1 and 7.2.1). These studies required a more in-depth evaluation of each EOC, and decisions about the use of each EOC in the measurement construction, as well as rolling up of EOCs into contiguous periods of stay (POS). A complete hospital admission is defined as the total time spent in the hospital from initial admission to hospital until discharge or death. Length of stay for each episode is calculated as a difference between episode separation and admission dates.

Figure 3.2 depicts how complete hospital admissions were constructed. Nested transfers add complexity in calculating POS, as their admission and separation dates lie within another EOC. Nested separations occur when a person is transferred from one hospital to another for a short stay (e.g. surgery) and then transferred back to the original hospital. It is important to flag these nested EOCs and use information about diagnoses and procedures performed when constructing exposure measures, with inclusion/exclusion of these EOCs dependent on the outcome of interest.

Figure 3.2. Construction of hospital stays



3.3 Defining measures used in the thesis

3.3.1 Key exposures of interest

Multimorbidity

The key concept of multimorbidity is defined as having two or more chronic conditions. At the time of writing this thesis, there was no consensus on the list of chronic conditions to be used in multimorbidity measurement, with the choice of multimorbidity measurement dependant on the purpose. The inclusion of chronic conditions used in this Thesis was thus chosen based on the data source at hand, supplemented with chronic conditions lists

commonly identified in systematic reviews on multimorbidity.[196, 197] For administrative data sources, diagnoses index episodes and prior hospitalisations ('lookback') were used to ascertain chronic conditions, using the Charlson and Elixhauser Indices.[198]

The full list of conditions used in the thesis is included in Table 3.4. Detailed rationale for their use is outlined in each published/submitted paper.

Frailty

Study 3 (Chapter 6) uses Hospital Frailty Risk Score (HFRS), a validated measure of frailty risk in hospitalised patients, developed by Gilbert et al.[87] HFRS helps identify patients with characteristics of frailty, and at risk of adverse healthcare outcomes including mortality, prolonged hospital stays and unplanned readmissions. The score, derived from a list of 109 ICD-10 diagnosis codes, has been validated in medical[199, 200] and surgical[201, 202] patients. It was purposefully built to be used with administrative data, and although a continuous measure (ranging from 0-99), due to its right skewness it was originally categorised into three groups: low risk (HFRS < 5), intermediate risk (HFRS 5-15) and high risk (>15).

For this thesis, the HRFS was derived using all hospital diagnoses from each EOC and 'lookback' EOCs, coded using ICD-10-AM. A lookback of two years was used in line with the original HFRS development study

Dichotomous frailty groups were used: low frailty (HFRS <5) and elevated frailty risk (HFRS≥5, combining intermediate and high frailty). Sensitivity analyses using three HFRS groups were also undertaken.

Table 3.4. List of conditions included in multimorbidity ascertainment

Thesis Chapter	Number of conditions	Dataset	Chronic conditions	Ascertainment
Chapter 4	6	45 Up	Diabetes, heart disease, hypertension, stroke	Has a doctor EVER told you that you have (*condition*)
			Obesity	BMI > 30 (calculated from self-reported height and weight)
			Smoking	Are you a regular smoker now?
Chapter 5	8	45 Up	Diabetes, heart disease, hypertension, stroke, cancer, asthma, depression, Parkinson's disease	Has a doctor EVER told you that you have (*condition*)
		APDC		ICD-10-AM codes using codes from the CCI and Elixhauser Index, with advice from clinical coder
		PBS		ATC codes from Rx-Risk-V
Chapter 6	32	APDC	AIDS/HIV, alcohol abuse, asthma, cancer, cardiac arrhythmia, CVD, chronic IHD, CKD, chronic pulmonary disease, coagulopathy, CHF, dementia, depression, drug abuse, epilepsy, hypertension, hypothyroidism, liver disease, MS, MI, Parkinson's disease, peptic ulcer disease, peripheral vascular disease, psychoses, pulmonary circulation disorders, rheumatoid arthritis, valvular disease, paralysis	ICD-10-AM codes using codes from the CCI and Elixhauser Index, supplemented with systematic reviews
Chapter 7	31	APDC	AIDS/HIV, alcohol abuse, blood loss anemia, cardiac arrhythmia, chronic pulmonary disease, coagulopathy, CHF, deficiency anemia, depression, diabetes (complicated), diabetes (uncomplicated), drug abuse, fluid and electrolyte disorders, hypertension (complicated), hypertension (uncomplicated), hyperthyroidism, liver disease, lymphoma, metastatic cancer, obesity, other neurological disorders, paralysis, peptic ulcer disease, peripheral vascular disorders, psychosis, pulmonary circulation disorders, renal failure, rheumatoid arthritis/collagen vascular disease, solid tumor without metastasis, valvular disease, weight loss	ICD-10-AM codes from Elixhauser index

3.3.2 Other risk adjustment factors

Variables used for risk adjustment purposes were determined by the data source and availability of data. For studies 1 and 2, which used survey data, and which provided more comprehensive information about patients' sociodemographic, lifestyle and health behaviours, self-report data from the 45 and Up Study baseline survey were used. Hospital-level variables came from APDC data, either using variables provided in the dataset (e.g. hospital type, size), or derived through analysis of the data (e.g. depth of coding, aggregate number of procedures performed).

A full list of risk adjustment variables by study and data source used is outlined in Table 3.5.

Table 3.5. Person-, area- and hospital-level variables used in risk adjustment

Study (Chapter)	Level	Variable	Data source used
Study 1 (Chapter 4)	Patient	Age, sex, highest educational attainment, country of birth, annual household income, functional limitation	45 Up Study
	Hospital	Type (public, private), peer group, depth of coding*	APDC
	Area	Remoteness of hospital*	APDC
Study 2 (Chapter 5)	Patient	Age, sex, highest educational attainment, Aboriginal or Torres Strait Islander origin, country of birth, speaks language other than English at home, annual household income, marital status	45 and Up Study
	Area	Remoteness of residence*	45 and Up Study
Study 3	Patient	Age, sex, number of prior admissions*	APDC
	Area	Socio-economic status*	
	Hospital	Hospital identifier (as a random intercept)	
Study 4	Patient	Age, sex, multimorbidity*	APDC
	Patient	BMI, ASA score	AOANJRR
	Hospital	Hospital identifier (as a random intercept)	APDC

* Denotes user derived variables. AOANJRR - Australian Orthopaedic Association National Joint Replacement Registry, APDC – Admitted Patient Data Collection, ASA – American Society of Anaesthesiologists, BMI – Body Mass Index

3.3.3 Study outcomes

Each of the Studies uses differing outcomes in the analysis. They are briefly summarised in Table 3.6.

Table 3.6. List of outcomes used in thesis Studies

Study	Dataset(s)	Outcome	Description
Study 1	45 Up, APDC	Agreement	Agreement between self-reported data (45 Up) and APDC health condition (six conditions reported separately)
Study 2	45 Up	Multimorbidity	Two or more conditions from a list of eight, self-reported
	APDC	Multimorbidity	Two or more conditions from a list of eight, using ICD-10-AM codes
	PBS	Multimorbidity	Two or more conditions from a list of eight, using ATC codes
Study 3	APDC	Mortality	30-day mortality post admission
	APDC	Long LOS	Prolonged length of stay (>10 days)
	APDC	Readmission	30-day unplanned* readmission post discharge (among patients discharged alive)
Study 4	APDC	Readmission	30-day all-cause* readmission post discharge (among patients discharged alive) 30-day unplanned** readmission

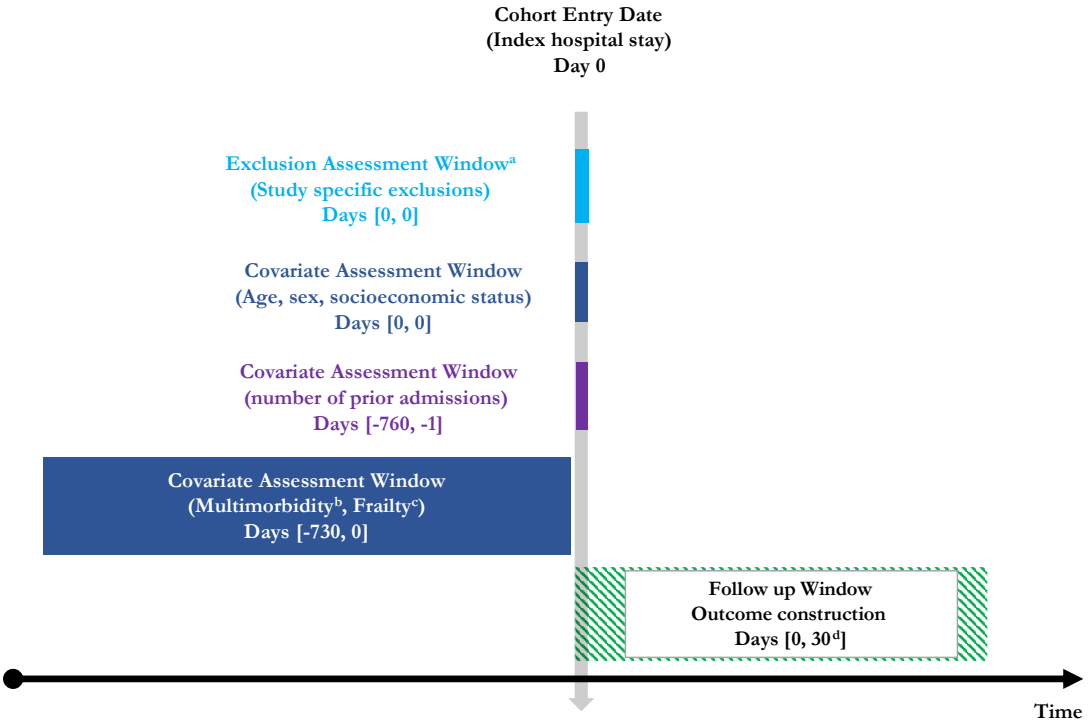
* Assigned using urgency status variable = 'emergency'; ** Assigned using specific ICD-10-AM diagnoses codes (Appendix 6, Table 1). APDC – Admitted Patient Data Collection, ATC – Anatomical Therapeutic Chemical, LOS – length of stay, PBS – Pharmaceutical Benefits Schedule

3.3.4 Construction of exposure and outcomes using linked data

For studies 3 (Chapter 6) and 4 (Chapter 7), which solely rely on the use of administrative data, the construction of outcomes and key exposures of interest required extra data preparation involving longitudinal data wrangling. The basic principle is outlined in Figure 3.3 as per study design visualisation framework.[203]

Within the available data window, each person's records were sequenced by earliest admission and separation dates to form a chronological admission trajectory. An 'index' admission was chosen to denote the EOC or POS, usually selected as the earliest admission (Chapter 7), or randomly selected within a pre-defined two-year period (Chapter 6). Outcome variables were then calculated from the index admission onwards. Exposure variables (multimorbidity and HFRS) were constructed using diagnoses from the index admission and those in the lookback periods (usually within two years prior to the index admission). Two-year lookback was chosen to pick up morbidities and risk factors not always recorded in hospital data, in line with international literature.[204]

Figure 3.3. Construction of exposure and outcome variable



a. Hospital data exclusions based on index stay
b. Multimorbidity using ICD-10-AM diagnoses
c. Frailty using HFRS calculations from ICD-10 codes only (Chapter 6)
d. Earliest of: outcome of interest (readmission, mortality), death, study end period

Figure adapted from Schneeweiss et al.[203] and https://www.repeatinitiative.org/projects.html

3.4 Statistical methods

3.4.1 Overview of statistical methods

In this thesis I use standard advanced statistical methods to obtain the results. All data were analysed using SAS 9.3, with the exception of multilevel modelling for which I used MLwiN software. Broad analytic approaches used in the thesis are outlined in Table 3.7.

Table 3.7. Statistical methods used in the thesis

Study (Chapter)	Analytic approach used	Description
Study 1 (Chapter 4)	Concordance Multilevel logistic regression	$\varkappa$ with 95% CI 2-levels, reporting MOR and ICC
Study 2 (Chapter 5)	Concordance and agreement measures Logistic regression	Sn, Sp, PPV, NPV, $\varkappa$ – all with 95% CI aORs
Study 3 (Chapter 6)	Multilevel Poisson regression	2-levels, reporting aRR
Study 4 (Chapter 7)	Stepwise single and multilevel logistic regression	2-levels, reporting aRR, VPC, AUC

aRR- adjusted relative risk, AUC – area under the receiver operating characteristic curve, CI – confidence interval, ICC – intraclass correlation coefficient, MOR – median odds ratio, NPV – negative predictive value, PPV – positive, Sn – Sensitivity, Sp – Specificity, predictive value, VPC – variance partitioning coefficient

3.4.2 Concordance and agreement measures

Studies 1 and 2 centred on validating the recording of common health conditions in hospital data (Chapter 4), and agreement between measurements of multimorbidity obtained from different data sources (Chapter 5). Cohen's kappa (κ) was used to measure agreement accounting for chance, calculated as κ = (observed agreement – expected agreement)/(1-expected agreement).[205]

To assess agreement of multimorbidity and individual chronic conditions using self-reported and administrative data, self-reported data were taken as the reference standard, as chronic disease capture in administrative data is incomplete. Sensitivity (Sn), specificity

(Sp), positive predictive value (PPV) and negative predictive value (NPV) were constructed using the following calculations:

		Reference standard Condition present?		**Total**
		Yes	No	
Administrative data	Yes	a	b	a + b
Condition present?	No	c	d	c+ d
Total		a + c	b + d	n = a + b + c + d

Table adapted from Watson & Petrie[206]

Sn = Proportion of cases self-reporting a condition that have a record within administrative data: $a / (a + c)$

Sp = Proportion of cases without a self-reported condition that did not have a record on such in administrative data: $d / (b + d)$

PPV = Proportion of those with a condition identified in administrative data that have a self-reported condition: $a / (a + b)$

NPV = Proportion of those without a condition identified in administrative data that do not have a self-reported condition: $d / (c + d)$

3.4.3 Multilevel models

Traditional statistical models used in epidemiological studies of observational data have assumptions which might not be met in the real-world data use. One such assumption is the independence of the observations. However, as multiple hospital admissions within an individual are possible, and as there are admissions which belong to the same hospital, the independence assumption is often violated. This results in potential underestimation of standard errors, leading to overestimation of statistical significance (lower *p*-values). To correctly account for the presence of clustering within the data, multilevel models (sometimes called hierarchical, mixed effects or random effects models) should be used.

Multilevel models recognise the existence of clustering and hierarchy within the dataset and allow estimation of both fixed and random effects, and partitioning of residual variation between levels. Multilevel models can be hierarchical (where lower levels are clustered entirely within higher ones), or non-hierarchical (where members within lower levels can be present in multiple higher level units).[207] In hospital data, numerous levels can be examined, depending on the level of influence that is of interest. For example, EOCs are clustered

within an individual, individuals are clustered within hospitals, and hospitals within health areas.

The standard logistic regression model can be represented as

$$logit(\Pr(Y_i = 1)) = \beta_0 + \sum_{n=1}^{N} \beta_n x_{ni} + e_i$$

where Y_i denotes the binary response variable for individual *i*, and $Y_i = 1$ denotes occurrence of the event; β_0 the intercept, β_n regression coefficients, x_{1i} through x_{ni} denote the *n* predictors or explanatory variables measured on the individual *i*; and e_i denotes the residual error term for individual *i*.

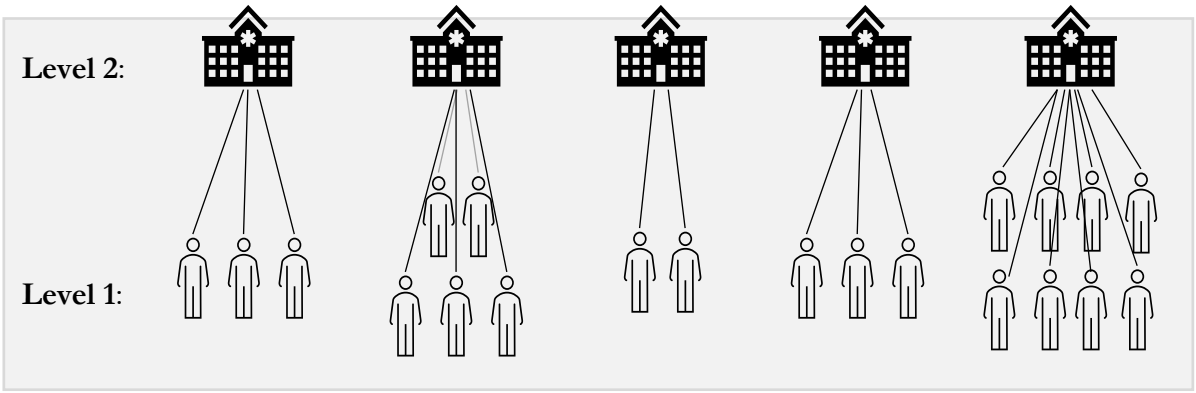
A multilevel logistic regression model on the other hand is represented as

$$logit\big(\Pr\big(Y_{ij} = 1\big)\big) = \beta_0 + \sum_{n=1}^{N} \beta_n x_{ni} + \sum_{p=1}^{P} \beta_p x_{pj} + u_j + e_{ij}$$

where $Y_{ij} = 1$ is the event within person *i* clustered within level *j* (e.g. hospital), x_{ni} and x_{pj} denote N predictors for person-level and P predictors for hospital-level variables, β_0 the intercept, β_n and β_p regression coefficients for person-level and hospital-level variables, and e_{ij} and u_j represent the residual error at the person and hospital levels.

Multilevel models were used in studies 1, 3 and 4, with the same underlying two-level hierarchical structure: patients clustered within hospitals (Figure 3.4).

Figure 3.4. Hierarchical structure of the data



Multilevel models separate the variance in the outcome into parts associated with each of the levels included in the model. Models with three or more levels or those with dichotomous outcomes require more complex calculations than the simple intraclass correlation coefficient (ICC) measure used for continuous outcomes[207] The proportion of the total variance that is attributable to a particular level in the model is called the variance partition coefficient (VPC). In studies 1 and 4, in which I used multilevel logistic regression models, VPC was calculated using the latent variable method from Snijders and Bosker [202] as $\frac{\sigma_u^2}{\sigma_u^2+\pi^2/_3}$, with σ_u^2 denoting higher-level (e.g. hospital) variance. Variation at the hospital level was expressed as a median odds ratio (MOR), denoting the median of odds ratios comparing persons with identical covariates randomly chosen between hospitals. MOR was calculated as $\exp(0.954 \times \sqrt{\sigma_u^2})$, with σ_u^2 denoting hospital variance.[207]

In study 3, where the aim was not to partition variation or explore hospital-level variance *per se*, the multilevel models were fitted to account for clustering within the data and estimate standard errors to draw correct inference, rather than estimate variance components.

3.5 Ethics approvals

The studies used in this thesis were nested within broader NHMRC funded projects, with ethics approval details as outlined in Table 3.8. Use of the data for the research in this PhD thesis was approved by each of the noted ethics committees as either an amendment (Study 4) or falling in scope of the original project application.

Table 3.8 Ethics approvals

Study	Project title	Ethics ID	Ethics committee
Studies 1 and 2	Use of primary care, health events, health service use and costs in the 45 and Up Study	2011/12/362	PHSREC
		832/11	AH&MRC
Study 3	Exploring the contributions of individual-, area- and service-level factors to Indigenous health outcomes	2009/03/141	PHSREC
		684/09	AH&MRC
Study 4	Variations in surgical outcomes in New South Wales	2019/ETH00423	PHSREC

CHAPTER 4

Variation in the recoding of common health conditions in routine hospital data: study using linked survey and administrative data in New South Wales, Australia

4.1 Background and aims

Administrative hospital inpatient data are known to under-report chronic diseases on patient discharge data due to the nature of coding diagnoses on each hospital stay. This study examines:

a) Agreement between self-reported morbidity and hospital discharge data for six common chronic conditions and health risk factors
b) Variation in the recording of this agreement and quantifying the contributions of patient- and hospital-level factors
c) Patient and hospital characteristics that predicted agreement levels.

4.2 Key findings

The recording of common comorbid conditions in routine hospital inpatient data is highly variable and, for some conditions, very poor. Recording varies considerably among hospitals, presenting the potential to introduce bias into risk-adjusted comparisons of hospital performance, especially for indicators that use heart disease or hypertension for risk adjustment. Between-hospital variation is even more amplified when smaller and private hospitals are included in the analyses.

4.3 Publication details

Lujic S, Watson DE, Randall DA, Simpson JM, Jorm LR

Variation in the recording of common health conditions in routine hospital data: study using linked survey and administrative data in New South Wales, Australia.

BMJ Open 2014;**4:**e005768. doi: 10.1136/bmjopen-2014-005768

SUPPORTING INFORMATION

Supplementary Tables 1-3 of this publication are shown in Appendix 3.

4.4 Student contribution

I had the overall responsibility for the design of this study, data management, carrying out the statistical analysis, interpreting results, drafting the initial manuscript, and reviewing and revising the manuscript in response to co-authors and reviewers. Co-authors Diane Watson and Louisa Jorm contributed to the conception and design of the study. Louisa Jorm helped with data acquisition and provided oversight for all analyses. Deborah Randall and Judy Simpson provided oversight and advice for the design and interpretation of the statistical analyses. All authors read and approved the final version as published.

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Variation in the recording of common health conditions in routine hospital data: study using linked survey and administrative data in New South Wales, Australia

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ABSTRACT

Objectives: To investigate the nature and potential implications of under-reporting of morbidity information in administrative hospital data.

Setting and participants: Retrospective analysis of linked self-report and administrative hospital data for 32 832 participants in the large-scale cohort study (45 and Up Study), who joined the study from 2006 to 2009 and who were admitted to 313 hospitals in New South Wales, Australia, for at least an overnight stay, up to a year prior to study entry.

Outcome measures: Agreement between self-report and recording of six morbidities in administrative hospital data, and between-hospital variation and predictors of positive agreement between the two data sources.

Results: Agreement between data sources was good for diabetes (κ=0.79); moderate for smoking (κ=0.59); fair for heart disease, stroke and hypertension (κ=0.40, κ=0.30 and κ =0.24, respectively); and poor for obesity (κ=0.09), indicating that a large number of individuals with self-reported morbidities did not have a corresponding diagnosis coded in their hospital records. Significant between-hospital variation was found (ranging from 8% of unexplained variation for diabetes to 22% for heart disease), with higher agreement in public and large hospitals, and hospitals with greater depth of coding.

Conclusions: The recording of six common health conditions in administrative hospital data is highly variable, and for some conditions, very poor. To support more valid performance comparisons, it is important to stratify or control for factors that predict the completeness of recording, including hospital depth of coding and hospital type (public/private), and to increase efforts to standardise recording across hospitals. Studies using these conditions for risk adjustment should also be cautious of their use in smaller hospitals.

Strengths and limitations of this study

- The study was based on linked data from a large-scale cohort study and administrative hospital data to evaluate four health conditions and two health risk factors, as well as their combinations.
- The study used advanced multilevel modelling methods to comprehensively evaluate the recording of each morbidity in administrative data and quantify between-hospital variation.
- The study provides detailed information about how the validity of morbidity reporting varies among hospitals after accounting for patient factors.
- Limitations include the use of self-reported data in the absence of a 'gold standard' such as medical records.

INTRODUCTION

Most nations with advanced economies publicly report on the comparative performance of hospitals with a view to accelerating and informing efforts to improve quality and allowing patients to make informed choices. Diagnoses recorded in administrative hospital data are commonly used in the construction and case-mix adjustment of hospital performance metrics, as well as for risk adjustment in epidemiological studies.

The construction of reliable health metrics relies on statistical methods that take into account the degree to which patients treated in different facilities have different morbidity and risk profiles that predispose them to requiring different interventions or to achieving different outcomes. These statistical methods, known as case-mix or risk adjustment, account for patient-related factors that are above and beyond the immediate control of healthcare professionals.

Thus, properly constructed performance metrics fairly reflect differences in healthcare experiences, patient outcomes and risks of adverse events. There has been some criticism of case-mix adjustments because they are subject to measurement error,[1] but

case-mix adjustment is still considered to be less biased than unadjusted comparisons.[2]

Most methods of case-mix adjustment rely principally on demographic and diagnostic information that is captured in administrative hospital data collections. The hospital data are collected and recorded in a database for administrative purposes, with clinical coders coding diagnostic information based on the patient's medical records.[3] This approach may be suboptimal[4 5] because evidence from many countries suggests that administrative hospital data under-report the morbidity information needed to fully account for differences between hospitals in patient-related factors that predispose them to differences in measured outcomes.[6–13] However, the impact of this under-reporting on comparative measures of hospital performance depends on whether it varies systematically among hospitals, because of differences in factors such as training or practice among coding staff, the comprehensiveness of clinicians' notes or 'upcoding' relating to funding models or incentives.[14]

This issue is relatively unexplored, aside from the work by Mohammed *et al*,[2] which reported a non-constant relationship between case-mix variables and mortality among hospitals in the UK, explained by differences in clinical coding and admission practices across hospitals. These variations in coding accuracy were shown to be related to geographic location and bed size, with small rural facilities performing better than large urban hospitals.[15 16] In Australia, variations in the reporting and coding of secondary diagnoses in administrative hospital data have been shown to exist in public hospitals among Australian states,[17] and also among hospitals within the state of New South Wales (NSW), with greater under-reporting in private and rural hospitals.[3] However, the relative contributions of patient and hospital factors to these variations have not been identified, nor has this variation been formally quantified.

This study, using data linkage of survey and administrative data, aimed to further investigate the nature and potential implications of under-reporting of morbidity information in administrative hospital data by: (1) measuring the agreement between self-reported morbidity information and coded diagnoses; (2) quantifying the amount of between-hospital variation in this agreement and (3) identifying patient and hospital characteristics that predict higher or lower levels of agreement. We focused on clinical conditions common to case-mix and risk-adjustment models—diabetes, heart disease, hypertension and stroke. We also focus on smoking and obesity, due to their impact on health trajectories, rapid shifts in prevalence, substantial geographic variation in rates[18] and paucity of international evidence on completeness of coding.

METHODS

Data sources

The 45 and Up Study

The 45 and Up Study is a large-scale cohort study involving 267 153 men and women aged 45 years and over from the general population of NSW, Australia. The study is described in detail elsewhere.[19] Briefly, participants in the 45 and Up Study were randomly sampled from the database of Australia's universal health insurance provider, Medicare Australia, which provides near-complete coverage of the population. People 80+ years of age and residents of rural and remote areas were oversampled. Participants joined the Study by completing a baseline questionnaire (available at https://www.saxinstitute.org.au/our-work/45-up-study/questionnaires/) between January 2006 and December 2009 and giving signed consent for follow-up and linkage of their information to routine health databases. About 18% of those invited participated and participants included about 11% of the NSW population aged 45 years and over.[19]

The NSW Admitted Patient Data Collection

The Admitted Patient Data Collection (APDC) includes records of all public and private hospital admissions ending in a separation, i.e. discharge, transfer, type-change or death. Each separation is referred to as an episode of care. Diagnoses are coded according to the Australian modification of the International Statistical Classification of Diseases and Health Related Problems 10th Revision (ICD-10-AM).[20] Up to 55 diagnoses codes are recorded on the APDC, including the principal diagnosis and up to 54 additional diagnoses. Additional diagnoses are defined as "a condition or complaint either coexisting with the principal diagnosis or arising during the episode of care" in the Australian Coding Standards and should be interpreted as conditions that affect patient management.[21] Assignment of diagnosis codes is done by trained clinical coders, using information from the patient's medical records.

The APDC from 1 July 2000 to 31 December 2010 was linked probabilistically to survey information from the 45 and Up Study by the NSW Centre for Health Record Linkage (http://www.cherel.org.au) using the 'best practice' protocol for preserving privacy.[22]

Study population

The study population comprised patients aged 45 years and above who participated in the 45 and Up Study and who had a hospitalisation lasting at least one night in the period up to 365 days prior to filling out the baseline 45 and Up Study survey. Day stay patients were excluded from the analysis to make the study more robust and generalisable beyond NSW and Australia, as there are differences in admission practices for same day patients between Australia and most other comparable countries.[23] NSW is home to 7.4 million people, or one-third of the population of Australia.

Measuring morbidity

We examined four health conditions (diabetes, heart disease, hypertension and stroke) and two health risk factors (obesity and smoking), referred to hereafter collectively as 'morbidities'. For each participant, these

health conditions were measured using self-report and administrative hospital data.

Self-reported morbidities were ascertained on the basis of responses to questions in the baseline 45 and Up Study survey. Diabetes, hypertension, stroke and heart disease were identified using the question "Has a doctor ever told you that you have [name of condition]?" Participants who did not answer the question were excluded from analyses (n=1242).

Smoking was classified on the basis of answering "yes" to both of the questions "Have you ever been a regular smoker?" and "Are you a regular smoker now?" Participants' responses to the questions "How tall are you without shoes?" and "About how much do you weigh?" were used to derive body mass index (BMI), defined as body weight divided by height squared (kg/m^2). The WHO's[24] classification system was used to categorise individuals as obese (BMI $\geq 30\ kg/m^2$).

Morbidity information in administrative hospital data was ascertained using all 55 diagnosis codes in the APDC records (ICD-10-AM: E10–E14 for diabetes, I20–I52 for heart disease, I60–I69, G45, G46 for stroke, I10–I15 and R03.0 for hypertension, F17.2 or Z72.0 for smoking and E66 for obesity). The inclusion of broader ICD-10-AM codes for heart disease and stroke was chosen because of the broad definition of disease type in the self-reported data. Thus, heart disease codes were inclusive of coronary heart disease, pulmonary heart disease and other forms of heart diseases, including heart failure and arrhythmias. Stroke codes included cerebrovascular diseases without infarction among others.

Predictors of agreement

We explored patient-level as well as hospital-level factors as predictors of agreement between the two data sources.

Patient-level factors were self-reported in the 45 and Up Study baseline survey and included age, sex, education, country of birth, income and functional limitation. Functional limitation was measured using the Medical Outcomes Study-Physical Functioning scale,[25] and classified into 5 groups: no limitation (score of 100), minor limitation (score 95–99), mild limitation (score 85–94), moderate limitation (60–84) and severe limitation (score 0–59).

Facility-level factors were type of hospital (public/private), hospital peer group (akin to hospital size defined by number of case-mix weighted separations,[26] which includes hospital remoteness in the classification), remoteness of hospital and depth of coding. Remoteness of the Statistical Local Area in which the hospital was located was classified according to the Accessibility/Remoteness Index of Australia (ARIA+), grouped into four categories (major city, inner regional, outer regional, remote/very remote).[27] Depth of hospital coding was the mean number of additional diagnoses coded per episode of care for each hospital, calculated using all overnight hospitalisations for the full 45 and Up Study cohort from 2000 to 2010, and divided into four groups at the 25th, 50th and 75th centile. Hospital peer groups were divided into 5 categories: principal referral (≥25 000 separations per year), major (10 000–24 999 separations per year), district (2000–9999 separations per year), community (up to 2000 separations per year) and other (non-acute, unpeered hospitals). Missing information was treated as a separate category for any variables with missing data.

Statistical methods

We examined patient-level agreement between data sources for each of the six morbidities individually, as well as for their 15 two-way combinations. We compared the self-reported responses (yes/no) with all the diagnoses provided in the hospital records both for 'index' admissions and for the 'lookback' period admissions.[28] The 'index' admission was the overnight hospital stay with admission date closest to the survey completion date and no longer than a year prior. Morbidity was coded as 'yes' if any of the diagnoses during that stay contained a mention of that morbidity. The 'lookback' admissions included all overnight stays in the 365-day period that preceded and included the 'index' admission. Morbidity was coded as 'yes' if any of the diagnoses from any lookback admissions contained a mention of that morbidity.

Agreement between the two data sources (yes/no) was measured using Cohen's κ statistic. κ Values above 0.75 denote excellent agreement, 0.40–0.75 fair to good agreement and below 0.45 poor agreement.[29] Agreement was computed for all 313 hospitals in the state, regardless of size, as well as for the 82 largest public hospitals, for which performance metrics are publicly reported.

Multilevel logistic regression was used to estimate OR with 95% CIs for patient-level and hospital-level factors that predicted positive agreement between the two data sources. Multilevel models were chosen because of the clustering of patients within hospitals. Models were run for each of the six morbidities separately. These analyses were constrained to only those participants who self-reported the morbidity of interest, and the outcome was whether the index hospital record contained a mention of the morbidity or not. Addition of the hospital-level characteristics was done one at a time, due to the collinearity between variables. All ORs presented are adjusted for all other demographic variables in the model.

Variation at the hospital level was expressed as a median OR (MOR), which is the median of the ORs of pairwise comparisons of patients taken from randomly chosen hospitals, calculated as $\exp^{0.954\times\sqrt{\text{variance}}}$;[30] and the intraclass correlation coefficient (ICC), which is the percentage of the total variance attributable to the hospital level.[31] Large ICCs indicate that differences among hospitals account for a considerable part of the variation in the outcome, whereas a small ICC means that the hospital effect on the overall variation is minimal. The

relative influence of the hospital on reporting of morbidity was calculated using a variance partitioning coefficient expressed as a percentage of the total variance using the Snijders and Bosker latent variable approach.[31]

All data management was done using SAS V.9.2[32] and multilevel modelling using MLwiN V.2.24.[33]

The conduct of the 45 and Up Study was approved by the University of New South Wales Human Research Ethics Committee (HREC).

RESULTS

Descriptive characteristics

A total of 32 832 study participants were admitted to 313 hospitals up to a year prior to completing the 45 and Up Study baseline survey. Just over half of the index admissions (53%) were planned stays in hospital, and 57% were to a public hospital. Around one-third of the index admissions occurred within the 3 months before study entry, and the mean length of stay was 4.8 days (median=3 days). Just under half of the sample (47%) reported having hypertension, with heart disease or obesity reported by 25% and current smoking by 6.1% of the sample. One-third (34%) of participants had two or more morbidities (data not shown). Other characteristics of the sample at their index admission are shown in table 1. Characteristics of hospitals are summarised in table 2.

Concordance between self-report and hospital records

Overall, reporting of morbidity differed between the two data sources with 23 257 (71%) participants having at least one of the six self-reported morbidities, and 11 977 (36.5%) and 14 335 (43.7%) of the sample having at least one morbidity recorded on their index or lookback hospital admissions, respectively.

Table 3 gives the summary concordance measures for each morbidity and two-way morbidity combination. For the index admission, good agreement was found for diabetes (κ=0.79); moderate agreement for smoking (κ=0.59); fair agreement for heart disease (κ=0.4); and poor agreement for stroke (κ=0.3), hypertension (κ=0.24) and obesity (κ=0.09). In two-way combinations, moderate levels of agreement were found only for diabetes combinations (with smoking, hypertension and heart disease).

Incorporating a 1-year lookback period increased the numbers of participants with a morbidity recorded in a hospital record, with average relative increases in the κ values of 20% (ranging from 2% increase for smoking to 41% increase for obesity). Good to excellent level of agreements were still found only for diabetes (κ=0.83) and smoking (κ=0.6).

Agreement was only slightly higher among the 82 large public hospitals (see online supplementary table S1) with relative κ values higher by 4%, on average.

Table 1 Characteristics of the study sample at their index admission

	All participants (N=32 832)	
	N	Per cent
Demographic characteristics		
Sex		
Male	16 812	51.2
Female	16 020	48.8
Age		
45–59	9666	29.4
60–79	16 624	50.6
80+	6540	19.9
Country of birth		
Australia	25 001	76.2
Other	7448	22.7
Unknown	383	1.2
Highest education level		
No school	5196	15.8
Year 10 or equivalent	7894	24.0
Year 12 or equivalent	2975	9.1
Trade	4270	13.0
Certificate	6109	18.6
University degree	5662	17.3
Unknown	726	2.2
Household income ($, per annum)		
<20 000	9077	27.7
20 000–<50 000	8223	25.1
500 000–<70 000	2560	7.8
70 000+	5042	15.4
Not disclosed	6003	18.3
Missing	1927	5.9
Functional status		
No limitation	4915	15.0
Mild limitation	6011	18.3
Moderate limitation	8701	26.5
Severe limitation	10 121	30.8
Missing	3084	9.4
Admission characteristics		
Admission type		
Surgical	15 464	47.1
Other	1439	4.4
Medical	15 929	48.5
Emergency status		
Emergency	13 484	41.1
Planned	17 544	53.4
Other	1803	5.5
Hospital of admission		
Hospital type		
Public	18 734	57.1
Private	14 096	42.9
Hospital remoteness		
Major city	19 754	60.2
Inner regional	8424	25.7
Outer regional	4137	12.6
Remote/very remote	363	1.1
Hospital depth of coding		
1—least comprehensive	1629	5.0
2	8803	26.8
3	11 543	35.2
4—most comprehensive	10 857	33.1
Hospital peer group		
Principal referral	6329	19.3
Major	11 052	33.7
District	6862	20.8
Community	7018	21.4
Other	1571	4.8

Table 2 Characteristics of the hospital of admission

	All hospitals (N=313)	
	N	Per cent
Hospital type		
Public	224	71.6
Private	88	28.1
Hospital remoteness		
Major city	124	39.6
Inner regional	72	23.0
Outer regional	94	30.0
Remote/very remote	20	6.4
Hospital depth of coding		
1—least comprehensive	48	15.3
2	91	29.1
3	89	28.4
4—most comprehensive	85	27.2
Hospital peer group		
Principal referral	14	4.5
Major	33	10.5
District	51	16.3
Community	121	38.7
Other	94	30.0

Patient-level and hospital-level predictors of positive agreement

The patient factors, which predicted positive agreement between the two data sources, differed between morbidities (table 4). Male sex was associated with better agreement for diabetes (OR=1.37, 95% CI 1.19 to 1.58), heart disease (OR=1.30, 95% CI 1.17 to 1.44) and hypertension (OR=1.28, 95% CI 1.18 to 1.38; see online supplementary table S2).

Older patients were significantly less likely to have smoking (80+years OR=0.48, 95% CI 0.31 to 0.74) and obesity (OR=0.14, 95% CI 0.08 to 0.26) recorded in their hospital records and significantly more likely to have hypertension recorded (OR=1.32, 95% CI 1.16 to 1.49), compared with younger patients (45–59 years). People with higher levels of functional limitation were significantly more likely to have hypertension, diabetes and obesity recorded on their most recent hospital stay. Planned admissions to hospital had lower odds of having any of the six conditions recorded, as did medical admissions (for diabetes, smoking and obesity only). Agreement did not vary significantly for any other patient factors.

The four hospital-level covariates (hospital type, hospital peer group, hospital remoteness and depth of coding) were added to multilevel models (including a random intercept for hospital) one at a time, separately. Positive agreement between self-report and hospital records was significantly lower for hospitals with lower depth of coding across all morbidities. The odds of recording were also lower among private hospitals for all six morbidities, with this difference being statistically significant for hypertension, heart disease and stroke only. Records from smaller hospitals (district and community peer groups) were significantly less likely to agree with self-reported data on hypertension, diabetes and heart disease. Positive agreement did not vary significantly with remoteness of hospital, with the exceptions of diabetes (lower agreement for outer regional, remote and very remote hospitals) and smoking (lower agreement for remote and very remote hospitals; see online supplementary table S3).

Quantifying variation between hospitals

Before any hospital-level variables were added into the multilevel model, ICC indicated that between 8% (diabetes) and 22% (heart disease) of the residual (unexplained) variation in agreement was attributable to the hospital after adjustment for the patient-level factors (table 5). This equated to MORs of 1.64 and 2.48, respectively, indicating that a patient in one hospital had an average of between 64% and 148% higher odds of having a particular morbidity recorded than a patient in a hospital with lower levels of recording. Less variation at the hospital level was found for the recording of diabetes, smoking and stroke, while more variation at the hospital level was found for the recording of hypertension, heart disease and obesity. When the analyses were restricted to 82 large public hospitals only, the between-hospital variation decreased to between 2% (stroke) and 13% (hypertension), or MOR of 1.24 and 1.94 (figure 1). This between-hospital variation was still significant for all morbidities except for stroke. Between-hospital variation was further reduced once lookback admissions were used to identify morbidities.

The addition of hospital-level variables to multilevel models, one at a time, separately, helped ascertain which factors explained the variation between hospitals (table 5). The addition of hospital-level factors contributed to explaining (i.e. decreasing) the residual variation for all conditions, except obesity. For the other morbidities, differences in the depth of coding explained from 16% (smoking) to 42% (hypertension) of residual variation between hospitals, while hospital type (public/private) explained from 0% (smoking) to 59% (stroke), and hospital peer group explained from 10% (hypertension) to 27% (diabetes) residual variation between hospitals.

DISCUSSION

Our study found that the concordance of administrative hospital and self-reported data varied between the six morbidities examined, with agreement ranging from good for diabetes; moderate for smoking; through to fair for heart disease; and poor for hypertension, stroke and obesity. We demonstrated considerable between-hospital variation in the recording of these common health conditions. Smaller, but still significant, between-hospital variation was found when restricting the analyses to the largest public hospitals in the state.

Previous studies have validated information recorded in NSW administrative hospital data for demographic factors,[34 35] and recording of perinatal conditions,[36–39]

Table 3 Agreement measures between self-report and hospital data, index and lookback admissions, all public and private hospitals in New South Wales, Australia (n=313)

	Index admission						Lookback admissions					
	45 and Up yes		45 and Up no		κ		45 and Up yes		45 and Up no		κ	
Morbidities*	APDC yes	APDC no	APDC yes	APDC no	Per cent	95% CI	APDC yes	APDC no	APDC yes	APDC no	Per cent	95% CI
Hypertension	4767	10 512	1434	16 119	24.0	(22.9 to 25.0)	6260	9019	2051	15 502	30.2	(29.1 to 31.2)
Heart disease	3639	4668	1942	22 583	40.3	(39.0 to 41.5)	4673	3634	2697	21 828	47.0	(45.8 to 48.2)
Diabetes	3560	1234	347	27 691	79.1	(78.1 to 80.1)	3928	866	479	27 559	83.0	(82.1 to 83.9)
Stroke	541	1939	306	30 046	29.8	(27.0 to 32.6)	776	1704	488	29 864	38.3	(35.8 to 40.8)
Smoking	1205	804	727	30 096	58.7	(56.7 to 60.7)	1411	598	1076	29 747	60.1	(58.2 to 61.9)
Obesity	551	7611	114	24 556	9.1	(7.3 to 10.9)	810	7352	209	24 461	12.8	(11.1 to 14.6)
Hypertension+heart disease	1172	3481	1270	26 909	25.8	(23.8 to 27.7)	1807	2846	2008	26 171	34.3	(32.6 to 36.0)
Hypertension+diabetes	1819	1238	759	29 016	61.3	(59.6 to 62.9)	2186	871	1021	28 754	66.6	(65.2 to 68.1)
Hypertension+stroke	203	1317	189	31 123	19.7	(15.7 to 23.7)	329	1191	340	30 972	28.0	(24.5 to 31.5)
Hypertension+smoking	133	598	180	31 921	24.5	(19.2 to 29.7)	199	532	319	31 782	30.6	(26.0 to 35.2)
Hypertension+obesity	234	4574	93	27 931	7.4	(4.9 to 9.8)	383	4425	183	27 841	11.5	(9.2 to 13.9)
Heart disease+diabetes	646	1154	404	30 628	43.0	(40.3 to 45.8)	904	896	661	30 371	51.2	(48.9 to 53.6)
Heart disease+stroke	76	973	126	31 657	11.2	(6.1 to 16.4)	149	900	261	31 522	19.0	(14.4 to 23.5)
Heart disease+smoking	76	294	222	32 240	22.0	(15.3 to 28.6)	118	252	373	32 089	26.5	(20.8 to 32.2)
Heart disease+obesity	79	1938	79	30 736	6.4	(2.5 to 10.4)	151	1866	169	30 646	11.4	(7.7 to 15.2)
Diabetes+stroke	85	555	58	32 134	21.1	(15.0 to 27.3)	140	500	119	32 073	30.4	(24.9 to 35.8)
Diabetes+smoking	143	161	108	32 420	51.1	(45.3 to 56.9)	171	133	176	32 352	52.1	(46.7 to 57.4)
Diabetes+obesity	232	1701	65	30 834	19.5	(15.9 to 23.2)	351	1582	120	30 779	27.5	(24.2 to 30.9)
Stroke+smoking	13	142	28	32 649	13.1	(0.1 to 26.1)	23	132	57	32 620	19.3	(7.8 to 30.8)
Stroke+obesity	6	558	9	32 259	2.0	(0.0 to 10.0)	13	551	21	32 247	4.2	(0.0 to 11.9)
Smoking+obesity	27	447	29	32 329	9.9	(1.9 to 17.9)	38	436	47	32 311	13.2	(5.5 to 20.9)

*ICD-10-AM codes: hypertension (I10–I15, R03.0), heart disease (I20–I52), diabetes (E10–E14), stroke (I60–I69, G45, G46), smoking (F17.2, Z72.0), obesity (E66).
APDC, Admitted Patient Data Collection; ICD-10-AM, International Statistical Classification of Diseases and Health Related Problems 10th Revision, Australian modification.

Table 4 Factors that predict positive agreement between self-report and hospital data, using multilevel modelling, all public and private hospitals in New South Wales, Australia (n=313)

	Hypertension (N=15 279)	Diabetes (N=4794)	Heart disease (N=8307)	Stroke (N=2480)	Smoking (N=2099)	Obesity (N=8162)
Person-level variables						
Sex†	**	**	**			
Age†	**				**	**
Education†			*		**	
Country of birth†				**		
Functional limitation†	**	**				**
Income†						
Admission type‡	**	**	**	**	**	**
Emergency status‡	**	**	**	**		**
Hospital-level variables						
Hospital type (public/private)§	**		**	**		
Hospital remoteness§					*	
Hospital depth of coding§	**	**	**	**	**	**
Hospital peer group§	**	**	**		**	

*Significant at 5% level.
**Significant at 1% level.
†Model 0: adjusted for demographic factors+random intercept for hospital.
‡Model 0+admission type+emergency status.
§Model 0+hospital-level variables (entered one at a time).

but there have been limited studies of the accuracy of the recording of health conditions commonly used for case-mix or risk adjustment. Our findings regarding agreement for the recording of diabetes (κ=0.83) were similar to previous Australian studies,[3 10] while agreement for hypertension (κ=0.3) and heart disease (κ=0.47) was considerably lower in our study. These differences may be due to the fact that both previous studies used medical records as a 'gold standard', while we used self-report. Lower agreement rates for heart disease could be due to the broader range of heart disease types included in our study, with known lower levels of agreement for heart failure compared with myocardial infarction.[9 40] Higher sensitivities reported in a study from the state of Victoria[10] could also be attributable to the differences in public hospital funding models between the two states. Specifically, Victoria has used activity-based funding since 1993, while this method of funding was introduced in NSW and other Australian states only subsequent to our study period.[41] Introduction of activity-based funding has been shown to increase recording of additional diagnoses and procedures in Europe.[42]

Some of the apparent discrepancies in the levels of coding between conditions can be attributed to the coding rules that govern whether or not a diagnosis is recorded in administrative hospital data. Additional diagnoses, recorded on administrative hospital data, are coded only if they affect the patient's treatments received, investigations required and/or resources used during the hospital stay. Thus, diagnoses that relate to an earlier episode, and which have no bearing on the current hospital stay, are not coded for that particular stay. Therefore, it is not surprising that (managed) hypertension, in particular, might not be recorded in hospital data relating to, e.g. elective surgery. On the other hand, we found that diabetes is well recorded, suggesting that it is considered to affect patient management in most hospital stays, and possibly reflecting the impact of changes to the Australian Coding Standards for diabetes such that between 2008 and 2010, diabetes with complications could be coded even where there was no established cause and effect relationship between diabetes and the complication.[43] It is for these reasons that researchers using administrative data sets are encouraged to incorporate information from previous hospitalisations, to increase the likelihood of capturing morbidity, as demonstrated in this as well as other Australian studies.[44]

As well as looking at single morbidities, ours is the first study, to our knowledge, to explore the variations of recording of multiple conditions in hospital data. Concordance of two-way condition combinations was very low, with best results found for combinations of diseases involving diabetes, which had the highest single-condition level of agreement with self-reported data (κ=0.83). Agreement measures for two-way combinations were found to be fair to good at best, with agreement on

Table 5 Variance and ICC for hospital-level random effects from multilevel logistic regression, all public and private hospitals in New South Wales, Australia (n=313)

		Hypertension (N=15 279)	Diabetes (N=4794)	Heart disease (N=8307)	Stroke (N=2480)	Smoking (N=2099)	Obesity (N=8162)
Hospital-level variance (SE)*							
Model 0	Patient factors	0.80 (0.10)	0.27 (0.06)	0.91 (0.12)	0.38 (0.10)	0.35 (0.09)	0.68 (0.14)
Model 1	Model 0 +hospital type (public/private)	0.65 (0.08)	0.27 (0.06)	0.71 (0.10)	0.16 (0.06)	0.35 (0.09)	0.69 (0.14)
Model 2	Model 0 +hospital remoteness	0.77 (0.09)	0.25 (0.05)	0.92 (0.12)	0.37 (0.10)	0.33 (0.08)	0.68 (0.14)
Model 3	Model 0 +hospital depth of coding	0.46 (0.06)	0.20 (0.05)	0.56 (0.08)	0.26 (0.08)	0.29 (0.08)	0.68 (0.14)
Model 4	Model 0 +hospital peer group	0.72 (0.09)	0.21 (0.05)	0.75 (0.10)	0.34 (0.09)	0.31 (0.08)	0.67 (0.14)
(ICC (%)†		19.5	7.6	21.6	10.4	9.6	17.1
(MOR†		2.34	1.64	2.48	1.80	1.76	2.19

*Patient-level variance in a logistic regression is set at $\pi^2/3=3.29$.[31]
†ICC and MOR calculated from model 0 (ICC=hospital-level variance divided by total variance (hospital-level+patient-level); MOR is calculated as $\exp^{0.954\times\sqrt{\text{variance}}}$).[30]
ICC, intraclass correlation coefficient; MOR, median OR; N, number of patients who self-reported condition.

three-way condition combinations (not investigated here) expected to be even lower. These findings have implications for research into multimorbidity (the co-occurrence of multiple chronic or acute diseases and medical conditions within one person[45]). We suggest that researchers who use administrative data for research into multimorbidity should use linked data to increase ascertainment and, if possible, supplement this information from other data sources, such as physician claims data or self-reported data.

We identified considerable between-hospital variability in the levels of recording of common health conditions, with between 8% and 22% of the variation attributable to hospital-level factors, after adjustment for patient factors. This was similar in magnitude to the variability previously reported for performance measures (varying from patient satisfaction, mortality, length of stay to quality of care) clustered at the facility level (0–51%)[46] and hospital-level variations in the use of services.[47–49] Significant between-hospital variation was still present after constraining the analyses to the 82 largest public hospitals in the state.

The recording of hypertension and heart disease was particularly variable between hospitals, those with better reporting having on average 2.3 and 2.5 times, respectively, the odds of recording these conditions than those with lower levels of reporting. The corresponding figures were 1.9 and 1.6 times for the 82 largest hospitals in the state. These findings indicate the potential for reporting bias to influence comparisons of health performance indicators between hospitals, especially for indicators that use conditions such as heart disease or hypertension for case-mix adjustment. To our knowledge, no previous studies have provided detailed information about how

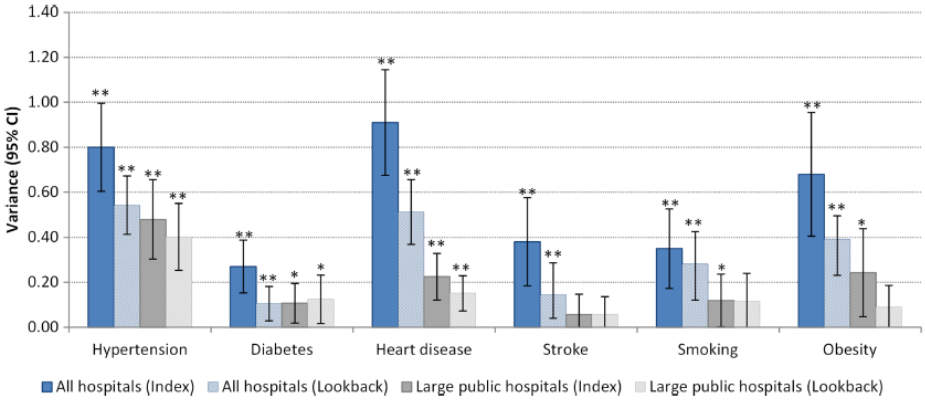

Figure 1 Variance for hospital-level random effects from multilevel logistic regression, for index and lookback admissions, by hospital size. *Significantly different from 0 at 5% level; **significantly different from 0 at 1% level.

the validity of morbidity reporting varies among hospitals after accounting for patient factors.

Furthermore, we have shown that variations in the accuracy of morbidity reporting between hospitals are predominantly driven by the hospital's depth of coding —concordance between self-reported and hospital data is lower in hospitals with a lower average number of additional diagnoses recorded. Up to 42% of the variation in recording at the hospital level could be attributed to differences in hospital depth of coding. Even though the measure of depth of coding we used was crude, and related to hospital size, it still helps in highlighting the impact of coding practices on variations among hospitals. Other research using the same depth of coding measure has shown that the lower depth of coding can disproportionately disadvantage hospitals' standardised mortality ratios, one of the commonly reported measures of hospital performance.[2] It will be important to track changes in the levels of the depth of coding across Australian states, and to consider the implications of these for state-based performance comparisons, following the national rollout of activity-based funding and comparative performance reporting.

Several factors might explain variation in depth of coding between hospitals. Clinical coders can code only information that has been recorded in the patient's medical record, so varying level of details recorded by clinicians will influence what gets coded. The training and professional development opportunities for coding staff might also influence the depth of coding. Also, case-mix funding systems, such as the Diagnosis Related Group (DRG) classification, are prone to 'upcoding' in order for services to receive higher reimbursement costs.[14]

We found that the reporting of conditions varied with hospital size, larger metropolitan hospitals having higher concordance, with κ values higher by 7% on average when comparing large tertiary with smaller urban hospitals. This finding echoes those of Powell *et al*[3] in NSW, Australia, during 1996–1998 and Rangachari[16] in the USA, during 2000–2004. Our study showed that large tertiary hospitals had better concordance for the recording of hypertension and heart disease than smaller urban hospitals, but the reverse was true for stroke and smoking. Our finding that between-hospital variation in the recording of morbidities was up to two times higher when all hospitals, rather than just the largest ones, were included has implications for further research using data from smaller hospitals. This high variability in concordance among smaller hospitals may mean that morbidity-adjusted comparisons are not as valid as for larger hospitals. Researchers using information from these hospitals are encouraged to supplement their data with either self-report information and/or data linkage. The value-add of incorporating previous hospitalisations was also highlighted in our results for stroke and obesity, with 43–47% more patients identified using lookback admissions than from a single admission only.

A particular strength of our study lies in the use of linked data from a large-scale cohort study to comprehensively evaluate the recording of common conditions in hospital data, and explore the variation in recording among hospitals. The 45 and Up Study contains records for one in every 10 persons aged 45 and over in NSW, so it provides a rich resource to answer research questions. Additionally, we used advanced multilevel modelling methods to quantify the amount of between-hospital variation in the level of recording of common health conditions, a finding which is of importance for research and policy paradigms due to its impact on adjusted comparisons among hospitals and the highlighted need to improve consistency of recording in hospitals across the state. To date, hospital-level variation has only been explored with a set outcome (e.g. mortality, readmission) in mind.

A potential limitation of our study was its use of self-reported information to explore concordance, in the absence of another 'gold standard', such as medical records. Access to medical records was not possible given the de-identified nature of our data and the large number of records in the data set. Moreover, studies that have examined accuracy of self-reported conditions against medical records have found high levels of agreement, ranging from 81%[50] to 87%[51] for hypertension, 66%[40] to 96%[50 51] for diabetes and 60%[50] to 98%[52] for acute myocardial infarction. Validation studies in the 45 and Up Study cohort have reported strong correlations and excellent levels of agreement between self-reported and measured height and weight, and derived BMI[53] as well as self-reported diabetes.[54] Although the 45 and Up Study had a response rate of 18%, the study sample is very large and has excellent heterogeneity. Furthermore, exposure–outcome relationships estimated from the 45 and Up Study data have been shown to be consistent with a large 'representative' population survey of the same population.[55]

CONCLUSION

The recording of common comorbid conditions in routine hospital data is highly variable and, for some conditions, very poor. Recording varies considerably among hospitals, presenting the potential to introduce bias into risk-adjusted comparisons of hospital performance, especially for indicators that use heart disease or hypertension for risk adjustment. Furthermore, between-hospital variation is amplified when smaller and private hospitals are included in the analyses. Stratification of analyses according to factors that predict the completeness of recording, including hospital depth of coding and hospital type and size, supplementing morbidity information with linked data from previous hospitalisations and increases in efforts to standardise recording across hospitals, all offer potential for increasing the validity of risk-adjusted comparisons.

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Contributors SL had overall responsibility for the design of this study, data management, statistical analysis and drafting this paper. DEW and LRJ contributed to the conception and design of the study. LRJ helped with data acquisition and provided oversight for all analyses. DAR and JMS provided oversight and advice for the design and interpretation of the statistical analyses. All authors contributed to the interpretation of the findings, the writing of the paper and approved the final draft.

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Competing interests None.

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4.5 Knowledge building

This Chapter used linkage of two data sources (survey and hospital data) and found that the recording of common comorbid conditions varies between conditions, and between hospitals. It highlighted the value-add of incorporating prior hospitalisations in identifying patients with morbidities. Informed by these findings, lookback periods were used to ascertain morbidities in the remaining thesis chapters.

Ascertainment of chronic diseases using a third source of data – medications – as well as comparison of prevalence of multimorbidity between all three data sources was carried out in Chapter 5.

Due to the differences in between-hospital variation of recording of morbidities, stratification/restriction of results by hospital type was undertaken in Chapter 7 to alleviate the possibility of bias for hospital-based performance reporting.

CHAPTER 5

Multimorbidity in Australia: Comparing estimates derived using administrative data sources and survey data

5.1 Background and aims

Multimorbidity estimates have most commonly been derived using primary health care data sources. However, Australian does not yet have a national primary health care dataset that would allow for accurate estimation of the burden of multimorbidity within the primary care setting.

The current study uses record linkage of self-report survey data from a large cohort study with two sets of administrative data to compare ascertainment of multimorbidity. Specifically, it investigates:

a) The concordance of identification of multimorbidity using self-report and administrative datasets
b) the similarities and differences between people with multimorbidity ascertained using different datasets and
c) whether the same individuals are classified as multimorbid using different data sources.

5.2 Key findings

The study shows that the ascertainment of multimorbidity, using the same list of chronic conditions and the same individuals, varies between data sources, and that, even where the estimated prevalence of multimorbidity is similar for two data sets, the concordance in classification as multimorbid for individual patients is low.

5.3 Publication details

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SUPPORTING INFORMATION

S1 Fig and S1 Table of this publication are shown in Appendix 4.

5.4 Student contribution

I conceptualised and designed the study with the help from co-authors. I carried out data curation and management, performed statistical analysis and visualisations, drafted the initial manuscript, and reviewed and revised the manuscript following co-authors' and reviewers' comments. Louisa Jorm acquired the data. Supervisors (Louisa Jorm and Judy Simpson) provided oversight of the analysis and contributed to the study result interpretations. Co-authors Nicholas Zwar and Hassan Hosseinzadeh provided advice on the study interpretation.

PLOS ONE

RESEARCH ARTICLE

Multimorbidity in Australia: Comparing estimates derived using administrative data sources and survey data

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Data Availability Statement: The 45 and Up Study is an open research resource which is managed by the Sax Institute. The datasets for this article were created by linkage of the 45 and Up Study baseline survey data to Australian Government and NSW state data sources with support from the NSW Centre for Health Record Linkage (www.cherel.org.au), and permission from the custodians of the datasets (Department of Human Services for PBS dataset, NSW Ministry of Health for APDC dataset) under specific ethics approvals. Interested researchers can contact the Sax Institute

Abstract

Background

Estimating multimorbidity (presence of two or more chronic conditions) using administrative data is becoming increasingly common. We investigated (1) the concordance of identification of chronic conditions and multimorbidity using self-report survey and administrative datasets; (2) characteristics of people with multimorbidity ascertained using different data sources; and (3) whether the same individuals are classified as multimorbid using different data sources.

Methods

Baseline survey data for 90,352 participants of the 45 and Up Study—a cohort study of residents of New South Wales, Australia, aged 45 years and over—were linked to prior two-year pharmaceutical claims and hospital admission records. Concordance of eight self-report chronic conditions (reference) with claims and hospital data were examined using sensitivity (Sn), positive predictive value (PPV), and kappa (κ).The characteristics of people classified as multimorbid were compared using logistic regression modelling.

Results

Agreement was found to be highest for diabetes in both hospital and claims data (κ = 0.79, 0.78; Sn = 79%, 72%; PPV = 86%, 90%). The prevalence of multimorbidity was highest using self-report data (37.4%), followed by claims data (36.1%) and hospital data (19.3%). Combining all three datasets identified a total of 46 683 (52%) people with multimorbidity, with half of these identified using a single dataset only, and up to 20% identified on all three datasets. Characteristics of persons with and without multimorbidity were generally similar. However, the age gradient was more pronounced and people speaking a language other than English at home were more likely to be identified as multimorbid by administrative data.

(45andup.research@saxinstitute.org.au) and NSW Centre for Record Linkage (cherel.mail@moh.health.nsw.gov.au) for data access approval procedures.

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Competing interests: The authors have declared that no competing interests exist.

Conclusions

Different individuals, with different combinations of conditions, are identified as multimorbid when different data sources are used. As such, caution should be applied when ascertaining morbidity from a single data source as the agreement between self-report and administrative data is generally poor. Future multimorbidity research exploring specific disease combinations and clusters of diseases that commonly co-occur, rather than a simple disease count, is likely to provide more useful insights into the complex care needs of individuals with multiple chronic conditions.

Introduction

Chronic diseases are the leading cause of illness, disability and death, accounting for 68% of global [1] and 90% of all Australian deaths [2]. The prevalence of chronic conditions has been increasing over the past forty years [3], with the greatest growth seen in the concurrent presence of multiple chronic diseases (known as multimorbidity [4]), attributable to the ageing population, and advances in medical care and public health policy [5, 6]. One third of the Australian population [7] are estimated to have multimorbidity, with up to 80% of those aged 65 and over having three or more chronic conditions [8].

Appropriate and accurate measurement of the prevalence of chronic disease and multimorbidity is essential in order to monitor trends, estimate burden of disease, target preventive measures, and plan treatment and care delivery. A variety of data sources are used for monitoring, including population health surveys, disease registries and administrative databases (including primary health care, hospitalisation and medication data), with the use of the latter becoming increasingly common due to its efficient capture, ease of use and inexpensive nature [9]. However, the use of administrative data is not without drawbacks. These data have different levels of capture of chronic disease, and variable data quality [10–14]. Furthermore, not all patients with chronic diseases use hospital services, and even when they do, their admission record may not capture all of their conditions. Medication data, on the other hand, present a different set of challenges. In some instances, prescribed medications are clearly linked to the treatment of a specific chronic condition (e.g. insulin in diabetic patients). In other cases, medications may have multiple indications (e.g. β-blockers for heart failure and high blood pressure). The majority of Australian studies of multimorbidity have estimated multimorbidity using self-report data [15–19].

Research on comparative estimates of multimorbidity derived using different data sources is scarce. The majority of multimorbidity studies use only one dataset (for example [17–21]), with only a handful of studies [22–27] examined the difference in prevalence estimates between data sources. These studies found differences in estimates of multimorbidity, but these were largely attributable to differing study populations and numbers of conditions counted in the multimorbidity definition. Even when trying to standardise the multimorbidity definition by using the same list of chronic conditions [26] or comparing multimorbidity within the same sample [24], no study has examined whether the same people, using the same list of chronic conditions, are classified as multimorbid using different data sources.

The current study used record linkage of self-report survey data from a large cohort study with two sets of administrative data to compare ascertainment of common chronic conditions. Specific aims were to investigate: (1) the concordance of identification of chronic conditions

and multimorbidity using self-report and administrative datasets; (2) the similarities and differences between people with multimorbidity ascertained using different datasets; and (3) whether the same individuals are classified as multimorbid using different data sources.

Methods

Data sources

The 45 and Up Study. The 45 and Up Study is a large-scale cohort study involving 266,950 men and women aged 45 years and over from the general population of New South Wales, Australia's most populous state. The study is described in detail elsewhere [28]. In brief, participants in the 45 and Up Study were randomly sampled from the Department of Human Services (formerly Medicare Australia) enrolment database, which provides near complete coverage of the population. People 80+ years of age and residents of rural and remote areas were oversampled. Participants joined the Study by completing a baseline questionnaire between February 2005 and March 2009 and giving signed consent for linkage of their information to routine health databases [28]. Of those invited, about 18% participated and these comprised about 11% of the NSW population aged 45 and over [28]. The baseline questionnaire was modified over time in an attempt to better capture self-report or doctor-diagnosed common illnesses. There were three versions of the questionnaire. In version 1, asthma, hayfever and depression were not included. In versions 2 and 3 separate questions for asthma, hayfever and depression were present [29].

Pharmaceutical Benefits Scheme (PBS). The PBS database contains information on Commonwealth subsidised claims for prescribed medicines listed on the Schedule of Pharmaceutical Benefits [30]. The main PBS beneficiaries include concession card holders (people aged 65 and over who meet an income test, people with disability, low income or facing a large burden of dependants) and general beneficiaries. Prior to 2012, only records for PBS-listed prescription medications for which a government subsidy was paid were recorded on the PBS data. This resulted in differential capture of prescribed medicines by concession card holders and general beneficiaries. Capture for concession card holders was complete, as all prescription medicines cost more that the concession threshold. However, PBS-medicines falling below the co-payment threshold for general beneficiaries were not captured in the PBS data. We therefore restricted our analyses to concession card holders only, to avoid potential incomplete capture of medicines dispensed to general beneficiaries. PBS data from 1 September 2005 to 20 December 2011 were linked deterministically to 45 and Up Study questionnaire data by the Sax Institute, using a unique identifier that was provided to the Department of Human Services (DHS). PBS data included date of dispensing, beneficiary status, PBS item code, Anatomical Therapeutic Chemical (ATC) code [31] and quantity supplied. Unless otherwise specified, the term medication data in the paper refers to the PBS data.

The NSW Admitted Patient Data Collection (APDC). The APDC includes records of all public and private hospital admissions ending in a separation, i.e. discharge, transfer, type-change or death. Diagnoses are coded according to the Australian modification of the International Statistical Classification of Diseases and Related Problems 10th Revision, ICD-10-AM [32]. Up to 55 diagnoses codes are recorded on the APDC, including the principal diagnosis and up to 54 additional diagnoses. The APDC from 1 July 2000 to 31 December 2013 was linked probabilistically to survey information from the 45 and Up Study by the NSW Centre for Health Record Linkage (www.cherel.org.au) using the 'best practice' protocol for preserving privacy [33]. Unless otherwise specified, the term hospital data in the paper refers to the APDC data.

Study population

People aged 45 years and over were included in the analysis if they: (a) completed the 45 and Up Study baseline study questionnaire between 1 September 2007 and 2 March 2009; and (b) had a PBS record for any prescription medication within 2 years preceding the questionnaire date (longest lookback available). Only those with consistent PBS concession card holder status within the 2-year period were included. Information about hospitalisations for these participants was also obtained from the APDC data, restricted to the same 2-year period as the PBS data. People who answered version 1 of the 45 and Up Study baseline questionnaire (n = 37 088) were excluded, as it was not possible to ascertain self-report of doctor-diagnosed depression for these participants. Holders of a Department of Veterans' Affairs health card (n = 6 299) were also excluded, as the PBS does not capture all the services provided to these individuals. A total of 90 352 people with consistent PBS concession card holder status were included in the analysis: 46,766 persons with claims data only (medication only); and 43 586 persons with both claims and hospitalisation records (medication + hospitalisation) (S1 Fig)

Morbidity measures

A total of eight chronic conditions (hypertension, cancer, heart disease, stroke, diabetes, asthma, depression and Parkinson's disease–hereafter referred to as 'morbidities') were selected for analysis, based on their availability in both self-report and administrative data.

Self-report morbidities were ascertained on the basis of responses to a single question "Has a doctor ever told you that you have (*name of condition*)?" in the baseline 45 and Up Study survey.

Morbidity in the hospital data was ascertained using ICD-10-AM codes in any of the 55 diagnosis fields (S1 Table). The initial list of eligible ICD-10 codes was obtained from the Charlson Index [34, 35] and Elixhauser Index [36, 37], and refined following advice from a clinical coder. If a condition was coded at least once in the 2-year lookback period, then a person was coded as having that condition in the hospital data.

Morbidity in the medication data was ascertained using ATC codes obtained from Rx-Risk-V [38, 39], published reports [40], and research articles [41–47]. A person was coded as having conditions of interest if a specific ATC code was present in the medication data at least twice in the 2-year lookback period, as it was expected that chronic condition medications would be used regularly. Where published literature had different ATC codes, we chose the codes that had the highest positive predictive value (S1 Table).

A count of conditions in each of the three datasets (self-report, medication and hospital) was created by summing the total number of chronic conditions, ranging from 0 to 8, as well as the total when stroke was excluded. Multimorbidity was defined as having two or more chronic conditions, which is the most commonly used definition in the literature [48]. Complex multimorbidity was defined as having three or more chronic conditions affecting three or more body systems [49].

Statistical methods

Measures of agreement. Agreement between the three data sources was measured by estimating sensitivity (Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and Cohen's kappa statistic (κ) using self-report morbidity measures as the reference. Sensitivity represents the percentage of those with a condition (according to self-report) who were correctly identified as having that condition in administrative data. Specificity represents the percentage of those without a self-report condition who did not have a condition in administrative data. PPV represents the percentage of those identified as having a condition of

interest in the administrative data, who actually had the condition, according to self-report. NPV represents the percentage of those identified as not having a condition of interest in the administrative data, who did not have a condition according to the self-report. The kappa statistic (κ) represents the proportion agreement corrected for chance. Kappa values above 0.75 denote excellent agreement, 0.40 to 0.75 fair to good agreement and below 0.45 poor agreement [50].

Analysis. Logistic regression was used to model the odds of multimorbidity, within each dataset separately. All analyses were adjusted for age (categorised into four 10-year age groups and 85+) and sex, and adjusted odds ratios (aORs) and their corresponding 95% confidence intervals (CI) were calculated. A range of categorical variables were examined, including remoteness of residence, highest education attainment, Aboriginal or Torres Strait Islander origin, country of birth, language other than English spoken at home, household income and marital status. Information about these variables was obtained from the 45 and Up Study baseline questionnaire. All data management and analyses were conducted using SAS software, version 9.3 [51].

Ethical approvals

Ethics approvals for this study were obtained from the NSW Population and Health Services Research Ethics Committee and the Aboriginal Health & Medical Research Ethics Committee. The conduct of the 45 and Up Study was approved by the University of New South Wales Human Research Ethics Committee.

Results

Sample characteristics

The sample comprised 90 352 participants, who all had a PBS record within the 2 years prior to joining the 45 and Up Study. Forty eight percent of participants also had a hospitalisation in the same timeframe. The mean age at survey completion was 70.2 years in the full sample, and 71.8 years among those with a hospital record. The median number of self-report conditions was 1, with hypertension being the most commonly reported. Other characteristics of the study population are presented in Table 1.

Agreement measures

Table 2 summarises agreement measures for self-report and administrative data for all eight chronic conditions and multimorbidity definitions. Excellent levels of agreement beyond chance were only found for diabetes, in both medication and hospital datasets. Fair to good agreement was found for hypertension, asthma, depression and Parkinson's disease in the medication data only. The agreement between self-report and hospital data was generally poor.

Except for cancer, sensitivity values were found to be higher in medication data (range 51.5% - 72.4%) than the hospital data (range 6.1% - 78.6%) (Fig 1). However, hospital data exhibited higher levels of PPV across all conditions, with the majority of PPVs higher than 70%. The highest PPV was for cancer (89%) in hospital data, and diabetes (90%) in medication data.

Prevalence of individual chronic conditions varied by data source, with hypertension identified in nearly 50% of the sample. Stroke prevalence estimates were found to be four times greater using medication data than self-report data (22.5% vs 5.6%), so stroke was excluded from the count of conditions in the remaining analyses.

Table 1. Characteristics of the study population.

	Medication + Hospitalisation (N = 43,586)		Full sample (N = 90,352)	
Mean age, years (standard deviation)	71.8 (9.7)		70.2 (10.2)	
Median number of self-report chronic conditions (range)	1 (0–8)		1 (0–8)	
Median number of self-report chronic conditions (exc stroke) (range)	1 (0–7)		1 (0–7)	
Male sex, n (%)	20,509 (47.1)		40,032 (44.3)	
Born overseas, n (%)	10,300 (23.6)		22,575 (25.0)	
Speaks language other than English at home, n (%)	4,173 (9.6)		9,525 (10.5)	
Aboriginal or Torres Strait Islander, n (%)	410 (0.9)		904 (1.0)	
Self-report conditions:	% with this condition	% with 1+ other conditions	% with this condition	% with 1+ other conditions
Hypertension	48.7	70.6	46.2	63.8
Cancer	26.4	75.2	20.9	73.1
Heart disease	23.9	82.2	18.5	80.6
Stroke	7.3	88.8	5.6	87.8
Diabetes	15.2	87.7	13.6	84.4
Asthma	14.0	82.3	12.6	77.8
Depression	16.2	79.0	15.7	72.8
Parkinson's	1.2	85.5	1.0	83.3

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Prevalence of multimorbidity

The prevalence of multimorbidity in the study sample was highest using the self-report data (37.4% in the overall sample, 44.2% among those hospitalised), followed by medication data (36.1%) and hospital data (19.3%) (Table 2). The highest level of complex multimorbidity was found among hospitalised patients using the self-report multimorbidity definition (11%).

The prevalence of multimorbidity was higher in males, and increased with age, using all three data definitions (Fig 2). For those aged under 75 years, the highest prevalence was found using self-report data. For people aged over 75 years, the estimates, particularly in women, were higher using medication data. The proportion of persons with multimorbidity was consistently lower in hospital data compared to the other two datasets.

Associations between multimorbidity and key demographic variables were found to be consistent between datasets, with some differences in the magnitudes of these relationships. The odds of multimorbidity were higher in people who were male, older, of Aboriginal or Torres Strait Islander origin, widowed/divorced/separated, or lived in remote/very remote areas (Table 3). Males had higher odds of multimorbidity using hospital data than with medication data (OR = 1.49 versus OR = 1.07). The age gradient in multimorbidity was more pronounced using administrative data than self-report data (OR >2.5 versus OR = 1.83 for those aged 75–84). People speaking a language other than English at home had 6% higher odds of having multimorbidity (OR = 1.06, 95% CI 1.01–1.10) using medication data and 32% higher odds using hospital data (OR = 1.32, 95% CI 1.22–1.42), but 20% lower odds (OR = 0.80, 95% CI 0.76–0.84) of multimorbidity using self-report data.

Agreement in multimorbidity between datasets

A total of 46 683 (52%) people were found to have multimorbidity in any of the three datasets–33 768 using self-report data, and an additional 12 915 using administrative data only. Of all multimorbid cases, half were identified using a single dataset only, and around one in ten

Table 2. Measures of agreement between self-report chronic conditions and administrative data, 2-year lookback.

Chronic condition	Sn (95% CI)	PPV (95% CI)	Sp (95% CI)	NPV (95%CI)	Kappa	Prevalence admin data	Prevalence self-report	Relative difference
Hospital data (n = 43,586)[3]								
Hypertension	34.5 (33.9–35.2)	72.7 (71.8–73.6)	87.7 (87.2–88.1)	58.5 (57.9–59.0)	0.23	23.1%	48.7%	-53%
Cancer	17.9 (17.2–18.6)	89.0 (87.7–90.2)	99.2 (99.1–99.3)	77.1 (76.7–77.5)	0.23	5.3%	26.4%	-80%
Heart disease	44.4 (43.4–45.3)	59.0 (57.9–60.1)	90.3 (90.0–90.6)	83.8 (83.4–84.2)	0.38	18.0%	23.9%	-25%
Stroke	13.2 (12.0–14.4)	74.7 (71.0–78.2)	99.7 (99.6–99.7)	93.6 (93.4–93.8)	0.21	1.3%	7.3%	-82%
Diabetes	78.6 (77.6–79.6)	86.1 (85.2–86.9)	97.7 (97.6–97.9)	96.2 (96.0–96.4)	0.79	13.8%	15.2%	-9%
Asthma	6.9 (6.3–7.5)	80.8 (77.2–83.9)	99.7 (99.7–99.8)	86.8 (86.5–87.1)	0.11	1.2%	14.0%	-91%
Depression	6.1 (5.6–6.7)	70.5 (66.7–73.9)	99.5 (99.4–99.6)	84.6 (84.2–84.9)	0.09	1.4%	16.2%	-91%
Parkinsons's	29.1 (25.4–33.0)	82.5 (76.5–87.3)	99.9 (99.9–99.9)	99.1 (99.0–99.2)	0.43	0.4%	1.2%	-65%
MM[1]	33.5 (32.8–34.2)	76.7 (75.8–77.6)	91.9 (91.6–92.3)	63.6 (63.1–64.1)	0.27	19.3%	44.2%	-56%
Complex MM[2]	7.4 (6.7–8.1)	67.9 (63.8–71.8)	99.6 (99.5–99.6)	89.7 (89.4–90.0)	0.11	1.2%	11.0%	-89%
Medication data (n = 90,352)[4]								
Hypertension	62.2 (61.7–62.6)	79.9 (79.4–80.3)	86.6 (86.3–86.9)	72.7 (72.4–73.1)	0.50	35.9%	46.2%	-22%
Cancer	4.5 (4.2–4.8)	47.6 (45.3–50.0)	98.7 (98.6–98.8)	79.6 (79.3–79.9)	0.05	2.0%	20.9%	-91%
Heart disease	67.9 (67.2–68.6)	35.3 (34.7–35.8)	71.7 (71.3–72.0)	90.8 (90.5–91.0)	0.29	35.7%	18.5%	93%
Stroke	64.1 (62.8–65.4)	16.0 (15.5–16.5)	80.0 (79.8–80.3)	97.4 (97.3–97.5)	0.18	22.5%	5.6%	300%
Diabetes	72.4 (71.7–73.2)	90.0 (89.4–90.5)	98.7 (98.6–98.8)	95.8 (95.6–95.9)	0.78	11.0%	13.6%	-19%
Asthma	65.4 (64.6–66.3)	57.3 (56.5–58.2)	93.0 (92.8–93.2)	94.9 (94.8–95.1)	0.55	14.4%	12.6%	14%
Depression	51.5 (50.7–52.3)	66.4 (65.5–67.3)	95.1 (95.0–95.3)	91.3 (91.1–91.5)	0.51	12.2%	15.7%	-22%
Parkinson's	58.9 (55.7–62.0)	53.3 (50.3–56.4)	99.5 (99.4–99.5)	99.6 (99.5–99.6)	0.56	1.1%	1.0%	10%
MM[1]	60.4 (59.8–60.9)	62.5 (62.0–63.0)	78.4 (78.0–78.7)	76.8 (76.5–77.2)	0.39	36.1%	37.4%	-3%
Complex MM[2]	24.7 (23.7–25.6)	56.2 (54.5–57.8)	98.2 98.1–98.2)	93.2 (93.0–93.3)	0.31	3.8%	8.7%	-56%
Medication or hospital data (n = 90,352)[5]								
Hypertension	66.2 (65.8–66.7)	78.0 (77.6–78.5)	84.0 (83.7–84.3)	74.4 (74.0–74.7)	0.51	39.2%	46.2%	-15%
Cancer	13.1 (12.6–13.5)	68.5 (66.9–70.0)	98.4 (98.3–98.5)	81.0 (80.8–81.3)	0.16	4.0%	20.9%	-81%
Heart disease	73.1 (72.4–73.8)	35.7 (35.2–36.2)	70.0 (69.7–70.4)	92.0 (91.7–92.2)	0.31	38.0%	18.5%	105%
Stroke	65.8 (64.5–67.1)	16.3 (15.8–16.8)	79.9 (79.7–80.2)	97.5 (97.4–97.6)	0.19	22.6%	5.6%	303%

(*Continued*)

Table 2. (*Continued*)

Chronic condition	Sn (95% CI)	PPV (95% CI)	Sp (95% CI)	NPV (95%CI)	Kappa	Prevalence admin data	Prevalence self-report	Relative difference
Diabetes	80.4 (79.7–81.1)	86.8 (86.2–87.4)	98.1 (98.0–98.2)	96.9 (96.8–97.1)	0.81	12.6%	13.6%	-7%
Asthma	65.8 (65.0–66.7)	57.3 (56.5–58.2)	92.9 (92.8–93.1)	95.0 (94.8–95.1)	0.55	14.5%	12.6%	15%
Depression	52.0 (51.1–52.8)	66.2 (65.3–67.0)	95.0 (94.9–95.2)	91.4 (91.1–91.6)	0.52	12.4%	15.7%	-21%
Parkinson's	59.5 (56.3–62.6)	52.6 (49.6–55.6)	99.4 (99.4–99.5)	99.6 (99.5–99.6)	0.55	1.2%	1.0%	13%
MM[1]	80.4 (80.0–80.8)	59.7 (59.2–60.1)	65.1 (64.7–65.5)	83.8 (83.4–84.1)	0.43	39.2%	37.4%	5%
Complex MM[2]	72.0 (71.2–72.7)	35.9 (35.4–36.5)	78.5 (78.2–78.8)	94.4 (94.2–94.5)	0.36	5.1%	8.7%	-41%

Sn: sensitivity; PPV: positive predictive value; Sp: specificity; NPV: negative predictive value

[1] Multimorbidity (MM): Presence of two or more chronic conditions, excluding stroke

[2] Complex MM: Presence of three or more chronic conditions affecting 3 or more body systems, excluding stroke

[3] Conditions ascertained from hospital diagnoses

[4] Conditions ascertained from medication codes

[5] Conditions ascertained from medication codes (for those without a hospitalisation), or medication or hospitalisation codes (for those with a hospitalisation)

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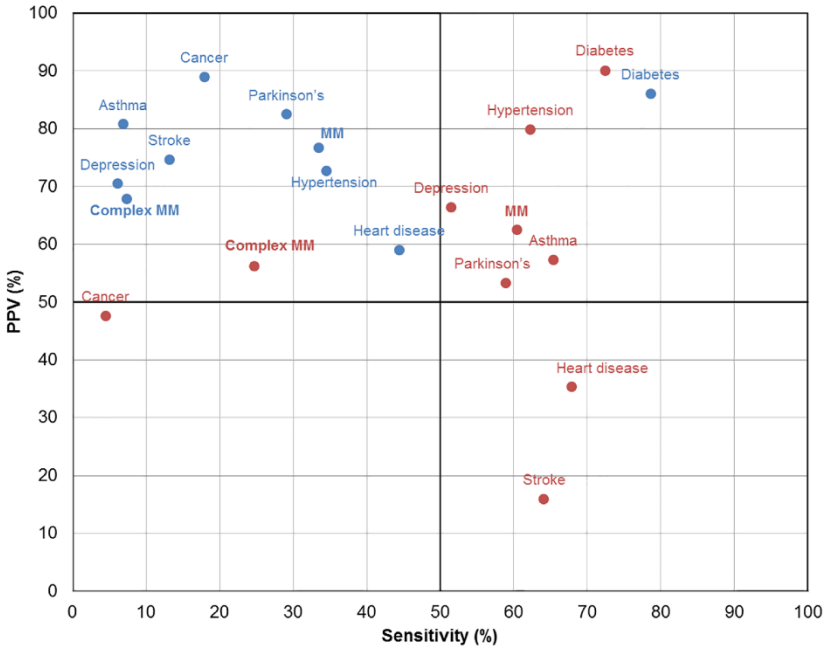

Fig 1. Agreement between self-report and administrative data sources. Blue circles–Hospital, Red circles–Medication. Abbreviations: MM–multimorbidity (2+ chronic conditions, excluding stroke); Complex MM–complex multimorbidity (3+ chronic conditions affecting 3 or more body systems, excluding stroke).

https://doi.org/10.1371/journal.pone.0183817.g001

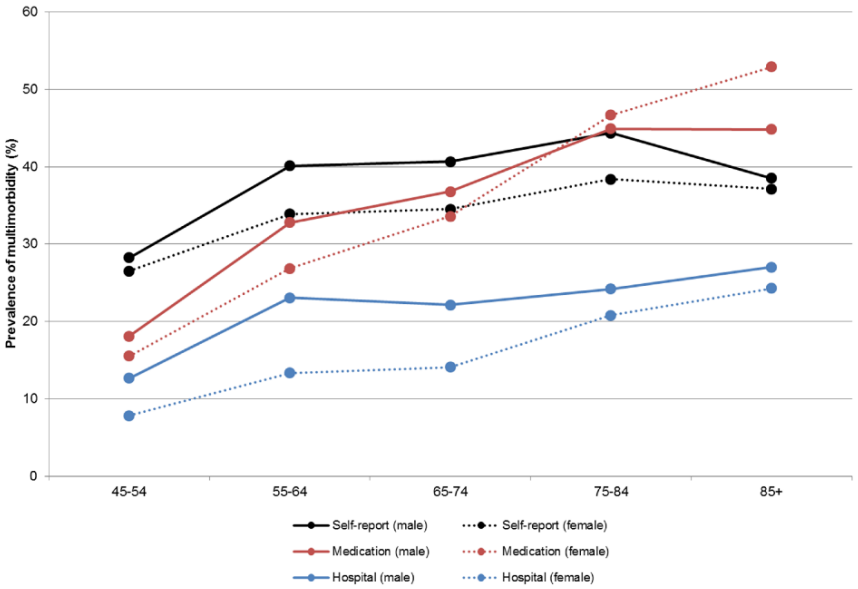

Fig 2. Prevalence of multimorbidity, by age group and data source. Black circles, solid line–Self-report (male); Black circles, broken line–Self-report (female); Red circles, solid line–Medication (male); Red circles, broken line–Medication (female); Blue circles, solid line–Hospital (male); Blue circles, broken line–Hospital (female).

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(n = 5 333, 11%) were multimorbid on all three datasets (Fig 3A). When the analyses were restricted to hospitalised patients, the overlap in the datasets increased to 20% (Fig 3B). The agreement on multimorbidity between datasets was poor, with kappa between 0.27 and 0.39, increasing to 0.43 when both hospital and medication data were combined (Table 2).

People identified as being multimorbid in only the self-report data had higher prevalence of cancer, depression, asthma and Parkinson's disease than those identified only in the administrative datasets. The most common self-report two-way combinations of morbidities were cancer and hypertension (n = 2 177), hypertension and depression (n = 1 243) and a three-way combination of cancer, hypertension and heart disease (n = 376).

Administrative data, however, were more likely to identify hypertension and heart disease than self-report, with the heart disease and hypertension two-way combination being the most prevalent in both medication (n = 7 291) and hospital datasets (n = 323) (data not shown).

Discussion

This record linkage study of self-report, hospital admission and medication data compared their use for identifying individuals with multimorbidity, based on the most common chronic conditions in Australia. It showed that the ascertainment of multimorbidity varied between data sources, and that, even where the estimated prevalence of multimorbidity was similar for two data sets, the concordance in classification as multimorbid for individual patients was low.

We investigated the level of concordance of identification of eight chronic conditions between self-report and administrative data. We found that chronic conditions identified in hospital data had higher PPVs and low sensitivities, indicating that although the hospital data does not identify all the people with a chronic condition, when such condition is identified, it is generally accurate. Diagnoses may not always be recorded during inpatient episodes of stay,

Table 3. Odds of multimorbidity, by data source.

Variable	n (%)[1]	Self-report data aOR (95% CI)	Medication data aOR (95% CI)	Hospital data aOR (95% CI)	Medication or Hospital data aOR (95% CI)
Age group[2]					
45–54 (ref)	8,388 (9.3)	1	1	1	1
55–64	15,830 (17.5)	1.51 (1.43, 1.60)	2.08 (1.94,2.22)	1.93 (1.67,2.23)	2.14 (2.00,2.28)
65–74	35,689 (39.5)	1.56 (1.48, 1.64)	2.73 (2.57,2.91)	1.98 (1.73,2.27)	2.81 (2.65,2.99)
75–84	25,441 (28.2)	1.83 (1.73, 1.93)	4.25 (3.99,4.53)	2.59 (2.26,2.96)	4.53 (4.26,4.81)
85+	5,004 (5.5)	1.62 (1.50, 1.74)	5.13 (4.73,5.55)	3.22 (2.76,3.75)	5.74 (5.31,6.22)
Sex[3]					
Female (ref)	50,320 (55.7)	1	1	1	1
Male	40,032 (44.3)	1.27 (1.23, 1.30)	1.07 (1.04,1.10)	1.49 (1.42,1.57)	1.13 (1.10,1.16)
Remoteness of residence[4]					
Major city (ref)	37,191 (41.2)	1	1	1	1
Inner regional	33,839 (37.5)	1.06 (1.03, 1.09)	0.97 (0.94,1.01)	0.92 (0.87,0.97)	0.97 (0.94,1.00)
Outer regional	17,506 (19.4)	1.00 (0.96, 1.04)	0.98 (0.94,1.02)	0.85 (0.79,0.91)	0.96 (0.93,1.00)
Remote/very remote	1,803 (2.0)	1.14 (1.03, 1.26)	1.11 (1.00,1.23)	1.28 (1.08,1.53)	1.10 (0.99,1.21)
Highest education[4]					
Did not complete school (ref)	42,789 (47.4)	1	1	1	1
High school, apprenticeship, grad dip	35,423 (39.2)	0.95 (0.92, 0.98)	0.80 (0.78,0.83)	0.83 (0.79,0.88)	0.80 (0.78,0.83)
University or higher	9,778 (10.8)	0.90 (0.86, 0.94)	0.65 (0.62,0.68)	0.72 (0.66,0.78)	0.65 (0.62,0.68)
Aboriginal or Torres Strait Islander [4]					
Non Aboriginal (ref)	87,142 (96.5)	1	1	1	1
Aboriginal	904 (1.0)	1.57 (1.38, 1.80)	1.60 (1.39,1.83)	2.09 (1.68,2.61)	1.66 (1.45,1.91)
Speaks language other than English at home[4]					
English only (ref)	80,827 (89.5)	1	1	1	1
Other language	9,525 (10.5)	0.80 (0.76, 0.84)	1.06 (1.01,1.10)	1.32 (1.22,1.42)	1.05 (1.00,1.10)
Country of birth[4]					
Australia (ref)	66,568 (73.7)	1	1	1	1
Overseas	22,575 (25.0)	0.78 (0.76, 0.81)	0.86 (0.83,0.89)	1.05 (0.99,1.11)	0.86 (0.83,0.89)
Household incom[4]					
<20,000 (ref)	35,726 (39.5)	1	1	1	1
20-50k	26,612 (29.5)	0.79 (0.77, 0.82)	0.73 (0.70,0.75)	0.65 (0.61,0.69)	0.72 (0.70,0.75)
50 - 70k	3,298 (3.7)	0.64 (0.59, 0.69)	0.53 (0.49,0.58)	0.49 (0.42,0.58)	0.54 (0.49,0.58)
70k+	1,495 (1.7)	0.58 (0.52, 0.66)	0.49 (0.43,0.55)	0.50 (0.40,0.63)	0.47 (0.42,0.53)
Not stated	15,862 (17.6)	0.75 (0.72, 0.78)	0.85 (0.81,0.88)	0.82 (0.77,0.88)	0.85 (0.82,0.88)
Marital status[4]					
Single (ref)	5,774 (6.4)	1	1	1	1
Married/de-facto	58,655 (64.9)	0.88 (0.83, 0.94)	0.96 (0.90,1.02)	0.88 (0.80,0.98)	0.94 (0.89,1.00)
Widowed/divorced/separated	25,246 (27.9)	1.10 (1.03, 1.17)	1.09 (1.02,1.16)	1.09 (0.98,1.22)	1.09 (1.02,1.16)

aOR–odds ratio adjusted for age and sex, unless stated otherwise.

[1] –percentages do not add up to 100 due to missing data.

[2] –adjusted for sex only.

[3] –adjusted for age only.

[4] –adjusted for age and sex.

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and there is variation in the level or recording between hospitals [10, 11]. In Australia, until recently, there was no mechanism to code diagnoses that do not contribute to hospital stay. Prior to 2015, only diagnoses affecting patient management in a particular episode of care were coded in administrative hospital data. In 2015 codes for temporary use in Australia were

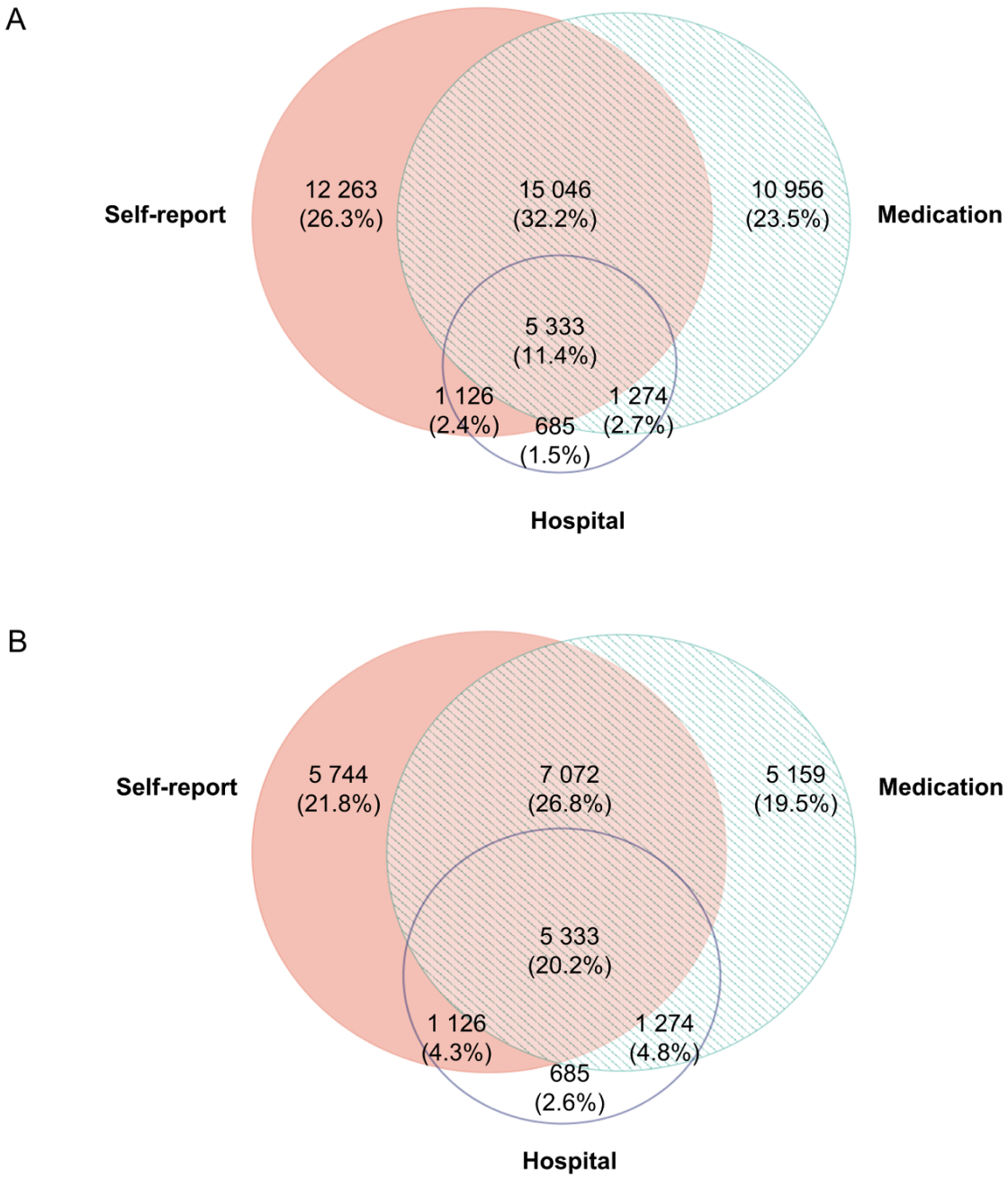

Fig 3. Venn diagram of the prevalence of multimorbidity according to data source. (A) All data. (B) Hospitalised patients only. Percentages (%) represent the proportion of all multimorbidity cases ascertained from any of the data sources. Venn diagram constructed using Euler*APE*: http://www.eulerdiagrams.org/eulerAPE/.

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assigned to 29 chronic conditions that are present on admission, where the condition does not meet the criteria for coding [52]. We anticipate that this introduction of supplementary codes for chronic conditions will have a positive impact on the sensitivities calculated in the future studies. For studies that do not have supplementary codes, it is advised to incorporate longer lookback periods in order to increase ascertainment of chronic conditions in hospital data [10, 53].

We found that using medication data identifies more cases (higher sensitivity), but at the cost of lower PPV. The lowest PPVs in medication data were found for stroke (16%) and heart disease (35%), the definitions for both of which capture drugs with multiple indications for prescribing. Strong levels of agreement for diabetes, hypertension and Parkinson's disease are consistent with previous research [41, 54–56], indicating that medication data can potentially be used for capturing these conditions. Low sensitivity and agreement for cancer in our study is congruent with previous Australian studies [54, 57], explained by the fact that chemotherapy drugs are only captured in the PBS data whilst patients are undergoing active treatment. Ascertainment of such cases can be increased by incorporating longer lookback periods. Higher sensitivities for diabetes, hypertension and depression found in our study, compared with a previous Australian study [57], could be attributable to a small sample size in that study, as well as our modified list of depression medications. Namely, we excluded tricyclic antidepressants, as they are commonly prescribed for insomnia and pain. This modification increased our PPV from 55% to 66%.

Selection of the most appropriate set of chronic conditions for other studies will depend on the study's purpose and the availability of data. Studies requiring accurate case ascertainment should use hospital data (noting that under-ascertainment is likely), or medication data for conditions for which medications are indicated only for that condition (e.g. diabetes) and where there is enough lookback time available. If a comprehensive profile of a patient's morbidity is needed, we suggest using a combination of data sources in order to increase sensitivity for identifying certain conditions. Caution should be applied when using hospital data for event-based conditions such as stroke, as these may have occurred outside of the time period of data capture, and would thus be under-reported. Identification of stroke patients using medications is also problematic, as the most commonly dispensed medication (Aspirin) is used for a variety of purposes. Furthermore, we recommend caution when interpreting the prevalence of disease or multimorbidity when using a single data source, in line with previously published work [26].

To the best of our knowledge, this is the first study to evaluate the differences in estimates of multimorbidity, using the same list of chronic conditions and the same individuals. Previous data linkage studies have evaluated differences in estimates of chronic disease prevalence within the same individuals [9, 55, 57–60], but did not formally compare case ascertainment of multimorbidity. Pache et al. [24] assessed the prevalence of multimorbidity using three definitions within the same sample, and found that one-third of participants diagnosed with multimorbidity were jointly diagnosed by all three definitions used. In our sample, this estimate was lower (11% - 20%), but this is explained by the smaller number of chronic conditions (8 vs 27), and the standardised list of chronic conditions used in our study, while Pache et al. used a different set of conditions in each of their three definitions,. Van den Bussche et al. [26] used an identical list of chronic conditions in the same setting, albeit among different people, and found that the prevalence of individual chronic conditions was one-third lower in claims data than in primary care data.

The odds of multimorbidity in our study were found to be higher among males, those of older age and those speaking a language other than English at home. The age gradient was noticeable in both hospital and medication datasets, especially with older ages. However, the

same gradient was not observed in the self-report data for those aged 85 and over, indicating a possible under-ascertainment of multimorbidity when relying on self-report data only for this age group. Males in our sample had between 7% (PBS data) and 49% (APDC data) higher odds of multimorbidity than females. This is in contrast to other Australian studies, which either found no difference [61] or higher prevalence among females [17], albeit there are differences between the study samples in each of the studies. Compared with the current study, the National Health Survey reported higher prevalence of the most common chronic conditions–hypertension, heart disease and diabetes–among males aged 45 and over [62]. People speaking a language other than English at home in our study were found to have increased odds of having multimorbidity in the administrative data but decreased odds in the survey data. These findings are novel, and have not been reported in the published literature, to the best of our knowledge. A possible explanation is that those speaking another language might have difficulties in understanding medical terminology, which translates to underreporting of conditions in the survey data.

The use of a large-scale cohort study linked with administrative data is a particular strength of our study. This allowed us to use a homogenous population and a common set of chronic conditions to explore ascertainment of multimorbidity using different data sources, which, to the best of our knowledge, has not been done before. Administrative data used in this study are available in most Australian states and territories, allowing replication of results.

Our research has implications for studies examining chronic conditions from a single data source and those examining multimorbidity. We have shown that agreement between self-report and administrative data sources is generally poor, except for a handful of conditions, implying that morbidity and multimorbidity prevalence estimates will vary depending on which data are used. Caution should be applied whenever a single data source is used, taking care to note different levels of capture of chronic disease between data sources. Self-report studies are subject to recall bias, hospitalisation data can only capture conditions for those admitted to hospital and if they are coded during the stay, and medication data may overestimate certain conditions because drugs may have multiple indications. In the case of administrative data, extra care should be taken regarding the time period which is used to ascertain morbidity, with longer times needed to capture more conditions of interest. Choice of which data to use also depends on the purpose of the study. For example, if the aim of the study is to monitor 'active' chronic conditions, data linkage of multiple administrative data sources may be more useful than self-report of ever-diagnosis. Furthermore, our study's finding regarding different individuals, with different combinations of conditions being identified as multimorbid, depending on which datasets are used, poses a challenge when interpreting results of studies examining outcomes of multimorbidity. Careful consideration of individual conditions (which may be under- or over-reported) is needed in order to provide meaningful recommendations for patients with complex care needs.

Although this research generated interesting results, it has some limitations. We based the analyses on a limited set of chronic conditions (arthritis and osteoporosis were notable omissions) available in all three data sources, as well as the available lookback period length. The prevalence of multimorbidity would have been different if a larger set of chronic conditions or a longer lookback period was used. However, all of the conditions used in the current study are National Health Priority Areas [63] as they represent the most common long-term conditions and most commonly managed conditions by GPs [2], significantly contributing to the burden of disease in the Australian community. They are also used in the majority of previously published research [64]. We have used the longest lookback period that the data allowed (2 years), which is longer than the 1-year lookback used in some studies [54, 59].

In the absence of readily available linked primary health care clinical data in Australia, and due to different levels of capture of chronic diseases in administrative datasets, we have used self-report chronic conditions as the reference when examining the concordance between data sets. Although the use of self-report data for identification of chronic disease has been cautioned by some [61], numerous other Australian studies use self-report data to ascertain multimorbidity [17–21]. Validation studies involving participants in the 45 and Up Study found excellent levels of agreement between self-report diabetes [65], country of birth [66] and height and weight [67]. Our data suggest that self-report may be less reliable after the age of 85 and in people speaking a language other than English at home. The use of another data source as a reference could have produced different results.

The use of administrative data poses a different set of challenges. Identification of chronic conditions using APDC data is limited to people who have been admitted to hospital, and having a chronic condition recorded if this was not directly related to the hospital stay, so it is likely to identify only the most severe cases. Medication dispensing information is dependent on the capture of data in the PBS dataset. We were limited to use of PBS-subsidised prescription medicines, which does not include over-the-counter and private prescriptions.

Conclusions

As administrative data become more widely used for research and evaluation, it is increasingly important to understand their strengths and limitations for ascertaining chronic disease and multimorbidity. This study showed that administrative data has high predictive value for identifying some chronic conditions, but that sensitivity is generally low. Further, it showed that different individuals, with different combinations of conditions, are identified as multimorbid when different data sources are used. Research that explores specific disease combinations and clusters of diseases that commonly co-occur, rather than simple disease counts, is likely to provide more useful insights into the complex care needs of individuals with multiple chronic conditions.

Supporting information

S1 Fig. Construction of study population. APDC–Admitted Patient Data Collection, PBS–Pharmaceutical Benefits Scheme.
(TIF)

S1 Table. Morbidities and ICD-10-AM and ATC codes.
(DOCX)

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5.5 Knowledge building

The findings from this chapter highlight the gaps in ascertainment of multimorbidity using a single data source and using hospital data in particular. The list of chronic conditions used in this chapter was limited to the conditions listed in the 45 and Up Study, which is why the next phase of the research moved to using an expanded list of chronic conditions and population-level data. In Chapter 6, state-based hospital data was used, with multimorbidity measured using a combination of Charlson and Elixhauser indices. Beyond simply measuring multimorbidity, Chapters 6 and 7 also examine the outcomes of people with multimorbidity.

CHAPTER 6

Interaction effects of multimorbidity and frailty on adverse health outcomes in elderly hospitalised patients: Australian observational study using hospital records for 257,535 patients

6.1 Background and aims

Multimorbidity and frailty have been shown to be independently associated with higher healthcare utilisation, costs and worse outcomes, with health policy planners using both metrics to identify high-need patients and those at risk of adverse health events. The extent to which these two states interact with one another is relatively unexplored, particularly in the hospital setting. This study:

a) Quantifies the associations between hospital frailty risk score and multimorbidity and adverse hospital outcomes
b) Characterises the type of interaction between multimorbidity and frailty

6.2 Key findings

Multimorbidity and frailty coexist and have varying and interacting effects on adverse health outcomes. The largest adverse effects on mortality, unplanned readmission and prolonged lengths of stay are seen in patients with both multimorbidity and elevated frailty risk, with larger effects in surgical patients than medical patients. Consideration of both multimorbidity and frailty can help identify those patients at highest risk of post-discharge complications.

6.3 Student contribution

I conceived and designed the study with oversight from all other authors. I performed the statistical analyses, interpreted results, drafted the initial manuscript and reviewed and revised the manuscript following advice from co-authors. Louisa Jorm acquired the data. Deborah Randall, Judy Simpson and Michael Falster supervised the statistical analyses and reviewed the manuscript. Deborah Randall performed the initial data cleaning of the IHOPE dataset. All authors read and approved the submitted version, as presented here.

6.4 Submitted paper

Interaction effects of multimorbidity and frailty on adverse health outcomes in elderly hospitalised patients: Australian observational study using hospital records for 257,535 patients

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ABSTRACT

Objective

To quantify the interaction of multimorbidity and frailty and their impact on adverse health outcomes in the hospital setting.

Methods

Retrospective cohort study of persons aged ≥75 years, admitted to hospital during 2010-2012 in New South Wales, Australia, linked with mortality data. Multimorbidity, frailty risk and outcomes: prolonged length of stay (LOS), 30-day mortality and 30-day unplanned

readmissions were constructed. Relative risks (RR) of outcomes were obtained using Poisson models with random intercept for hospital.

Results

Among 257,535 elderly inpatients, 33.6% had multimorbidity and elevated frailty risk, 14.7% had multimorbidity only, 19.9% had elevated frailty risk only and 31.8% had neither. Additive interactions were present for all outcomes, with a further multiplicative interaction for mortality and LOS. Mortality risk was 4.2 (95% CI 4.1 – 4.4), prolonged LOS 3.3 (95% CI 3.3 – 3.4) and readmission 1.8 (95% CI 1.7 – 1.9) times higher in patients with both factors present compared with patients with neither.

Conclusions

Multimorbidity and frailty coexist in older hospitalized patients and interact to increase the risk of adverse outcomes beyond the sum of their individual effects. Their joint effect should be considered in health outcomes research and when administering hospital resources.

INTRODUCTION

Frailty and multimorbidity are gaining attention with the noted global increase in the average age of populations. Frailty denotes a state of increased vulnerability of individuals to stressors from the accumulated consequences of morbidities or their treatments[79] and multimorbidity is a co-occurrence of multiple chronic diseases within an individual.[4] Both states have been associated with higher healthcare utilisation, costs and mortality,[38, 55, 81, 209] and are used by health policy planners to identify both high-need patients and those at risk of adverse health events. However, while patients experiencing frailty and multimorbidity often require additional care, the specific care needs and prognosis may vary between them.[90]

Currently there is no consensus on standardised measurement of either multimorbidity or frailty, with choice of the measure often driven by data availability and the study setting. Routinely collected data are increasingly being used in ageing health research,[26] giving opportunities to define frail and multimorbid individuals from their full health care history. A range of claims-based frailty indices were developed recently,[81] with one such measure using administrative data for hospitalised patients being the Hospital Frailty Risk Score

(HFRS).[87] HFRS helps identification of patients with characteristics of frailty, and at risk of adverse healthcare outcomes including mortality, prolonged hospital stays and unplanned readmissions. The score has been validated in medical[199, 200] and surgical[201, 202] patients.

While various definitions of frailty and multimorbidity exist, they are intrinsically linked with each other, with most frail patients being multimorbid, and one-sixth of multimorbid adults presenting with frailty.[74] The National Institute for Health and Care Excellence (NICE) guidelines recommends frailty to be considered when managing older adults with multimorbidity.[93] Since many patients experience both multimorbidity and frailty, there is potential that they interact to increase risk of adverse outcome. For example, multimorbid patients who are in a frail state may experience higher risk of complications, or be predisposed to more severe and ongoing complications, than multimorbid patients with low frailty. Investigating how an additional health state impacts on the health outcomes in patients already experiencing another is of importance as it can help identify those at greater risk and in need of further targeted health services.

Interactions between multimorbidity and frailty can be measured on different scales. Interaction on an additive scale would imply that the combined effect of multimorbidity and frailty is greater than the sum of their individual effects, whereas interaction on a multiplicative scale would imply that their combined effect is greater than the product of their individual effects. While interactions on an additive scale are more important in public health[210, 211] due to the ease of interpretation of absolute rather than relative numbers of patients who might benefit from an intervention, quantifying the magnitude and scale of the interaction is crucial for understanding the extent to which the presence of one condition amplifies the effect of the other. Given there has been a rapid increase in the prevalence of both multimorbidity and frailty in patient populations,[212, 213] identifying such amplifying factors is critical to inform future health care resource planning.

To our knowledge, no studies to date have examined interaction between the two factors in hospital patients, who are at higher risk of complications and adverse outcomes. The purpose of our study was to quantify the interaction of multimorbidity and frailty, and their impact on adverse health outcomes, in a large observational cohort of elderly Australian hospital patients. Specifically, we aimed to 1) estimate the joint effect of HFRS and multimorbidity with hospital outcomes (30-day mortality, 30-day readmission, prolonged length of stay), and 2) characterise the type of interaction between multimorbidity and frailty.

METHODS

Study design

We conducted a retrospective cohort study using routinely collected administrative hospital and mortality data.

Setting and data

New South Wales (NSW) is Australia's most populous state with 7.2 million residents in 2012.[214] We used NSW Admitted Patient Data collection (hospital data) linked with mortality data for a period 1 January 2008 – 31 March 2013. The hospital data included records for all public and private hospital admissions ending in discharge, transfer, type change or death. Hospital admissions were coded using the International Statistical Classification of Diseases and Related Problems, tenth revision, Australian modification (ICD-10-AM) and Australian Refined Diagnosis Related Group (AR-DRG) codes.[191] The Centre for Health Record Linkage linked the two datasets using probabilistic methods, with false positive and false negative rates of 0.5%.[195]

Study cohort construction

Our study replicated inclusion criteria of the original HFRS publication[87] with a cohort containing NSW residents, aged 75 and over, having at least one unplanned admission to an acute hospital during 1 January 2010 – 31 December 2012. For admissions ending in type change (e.g. from acute to sub-acute care) or transfer, contiguous periods of stay were constructed using admission dates and admission status from the first episode and separation dates and separation type from the last episode of care. We selected a single random hospital stay for each patient as their 'index' admission.

Predictors and outcomes

We classified the two main analysis variables of interest, multimorbidity and frailty risk, using the ICD-10-AM diagnoses codes from the index admission and any hospitalisations in the preceding two-year period. We ascertained multimorbidity – presence of two or more chronic conditions – from a list of 29 chronic conditions from the Charlson and Elixhauser indices,[198] supplemented with core morbidities from more recent systematic reviews[14, 197] (Appendix 5, Table 4). We calculated a continuous HFRS using the ICD-10 codes from Gilbert et al,[87] adapted to the Australian modification (ICD-10-AM) (Appendix

5, Table 5). The HFRS captures comorbidities associated with frailty, as well as functional deficits and symptoms. We created dichotomous frailty groups of low frailty (HFRS <5) and elevated frailty risk (HFRS≥5, combining intermediate and high frailty) using the validated cut points from Gilbert et al.[87] Sensitivity analysis using all three frailty categories (low, intermediate, and high frailty) was also carried out.

We constructed a composite variable of multimorbidity and frailty risk with four categories: neither multimorbid nor at elevated risk of frailty, elevated frailty risk only, multimorbid only, and both multimorbid and with elevated frailty risk.

Other covariates included age at index admission (in five-year age groups), sex, quantiles of socioeconomic status based on the Australian Bureau of Statistics Socioeconomic Indices of Areas (SEIFA) Index of Relative Socio-economic Advantage and Disadvantage (IRSAD), and number of hospital admissions in the preceding two-year period (none, one, two or more).

Outcomes of interest included those from HFRS study:[87] mortality within 30 days of index admission; prolonged hospital stay (>10 days in hospital); unplanned readmission within 30 days of discharge (for patients discharged alive). Results were stratified by admission type, grouped into medical (not involving an operating room procedure), surgical (involving significant operating room procedure) and other (involving non-operating room procedure) admissions based on AR-DRG procedures.[215]

Statistical analysis

We used descriptive statistics to compare demographic characteristics and crude outcome proportions between multimorbidity and frailty risk groups.

We built Poisson random intercept models to quantify the association of outcomes with multimorbidity and frailty accounting for clustering within hospitals, and adjusted for age group, sex, socio-economic status, and number of prior admissions. Effects are reported as relative risks (RR), given the high frequency of the outcomes.[216, 217]

We calculated and presented the analyses of interaction as recommended by Knol and VanderWeele.[210] Interaction on an additive scale was estimated using the relative excess risk due to interaction ($RERI_{RR}$), with adjustments for clustered data.[218] $RERI_{RR} = 0$ implies no interaction (exact additivity), $RERI_{RR} > 0$ denotes interaction more than additivity and $RERI_{RR} < 0$ means interaction less than additivity. Interaction on a multiplicative scale was

assessed via the inclusion of an interaction term in the adjusted Poisson model including both main effects (multimorbidity and frailty) and interaction term (multimorbidity*frailty). Significance of an interaction on the multiplicative scale is denoted where relative risk of the interaction term is different from 1, and on additive scale if RERI is different from 0.

We used SAS version 9.4 (SAS Institute Inc., Cary, NC) for data management and analysis.

We obtained ethics approvals from the NSW Population and Health Services Research (reference 2009/03/141) and the Aboriginal Health and Medical Research Council (reference 684/09) Ethics Committees.

RESULTS

Study cohort

Our cohort included a total of 257535 patients aged 75 and over with an unplanned hospital admission during 2010-2012. The majority of the admissions (86%) were medical in nature, with a smaller proportion (9.1%) being for surgery, and the remainder in the other category. The median patient age was 83.3 years (interquartile range 79.2 – 87.7) and most patients were female (57.2%). Other cohort characteristics are shown in Table 6.1.

Frailty and multimorbidity

The HFRS ranged from 0 to 88, with 53.5% of the patients having an elevated frailty risk score, including 35.6% at intermediate and 17.9% at high risk (Appendix 5, Table 1). Multimorbidity was present in 124468 (48.4%) of the study cohort, with median number of chronic conditions among multimorbid patients being 3 (interquartile range 2 – 4).

In our study cohort, 33.6% patients had both multimorbidity and elevated frailty risk, 19.9% had elevated frailty risk only, 14.7% had multimorbidity only and the remaining 31.8% had neither. Hospitalised patients experiencing both states tended to be older (median age 84 years), have more hospital stays (65% had two or more stays), and have both higher HFRS scores and a larger number of chronic conditions. Patients with neither factor were younger and with fewer prior admissions (Table 6.1).

Table 6.1 Cohort description at the time of index hospitalisation 2010-2012, by multimorbidity and frailty risk

	Total	Multimorbidity and frailty risk				
		Neither	Elevated frailty risk only	Multimorbid only	Both	*p-value*
	N = 257,535	*n = 81,788*	*n = 51,279*	*n = 37,949*	*n = 86,519*	
Sex, n (%)						
Male	110,125 (42.8)	34,363 (42.0)	17,134 (33.4)	19,587 (51.6)	39,041 (45.1)	<0.01
Female	147,410 (57.2)	47,425 (58.0)	34,145 (66.6)	18,362 (48.4)	47,478 (54.9)	
Median age (IQR)	83.3 (79.2 – 87.7)	81.9 (78.3 – 86.2)	84.9 (80.6 – 89.3)	82.0 (78.4 – 86.1)	84.4 (80.1 – 88.6)	<0.01
Age, n (%)						
75-79	76,233 (29.6)	30,169 (36.9)	11,343 (22.1)	13,716 (36.1)	21,005 (24.3)	<0.01
80-84	78,766 (30.6)	26,181 (32.0)	14,550 (28.4)	12,509 (33.0)	25,526 (29.5)	
85-89	63,894 (24.8)	16,824 (20.6)	14,359 (28.0)	8,098 (21.3)	24,613 (28.4)	
90+	38,642 (15.0)	8,614 (10.5)	11,027 (21.5)	3,626 (9.6)	15,375 (17.8)	
Aboriginal and Torres Strait Islander status, n (%)						
Non-Aboriginal	256,100 (99.4)	81,332 (99.4)	51,074 (99.6)	37,697 (99.3)	85,997 (99.4)	<0.01
Aboriginal	1,435 (0.6)	456 (0.6)	205 (0.4)	252 (0.7)	522 (0.6)	
Socioeconomic status quartiles, n(%)						
Most disadvantaged	66,279 (25.7)	21,889 (26.8)	12,215 (23.8)	10,597 (27.9)	21,578 (24.9)	<0.01
2	54,192 (21)	17,996 (22.0)	10,491 (20.5)	8,137 (21.4)	17,568 (20.3)	
3	46,441 (18)	14,943 (18.3)	9,478 (18.5)	6,694 (17.6)	15,326 (17.7)	
4	47,350 (18.4)	14,512 (17.7)	9,868 (19.2)	6,600 (17.4)	16,370 (18.9)	
Most advantaged	40,911 (15.9)	11,904 (14.6)	8,687 (16.9)	5,681 (15.0)	14,639 (16.9)	
Missing	2,362 (0.9)	544 (0.7)	540 (1.1)	240 (0.6)	1,038 (1.2)	
Admission type, n (%)						
Medical	224,949 (87.3)	71,714 (87.7)	44,897 (87.6)	32,486 (85.6)	75,852 (87.7)	<0.01
Surgical	23,339 (9.1)	7,020 (8.6)	5,374 (10.5)	3,010 (7.9)	7,935 (9.2)	
Other	9,247 (3.6)	3,054 (3.7)	1,008 (2.0)	2,453 (6.5)	2,732 (3.2)	
Number of prior admissions over 2 years, excluding index admission, n (%)						
0	84,775 (32.9)	43,072 (52.7)	17,527 (34.2)	11,471 (30.2)	12,705 (14.7)	<0.01
1	62,827 (24.4)	20,433 (25.0)	14,370 (28.0)	10,092 (26.6)	17,932 (20.7)	
2 or more	109,933 (42.7)	18,283 (22.4)	19,382 (37.8)	16,386 (43.2)	55,882 (64.6)	
Median HFRS (IQR)	5.5 (1.9 – 12.0)	1.6 (0 – 3)	9.0 (6.6 – 13.2)	2.0 (0.7 – 3.4)	13.3 (8.6 – 20.3)	<0.01
Median number of chronic conditions (IQR)	1 (0 – 3)	0 (0 – 1)	1 (0 – 1)	2 (2 – 3)	3 (2 – 5)	<0.01

HFRS – Hospital frailty risk score, IQR – interquartile range

Outcomes

Overall 30-day mortality and readmission rates in our study were both 11%, with 30% of patients staying longer than 10 days in hospital. Crude incidence rates for each outcome were higher in those with elevated frailty risk or multimorbidity, with highest rates observed in patients who were both multimorbid and at elevated risk of frailty (Table 6.2).

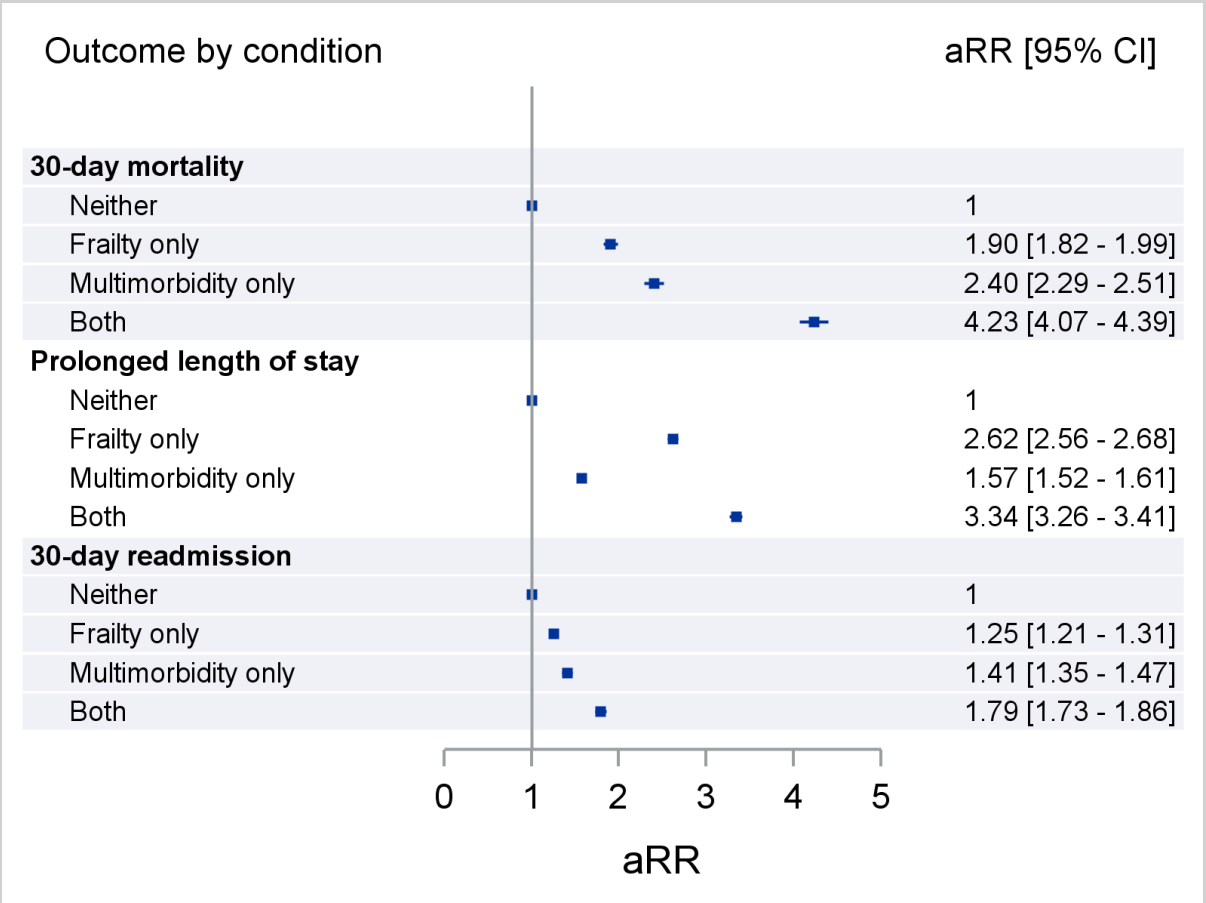
Table 6.2 Crude patient outcomes by multimorbidity and frailty risk

	Total	***Multimorbidity by Frailty risk***				
	N (%)	Neither *n = 81,788*	Elevated frailty risk only *n = 51,279*	MM only *n = 37,949*	Both *n = 86,519*	*p-value**
Mortality within 30-days	28886 (11.2)	3854 (4.7)	4731 (9.2)	4046 (10.7)	16255 (18.8)	<0.001
Median LOS (days) (IQR)	5 (2-12)	2 (1-6)	6 (2-16)	4 (2-8)	8 (3-19)	<0.001
Prolonged LOS (>10 days)	76585 (29.7)	11855 (14.5)	19181 (37.4)	8001 (21.1)	37548 (43.4)	<0.001
Readmission within 30-days	26264 (11.2)	5457 (6.9)	4727 (10.0)	3960 (11.4)	12120 (16.5)	<0.001

* Differences in proportions tested using χ^2 test, and medians using Kruskal Wallis test

Figure 6.1 shows the results from the Poisson random intercept models, adjusting for age group, sex, socioeconomic status and the number of prior admissions. The relative risk of adverse outcomes continued to be higher in multimorbid and elevated frailty risk individuals after risk-adjustment. Patients who experienced both health states had the highest risks of adverse outcomes. Multimorbid individuals with elevated frailty risk had 4.2 (95% CI 4.1 – 4.4) times higher risk of mortality, 3.3 (95% CI 3.3 – 3.4) times higher risk of prolonged hospital stays and 1.8 (95% CI 1.7 – 1.9) times higher risk of 30-day unplanned readmission than those with neither, with risks also being higher in patients with only one health state.

Figure 6.1 Adjusted relative risk (aRR) between multimorbidity and elevated frailty risk with adverse outcomes



Interaction effect results are shown in Table 6.3. Significant interactions between multimorbidity and frailty were observed on both additive and multiplicative scales for mortality ($RERI_{RR}$ 0.93 (95% CI 0.81 – 1.04), ratio of RR 0.93 (95% CI 0.88 – 0.98)) and prolonged length of stay ($RERI_{RR}$ 0.15 (95% CI 0.09 – 0.21), ratio of RR 0.81 (0.79 – 0.84)), and additive scale only for readmission ($RERI_{RR}$ 0.13 (95% CI 0.06 – 0.20), ratio of RR 1.02 (95% CI 0.96 – 1.07)). Sensitivity analysis of interactions using 3-categories of HFRS yielded the same conclusions (Appendix 7, Table 7.1.5)

Table 6.3 Additive and multiplicative Interaction effects of multimorbidity and frailty risk on adverse patient outcomes, full cohort

Mortality within 30-days post admission	**Low frailty risk**			**Elevated frailty risk**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	%outcome	aRR (95% CI)
No multimorbidity	3854	4.7	1	4,731	9.2	1.90 (1.82 – 1.99)
Multimorbidity	4,046	10.7	2.40 (2.29 – 2.51)	16,255	18.8	4.23 (4.07 – 4.39)

[a]*Measure of effect modification on additive scale: RERI (95% CI) = 0.93 (0.81 – 1.04)**

[a]*Measure of effect modification on multiplicative scale: ratio of RR= 0.93 (0.88 – 0.98), p-value =0.006**

Prolonged LOS	**Low frailty risk**			**Elevated frailty risk**		
	N with outcome	% outcome	aRR (95% CI)	N with	%outcome	aRR (95% CI)
No multimorbidity	11855	14.5	1	19,181	37.4	2.62 (2.56 – 2.68)
Multimorbidity	8,001	21.1	1.57 (1.52 – 1.61)	37,548	43.4	3.34 (3.26 – 3.41)

[a]*Measure of effect modification on additive scale: RERI (95% CI) =0.15 (0.09 – 0.21)**

[a]*Measure of effect modification on multiplicative scale: ratio of RR= 0.81 (0.79 – 0.84), p-value <0.001**

Readmission within 30-days post discharge	**Low frailty risk**			**Elevated frailty risk**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	%outcome	aRR (95% CI)
No multimorbidity	5,457	6.9	1	4,727	9.9	1.25 (1.21 – 1.31)
Multimorbidity	3,960	11.4	1.41 (1.35 – 1.47)	12,120	16.5	1.79 (1.73 – 1.86)

[a]*Measure of effect modification on additive scale: RERI (95% CI) =0.13 (0.06 – 0.20)**

[a]*Measure of effect modification on multiplicative scale: ratio of RR= 1.02 (0.96 – 1.07), p-value =0.57*

* Denotes significance at 5% level.

[a] Significance of an interaction on an additive scale is denoted where RERI is different from 0, and on the multiplicative scale if ratio of RR is different from 1.

Stratified analysis

We found similar interaction effects for 30-day mortality and readmissions when stratified by admission type, although with larger effect sizes for surgical patients, among whom those with both multimorbidity and elevated frailty had a high risk of 30-day mortality (aRR: 7.2; 95% CI 6.1 – 8.5) and 30-day readmission (aRR: 2.6; 95% CI 2.3 – 3.0) compared with those with neither (Appendix 5, Table 2). The results for prolonged length of stay in this group were attenuated in the surgical cohort compared with the medical cohort (Appendix 5, Table 3).

DISCUSSION

Our study shows that multimorbidity and frailty risk occur both jointly and in isolation in our cohort of older Australians with unplanned admissions to hospital, and have varying and interacting effects on adverse health outcomes. We observed the largest adverse effects on mortality, readmission and prolonged lengths of stay in those patients with both multimorbidity and elevated frailty risk, with greater risks of mortality and readmission in surgical patients. To our knowledge, no prior studies have explored the nature of any interactions between HFRS and multimorbidity in hospital patients, nor reported their joint effects. Our findings highlight that when identifying older hospitalised patients at risk of complications, accounting for both the patient's burden of chronic disease and vulnerability to stressors of treatment will both increase the breadth of patients identified, and help separate those at even higher risk of complication.

Measures of additive interaction are not frequently reported in the literature, despite their value for identifying individuals who would most benefit from treatment or need more monitoring for complications or adverse health outcomes [211]. Our findings, congruent with other research,[90, 94, 96, 219, 220] show that both multimorbidity and frailty have important independent impacts on health outcomes, but further demonstrate that their joint effects on mortality and length of stay are amplified, while their effects on readmission are additive. The different scale of interaction between outcomes may reflect the fact that readmissions are only measured for patients who survived to discharge (in our study 91% of patients) – thus attenuating some of the excess risk. Our findings indicate that the presence of not only multimorbidity and frailty, but also their co-occurrence, in patient populations are important inputs to hospital care resource projections and planning. These

findings will inform future revisions to patient classifications used for activity-based funding, such as Australian Diagnosis Related Groups (AR-DRGs).[215] Routine screening and identification of patients with multimorbidity and elevated risk of frailty could potentially be used to better target further interventions, such as comprehensive geriatric assessment, home care planning, and end-of-life care planning.

Our study also highlights that, although a high proportion of elderly patients experience both health states, a notable portion of hospitalised patients are multimorbid without exhibiting elevated frailty risk, and vice versa. Multimorbid-only individuals had higher age-adjusted mortality and readmission risks than frail-only individuals, reflecting the ongoing risk of complications experienced by people with multiple chronic diseases. Conversely, patients with elevated frailty risk had higher risk of prolonged hospitalisation than multimorbid-only patients, reflecting the vulnerability of these patients to acute complications of care. Using only one of these factors to identify at-risk patients will not only fail to account for the interactive effect found in this study, but also potentially fail to identify patients at-risk of different types of complications.

A recent systematic review by Vetrano et al.[74] reported that 72% of frail individuals had multimorbidity, and 16% of multimorbid individuals were frail. In our study these proportions were 63% and 70% respectively. The differences in our estimates could be attributed to the study populations and methods of frailty assessment. We studied older hospitalised patients presenting as unplanned cases, with frailty risk ascertained from routinely collected data. The majority of the studies included in the systematic review investigated community dwelling participants, with frailty ascertained using Fried et al.[82] Frail Phenotype based on physical signs and symptoms.

There are several limitations to our study. First, while the indices of multimorbidity and frailty are commonly used and validated, there remain aspects of patient frailty that are unable to be captured in administrative data, as well as possible under-ascertainment of some morbidities. Second, there is overlap between the ICD-10 diagnoses codes used in frailty risk and comorbidity ascertainment which makes it difficult to disentangle their effects, although prior research indicates only a weak correlation between HFRS and the Charlson Index.[221] Third, there might be under-ascertainment of frailty and multimorbidity in patients with few or no prior hospitalisations. Fourth, whilst we used the most commonly applied dichotomous definition of multimorbidity, this may have resulted in information loss and reduced study power. Lastly, our restriction to unplanned admissions

limits generalisability of our findings to broader patient populations such as those undergoing elective surgery.

The strengths of this study include its large size and the use of linked population-based data on hospitalisations and mortality, enabling calculation of patient outcomes within and beyond the index hospital stay. Furthermore, ascertainment of multimorbidity and HFRS used administrative data only and ICD-10 diagnosis codes, presenting an approach that is amenable to incorporation into hospital forecasting planning and models.

CONCLUSION

Multimorbidity and frailty coexist in older hospitalised patients and interact to increase the risk of adverse outcomes beyond the sum of their individual effects. The risk of mortality, readmission and prolonged lengths of stay among multimorbid individuals with elevated frailty risk is two to four times higher than for those without either factor, and larger than in patients with only one factor. Joint effects of multimorbidity and frailty should be considered in health outcomes research and when administering hospital resources.

ACKNOWLEDGEMENTS

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AUTHOR CONTRIBUTIONS

S.L. conceived and designed the study with oversight from all other authors. L.J. acquired the data. S.L. performed the statistical analyses, interpreted results, drafted the initial manuscript and reviewed and revised the manuscript. D.R., J.S., M.F. supervised the statistical analyses and reviewed the manuscript. L.J., J.S. and M.F. critically reviewed and revised the manuscript for important intellectual content. All authors read and approved the submitted version.

COMPETING INTERESTS

The authors declare no competing interests.

6.5 Knowledge building

This chapter explored two drivers of adverse health outcomes in the elderly – multimorbidity and frailty. Both are reflective of patient complexity and were shown to have significant effects on mortality and prolonged lengths of stay. However, the measurement of these was based solely on administrative hospital data. There may be additional patient characteristics and markers of patients' complexity that contribute to patient outcomes such as readmissions, which complement what is captured in administrative data and refine how we consider multimorbidity. Chapter 7 explores how the inclusion of clinical registry data adds to the explanation of 30-day readmissions over and above administrative hospital data.

CHAPTER 7

Supplementing multimorbidity measures using administrative data with clinical registry data

7.1 Background and aims

Multimorbidity measures derived from administrative data sources are used for risk-adjustment of performance indicators for hospital quality of care. These measures are better able to predict mortality than readmissions,[190] leaving room for exploration of additional patient characteristics that might contribute to higher risks of readmission. However administrative hospital inpatient data contain limited information about other aspects of patient complexity, such as the clinical assessment of patient's overall health. Linkage with clinical registries provides opportunities to highlight the benefit of supplementing multimorbidity measures based on administrative data with additional clinical information for quality improvement purposes.

This study addressed these questions

(a) how does multimorbidity contribute to variations in hospital-level outcome indicators used for performance measurement?
(b) does the addition of variables from clinical registries improve predictive ability (discriminative performance) of models used to monitor health performance metrics?

7.2 Key Findings

This study used de-novo linkage of the hospital data with the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR). Current models for 30-day readmission post THA/TKA used by the NSW Bureau of Health Information (BHI) for hospital profiling use predisposing factors (age, sex) and illness level (Elixhauser morbidities) in the risk adjustment.[222,223] This study found that multimorbidity was

significantly associated with 30-day readmission following THA/TKA, whether measured using binary, ordinal or individual morbidity measures. The addition of information from the registry data (BMI and ASA) provided modest improvements to predictive ability of 30-day readmission models currently used by the BHI. Less than 1.4% of the overall individual variation in readmission was attributable to the hospital where the surgery was performed, indicating that reductions in readmissions are most likely to be achieved by interventions that are targeted towards patients at high risk of readmission, rather than focussed at the hospital level.

7.3 Further exploratory work

Since July 2015, 29 clinically important chronic conditions, which had not previously met the criteria for coding additional diagnoses,[121] have started being coded when documented as being present during an episode of admitted care in Australia.[122]These supplementary chronic disease codes ('U codes') present an opportunity to increase ascertainment of morbidity and multimorbidity using administrative data.

I examined the impact of supplementary chronic disease codes on ascertainment of chronic conditions in THA/TKA cohorts, with the results shown in Table 7.1. The largest relative increases were found for asymptomatic, and seemingly non-complex and clinically insignificant conditions.[226] I did not use the supplementary codes for multimorbidity measurement in this Chapter for two reasons:

1) Not all chronic conditions are captured by the supplementary U codes, which could have led to differential ascertainment of conditions.
2) There is a possibility of between-hospital variations of recording of health conditions[224,225], which could have introduced bias into study results.

Supplementary codes were only used for obesity for descriptive and validation purposes.

Table 7.1 Impact of supplementary chronic disease codes on ascertainment of chronic diseases in hospital data

	THA n (%)			TKA n (%)		
Elixhauser Index morbidities	ICD-10-AM codes	ICD-10-AM + supplementary codes	Relative increase %	ICD-10-AM codes	ICD-10-AM + supplementary codes	Relative increase %
AIDS/HIV	n.p.	n.p.	0	n.p.	n.p.	
Alcohol abuse	121 (2.1)	121 (2.1)	0	124 (1.2)	124 (1.2)	0
Blood loss anemia	35 (0.6)	35 (0.6)	0	54 (0.5)	54 (0.5)	0
Cardiac arrhythmia	584 (10.0)	584 (10.0)	0	887 (8.7)	887 (8.7)	0
Chronic pulmonary disease[s]	136 (2.3)	545 (9.3)	301	189 (1.9)	865 (8.5)	358
Coagulopathy	79 (1.3)	79 (1.3)	0	95 (0.9)	95 (0.9)	0
Congestive heart failure[s]	88 (1.5)	157 (2.7)	78	135 (1.3)	259 (2.5)	92
Deficiency anemia	142 (2.4)	142 (2.4)	0	239 (2.3)	239 (2.3)	0
Dementia[s]	27 (0.5)	46 (0.8)	70	34 (0.3)	59 (0.6)	74
Depression[s]	56 (1.0)	85 (1.5)	52	78 (0.8)	119 (1.2)	53
Diabetes (uncomplicated)	461 (7.9)	461 (7.9)	0	1215 (11.9)	1215 (11.9)	0
Diabetes (complicated)	709 (12.1)	709 (12.1)	0	1768 (17.4)	1768 (17.4)	0
Drug abuse	54 (0.9)	54 (0.9)	0	57 (0.6)	57 (0.6)	0
Fluid and electrolyte disorders	685 (11.7)	685 (11.7)	0	1075 (10.6)	1075 (10.6)	0
Hypertension (complicated)	n.p.	n.p.	0	8 (0.1)	8 (0.1)	0
Hypertension (uncomplicated) [s]	488 (8.3)	3130 (53.5)	541	918 (9.0)	6428 (63.1)	600
Hyperthyroidism	15 (0.3)	15 (0.3)	0	25 (0.2)	25 (0.2)	0
Liver disease[s]	112 (1.9)	112 (1.9)	0	161 (1.6)	161 (1.6)	0
Lymphoma	20 (0.3)	20 (0.3)	0	11 (0.1)	11 (0.1)	0
Metastatic cancer	30 (0.5)	30 (0.5)	0	35 (0.3)	35 (0.3)	0
Obesity [s]	78 (1.3)	764 (13.0)	879	182 (1.8)	1997 (19.6)	997
Other neurological disorders [s]	48 (0.8)	134 (2.3)	179	52 (0.5)	206 (2.0)	296
Paralysis [s]	24 (0.4)	30 (0.5)	25	42 (0.4)	49 (0.5)	17
Peptic ulcer disease	20 (0.3)	20 (0.3)	0	31 (0.3)	31 (0.3)	0
Peripheral vascular disorders	53 (0.9)	53 (0.9)	0	87 (0.9)	87 (0.9)	0
Psychoses [s]	15 (0.3)	40 (0.7)	167	18 (0.2)	53 (0.5)	194
Pulmonary circulation disorders	46 (0.8)	46 (0.8)	0	91 (0.9)	91 (0.9)	0
Renal failure [s]	124 (2.1)	290 (5.0)	134	243 (2.4)	515 (5.1)	112
Rheumatoid arthritis/collagen vascular disease [s]	72 (1.2)	92 (1.6)	28	129 (1.3)	143 (1.4)	11
Solid tumor without metastasis	128 (2.2)	128 (2.2)	0	210 (2.1)	210 (2.1)	0
Valvular disease	56 (1.0)	56 (1.0)	0	83 (0.8)	83 (0.8)	0
Weight loss	119 (2.0)	119 (2.0)	0	85 (0.8)	85 (0.8)	0
Multimorbidity†	1102 (18.8)	2359 (40.3)	114	2038 (20.0)	4715 (46.3)	131

[s] Has a corresponding supplementary code. † Presence of 2 of more Elixhauser Index morbidities

7.4 Student contribution

I conceived and designed the study with the oversight from my supervisors (Louisa Jorm, Judy Simpson and Michael Falster). Data management, statistical analyses and full draft of the paper were also done by me. Ian Harris provided clinical advice and contributed to result interpretation. Michelle Lorimer prepared the AOANJRR data extraction and edited the draft manuscript.

Initial study results were presented and discussed with the 'Enhancing Joint Replacement Outcomes through National Data Linkage' research group, who instigated the linkage of the AOANJRR data. Further comments on the written paper, as presented in section 7.4, will be sought from the Group prior to the submission to the Medical Journal of Australia.

7.5 Paper (formatted as MJA journal submission)

Supplementing administrative data with clinical registries: an example using total hip (THA) and total knee arthroplasty (TKA) readmission rates for hospital performance measurement

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Abstract

Objectives: To examine a) the impact of multimorbidity on THA/TKA readmission rates and b) assess whether the inclusion of clinical registry information (body mass index (BMI) and American Society of Anaesthesiologists Physical Status score (ASA)) improves predictive ability of models currently used to monitor hospital performance metrics

Design, setting, participants: Retrospective cohort study of patients aged ≥18 years, admitted for total hip or knee arthroplasty (THA/TKA) in public hospitals in New South Wales between 1 July 2016 and 30 June 2018 using hospital records linked with the Australian Orthopaedic Association National Joint Replacement Registry data (AOANJRR).

Main outcome measures: 30-day post discharge all-cause readmission

Results: A total of 5855 THA and 10183 TKA patients underwent surgery, of whom 430 (7.3%) THA and 837 (8.2%) TKA patients were readmitted for any reason within 30 days following separation from acute care. Recording of patient's overweight/obese status was higher in the AOANJRR registry (76.9% of THA and 87.0% of TKA patients) than in hospital diagnosis codes (10.6% of THA and 16.5% of TKA patients). Using stepwise multilevel logistic regression, we found modest improvements in the discriminatory accuracy with the addition of registry data (ASA for THA, ASA and BMI for TKA), even after adjusting for multimorbidity. After risk-adjustment, less than 1.4% of the variation in 30-day readmissions was attributable to the hospital where the procedure was performed.

Conclusions: Inclusion of registry data, especially ASA scores, improves risk adjustment for hospital readmission performance measures for THA/TKA, demonstrating the potential benefits of integrating registry and administrative datasets. Reductions in readmissions following joint replacement surgery are most likely to be achieved by interventions that are targeted towards patients at high risk of readmission, rather than focussed at the hospital level.

The known

- Readmission rates following total hip or knee arthroplasty (THA/TKA) are influenced by factors such as body mass index (BMI) and American Society of

Anaesthesiologists Physical Status (ASA) score, which are not captured in administrative data used for hospital performance measurement

The new

- Addition of ASA and BMI improved the discriminatory accuracy of multilevel models for 30-day all-cause readmission, compared with models using administrative data only. After risk-adjustment, less than 1.4% of the variation in 30-day readmissions was attributable to the hospital where the procedure was performed.

The implications

- Inclusion of registry data, especially ASA scores, improves risk adjustment for hospital readmission performance measures for THA/TKA, demonstrating the potential benefits of integrating registry and administrative datasets.

Introduction

Osteoarthritis is a long-term progressive disease affecting nearly 1 in 11 Australians,[227] and costing the Australian health system an estimated $3.5 billion.[140] Australian clinical practice guidelines recommend joint replacement surgery for severe disease when conservative options, such as weight management and increase in physical activity, have failed.[228] The demand for surgical interventions has steadily increased over time, owing to a rise in obesity, aging populations and joint injuries.[229]

A substantial increase in both the rates and volume of joint replacement surgeries are expected in the Australian population over the next 25 years. Incidence rates of total hip arthroplasty (THA) and total knee arthroplasty (TKA) are expected to rise by 73% and 31% respectively from 2014 to 2046, with a noted projected increase in surgical volume of 198% and 126%.[230] Performance metrics for THA/TKA, such as all-cause and unplanned readmissions, are widely used to drive improvements in patient care both internationally and nationally. In the United States, measures including penalising hospitals with excess readmission rates and bundling payments to cover costs of the entire postoperative period[231] are applied, despite recent critiques due to the lack of the variation in readmission rates attributable to hospitals.[232] In Australia, readmission indicators for hip and knee

replacements are part of the national core hospital-based outcome indicators to improve safety and quality in patient care[189] and are used for state level reporting of public hospital performance. In NSW, the Bureau of Health Information (BHI) reports THA/TKA readmission rates for public hospitals, using age, sex and Elixhauser morbidities for risk adjustment.[222]

THA/TKA readmission rates are influenced by a variety of patient, clinical and care factors. Recent systematic and literature reviews[233,234] identified age, sex, comorbidities, socioeconomic status, race/ethnicity, American Society of Anaesthesiologists Physical Status (ASA) score, body mass index (BMI), discharge disposition (home, rehabilitation, nursing home) and length of stay to be significantly associated with higher readmission rates. While adjusting for socioeconomic status, race/ethnicity and process level factors may blunt the ability of performance measures to characterise quality of care,[243] BMI and ASA score can appropriately be used to adjust for patient complexity. Their use, however, has not been studied in Australia due to the lack of available information in administrative health data sources.

Clinical registries provide additional sources of information which potentially can be used to enhance risk-adjustment of performance metrics, and integration of clinical quality data with major health care datasets is a vision of the first Australian National Clinical Quality Registry and Virtual Registry Strategy 2020-2030.[127] However, the potential contribution of information captured in registries to risk adjustment of performance metrics is largely unknown.

In this first study of Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) data linked with hospital data we aim to (a) examine the impact of multimorbidity on THA/TKA readmission rates, (b) assess whether the inclusion of registry-level variables (BMI, ASA score) improves predictive ability of models used to monitor hospital performance metrics and (c) quantify the extent to which variation in 30-day readmissions is attributable to differences among hospitals.

Methods

Study design

We undertook an observational cohort study of routinely linked New South Wales (NSW) hospital data and registry data.

Data sources

We used NSW Admitted Patient Data Collection (hospital data), linked with the AOANJRR (registry data) and Registry of Births, Deaths and Marriages mortality data. Data linkage was carried out by the NSW Centre for Health Record Linkage (CHeReL), with an estimated false positive and false negative rate of <0.5%.[195] Hospital data include all admissions to public and private hospitals in the state resulting in discharge, transfer, type change or death. Hospital diagnoses are coded using International Statistical Classification of Diseases and Related Problems, tenth revision, Australian modification (ICD-10-AM) and procedures using the Australian Classification of Health Interventions (ACHI).[191] The AOANJRR collects data on individuals receiving primary or revision joint arthroplasty surgery at public and private hospitals in Australia, with almost complete coverage (97.8%).[192] Registry data are collected via forms filled out at the time of surgery and include information on BMI, ASA, diagnoses, type and reason for arthroplasty, surgical technique and components inserted.

Study population

The study population comprised adult patients (aged 18 years and over), admitted to acute care in public hospitals with primary or secondary procedure for total knee arthroplasty (TKA) or total hip arthroplasty (THA), and discharge dates between 1 July 2016 and 30 June 2018. Non-NSW residents and patients with fractures, those who died in hospital, were discharged at own risk or transferred between hospitals were excluded (Appendix 6, Supplementary Figures 1, 2).

Predictors and outcomes

Person-level factors used to model readmissions were age group, sex, and comorbidities from hospital data and ASA and BMI from registry data.

Thirty-one morbidities from the Elixhauser index[198] were summarised from the principal and secondary diagnoses at the time of THA/TKA and two years preceding the surgery. Total number of morbidities was summed and categorised into groups of 0, 1, 2 and 3 or

more. Sensitivity analysis using dichotomous measure of multimorbidity – presence of two or more Elixhauser morbidities – was carried out.

BMI from the AOANJRR was categorised into the World Health Organisation[235] categories: underweight (<18.5), normal weight (18.5-24.99), overweight (25-29.99), obesity class I (30-34.99), obesity class II (35-39.99) and obesity class III (≥40). Ascertainment of overweight/obesity in hospital data was made using ICD-10-AM diagnosis code "E66" and the supplementary chronic disease code of obesity "U78.1".

ASA is a five-category classification ranging from 1 for a heathy patient to 5 for a moribund patient not expected to survive the surgery.[236] In our cohort the ASA ranged from 1 to 4.

We constructed periods of stay by rolling up contiguous acute and sub-acute (e.g. rehabilitation) episodes of care. End dates from an acute episode of care were used to construct a readmission to the next acute admission within a new period of stay. We considered acute all-cause and unplanned readmissions (Appendix 6, Supplementary Table 1) within 30 days of discharge from index admission excluding planned hospitalisation for haemodialysis, chemotherapy, radiotherapy and cataract surgery (Appendix 6, Supplementary Table 1). Readmissions for THA and TKA were modelled separately, as binary outcomes.

Statistical analysis

We used a novel methodological approach of stepwise multilevel logistic regression analysis of discriminatory accuracy[237] to classify patients by their 30-day readmission likelihood. Multilevel models were chosen because of the nesting of patients within hospitals. For each outcome we fitted three logistic regression models, computing the area under the receiver operator characteristic curve (AUC), as a measure of the model's discriminatory ability to correctly classify patients with and without an outcome (30-day readmission). AUC values range from 0.5 to 1, with 0.5 indicating no discrimination, and 1 perfect discrimination.[238]

Model 1 includes a single-level logistic regression to evaluate the contributions of age and sex to the outcome.

In Model 2h we added Elixhauser morbidities to Model 1, in line with the current hospital data risk-adjustment BHI methodology.[222] In model 2h,r we added registry variables (BMI, ASA) to Model 2h. Differences between AUC of Models 2 and 1 were used to examine the

improvement in classification of patients. ASA score was included as a continuous variable because there was an increasing trend in proportion readmitted with increasing score for both THA and TKA.

In Model 3, we expanded on Model 2 by adding a random intercept for hospitals (multilevel model) to quantify the contribution of hospitals to variation in the outcome (measured using the variance partition coefficient (VPC)) and discrimination accuracy (measured using the difference between AUC of Models 3 and 2d). Hospital-level variables were not including in multilevel models because they may exist on a causal pathway to the outcome, rather than being confounders.[243]

The VPC uses the estimated hospital-level variance in the calculation,[239] and ranges between 0% and 100%, with higher values representing a higher proportion of the observed individual variation attributable to between-hospital variation.

Data management and analyses were carried out using SAS version 9.3 software.[240] We obtained ethics approval from the NSW Population & Health Services Research Committee (Ref 2019/ETH00436).

Results

Between 1 July 2016 – 30 June 2018 we identified 5855 patients with THA (103, 1.8% bilateral) in 45 NSW public hospitals (median number of patients per hospital=116 [IQR 71-163]), and 10183 (688, 6.8% bilateral) patients with TKA in 43 hospitals (median number of patients per hospital =206 [IQR 110-321]). Mean age of the THA cohort was 66.7 years (SD 11.9), and 68.9 years (SD 9.1) for TKA. 19% of the THA and 20% of the TKA cohort were multimorbid, with diabetes, hypertension, cardiac arrhythmias, chronic ischaemic heart disease, chronic kidney disease and cancer most prevalent (Table 7.2).

Overweight/obesity was present in 10.6% of THA and 16.5% of TKA patients, using hospital diagnoses (Table 7.2). Obesity, measured using BMI, was present in 43.7% of THA and 61.5% of TKA patients, with morbid obesity present in 6.3% of THA and 12.3% of TKA patients (Table 7.2). Ascertainment of overweight and obesity in hospital data was low, with only 13% of THA and 18% of TKA patients with BMI >25kg/m^2 identified using diagnosis or supplementary codes, but with high validity (sensitivities > 99%)

(Appendix 6, Table 2). Weak correlations between the ASA and Elixhauser Index were noted (Spearman ρ=0.35 in THA and ρ =0.30 in TKA).

There were 430 (7.3%) all-cause readmissions and 149 (2.5%) unplanned readmissions within 30 days of discharge from THA, and 837 (8.2%) all-cause and 357 (3.5%) unplanned readmissions following TKA. Patients who are older, have higher ASA score, more morbidities or who are morbidly obese (in TKA cohort only) have higher readmission rates (Table 7.2). Leading reasons for readmission are shown in Appendix 6, Table 3.

Table 7.2 Characteristics of patients undergoing THA or TKA between 1 July 2016 and 30 June 2018

	THA (N = 5855)		TKA (N = 10183)	
	Total	30-day readmission	Total	30-day readmission
Sex	n (%)	(N = 430, 7.3%)	n (%)	(N = 837, 8.2%)
Male	2857 (48.8)	219 (7.7)	4382 (43.0)	383 (8.7)
Female	2998 (51.2)	211 (7.0)	5801 (57.0)	454 (7.8)
Age				
<60	1571 (26.8)	88 (5.6)	1771 (17.4)	130 (7.3)
60-64	805 (13.7)	45 (5.6)	1545 (15.2)	106 (6.9)
65-69	979 (16.7)	68 (6.9)	2053 (20.2)	157 (7.6)
70-74	992 (16.9)	83 (8.4)	2078 (20.4)	193 (9.3)
75-79	785 (13.4)	73 (9.3)	1618 (15.9)	146 (9.0)
80+	723 (12.3)	73 (10.1)	1118 (11.0)	105 (9.4)
Procedure type				
Bilateral	103 (1.8)	4 (3.9)	688 (6.8)	41 (6.0)
Unilateral	5752 (98.2)	426 (7.4)	9495 (93.24)	796 (8.4)
Overweight/obesity				
No	5235 (89.4)	375 (7.2)	8502 (83.5)	676 (8.0)
Yes	620 (10.6)	55 (8.9)	1681 (16.5)	161 (9.6)
BMI				
Underweight	47 (0.8)	n.p.	19 (0.2)	n.p.
Normal	1077 (18.4)	75 (7.0)	860 (8.4)	60 (7.0)
Overweight	1963 (33.5)	148 (7.5)	2657 (26.1)	218 (8.2)
Obese I	1487 (25.4)	107 (7.2)	3097 (30.4)	227 (7.3)
Obese II	702 (12.0)	47 (6.7)	1910 (18.8)	168 (8.8)
Obese III	349 (6.0)	32 (9.2)	1194 (11.7)	130 (10.9)
Missing/invalid	230 (3.9)	19 (8.3)	446 (4.4)	32 (7.2)
ASA				
1 - Healthy	371 (6.3)	14 (3.8)	320 (3.1)	12 (3.8)
2 - Mild disease	3240 (55.3)	202 (6.2)	5696 (55.9)	382 (6.7)
3 - Severe disease	2164 (37.0)	199 (9.2)	4048 (39.8)	429 (10.6)
4 - Incapacitating	62 (1.1)	13 (21.0)	83 (0.8)	14 (16.9)
Missing	18 (0.3)	0 (0)	36 (0.4)	n.p.
Elixhauser Index				
0	3318 (56.7)	166 (5.0)	5435 (53.4)	347 (6.4)
1	1439 (24.6)	131 (9.1)	2718 (26.7)	234 (8.6)
2	582 (9.9)	61 (10.5)	1163 (11.4)	125 (10.8)
3 or more	516 (8.8)	72 (14.0)	867 (8.5)	131 (15.1)
Multimorbidity†				
No	4757 (81.3)	297 (6.2)	8153 (80.1)	581 (7.1)
Yes	1098 (18.7)	133 (12.1)	2030 (19.9)	256 (12.6)
Individual morbidities				
AIDS/HIV	n.p.	n.p.	n.p.	n.p.
Alcohol abuse	121 (2.1)	17 (14.0)	124 (1.2)	19 (15.3)
Blood loss anemia	35 (0.6)	5 (14.3)	54 (0.5)	12 (22.2)
Cardiac arrhythmia	584 (10.0)	66 (11.3)	887 (8.7)	129 (14.5)

	THA (N = 5855)		TKA (N = 10183)	
	Total	**30-day readmission**	**Total**	**30-day readmission**
Chronic pulmonary disease	136 (2.3)	24 (17.6)	189 (1.9)	26 (13.8)
Coagulopathy	79 (1.3)	16 (20.3)	95 (0.9)	19 (20.0)
Congestive heart failure	88 (1.5)	13 (14.8)	135 (1.3)	19 (14.1)
Deficiency anemia	142 (2.4)	15 (10.6)	239 (2.3)	31 (13.0)
Depression	56 (1.0)	n.p.	78 (0.8)	15 (19.2)
Diabetes, complicated	461 (7.9)	59 (12.8)	1215 (11.9)	144 (11.9)
Diabetes, uncomplicated	709 (12.1)	72 (10.2)	1768 (17.4)	166 (9.4)
Drug abuse	54 (0.9)	8 (14.8)	57 (0.6)	12 (21.1)
Fluid and electrolyte disorders	685 (11.7)	76 (11.1)	1075 (10.6)	140 (13.0)
Hypertension (complicated)	n.p.	n.p.	8 (0.1)	n.p.
Hypertension (uncomplicated)	488 (8.3)	49 (10.0)	918 (9.0)	116 (12.6)
Hyperthyroidism	15 (0.3)	n.p.	25 (0.2)	n.p.
Liver disease	112 (1.9)	17 (15.2)	161 (1.6)	18 (11.2)
Lymphoma	20 (0.3)	n.p.	11 (0.1)	n.p.
Metastatic cancer	30 (0.5)	5 (16.7)	35 (0.3)	n.p.
Obesity	78 (1.3)	7 (9.0)	182 (1.8)	17 (9.3)
Other neurological disorders	48 (0.8)	5 (10.4)	52 (0.5)	7 (13.5)
Paralysis	24 (0.4)	n.p.	42 (0.4)	n.p.
Peptic ulcer disease	20 (0.3)	n.p.	31 (0.3)	n.p.
Peripheral vascular disorders	53 (0.9)	5 (9.4)	87 (0.9)	11 (12.6)
Psychoses	15 (0.3)	n.p.	18 (0.2)	n.p.
Pulmonary circulation disorders	46 (0.8)	n.p.	91 (0.9)	11 (12.1)
Renal failure	124 (2.1)	16 (12.9)	243 (2.4)	40 (16.5)
Rheumatoid arthritis/collagen vascular disease	72 (1.2)	9 (12.5)	129 (1.3)	11 (8.5)
Solid tumor without metastasis	128 (2.2)	13 (10.2)	210 (2.1)	24 (11.4)
Valvular disease	56 (1.0)	8 (14.3)	83 (0.8)	12 (14.5)
Weight loss	119 (2.0)	15 (12.6)	85 (0.8)	10 (11.8)

n.p. Not reported (<5), ǂ Presence of 2 of more Elixhauser Index morbidities

Patient-level effects

In the THA cohort, factors that were significantly associated with 30-day readmission include older age and more morbidities (Table 7.3), particularly chronic pulmonary disease, coagulopathy, alcohol abuse and diabetes with complications (Appendix 6, Table 4). Multimorbid patients had 87% higher odds of readmission compared to those that were not (Appendix 6, Table 5). BMI was not found to be significantly associated with readmission following age and sex adjustments, and the association between ASA and readmission remained significant following adjustments for Elixhauser Index. Inclusion of Elixhauser Index increased the AUC from 0.59 to 0.64 (95%CI 0.62-0.67), with a further modest increase to 0.65 (95% CI 0.62-0.68) once ASA was added.

Table 7.3 Measures of variation in 30-day readmissions by person and hospital effects, THA

	Single-level models			Multilevel models	
	Model 1 OR (95% CI)	Model 2_h OR (95% CI)	Model $2_{h,r}$ OR (95% CI)	Model 3_h OR (95% CI)	Model $3_{h,r}$ OR (95% CI)
Patient-level effects					
Sex					
Male	1.26 (1.03-.154)	1.22 (1.00-1.50)	1.23 (1.00-.152)	1.23 (1.00-1.51)	1.24 (1.01-1.53)
Age					
<60	Reference	Reference	Reference	Reference	Reference
60 - 64	1.10 (0.75-1.63)	1.02 (0.69-1.50)	1.00 (0.67-1.47)	1.01 (0.69-1.50)	1.00 (0.67-1.48)
65 - 69	1.46 (1.04-2.06)	1.31 (0.93-1.84)	1.26 (0.90-1.79)	1.31 (0.93-1.85)	1.27 (0.90-1.79)
70 - 74	1.78 (1.29-2.47)	1.55 (1.11-2.15)	1.47 (1.05-2.05)	1.55 (1.11-2.16)	1.47 (1.05-2.06)
75 - 79	2.08 (1.49-2.92)	1.73 (1.23-2.44)	1.61 (1.14-2.28)	1.73 (1.23-2.45)	1.62 (1.15-2.30)
80 and over	2.30 (1.64-3.23)	1.79 (1.27-2.54)	1.66 (1.17-2.36)	1.79 (1.27-2.54)	1.67 (1.17-2.37)
Elixhauser Index					
0		Reference	Reference	Reference	Reference
1		1.86 (1.45-2.37)	1.75 (1.36-2.24)	1.87 (1.46-2.39)	1.77 (1.37-2.27)
2		2.06 (1.50-2.84)	1.87 (1.35-2.60)	2.07 (1.50-2.85)	1.88 (1.35-2.61)
3 or more		2.77 (2.03-3.78)	2.42 (1.75-3.35)	2.77 (2.03-3.78)	2.43 (1.75-3.37)
ASA class			1.29 (1.07-1.55)		1.28 (1.07-1.55)
Hospital-level effects					
Hospital-level intercept(SE)				0.03 (0.03)	0.03 (0.03)
VPC				0.94%	0.84%
Discriminatory accuracy					
AUC	0.59 (0.56-0.62)	0.64 (0.62-0.67)	0.65 (0.62-0.68)	0.64 (0.62-0.67)	0.65(0.62-0.68)
AUC difference	Reference	0.05[a]	0.06[a]	0.00[b]	0.00[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2

Model 1: single-level model with age, sex only; Model 2_h: Model 1 and hospital data information (Elixhauser Index); Model $2_{h,r}$: Model 1 and hospital and registry information (Elixhauser Index, ASA); Model 3_h: Model 2_h plus hospital-level random effect; Model $3_{h,r}$: Model $2_{h,r}$ plus hospital-level random effect. ICC: intraclass correlation coefficient, VPC: variance partition coefficient, AUC: area under the receiver operating characteristic curve

Adjusted 30-day readmissions in the TKA cohort were significantly higher among individuals with more morbidities and increasing ASA scores (Table 7.4) and among those with drug abuse, blood loss anaemia, cardiac arrhythmias, fluid and electrolyte disorders, diabetes with complications and hypertension (Appendix 6, Table 6). Odds of readmission were 92% higher among patients that were multimorbid (Appendix 6, Table 7). BMI was

significantly associated with readmission after adjustment for age, sex and comorbidities only (Appendix 6, Table 5), but not when ASA was added to the model. The addition of Elixhauser Index increased the AUC from 0.54 to 0.60 (95%CI 0.58-0.62), and addition of ASA increased the AUC further to 0.61 (0.59-0.63).

Table 7.4 Measures of variation in 30-day readmissions by person and hospital effects, TKA

	Single-level models			Multilevel models	
	Model 1 OR (95% CI)	Model 2_h OR (95% CI)	Model $2_{h,r}$ OR (95% CI)	Model 3_h OR (95% CI)	Model $3_{h,r}$ OR (95% CI)
Patient-level effects					
Sex					
Male	1.14 (0.99-1.32)	1.11 (0.96-1.28)	1.11 (0.96-1.28)	1.10 (0.95-1.28)	1.10 (0.95-1.28)
Age					
<60	Reference	Reference	Reference	Reference	Reference
60 - 64	0.93 (0.71-1.22)	0.90 (0.68-1.18)	0.89 (0.67-1.16)	0.90 (0.68-1.18)	0.89 (0.68-1.17)
65 - 69	1.06 (0.83-1.36)	0.98 (0.77-1.26)	0.96 (0.75-1.24)	0.99 (0.77-1.27)	0.97 (0.76-1.25)
70 - 74	1.33 (1.05-1.68)	1.20 (0.95-1.53)	1.16 (0.91-1.48)	1.21 (0.95-1.53)	1.17 (0.92-1.48)
75 - 79	1.24 (0.96-1.60)	1.09 (0.84-1.41)	1.04 (0.80-1.35)	1.08 (0.84-1.40)	1.03 (0.80-1.34)
80 and over	1.29 (0.98-1.70)	1.09 (0.82-1.45)	1.02 (0.77-1.35)	1.08 (0.81-1.43)	1.01 (0.76-1.34)
Elixhauser Index					
0		Reference	Reference	Reference	Reference
1		1.41 (1.18-1.68)	1.31 (1.10-1.57)	1.40 (1.17-1.67)	1.31 (1.09-1.57)
2		1.83 (1.47-2.28)	1.63 (1.30-2.04)	1.83 (1.47-2.28)	1.63 (1.30-2.05)
3 or more		2.71 (2.17-3.39)	2.30 (1.82-2.91)	2.71 (2.16-3.39)	2.31 (1.82-2.92)
ASA class			1.40 (1.22-1.61)		1.40 (1.22-1.61)
Hospital-level effects					
Hospital-level intercept (SE)				0.05 (0.02)	0.04 (0.02)
VPC				1.38%	1.34%
Discriminatory accuracy					
AUC	0.54 (0.52-0.56)	0.60 (0.58-0.62)	0.61 (0.59-0.63)	0.60 (0.58-0.62)	0.61(0.59-0.63)
AUC difference	Reference	0.06[a]	0.07[a]	0.00[b]	0.00[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2

Model 1: single-level model with age, sex only; Model 2_h: Model 1 and hospital data information (Elixhauser Index); Model $2_{h,r}$: Model 1 and hospital and registry information (Elixhauser Index, ASA); Model 3_h: Model 2_h plus hospital-level random effect; Model $3_{h,r}$: Model $2_{h,r}$ plus hospital-level random effect. ICC: intraclass correlation coefficient, VPC: variance partition coefficient, AUC: area under the receiver operating characteristic curve

Hospital-level effects

Variation at hospital level was small in both the THA and TKA cohorts, with VPC of 1.34% and 0.84% respectively, indicating that less than 1.4% of the adjusted individual

variation in 30-day readmission rates was attributable to the hospital. Similarly, the AUC of Model 3, which includes a hospital-level random intercept, showed no increase in discriminatory accuracy.

Discussion

Our study is the first to link the AONJRR to hospital administrative data and to examine how the inclusion of registry information (BMI and ASA scores) adds to the explanation of 30-day readmission rates over and above measures used for hospital performance profiling. This linkage also allowed us to evaluate whether there is variation among hospital outcomes beyond that which is explained by patient characteristics.

Using stepwise multilevel logistic regression analysis, we showed that, after inclusion of Elixhauser Index, there were modest improvements in the discriminatory accuracy with the addition of clinical registry data (ASA for THA, ASA or BMI for TKA). After full adjustment, the ASA score was a significant predictor of readmissions for both THA and TKA. These findings suggest integration of clinical registry data may improve capacity to identify at-risk patients following these procedures more than traditional approaches using administrative data alone- such as reporting on between-hospital variation.

In our study, higher ASA score was associated with an increased risk of readmission in age-sex adjusted models and maintained a significant independent association following Elixhauser Index adjustment in both the THA and TKA cohorts. ASA has been one of the more cited factors contributing to increased readmission,[233] and we have shown its contribution to the Australian joint replacement surgery cohorts, with higher ASA being associated with increased odds of readmissions. Modest improvements in discriminatory accuracy seen with the addition of ASA scores in our study may be due to homogeneity in THA/TKA cohorts, with effect sizes likely to have a greater impact in clinical registries with a greater range of illness severity. The correlation between the ASA and Elixhauser index was not strong, highlighting that ASA captures different aspects of a patient's overall health. Although the ASA was not designed to predict outcomes,[236] but rather to assess patients' pre-anaesthesia comorbidity, its delineation between patients with minimal to severe systemic disease can be viewed as a proxy of patient complexity, over and above the weighted disease count of Elixhauser comorbidity index. Furthermore, ASA is assessed by a clinician who has examined the patient, rather than being assigned on the basis of coded diagnoses, the quality of which varies widely.[241] The inclusion of additonal measures of

patient complexity, such as severity of illness, in clinical registries which collect such data, could provide further means to improve risk adjustment for hosptial performance metrics.

The contribution of BMI, as captured in registry data, to 30-day readmissions differed between the two cohorts. BMI was not a significant predictor of readmission in the THA cohort analysis adjusted for age and sex, but morbidly obese individuals (obesity class III) were significantly more likely to have a readmission following TKA. These mixed results for the effects of obesity are also observed in prior studies.[242] We also showed that obesity was prevalent in both THA and TKA cohorts, with low capture but high validity within hospital data. Adjustments for obesity using hospital data alone should therefore be viewed with caution, noting high under-enumeration of obesity in the administrative data sources.

Readmission literature for joint replacements indicates several other factors that are associated with higher readmission rates. A recent systematic review[233] found that factors such as socioeconomic status, race/ethnicity, length of stay and disposition at discharge are predictive of readmission following arthroplasty. More recent research indicated that hospital frailty risk scores (HFRS) provide better discriminative ability to classify patients with and without adverse events.[201] And HFRS[87] can be derived from administrative data, it includes markers of quality of care, such as hospital-acquired complications, so using it to adjust indicators may mask genuine differences in hospital performance.

We found that less than 1.4% of the overall individual variation in readmission was attributable to the hospital where the surgery was performed. Our findings are in line with previous studies of hospital differences in orthopaedic surgery.[244, 245] Hollis et al.[244] found 1.5% of variation in US orthopaedic 30-day readmission rates was attributable to hospitals and Kristensen et al.[245] found up to 0.9% of the variation in orthopaedic 30-day mortality rates in Denmark to be attributable to hospitals. These findings support the notion that reductions in readmissions following joint replacement surgery are most likely to be achieved by interventions that are targeted at the individual level, towards patients at high risk of readmission, rather than focussed at the hospital level.

The key strength of this study is the use of linked AOANJRR registry and population-level hospital data, and the novel analytical approach to unpack the relative contributions of data sources to explaining patient outcomes. However, it does have several limitations. The information about BMI and ASA in the registry data was collected from year 2015 only, limiting the number of years of the data we could analyse. We could not include patients

who had joint replacement procedures from private hospitals because we did not have complete data for them.

Future planned integration of clinical registry data can help to identify at-risk patients following THA/TKA procedures and improve risk adjustment for hospital readmission performance measures. Reductions in readmissions following joint replacement surgery are most likely to be achieved by interventions that are targeted towards patients at high risk of readmission, rather than focussed at the hospital level.

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AUTHOR CONTRIBUTION

S.L. designed the study with the oversight from other co-authors. L.R.J. acquired the funding and data. J.M.S and M.O.F. supervised statistical analyses. S.L. performed data curation, carried out statistical analyses, interpretation of findings, drafted the manuscript, reviewed and revised it following input from all co-authors. I.A.H provided clinical advice and contributed to result interpretation. M.F.L prepared AOANJRR data for linkage by CHeReL. All authors interpreted the results, revised and approved the manuscript.

CHAPTER 8

Discussion

8.1 Thesis motivation and aims

People with multiple chronic conditions have adverse health outcomes (mortality, hospitalisations, prolonged lengths of stay, etc), higher levels of disability[64, 65, 90, 220] and reduced quality of life.[63, 75] Multimorbidity increases healthcare utilisation[69, 196, 246] and healthcare costs.[58, 67] Growing numbers of individuals living with multimorbidity, with the associated higher utilisation of primary and acute care services, is a challenge facing many healthcare systems internationally. Multimorbidity has been hailed a priority for research, by the Academy of Medical Sciences,[8] medical practice, by the NICE,[92] and health policy reform.[187, 247, 248] Research on multimorbidity has grown considerably in the past decade.

Population-level research on multimorbidity and its outcomes is impeded by a lack of available data that permit identification of people with multiple chronic diseases and longitudinal tracking of their subsequent service use and health outcomes. Australia is on the cusp of creating enduring linked data assets for Australian health research,[249] which will bolster national research in health priority areas, including multimorbidity. Until this occurs, Australian researchers rely on ad-hoc linkages of health data sources, often with long lead times and at considerable cost.

In this thesis I aimed to explore measurement of multimorbidity, its interplay with frailty, and associations with outcomes for patients, via a series of studies using Australian administrative health data linked with survey and national registry data from three separate NHMRC projects. The first two studies used the data from the 45 and Up Study, Australia's largest cohort study of health and ageing (https://www.saxinstitute.org.au/our-work/45-up-study/). The remaining two studies included population-level hospital data for NSW, Australia's most populous state.[109]

Specific aims of the thesis included addressing the following research questions:

1. Is there agreement between self-repoted health conditions and coded diagnoses in routine hospital inpatient data? What patient- and hospital-level factors explain this agreement?
2. Do multimorbidity prevalence estimates vary according to data source? Are different individuals identified as multimorbid using different data sources?
3. What effects do the different measures of multimorbidity and frailty have on adverse patient outcomes? How do multimorbidity and frailty interact?
4. How does multimorbidity contribute to the variations in hospital-level outcome indicators used for performance measurement? Does the addition of variables from clinical registries improve predictive ability (discriminative performance) of modes used to monitor health performance metrics?

8.2 Key thesis findings

8.2.1 Study 1: Variation in recording health conditions in hospital data

Routinely collected hospital data are increasingly being used in health research, with hospital coded diagnoses commonly used for risk adjustment in epidemiological studies. These data are prone to underreporting of morbidities,[28, 29, 225] with a potential to introduce bias in risk-adjustment, particularly when used to report on hospital-performance measures.

Chapter 4 investigated the variation in recording of single and multiple conditions in hospital data in NSW, using linked data for 32,832 people admitted to 313 hospitals in the state. I used multilevel modelling in this work to account for clustering of people within hospitals, thus properly considering contextual influences that can explain the variation in recording of conditions. My research demonstrated considerable between-hospital variation in the recording of six morbidities: diabetes, heart disease, hypertension, stroke, smoking and obesity, and showed that this variation is predominantly driven by the average number of diagnosis codes for each patient that is coded by hospitals (i.e. 'depth of coding').

Concordance between self-reported and hospital-coded morbidities varied among the six conditions and their combinations, and was found to be good for diabetes, moderate for smoking, fair for heart disease and poor for hypertension, stroke, and obesity. My study, to the best of my knowledge, was the first to explore variations in recording of multiple conditions in hospital data. I found that the concordance of two-way morbidity

combinations was very low, and was fair or good at best, and generally higher among combinations of diseases involving diabetes.

My research highlighted the value-add of incorporating prior hospitalisations in identifying patients with morbidities. Concordance between self-reported and hospital-coded morbidities increased with the inclusion of prior hospital admissions (lookback). I found that close to half (41-56%) of the patients with hypertension and heart disease can be ascertained using a lookback period, compared with 31% and 44%, respectively, using information from a single admission only.

My research found considerable hospital-level variation in the recording of health conditions, with between 8% (diabetes) and 22% (heart disease) of variation attributable to hospital-level factors, after adjustments for patient characteristics. There was less hospital-level variation in the recording of diabetes, smoking and stroke, and more hospital-level variation in the recording of hypertension, heart disease and obesity. Recording of hypertension and heart disease varied greatly, the hospitals with better reporting having over two times higher odds of recording these conditions than hospitals with lower levels of reporting. These findings were novel, and for the first time provided detailed information about how the validity of morbidity coding varied between hospitals.

In this research I also explored hospital-level factors that contributed to variations in the coding between the six chosen morbidities. Hospital-level variables (depth of coding, hospital size (peer group), hospital type (public/private) and hospital remoteness) were added one at a time to examine their contribution to between-hospital variation. Depth of coding was found to explain the highest proportion of the variation and explained between 16% (smoking) and 42% (hypertension) of residual variation among hospitals. Hospital type explained from 0% (smoking) to 59% (stroke), and hospital size explained from 10% (hypertension) to 27% (diabetes) of the hospital-level variation.

These findings have implications for multimorbidity ascertainment in acute care settings and highlight the advantages of incorporating prior hospitalisation history or supplementing the data using other administrative or self-reported data sources. Differences in between-hospital variation of recording, as shown in in this and a subsequent study,[240] highlight the possibility of introducing biases for hospital-based performance reporting and activity-based funding if all hospitals are included. Stratification by hospital type (public, private) and hospital peer group, and risk-adjustment for

comorbidity, is suggested when reporting hospital results to help mitigate such potential bias.

8.2.2 Study 2: Comparing estimates of multimorbidity between data sources

Accurate and reliable measures of the prevalence of chronic disease and multimorbidity are essential for monitoring trends, estimating burden of disease, targeting preventive measures and planning healthcare resources. With a variety of data sources available, it is increasingly important to define consistent measures of multimorbidity.

In Chapter 5 I explored concordance in identification of eight common chronic conditions, estimates of multimorbidity and complex multimorbidity, and similarities and differences between individuals with multimorbidity using self-reported and administrative (hospital and medication) datasets for 90,352 NSW residents. My research found that different individuals, with different combinations of conditions, are identified as multimorbid when different data sources are used.

My analysis showed that there is a variable level of agreement between self-reported and administrative data. Excellent levels of agreement were found for diabetes in both hospital and medication datasets. Fair to good agreement was found in medication data for hypertension, asthma, depression, and Parkinson's disease. The agreement between hospital and self-reported data was generally poor, but hospital diagnoses had high levels of positive predictive value (PPV) across all examined conditions, indicating that although not all chronic conditions are identified in hospital data, when recorded they are generally accurate.

My analysis was the first, to my knowledge, to evaluate the differences between data sources in estimates of multimorbidity using the same list of chronic conditions in the same individuals. In my research, the estimates of multimorbidity prevalence varied by the data source used, with highest prevalence of multimorbidity and complex multimorbidity found using self-reported data, followed by medication data and hospital data. Combining hospital and medication data brought the overall multimorbidity estimates of the self-report and administrative data closer together, but there was still 41% relative difference in the estimated prevalence of complex multimorbidity between the data sources.

My research also showed that the odds of multimorbidity were higher among males, older people and those speaking a language other than English at home. The increasing age gradient in odds of multimorbidity was more pronounced in administrative than self-reported data for those aged 75 years and over, indicating a potential under numeration of morbidities when relying on self-reported data alone. My research found that people speaking English as a second language had increased odds of having multimorbidity in the administrative data, but decreased odds in the survey data. These findings were novel, and had not been reported in the literature, to the best of my knowledge.

The findings from this research highlight the gaps in the ascertainment of multimorbidity using single data sources. Reliance on self-reported data will under-ascertain morbidities for persons speaking English as a second language, and people aged over 75 years of age. Reliance on administrative data will under-ascertain multimorbidity but could potentially be used to identify cohorts of individuals with chronic disease, with high specificity. The gaps in the current data collections can be overcome, in part, by supplementing chronic disease information using different data sources. And these gaps can further be closed once additional data sources, in particular national primary health care datasets, become available.

8.2.3 Study 3: Multimorbidity and frailty

Multimorbidity and frailty are distinct entities reflecting different aspects of patient complexity. Many patients experience both, presenting the potential that they interact to increase the risk of adverse outcomes. In Chapter 6 I used whole-of-population data for NSW patients aged 75 and over (n=257,535) to explore the interaction between multimorbidity and frailty in hospitalised patients and their combined effects on adverse patient outcomes. To the best of my knowledge, no other studies have examined interaction between the two factors in hospital patients, nor reported the joint effects of multimorbidity and frailty.

The study used advanced statistical techniques to model patient outcomes of 30-day mortality, 30-day unplanned readmission to hospital and prolonged length of stay. Clustering of patients within hospitals was taken into account using multilevel models, to allow for similarities in patients treated within the same hospital. Poisson regression was used rather than logistic regression, given that odds ratios may not approximate relative risk

in common outcomes.[250] Study findings were reported using recognised best practice for the reporting of interaction results.[210, 2211, 251]

My research showed that one-third of hospitalised patients had both multimorbidity and elevated risks of frailty, close to 20% had an elevated frailty risk only, 15% were multimorbid only and the remaining 30% had neither. People with both multimorbidity and frailty were found to have worse outcomes than those with one or neither factor. Synergistic effects between multimorbidity and frailty were found for mortality and prolonged lengths of stay, and an additive effect for readmission. Compared with patients with neither multimorbidity nor at increased risk of frailty, patients with multimorbidity and frailty had 4.23 (95% CI 4.07-4.39) times the risk of 30-day mortality, 3.34 (95% CI 3.26-3.41) times the risk of prolonged length of stay and 1.79 (95% CI 1.73-1.86) times the risk of unplanned readmission within 30 days post discharge. Even larger effects of multimorbidity and frailty on adverse outcomes were found among surgical patients, with 30-day mortality risk 7.2 (95% CI 6.1-8.5) times higher in those with both multimorbidity and elevated frailty and 2.6 (95% CI 2.3-3.0) times higher 30-day readmission risk.

The findings from this study highlight the fact that both multimorbidity and frailty ought to be used to identify patients at risk of different types of complications. Multimorbidity and claims-based frailty, via HFRS, can readily be measured using administrative data containing ICD-10 codes, and can potentially be used for risk-stratification purposes. However, an overlap in some of the ICD-10 codes used in the two measures, and the capture of in-hospital complications contained within the HFRS, suggests further work is required to refine their application. For the latter, incorporation of condition onset flags (sometimes known as present on admission flags) into the HFRS coding algorithm could alleviate the problem of adjusting for factors that may represent adverse outcomes of care, potentially masking the between-hospital differences that performance indicators were designed to discover.

8.2.4 Study 4: Supplementing multimorbidity measured using administrative data with clinical registry data

Performance monitoring of patient care and outcomes is usually undertaken using administrative data. There is strong interest in integrating clinical registries with such major health care datasets, for example to improve risk adjustment of performance metrics.

However, there are few such linkages in Australia, and the potential added value of clinical registries is largely unknown.

In Chapter 7 I extended the exploration of 30-day readmission work from Chapter 6, and supplemented administrative data with registry information to examine readmissions following joint replacement surgery – one of the national core, hospital-based outcome indicators for measuring hospital performance.[189] Both Australian[222] and US[243] indicators of readmission for THA/TKA risk adjust for age, sex and comorbidity. However, readmissions for THA/TKA have been shown to increase with increasing ASA scores and BMI,[233, 242] both of which are captured in clinical registry data. In this work I used the linked data from hospitals and the AOANJRR, the oldest and most comprehensive clinical quality registry in Australia.[252]

The analysis in Chapter 7 was designed to fill a gap in the research on exploration of variation in patient outcomes. Using unique linked hospital and registry data for a population cohort and applying a methodological approach of stepwise multilevel models, I unpacked the relative contribution of patient factors and between-hospital variation in prediction of readmission following THA/TKA. This was the first study to examine the value of including registry data, over and above multimorbidity as measured using administrative data, in the prediction of readmission following THA/TKA for hospital performance measurement.

Around 7% of THA and 8% of TKA patients had a readmission within 30 days of discharge from surgery, with patients who are older, have multimorbidity or higher ASA scores having higher readmission rates. My research found that the variation at hospital-level was small, with less than 1.4% of the adjusted individual variation in readmission rates attributable to hospitals. Despite public reporting of NSW hospital performance for THA/TKA by the NSW BHI, this was the first-time between hospital-level variation in TKA/TKA has formally been quantified.

THA and TKA patients who had multimorbidity were more likely to experience readmissions following surgery, with noted increase in the likelihood of readmission for conditions such as chronic pulmonary disease, coagulopathy, alcohol abuse and diabetes with complications in the THA cohort, and drug abuse, blood loss anaemia, cardiac arrhythmia, fluid and electrolyte disorders and hypertension in the TKA cohort. There was a weak correlation between ASA score from the AOANJRR, and Elixhauser Index derived from hospital administrative data. The addition of ASA score to a model containing age,

sex and morbidity increased the model's discriminatory power (measured using increase in the AUC value) by a modest amount in both THA and TKA cohorts, with ASA score remaining a significant predictor of readmissions over and above morbidity adjustments.

Aside from the above, I showed that ascertainment of obesity in hospital data is low, with only 13% of overweight/obese patients with BMI from registry data being identified using hospital diagnoses or supplementary codes. This finding echoes the results from Chapter 4, where poor levels of agreement were found between self-reported BMI and hospital diagnosis.

These results demonstrate there is value in supplementing measures of multimorbidity from administrative data with information from registries. More direct clinical information (such as the ASA score) can increase our capacity to identify and risk-adjust for high-risk individuals. Furthermore, clinical registries may provide more complete information on risk factors (e.g. BMI) where ascertainment within administrative data is poor.

8.3 Reach and impact of the research

Findings from the thesis have been presented at a number of national and international conferences and meetings including the 45 and Up Collaborators meetings in 2013 and 2014 in Sydney, the Health Services and Policy Research conferences in 2013 in Wellington, New Zealand, and 2015 in Adelaide, the Scottish Health Informatics Program (SHIP) conference in St Andrews, Scotland, in 2013, and the International Health Data Linkage conference in Vancouver, Canada, in 2014. The results from Chapters 4 and 5 were presented at invited talks at the NSW Ministry of Health, National Centre for Classification in Health, and various research centres across UNSW and beyond (details on page xvi).

Published papers from Chapters 4 and 5 have been cited by 27[253] and 25[254] articles respectively, as measured by Dimensions software.[255] The articles were cited by various researchers around the globe, including 25 (47%) citations from Australia, 7 (13%) citations from Canada, 6 (11%) from UK, 5 (9%) from Spain, 4 (8%) from the US, and 6 (11%) citations from other countries. My Chapter 5 publication has received a lot of interest recently,[254] with the results included in four systematic reviews[256-259] of prevalence of multimorbidity in community settings,[256] validation studies of claims-based data,[257] identification of asthma patients using administrative data,[258] and social determinants of

multimorbidity.[259] This work has also recently been cited in a 2021 government report on chronic condition multimorbidity by the AIHW.[260]

Aside from the scholarly research, I have contributed to the field of multimorbidity via participating in the current work on exploring an international consensus of the definition and measurement of multimorbidity via a series of Delphi surveys,[261] as well as being a reviewer for a number of articles for the Journal of Comorbidity, now known as the Journal of Multimorbidity and Comorbidity.

My contribution also extends to policy processes on the refinement of the national core, hospital-based outcome indicator (CHBOI) indicator specifications[189] by the Australian Commission on Safety and Quality in Health Care, including the development of the flowchart approach used in the current indicator specifications, and undertaking commissioned rapid literature reviews for mortality and readmission indicators. I lead the two rapid literature reviews, drafted key summaries for condition-specific indicator workshops, participated these workshops alongside clinicians, coders and data specialists, as well as led the drafting of final reports. The final reports included an overview and critical appraisal of published literature, summaries and comparisons of international readmission indicators, as well discussions and recommendations around validity of indicators, risk-adjustment methods, and implications for Australian metrics.

8.4 Implications for policy and practice

8.4.1 The need to accurately capture chronic diseases in administrative data

The population incidence and prevalence of chronic disease is monitored using both self-reported information from national health surveys and administrative data sources. Relying on a single source gives a limited view of chronic disease,[204] as self-reported data can be prone to recall bias and usually captures limited numbers of chronic diseases, whereas administrative data are captured only when people use health services and may be subject to data quality issues.

In Studies 1 and 2 I explored consistency of ascertainment of chronic disease using self-reported and administrative data and found that there is variability in condition

ascertainment between data sources and between individuals. These findings are consistent with other research,[225, 204,262,263] highlighting the importance of using multiple data sources to ascertain chronic disease, rather than relying on the information within a single source alone.

There is also potential to further improve capture of chronic disease in Australia through linkage to further physician claims and EMR data. Physician claims database coverage and completeness varies between countries. In countries like Canada[254-266], UK[42, 267], US[268] and Germany,[269] physician claims data contain coded diagnoses which can be used to identify individuals with particular diseases. There are few sources of primary health care data in Australia,[124] and no state-based reporting systems containing detailed clinical information, limiting our capacity to use claims-based data for chronic disease surveillance and monitoring to the extent possible overseas. However, data extraction from GP electronic health records (EHRs) is possible from individual providers or programs such as NPS MedicineInsight.[270] NPS MedicineInsight includes longitudinal data from EHRs from approximately 8% of general practices in Australia,[106] providing an avenue for furthering the research into chronic disease. However, NPS MedicineInsight data are currently unable to link patients across different general practice sites, or to other data sources, but linkages are planned in the future.[106] Linkage of EHR data to hospital and survey data will advance Australian efforts to evaluate algorithms for monitoring and estimating disease prevalence, in line with international specifications.[271]

My findings highlight that, despite the presence of coding standards in Australia, there is large variability in recording of chronic disease - and that further improvements can be made. Comparisons of estimates of chronic disease within hospitalised patients is reliant on accurate and consistent coding at discharge from hospital. But accuracy of discharge coding is found to be variable between countries (51 – 98%),[241] with differences found both in terms of the maximum allowable number of coded diagnoses and how main diagnoses are defined. Barriers to accurate coding include chart documentation and clinical coding practices,[120, 226] with under-coding of conditions identified as a major issue in administrative data bases.[27-29] Improvements in the validity of coding can be made if conditions are coded regardless of their implication for hospital resources and costs.[27] This has been the case in Australia since the introduction of supplementary codes for chronic diseases in 2015.[122] During 2017-18, around one third of the separations in NSW hospitals included supplementary codes, averaging between 1.8 supplementary codes per separation in public

and 1.5 in private hospitals.[272] My research in Chapter 7 demonstrated a dramatic increase in the coding of overweight and obesity using supplementary codes, highlighting the benefit of the inclusion of additional information within hospital data. It is important to note that validation studies of supplementary codes are yet to be done and, informed by my research in Chapter 4 and a subsequent Australian study,[225] these should be carried out in representative samples of public and private hospitals of different sizes, due to the variability in coding practices between these hospital types.

8.4.2 The challenges in measurement of multimorbidity using administrative data

The estimated prevalence of multimorbidity can vary considerably based on how it is measured, with differences, for example, in the list of conditions used (chronic only, both chronic and acute, including or excluding symptoms), number of conditions included (ranging between 4 and 138[11, 273]), data collections used (surveys, medical chart extraction, administrative databases) and settings (general population, primary care, hospital, nursing home). A 2012 systematic review by Fortin et al.[32] found that the prevalence is higher in primary care samples (42 – 52%) than in the general population (10% - 13%). Large differences in prevalence estimates between settings were also noted by Schram et al.,[274] with multimorbidity most common in the nursing home setting (82%), followed by the general population and general practitioner registries (56%-72%) and least prevalent in the hospital setting (22%).

My research in Chapter 5 demonstrated that the ascertainment of multimorbidity is highest using self-reported data, followed by pharmaceutical claims and hospital data. Recent studies, citing my research, have also shown that the prevalence of multimorbidity is higher based on self-reported[262] or pharmaceutical claims data[275] compared with hospital data. This research highlights the importance of supplementing data sources when reporting on the prevalence of multimorbidity, particularly if focusing on the inpatient setting alone. However, incorporation of data from multiple sources is often constrained by the cost, lead times in data procurement, and data availability.

Using a combination of data sources, including administrative (such as hospital data, claims data – pharmaceuticals, physician claims) and registry data will help overcome the gaps and limitations of using a single data source – for example in increasing case identification.

Algorithms to identify chronic diseases using single and multiple administrative data sets have been studied in Canada,[204, 264, 276] US,[277] New Zealand[278, 279] and Sweden[15]. Australian development has been slow, due to the difficulties in accessing linked population-level data (e.g. linked pharmaceutical claims and administrative hospital databases), as well as the lack of national primary care data. However, recent advances on this front are emerging. Increased calls for creation of an Australian primary care minimum dataset[280, 281] have resulted in work to commence development of a National Primary Health Care Data Asset,[107, 271] as well as state-based initiatives, such as the Lumos programme in NSW, linking general practice data with patient records from acute and other settings.[282] Linkages of the primary health care data will help to further our understanding of the patient journeys in the primary care setting and provide opportunities for improving patient care and care coordination.

There can also be systematic underreporting of some types of chronic conditions within different data sources. Capture of (multi)morbidity using administrative data sources is driven by coded diagnoses, and the use of validated indices, such as the Charlson and Elixhauser indices. In this thesis, a combination of Elixhauser and Charlson indices was used, due to the lack of inclusion of mental health related comorbidities in the Charlson Index. The inclusion of mental health conditions in the measurement of multimorbidity has been noted in multimorbidity literature[11, 278] which found increase in the prevalence of mental health disorders with increasing number of physical conditions.[42, 73] Chapter 5 of this thesis showed that the prevalence of depression within a hospitalised cohort was much higher when using self-reported data than hospital diagnosis codes, with differences in estimates being closer together once medication data was included. This finding, along with more recent research,[27] highlights the gap in hospital data completeness of asymptomatic conditions treated in primary care. A 2021 systematic review[283] found that serious mental illness was associated with higher inpatient costs, prolonged lengths of stay and higher readmissions, reflecting the importance of screening or capture of mental disorders to improve patient outcomes. Additional analyses of data in Chapter 7 indicated that the inclusion of supplementary chronic diagnosis codes increased ascertainment of depression over ten-fold, highlighting the need to capture a broader variety of coded diagnoses in the hospital data, especially if this will help in identifying patients in need of optimising care.

8.4.3 The need for a multifaceted view of patient complexity

Multimorbidity increases the risk of adverse health outcomes for people of all ages, but particularly older adults. However, there are other drivers of adverse outcomes in the elderly – such as frailty.[80] The relationship between frailty and multimorbidity is complex, as both are reflective of patient complexity, but with recognition that they are distinct concepts[84] and with evidence of a bidirectional association.[74] My study in Chapter 6 describes additive and synergistic effects of multimorbidity and frailty in hospitalised older adults, over and above the effects of age alone. These findings highlight the potential to identify patients at increased risk of different types of complications, with multimorbid-only individuals having higher age-adjusted mortality and readmission risks than frail-only individuals, and elevated frailty risk patients only having higher risk of prolonged hospital stay.

We need to identify multiple facets of patient complexity. Indeed, frailty screening among patients with multimorbidity in primary care are recommended in the NICE guidelines,[93, 284] and systematic identification of frailty in primary care is performed routinely in England using the electronic Frailty Index (eFI).[285] Identification of individuals at elevated risks of frailty in the hospital setting is possible with the HFRS, and can be implemented at the point of admission to hospital to help prompt geriatric-based assessments, as required. Furthermore, tracking of frailty within hospital can help with service-level planning of resources required to care for patients with most complex needs.

8.4.4 The need for enduring linked data sources for research

This thesis presents a series of studies on multimorbidity using administrative health data. It highlights the paucity of Australian studies of multimorbidity beyond estimates of multimorbidity in primary care, or self-reported outcomes, and shows how 'big data' can be used to further Australian multimorbidity research.

Data linkage capabilities across Australian states and territories have been steadily growing since the establishment of the first data linkage unit in Western Australia in 1995.[286] However, access to and use of linked data, and particularly Commonwealth health data, is hampered by complex, lengthy and often duplicative approvals processes,[287] and long lead times in receiving linked data. Furthermore, separate data linkages, approvals and data

extractions are required for each individual research study of interest, contributing to research inefficiencies and waste. In this thesis I used data from three NHMRC-funded projects, which required multiple ethics and data custodian approvals, as well as multiple data extractions. The existence of an enduring linked data set would have provided quicker and easier access to data.

Enduring linked data, which provide consistent access for multiple data users, are the key for efficient, timely and cost-effective research. The Australian government has recognised the value of integration of data assets,[288] with demand for national cross-sectoral and cross-jurisdictional data resulting in the creation of the National Integrated Health Services Infrastructure (NIHSI) by the AIHW,[249] linking information from hospitals, emergency departments, MBS, PBS, residential aged care and national death datasets.[289] Initial excitement of NIHSI construction has however been dampened by the restricted access to organisations providing the data (AIHW, state and territory health departments and Department of Health). However, governance models for third-party access to such data are in development, such as in the Australian Research Data commons funded project led by the University of New South Wales, in partnership with AIHW, government departments and research organisations, to establish the LINked Data Asset for Australian Health Research (LINDAHR).[290]

Numerous developments in data access, and creation and integration of health data are underway in Australia. A National Primary Health Data Asset is under development,[107, 271] integration of clinical quality registry data is proposed,[127] and significant investment in digital future in the recently announced Federal Budget[291] promises to bolster data-intensive health research in Australia.

8.5 Strengths and limitations

The strengths of this thesis lie in the use of large population-level hospital data, linked to claims-based, survey and registry data, to bring together information about individuals with multimorbidity. The use of advanced and novel analytical approaches was also advantageous in unpacking the relative contributions of data sources in measuring patient outcomes, and delineating patients most at risk of adverse events.

Most of the previous Australian research on multimorbidity used information from single data sources, often with limited sample sizes. The use of linked data in this thesis allowed me to further the research about multimorbidity within an Australian setting and provide evidence of ascertainment of multimorbidity using data for large numbers of older adults from survey, inpatient and pharmaceutical claims data. The results provided the first Australian evidence for the contrasting estimates of prevalence that are generated from different datasets for the same sample of individuals and the same set of chronic conditions.

The value of linked data sources for multimorbidity research was highlighted in Chapters 6 and 7, which used longitudinal information about patients with multimorbidity to examine patient outcomes. Harnessing the power of linked administrative data on a population level, provides an efficient way of tracking patients over time, exploring their interactions with health services and identifying how multimorbidity affects health outcomes.

However, this research has some limitations. Study-specific limitations are presented within each analytical chapter. This section outlines general limitations.

The use of administrative data has a unique set of challenges. These data are collected mainly for administrative purposes, meaning that factors such as disease acuity, general health status, pathology results, lifestyle behaviours and detailed clinical information are not captured. This may potentially result in residual confounding when estimating the effects of multimorbidity on health outcomes[292] – for example the analyses in Chapters 6 and 7. Findings from both these chapters suggest there is value identifying further measures of patient complexity beyond multimorbidity, and new sources of patient information should continue to be explored.

Results from Chapters 4 and 5 indicate that hospital data have low sensitivity but high positive predictive values for identifying chronic conditions. Ascertainment of conditions in Chapters 5 and 6 was increased though incorporation of a two-year lookback period, but it is highly likely that under-enumeration of some conditions remained.[293] Also, it was not possible to distinguish between comorbidities present on admission and complications of care in the analyses presented in Chapters 4-6. Although this would not impact on the results presented in Chapters 4 and 5, it has implications for those presented in Chapter 6, with some of the HFRS diagnoses potentially arising during hospital admission. For this reason, HFRS was not used for risk-adjustment of hospital readmission performance

indicators in Chapter 7, as adjustment for adverse outcomes occurring during hospital stay is not appropriate for an indicator that is intended to measure quality of hospital care.

Prior research[60] has shown that single indices of multimorbidity may be inadequate to predict multiple outcomes, with calls for multiple indices of multimorbidity to be used.[11] In Chapter 6, in which three outcomes were reported (mortality, readmissions, prolonged length of stay), a combination of Charlson and Elixhauser indices was applied. The combined Charlson/Elixhauser index was validated for examining mortality[294, 295] and readmissions outcomes[296] but not for prolonged length of stay. The research presented in Chapter 7 used only the Elixhauser index to measure multimorbidity, in line with methods used for risk adjustment for hospital readmission indicators for THA/TKA in NSW,[222] and the inclusion of an additional measure, preoperative risk via ASA score, was shown to improve risk adjustment for these hospital performance measures.

Another limitation pertains to the generalisability of the results for studies in Chapters 4 and 5, which used the 45 and Up Study. Although comprising a large and heterogeneous population owing to the large number of individuals, the Study's response rate was 18%.[132] The participants in the Study are older and healthier than the general population[132] but estimates of within-cohort comparisons are still valid.[297]

Finally, linkage of data using probabilistic linkage methods results in false positive as well as false negative (missed) links between individuals across data sources. The CHeReL estimates that rates of both false positive and false negative links are approximately 5/1,000 (0.5%),[195] so the impact on the results presented in the thesis is likely to be small. Some individuals with false positive links could be identified during the data cleaning process (e.g. hospital records occurring after a death record) and were excluded from the analyses, but adjustments for missed links were not possible.

8.6 Future research directions

8.6.1 Standardising definition and measurement of multimorbidity

Consensus on the preferred method of multimorbidity measurement is still developing, owing to the differences in international healthcare systems, data collections, classifications systems, populations and settings of interest, as well as the purpose of measuring

multimorbidity. These differences are impeding international comparisons[32] and diminishing the widespread utility of measures developed using data-driven algorithms which include a mixture of data sources.

An operational measure of multimorbidity developed by Calderón-Larrañaga in 2017,[15] using a clinically driven list of chronic conditions decided upon by an international and multidisciplinary team, provides a promising avenue for standardising multimorbidity measurement using administrative and clinical data. It is yet to be validated in the Australian setting. In the first instance, this work could be undertaken using the 45 and Up Study linked with hospital and PBS data (as presented in Chapter 5) and expanded to population-level data once enduring linked data sources are constructed.

Current work by researchers in Scotland aims to explore an international consensus on the definition and measurement of multimorbidity via a series of Delphi surveys.[261] A variety of participants including researchers, clinicians, care providers, policy makers and general public were invited to take part in the study over three rounds of panel discussions. I took part in all three rounds. Once the study results are available, harmonising the findings with the operational measure described above could be used to develop an agreed measure of which individual morbidities should be counted.

Following international consensus on the definition of multimorbidity, more work will be required regarding how to capture the conditions across data sources. This work can be guided by prior research,[264, 276, 278, 279] taking note of differences in data availability among countries. Where possible, incorporation of primary care databases with hospitalisation and pharmaceutical claims data is recommended in order to examine longitudinal trajectories for patients with multimorbidity. Within Australia, there is still much work to be done in extracting and standardising local EHR data for use in performance monitoring and research. However, this infrastructure is being developed, for example with NPS MedicineInsight linked records within and across databases, or development of a National Primary Health Care Data Asset. Creation of chronic disease flags across data sources, such as in the US Centers for Medicare and Medicaid Services' Chronic Condition Data Warehouse which uses diagnosis codes from Medicare claims data,[298, 299] could be implemented in Australia to further streamline research into chronic disease.

8.6.2 Future of Australian research into multimorbidity

Australia is on the cusp of a number of significant data developments which will further enable cutting edge research in multimorbidity, provided that data siloing and data availability are addressed. Longitudinal research into disease accumulation, and progression to multimorbidity, will be possible once enduring data sets become available. Furthering the work in clustering of commonly co-occurring chronic conditions[161, 170, 300, 301] by examining social determinants of health and patient care pathways will help in identifying patient subgroups with varying clusters of chronic disease, helping to develop required preventive interventions targeted to each subgroup of interest.

A 2019 scoping review[302] identified 87 documents assessing quality of care in multimorbid patients and found that the use of 'disease-oriented' models by care organisations is a major challenge for high healthcare performance. New models of integrated care, for example the Integrated Care for People with Chronic Conditions (ICPCC) model developed by NSW Health Integrated Care strategy, aim to develop and enhance relationships between health services and primary care.[303] Identifying the target cohort for the ICPCC, individuals with one or more chronic diseases who are at increased risk of hospitalisation, can be guided by the work proposed in section 8.5.1. Identification of the cohort should be driven by a combination of data sources, with the inclusion of EHR data wherever possible.

The lack of availability of person-centred outcomes in administrative data is being addressed in NSW by state-wide rollout of the Patients Reported Measures (PRM) program, which captures patient reported measures about needs and expectations at the point of care via electronic patient surveys.[304] In NSW, the newly operational Health Outcomes and Patient Experience (HOPE) system will capture electronic data and feed it into integrated and linked datasets, helping to guide individual-, service- and system-level decision making.[305] These datasets are pivotal to advancing the much-needed work on evaluating the impacts of multimorbidity and frailty on multiple facets of patient health.[306]

The planned integration of new data sources, including clinical quality registries and EHRs, provides another exciting avenue for furthering health research in Australia. The newly developed National Clinical Quality Registry and Virtual Registry Strategy 2020-2030[127] aims to integrate clinical quality outcomes data with heath and non-health datasets, to drive improvements in patient outcomes, and value and quality of care. The inclusion of these data will help fill the gaps in detailed clinical information in administrative data sources.

A new era of health research in Australia is coming. New and exciting developments in data capture and integration to support a focus on patient-centred care have the potential to better the outcomes of patients across the health care system. Researchers and analysts are ready to embrace the data deluge and help develop solutions to improve the health of the Australian population. The future of health research is looking promising, and the people who benefit the most will be patients, including those with complex care needs, such as those with multimorbidity.

8.7 Conclusions

Australian studies of multimorbidity are impeded by the lack of researcher access to data, data silos and limited information contained within the data that are available. These hindrances point to the need for linkage over time and across sectors to understand longitudinal patterns of morbidity and outcomes, examples of which are presented in this thesis. The research presented here highlights the benefits of the use of linked data in Australian multimorbidity research in three ways. First, it underlines the need for incorporation of chronic disease information from multiple databases, including inpatient, and claims-based data to accurately capture the extent of chronic disease and to identify people with multimorbidity. Second, it emphasises the need to examine complexities in the interplay between drivers of adverse outcomes – including multimorbidity, frailty and clinical assessment of a patient's overall health – in identifying patients with increased risk of complications and informing future hospital resource planning. And third, it demonstrates the value of integrating new data sources, such as clinical registries with linked administrative data for improving risk adjustment of hospital performance measures, with potentially much wider applications in health outcomes research and program evaluation. With a policy focus on patient-centred care, and burgeoning new sources of clinical data including registries and EHRs, the importance of cross-sectoral and cross-jurisdictional data linkage has never been greater. Availability and use of these data will be crucial for bettering patient outcomes and experience and providing an evidence base to support service providers and health system planners in (re)designing care to benefit the Australian population.

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Appendix 1. Australian studies on multimorbidity

PubMed search: (Multimorbid*(Title/Abstract)) AND (Australia*(Title/Abstract)) from 1996 to January 2021

Table 1 List of Australian studies on multimorbidity

Table 2 List of Australian studies on multimorbidity in the context of index disease

Table 3 Outcomes studied in Australian publications on multimorbidity

Table 1 List of Australian studies on multimorbidity, PubMed search, 1996 – 2021

First author, year	Sample N	Study setting	Age	Linked data?	Chronic condition		Data source					
					Measurement	N conditions	Medical records	Trial, RCT	Survey	Cohort	Hospital, ED	MBS	PBS
Quantitative studies													
Arnold-Reed 2018	4,285	Primary care	All	No	Diagnosis (CIRS)		Yes						
Barker 2018	17	Tertiary care	≥ 18	No	Diagnosis: CIRS(G), (FCI), (MULTIPleS), (DUSOI)	MM patients only already	Yes						
Brett 2013	7,247	Primary care	All	No	Diagnosis (CIRS)	14	Yes						
Brett 2014	7,170	Primary care	All	No	Diagnosis (CIRS)	14	Yes						
Britt 2008	9,156	Primary care	All	No	Diagnosis (CIRS)	14			BEACH				
Carpenter 2015	4,574	General population	≥ 50	No	Self-report	11			NSA				
González-Chica 2017	2,912	General population	≥ 20	No	Self-report	17			South Australian Omnibus Survey				
Gunn 2012	7,620	Primary care	≥ 18	No	Self-report	12			GP attendee survey				
Ha 2020	229,964	General population	≥ 45	Yes	Rx-Risk-V	22				45 and Up	Yes	Yes	Yes
Harrison 2014	8,707	Primary care	All	No	Diagnosis: CIRS, ICPD-2 chapter, ICD-10 chapter				BEACH				

Appendix 1: Australian studies on multimorbidity

First author, year	Sample N	Study setting	Age	Linked data?	Chronic condition		Data source					
					Measurement	N conditions	Medical records	Trial, RCT	Survey	Cohort	Hospital, ED	MBS	PBS
Harrison 2016	8,707	Primary care	All	No	Diagnosis: ICPC-2-chapter, diagnosis (GP)	28			BEACH				
Harrison 2017	43,501	Primary care	All	No	ICPC-2 chapter				BEACH				
Held 2016	1,464	General population	≥ 70, men	No	Self-report	17				CHAMP			
Holden 2011	78,000	General population	≥ 18	No	Self-report	28			WORC				
Ishida 2020	Varied	General population	≥ 15	No	Self-report	11				HILDA			
Islam 2015	2,540	General population	≥ 50	No	Self-report	12			NSA				
Islam 2014	4,574	General population	≥ 50	No	Self-report	11			NSA				
Jackson 2015	4,865	General population	≥ 45, women	No	Self-report	31				ALSWH			
Jackson 2016	4,896	General population	≥ 45, women	No	Self-report	31				ALSWH			
Jackson 2015	7,270	General population	≥ 45, women	No	Self-report	31				ALSWH			
John 2020	616	Primary care	≥ 40	No	Diagnosis (GP)	6		Yes					
John 2020	636	Primary care	≥ 40	No	Diagnosis (GP)	6		Yes					

Appendix 1: Australian studies on multimorbidity

First author, year	Sample N	Study setting	Age	Linked data?	Chronic condition		Data source						
					Measurement	N conditions	Medical records	Trial, RCT	Survey	Cohort	Hospital, ED	MBS	PBS
Jowsey 2013	2,540	General population	≥ 50	No	Self-report	12			NSA				
Lind 2020	9,436	Tertiary care	≥ 65	No	EHR free text, ATC codes	60	Yes						
McRae 2013	4,574	General population	≥ 50	No	Self-report	11							
Ng 2020	2,039	General population	38-85, men	Yes	Self-report	8				FAMAS		Yes	
Ofori-Asenso 2018	Varied	General population	≥ 65	No	Rx-Risk-V	22							Yes
Ruel 2014	1,854	General population	≥ 18	No	Self-report	8				NWAHS			
Shang 2020	53,867	General population	≥ 45	Yes	MBS, PBS	11				45 and Up		Yes	Yes
Sharpe 2017	1,281	Primary care	≥ 65	No	Self-report	13		Yes					
Shi 2015	36,663	General population	≥ 16	No	Self-report	9			South Australian Monitoring and Surveillance System				
Sum 2020	6,382	General population	≥ 50	No	Self-report	12				HILDA			
Thiruchelvam 2020	10,334	General population	77-96	Yes	Self-report	11				ALSWH			Yes

Appendix 1: Australian studies on multimorbidity

First author, year	Sample N	Study setting	Age	Linked data?	Chronic condition		Data source					
					Measurement	N conditions	Medical records	Trial, RCT	Survey	Cohort	Hospital, ED	MBS	PBS
Thompson 2018	696	General population	≥ 65	No	Self-report	Unclear				NWAHS			
Tyack 2018	351	Tertiary care	≥ 18	No	Self-report	21		Yes					
Westley-Wise 2020	38,156	Tertiary care	≥ 15	Yes	Diagnoses	19					Yes		
Wister 2016	5,532	General population	≥ 45	No	Self-report	7				HILDA			
Xia 2020	67,474	Primary care	≥ 65	Yes	Free text, MBS data	13	Yes				Yes		
Xu 2018	13,714	General population	45-50	No	Self-report	3				HILDA			
Tooth 2008	10,434	General population	73-78, women	No	Self-report	19				ALSWH			
Tyack 2016	351	Tertiary care	≥ 18	No	Self-report	25		Yes					
Wang 2017	8,841	General population	≥ 16	No	Self-report	9			Australian National Survey of mental health and Wellbeing				

ASLWH – Australian Longitudinal Study on Women's Health, BEACH – Bettering the Evaluation and Care of Health, CHAMP – *Concor*d Health and Ageing in Men Project, EMR – electronic medical record, FAMAS – Florey Adelaide Male Ageing Study, HILDA – Household, Income and Labour Dynamics in Australia, MM – multimorbidity, NSA – National Seniors Australia, PBS – Pharmaceutical Benefits Scheme , MBS – Medicare Benefits Schedule, NWAHS - North West Adelaide Longitudinal Health Study, , WORC – Australian Work Outcomes Research Cost-benefit

Table 1 List of Australian studies on multimorbidity, PubMed search, 1996 – 2021, *cont.*

First author, year	Sample N	Study setting/data source
Qualitative studies		
Jeon 2012	40 members of National Seniors Australia	General population (Semi-structured interview)
Jones 2018	13 GPs and registrars from Aboriginal Health Care service	Primary care (semi-structured interview)
Mc Namara 2017	26 healthcare professionals from metropolitan and rural Victoria and South Australia	Primary care (semi-structured interview)
Peat 2020	29 health care providers of care coordination in Melbourne	Primary care (semi-structured interview)
Reviews		
Aspin 2010	46 policy documents	
Caughey 2008	25 studies on MM prevalence	
Chandraratne 2018	56 policies, guidelines (international)	Primary care
Damarell 2021	10 clinical practice guidelines	Primary care
Ng 2018	41 studies	
O'Connell 2018	8 frameworks (international)	
Rosbach 2017	9 studies on burden of MM	
Walker 2015	88 studies	
Young 2015	13 guidelines	
Young 2016	16 care plans	

Appendix 1: Australian studies on multimorbidity

Table 2. List of Australian studies on multimorbidity in the context of index disease, 1996 – 2021

Index condition	Author (year)	Study setting
Acquired brain injury	Jackson (2020)	Primary health care
Acute coronary syndrome	Ofori-Asenso (2019)	Tertiary care
Alzheimer's	Eshetie (2019)	Primary health care
Atherothrombotic disease	Hussain (2018)	Tertiary care
Atrial fibrillation	Nishtala (2016)	Residential aged care
Cancer	Ng (2018), Ng (2020)	General population
Cardiovascular disorders	Price (2014)	Primary health care
Chronic kidney disease	Lo (2016), Venuthurupalli (2019)	Tertiary care
Depression	Morgan (2015), Stanners (2012), Xu (2019)	Primary health care, General population
Diabetes (T2)	Chiang (2020)	Primary health care
Heart failure	Caughey (2019), Taylor (2017), Wiley (2018)	DVA, primary health service, tertiary care
HIV	Dharan (2020), Edmiston (2015)	Primary health care
Hypertension	John (2020)	Primary health care
Intellectual disability	Hussain (2020)	General population
Musculoskeletal conditions	Lowe (2015), Lowe (2016), Lowe (2017)	General population
Psychosis	Charlson (2021)	Primary health care

Appendix 1: Australian studies on multimorbidity

Table 3. Outcomes studies in Australian publications on multimorbidity

Outcome	Author (year)	Sample size range	Chronic disease ascertainment	Outcome measurement
Depressive symptoms	Gunn (2012), Sharpe (2017)	1,281 - 7,620	Self-report	Self-report
Disease burden	Tyack (2018)	351	Self-report	Self-report
Frailty	Held (2016), Thompson (2018)	696 - 1,464	Self-report	Self-report
Functional ability	Barker (2018), Jackson (2015), Wister (2016), Tooth (2008)	16 - 10,434	Self-report	Self-report
Health related Quality of life	Barker (2018), González-Chica (2017), Ishida (2020), John (2020), Tooth(2008), Tyack (2016), Wang (2017)	16 - 17,529	Self-report	Self-report
Health service use	Ishida (2020), Ng (2020)*, Sum (2020), Wister (2016), Xia (2020)*, Tooth (2008)	2,039 - 67,474	Majority self-report, 1 with EMR	Self-report, MBS, ED data
Incident multimorbidity	Jackson (2015), Shang (2020)*, Xu (2018)	4,865 - 53,867	Majority self-report, 1 with PBS/MBS	Self-report, PBS data
Life satisfaction	Wister (2016)	5,532	Self-report	Self-report
Loneliness	Wister (2016)	5,532	Self-report	Self-report
Medication dispensation	Thiruchelvam (2020)*	10,334	Self-report	PBS data
Mobility restriction	Wister (2016)	5,532	Self-report	Self-report
Mortality	Tooth (2008)*	10,434	Self-report	Death data

* Used linked data

Table 3. Outcomes studies in Australian publications on multimorbidity, *cont.*

Outcome	Author (year)	Sample size range	Chronic disease ascertainment	Outcome measurement
Out-of-pocket medical expenses	Carpenter (2015), McRae (2013)	4,574	Self-report	Self-report
Patient self management	John (2020)	636	Unknown	Self-report
Perceived health	Wister (2016)	5,532	Self-report	Self-report
Potentially avoidable hospitalisations	Ha (2020)*	229,964	PBS data	Hospital data
Readmission	Westley-Wise (2020)*	38,156	Hospital diagnoses	Hospital data
Time spent on health related activities	Islam (2015), Jowsey (2013)	2,540	Self-report	Self-report
Work productivity	Ishida (2020)	13,284 - 17,529	Self-report	Self-report

* Used linked data, ED – Emergency Department, EMR – Electronic Medical Record, PBS – Pharmaceutical Benefits Scheme , MBS – Medicare Benefits Schedule

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Appendix 1: Australian studies on multimorbidity

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Appendix 2. 45 and Up Study questionnaire

THE 45 AND UP STUDY
Research to improve health and wellbeing

45 and Up Study Questionnaire for Women

The *45 and Up Study* relies on the willingness of people in New South Wales to share information about their lives and experiences, to provide knowledge that will help people live healthy and fulfilling lives for as long as possible. Participation is completely voluntary, and you are free to withdraw from the Study at any time. To take part, please read the participant information leaflet, then complete the questionnaire and consent form and return them in the envelope provided. We very much hope you will be able to take part.

Any questions or comments? Please call the Study helpline: **1300 45 11 45** or go to **www.45andUp.org.au**

Auspiced by: the saxinstitute — Research Partnerships for Better Health

In collaboration with: The Cancer Council New South Wales; Heart Foundation; NSW Health; beyondblue; New South Wales Government; DADHC Department of Ageing, Disability & Home Care

Your answers and experiences are important to us.
To help us read your answers, please write as clearly as possible using a **BLACK** or **BLUE** pen, and be sure to complete the questionnaire as shown:

Please put a cross in the appropriate box(es) [X] Yes [ ] No
OR put numbers in the appropriate box, e.g. *21st June 1945*
2 1 / 0 6 / 1 9 4 5 age 6 2

General questions about you

1. **What is your date of birth?** day / month / year: / / 1 9
2. **What is today's date?** day / month / year: / / 2 0
3. **How tall are you without shoes?** (please give to the nearest cm or inch) ____ cm OR ____ feet ____ inches
4. **About how much do you weigh?** ____ kg OR ____ stone ____ lbs
5. **What is the highest qualification you have completed?** (please put a cross in the most appropriate box)
   - [ ] no school certificate or other qualifications
   - [ ] school or intermediate certificate (or equivalent)
   - [ ] higher school or leaving certificate (or equivalent)
   - [ ] trade/apprenticeship (e.g. hairdresser, chef)
   - [ ] certificate/diploma (e.g. child care, technician)
   - [ ] university degree or higher
6. **Are you of Aboriginal or Torres Strait Islander origin?** (you can cross more than one box)
   - [ ] No [ ] Yes, Aboriginal [ ] Yes, Torres Strait Islander
7. **In which country were you born?**
   - [ ] Australia ▶ please go to question 9
   - [ ] UK [ ] Ireland [ ] Italy [ ] China
   - [ ] Greece [ ] New Zealand [ ] Germany [ ] Lebanon
   - [ ] Philippines [ ] Netherlands [ ] Vietnam [ ] Malta
   - [ ] Poland [ ] other *(please specify)* _____
8. **What year did you first come to live in Australia for one year or more?** (e.g. 1970) ____
9. **What is your ancestry?** (please cross up to 2 boxes)
   - [ ] Australian [ ] English [ ] Irish [ ] Chinese
   - [ ] Italian [ ] Greek [ ] Scottish [ ] German
   - [ ] Lebanese [ ] Dutch [ ] Maltese [ ] Polish
   - [ ] Filipino [ ] Indian [ ] Croatian [ ] Vietnamese
   - [ ] other *(please specify)* _____
10. **Do you speak a language other than English at home?**
    - [ ] Yes [ ] No
11. **Have you ever been a regular smoker?**
    - [ ] Yes ▼ [ ] No ▶ *If No – please go to question 12*

    How old were you when you started smoking regularly? ____ years old
    Are you a regular smoker now? [ ] Yes [ ] No
    If No – how old were you when you stopped smoking regularly? ____ years old
    About how much do you/did you smoke on average each day?
    (If you are an ex-smoker, how much did you smoke on average when you smoked?)
    ____ cigarettes per day ____ pipes and cigars per day
12. **About how many alcoholic drinks do you have each week?**
    one drink = a glass of wine, middy of beer or nip of spirits
    (put "0" if you do not drink, or have less than one drink each week)
    ____ number of alcoholic drinks each week
13. **On how many days each week do you usually drink alcohol?** ____ days each week

BLFF0710

14. What best describes your current situation? (please cross one box)

☐ single ☐ married ☐ de facto/living with a partner
☐ widowed ☐ divorced ☐ separated

15. What best describes your current housing? (please cross one box)

☐ house ☐ flat, unit, apartment ☐ house on farm
☐ hostel for the aged ☐ mobile home ☐ other
☐ nursing home ☐ retirement village, self care unit

16. How many TIMES did you do each of these activities LAST WEEK?
(put "0" if you did not do this activity)

	times in the last week
Walking continuously, for at least 10 minutes *(for recreation or exercise or to get to or from places)*	☐☐
Vigorous physical activity *(that made you breathe harder or puff and pant, like jogging, cycling, aerobics, competitive tennis, but not household chores or gardening)*	☐☐
Moderate physical activity *(like gentle swimming, social tennis, vigorous gardening or work around the house)*	☐☐

17. If you add up all the time you spent doing each activity LAST WEEK, how much time did you spend ALTOGETHER doing each type of activity?
(put "0" if you did not do this activity)

	hours	minutes
Walking continuously, for at least 10 minutes *(for recreation or exercise or to get to or from places)*	☐☐ :	☐☐
Vigorous physical activity *(that made you breathe harder or puff and pant, like jogging, cycling, aerobics, competitive tennis, but not household chores or gardening)*	☐☐ :	☐☐
Moderate physical activity *(like gentle swimming, social tennis, vigorous gardening or work around the house)*	☐☐ :	☐☐

Questions about your family

18. Have your mother, father, brother(s) or sister(s) ever had:
(blood relatives only: please put a cross in the appropriate box(es))

	mother	father	brother/ sister		mother	father	brother/ sister
heart disease	☐	☐	☐	breast cancer	☐	☐	☐
high blood pressure	☐	☐	☐	bowel cancer	☐	☐	☐
stroke	☐	☐	☐	lung cancer	☐	☐	☐
diabetes	☐	☐	☐	melanoma	☐	☐	☐
dementia/Alzheimer's	☐	☐	☐	prostate cancer		☐	☐
Parkinson's disease	☐	☐	☐	ovarian cancer	☐		☐
severe depression	☐	☐	☐	osteoporosis	☐	☐	☐
severe arthritis	☐	☐	☐	hip fracture	☐	☐	☐
do not know	☐	☐	☐				

19. How many children have you given birth to? ☐☐ children
(please include stillbirths but do not include miscarriages, please write "0" if you have not had any children)

How old were you when you gave birth to your FIRST child? ☐☐ years old

How old were you when you gave birth to your LAST child? ☐☐ years old

For how many months, in total, have you breastfed? ☐☐ months
(please add together all the time you spent breastfeeding all of your children; put "0" if you never breastfed)

Questions about your health

20. About how many hours a week are you exposed to someone else's tobacco smoke?

hours per week ☐☐ at home — hours per week ☐☐ in other places *(e.g. work, going out, cars)*

21. Have you ever used the pill or other hormonal contraceptives?
(e.g. the combined pill, mini pill, contraceptive implant or injections)

☐ Yes ▼ ☐ No

If Yes, for how long altogether have you used hormonal contraceptives? ☐☐ years
(please write '0' if you used them for less than a year in total)

If Yes, how old were you when you LAST used hormonal contraceptives? ☐☐ age
(please write your current age if you are still using them)

Which type of pill or other hormonal contraceptive did you use MOST RECENTLY?

☐ "the pill", combined pill *(e.g. Microgynon, Levlen)*
☐ progesterone-only pill ("mini pill") *(e.g. Micronor, Noriday, Microval)*
☐ Depo Provera
☐ contraceptive implant *(e.g. Implanon, Norplant)*
☐ do not know

22. Have you ever used hormone replacement therapy (HRT)?

☐ Yes ▼ ☐ No

If Yes, for how long altogether have you used HRT? ☐☐ years
(please write '0' if you used HRT for less than a year in total)

Are you currently taking HRT? ☐ Yes ☐ No

If No, at what age did you stop? ☐☐ age

23. Have you taken any medications, vitamins or supplements for most of the last 4 weeks, including HRT and the pill?

☐ Yes ▼ ☐ No

If Yes, was it:

☐ multivitamins + minerals	☐ multivitamins alone	☐ fish oil
☐ glucosamine	☐ omega 3	☐ paracetamol
☐ aspirin for the heart	☐ aspirin for other reasons	☐ Lipitor
☐ Avapro, Karvea	☐ warfarin, Coumadin	☐ Pravachol
☐ Coversyl, Coversyl Plus	☐ Lasix, frusemide	☐ Zocor, Lipex
☐ Cardizem, Vasocordol	☐ Micardis	☐ Nexium
☐ Norvasc	☐ Fosamax	☐ Somac
☐ Tritace	☐ Caltrate	☐ Losec, Acimax *omeprazole*
☐ Noten, Tenormin *atenolol*	☐ Oroxine *thyroxine*	☐ Ventolin *salbutamol*
☐ Zyloprim, Progout 300 *allopurinol*	☐ Diabex, Diaformin *metformin*	☐ Zoloft *sertraline*
☐ Cipramil *citaloprim*	☐ Efexor *venlafaxine*	

please list any other regular medications or supplements here

24. Has a doctor EVER told you that you have:
(If YES, please cross the box and give your age when the condition was first found)

	Yes	Age when condition was first found
skin cancer (not melanoma)	☐	☐☐ age
melanoma	☐	☐☐ age
breast cancer	☐	☐☐ age
other cancer	☐	☐☐ age
type of cancer *(please describe)*		
heart disease	☐	☐☐ age
type of heart disease *(please describe)*		
high blood pressure – when pregnant	☐	☐☐ age
high blood pressure – when not pregnant	☐	☐☐ age
stroke	☐	☐☐ age
diabetes	☐	☐☐ age
blood clot (thrombosis)	☐	☐☐ age
asthma	☐	☐☐ age
hayfever	☐	☐☐ age
depression	☐	☐☐ age
anxiety	☐	☐☐ age
Parkinson's disease	☐	☐☐ age
none of these	☐	

25. In the last month have you been treated for:
(If YES, please cross the box and give your age when the treatment started)

	Yes	Age started treatment
cancer	☐	☐☐ age
heart attack or angina	☐	☐☐ age
other heart disease	☐	☐☐ age
high blood pressure	☐	☐☐ age
high blood cholesterol	☐	☐☐ age
blood clotting problems	☐	☐☐ age
asthma	☐	☐☐ age
osteoarthritis	☐	☐☐ age
thyroid problems	☐	☐☐ age
osteoporosis or low bone density	☐	☐☐ age
depression	☐	☐☐ age
anxiety	☐	☐☐ age
none of these	☐	

26. Are you NOW suffering from any other important illness?
☐ Yes ▼ ☐ No

Please describe this illness and its treatment

27. Do you regularly need help with daily tasks because of long-term illness or disability?
(e.g. personal care, getting around, preparing meals)
☐ Yes ☐ No

28. Does your health now LIMIT YOU in any of the following activities?

	yes, limited a lot	**yes**, limited a little	**no**, not limited at all
VIGOROUS activities *(e.g. running, strenuous sports)*	☐	☐	☐
MODERATE activities *(e.g. pushing a vacuum cleaner, playing golf)*	☐	☐	☐
lifting or carrying shopping	☐	☐	☐
climbing several flights of stairs	☐	☐	☐
climbing one flight of stairs	☐	☐	☐
walking one kilometre	☐	☐	☐
walking half a kilometre	☐	☐	☐
walking 100 metres	☐	☐	☐
bending, kneeling or stooping	☐	☐	☐
bathing or dressing yourself	☐	☐	☐

29. Have you ever had any of the following operations?
(If YES, please cross the box and give your age when you had the operation; give your age at the **most recent operation** if you have had more than one)

	Yes	Age when had operation
removal of skin cancer	☐	☐☐ age
hysterectomy	☐	☐☐ age
both ovaries removed	☐	☐☐ age
sterilisation (tubes tied)	☐	☐☐ age
repair of prolapsed womb, bladder or bowel	☐	☐☐ age
knee replacement	☐	☐☐ age
hip replacement	☐	☐☐ age
gallbladder removed	☐	☐☐ age
heart or coronary bypass surgery *(include stents and balloons)*	☐	☐☐ age

other *(please describe any other operations you have had in the last 10 years, with your age when you had them)*

30. Do you regularly care for a sick or disabled family member or friend?

☐ Yes ▼ ☐ No

If Yes, about how much time each week do you usually spend caring for this person?

☐ full time OR ☐☐ hours/wk

31. In general, how would you rate your:

	excellent	very good	good	fair	poor
overall health?	☐	☐	☐	☐	☐
quality of life?	☐	☐	☐	☐	☐
eyesight? *(with glasses or contact lenses, if you wear them)*	☐	☐	☐	☐	☐
memory?	☐	☐	☐	☐	☐
teeth and gums?	☐	☐	☐	☐	☐

32. Do you feel you have a hearing loss? ☐ Yes ☐ No

33. How many of your own teeth do you have left?

☐ None – all of my teeth are missing ☐ 1-9 teeth left
☐ 10-19 teeth left ☐ 20 or more teeth left

34. During the past 12 months, how many times have you fallen to the floor or ground? (put "0" if you haven't fallen in this time)

☐☐ times

35. Have you had a broken/fractured bone in the last 5 years?

☐ Yes ▼ ☐ No

If Yes, which bones were broken?

☐ wrist ☐ arm ☐ hip ☐ ankle
☐ rib ☐ finger/toe ☐ other _____

How old were you when it happened? (give age at most recent fracture if more than one) ☐☐ years old

36. About how many times a week are you usually troubled by leaking urine?

☐ never ☐ once a week or less ☐ every day
☐ 2-3 times ☐ 4-6 times

37. Have you been through menopause?

☐ No
☐ Not sure *(because hysterectomy, taking HRT, etc.)*
☐ My periods have become irregular
☐ Yes – How old were you when you went through menopause? ☐☐ years old

38. Have you ever been for a breast screening mammogram?

☐ Yes ▼ ☐ No

If Yes, what year did you have your last mammogram? (e.g. 2005) ☐☐☐☐

How many times have you been for breast screening altogether? ☐☐ times

39. Have you ever been screened for colorectal (bowel) cancer?

☐ Yes ▼ ☐ No

If Yes, please indicate which test(s) you had:

☐ faecal occult blood test *(test for blood in the stool/faeces)*
☐ sigmoidoscopy *(a tube is used to examine the lower bowel: this is usually done in a doctor's office without pain relief)*
☐ colonoscopy *(a long tube is used to examine the whole large bowel; you would usually have to have an enema or drink large amounts of special liquid to prepare the bowel for this)*

What year did you have the most recent one of these tests? (e.g. 2005) ☐☐☐☐

Questions about your diet

40. About how many times each week do you eat:
(please count all meals and snacks. put '0' if never eaten or eaten less than once a week)

	number of times eaten each week
beef, lamb or pork	☐☐
chicken, turkey or duck	☐☐
processed meat *(include bacon, sausages, salami, devon, burgers, etc)*	☐☐
fish or seafood	☐☐
cheese	☐☐

41. About how many of the following do you usually eat:

slices or pieces of brown/wholemeal bread each week *(also include multigrain, rye bread, etc.)* ☐☐

bowls of breakfast cereal each week ☐☐

If you eat breakfast cereal is it usually: (please cross)

☐ bran cereal *(allbran, branflakes, etc.)* ☐ muesli
☐ biscuit cereal *(weetbix, shredded wheat, etc.)* ☐ other *(cornflakes, rice bubbles,etc.)*
☐ oat cereal *(porridge, etc.)*

42. Which type of milk do you mostly have?

☐ whole milk ☐ reduced fat milk ☐ skim milk
☐ soy milk ☐ other milk ☐ I don't drink milk

43. About how many serves of vegetables do you usually eat each day? A serve is half a cup of cooked vegetables or one cup of salad (please include potatoes and put "0" if less than one a day)

☐☐ number of serves of cooked vegetables each day
☐☐ number of serves of raw vegetables each day (e.g. salad)
☐ I don't eat vegetables

44. About how many serves of fruit or glasses of fruit juice do you usually have each day? A serve is 1 medium piece or 2 small pieces or 1 cup of diced or canned fruit pieces (put "0" if you eat less than one serve a day)

☐☐ number of serves of fruit each day
☐☐ number of glasses of fruit juice each day
☐ I don't eat fruit

45. Please put a cross in the box if you NEVER eat:

☐ red meat ☐ chicken/poultry ☐ pork/ham ☐ dairy products
☐ any meat ☐ eggs ☐ sugar ☐ wheat products
☐ fish ☐ seafood ☐ cream ☐ cheese

Questions about time and work

46. What is your usual yearly HOUSEHOLD income before tax, from all sources? (please include benefits, pensions, superannuation, etc)

☐ less than $5,000 per year ☐ $30,000-$39,999 per year
☐ $5,000-$9,999 per year ☐ $40,000-$49,999 per year
☐ $10,000-$19,999 per year ☐ $50,000-$69,999 per year
☐ $20,000-$29,999 per year ☐ $70,000 or more per year
☐ I would rather not answer this question

47. What is your current work status? (you can cross more than one box)

- ☐ in full time paid work
- ☐ in part time paid work
- ☐ completely retired/pensioner
- ☐ partially retired
- ☐ disabled/sick
- ☐ other
- ☐ self-employed
- ☐ doing unpaid work
- ☐ studying
- ☐ looking after home/family
- ☐ unemployed

48. If you are partially or completely retired, how old were you when you retired? ☐☐ years old

Why did you retire? (you can cross more than one box)

- ☐ reached usual retirement age
- ☐ to care for family member/friend
- ☐ made redundant
- ☐ other
- ☐ lifestyle reasons
- ☐ ill health
- ☐ could not find a job

49. About how many HOURS each WEEK do you usually spend doing the following? (please put "0" if you do not spend any time doing it)

hours per week ☐☐ paid work

hours per week ☐☐ voluntary/unpaid work

50. Which of the following do you have? (excluding Medicare)

- ☐ Private health insurance – with extras
- ☐ Private health insurance – without extras
- ☐ Department of Veterans' Affairs white or gold card
- ☐ Health care concession card
- ☐ none of these

51. What best describes the colour of the skin on the inside of your upper arm, that is your skin colour without any tanning?

- ☐ very fair
- ☐ fair
- ☐ light olive
- ☐ dark olive
- ☐ brown
- ☐ black

52. What would happen if your skin was repeatedly exposed to bright sunlight during summer without any protection? Would it:

- ☐ Get very tanned?
- ☐ Get moderately tanned?
- ☐ Get mildly or occasionally tanned?
- ☐ Never tan, or only get freckled?

53. About how many hours a DAY would you usually spend outdoors on a weekday and on the weekend?

hours per day ☐☐ weekday

hours per day ☐☐ weekend

54. About how many HOURS in each 24 hour DAY do you usually spend doing the following?
(please put "0" if you do not spend any time doing it)

hours per day		hours per day	
☐☐	sleeping (including at night & naps)	☐☐	sitting
☐☐	watching television or using a computer	☐☐	standing

55. How many TIMES in the LAST WEEK did you:
(please put "0" if you did not spend any time doing it)

	times in the last week
spend time with friends or family who do not live with you?	☐☐
talk to someone (friends, relatives or others) on the telephone?	☐☐
go to meetings of social clubs, religious groups or other groups you belong to?	☐☐

56. How many people outside your home, but within one hour of travel, do you feel you can depend on or feel very close to? ☐☐ people

57. During the past 4 weeks, about how often did you feel:

	none of the time	a little of the time	some of the time	most of the time	all of the time
tired out for no good reason?	☐	☐	☐	☐	☐
nervous?	☐	☐	☐	☐	☐
so nervous that nothing could calm you down?	☐	☐	☐	☐	☐
hopeless?	☐	☐	☐	☐	☐
restless or fidgety?	☐	☐	☐	☐	☐
so restless that you could not sit still?	☐	☐	☐	☐	☐
depressed?	☐	☐	☐	☐	☐
that everything was an effort?	☐	☐	☐	☐	☐
so sad that nothing could cheer you up?	☐	☐	☐	☐	☐
worthless?	☐	☐	☐	☐	☐

58. During the past 4 weeks, have you had any of the following problems with your work or daily activities because of any emotional problems (such as being depressed or anxious)?

cut down on the amount of time you spent on work or other activities	☐ Yes	☐ No
achieved less than you would have liked to	☐ Yes	☐ No
did work or other activities less carefully than usual	☐ Yes	☐ No

Thank you very much for filling in the questionnaire
DON'T FORGET TO SIGN THE CONSENT FORM OVERLEAF

Are your name and address correct on the front of this questionnaire? ☐ Yes ☐ No

If INCORRECT, give details below.

Surname:

Given name(s):

Postal address:

Town or Suburb:

State or Territory: Postcode:

Consent form

THE 45 AND UP STUDY
Research to improve health and wellbeing

The *45 and Up Study* relies on the willingness of people in New South Wales to share information about their lives and experiences and to have their health followed over time. By signing this form you are agreeing to take part in the *45 and Up Study* and for the Study team to follow your health over time. Participation is completely voluntary, and you are free to ask questions or to withdraw from the Study at any time, by calling the Study helpline on 1300 45 11 45. More information on the Study can be found at www.45andup.org.au

I agree to have my health followed over time through:

the 45 and Up Study team following health and other records relating to me, including NSW hospital records, cancer records, death records and other health-related records, as outlined in the Study leaflet: *The 45 and Up Study: Information for participants*;

Medicare Australia releasing to the 45 and Up Study my enrolment details, including Medicare number, and information concerning services provided to me under Medicare, the Department of Veterans' Affairs, the Pharmaceutical Benefits Scheme and the Repatriation Pharmaceutical Benefits Scheme, including past information, until the end of the Study or for the duration of my involvement in the Study;

being contacted in the future to provide information on changes to my health and lifestyle. I may also be asked to provide further information including questionnaire responses or biological samples; my participation in any of these would be completely voluntary.

I give my consent on the understanding that:

my information will only be used for the purposes outlined in the Study leaflet entitled *The 45 and Up Study: Information for participants*, of which I have a copy;

my information will be kept strictly confidential and will be used for health research only;

reports and publications from the Study will be based on de-identified information and will not identify any individual taking part;

my participation in this Study is entirely voluntary and my consent will continue to be valid following death or disablement unless withdrawn by my next of kin or other person responsible. I am free to withdraw from the Study at any time by calling the **Study helpline on 1300 45 11 45;**

my decision on whether or not to take part in the Study or in any additional research will not disadvantage me or affect my future health care in any way.

I have been provided with information about the 45 and Up Study including how it will gather, store, use and disclose information about me, in the Study leaflet. I have been given an opportunity to ask questions and have been fully informed about the Study.

Name (Print): _____

Signature: _____ Date today: day ☐☐ / month ☐☐ / 2 0 ☐☐

Extra contact details

It would be very helpful and reduce Study costs if we could contact you in future by email. If you are happy for us to do this, please write your email address here:

Email address: _____

Sometimes we find that people have moved when we try to contact them again. It would be very helpful if you could give us your mobile phone number and/or the contact details of someone close to you (such as a relative or friend) who would be happy for us to contact them if we are unable to reach you. We would only get in touch with that person if we were unable to contact you directly and we would need to tell them our reason for contacting you. Please leave this section blank if you do not wish to provide these extra contact details.

Your home phone number: ( ) _____ Your mobile phone number: _____

Full name of contact person: _____

Phone number of contact person: ( ) _____

If you have any questions about the Study, please ring the Study helpline on **1300 45 11 45**.
You can also write to or send your questionnaire (no stamp required) directly to:

Associate Professor Emily Banks, Scientific Director,
The 45 and Up Study, Reply paid 5289, Sydney NSW 2001.

Thank you very much for taking part

Appendix 3. Supplementary materials from Chapter 4 publication

Supplementary Table 1. Agreement measures between self-report and hospital data, index and lookback admissions, large public hospitals in New South Wales, Australia (n=82)

Supplementary Table 2. Adjusted ORs for patient-level variables from the multilevel logistic regression with random intercept for hospital of admission, all public and private hospitals in New South Wales, Australia (n=313)

Supplementary Table 3. Adjusted ORs for hospital-level variables from the multilevel logistic regression with random intercept for hospital of admission, all public and private hospitals in New South Wales, Australia (n=313)

Supplementary Table 1. Agreement measures between self-report and hospital data, index and lookback admissions, large public hospitals in New South Wales, Australia (n=82)

Morbidities	Index admission						Lookback admissions					
	45 and Up Yes:		45 and Up No:		Kappa		45 and Up Yes:		45 and Up No:		Kappa	
	APDC yes	APDC no	APDC yes	APDC no	%	95% CI	APDC yes	APDC no	APDC yes	APDC no	%	95% CI
Hypertension	3,061	4,803	983	7,634	**28.1**	(26.6-29.6)	3,829	4,035	1,339	7,278	**33.7**	(32.2-35.1)
Heart disease	2,306	2,455	1,309	10,411	**40.1**	(38.5-41.8)	2,910	1,851	1,710	10,010	**46.9**	(45.4-48.5)
Diabetes	2,168	661	214	13,438	**80.1**	(78.8-81.4)	2,355	474	289	13,363	**83.3**	(82.1-84.4)
Stroke	414	1,210	213	14,644	**33.1**	(29.8-36.4)	563	1,061	311	14,546	**41**	(38.0-44.0)
Smoking	820	507	468	14,686	**59.5**	(57.0-62.0)	948	379	692	14,462	**60.4**	(58.1-62.7)
Obesity	265	3,857	61	12,298	**8.6**	(6.1-11.1)	414	3,708	114	12,245	**12.9**	(10.4-15.3)
Hypertension + heart disease	799	1,878	893	12,911	**27.4**	(25.0-29.9)	1,159	1,518	1,327	12,477	**34.7**	(32.5-36.9)
Hypertension + diabetes	1,129	670	518	14,164	**61.5**	(59.4-63.6)	1,317	482	662	14,020	**65.8**	(63.9-67.7)
Hypertension + stroke	160	825	145	15,351	**22.6**	(17.9-27.3)	238	747	237	15,259	**29.9**	(25.6-34.1)
Hypertension + smoking	106	399	135	15,841	**27**	(20.9-33.1)	154	351	237	15,739	**32.6**	(27.2-37.9)
Hypertension + obesity	157	2,291	62	13,971	**9.6**	(6.2-13.0)	251	2,197	117	13,916	**14.5**	(11.3-17.7)
Heart disease + diabetes	452	686	293	15,050	**45**	(41.7-48.3)	620	518	442	14,901	**53.2**	(50.4-56.1)
Heart disease + stroke	61	641	93	15,686	**12.9**	(6.8-19.1)	107	595	171	15,608	**19.9**	(14.4-25.4)
Heart disease + smoking	65	209	163	16,044	**24.8**	(17.2-32.3)	98	176	280	15,927	**28.7**	(22.2-35.1)
Heart disease + obesity	63	1,145	62	15,211	**8.2**	(3.2-13.2)	117	1,091	119	15,154	**14.1**	(9.5-18.8)
Diabetes + stroke	66	374	38	16,003	**23.5**	(16.2-30.8)	110	330	69	15,972	**34.5**	(28.2-40.9)
Diabetes + smoking	107	112	83	16,179	**51.7**	(45.0-58.5)	130	89	132	16,130	**53.4**	(47.3-59.5)
Diabetes + obesity	150	994	39	15,298	**20.9**	(16.3-25.6)	229	915	76	15,261	**29.5**	(25.3-33.8)
Stroke + smoking	13	106	23	16,339	**16.5**	(2.1-30.8)	19	100	41	16,321	**20.8**	(7.8-33.9)
Stroke + obesity	4	368	7	16,102	**2**	(0.0-11.8)	9	363	13	16,096	**4.3**	(0.0-13.9)
Smoking + obesity	17	292	18	16,154	**9.5**	(0.0-19.5)	25	284	29	16,143	**13.3**	(3.8-22.8)

[a] ICD-10-AM codes: hypertension (I10-I15, R03.0), heart disease (I20-I25, I26-I28, I30-I52), diabetes (E10-E14), smoking (F17.2, Z72.0), obesity (E66)

Supplementary Table 2. Adjusted ORs[a] for patient-level variables from the multilevel logistic regression with random intercept for hospital of admission, all public and private hospitals in New South Wales, Australia (n=313)

Patient characteristics	Hypertension (N = 15,279)		Diabetes (N = 4,794)		Heart disease (N = 8,307)		Stroke (N = 2,480)		Smoking (N = 2,099)		Obesity (N = 8,162)	
	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]
Sex												
Female	1		1		1		1		1		1	
Male	1.28	(1.18,1.38)	1.37	(1.19,1.58)	1.30	(1.17,1.44)	1.13	(0.91,1.40)	1.14	(0.94,1.40)	0.85	(0.70,1.04)
Age												
45-59	1		1		1		1		1		1	
60-79	1.27	(1.15,1.41)	0.97	(0.81,1.16)	0.94	(0.82,1.09)	1.08	(0.78,1.52)	0.80	(0.65,0.99)	0.57	(0.47,0.70)
80+	1.32	(1.16,1.49)	1.00	(0.80,1.25)	1.01	(0.86,1.19)	1.02	(0.72,1.46)	0.48	(0.31,0.74)	0.14	(0.08,0.26)
Education												
None	1		1		1		1		1		1	
Trade	0.90	(0.79,1.03)	0.93	(0.73,1.18)	0.80	(0.68,0.94)	1.08	(0.76,1.54)	0.67	(0.48,0.94)	1.42	(1.01,2.02)
School certificate	0.96	(0.86,1.07)	1.00	(0.82,1.23)	0.90	(0.78,1.05)	1.22	(0.90,1.66)	0.87	(0.66,1.16)	1.04	(0.77,1.41)
HSC	0.99	(0.85,1.15)	0.89	(0.68,1.17)	0.91	(0.75,1.11)	2.23	(1.51,3.30)	0.53	(0.37,0.76)	1.24	(0.84,1.83)
Diploma	0.96	(0.84,1.09)	0.90	(0.72,1.14)	0.87	(0.74,1.03)	1.08	(0.75,1.56)	1.00	(0.73,1.37)	1.15	(0.83,1.59)
University	0.85	(0.74,0.98)	0.90	(0.70,1.16)	0.72	(0.60,0.86)	1.23	(0.83,1.81)	0.54	(0.37,0.80)	1.25	(0.88,1.79)
County of birth												
Australia	1		1		1		1		1		1	
Overseas	1.00	(0.91,1.09)	0.95	(0.81,1.11)	1.10	(0.98,1.23)	1.19	(0.94,1.51)	1.17	(0.92,1.48)	0.89	(0.69,1.14)
Functional limitation												
No limitation	1		1		1		1		1		1	
Mild	1.07	(0.91,1.25)	0.91	(0.68,1.23)	1.02	(0.82,1.28)	0.82	(0.48,1.42)	0.92	(0.65,1.30)	1.07	(0.72,1.60)
Moderate	1.23	(1.07,1.42)	1.14	(0.87,1.50)	0.92	(0.75,1.13)	0.68	(0.42,1.11)	0.79	(0.57,1.09)	1.06	(0.73,1.53)
Severe	1.53	(1.33,1.76)	1.54	(1.18,2.01)	0.97	(0.79,1.19)	0.84	(0.53,1.33)	0.82	(0.60,1.12)	2.27	(1.59,3.24)
Income												

<20,000	1		1		1		1		1		1	
20-50,000	0.89	(0.81,0.99)	0.95	(0.79,1.14)	1.03	(0.91,1.17)	1.14	(0.87,1.49)	1.17	(0.90,1.53)	0.76	(0.57,1.00)
50-70,000	0.89	(0.75,1.05)	0.87	(0.64,1.19)	1.11	(0.89,1.38)	1.16	(0.68,1.99)	1.37	(0.93,2.02)	0.89	(0.60,1.30)
>70,000	0.86	(0.74,1.00)	1.03	(0.77,1.38)	1.24	(1.02,1.50)	1.07	(0.63,1.82)	0.95	(0.66,1.36)	1.15	(0.83,1.59)
Not disclosed	1.00	(0.90,1.12)	1.04	(0.86,1.27)	1.14	(0.99,1.31)	1.18	(0.89,1.56)	1.36	(1.02,1.80)	1.07	(0.81,1.41)
Admission type[c]												
Surgical	1		1		1		1		1		1	
Other	1.45	(1.23,1.72)	1.01	(0.72,1.42)	2.34	(1.91,2.87)	0.47	(0.16,1.37)	0.69	(0.41,1.14)	0.62	(0.36,1.09)
Medical	1.14	(1.03,1.27)	0.66	(0.55,0.80)	0.97	(0.84,1.11)	4.36	(3.02,6.29)	0.50	(0.38,0.65)	0.64	(0.50,0.84)
Emergency status[c]												
Emergency	1		1		1		1		1		1	
Planned	0.63	(0.56,0.71)	0.64	(0.52,0.77)	0.42	(0.36,0.49)	0.65	(0.48,0.88)	0.86	(0.65,1.13)	0.58	(0.44,0.78)
Other	0.96	(0.80,1.15)	0.98	(0.72,1.33)	1.02	(0.81,1.28)	1.19	(0.80,1.76)	1.03	(0.65,1.62)	0.80	(0.50,1.28)

[a] Odds ratio of a hospital record of a condition, among those that self-reported having a condition. Adjusted for age, sex, income, education, country of birth and functional limitation

[b] Confidence interval

[c] Model included both admission type and emergency status together with other listed patient characteristics

Supplementary Table 3. Adjusted ORs[a] for hospital-level variables from the multilevel logistic regression with random intercept for hospital of admission**,** all public and private hospitals in New South Wales, Australia (n=313)

Hospital characteristics	Hypertension (N = 15,279)		Diabetes (N = 4,794)		Heart disease (N = 8,307)		Stroke (N = 2,480)		Smoking (N = 2,099)		Obesity (N = 8,162)	
	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]	OR[a]	(95%CI)[b]
Hospital type[c]												
Public	1		1		1		1		1		1	
Private	0.49	(0.38,0.63)	0.98	(0.78,1.23)	0.35	(0.26,0.47)	0.31	(0.22,0.43)	0.99	(0.72,1.35)	0.91	(0.64,1.31)
Hospital remoteness[c]												
Major city	1		1		1		1		1		1	
Inner regional	0.89	(0.64,1.23)	0.86	(0.67,1.11)	1.01	(0.70,1.47)	1.29	(0.91,1.83)	1.04	(0.75,1.45)	0.91	(0.60,1.38)
Outer regional	0.75	(0.55,1.02)	0.69	(0.52,0.91)	0.97	(0.67,1.41)	1.09	(0.72,1.67)	0.82	(0.57,1.18)	0.91	(0.58,1.44)
Remote/very remote	1.05	(0.57,1.94)	0.53	(0.28,1.00)	1.70	(0.81,3.59)	0.66	(0.22,1.98)	0.33	(0.15,0.71)	0.52	(0.16,1.68)
Hospital size[c]												
Principal referral	1		1		1		1		1		1	
Major	0.59	(0.34,1.01)	0.89	(0.62,1.27)	0.76	(0.44,1.34)	0.93	(0.58,1.47)	1.03	(0.66,1.61)	1.10	(0.59,2.05)
District	0.45	(0.27,0.76)	0.83	(0.58,1.19)	0.45	(0.26,0.78)	0.97	(0.60,1.55)	0.73	(0.47,1.15)	1.02	(0.55,1.91)
Community	0.41	(0.25,0.68)	0.61	(0.43,0.87)	0.35	(0.20,0.59)	0.57	(0.35,0.94)	0.89	(0.56,1.39)	0.88	(0.47,1.62)
Other	0.52	(0.30,0.89)	0.44	(0.29,0.68)	0.35	(0.19,0.65)	1.19	(0.66,2.14)	0.39	(0.22,0.68)	1.22	(0.59,2.53)
Depth of coding[c]												
1 - least comprehensive	0.17	(0.11,0.27)	0.26	(0.17,0.40)	0.09	(0.04,0.17)	0.38	(0.17,0.82)	0.22	(0.12,0.42)	0.28	(0.12,0.65)
2	0.29	(0.22,0.38)	0.66	(0.52,0.85)	0.41	(0.29,0.56)	0.31	(0.21,0.48)	0.74	(0.52,1.06)	0.59	(0.38,0.92)
3	0.58	(0.45,0.76)	0.85	(0.66,1.08)	0.75	(0.55,1.02)	0.66	(0.48,0.91)	0.89	(0.65,1.24)	0.65	(0.43,0.99)
4 - most comprehensive	1		1		1		1		1		1	

[a] Odds ratio of a hospital record of a condition, among those that self-reported having a condition. Adjusted for age, sex, income, education, country of birth and functional limitation

[b] Confidence interval

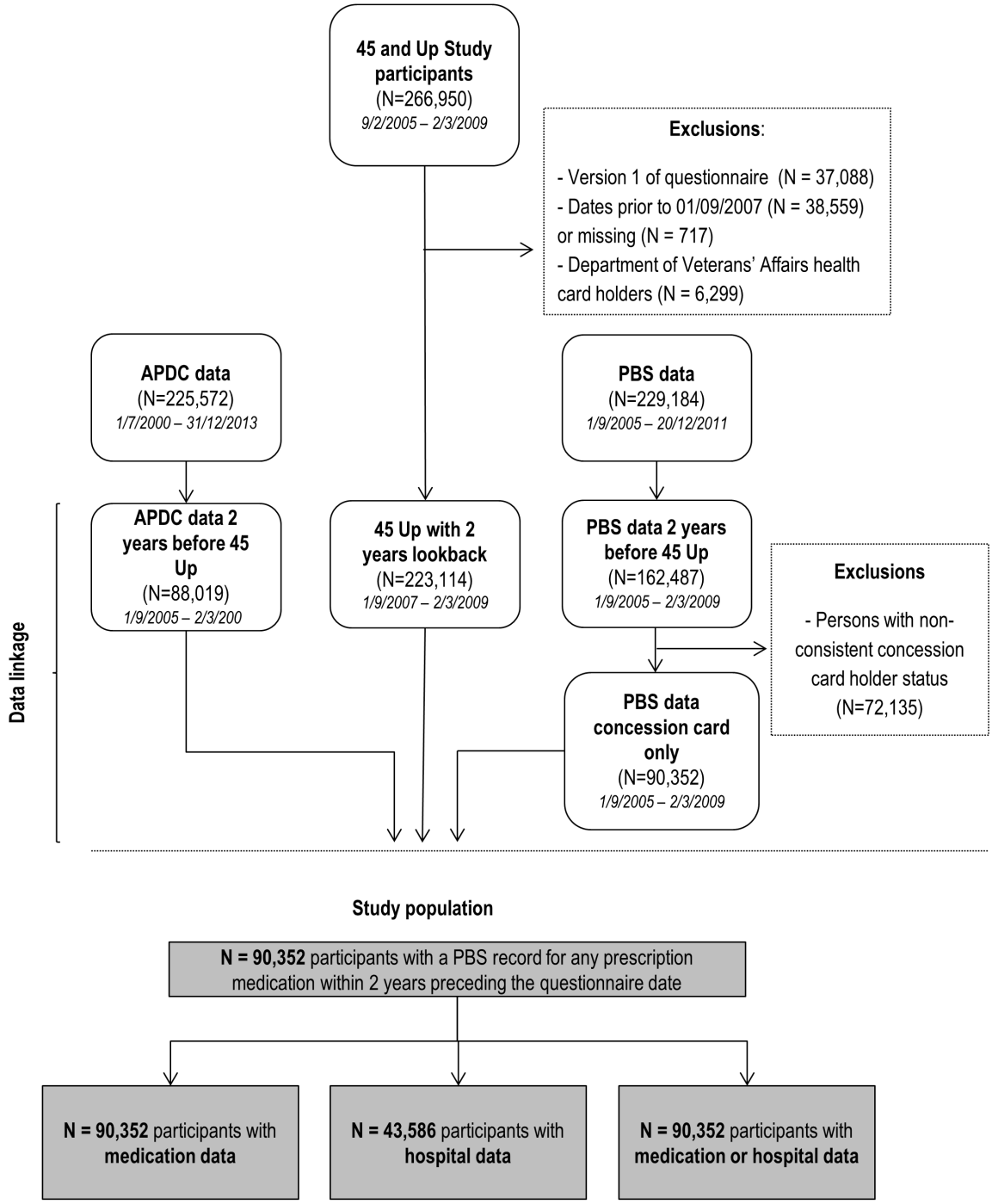
[c] Hospital-level covariates added one at a time, separately

Appendix 4. Supplementary materials from Chapter 5 publication

S1 Fig. Construction of study population. APDC – Admitted Patient Data Collection, PBS – Pharmaceutical Benefits Scheme

S1 Table. Morbidities and ICD-10-AM and ATC codes

S1 Fig. Construction of study population. APDC – Admitted Patient Data Collection, PBS – Pharmaceutical Benefits Scheme



S1 Table. Morbidities and ICD-10-AM and ATC codes

Chronic condition	Medication data		Hospital data	
	ATC codes	**Based on**	**ICD-10-AM codes**	**Based on**
Cancer	L01AA01, L01AA02, L01AA03, L01AA06, L01AB01, L01AX03, L01BA01, L01BA03, L01BA04, L01BB02, L01BB03, L01BB04, L01BC01, L01BC02, L01BC05, L01BC06, L01CA01, L01CA02, L01CA04, L01CB01, L01CD01, L01CD02, L01DB01, L01DB07, L01DC01, L01XA01, L01XA02, L01XC02, L01XC03, L01XE01, L01XE06, L01XE07, L01XX05, L01XX19, L01XX32	Rx-Risk-V [35]	C00-C97 (excluding C44)	Charlson Index (32), modified to exclude skin cancer
Heart disease	C01DA02, C01DA08, C01DA14, C07AA02, C07AA03, C07AA05, C07AB02, C07AB03, C07AB07, C07AB12, C07AG01, C07AG02, C08CA01, C08CA02, C08CA05, C08CA13, C08DA01, C08DB01	Olesen et al. [44] At least two classes: α adrenergic blockers, non-loop diuretics, vasodilators, β blockers, calcium channel blockers, renin-antiotensin system inhibitors	I20-I52	
Hypertension	C02AB01, C02AB02, C02AC01, C02AC05, C02DB02, C02DC01, C02KX01, C02KX02, C02KX03, C03AA03, C03BA04, C03BA11, C03DA01, C03DA04, C03DB01, C03EA01, C09BA02, C09BA04, C09BA06, C09BA09, C09BB02, C09BB05, C09BB10, C09DA02, C09DA04, C09DA06, C09DA07, C09DA08	Rx-Risk-V [35]	I10, I11-I13, I15	Elixhauser Index (34)
Stroke	B01AA03, B01AB01, B01AB04, B01AC04, B01AC05, B01AC06, B01AC07, B01AC30	Lix et al. [37]	I60-I64	
Diabetes	A10AB01, A10AB02, A10AB04, A10AB05, A10AB06, A10AC01, A10AC02, A10AD, A10AD01, A10AD04, A10AE04, A10AE05, A10B, A10BA02, A10BB01, A10BB07, A10BB09, A10BB12, A10BD02, A10BD03, A10BF01, A10BG02, A10BG03, A10BH01	Rx-Risk-V [35]	E10-E14	Elixhauser Index (34) Charlson Index (32)
Asthma	R03AC02, R03AC03, R03AC12, R03AC13, R03AK06, R03BA01, R03BA02, R03BA05, R03BB01, R03BC01, R03BC03, R03CC02, R03CC03, R03DA04, R03DC03	Lix et al. [37]	J45, J46	
Depression	N06AB03, N06AB04, N06AB05, N06AB06, N06AB08, N06AB10,	Rx-Risk-V [35], modified	F32, F33	

	N06AF03, N06AF04, N06AG02, N06AX03, N06AX11, N06AX16, N06AX18, N06AX21	(excluding tricyclic antidepressants)	
Parkinson's	N04AA01, N04AA02, N04AC01, N04BA02, N04BA03, N04BB01, N04BC01, N04BC02, N04BC05, N04BC06, N04BD01, N04BX02	Rx-Risk-V [35]	G20, F02.3

Appendix 5. Supplementary materials from Chapter 6

Table 1. Baseline characteristics by multimorbidity and frailty at index hospital stay (2010 – 2012)

	Total	Frailty risk category			Multimorbidity		
		Low risk	*Elevated risk*	*p-value*	*No*	*Yes*	*p-value*
	N = 257,535	*n = 119,737*	*n = 137,798*		*n = 133,067*	*n = 124,468*	
Sex, n (%)							
Male	110,125 (42.8)	53,950 (45.1)	56,175 (40.8)	<0.01	51,497 (38.7)	58,628 (47.1)	<0.01
Female	147,410 (57.2)	65,787 (54.9)	81,623 (59.2)		81,570 (61.3)	65,840 (52.9)	
Median age [IQR]							
	83.3 [79.2 – 87.7]	81.9 [78.3 – 86.2]	84.6 [80.3 – 88.8]	<0.01	83.0 [79.0 – 87.5]	83.6 [79.5 – 87.9]	<0.01
Age, n (%)							
75-79	76,233 (29.6)	43,885 (36.7)	32,348 (23.5)	<0.01	41,512 (31.2)	34,721 (27.9)	<0.01
80-84	78,766 (30.6)	38,690 (32.3)	40,076 (29.1)		40,731 (30.6)	38,035 (30.6)	
85-89	63,894 (24.8)	24,922 (20.8)	38,972 (28.3)		31,183 (23.4)	32,711 (26.3)	
90+	38,642 (15)	12,240 (10.2)	26,402 (19.2)		19,641 (14.8)	19,001 (15.3)	
Aboriginal and Torres Strait Islander status, n (%)							
Non-Aboriginal	256,100 (99.4)	119,029 (99.4)	137,071 (99.5)	0.03	132,406 (99.5)	123,694 (99.4)	<0.01
Aboriginal	1,435 (0.6)	708 (0.6)	727 (0.5)		661 (0.5)	774 (0.6)	
Socioeconomic status quartiles, n(%)							
Most disadvantaged	66,279 (25.7)	32,486 (27.1)	33,793 (24.5)	<0.01	34,104 (25.6)	32,175 (25.9)	<0.01
2	54,192 (21)	26,133 (21.8)	28,059 (20.4)		28,487 (21.4)	25,705 (20.7)	
3	46,441 (18)	21,637 (18.1)	24,804 (18)		24,421 (18.4)	22,020 (17.7)	
4	47,350 (18.4)	21,112 (17.6)	26,238 (19)		24,380 (18.3)	22,970 (18.5)	
Most advantaged	40,911 (15.9)	17,585 (14.7)	23,326 (16.9)		20,591 (15.5)	20,320 (16.3)	
Missing	2,362 (0.9)	784 (0.7)	1,578 (1.1)		1,084 (0.8)	1,278 (1)	
Admission type, n (%)							
Medical	224,949 (87.3)	104,200 (87)	120,749 (87.6)	<0.01	116,611 (87.6)	108,338 (87)	<0.01
Surgical	23,339 (9.1)	10,030 (8.4)	13,309 (9.7)		12,394 (9.3)	10,945 (8.8)	
Other	9,247 (3.6)	5,507 (4.6)	3,740 (2.7)		4,062 (3.1)	5,185 (4.2)	
Number of prior admissions over 2 years, excluding index admission, n (%)							
0	84,775 (32.9)	54,543 (45.6)	30,232 (21.9)	<0.01	60,599 (45.5)	24,176 (19.4)	<0.01
1	62,827 (24.4)	30,525 (25.5)	32,302 (23.4)		34,803 (26.2)	28,024 (22.5)	
2 or more	109,933 (42.7)	34,669 (29)	75,264 (54.6)		37,665 (28.3)	72,268 (58.1)	
HFRS category							
Low risk	119,737 (46.5)	119,737 (100)			81,788 (61.5)	37,949 (30.5)	<0.01
Elevated risk	137,798 (53.5)		137,798 (100)		51,279 (38.5)	86,519 (69.5)	
Multimorbidity							
No	133,067 (51.7)	81,788 (68.3)	51,279 (37.2)	<0.01	133,067 (100)		
Yes	124,468 (48.3)	37,949 (31.7)	86,519 (62.8)			124,486 (100)	
Median HFRS [IQR]							
	5.5 [1.9 – 12.0]	1.8 [0 – 3.2]	11.3 [7.6 – 17.6]	<0.01	3.4 [1.1 – 7.5]	9.1 [3.9 – 16.7]	<0.01
Median number of chronic conditions [IQR]							
	1 [0 – 3]	1 [0 – 2]	2 [1 – 4]	<0.01	0 [0 – 1]	3 [2 – 4]	<0.01

HFRS – Hospital frailty risk score, IQR – interquartile range

Table 2. Additive and multiplicative Interaction effects of multimorbidity and frailty risk on adverse patient outcomes, surgical cohort

Mortality within 30-days post discharge	**Non-frail**			**Frail**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	% outcome	aRR (95% CI)
No multimorbidity	171	2.4	1	379	7.1	2.75 (2.29 – 3.31)
Multimorbidity	229	7.6	3.21 (2.63 – 3.93)	1,339	16.9	7.24 (6.14 – 8.54)
*Measure of effect modification on additive scale: RERI (95% CI) = 2.27 (1.58 – 2.96) **						
Measure of effect modification on multiplicative scale: ratio of RR= *0.82 (0.65 – 1.03), p-value =0.086*						

Prolonged LOS	**Non-frail**			**Frail**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	% outcome	aRR (95% CI)
No multimorbidity	2,735	39.0	1	3,921	73.0	1.76 (1.67 – 1.85)
Multimorbidity	1,239	41.2	1.05 (0.98 – 1.12)	6,088	76.7	1.91 (1.82 – 2.00)
*Measure of effect modification on additive scale: RERI (95% CI) =0.10 (0.00 – 0.20)**						
Measure of effect modification on multiplicative scale: ratio of RR=*1.03 (0.96 – 1.12) , p-value =0.391*						

Readmission within 30-days post discharge	**Non-frail**			**Frail**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	% outcome	aRR (95% CI)
No multimorbidity	281	4.1	1	356	7.0	1.64 (1.40 – 1.92)
Multimorbidity	263	9.4	1.99 (1.68 – 2.36)	863	13.2	2.63 (2.28 – 3.03)
Measure of effect modification on additive scale: RERI (95% CI) =0.01 (-0.36 – 0.37)						
Measure of effect modification on multiplicative scale: ratio of RR= *0.81 (0.66 – 1.00), p-value =0.046**						

* Significant at 5% level. [a] Significance of an interaction on an additive scale is denoted where RERI is different from 0, and on the multiplicative scale if ratio of RR is different from 1.

Table 3. Additive and multiplicative Interaction effects of multimorbidity and frailty risk on adverse patient outcomes, medical cohort

Mortality within 30-days post discharge	**Non-frail**			**Frail**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	% outcome	aRR (95% CI)
No multimorbidity	3,572	5.0	1	4,227	9.4	1.84 (1.76 – 2.92)
Multimorbidity	3,596	11.1	2.35 (2.25 – 2.47)	14,267	18.8	4.00 (3.84 – 4.16)
*Measure of effect modification on additive scale: RERI (95% CI) = 0.81 (0.69 – 0.93)**						
Measure of effect modification on multiplicative scale: ratio of RR*= 0.92 (0.87 – 0.98), p-value =0.008**						

Prolonged LOS	**Non-frail**			**Frail**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	% outcome	aRR (95% CI)
No multimorbidity	6,726	9.4	1	11,819	26.3	2.80 (2.73 – 2.88)
Multimorbidity	4,642	14.3	1.68 (1.62 – 1.73)	24,096	31.8	3.70 (3.61 – 3.80)
*Measure of effect modification on additive scale: RERI (95% CI) =0.23 (0.15 – 0.30)**						
Measure of effect modification on multiplicative scale: ratio of RR*= 0.79 (0.76 – 0.82), p-value <0.001**						

Readmission within 30-days post discharge	**Non-frail**			**Frail**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	% outcome	aRR (95% CI)
No multimorbidity	4,996	7.2	1	4,272	10.2	1.23 (1.18 – 1.28)
Multimorbidity	3,461	11.7	1.36 (1.31 – 1.43)	10,835	16.8	1.72 (1.66 – 1.79)
*Measure of effect modification on additive scale: RERI (95% CI) =0.13 (0.06 – 0.20)**						
Measure of effect modification on multiplicative scale: ratio of RR*=1.03 (0.97 – 1.09), p-value =0.367*						

* Significant at 5% level. Significance of an interaction on an additive scale is denoted where RERI is different from 0, and on the multiplicative scale if ratio of RR is different from 1.

Table 4: List of ICD-10 codes for multimorbidity ascertainment, and prevalence within cohort and by multimorbidity and frailty risk status

Name	ICD-10-AM Codes	Source	Cohort		% within group			
			N	%	Neither	Frail only	MM only	Both
AIDS/HIV	B20.x-B22.x, B24.x	Elixhauser	23	0.0	<5	<5	26	70
Alcohol abuse*	F10.x*, E52.x, G62.1, I42.6, K29.2, K70.0, K70.3, K70.9, T51.x, Z50.2*, Z71.4, Z72.1	Elixhauser	4,028	1.6	8	11	13	68
Asthma and bronchiectasis	J45.x, J46.x, J47.x	New	5,063	2.0	14	5	27	54
Cancer	C00.x -C26.x, C30.x -C34.x, C37.x -C41.x, C43.x, C45.x -C58.x, C60.x -C76.x, C77.x -C80.x, C81.x-C85.x, C88.x, C96.x, C90.0, C90.2, C97.x	Elixhauser (combining: 'Lymphoma', 'Metastatic cancer' and 'Solid tumor without metastasis')	24,036	9.3	18	13	18	51
Cardiac arrhythmias, including atrial fibrillation*	I44.1-I44.3, I45.6, I45.9, I47.x-I49.x, R00.0*, R00.1*, R00.8*, T82.1, Z45.0, Z95.0	Elixhauser Index	69,883	27.1	11	6	24	59
Cerebrovascular disease, including stroke/TIA (CVD)*	G45.x*, G46.x, H34.0, I60.x-I69.x*	Charlson Index	27,497	10.7	7	4	16	74
Chronic IHD	I25.x	New	26,050	10.1	4	1	40	56
Chronic kidney disease*	N00.x–N08.x, N11.x, N12.x, N14.x–N16.x, N18.x*, N19.x*, N25.x–N28.x*, N39.1*, N39.2*, Q60.x–Q63.x, T82.4, T86.1, V56.0, V56.8, V42.0, V45.1, Z49.x, Z94.0, Z99.2*	New –expanded version of renal disease in both Charlson and Elixhauser indices	29,169	11.3	2	5	13	80

Chronic pulmonary disease	I27.8, I27.9, J40.x -J44.x, J60.x -J67.x, J68.4, J70.1, J70.3	Elixhauser (excluding J45-J47, now in a new category: 'Asthma or bronchiectasis')	24,227	9.4	14	6	25	56
Coagulopathy	D65.x-D68.x, D69.1, D69.3-D69.6	Elixhauser	11,079	4.3	5	4	17	74
Congestive heart failure	I09.9, I11.0, I13.0, I13.2, I42.0, I42.5-I42.9, I43.x, I50.x, P29.0	Elixhauser (excluding I25.5, included in the new category CIHD above)	37,770	14.7	4	3	26	68
Dementia*	F00.x-F03.x*, F05.1*, G30.X*, G31.1*	Charlson	33,319	12.9	4	25	5	66
Depression*	F20.4, F31.3-F31.5, F32.x*, F33.x, F34.1, F41.2, F43.2	Elixhauser	7,585	2.9	6	7	11	77
Diabetes	E10.x- E14.x	Elixhauser (combining uncomplicated and complicated diabetes)	32,374	12.6	8	5	25	63
Drug abuse	F11.x -F16.x, F18.x, F19.x, Z71.5, Z72.2	Elixhauser	603	0.2	2	7	9	81
Epilepsy*	G40.x*, G41.x	New	1,523	0.6	5	9	9	77
Hypertension	I10.x -I13.x, I15.x	Elixhauser (combining uncomplicated and complicated hypertension)	77,940	30.3	6	4	27	63
Hypothyroidism	E00.x -E03.x, E89.0	Elixhauser	3,007	1.2	3	5	17	75
Liver disease	B18.x, I85.x, I86.4, I98.2, K70.x, K71.1, K71.3-K71.5, K71.7, K72.x -K74.x, K76.0, K76.2-K76.9, Z94.4	Elixhauser	2,595	1.0	5	4	19	71
Multiple sclerosis	G35.x, G36.x, G367.x, H46.x	New	56	0.0	11	9	18	63
Myocardial infarction	I21.x, I22.x	Charlson (excluding I25.2 included in the new category CIHD above)	19,227	7.5	3	1	35	61
Parkinson's*	G20.x*, G21.x, G22.x	New	5,203	2.0	4	14	7	75

Peptic ulcer disease excluding bleeding*	K25.7, K25.9, K26.7*, K26.9*, K27.7, K27.9, K28.7, K28.9	Elixhauser Index	1,967	0.8	13	8	18	61
Peripheral vascular disorders	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9	Elixhauser Index	11,724	4.6	8	4	22	65
Psychoses	F20.x, F22.x -F25.x, F28.x, F29.x, F30.2, F31.2, F31.5	Elixhauser Index	1,493	0.6	8	7	13	71
Pulmonary circulation disorders	I26.x, I27.x, I28.0, I28.8, I28.9	Elixhauser Index	9,290	3.6	6	3	25	67
Rheumatoid arthritis / collagen vascular diseases	L94.0, L94.1, L94.3, M05.x, M06.x, M08.x, M12.0, M12.3, M30.x, M31.0-M31.3, M32.x -M35.x, M45.x, M46.1, M46.8, M46.9	Elixhauser Index	3,253	1.3	8	10	16	66
Valvular disease	A52.0, I05.x -I08.x, I09.1, I09.8, I34.x -I39.x, Q23.0-Q23.3, Z95.2-Z95.4	Elixhauser Index	11,635	4.5	3	2	29	67
Paralysis*	G04.1, G11.4, G80.1, G80.2, G81.x*, G82.x, G83.0–G83.4, G83.9	Elixhauser Index	12,086	4.7	0	1	3	95

* Overlapping ICD-10 codes with HFRS diagnoses

Table 5: List of ICD-10 codes for HFRS calculation, and prevalence within cohort and by multimorbidity and frailty risk status

ICD-10 code	Description	Cohort		% within group			
		N	%	Neither	Frail only	MM only	Both
A04	Other bacterial intestinal infections	2348	0.9	10	24	3	63
A09	Diarrhoea and gastroenteritis of presumed infectious origin	17,792	6.9	16	24	5	54
A41	Other septicaemia	13,205	5.1	5	22	3	69
B95	Streptococcus and staphylococcus as the cause of diseases classified to other chapters	17,635	6.8	6	24	3	68
B96	Other bacterial agents as the cause of diseases classified to other chapters (secondary code)	39,039	15.2	2	34	1	63
D64	Other anaemias	24,300	9.4	11	20	9	61
E05	Thyrotoxicosis [hyperthyroidism]	1,331	0.5	8	16	13	63
E16	Other disorders of pancreatic internal secretion	971	0.4	7	19	4	69
E53	Deficiency of other B group vitamins	2,778	1.1	4	30	3	63
E55	Vitamin D deficiency	4,801	1.9	4	29	3	64
E83	Disorders of mineral metabolism	10,255	4.0	7	19	7	67
E86	Volume depletion	39,117	15.2	8	28	3	62
E87	Other disorders of fluid, electrolyte and acid- base balance	40,037	15.5	6	23	5	67
F00*	Dementia in Alzheimer's disease	6,408	2.5	0	35	0	65
F01*	Vascular dementia	2,995	1.2	3	17	4	76
F03*	Unspecified dementia	22,837	8.9	5	24	5	66
F05*	Delirium, not induced by alcohol and other psychoactive substances	21,983	8.5	2	29	1	69
F10*	Mental and behavioural disorders due to use of alcohol	3,417	1.3	8	12	11	68
F32*	Depressive episode	5,986	2.3	5	7	9	78
G20*	Parkinson's disease	4,986	1.9	4	14	7	75
G30*	Alzheimer's disease	6,460	2.5	0	34	0	66
G31*	Other degenerative diseases of nervous system, not elsewhere classified	1,680	0.7	6	19	4	71
G40*	Epilepsy	1,423	0.6	5	9	9	77
G45*	Transient cerebral ischaemic attacks and related syndromes	7,682	3.0	15	6	21	58
G81*	Hemiplegia	11,292	4.4	0	1	2	97
H54	Blindness and low vision	3,197	1.2	6	24	5	66
H91	Other hearing loss	3,198	1.2	6	25	5	64
I63*	Cerebral Infarction	8,471	3.3	2	2	11	84
I67*	Other cerebrovascular diseases	1,643	0.6	2	5	6	86
I69*	Sequelae of cerebrovascular disease (secondary codes)	4,506	1.7	0	2	1	97
I95	Hypotension	38,267	14.9	8	22	7	63
J18	Pneumonia, organism unspecified	28,718	11.2	16	17	11	56
J22	Unspecified acute lower respiratory infection	15,497	6.0	15	17	11	57
J69	Pneumonitis due to solids and liquids	7,831	3.0	6	19	3	72
J96	Respiratory failure, not elsewhere classified	7,695	3.0	7	12	9	71
K26*	Duodenal ulcer	1,520	0.6	15	18	8	59
K52	Other noninfective gastroenteritis and colitis	4,109	1.6	15	20	8	57
K59	Other functional intestinal disorders	33,072	12.8	10	28	4	58

K92	Other diseases of digestive system	14,405	5.6	23	17	10	50
L03	Cellulitis	19,021	7.4	15	23	5	57
L08	Other local infections of skin and subcutaneous tissue	1,068	0.4	11	22	5	62
L89	Decubitus ulcer	12,691	4.9	3	24	2	71
L97	Ulcer of lower limb, not elsewhere classified	8,187	3.2	5	23	3	69
M15	Polyarthrosis	597	0.2	8	22	6	63
M19	Other arthrosis	4,154	1.6	8	22	7	62
M25	Other joint disorders, not elsewhere classified	9,564	3.7	12	29	4	55
M41	Scoliosis	607	0.2	11	30	3	57
M48	Spinal stenosis (secondary code only)	4,155	1.6	17	27	7	49
M79	Other soft tissue disorders, not elsewhere classified	5,069	2.0	15	22	6	57
M80	Osteoporosis with pathological fracture	21,568	8.4	20	20	12	47
M81	Osteoporosis without pathological fracture	15,348	6.0	12	21	10	56
N17	Acute renal failure	28,079	10.9	3	17	5	76
N18*	Chronic renal failure	24,658	9.6	1	4	12	83
N19*	Unspecified renal failure	3,191	1.2	2	7	11	80
N20	Calculus of kidney and ureter	1,588	0.6	30	19	9	43
N28*	Other disorders of kidney and ureter, not elsewhere classified	1,350	0.5	5	8	13	74
N39*	Other disorders of urinary system (includes urinary tract infection and urinary incontinence)	50,226	19.5	3	36	1	61
R00*	Abnormalities of heart beat	15,834	6.1	12	8	18	62
R02	Gangrene, not elsewhere classified	643	0.2	8	20	3	68
R11	Nausea and vomiting	14,826	5.8	19	22	8	51
R13	Dysphagia	15,837	6.1	7	18	4	70
R26	Abnormalities of gait and mobility	12,644	4.9	4	28	2	66
R29	Other symptoms and signs involving the nervous and musculoskeletal systems (R29·6 Tendency to fall)	18,269	7.1	2	30	1	68
R31	Unspecified haematuria	7,939	3.1	10	25	4	61
R32	Unspecified urinary incontinence	19,010	7.4	3	26	2	69
R33	Retention of urine	15,590	6.1	9	26	4	61
R40	Somnolence, stupor and coma	3,526	1.4	4	22	2	72
R41	Other symptoms and signs involving cognitive functions and awareness	20,367	7.9	4	28	2	66
R44	Other symptoms and signs involving general sensations and perceptions	1,727	0.7	5	23	3	68
R45	Symptoms and signs involving emotional state	3,690	1.4	3	21	3	73
R47	Speech disturbances, not elsewhere classified	10,193	4.0	4	7	7	82
R50	Fever of unknown origin	6,824	2.6	16	20	10	54
R54	Senility	1,373	0.5	5	30	3	62
R55	Syncope and collapse	19,639	7.6	21	25	8	47
R56	Convulsions, not elsewhere classified	2,789	1.1	9	20	3	69
R63	Symptoms and signs concerning food and fluid intake	6,732	2.6	12	23	6	60
R69	Unknown and unspecified causes of morbidity	234	0.1	20	22	5	53
R79	Other abnormal findings of blood chemistry	1,219	0.5	16	19	9	56
R94	Abnormal results of function studies	6,972	2.7	9	20	8	63
S00	Superficial injury of head	10,134	3.9	5	42	0	53
S01	Open wound of head	11,939	4.6	14	36	2	48
S06	Intracranial injury	5,133	2.0	7	39	1	53
S09	Other and unspecified injuries of head	2,606	1.0	12	33	2	54
S22	Fracture of rib(s), sternum and thoracic spine	6,206	2.4	11	35	2	52
S32	Fracture of lumbar spine and pelvis	7,682	3.0	11	40	2	47

S42	Fracture of shoulder and upper arm	4,887	1.9	13	41	1	45
S51	Open wound of forearm	5,935	2.3	11	30	2	56
S72	Fracture of femur	15,651	6.1	14	37	2	47
S80	Superficial injury of lower leg	3,937	1.5	8	37	1	54
T83	Complications of genitourinary prosthetic devices, implants and grafts	3,098	1.2	2	27	1	70
U80	Agent resistant to penicillin and related antibiotics	0	0.0	0	0	0	0
W01	Fall on same level from slipping, tripping and stumbling	25,913	10.1	23	31	3	43
W06	Fall involving bed	4,648	1.8	9	29	2	60
W10	Fall on and from stairs and steps	4,362	1.7	27	33	3	37
W18	Other fall on same level	21,710	8.4	10	35	2	53
W19	Unspecified fall	21,559	8.4	5	38	1	57
X59	Exposure to unspecified factor	5,095	2.0	12	26	3	58
Y84	Other medical procedures as the cause of abnormal reaction of the patient	10,872	4.2	8	18	10	64
Y95	Nosocomial condition	1,156	0.4	2	18	2	77
Z22	Carrier of infectious disease	3,024	1.2	5	17	3	75
Z50*	Care involving use of rehabilitation procedures	25,433	9.9	3	23	2	72
Z60	Problems related to social environment	29,613	11.5	12	29	6	52
Z73	Problems related to life-management difficulty	789	0.3	9	27	4	61
Z74	Problems related to care-provider dependency	23,475	9.1	6	27	3	65
Z75	Problems related to medical facilities and other health care	17,564	6.8	6	22	6	66
Z87	Personal history of other diseases and conditions	4,131	1.6	29	23	13	36
Z91	Personal history of risk-factors, not elsewhere classified	4,493	1.7	8	14	10	68
Z93	Artificial opening status	3,634	1.4	9	24	4	63
Z99*	Dependence on enabling machines and devices	3,198	1.2	6	17	7	70

* Overlapping ICD-10 codes with multimorbidity list

Appendix 6. Supplementary materials from Chapter 7

Figure 1. Flowchart of THA cohort construction

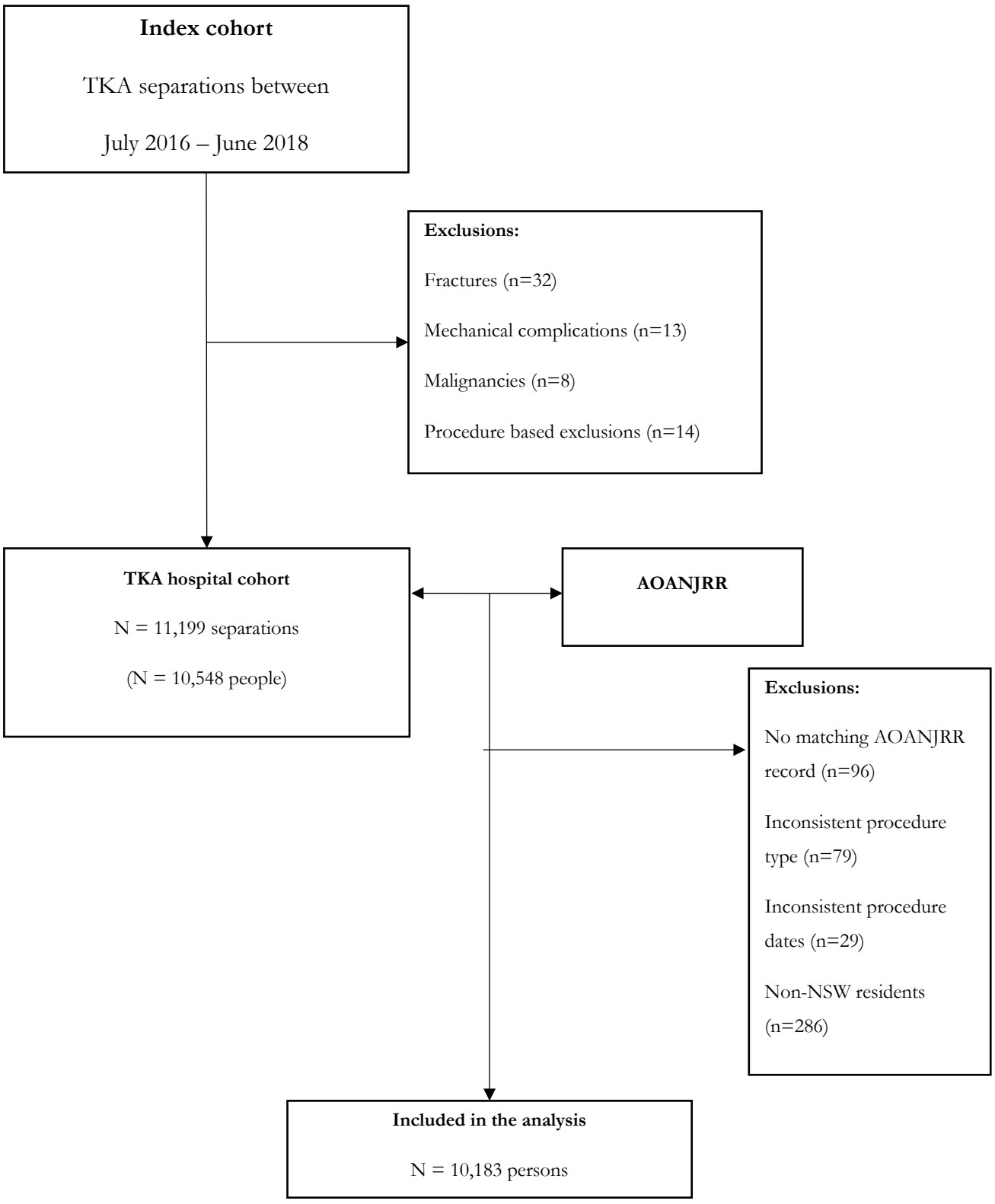


Figure 2. Flowchart of TKA cohort construction

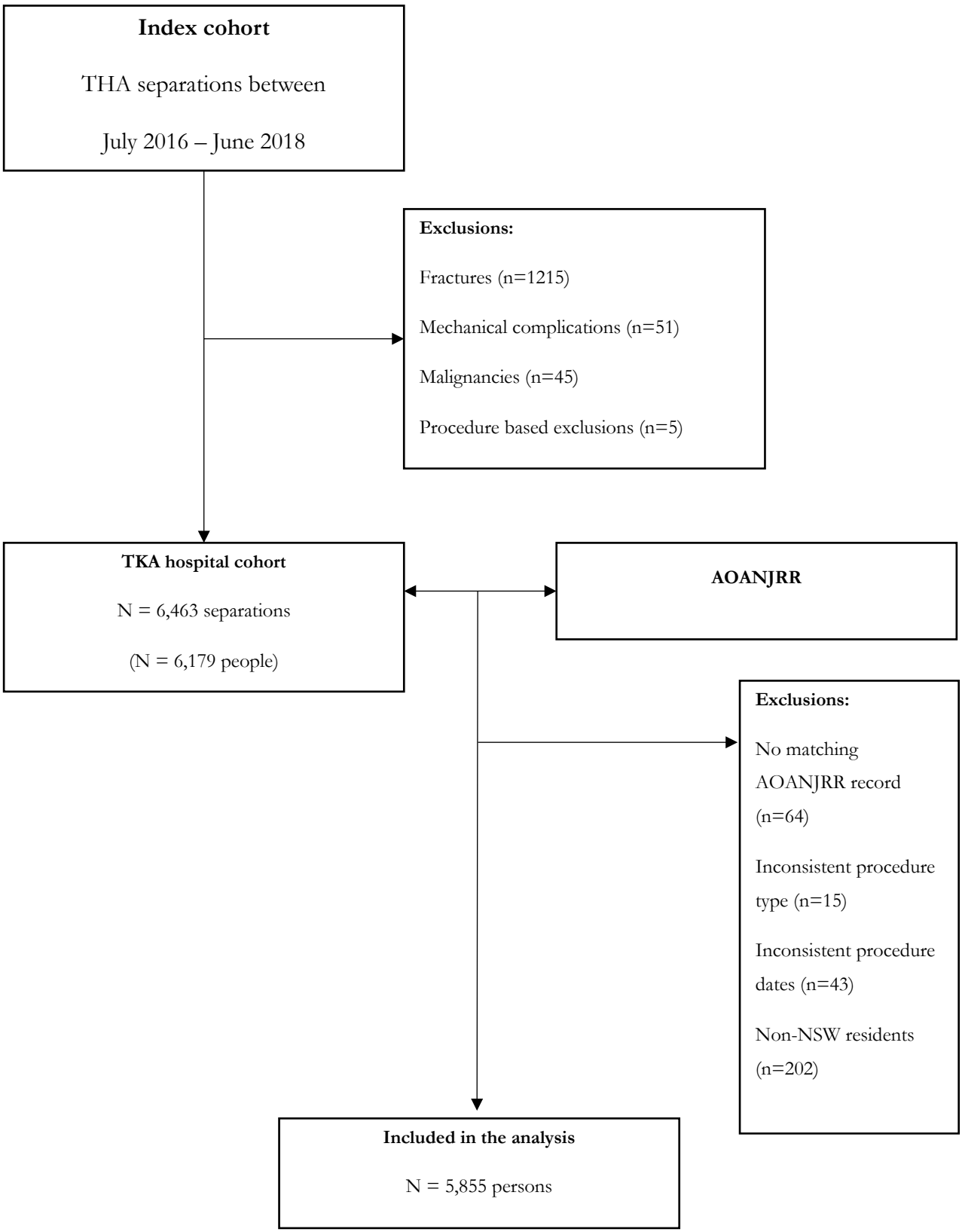


Table 1. Codes for exclusions and unplanned readmissions (ICD-10-AM)

Exclusions
• Dialysis: Z49.1, Z49.2, Z94.0, Z99.2 (ICD-10-AM diagnosis codes) • Cataract: 42698-00, 42698-01, 42698-02, 42698-03, 42698-04, 42698-05, 42702-00, 42702-01, 42702-02, 42702-03, 42702-04, 42702-05, 42702-06, 42702-07, 42702-08, 42702-09, 42702-10, 42702-11, 42716-00, 42719-00, 42719-02, 42722-00, 42731-00, 42731-01, 42734-00, 42788-00 (ACHI procedure code) • Chemotherapy: Z51.1 (ICD-10-AM diagnosis code) • Radiotherapy: Z51.0 (ICD-10-AM diagnosis code)

Unplanned readmission for TKA[a]
• Principal diagnosis code for readmission: • I2I,I26,I50,I74,M17,M23,N13,R33,S89,T81,T84,I80.1,I80.2,I97.8,J15.1,J18.0,J18.9,J95.8,L89.2, M24.6,M25.6,N39.0,S82.0,T88.7,L03.11,S72.10,S83.44,T85.78,T85.88
Unplanned readmission for THA[a]
• G46,I21,I26,I50,I74,I80,J15,L89,N13,N30,R33,S73,T84,T89,I62.1,I63.3,I97.8,J18.0,J18.9,J95.8, L03.9,M25.6,M96.8,N390,T81.1,T81.3,T81.5,T81.6,T81.8,T81.9,T85.9,T88.7, L03.11,S72.00,S72.08,T85.87,T85.88

[a] Department of Health and Human Services. Victorian Health Services Performance monitoring framework 2018–19. Melbourne: Department of Health and Human Services; 2018. Available at https://www2.health.vic.gov.au/hospitals-and-health-services/funding-performance-accountability/performance-monitoring

Table 2. Validity of ICD-10-am codes for presence of overweight/obesity

		Registry information			Hospital information	
	N	BMI ≥ 25kg/m²	BMI < 25kg/m²	No BMI recorded	Overweight/obese diagnosis code[a]	No overweight/obese diagnosis code
		n (%)	n (%)	n (%)	n (%)	n (%)
All[b]	16038	13359 (83.3)	2003 (12.5)	676 (4.2)	2301 (14.3)	13737 (85.7)
Procedure						
TKA	10183	8858 (87.0)	879 (8.6)	446 (4.4)	1681 (16.5)	8502 (83.5)
THA	5855	4501 (76.9)	1124 (19.2)	230 (3.9)	620 (10.6)	5235 (89.4)
Diagnosis code[a]						
ICD-10-AM E66	135	117 (86.7)	1 (0.7)	17 (12.6)		
Supplementary U78.1	2166	2060 (95.1)	8 (0.4)	98 (4.5)		
Gender						
Male	7239	6129 (84.7)	817 (11.3)	293 (4.0)	960 (13.3)	6279 (86.7)
Female	8799	7230 (82.2)	1186 (13.5)	383 (4.4)	1341 (15.2)	7458 (84.8)
Age						
<60	3342	2787 (83.4)	386 (11.6)	169 (5.1)	573 (17.2)	2769 (82.8)
60-64	2350	2008 (85.5)	246 (10.4)	96 (4.1)	397 (16.9)	1953 (83.1)
65-69	3032	2607 (86.0)	317 (10.5)	108 (3.6)	474 (15.6)	2558 (84.4)
70-74	3070	2613 (85.1)	338 (11.0)	119 (3.9)	454 (14.7)	2616 (88.5)
75-79	2403	1981 (82.4)	316 (13.2)	106 (4.4)	277 (11.5)	2126 (88.5)
80+	1841	1363 (74.0)	400 (21.7)	78 (4.2)	156 (6.8)	1715 (93.2)

[a] Using E66 or U78.1 codes in any of the diagnoses fields in hospital data
[b] Information from hospital data

	Metrics	
	Sensitivity	PPV
All	16.3 (15.7 - 16.9)	99.6 (99.2 - 99.8)
Procedure		
TKA	17.9 (17.1 - 18.7)	99.6 (99.1 - 99.8)
THA	13.1 (12.1 - 14.1)	99.7 (98.7 - 99.9)
Male	15.0 (14.2 - 16.0)	99.6 (98.9 - 99.8)
Female	17.4 (16.5 - 18.3)	99.6 (99.1 - 99.8)
Age		
<60	19.0 (17.5 - 20.5)	99.8 (98.7 - 100)
60-64	18.9 (17.2 - 20.7)	99.7 (98.2 - 100)
65-69	17.0 (15.6 - 18.5)	99.6 (98.2 - 100)
70-74	16.7 (15.3 - 18.2)	99.3 (97.9 - 99.8)
75-79	13.7 (12.0 - 15.3)	99.6 (97.5 - 100)
80+	8.7 (7.3 - 10.4)	99.2 (94.3 - 99.9)

Table 3. Leading reasons for readmission, by surgical type

ICD-10-AM code	Description	N (%)
	THA	
T84.5	Infection and inflammatory reaction due to internal joint prosthesis	27 (6.3)
M25.55	Pain in a joint, pelvic region and thigh	18 (4.2)
L03.13	Cellulitis of lower limb	16 (3.7)
T81.4	Wound infection following a procedure, not elsewhere classified	15 (3.5)
T84.8	Other complications of internal orthopaedic prosthetic devices, implants and grafts	14 (3.3)
M79.86	Other specified soft tissue disorders, lower leg	12 (2.8)
S73.01	Posterior dislocation of hip	9 (2.1)
I26.9	Pulmonary embolism without mention of acute cor pulmonale	7 (1.6)
K92.2	Gastrointestinal haemorrhage, unspecified	7 (1.6)
T81.0	Haemorrhage and haematoma complicating a procedure, not elsewhere classified	7 (1.6)
T84.0	Mechanical complication of internal joint prosthesis	7 (1.6)
K59.0	Constipation	6 (1.4)
M16.1	Other primary coxarthrosis	6 (1.4)
N39.0	Urinary tract infection, site not specified	6 (1.4)
T84.81	Haemorrhage and haematoma following insertion of internal orthopaedic prosthetic devices, implants and grafts	6 (1.4)
Z48.8	Other specified surgical follow-up care	6 (1.4)
I48.9	Atrial fibrillation and atrial flutter, unspecified	5 (1.2)
M79.66	Pain in limb, lower leg	5 (1.2)
R11	Nausea and vomiting	5 (1.2)
R50.9	Fever, unspecified	5 (1.2)
R60.0	Localised oedema	5 (1.2)
S73.02	Anterior dislocation of hip	5 (1.2)
Z47.8	Other specified orthopaedic follow-up care	5 (1.2)

Table 3. Leading reasons for readmission, by surgical type, *cont.*

ICD-10-AM code	Description	N (%)
	TKA	
T81.4	Wound infection following a procedure, not elsewhere classified	71 (8.5)
T84.5	Infection and inflammatory reaction due to internal joint prosthesis	61 (7.3)
M25.56	Pain in a joint, lower leg	48 (5.7)
L03.13	Cellulitis of lower limb	45 (5.4)
T84.8	Other complications of internal orthopaedic prosthetic devices, implants and grafts	30 (3.6)
K59.0	Constipation	17 (2.0)
M17.1	Other primary gonarthrosis	17 (2.0)
Z48.8	Other specified surgical follow-up care	17 (2.0)
R07.4	Chest pain, unspecified	15 (1.8)
I26.9	Pulmonary embolism without mention of acute cor pulmonale	14 (1.7)
T84.81	Haemorrhage and haematoma following insertion of internal orthopaedic prosthetic devices, implants and grafts	14 (1.7)
M25.06	Haemarthrosis, lower leg	12 (1.4)
A09.9	Gastroenteritis and colitis of unspecified origin	11 (1.3)
T81.3	Disruption of operation wound, not elsewhere classified	11 (1.3)
T81.8	Other complications of procedures, not elsewhere classified	11 (1.3)
T81.83	Pain following a procedure, not elsewhere classified	11 (1.3)
T84.83	Pain following insertion of internal orthopaedic prosthetic devices, implants and grafts	11 (1.3)
M79.66	Pain in limb, lower leg	10 (1.2)
M79.86	Other specified soft tissue disorders, lower leg	10 (1.2)
M25.46	Effusion of joint, lower leg	9 (1.1)
R06.0	Dyspnoea	9 (1.1)
I97.8	Other intraoperative and postprocedural disorders of circulatory system, not elsewhere classified	8 (1.0)
R11	Nausea and vomiting	8 (1.0)
T81.89	Other complications following a procedure, not elsewhere classified	8 (1.0)
T84.7	Infection and inflammatory reaction due to other internal orthopaedic prosthetic devices, implants and grafts	8 (1.0)
I48.9	Atrial fibrillation and atrial flutter, unspecified	7 (0.8)
I80.20	Phlebitis and thrombophlebitis of deep vessels of lower extremities, not elsewhere classified	6 (0.7)
R42	Dizziness and giddiness	6 (0.7)
R55	Syncope and collapse	6 (0.7)
Z46.6	Fitting and adjustment of urinary device	6 (0.7)
Z47.8	Other specified orthopaedic follow-up care	6 (0.7)
H81.1	Benign paroxysmal vertigo	5 (0.6)
I80.2	Phlebitis and thrombophlebitis of other deep vessels of lower extremities	5 (0.6)
K92.2	Gastrointestinal haemorrhage, unspecified	5 (0.6)
R10.1	Pain localised to upper abdomen	5 (0.6)
S89.9	Unspecified injury of lower leg	5 (0.6)
T81.0	Haemorrhage and haematoma complicating a procedure, not elsewhere classified	5 (0.6)
T84.82	Embolism and thrombosis following insertion of internal orthopaedic prosthetic devices, implants and grafts	5 (0.6)

Table 4. Regression estimates for 30-day readmissions by person and hospital effects, THA

	Single-level models				Multilevel models	
	Model 1	Model 2_a	Model 2_b	Model 2_c	Model 3_a	Model 3_c
Male	**1.26 (1.03-.54)**	1.21 (0.98-1.50)	1.21 (0.98-1.50)	1.22 (0.99-1.51)	122 (0.99-1.51)	1.23 (1.00-1.52)
Age						
<60	Reference	Reference	Reference	Reference	Reference	Reference
60 - 64	1.10 (0.75-1.63)	1.08 (0.73-1.60)	1.08 (0.73-1.61)	1.05 (0.71-1.56)	1.08 (0.73-1.60)	1.05 (0.71-1.56)
65 - 69	**1.46 (1.04-2.06)**	1.40 (0.99-1.99)	**1.42 (1.00-2.01)**	1.35 (0.95-1.92)	1.40 (0.99-1.99)	1.35 (0.95-1.93)
70 - 74	**1.78 (1.29-2.47)**	**1.71 (1.22-2.40)**	**1.75(1.24-2.45)**	**1.61 (1.15-2.27)**	**1.71 (1.22-2.40)**	**1.62 (1.15-2.28)**
75 - 79	**2.08 (1.49-2.92)**	**1.93 (1.36-2.74)**	**1.96(1.38-2.80)**	**1.79 (1.26-2.56)**	**1.93 (1.36-2.75)**	**1.80 (1.26-2.57)**
80 and over	**2.30 (1.64-3.23)**	**2.08 (1.46-2.96)**	**2.16(1.51-3.08)**	**1.90 (1.33-2.72)**	**2.07 (1.46-2.96)**	**1.90 (1.33-2.73)**
Individual Elixhauser morbidities						
CHF		1.16 (0.59-2.27)	1.11 (0.57-2.18)	1.09 (0.56-2.14)	1.15 (0.59-2.25)	1.08 (0.55-2.12)
Cardiac arrhythmia		1.30 (0.95-1.76)	1.30 (0.96-1.76)	1.25 (0.92-1.70)	1.30 (0.95-1.77)	1.25 (0.92-1.70)
Hypertension (uncomplicated)		1.07 (0.76-1.50)	1.07 (0.77-1.50)	1.05 (0.75-1.46)	1.07 (0.76-1.50)	1.04 (0.74-1.46)
Paralysis		2.24 (0.73-6.90)	2.22 (0.72-6.86)	2.08 (0.68-6.41)	2.24 (0.72-6.92)	2.08 (0.68-6.43)
Chronic pulmonary disease		**2.09 (1.29-3.40)**	**2.10 (1.29-3.42)**	**1.95 (1.20-3.18)**	**2.10 (1.29-3.42)**	**1.97 (1.21-3.21)**
Diabetes (uncomplicated)		1.20 (0.89-1.62)	1.20 (0.89-1.62)	1.17 (0.87-1.57)	1.21 (0.89-1.63)	1.17 (0.87-1.58)
Diabetes (complicated)		**1.51 (1.07-2.13**)	**1.44 (1.01-2.05)**	**1.41 (1.00-1.99)**	**1.52 (1.08-2.15)**	**1.42 (1.00-2.00)**
Renal failure		0.95 (0.52-1.75)	0.95 (0.52-1.74)	0.93 (0.51-1.69)	0.95 (0.52-1.74)	0.92 (0.50-1.68)
Liver disease		1.77 (0.94-3.35)	1.81 (0.95-3.43)	1.72 (0.91-3.25)	1.77 (0.94-3.35)	1.73 (0.91-3.26)
Lymphoma		2.39 (0.74-7.72)	2.32 (0.71-7.57)	2.27 (0.70-7.37)	2.40 (0.73-7.86)	2.33 (0.72-7.60)
Rheumatoid arthritis/collagen vascular disease		1.59 (0.73-3.43)	1.63 (0.75-3.53)	1.48 (0.68-3.20)	1.59 (0.73-3.45)	1.49 (0.69-3.23)
Coagulopathy		**2.06 (1.10-3.85)**	**2.16 (1.15-4.04)**	**1.91 (1.02-3.57)**	**2.06 (1.10-3.87)**	**1.92 (1.02-3.59)**
Weight loss anemia		1.14 (0.62-2.07)	1.27(0.69-2.35)	1.11 (0.61-2.03)	1.14 (0.62-2.08)	1.12 (0.61-2.04)
Fluid and electrolyte disorders		1.20 (0.89-1.62)	1.21 (0.89-1.63)	1.19 (0.88-1.60)	1.21 (0.89-1.63)	1.19 (0.88-1.61)
Alcohol abuse		**1.93 (1.07-3.48)**	**1.95 (1.08-3.52)**	**1.87 (1.04-3.37)**	**1.92 (1.06-3.47)**	**1.86 (1.03-3.35)**
Drug abuse		1.29 (0.49-3.38)	1.30 (0.49-3.44)	1.20 (0.46-3.15)	1.29 (0.49-3.38)	1.19 (0.45-3.13)
Body Mass Index						
Underweight			0.42 (0.10-1.89)			
Normal weight			Reference			
Overweight			1.14 (0.85-1.54)			
Obese I			1.05 (0.77-1.45)			
Obese II			1.03 (0.69-1.52)			
Obese III			1.49 (0.94-2.36)			
ASA class				**1.29 (1.07-1.55)**		**1.28 (1.06-1.55)**
Hospital-level effects						
Hospital variability (SE)					0.03 (0.03)	0.03 (0.03)
VPC					0.92%	0.84%
Discriminatory accuracy						
AUC	0.59 (0.56-0.62)	0.64 (0.62-0.67)	0.64 (0.62-0.67)	0.65 (0.62-0.68)	0.64 (0.61-0.67)	0.65 (0.63-0.68)
AUC difference		0.05[a]	0.05[a]	0.06[a]	0.00[b]	0.00[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2

Table 5. Variation in 30-day readmissions by person and hospital effects, using dichotomous multimorbidity, THA

	Single-level models			Multilevel models	
	Model 1 OR (95% CI)	Model 2_h OR (95% CI)	Model $2_{h,r}$ OR (95% CI)	Model 3_h OR (95% CI)	Model $3_{h,r}$ OR (95% CI)
Patient-level effects					
Sex					
Male	1.26 (1.03-1.54)	1.24 (1.01-1.52)	1.25 (1.02-1.53)	1.24 (1.01-1.53)	1.25 (1.02-1.54)
Age					
<60	Reference	Reference	Reference	Reference	Reference
60 - 64	1.10 (0.75-1.63)	1.08 (0.73-1.59)	1.04 (0.71-1.54)	1.08 (0.73-1.59)	1.04 (0.71-1.54)
65 - 69	1.46 (1.04-2.06)	1.40 (0.99-1.97)	1.33 (0.94-1.87)	1.40 (1.00-1.98)	1.33 (0.94-1.88)
70 - 74	1.78 (1.29-2.47)	1.67 (1.20-2.32)	1.54 (1.11-2.15)	1.68 (1.21-2.33)	1.55 (1.11-2.16)
75 - 79	2.08 (1.49-2.92)	1.88 (1.34-2.65)	1.70 (1.21-2.40)	1.89 (1.35-2.67)	1.71 (1.21-2.42)
80 and over	2.30 (1.64-3.23)	1.98 (1.40-2.79)	1.76 (1.24-2.50)	1.98 (1.41-2.80)	1.77 (1.25-2.51)
Multimorbidity †					
No		Reference	Reference	Reference	Reference
Yes		1.87 (1.49-2.34)	1.65 (1.30-2.09)	1.86 (1.49-2.34)	1.65 (1.30-2.09)
ASA class			1.39 (1.16-1.67)		1.39 (1.16-1.67)
Hospital-level effects					
Hospital-level intercept (SE)				0.03 (0.03)	0.02 (0.03)
VPC				0.78%	0.66%
Discriminatory accuracy					
AUC	0.59 (0.56-0.62)	0.62 (0.59-0.65)	0.64 (0.61-0.66)	0.62 (0.59-0.65)	0.64(0.61-0.66)
AUC difference	Reference	0.03[a]	0.05[a]	0.00[b]	0.00[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2, † Presence of two or more Elixhauser Index morbidities

Model 1: single-level model with age, sex only; Model 2_h: Model 1 and hospital data information (Elixhauser Index); Model $2_{h,r}$: Model 1 and hospital and registry information (ASA); Model 3_h: Model 2_h plus hospital-level random effect; Model $3_{h,r}$: Model $2_{h,r}$ plus hospital-level random effect. ICC: intraclass correlation coefficient, VPC: variance partition coefficient, AUC: area under the receiver operating characteristic curve; Multimorbid - ≥2 Elixhauser morbidities

Table 6. Measures of variation in 30-day readmissions by person and hospital effects, TKA

	Single-level models				Multilevel models	
	Model 1	Model 2_a	Model 2_b	Model 2_c	Model 3_a	Model 3_c
Male	1.14 (0.99-1.32)	1.10 (0.95-1.27)	1.15 (0.98-1.33)	1.10 (0.95-1.27)	1.09 (0.94-1.27)	1.13 (0.97-1.31)
Age						
<60	Reference	Reference	Reference	Reference	Reference	Reference
60 - 64	0.93 (0.71-1.22)	0.91 (0.69-1.20)	0.94 (0.71-1.23)	0.90 (0.68-1.19)	0.92 (0.69-1.21)	0.92 (0.70-1.22)
65 - 69	1.06 (0.83-1.36)	1.00 (0.78-1.29)	1.04 (0.81-1.34)	0.98 (0.76-1.26)	1.01 (0.78-1.29)	1.02 (0.79-1.31)
70 - 74	**1.33 (1.05-1.68)**	1.22 (0.96-1.56)	1.29 (1.01-1.65)	1.18 (0.92-1.50)	1.22 (0.96-1.56)	1.23 (0.96-1.58)
75 - 79	1.24 (0.96-1.60)	1.11 (0.86-1.45)	1.21 (0.92-1.57)	1.06 (0.81-1.37)	1.10 (0.85-1.43)	1.12 (0.85-1.46)
80 and over	1.29 (0.98-1.70)	1.08 (0.81-1.44)	1.20 (0.89-1.62)	1.00 (0.75-1.33)	1.06 (0.79-1.41)	1.07 (0.79-1.45)
Individual Elixhauser morbidities						
CHF		0.83 (0.47-1.47)	0.81 (0.46-1.44)	0.81 (0.46-1.43)	0.81 (0.46-1.43)	0.78 (0.44-1.39)
Cardiac arrhythmia		**1.66 (1.33-2.07)**	**1.64 (1.32-2.05)**	**1.58 (1.26-1.97)**	**1.69 (1.35-2.12)**	**1.61 (1.29-2.02)**
Valvular disease		0.97 (0.48-1.94)	0.98 (0.49-1.97)	0.94 (0.47-1.88)	0.96 (0.48-1.93)	0.94 (0.47-1.89)
Hypertension (uncomplicated)		**1.37 (1.09-1.72)**	**1.32 (1.08-1.70)**	**1.34 (1.07-1.68)**	**1.38 (1.10-1.73)**	**1.34 (1.07-1.68)**
Hypertension (complicated)		3.50 (0.73-16.82)	3.55 (0.74-17.11)	3.10 (0.64-14.95)	3.53 (0.73-17.16)	3.27 (0.67-15.97)
Chronic pulmonary disease		1.24 (0.78-1.97)	1.22 (0.77-1.94)	1.14 (0.72-1.81)	1.22 (0.77-1.94)	1.13 (0.71-1.79)
Diabetes (uncomplicated)		1.06 (0.87-1.29)	1.08 (0.88-1.31)	1.02 (0.84-1.25)	1.06 (0.87-1.29)	1.04 (0.86-1.27)
Diabetes (complicated)		**1.41 (1.13-1.75)**	**1.30 (1.04-1.62)**	**1.30 (1.04-1.61)**	**1.41 (1.13-1.75)**	1.24 (0.99-1.56)
Renal failure		1.13 (0.75-1.70)	1.14 (0.76-1.73)	1.08 (0.72-1.63)	1.12 (0.74-1.70)	1.09 (0.72-1.65)
Liver disease		1.21 (0.71-2.05)	1.25 (0.74-2.13)	1.17 (0.69-1.98)	1.19 (0.70-2.03)	1.19 (0.70-2.03)
Coagulopathy		**1.76 (1.02-3.04)**	**1.78 (1.03-3.07)**	1.61 (0.93-2.78)	1.73 (1.00-3.00)	1.62 (0.93-2.81)
Fluid and electrolyte disorders		**1.47 (1.19-1.82)**	**1.49 (1.21-1.85)**	**1.43 (1.16-1.78)**	**1.47 (1.19-1.82)**	**1.46 (1.18-1.81)**
Blood loss anemia		**2.14 (1.07-4.26)**	**2.14 (1.08-4.28)**	**2.15 (1.08-4.30)**	**2.13 (1.06-4.27)**	**2.12 (1.06-4.27)**
Deficiency anemia		1.18 (0.78-1.78)	1.19 (0.78-1.80)	1.15 (0.76-1.75)	1.16 (0.76-1.77)	1.15 (0.76-1.76)
Alcohol abuse		1.17 (0.67-2.06)	1.21 (0.69-2.13)	1.17 (0.67-2.04)	1.19 (0.68-2.10)	1.22 (0.69-2.14)
Drug abuse		**2.58 (1.27-5.22)**	**2.60 (1.25-5.28)**	**2.47 (1.22-4.98)**	**2.54 (1.25-5.16)**	**2.44 (1.20-4.95)**
Psychoses		2.06 (0.63-6.70)	2.00 (0.62-6.51)	1.91 (0.59-6.17)	2.09 (0.64-6.82)	1.94 (0.60-6.30)
Depression		1.83 (0.97-3.44)	**1.91 (1.02-3.58)**	1.83 (0.98-3.43)	1.88 (1.00-3.53)	**1.92 (1.03-3.60)**
Body Mass Index						
Underweight			1.28 (0.28-5.87)			1.18 (0.25-5.50)
Normal weight			Reference			Reference
Overweight			1.23 (0.91-1.67)			1.22 (0.90-1.65)
Obese I			1.11 (0.82-1.50)			1.07 (0.79-1.45)
Obese II			1.35 (0.98-1.86)			1.25 (0.91-1.73)
Obese III			**1.72 (1.23-2.42)**			**1.49 (1.05-2.11)**
ASA class				**1.40 (1.22-1.60)**		
Hospital-level effects						
Hospital variance (SE)					0.05 (0.03)	0.05 (0.02)
VPC					1.48%	1.42%
Discriminatory accuracy						
AUC	0.54 (0.52-0.56)	0.60 (0.58-0.62)	0.61 (0.59-0.64)	0.61 (0.59-0.63)	0.60 (0.58-.62)	0.62 (0.60-0.64)
AUC difference		0.06[a]	0.07[a]	0.07[a]	0.00[b]	0.01[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2

Table 7. Measures of variation in 30-day readmissions by person and hospital effects, using dichotomous multimorbidity, TKA

	Single-level models			Multilevel models	
	Model 1 OR (95% CI)	Model 2_h OR (95% CI)	Model $2_{h,r}$ OR (95% CI)	Model 3_h OR (95% CI)	Model $3_{h,r}$ OR (95% CI)
Patient-level effects					
Sex					
Male	1.14 (0.99-1.32)	1.12 (0.97-1.30)	1.12 (0.96-1.29)	1.12 (0.96-1.29)	1.11 (0.96-1.29)
Age					
<60	Reference	Reference	Reference	Reference	Reference
60 - 64	0.93 (0.71-1.22)	0.91 (0.69-1.20)	0.89 (0.68-1.17)	0.91 (0.69-1.20)	0.90 (0.68-1.18)
65 - 69	1.06 (0.83-1.36)	1.00 (0.78-1.29)	0.98 (0.76-1.25)	1.01 (0.78-1.29)	0.98 (0.76-1.26)
70 - 74	1.33 (1.05-1.68)	1.24 (0.98-1.58)	1.19 (0.93-1.51)	1.25 (0.98-1.58)	1.19 (0.93-1.51)
75 - 79	1.24 (0.96-1.60)	1.14 (0.88-1.47)	1.07 (0.83-1.38)	1.13 (0.87-1.46)	1.06 (0.82-1.37)
80 and over	1.29 (0.98-1.70)	1.15 (0.87-1.52)	1.05 (0.79-1.39)	1.13 (0.85-1.50)	1.03 (0.78-1.37)
Multimorbidity†					
No		Reference	Reference	Reference	Reference
Yes		1.92 (1.64-2.26)	1.69 (1.43-2.00)	1.93 (1.64-2.26)	1.70 (1.44-2.01)
ASA class			1.46 (1.28-1.68)		1.46 (1.27-1.67)
Hospital-level effects					
Hospital-level intercept (SE)				0.05 (0.02)	0.05 (0.02)
VPC				1.45%	1.39%
Discriminatory accuracy					
AUC	0.54 (0.52-0.56)	0.58 (0.56-0.61)	0.60 (0.58-0.62)	0.58 (0.56-0.61)	0.60 (0.58-0.62)
AUC difference	Reference	0.04[a]	0.06[a]	0.00[b]	0.00[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2, †Presence of two or more Elixhauser Index morbidities

Model 1: single-level model with age, sex only; Model 2_h: Model 1 and hospital data information (Elixhauser Index); Model $2_{h,r}$: Model 1 and hospital and registry information (Elixhauser Index, ASA); Model 3_h: Model 2_h plus hospital-level random effect; Model $3_{h,r}$: Model $2_{h,r}$ plus hospital-level random effect. ICC: intraclass correlation coefficient, VPC: variance partition coefficient, AUC: area under the receiver operating characteristic curve; Multimorbid - ≥2 morbidities

Appendix 7. Statistical Appendices

7.1 Statistical Appendix for Chapter 6

Table 7.1.1 Data quality checks and list of exclusions

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Table 7.2.6 Summary of the sensitivity analysis for 30-day readmissions, with adjustments for competing risk of death, TKA

Table 7.2.7 Measures of variation in 30-day readmissions by person and hospital effects, TKA, excluding patients that died prior to readmission (for comparison with Table 7.4 in the main body of Thesis)

7.1 Statistical appendix for Chapter 6

Data quality and exclusions

Table 7.1.1 Data quality checks and list of exclusions

Check	Description	N of Records (n=355,766)	N of people (n=263,419)	Decision
Date checks				
Dates of admission not in a plausible range	Check if the requested data extract matches ethics application (2000 – 2014)	0		No changes needed
Dates of birth not in a plausible range	Check if dates of birth are outside the plausible range (1890 – 2014), leading to incorrect age calculations	0		No changes needed
2 or more dates of birth per person	Check if multiple DOBs exist per person. Probabilistic linkage software allows transposition of months/days in its algorithms	603		Chose the most frequent DOB
Date of death is before date of separation	Date of death (from RBDM data) appears before separation date of episode of care	**410**	**392**	**Delete records from analysis - possible false positive links**
Admission date after date of death	Possible incorrect linkage of death data with a hospital record after registered death	**86**	**71**	**Exclude all records for the person - possible false positive link**
Admission date after separation date	Checking for negative length of stay (implausible)	0		No changes needed
Same admission/separation dates and times	Check if duplicate entries exist based on the same admission dates and times. Check if other variables are the same within potential duplicate records	86		Leave the records as they denote nested admissions.
Inconsistencies and other checks				
Sex differently recorded across records for the same individual	Check if there is consistency across all records for a person on their sex. Chose the most frequent sex recorded	**31**	**25**	**Exclude person from analysis as potential false positive link**
Dates of death in RBDM and ABS records > 10 years apart	If there are differences in the recorded dates of death between registry (RBDM) and cause of death data (ABS)	2		Chose the latter date of death
Not a resident of NSW based on the SLA of residence	Non-residents of NSW are captured in APDC but their follow up or hospitalisations to other non-NSW hospitals are not captured	6378	5472	**Excluded from analysis due to incomplete data capture**
Total exclusions			**5888 (2.2%)**	

Assessment of model fit – multilevel models

Patients were admitted to 234 hospitals in NSW, with median number of patients per hospital being 145.5 (interquartile range 30 – 990).

Table 7.1.2. Model building for 30-day mortality outcome

	Model 1	Model 2
Fixed effects		
Group aRR (95% CI)		
Neither	1	1
Frail only	1.90 (1.82 – 1.99)	1.90 (1.82 – 1.99)
Multimorbid only	2.38 (2.28 – 2.49)	2.40 (2.29 – 2.51)
Both	4.18 (4.02 – 4.34)	4.23 (4.07 – 4.39)
Random effects		
Level-2 intercept (SE)		0.039 (0.008)
Model fit		
-2 Log Likelihood	173173.8	172877.6[a]
Fit for conditional distribution (χ^2/DF)		0.87

Model 1 denotes a single-level model, Model 2 is a 2-level multilevel model with patients nested within hospitals, [a] denotes a better fitting model

- ➔ Hospital level intercept is significant with z-value=4.75, *p*-value < 0.001
- ➔ Model 2 is a better fitting model with $\chi^2_{diff} = -2\,LL_{Model1} - -2\,LL_{Model2} = 296.2$, 1 df, *p*-value < 0.001
- ➔ Fit for conditional distribution (χ^2/DF<1) indicates that there is no residual dispersion

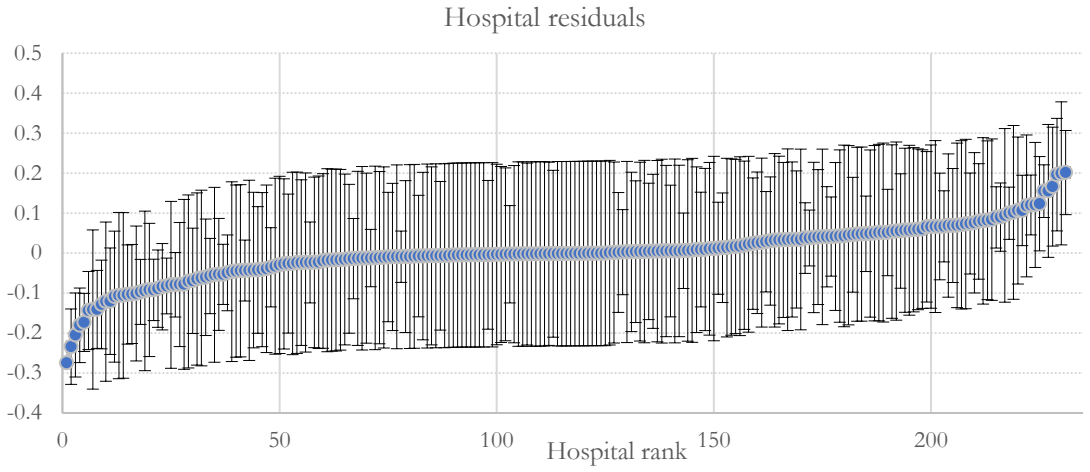


Table 7.1.3. Model building for prolonged length of stay

	Model 1	Model 2
Fixed effects		
Group aRR (95% CI)		
Neither	1	1
Frail only	2.64 (2.58 – 2.70)	2.62 (2.56 – 2.68)
Multimorbid only	1.58 (1.53 – 1.62)	1.57 (1.52 – 1.61)
Both	3.36 (3.29 – 3.44)	3.34 (3.26 – 3.41)
Random effects		
Level-2 intercept (SE)		0.050 (0.007)
Model fit		
-2 Log Likelihood	321820.2	320271.8[a]
Fit for conditional distribution (χ^2/DF)		0.70

Model 1 denotes a single-level model, Model 2 is a 2-level multilevel model with patients nested within hospitals, [a] denotes a better fitting model

- ➔ Hospital level intercept is significant with z-value=7.02, *p*-value < 0.001
- ➔ Model 2 is a better fitting model with $\chi^2_{diff} = -2\,LL_{Model1} - -2\,LL_{Model2} = 1548.4$, 1 df, *p*-value < 0.001
- ➔ Fit for conditional distribution (χ^2/DF<1) indicates that there is no residual dispersion

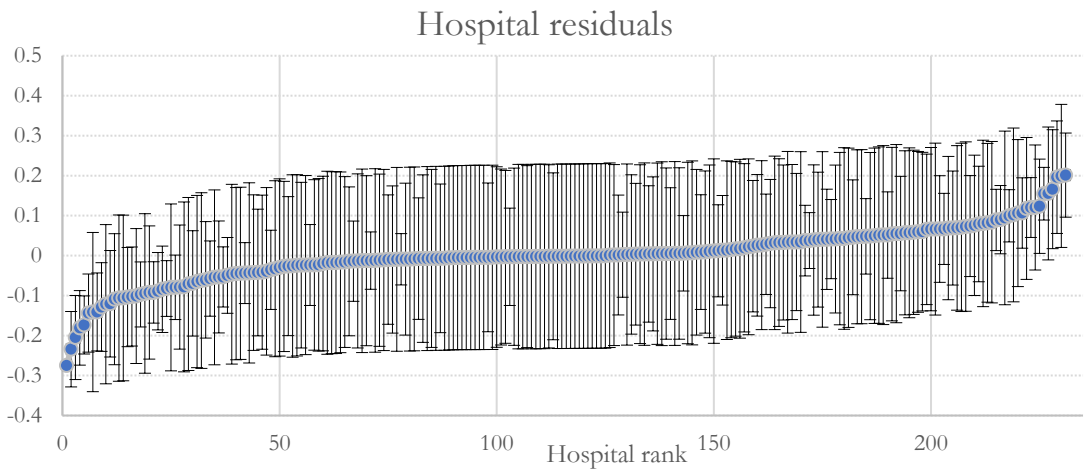


Table 7.1.4. Model building for 30-day readmissions

	Model 1	Model 2
Fixed effects		
Group aRR (95% CI)	1	1
Neither	1.25 (1.20 – 1.30)	1.25 (1.21 – 1.31)
Frail only	1.40 (1.34 – 1.45)	1.41 (1.35 – 1.47)
Multimorbid only	1.78 (1.72 – 1.84)	1.79 (1.73 – 1.86)
Both		
Random effects		
Level-2 intercept (SE)		0.014 (0.003)
Model fit		
-2 Log Likelihood	162109.2	161937.4[a]
Fit for conditional distribution (χ^2/DF)		0.89

Model 1 denotes a single-level model, Model 2 is a 2-level multilevel model with patients nested within hospitals, [a] denotes a better fitting model

- ➔ Hospital level intercept is significant with z-value=4.52, *p*-value < 0.001
- ➔ Model 2 is a better fitting model with χ^2_{diff} = -2 LL_{Model1} - -2 LL_{Model2} = 171.80, 1 df, *p*-value < 0.001
- ➔ Fit for conditional distribution (χ^2/DF<1) indicates that there is no residual dispersion

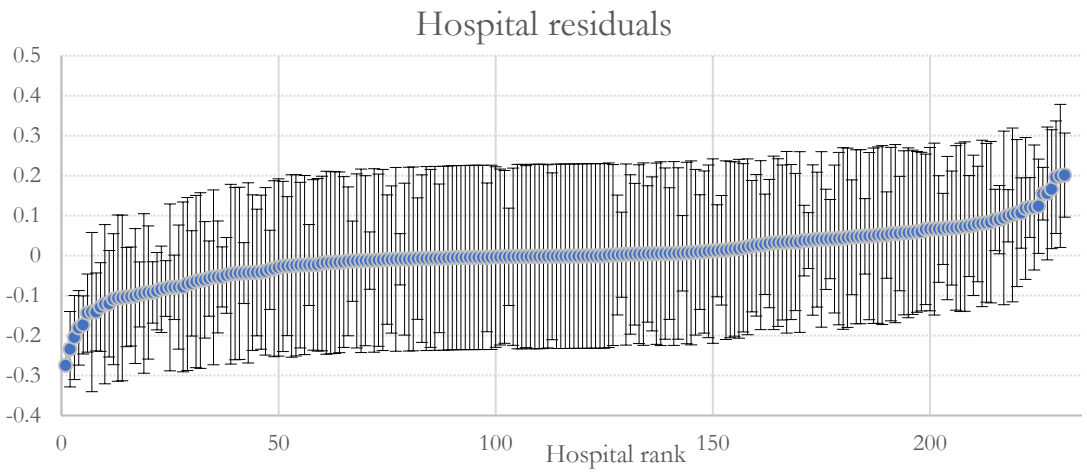


Table 7.1.5. Adjusted relative risk (aRR) between multimorbidity and 3 categories of HFRS with adverse outcomes

Outcomes	Single-level model	Multilevel model
	aRR	aRR
30-day mortality		
Group		
Neither	1	1
Mild frailty risk only	1.82 (1.74 – 1.91)	1.82 (1.74 – 1.91)
High frailty risk only	2.38 (2.22 – 2.55)	2.40 (2.24 – 2.57)
Multimorbid only	2.40 (2.29 – 2.51)	2.42 (2.31 – 2.53)
Multimorbid, mild frailty risk	3.97 (3.82 – 4.13)	4.02 (3.86 – 4.18)
Multimorbid, high frailty risk	4.64 (4.45 – 4.85)	4.75 (4.55 – 4.96)
Interaction *p*-value	<0.001	<0.001
Prolonged length of stay		
Group		
Neither	1	1
Mild frailty risk only	2.47 (2.41 – 2.53)	2.46 (2.40 – 2.53)
High frailty risk only	3.65 (3.52 – 3.78)	3.63 (3.50 – 3.76)
Multimorbid only	1.59 (1.55 – 1.64)	1.59 (1.54 – 1.63)
Multimorbid, mild frailty risk	3.10 (3.02 – 3.17)	3.09 (3.01 – 3.16)
Multimorbid, high frailty risk	3.97 (3.87 – 4.07)	3.97 (3.86 – 4.07)
Interaction *p*-value	<0.001	<0.001
30-day readmission		
Group		
Neither	1	1
Mild frailty risk only	1.22 (1.17 – 1.27)	1.22 (1.14 – 1.27)
High frailty risk only	1.41 (1.32 – 1.51)	1.42 (1.32 – 1.52)
Multimorbid only	1.40 (1.34 – 1.46)	1.41 (1.35 – 1.47)
Multimorbid, mild frailty risk	1.73 (1.66 – 1.79)	1.74 (1.68 – 1.81)
Multimorbid, high frailty risk	1.87 (1.80 – 1.95)	1.89 (1.81 – 1.97)
Interaction *p*-value	0.234	0.229

Table 7.1.6. Additive and multiplicative interaction effects of multimorbidity and frailty risk on adverse patient outcomes, full cohort, **single-level models**

Mortality within 30-days post admission	**Low frailty risk**			**Elevated frailty risk**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	%outcome	aRR (95% CI)
No multimorbidity	3854	4.7	1	4,731	9.2	1.90 (1.82 – 1.99)
Multimorbidity	4,046	10.7	2.38 (2.28 – 2.49)	16,255	18.8	4.18 (4.02 – 4.34)

[a]*Measure of effect modification on additive scale: RERI (95% CI) = 0.85 (0.75 – 0.96)**

[a]*Measure of effect modification on multiplicative scale: ratio of RR= 0.92 (0.87 – 0.97), p-value =0.003**

Prolonged LOS	**Low frailty risk**			**Elevated frailty risk**		
	N with outcome	% outcome	aRR (95% CI)	N with	%outcome	aRR (95% CI)
No multimorbidity	11855	14.5	1	19,181	37.4	2.64 (2.58 – 2.70)
Multimorbidity	8,001	21.1	1.58 (1.53 – 1.62)	37,548	43.4	3.36 (3.29 – 3.44)

[a]*Measure of effect modification on additive scale: RERI (95% CI) =0.16 (0.11 – 0.21)**

[a]*Measure of effect modification on multiplicative scale: ratio of RR= 0.81 (0.78 – 0.84), p-value <0.001**

Readmission within 30-days post discharge	**Low frailty risk**			**Elevated frailty risk**		
	N with outcome	% outcome	aRR (95% CI)	N with outcome	%outcome	aRR (95% CI)
No multimorbidity	5,457	6.9	1	4,727	9.9	1.25 (1.20 – 1.30)
Multimorbidity	3,960	11.4	1.40 (1.34 – 1.45)	12,120	16.5	1.78 (1.72 – 1.84)

[a]*Measure of effect modification on additive scale: RERI (95% CI) =0.13 (0.07 – 0.20)**

[a]*Measure of effect modification on multiplicative scale: ratio of RR= 1.02 (0.97 – 1.07), p-value =0.48*

* Denotes significance at 5% level.

[a] Significance of an interaction on an additive scale is denoted where RERI is different from 0, and on the multiplicative scale if ratio of RR is different from 1.

Table 7.1.7. Sensitivity analysis for 30-day readmissions, with adjustments for competing risk of death

Group	Original result	Sensitivity analysis 1*	Sensitivity analysis 2**
	aRR	aRR	aHR
Group			
Neither	1	1	1
Frail only	1.25 (1.21 – 1.31)	1.28 (1.23 – 1.33)	1.26 (1.22 – 1.32)
Multimorbid only	1.41 (1.35 – 1.47)	1.42 (1.36 – 1.48)	1.42 (1.36 – 1.47)
Both	1.79 (1.73 – 1.86)	1.87 (1.80 – 1.93)	1.84 (1.78 – 1.91)
Multiplicative interaction tests			
	1.02 (0.96 – 1.07) *p*-value = 0.57	1.03 (0.98 – 1.09) *p*-value = 0.29	1.03 (0.98 – 1.09) *p*-value = 0.26

* Excluding 6763 (2.9%) of patients that had a death prior to readmission

** Analysis using Fine Gray competing risks model accounting for competing risk of death

7.2 Statistical appendix for Chapter 7

Data quality and exclusions

Table 7.2.1 Data quality checks and list of exclusions

Check	Description	N of Records (n=21,209)	N of people (n=20,048)	Decision
Date checks				
Dates of admission not in a plausible range	Check if the requested data extract matches ethics application (2001 – 2019)	0		No changes needed
Dates of birth not in a plausible range	Check if dates of birth are outside the plausible range (1890 – 2019), leading to incorrect age calculations	0		No changes needed
Admission date after date of death	Possible incorrect linkage of death data with a hospital record after registered death	**13**	**13**	**Exclude all records for the person - possible false positive link**
Admission date after separation date	Checking for negative length of stay (implausible)	0	0	No changes needed
Date of birth after admission date	Implausible DOB	0	0	
Same admission/separation dates and times	Check if duplicate entries exist based on the same admission dates and times. Check if other variables are the same within potential duplicate records	32	32	Leave the records as they denote nested admissions.
Inconsistencies and other checks				
Inconsistent sex	Check if there is consistency across all records for a person on their sex. Chose the most frequent sex recorded	**75**	**71**	**Exclude person from analysis as potential false positive link**
Inconsistent date of birth	Check dates of birth and if they differ by more than 10 years	299	285	**Exclude person from analysis as potential false positive link**
Total exclusions		**373 (1.8%)**	**355 (1.8%)**	

Assessment of multilevel model fit

THA analysis

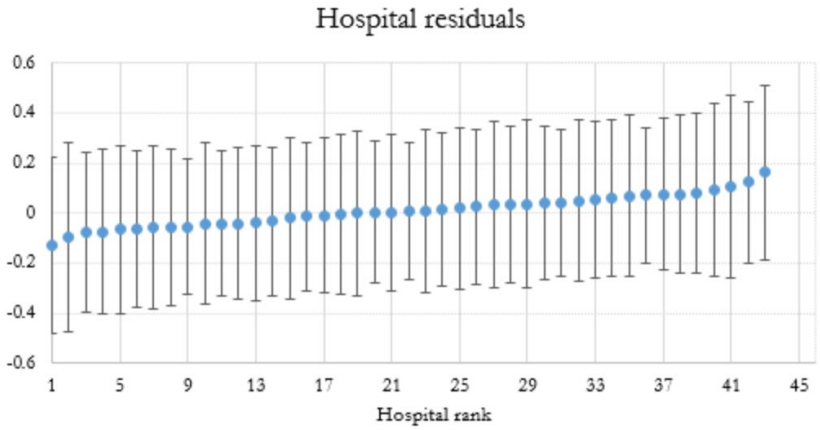
Patients were admitted to 45 hospitals in NSW, with median number of patients undergoing THA procedure per hospital being 116 (interquartile range 71 – 163).

Table 7.2.2 Comparison of single and multilevel models for 30-day readmissions following THA

	Model $2_{h,r}$	Model $3_{h,r}$
Fixed effects		
Elixhauser Index		
0	1	1
1	1.75 (1.36-2.24)	1.77 (1.37-2.27)
2	1.87 (1.35-2.60)	1.88 (1.35-2.61)
3 or more	2.42 (1.75-3.35)	2.43 (1.75-3.37)
ASA class	1.29 (1.07-1.55)	1.28 (1.07-1.55)
Random effects		
Hospital-level intercept (SE)		0.03 (0.03)
Model fit		
-2 Log Likelihood	2832.10[a]	2830.84
Fit for conditional distribution (χ^2/DF)		0.97

Model $2_{h,r}$ denotes a single-level model including hospital and registry data, Model $3_{h,r}$ is a 2-level multilevel model with patients nested within hospitals, [a] denotes a better fitting model

- ➔ Hospital level intercept is not significant with z-value=0.93, *p*-value=0.176, indicating no difference between readmission rates between hospitals
- ➔ Single level model is a better fitting model with $\chi^2_{\text{diff}} = -2\,LL_{\text{Model1}} - -2\,LL_{\text{Model2}} = 1.26$, 1 df, *p*-value=0.13
- ➔ Fit for conditional distribution of multilevel model (χ^2/DF<1) indicates that there is no residual dispersion



TKA analysis

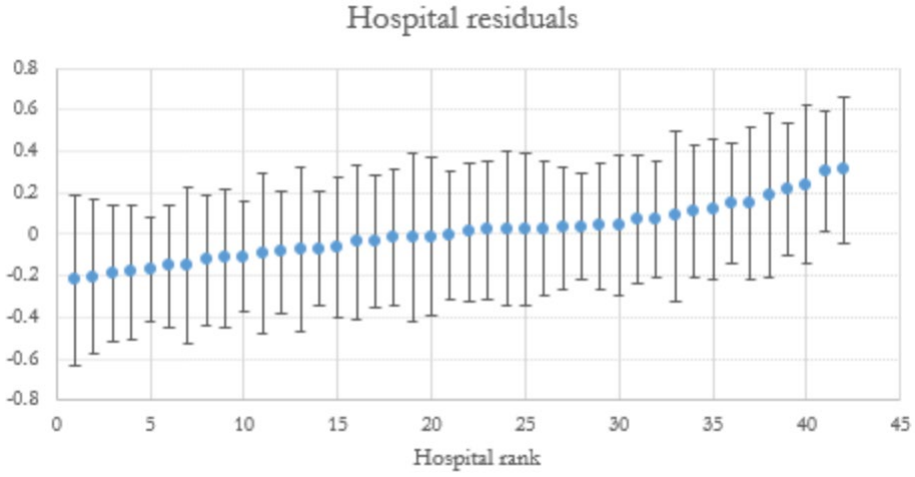
Patients were admitted to 43 hospitals in NSW, with median number of patients per hospital being 206 (interquartile range 110 – 321).

Table 7.2.3 Comparison of single and multilevel models for 30-day readmissions following TKA

	Model $2_{h,r}$	Model $3_{h,r}$
Fixed effects		
Elixhauser Index		
0	1	1
1	1.31 (1.10-1.57)	1.31 (1.09-1.57)
2	1.63 (1.30-2.04)	1.63 (1.30-2.05)
3 or more	2.30 (1.82-2.91)	2.31 (1.82-2.92)
ASA class	1.40 (1.22-1.61)	1.40 (1.22-1.61)
Random effects		
Hospital-level intercept (SE)		0.04 (0.02)
Model fit		
-2 Log Likelihood	5404.75	5396.17
Fit for conditional distribution (χ^2/DF)		0.98

Model $2_{h,r}$ denotes a single-level model including hospital and registry data, Model $3_{h,r}$ is a 2-level multilevel model with patients nested within hospitals, [a] denotes a better fitting model

- ➔ Hospital level intercept is significant with z-value=1.84, *p*-value=0.03
- ➔ Single level model is a better fitting model with $\chi^2_{diff} = -2\,LL_{Model1} - -2\,LL_{Model2} = 8.58$, 1 df, *p*-value=0.001
- ➔ Fit for conditional distribution of multilevel model (χ^2/DF<1) indicates that there is no residual dispersion



Sensitivity analyses

Table 7.2.4 Summary of the sensitivity analysis for 30-day readmissions, with adjustments for competing risk of death, THA

Group	Original result Model $2_{h,r}$		Sensitivity analysis 1* Model $2_{h,r}$		Sensitivity analysis 2** Model $2_{h,r}$	
	aRR	p-value	aRR	p-value	aHR	p-value
Sex						
Male	1.23 (1.00-0.52)	0.045	1.24 (1.01-1.52)	0.044	1.19 (0.98-1.45)	0.080
Age						
<60	1	0.015		0.015	1	0.020
60 - 64	1.00 (0.67-1.47)		0.99 (0.67-1.47)		1.00 (0.68-1.46)	
65 - 69	1.26 (0.90-1.79)		1.26 (0.89-1.78)		1.27 (0.90-1.77)	
70 - 74	1.47 (1.05-2.05)		1.46 (1.05-2.04)		1.46 (1.06-2.02)	
75 - 79	1.61 (1.14-2.28)		1.61 (1.14-2.28)		1.60 (1.14-2.25)	
80 and over	1.66 (1.17-2.36)		1.67 (1.17-2.37)		1.62 (1.14-2.30)	
Elixhauser Index						
0	1	<0.001		<0.001	1	<0.001
1	1.75 (1.36-2.24)		1.75 (1.37-2.25)		1.68 (1.32-2.14)	
2	1.87 (1.35-2.60)		1.87 (1.35-2.60)		1.83 (1.33-2.50)	
3 or more	2.42 (1.75-3.35)		2.44 (1.76-3.38)		2.32 (1.68-3.19)	
ASA class	1.29 (1.07-1.55)	0.008	1.29 (1.07-1.55)	0.008	1.26 (1.04-1.51)	0.016

* Excluding 6 (0.1%) of patients that had a death prior to readmission

** Analysis using Fine Gray competing risks model accounting for competing risk of death

Table 7.2.5 Measures of variation in 30-day readmissions by person and hospital effects, THA, excluding patients that died prior to readmission (for comparison with Table 7.3 in the main body of Thesis)

	Single-level models			Multilevel models	
	Model 1 OR (95% CI)	Model 2_h OR (95% CI)	Model $2_{h,r}$ OR (95% CI)	Model 3_h OR (95% CI)	Model $3_{h,r}$ OR (95% CI)
Patient-level effects					
Sex					
Male	1.26 (1.03-1.55)	1.23 (1.00-1.51)	1.24 (1.01-1.52)	1.23 (1.00-1.52)	1.24 (1.01-1.53)
Age					
<60	Reference	Reference	Reference	Reference	Reference
60 - 64	1.10 (0.75-1.62)	1.01 (0.69-1.50)	0.99 (0.67-1.47)	1.01 (0.68-1.50)	0.99 (0.67-1.47)
65 - 69	1.46 (1.04-2.05)	1.30 (0.92-1.84)	1.26 (0.89-1.78)	1.30 (0.92-1.84)	1.27 (0.89-1.79)
70 - 74	1.78 (1.28-2.47)	1.54 (1.11-2.15)	1.46 (1.05-2.04)	1.54 (1.11-2.15)	1.47 (1.05-2.05)
75 - 79	2.08 (1.48-2.92)	1.72 (1.22-2.43)	1.61 (1.14-2.27)	1.73 (1.22-2.43)	1.62 (1.14-2.29)
80 and over	2.31 (1.65-3.24)	1.80 (1.27-2.55)	1.67 (1.17-2.37)	1.80 (1.27-2.54)	1.67 (1.18-2.37)
Elixhauser Index					
0		Reference	Reference	Reference	Reference
1		1.86 (1.45-2.38)	1.75 (1.37-2.25)	1.87 (1.46-2.40)	1.77 (1.38-2.27)
2		2.06 (1.50-2.84)	1.87 (1.35-2.60)	2.06 (1.50-2.84)	1.88 (1.35-2.61)
3 or more		2.79 (2.05-3.80)	2.42 (1.75-3.35)	2.79 (2.04-3.80)	2.45 (1.77-3.39)
ASA class			1.29 (1.07-1.55)		1.28 (1.06-1.54)
Hospital-level effects					
Hospital-level intercept (SE)				0.03 (0.03)	0.03 (0.03)
VPC				0.94%	0.86%
Discriminatory accuracy					
AUC	0.59 (0.56-0.62)	0.64 (0.62-0.67)	0.65 (0.62-0.68)	0.64 (0.62-0.67)	0.65(0.62-0.68)
AUC difference	Reference	0.05[a]	0.06[a]	0.00[b]	0.00[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2

Model 1: single-level model with age, sex only; Model 2_h: Model 1 and hospital data information (Elixhauser Index); Model $2_{h,r}$: Model 1 and hospital and registry information (Elixhauser Index, ASA); Model 3_h: Model 2_h plus hospital-level random effect; Model $3_{h,r}$: Model $2_{h,r}$ plus hospital-level random effect. ICC: intraclass correlation coefficient, VPC: variance partition coefficient, AUC: area under the receiver operating characteristic curve

Table 7.2.6 Summary of the sensitivity analysis for 30-day readmissions, with adjustments for competing risk of death, TKA

Group	Original result Model $2_{h,r}$		Sensitivity analysis 1* Model $2_{h,r}$		Sensitivity analysis 2** Model $2_{h,r}$	
	aRR	p-value	aRR	p-value	aHR	p-value
Sex						
Male	1.11 (0.96-1.28)	0.179	1.11 (0.96-1.28)	0.173	1.11 (0.96-1.27)	0.160
Age						
<60	Reference	0.393	Reference	0.392	Reference	0.388
60 - 64	0.89 (0.67-1.16)		0.88 (0.67-1.16)		0.89 (0.68-1.16)	
65 - 69	0.96 (0.75-1.24)		0.96 (0.75-1.24)		0.97 (0.76-1.23)	
70 - 74	1.16 (0.91-1.48)		1.16 (0.91-1.48)		1.15 (0.92-1.45)	
75 - 79	1.04 (0.80-1.35)		1.04 (0.81-1.35)		1.04 (0.82-1.33)	
80 and over	1.02 (0.77-1.35)		1.02 (0.77-1.35)		1.01 (0.77-1.32)	
Elixhauser Index						
0	Reference	<0.001	Reference	<0.001		<0.001
1	1.31 (1.10-1.57)		1.31 (1.10-1.57)		1.30 (1.10-1.55)	
2	1.63 (1.30-2.04)		1.63 (1.30-2.04)		1.59 (1.29-1.97)	
3 or more	2.30 (1.82-2.91)		2.31 (1.83-2.91)		2.18 (1.76-2.71)	
ASA class	1.40 (1.22-1.61)	<0.001	1.40 (1.22-1.61)	<0.001	1.38 (1.21-1.57)	<0.001

* Excluding 3 (0.03%) of patients that had a death prior to readmission

** Analysis using Fine Gray competing risks model accounting for competing risk of death

Table 7.2.7 Measures of variation in 30-day readmissions by person and hospital effects, TKA, excluding patients that died prior to readmission (for comparison with Table 7.4 in the main body of Thesis)

	Single-level models			Multilevel models	
	Model 1 OR (95% CI)	Model 2_h OR (95% CI)	Model $2_{h,r}$ OR (95% CI)	Model 3_h OR (95% CI)	Model $3_{h,r}$ OR (95% CI)
Patient-level effects					
Sex					
Male	1.14 (0.99-1.32)	1.11 (0.96-1.28)	1.11 (0.96-1.28)	1.11 (0.95-1.28)	1.10 (0.95-1.28)
Age					
<60	Reference	Reference	Reference	Reference	Reference
60 - 64	0.93 (0.71-1.22)	0.90 (0.68-1.18)	0.88(0.67-1.16)	0.90 (0.68-1.18)	0.89 (0.68-1.17)
65 - 69	1.06 (0.83-1.36)	0.98 (0.77-1.26)	0.96 (0.75-1.24)	0.99 (0.77-1.27)	0.97 (0.76-1.25)
70 - 74	1.33 (1.05-1.68)	1.20 (0.95-1.53)	1.16 (0.91-1.48)	1.21 (0.95-1.53)	1.17 (0.92-1.48)
75 - 79	1.25 (0.97-1.61)	1.10 (0.85-1.42)	1.04 (0.81-1.35)	1.09 (0.84-1.41)	1.04 (0.80-1.34)
80 and over	1.29 (0.98-1.70)	1.09 (0.82-1.45)	1.02 (0.77-1.35)	1.08 (0.81-1.43)	1.00 (0.76-1.34)
Elixhauser Index					
0		Reference	Reference	Reference	Reference
1		1.41 (1.18-1.68)	1.31 (1.10-1.57)	1.40 (1.17-1.67)	1.31 (1.09-1.57)
2		1.83 (1.47-2.28)	1.63 (1.30-2.04)	1.83 (1.47-2.29)	1.63 (1.30-2.05)
3 or more		2.71 (2.17-3.40)	2.31 (1.83-2.91)	2.72 (2.17-3.40)	2.31 (1.82-2.92)
ASA class			1.40 (1.22-1.61)		1.40 (1.22-1.61)
Hospital-level effects					
Hospital-level intercept (SE)				0.05 (0.02)	0.04 (0.02)
VPC				1.38%	1.34%
Discriminatory accuracy					
AUC	0.54 (0.52-0.56)	0.60 (0.58-0.62)	0.61 (0.59-0.63)	0.60 (0.58-0.62)	0.61(0.59-0.63)
AUC difference	Reference	0.06[a]	0.07[a]	0.00[b]	0.00[b]

[a] Incremental increase from Model 1, [b] Incremental increase from Model 2

Model 1: single-level model with age, sex only; Model 2_h: Model 1 and hospital data information (Elixhauser Index); Model $2_{h,r}$: Model 1 and hospital and registry information (Elixhauser Index, ASA); Model 3_h: Model 2_h plus hospital-level random effect; Model $3_{h,r}$: Model $2_{h,r}$ plus hospital-level random effect. ICC: intraclass correlation coefficient, VPC: variance partition coefficient, AUC: area under the receiver operating characteristic curve