Australian National University

Living with cardiovascular disease (CVD) in Australia: Using large-scale linked data to investigate workforce participation and social interaction in relation to CVD diagnosis

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Declaration

Unless otherwise indicated, the work presented in this is my own.

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ABSTRACT

Cardiovascular disease (CVD) is a leading cause of global mortality and a major contributor to disability. The number of people living with CVD in Australia is expected to increase due to an aging population and improved treatment, leading to higher survival. Evidence on longer-term health care outcomes that matter to individuals living with CVD, including disability and social and economic participation (person-centred outcomes), is critical to provide appropriate support to these individuals and their carers. In particular, the ability to participate in the workforce and to have meaningful social interaction (e.g. social visits, phone calls or group meetings) are important person-centred outcomes that may be adversely affected by CVD. Yet we lack critical information on these outcomes.

The purpose of this thesis was to gain a better understanding of the relationship between CVD and both workforce participation and social interaction in middle-aged and older people in Australia. The thesis consists of two systematic reviews, which summarise important gaps in the evidence, and four empirical studies to address these gaps.

Using PubMed, Scopus, and Web of Science up to December 2019, I identified twenty-seven articles on the relationship of CVD to workforce participation and six on CVD and social interaction. The available evidence was largely descriptive, small-scale, and lacking a suitable comparison group. There was limited information on variation in outcomes according to CVD subtype, and by population characteristics. In particular, the role of physical disability in workforce participation and social interaction amongst people with CVD had not been examined.

For the empirical studies, I used data from the 45 and Up Study, a cohort study of 267,153 participants from New South Wales, Australia, with two waves of questionnaire data linked to hospitalisation and death data. I undertook two cross-sectional analyses, to quantify workforce participation and social interaction in people with existing versus no CVD. To better understand the likely causal role of CVD, I conducted two longitudinal analyses, examining

exit from the workforce, and becoming socially isolated after incident CVD in comparison to people without CVD. Regression models were adjusted for sociodemographic characteristics, and comorbidity where applicable.

Results showed that most people aged 45-64 years old with CVD were in the workforce, but workforce non-participation was 36% higher compared to those without CVD. People with incident CVD versus those without had a 28% higher risk of leaving the workforce.

People with CVD had slightly lower levels of social interaction compared to those without CVD. However, the risk of becoming socially isolated in people with incident CVD was similar to that seen in people without CVD.

The relationship of CVD to workforce participation and social interaction varied by CVD subtype and population characteristics in both cross-sectional and longitudinal results. Generally, workforce participation and social interaction outcomes were poorer for those with cerebrovascular disease or heart failure compared to other types of CVD. Workforce participation and social interaction were much more strongly related to physical disability than to CVD diagnosis itself; among people without disability, levels of workforce participation were similar in people with and without CVD and poorer outcomes were observed in people with severe disability regardless of CVD diagnosis.

I also examined loss to follow-up, a common problem in longitudinal studies, and found no evidence that it materially affected the findings.

This thesis enriches current the understanding of the relation of CVD to important person-centred outcomes; the evidence on variation by CVD subtype and the role of physical disability are key novel contributions. The evidence generated will inform people with CVD and those caring for them, as well as the organisations that aim to improve quality of life by those living with CVD.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ABS	Australian Bureau of Statistics
APDC	Admitted Patient Data Collection
ARIA+	Accessibility Remoteness Index of Australia Plus
BMI	Body Mass Index
CHD	Coronary heart disease
CHeReL	Centre for Health Record Linkage
CI	Confidence Interval
CVD	Cardiovascular disease
DALY	Disability-adjusted life year
DSSI	Duke Social Support Index
EU	European Union
HA	Heart attack
HD	Heart disease
HF	Heart failure
HR	Hazard ratio
ICD-AM	Interactional Classification of Disease- Australian Modification
ICD-9-CM	International Classification of Diseases, 9th Revision, Clinical Modification
ICH	Intracerebral haemorrhage
IHD	Ischaemic heart disease
IRR	Incident rate ratio
IS	Ischaemic stroke
K10	Kessler 10 Scale
MAR	Missing at random
MI	Myocardial infarction
MICE	Multiple imputation with chained equations
MCAR	Missing completely at random
MNAR	Missing not at random
MOS-PF	Medical Outcomes Score-Physical Functioning
MVNI	Multivariate normal imputation
NHS	National Health Survey
NSW	New South Wales
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
PAD	Peripheral artery disease

PFL	Physical functioning limitation
PR	Prevalence Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRR	Prevalence rate ratio
RR	Risk Ratio
SD	Standard Deviation
SE	Standard error of mean
SEEF	Social, Economic and Environmental Factors
SHR	Sub distribution hazard ratio
SOC	Sense of Coherence Scale
SOS	Social network and social support scale
TIA	Transient ischemia
UK	United Kingdom
USA	United States of America
VD	Vascular disease
VTE	Venous thromboembolism
WHO	World Health Organisation
YLD	Years lived with disability
YLL	Years of life lost

CHAPTER 1 Introduction

1.0 Chapter summary

This chapter provides the context and overview of the thesis. The context introduces cardiovascular disease (CVD) and person-centred outcomes, and important factors for the relationship of CVD and person-centred outcomes, such as CVD subtype, and population characteristics, particularly the role of physical disability. It then defines workforce participation and social interaction - as important person-centred outcomes - prior to outlining the overview which includes the aims, objectives, and structure of the thesis. Finally, the author's contribution and publications from the thesis are listed.

1.1 Context

1.1.1 Cardiovascular disease (CVD) globally, and in Australia

Cardiovascular disease (CVD) encompasses all types of diseases that affect the heart or blood vessels including but not limited to ischaemic heart disease, stroke, heart failure, and peripheral artery disease [1]. CVD is a leading cause of global mortality and a major contributor to disability [2, 3]. From 1990 to 2019, the prevalence of CVD doubled (from 271 million to 523 million people living with CVD), the number of CVD deaths increased (from 12.1 million to 18.6 million), disability-adjusted life years (DALYs) and years of life lost (YLL) increased significantly, and years lived with disability (YLD) doubled (from 17.7 million to 34.4 million) [2]. An estimated 1.2 million (5.6%) Australian adults aged 18 years and over had CVD in 2017–18 [4], and CVD was the underlying cause of death in 41,800 deaths in 2018 (26% of all deaths in Australia) [5]. The most recent burden of disease study in Australia [6] has estimated that in between 2003 and 2015, there is an overall decrease of CVD disease burden (35.9% decrease in DALY rate), but the decrease of non-fatal burden of CVD is lower (26.9% decrease in the YLD rate) than that of the fatal burden of CVD (38% decrease in the YLL rate). The Australian Heart Foundation's Heart Watch survey in 2020 has estimated that three-quarters of Australians are at risk of developing CVD [7, 8].

Various strategies available to practitioners and care providers to address the various stages of the natural history of CVD could be divided into the three levels: primary, secondary, and tertiary prevention [9]. Primary prevention aims to keep CVD from becoming established, secondary prevention aims to interrupt CVD progression and tertiary prevention aims to limit the physical impairment and social consequences from CVD [10, 11]. Improvements in CVD intervention over the last several decades have contributed to greater overall survival after a CVD event [12]. However, largely because of population ageing and other demographic changes [13], the overall global burden of CVD continues to increase, including increasing non-fatal CVD burden [2].

There is an increasing need to generate evidence on long-term survivorship issues that matter to individuals with CVD and to optimise CVD health and healthy aging [14], especially in a country like Australia where the number of people surviving with CVD is likely to continue to increase over the coming decades due to ageing of the population [15]. The Australian Bureau of Statistics (ABS) has projected that the population aged 75 years or more is expected to rise two-fold from 2012 to 2060, increasing from about 6.4 to 14.4 per cent of the total population [15]. By 2030, the prevalence of heart failure is projected to increase by 51% in men and 65% in women, compared to 2014 levels [16]. This highlights the significance of long-term health and wellbeing outcomes of CVD survivors, including attributes central to the ability of individuals and communities to lead happy and fulfilling lives [17].

1.1.2 Person-centred outcomes for people living with CVD

Person-centred outcomes include the longer-term health care outcomes that matter to individuals. People living with CVD have identified many person-centred outcomes of importance, including those related to mental wellbeing, physical wellbeing, ability to earn income, and ability to connect with the broader community through social participation and quality of life [18, 19]. The importance of person-centred outcomes for individuals living with CVD has been recognised by the systematic reviews and qualitative studies on the lived experience of people with CVD [18, 20]. Previous studies have also indicated that patient care models that incorporate person-centred outcomes in disease management plans provide a better quality of care for people living with CVD [21, 22].

CVD is a highly heterogeneous disease and recognising the diversity of survivorship experience is also important. The CVD subtypes with the greatest clinical impact, particularly for Australia, are ischaemic heart disease, myocardial infarction, heart failure, cerebrovascular disease, and peripheral arterial diseases [23, 24]. The onset of CVD, progression of CVD, and

functional recuperation differ substantially by these CVD subtypes. Previous studies also have indicated that person-centred outcomes vary substantively across different CVD subtypes [18]. Although it is well-established that people with CVD are concerned with person-centred outcomes, the magnitude of their concerns varies by different social-demographic and health-related characteristics. For example, among people with CVD, younger people with CVD care more about participating in social activities than older people [25], while women tend to be more disabled than men in various functional activities (e.g., eating, dressing, etc.) [26].

Physical disability is an important person-centred outcome [27]. It also has the potential to influence or underpin the relationship between CVD and other person-centred outcomes. Physical disability generally increases with age, and having good physical functioning is one of the key aspects of healthy ageing. It is also associated with different person-centred outcomes in elderly people [28, 29]. Previous studies have indicated that older people with CVD generally report having a greater physical disability than people without CVD, although underlying mechanisms are likely to vary depending on the subtype of CVD [30]. Thus, understanding how physical disability and CVD jointly affect person-centred outcomes might be of particular interest to explain the relationship of CVD to person-centred outcomes.

There is an increasing interest in research on person-centred outcomes around the world, including in Australia. Earlier investigations from Australia primarily focused on cancer in relation to physical, mental health, and quality of life person-centred outcomes [31, 32]. However, despite the rising number of people living with CVD, and the potential benefits of empirical evidence on CVD survivorship, little is known on how person-centred outcomes of people with versus without CVD vary in Australia. Available evidence from studies outside of Australia indicates that people diagnosed with CVD have a poor quality of life [33, 34], higher levels of depression [35, 36], lower physical activity [37, 38], lower workforce participation [39], and less social interaction [40] compared to people without CVD. However, the bulk of the

evidence is small-scale, focuses almost exclusively on a single CVD subtype, and does not account for different CVD subtypes, different population sub-groups, and other important factors such as physical disability [41, 42]. To add to the available evidence on person-centred outcomes of individuals living with CVD, in this thesis I have investigated two important but understudied person-centred outcomes which are relevant for financial and social wellbeing [43-45]: workforce participation and social interaction.

Untangling the relationship of CVD to both person-centred outcomes might be helpful in CVD management by informing people with CVD and their caregivers and organisations and programs that aim to support older people with CVD to have healthy ageing.

1.1.3 Workforce participation and CVD

The ability to earn one's livelihood (measured by the level of workforce participation) is an important person-centred outcome, and it is likely to be adversely affected by CVD diagnosis. Workforce participation status primarily aims to indicate a person's ability to earn a livelihood and it has similarity with the term is 'employment status' reported by ABS in its monthly 'Labour Force Survey' [46]. Aside from some technicalities in the definition of different categories of employment status, 'workforce participation status' and 'employment status' are just different ways of describing engagement in the workforce. Previous qualitative investigations have indicated that people of working age living with CVD generally want to continue work (either being self-employed or as an employee) and consider participation in the workforce as an important person-centred outcome [47, 48]. Working-age individuals value participation in the workforce as an important health indicator, are conscious of losing their jobs and expect to continue participating in the workforce, especially after a CVD diagnosis [18]. Participation in the workforce is associated with improved wellbeing for the individual concerned [49] and

maintaining workforce engagement is likely to have positive economic consequences at a community and national level [49, 50].

The occurrence of a CVD event is likely to adversely impact the ability to get and continue with a job [51]. While some studies have indicated that people living with CVD have lower workforce participation [52, 53], research on how workforce participation status varies among those with versus without CVD remains limited. There is limited evidence on how the relationship of CVD to workforce participation varies across different CVD subtypes, by population characteristics including the likely role of physical disability on the relationship (*further detail in chapter 2*).

1.1.4 Social interaction and CVD

Social wellbeing, including the ability to maintain social interaction, is another important person-centred outcome and is likely to be negatively affected by CVD. Social interaction is a dynamic sequence of social actions between individuals or groups, and its quantitative measurement is one of the indicators of social support and connection with others [54]. There are various types of social interaction (such as verbal or nonverbal communication) and many elements (such as social status, culture, social class) form the basis of social interaction [55].

Various terms (such as social engagement, social network, social support) have been used to indicate the level of social interaction, ranging from casual acquaintance to close familial connections. As evident from the systematic review (in chapter 3), there are different dimensions to meaningful social interaction, including the type of interaction, quality/level of interaction, one's willingness and ability to participate and how supported/connected one feels. From the person-centred perspective, a key indicator is ultimately whether or not one feels socially isolate.

Previous studies have shown that levels of social interaction are lower in people with CVD compared to those without CVD [56, 57]. However, these findings were not derived from large-scale population-based research. There is not adequate large-scale evidence on how the relationship varies across different CVD subtypes. There is also not any evidence on how the relationship of CVD to social interaction differs by population characteristics, including the likely role of physical disability on the relationship (*further detail in chapter 3*).

Understanding the relationship of CVD to two person-centred outcomes (workforce participation and social interaction), particularly how the relationship varies across different CVD subtypes, and by population characteristics would provide a stronger evidence-base to inform people living with CVD, their care providers and the organisations that aim to support them.

1.2 Aims, objectives and structure of the thesis

The ultimate purpose of this thesis is to improve CVD outcomes and care through generating reliable large-scale evidence on two person-centred outcomes—workforce participation and social interaction—in people with CVD compared to people not diagnosed with CVD. The overall aims of the thesis are to understand the relationship of CVD to (1) workforce participation and (2) social interaction by quantifying these outcomes in middle-aged and older people with CVD compared to those without CVD. The sequential steps for both aims are- compiling available evidence and gaps in knowledge by conducting systematic reviews, examining the magnitude of association using cross-sectional analyses, and finally estimating the likely causal role of incident CVD by longitudinal investigation. The detailed investigation examines workforce participation in people with different CVD subtypes and among different

population sub-groups, as well as quantifies the potential role of physical disability in these relationships.

Data from the largest Australian cohort study to date, the 45 and Up Study [58], were used in this thesis, including baseline and follow-up survey data linked to administrative data on hospitalisations and deaths. A substantial proportion of participants did not respond to the follow-up survey. Hence, I also investigated the implications of missing data due to the non-completion of the follow-up survey with a case study from the thesis. Therefore, the objectives in this thesis were:

1. To systematically review the evidence on the association between workforce participation and CVD among working-age older people published until December 2019 by using three databases (PubMed, Scopus, and Web of Science) and to identify the gaps in knowledge (Chapter 2).

2. To systematically review the evidence on the relationship between social interaction and CVD among older people published until December 2019 by using three databases (PubMed, Scopus, and Web of Science) and to identify the gaps in knowledge (Chapter 3).

3. To summarise the methods used in this thesis to analyse the relationship between CVD and workforce participation and social interaction, including data sources, general statistical methods, and ethics approval (Chapter 4).

4. To use cross-sectional analysis to quantify levels of workforce participation of working-age people with CVD compared with people without CVD and how this varies by CVD subtype, population sub-group, and physical disability (Chapter 5).

5. To use longitudinal analysis to investigate the relationship between incident CVD – ascertained from hospital and death records –and exit from the workforce – ascertained using follow-up survey data – among people without CVD and who had been working at baseline, and how this varies by incident CVD subtype, population sub-group, and physical disability (Chapter 5).

6. To use cross-sectional analysis to quantify the association between CVD and social interaction, using social isolation and four social interaction components (social visits per week, telephone contacts per week, social group meetings per week, and the number of people to depend on) from the Duke social support index subscale in people with CVD compared with people without CVD, as well as how the association varies by CVD subtype, population sub-group, and physical disability (Chapter 6).

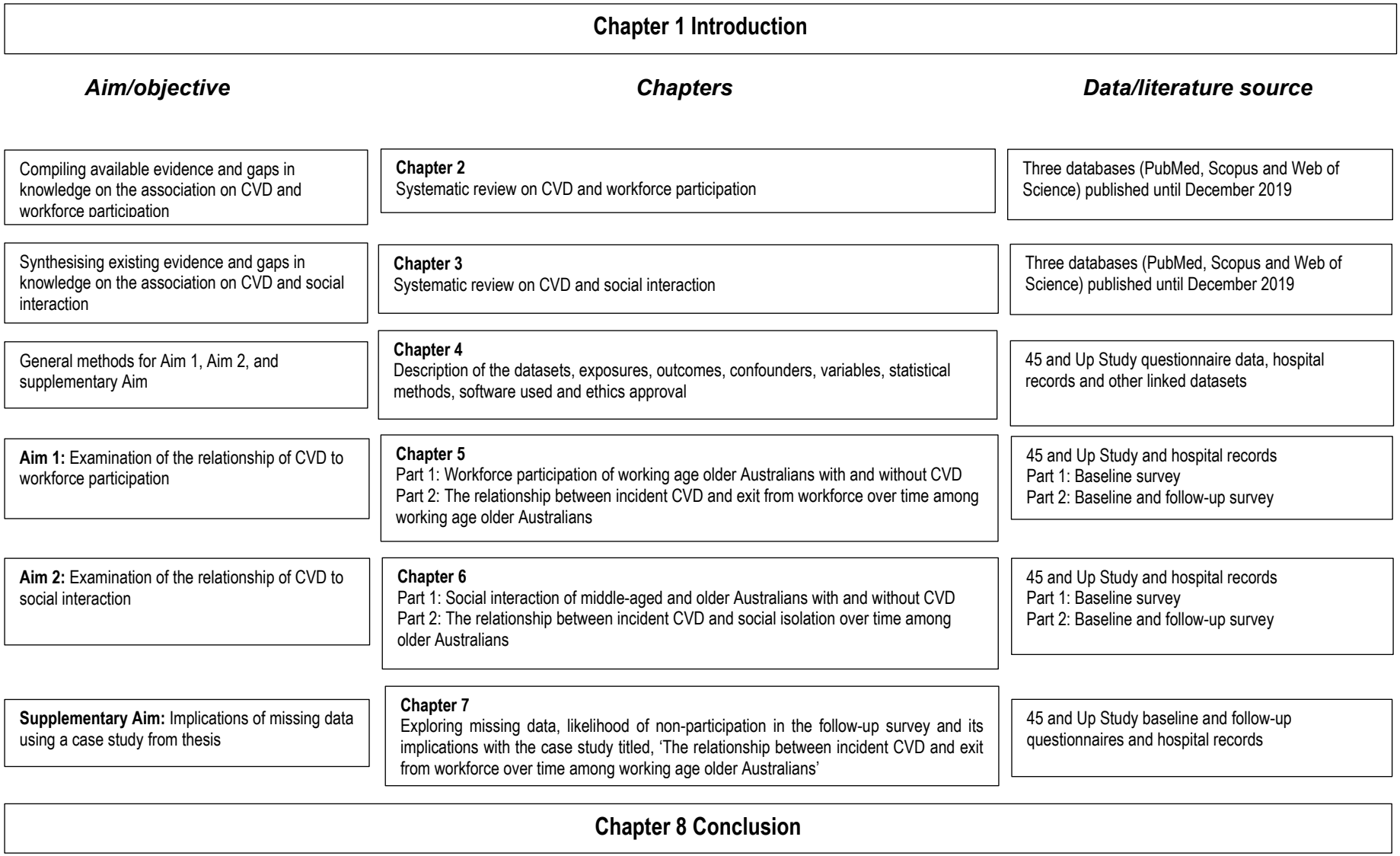
7. To use longitudinal analysis to examine the relationship between incident CVD and becoming socially isolated – ascertained using follow-up survey data – among people without CVD at baseline and who had not been socially isolated at baseline, and how this varies by incident CVD subtype, population sub-group, and physical disability (Chapter 6).

8. To investigate implications of missing data, particularly due to non-participation in the follow-up surveys (Chapter 7).

9. To bring together and discuss the importance of the findings across the different components of this thesis (Chapter 8).

The above-mentioned objectives will provide a thorough investigation on the relationship of CVD to two important person-centred outcomes – workforce participation and social interaction – and form the structure of this thesis (**Figure 1.1**).

Figure 1.1 Summary of thesis structure



1.3 Author's contribution

The projects on person-centred outcomes have been ongoing research within the Epidemiology for Policy and Practice group at the National Centre for Epidemiology and Population Health with the leadership of Professor Emily Banks. For my doctoral research, I was responsible for synthesising evidence on two person-centred outcomes for CVD survivors via conducting two systematic reviews, planning the analyses for each of the four empirical studies and one supplementary study, undertaking the analyses, and writing and interpreting the results of each study. The thesis panel provided feedback and input into each stage of the process particularly in the design of the analyses and input into drafting the manuscripts that some of the study chapters are based on. The panel included: Dr Grace Joshy, Associate Professor Rosemary Korda, Professor Emily Banks and Dr Ellie Paige, all from the Australian National University, Australia. In addition, Mr Md Moustafa Kamal and Dr Angus McLure,- both from the ANU, acted as independent reviewers for the screening of articles and quality assessment of the included articles for the two systematic reviews.

1.4 Conference presentations and publications

Chapters 2, 3, 5 and 6 are studies that formed the basis of manuscripts. In addition, chapter 7 was part of a conference paper [59] and is expected to be part of a full paper. My expertise and skills on coding for workforce participation definition as presented in chapter 5 of the thesis resulted in a contribution to one related published paper [60]. Aside from these, the core papers and conference presentations resulting from the thesis are listed below.

1.4.1 Conference presentations

1. Bin Sayeed MS, Joshy G, Banks E, Korda R. Social interaction of middle-aged and older people with and without cardiovascular disease in Australia. *World Congress of*

Epidemiology, 3-6 September 2021, Melbourne, Australia. (Int J Epidemiol. 2021 Sep; 50 (Supplement_1) dyab168-080, doi: 10.1093/ije/dyab168.080): (IEA World Congress of Epidemiology 2021 - Scientific Program Abstract).

2. Bin Sayeed MS, Joshy G, Banks E, Korda R. Incident CVD and change in workforce participation: A longitudinal study of older working-age Australians. *Society for Epidemiology Research Virtual Conference,* 15-18 December 2020.

3. Bin Sayeed MS, Kamal MM, McLure A, Paige E. A systematic review on workforce participation of people with cardiovascular disease compared to those without cardiovascular disease. *The International Alliance of Research Universities (IARU) – Ageing, Longevity and Health (ALH) Virtual graduate student conference,* 30 September -2 October 2020.

4. Bin Sayeed MS, Joshy G, Banks E, Korda R. Workforce participation of working age older people with cardiovascular disease in Australia. *Australasian Epidemiological Association Annual Scientific Meeting 2019*, 23-25 October, 2019, Brisbane, Queensland, Australia.

1.4.2 Publications as peer-reviewed articles and protocols

1. 4.2.1 Published

1. *Peer-reviewed article*

   - Bin Sayeed MS, Joshy G, Paige E, Banks E, Korda R. Cardiovascular disease subtypes, physical disability and workforce participation: A cross-sectional study of 163,562 middle-aged Australians. *PLoS One*. 2021 Apr 8;16(4):e0249738. doi: 10.1371/journal.pone.0249738 , PMID: 33831054. Clickable weblink to the published paper.

2. *Systematic review protocols*

   - Bin Sayeed MS, Kamal MM, McLure A, Paige E, Joshy G, Banks E, Korda R. Workforce participation following cardiovascular disease: protocol for a systematic review and meta-analysis. PROSPERO 2019 CRD42019119356 Available from: *https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019119356*

   - Bin Sayeed MS, Kamal MM, McLure A, Paige E, Joshy G, Banks E, Korda R. Social interactions following cardiovascular disease: protocol for a systematic review and meta-analysis. PROSPERO 2020 CRD42020165442 Available from: *https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020165442*

1. 4.2.2 Manuscript in preparation (for peer-reviewed articles)

1. Bin Sayeed MS, Kamal MM, McLure A, Paige E, Joshy G, Banks E, Korda R. A systematic review on workforce participation of people with cardiovascular disease compared to those without cardiovascular disease. (From Chapter 2).

2. Bin Sayeed MS, Kamal MM, Paige E, Joshy G, Banks E, Korda R. A systematic review on social interaction of people with cardiovascular disease compared to those without cardiovascular disease. (From Chapter 3).

3. Bin Sayeed MS, Joshy G, Banks E, Korda R. Incident CVD and change in workforce participation: A longitudinal study of older working-age Australians. (Second study from Chapter 5).

4. Bin Sayeed MS, Joshy G, Banks E, Korda R. Social interaction of middle-aged and older people with and without cardiovascular disease in Australia: A cross-sectional study of 266 504 middle-aged and older Australians. (First study from Chapter 6).

5. Bin Sayeed MS, Joshy G, Banks E, Korda R. Incident CVD and becoming socially isolated: A longitudinal study of middle-aged and older Australians. (Second study from Chapter 6).

CHAPTER 2 Systematic review on workforce participation and CVD

2.0 Chapter summary

An increasing number of people are living with cardiovascular disease (CVD), but the workforce participation of those with CVD compared to those without CVD is poorly understood. The aim was to review literature that assessed the association of workforce participation pattern of people living with CVD compared to those without CVD. A systematic search of studies published until December 2019, using PubMed, Scopus, and Web of Science databases was undertaken. Eligible studies were those that compared workforce participation patterns in people of working age with CVD to those of people without CVD. The study characteristics, details on analysis methods, and associations between exposures and outcomes were extracted. Twenty-seven articles were included with study populations from Europe, North America, Asia, and Australia. Workforce participation-related outcomes were divided into three types: non-participation in paid work, work performance, and pension receipt. Compared to those without CVD, people living with CVD had a higher tendency for non-participation, poor work performance, and higher pension receipts. However, there is limited evidence on whether workforce participation varies with CVD subtypes and population sub-groups, including physical disability. Therefore, further research is recommended to address the gaps as identified in this systematic review. These might improve the understanding of the relationship of CVD to workforce participation and provide evidence to choose appropriate interventions for people living with CVD or the population subgroups needing support to lead a better-quality life with CVD.

The PROSPERO registration number: **CRD42019119356.**

2.1 Introduction

Improved medical treatment and lifestyle changes have contributed to higher rates of survival of cardiovascular disease (CVD) all over the world [61, 62]. A rise in the proportion of working-age people living with CVD is expected because of higher CVD prevalence among the aging population and continual increase of retirement age [63]. Therefore, it is crucial to understand the long-term effects of CVD survivorship on workforce participation patterns to safeguard against the social and economic burden of an aging society [64].

A significant proportion of those living with CVD experiences different problems such as fatigue [65], cognitive deficits, anxiety, and depression [66, 67], all of which might be chronic. Persons living with CVD are more likely to fall into poverty [9, 68] and lose their income and savings due to needing to pay for health care [49, 69, 70]. The long-term effects of CVD may cause impairments that reduce physical, psychological and social functioning including the obtainment or continuation of paid work [18]. Because of the aging population, an increase in retirement age and higher survival after CVD diagnosis, the number and proportion of working-age people with CVD is increasing. However, previous studies have indicated that appropriate interventions can improve the quality of survivorship after diagnosis of CVD [71].

Many people living with CVD want to and are able to return to work after diagnosis and treatment [72]. Often returning to work after CVD is considered as indicative of complete recovery and regained normalcy, despite many people still needing support at the workplace [73]. Participation in the paid workforce is associated with a higher quality of life [50]. The encouragement of those living with CVD to return to work thus benefits aging societies by improving workforce participation reducing the number of people needing disability benefits and, for the individual, improving quality of life [74].

Some reviews suggest that CVD or specific subtypes of CVD like stroke and coronary heart disease (CHD) are associated with poor work performance [75], higher financial burden [18] and productivity loss [76]. What these reviews lack is the synthesis of evidence that demonstrates the direct comparison of workforce participation related outcomes of those with CVD versus healthy controls. There is also a limitation in understanding which CVD sub-types are most deleterious for exit from paid workforce. This literature review will improve the understanding of the association of workforce participation patterns with different CVD sub-types. An improved understanding of the effects of CVD on workforce participation will help not-for-profit organisations better support people living with CVD. This will also provide a stronger evidence base to support the return to work more optimally or continuation of work in those with CVD [77, 78].

This chapter aimed to summarise the literature on workforce participation related outcomes amongst working-age people with CVD compared with people without CVD. Secondarily, it examined whether there is variation in workforce participation across different subtypes of CVD or among different population subgroups.

2.2 Methods

2.2.1 Search strategy

We searched PubMed, Scopus, and Web of Science until December 31, 2019, to identify articles evaluating the association between CVD and workforce participation. The search terms were developed in consultation with Australian National University (ANU) librarian (Rachel Karasick, Information Access Coordinator, Hancock Library, ANU, Australia) and the search terms included combinations of: ‘atherosclerosis’, ‘cardiocerebrovascular disease’, ‘cardiovascular disease’, ‘cardiovascular event’, ‘cerebral infarction’, ‘cerebrovascular attack’, ‘cerebrovascular disease’, ‘cerebrovascular disorder’, ‘coronary artery disease’, ‘coronary disease’, ‘coronary heart disease’,

'heart attack', 'heart disease', 'heart failure', 'ischaemic heart disease', 'myocardial infarction', 'myocardial ischemia', 'myocardial ischaemia', 'peripheral arterial disease', 'stroke' and 'workforce participation', 'labour force participation', 'return to work', 'work resumption', 'employment', 'occupation', 'vocation', 'sick leave', 'disability pension', 'unemployment', 'early retirement', 'absenteeism', 'working hour', 'subsidized salary' and 'subsidized job'. The full search terms are presented in '*Appendix 1: S2.1'*. There was no restriction on study year or language. Cohort and cross-sectional studies were included. Conference abstracts, case reports, case series, and qualitative studies were excluded. The studies were excluded if exposure-outcome associations of interest were not available, there was no appropriate comparator group, results for people of working age were not reported or study participants had a pre-existing disease or health conditions (such as hyperlipidaemia). The study was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guideline [79] (*Appendix 1: Table S2.2.1*) and registered in PROSPERO (CRD42019119356).

2.2.2 Data extraction and quality assessment

All citations identified through our search strategy were imported into EndNote version X8 (Thompson Reuters, New York, NY, USA) and Covidence (*https://www.covidence.org*). The titles and abstracts of identified articles and full texts were reviewed independently by two reviewers (I and one of Md Moustafa Kamal or Angus McLure), with the final inclusion of studies decided through consensus. Data on exposures, outcomes, first author, year of publication, study design, geographical location, study setting (hospital or community), study period, participant age (mean, median or range), per cent men, number of participants with CVD, number in the comparison group, CVD type, outcomes, follow-up time, analysis method, effect measures (e.g., hazard ratio (HR), odds ratio (OR), etc), point estimates, 95% confidence interval (CI) and adjustments/stratifications were extracted.

2.2.3 Quality assessment

The methodological quality of included studies was assessed by using the Newcastle-Ottawa Scale (NOS) adapted for cohort [80] and cross-sectional [81] studies *(Appendix 1: S2.3)*. This validated scoring scale assesses the quality of a study across three domains: selection of participants; comparability of controls; and the ascertainment and reporting of outcomes. Another researcher (either Angus McLure or Md Moustafa Kamal) did the quality assessment independently and the final score of the studies was decided through consensus.

2.3 Results

After removing duplicates, there were a total of 4720 studies across the three databases. Of these, 4641 were excluded after reviewing the title and abstract. Of the remaining 79 studies, 52 studies were excluded following full-text review (*Appendix 1: Table S2.4.1, Table S2.4.2*), leaving 27 studies [39, 41, 52, 53, 82-104] for inclusion in this systematic review (**Figure 2.1**). Fourteen of the included studies were cohort studies among which six studies were of high quality [52, 84, 88, 91, 97, 104] and the remaining studies [85-87, 89, 90, 93, 101, 103] were of medium quality. All cross-sectional studies [39, 41, 53, 82, 83, 92, 94-96, 98-100, 102] were of medium quality (*Appendix 1: Table S2.5.1 and Table S2.5.2*).

2.3.1 Characteristics of the included studies

Twenty-seven studies included in this review had participants residing in twenty-five different countries, the majority of which were from Europe. The studies were primarily from population-level data published between 1999 and 2019. Most participants were aged <65years **(Table 2.1)**. Five cross-sectional studies [41, 83, 94, 98, 100] included participants beyond the usual working age. These studies were included because it was possible to derive workforce non-participation related outcomes among those in the working age. The number of included participants ranged

from 2,218 [91] to 7,803,694 [93] and the percentage of men varied from 18% [99] to 81.5% [97] (**Table 2.2**). The outcomes were categorized into four groups: non-participation in paid work, performance in paid work, pension receipt and miscellaneous exit from paid work (*Appendix 1: Table S2.5.3*). The reported exposures (CVD or its subtypes) were mostly self-reported (*Appendix 1: Table S2.5.4*).

Figure 2.1 PRISMA flow diagram of study selection in the systematic review on CVD and workforce participation

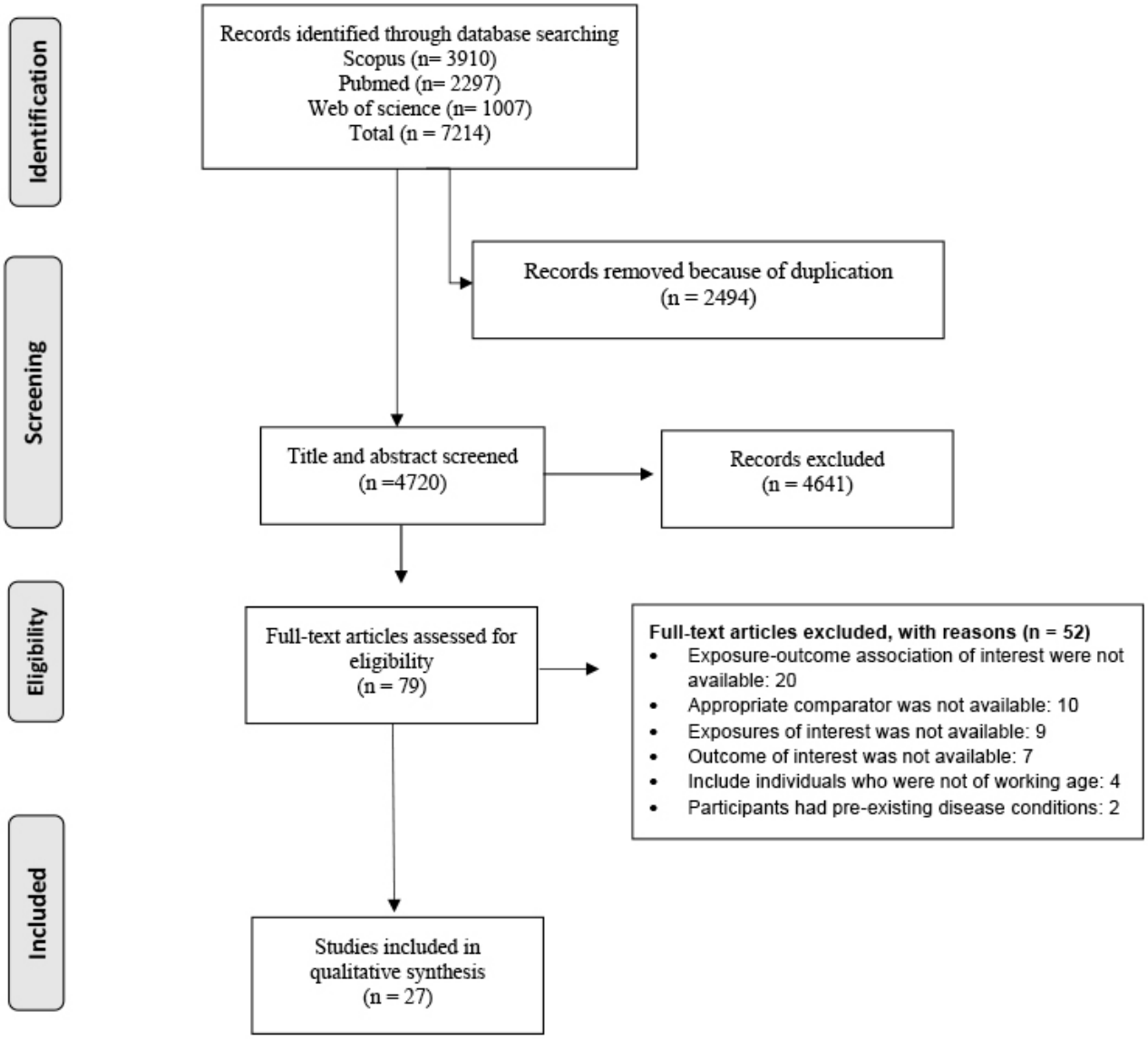


Table 2.1 Summary of study design, data sources and location for included studies in systematic review on CVD and workforce participation

Study	Study Design	Surveillance period	Data Source	Location
Alavinia 2008 [82]	Cross-sectional	2004	Survey on Health and Ageing in Europe (SHARE study)	10 European countries
Anesetti-Rothermel 2011 [39]	Cross-sectional	2007	Medical Expenditure Panel Survey (MEPS)	USA
Bielecky 2015 [83]	Cross-sectional	2003-2010	Canadian Community Health Survey (CCHS), 2003-2010	Canada
Brækkan 2016 [84]	Cohort	1994-2008	HUNT	Norway
deBoer 2018 [85]	Cohort	2007-2009	Netherlands Working Conditions Cohort Study (NWCCS)	Netherlands
Ervasti 2016 [86]	Cohort	2003-2004	Finnish Public Sector Study	Finland
Feigl et al 2019 [103]	Cohort	2004-2007 2010-2013 2015	Survey of Health, Ageing, and Retirement in Europe (SHARE)	21 European countries
Garland et al 2019 [104]	Cohort	2005-2010	Canadian Hospitalization and Taxation Database (C-HAT)	Canada
Hemingway 2007 [87]	Cohort	2000-2003	Finland postal survey	Finland
Holden 2011 [41]	Cross-sectional	2004-2005	The Australian Work Outcomes Research Cost–benefit (WORC) project	Australia
Holland 2009 [52]	Cohort	1996-2001	VAL, LOUISE	Sweden
Jespersen 2013 [88]	Cohort	1998-2009	Copenhagen City Heart Study (CCHS)	Denmark
Johansen 1999 [53]	Cross-sectional	1996-1997	National Population Health Survey (NPHS)	Canada
Kang 2015 [89]	Cohort	2006-2012	Korean Longitudinal Study of Ageing (KLoSA)	Korea
Kouwenhoven-Pasmooij 2016 [90]	Cohort	2004-2005	Survey of Health, Ageing, and Retirement in Europe (SHARE)	11 European countries
Kruse 2009 [91]	Cohort	1980-2003	Danish National Cohort Study (DANCOS)	Denmark
LiRanzi 2013 [92]	Cross-sectional	2004-2005	Italian Health Interview Survey	Italy
Maaijwee 2014 [93]	Cohort	1980-2010	FUTURE (Follow-Up of TIA and stroke patients and Unelucidated Risk factor Evaluation) study	Denmark
Marrett 2013 [94]	Cross-sectional	2010	5 EU National Health and Wellness survey (NHWS) and US NHWS	5 European countries and the USA
Nakaya 2016 [95]	Cross-sectional	2012	Shichigahama Health Promotion Project	Japan

Oude Hengel et al 2019 [101]	Cohort	2010-17	Study on Transitions in Employment, Ability and Motivation (STREAM)	Netherlands
Pit 2013 [96]	Cross-sectional	2006-2008	45 and up Study	Australia
Smedegaard 2017 [97]	Cohort	1997-2012	Danish nationwide retrospective cohort study	Denmark
Stein 2006 [98]	Cross-sectional	2000-2001	Canadian Community Health Survey (CCHS)	Canada
Schnitzler et al 2019 [102]	Cross-sectional	2008-2009	Disability Health Survey	France
vandenBerg 2017 [99]	Cross-sectional	2011-2012	Dutch health care employees	Netherlands
Zhang 2016 [100]	Cross-sectional	2010	Canadian Community Health Survey 2010	Canada

EU= European Union, USA= The United States of America, CVD= cardiovascular disease, VTE= Venous thromboembolism, CVD= cardiovascular disease, MI= Myocardial infarction, PAD= Peripheral arterial disease.

Table 2.2 Sample sizes and participant characteristics of included studies in systematic review on CVD and workforce participation

Study	Age (range or mean [SD])	Sample size	%Men*	CVD group (n=)[#]	Comparator group (n=)[#]
Alavinia 2008 [82]	50-64yr	11462	46% of total	720 (Heart attack (HA)) 234 (Stroke)	10742 (HA ref) 11228 (stroke ref)
Anesetti-Rothermel 2011 [39]	18-64yr	12860	51% of total	588 (Heart disease (HD)) 57 (Stroke)	12272 (HD ref) 12803 (stroke ref)
Bielecky 2015 [83]	25–74 yr	120005	52% of total	2591	117414
Brækkan 2016 [84]	41.3 (11.2) yr (no VTE) 45.1 (9.8) yr (VTE)	66005	49% among no VTE 53% among VTE	384	65621
deBoer 2018 [85]	15-62yr	Baseline= 21747 after1yr=10,038 after 2yr=7636	48% of total	296 (1-yr follow-up) 236 (2-yr follow-up)	6291=1-yr follow-up ref 4761=2-yr follow-up ref
Ervasti 2016 [86]	50.8 (7.7) for control 52.1 (7.4) for cardio	14514	26% in control 29% in heart or cerebrovascular disease	1282	9716
Feigl et al 2019 [103]	50-63 yr	Ranged from 27,395 to 10,490 in wave 1 to wave 6 surveys	Ranged from 43% to 46% in wave 1 to wave 6 surveys	not stated	not stated
Garland et al 2019 [104]	40-61 at the time of CVD event	Acute MI=1839773 Cardiac arrest= 308418 Stroke= 892876		Acute MI: 19 129 Cardiac arrest: 1043 Stroke: 4395	Acute MI: 1 820 644 Cardiac arrest: 307 375 Stroke: 888 481
Hemingway 2007 [87]	17-65yr	33148	20% of total	341	14392
Holden 2011 [41]	18-70yr	78430 =Absenteeism 77455 = presenteeism	35% of total	784=Absenteeism CVD 763=presenteeism CVD	77646=Absenteeism ref, 76680 =presenteeism ref
Holland 2009 [52]	31-59yr	717054	50% for ref. group 74% for IHD	968 but for calculation 600= qualified	716,086
Jespersen 2013 [88]	<65yr [40-56yr for reference and 48-61yr for study cohort]	7187	41% for angiography normal 62% for angiographically diffuse, 76% = 1 Vascular disease (VD), 86%= 2 VD, 89%= 3 VD and 46% for ref grp	4415	2772
Johansen 1999 [53]	35-64yr	33686	58% of total[$]	1182	32504
Kang 2015 [89]	54.33 (7) yr	3,371	68% of total	80 = cardiovascular disease 22= cerebrovascular disease	3291=CVD ref, 3349=cerebrovascular disease ref
Kouwenhoven-Pasmooij 2016 [90]	55.4 (3.6) yr at baseline	5182	55% of total	231= heart disease (HD) 47= stroke	4951 = HD ref 5135 = stroke ref
Kruse 2009 [91]	<70yr	2218	79% =CHD, 76%=Reference	549	1663
LiRanzi 2013 [92]	45–59 yr	18547	63% of total	259 = angina 578 =MI 203 = stroke	11122 =angina ref 17969=MI ref 18344= stroke ref

Maaijwee 2014 [93]	18–50 yr	7803694	41%=TIA 48%= ICH 43%= IS	215=TIA 54= ICH 425= IS	7,803,000
Marrett 2013 [94]	58.1(13.0) yr>PAD in 5EU 62.4 (11.3) yr>PAD in US 6.3 (15.8) yr >No PAD in 5EU 48.0 (16.5) yr>No PAD in US	57,805 =5EU 75,000 =US	47%>PAD in 5EU 60%>PAD in USA 49% >No PAD in 5EU 48%>No PAD in US	743=5EU 777=US	57062=5EU ref 74223=US ref
Nakaya 2016 [95]	20-64 yr	2588	50% of total, 58% of employed and 26% of unemployed	7= stroke and 47=myocardial infarction	2581 = stroke ref 2543= MI ref
Oude Hengel et al 2019 [101]	45–64 yr	9160	Not reported	984	4161
Pit 2013 [96]	45 - 64 yr	38112	43% of total	509 = heart disease 133= stroke	not clearly mentioned, those without HD
Smedegaard 2017 [97]	19->85years but the results of those aged 19-59 years were recorded	33,785	Not directly mentioned for 19-59 years old category	1725 but not directly mentioned for 19-59 years old category	The results for 19-59 years old were considered. The number was not clearly mentioned
Stein 2006 [98]	30 - 65 yr	122490	82% (both study and control)	20415	102075
Schnitzler et al 2019 [102]	12 yr and above	130880	49.30%	not clearly mentioned	not clearly mentioned
vandenBerg 2017 [99]	49 (11) yr	8364	18%	1066	2858
Zhang 2016 [100]	40.9(0.1)[#] yr	28678	54.60%	631	28047

*Rounded to whole number, [#] they may not add-up to the total because of outcomes missingness or selection of reference group as those who had no CVD and no other chronic disease, [#]Comparison to those of people without CVD or those without the specified CVD subtype, yr= Years, VTE= Venous thromboembolism, SD= standard deviation, CVD= cardiovascular disease, Ref= reference, HA= heart attack, HD= Heart disease, MI= myocardial infarction, TIA= Transient ischemia, ICH= intracerebral haemorrhage, IS= ischaemic stroke, CHD= coronary heart disease, VD= Vascular disease, [#]SE= Standard error of mean, *NR= Not reported, [$]this is obtained indirectly and the data used for analysis did not provide the ratio

2.3.2 Association of non-participation in paid work and cardiovascular disease

Seventeen studies [52, 53, 82, 85, 88-93, 95-97, 101-104] reported outcomes related to non-participation in paid work in people with versus without CVD. The exposures were CVD [53, 89, 90, 96] or a specific CVD subtype (such as stroke [82, 90, 92, 93, 95, 96, 104], MI [82, 92, 95, 97], angina [88, 92], cerebrovascular disease [89] and CHD [52, 91]). Though the studies were different in terms of study types, methods used, and adjustment variables considered, most showed the same direction for the relationship, which is- people with versus without CVD were more likely to have adverse outcomes.

There was some evidence that the strength of the association varied by the type of outcome (retired or unemployed), CVD subtype, and time since the CVD event. Within individual studies and overall, the relationship between CVD and retirement was stronger than the relationship between CVD and unemployment (**Table 2.3**). For example, working-age people with stroke were 2.6 times more likely to retire (OR=2.6 [95% CI: 1.66-4.07]) and 1.1 times more likely to be unemployed (OR=1.11 [0.53-2.32]) compared to those of people living without CVD [82]. Two studies examined non-participation in the workforce due to ill health, finding that those with CVD were 5.9 times more likely to not be employed due to illness (OR=5.9, 95% CI: 3.8-9.2) [53] and 1.87 times more likely to be fully retired (OR=1.87, 95% CI: 1.44-2.42) [96] compared with those without CVD. People with severe subtypes of CVD had a higher likelihood of being unemployed, but there is a lot of overlap in the confidence intervals. For example, compared to people without CVD, the likelihood of early retirement in people with stroke and MI was 58% (PR=1.58, (95% CI: (1.19-2.10)) and 36% (PR=1.36, (95% CI: (1.17-1.60)) higher respectively [92]. The role of time since CVD diagnosis is reported in one study [85] which has indicated that- compared to those without CVD, people with CVD had a 27% additional risk of leaving paid employment within one more year after incident CVD.

There were two cross-sectional studies that reported ‘homemaker’ and ‘homemaker/other’ as outcomes related to non-participation in paid-workforce in people with versus without CVD [82, 90]. Both studies had one exposure in common (stroke) but the definition of the outcomes did not match. Both studies have indicated a slightly higher likelihood of being homemaker/other in people with versus without CVD. However, the 95% CI included a null association point estimate (which is 1.00) indicating that the associations were not statistically significant (**Table 2.3**). Therefore, whether people living with CVD had a higher tendency to leave paid workforce via being a homemaker/miscellaneous way compared to that of people living without CVD could not be established based on these cross-sectional investigations.

Table 2.3 Effect sizes of outcomes related to non-participation in paid work of people with CVD in comparison to those without CVD

Study Reference	Exposure	Outcomes	Analysis	Measurement	Point estimate	CI95%
Alavinia 2008 [82]	Heart Attack	Retired	Multivariate association	OR	1.17	0.93-1.49
Alavinia 2008 [82]	Heart Attack	Unemployed	Multivariate association	OR	0.96	0.66–1.40
Alavinia 2008 [82]	Stroke	Retired	Multivariate association	OR	2.60	1.66–4.07
Alavinia 2008 [82]	Stroke	Unemployed	Multivariate association	OR	1.11	0.53–2.32
Alavinia 2008 [82]	Heart Attack	Homemaker	Multivariate association	OR	1.20	0.83–1.75
Alavinia 2008 [82]	Stroke	Homemaker	Multivariate association	OR	1.27	0.65–2.47
deBoer 2018 [85]	Cardiovascular disease	Exit from paid employment	Percent ratio***	RR	2.75	N/A
Feigl et al 2019 [103]	Heart disease	Employment	Poisson models	RR	0.85	0.80-0.89
Feigl et al 2019 [103]	Heart disease	Additional days missed/year (as count variable)	Zero-inflated Poisson regression		5.10	0.43-9.86
Feigl et al 2019 [103]	Heart disease	Additional hours missed/week (as count variable)	Zero-inflated Poisson regression		-1.19	-2.19, -0.18
Feigl et al 2019 [103]	Heart disease	Intention to retire early	Poisson models	RR	1.10	1.00-1.20
Feigl et al 2019 [103]	Stroke	Employment	Poisson models	RR	0.78	0.71-0.85
Feigl et al 2019 [103]	Stroke	Additional days missed/year (as count variable)	Zero-inflated Poisson regression		7.10	-7.7 to 22.1
Feigl et al 2019 [103]	Stroke	Additional hours missed/week (as count variable)	Zero-inflated Poisson regression		-2.56	-4.48 to -0.64
Feigl et al 2019 [103]	Stroke	Intention to retire early	Poisson models	RR	1.16	1.00 to 1.34
Garland et al 2019 [104]	Acute myocardial infarction	Working (three year after the event)	Difference in % (health event minus control)		-5.10	-
Garland et al 2019 [104]	Cardiac arrest	Working (three year after the event)	Difference in % (health event minus control)		-12.70	-
Garland et al 2019 [104]	Stroke	Working (three year after the event)	Difference in % (health event minus control)		-19.80	-
Holland 2009 [52]	Ischaemic heart disease	Likelihood of leaving employment	Binary logistic regression	OR	3.95	3.23–4.83
Jespersen 2013 [88]	Angiographically normal	Premature exit from workforce	Cox proportional hazard regression	HR	1.30	1.0-1.6
Jespersen 2013 [88]	Angiographically diffuse	Premature exit from workforce	Cox proportional hazard regression	HR	1.40	1.0-1.8

Johansen 1999 [53]	Heart disease	Not employed because illness/disability	Weighted logistic regression	OR	5.90	3.80-9.20
Johansen 1999 [53]	Heart disease	Employed	Weighted logistic regression	OR	0.40	0.30-0.70
Kang 2015 [89]	Cardiovascular disease	Early retirement	Cox proportional hazard regression	HR	2.12	0.98−4.59
Kang 2015 [89]	Cerebrovascular disease	Early retirement	Cox proportional hazard regression	HR	1.63	0.39−6.75
Kouwenhoven-Pasmooij 2016 [90]	Heart disease	Unemployment	Multinomial regression	OR	0.91	0.46–1.82
Kouwenhoven-Pasmooij 2016 [90]	Heart disease	Early retirement	Multinomial regression	OR	1.61	1.15–2.27
Kouwenhoven-Pasmooij 2016 [90]	Stroke	Unemployment	Multinomial regression	OR	1.36	0.41–4.53
Kouwenhoven-Pasmooij 2016 [90]	Stroke	Early retirement	Multinomial regression	OR	1.18	0.50–2.76
Kouwenhoven-Pasmooij 2016 [90]	Heart disease	Homemaker/other	Multinomial regression	OR	1.46	0.79–2.71
Kouwenhoven-Pasmooij 2016 [90]	Stroke	Homemaker/other	Multinomial regression	OR	1.68	0.49–5.69
Kruse 2009 [91]	Coronary heart disease	Unemployment	Percent ratio***	RR	1.20	N/A
Kruse 2009 [91]	Coronary heart disease	Early retired	Percent ratio***	RR	1.67	N/A
Kruse 2009 [91]	Coronary heart disease	Risk of labour market withdrawal	Cox regression	HR	1.32	1.11-1.57
LiRanzi 2013 [92]	Angina pectoris	Early retirement	Poisson regression model with robust standard error	PR	1.38	1.09–1.76
LiRanzi 2013 [92]	Stroke	Early retirement	Poisson regression model with robust standard error	PR	1.58	1.19–2.10
LiRanzi 2013 [92]	Myocardial infarction	Early retirement	Poisson regression model with robust standard error	PR	1.36	1.17–1.60
Maaijwee 2014 [93]	Stroke (TIA, ischemic stroke, or intracerebral haemorrhage)	Unemployment Full or partial	Multiple logistic regression	OR	2.30	1.80–2.90
Maaijwee 2014 [93]	Stroke (ischemic stroke, or intracerebral haemorrhage)	Unemployment Full or partial	Multiple logistic regression	OR	4.00	3.00–5.30

Nakaya 2016 [95]	Myocardial infarction	Unemployment	Logistic regression	OR	3.90	0.70–22.7
Nakaya 2016 [95]	Stroke	Unemployment	Logistic regression	OR	1.50	0.70–2.90
Oude Hengel et al 2019 [101]	Cardiovascular disease	Exit from paid work via disability pension	Proportional sub-hazard models measuring sub distribution hazard ratio	SHR	2.13	1.44 -3.16
Oude Hengel et al 2019 [101]	Cardiovascular disease	Exit from paid work via unemployment benefits	Proportional sub-hazard models measuring sub distribution hazard ratio	SHR	1.08	0.85-1.36
Oude Hengel et al 2019 [101]	Cardiovascular disease	Exit from paid work via early retirement benefits	Proportional sub-hazard models measuring sub distribution hazard ratio	SHR	1.03	0.86-1.23
Oude Hengel et al 2019 [101]	Cardiovascular disease	Exit from paid work via economically inactive	Proportional sub-hazard models measuring sub distribution hazard ratio	SHR	0.73	0.40-1.31
Pit 2013 [96]	Heart disease	Fully retired due to ill health	Multinomial logistic regression	OR	1.87	1.44-2.42
Pit 2013 [96]	Heart disease	Partly retired due to ill health	Multinomial logistic regression	OR	1.75	1.11-2.76
Pit 2013 [96]	Stroke	Fully retired due to ill health	Multinomial logistic regression	OR	2.83	1.69-4.74
Pit 2013 [96]	Stroke	Partly retired due to ill health	Multinomial logistic regression	OR	1.77	0.64-4.88
Smedegaard 2017 [97]	Myocardial infarction	Unemployment	Percent ratio***	PRR	4.07	N/A
Smedegaard 2017 [97]	Myocardial infarction	Early retirement	Percent ratio***	PRR	1.70	N/A
Smedegaard 2017 [97]	Myocardial infarction	Working	Percent ratio***	PRR	0.82	N/A
Schnitzler et al 2019 [102]	Stroke	Working	Prevalence ratio	PR	0.50	-

PR= prevalence rate, HR= hazard ratio, IRR= incident rate ratio, RR= relative risk ratio, PRR= prevalence rate ratio, OR= odds ratio, SHR= Sub distribution hazard ratio; ***(95%CI)*:** 95% confidence interval; N/A= not available; *** manually calculated. The study with multiple adjusted variable results, the effect sizes with maximally adjusted results were presented, study results at different follow-up periods, the effect size at the longest follow-up periods were reported

2.3.3 Association of work performance and cardiovascular disease

Ten studies [39, 41, 83, 84, 87, 94, 97-100] reported outcomes related to work performance. Some studies reported outcomes of those living with CVD [39, 41, 83, 98-100], with some CVD subtypes (such as angina [87], MI [97], stroke [39] and PAD [94]) in comparison to those of people without CVD or those without the specified CVD subtype. The outcomes related to work performance were reported as either quantitative variables (for example, 'disability days') or qualitative categorical variables (for example, presenteeism, the problem of workers' being on the job but, because of illness or other medical conditions, not fully functioning [105]). Although the strength of the association varied, overall studies showed that those with CVD compared to those without were more likely to be absent from work, show higher levels of presenteeism and had higher numbers of disability or sick leave days. For example, compared to people without CVD, those living with CVD had 4 times more disability days [39] and were 2 times more likely to show presenteeism [83]. Substantial differences in exposure outcomes, analytical methods, and adjustments meant that methods of pooling results (such as meta-analysis) were not possible (**Table 2.4**).

Table 2.4 Effect sizes of outcomes related to work performance of people with CVD in comparison to those without CVD

Study reference	Exposure	Outcomes	Analysis	Measurement	Point estimate	95%CI
Anesetti-Rothermel 2011 [39]	Heart disease	Disability days	Linear regression	Beta	4.06	1.18(SE)
Anesetti-Rothermel 2011 [39]	Stroke	Disability days	Linear regression	Beta	13.40	5.89(SE)
Bielecky 2015 [83]	Heart disease	Presenteeism	Modified Poisson regression	PR	2.01	1.60–2.53
Brækkan 2016 [84]	Venous thromboembolism	Work-related disability	Cox proportional hazard regression	HR	1.44	1.12–1.85
Hemingway 2007 [87]	Angina	Sickness absence	Cox proportional hazard regression	HR	2.90	2.51-3.36
Holden 2011 [41]	Cardiovascular disease	Absenteeism	Negative binomial logistic regression	IRR	1.17	1.03−1.32
Holden 2011 [41]	Cardiovascular disease	Presenteeism	Multinomial logistic regression	RRR	1.15	0.84−1.58
Marrett 2013 [94]	Peripheral arterial disease	Absenteeism	Percent ratio***	RR	3.83	N/A
Marrett 2013 [94]	Peripheral arterial disease	Overall work impairment	Percent ratio***	RR	1.70	N/A
Marrett 2013 [94]	Peripheral arterial disease	Presenteeism	Percent ratio***	RR	1.64	N/A
Smedegaard 2017 [97]	Myocardial infarction	Sick leave	Percent ratio***	PRR	4.54	N/A
Stein 2006 [98]	Heart disease	Work absence	Multiple logistic regression	OR	6.18	2.48–15.37
vandenBerg 2017 [99]	Cardiovascular disease	Sick leave	Logistic regression	OR	6.37	4.90-8.28
Zhang 2016 [100]	Heart disease	Absent workdays due to any health problems	Negative binomial regression	Ratio of expected count	1.73	1.19–2.50
Zhang 2016 [100]	Heart disease	Absent workdays due to chronic and other health problems	Negative binomial regression	Ratio of expected count	3.90	1.86–8.18

Beta= beta-coefficient of the linear regression model, PR= prevalence rate, HR= hazard ratio, IRR= incident rate ratio, RRR= relative risk ratio, PRR= prevalence rate ratio, OR= odds ratio, 95%C= 95% confidence interval; N/A= not available, SE= standard error of mean; *** manually calculated.

2.3.4 Association of pension receipt and cardiovascular disease

Five studies [86, 88, 90, 91, 97] reported outcomes related to receiving disability or aged pension. The exposures were CVD [88, 90] or CVD subtypes such as cerebrovascular disease [86], angina [88], stroke [90], CHD [91] and MI [97]. Though there were variations in the patterns of associations, the reported associations in all studies were in the same direction, were fairly strong, and the results were statistically significant (**Table 2.5**). The increased likelihood of pension receipt ranged from 2.70 (OR=2.68 [95% CI: 1.59-4.52]) for the relationship between CVD and disability pension [90] to 3.48 (OR=3.48 [1.31-9.23]) for the relationship between stroke and disability pension [90]. In presence of other co-morbid conditions, the risk varied for a particular CVD subtype. For example, the risk of getting a disability pension for angiographically normal and angiographically diffuse patients was 2.7 and 3 times higher respectively compared to people without CVD [88]. The risk of pension receipt also varied by the type of pension. For example, people with MI had 4, 1.5 and 5 times more likely to receive a disability pension, pension and subsidized job respectively compared to those of people living without MI [97]. Since there was also a small number of studies, it was not clear whether the relationship varied by CVD subtypes. Estimation of the pooled overall effect size by combining several studies was also not possible because of heterogeneity of reported associations and adjusted variables (**Table 2.5**).

Table 2.5 Effect sizes of outcomes related to pension receipt of people with CVD in comparison to those without CVD

Study Reference	Exposure	Outcomes	Analysis	Measurement	Point estimate	95%CI
Ervasti 2016 [86]	Heart or cerebrovascular disease	Disabiliy pension_All-cause disability pension	Cox proportional hazard regression	HR	2.88	2.50-3.31
Jespersen 2013 [88]	Angiographically normal	Disability pension	Cox proportional hazard regression	HR	2.70	2.00-3.60
Jespersen 2013 [88]	Angiographically diffuse	Disability pension	Cox proportional hazard regression	HR	3.00	2.00-4.40
Kouwenhoven-Pasmooij 2016 [90]	Heart disease	Disability pension	Multinomial regression	OR	2.68	1.59–4.52
Kouwenhoven-Pasmooij 2016 [90]	Stroke	Disability pension	Multinomial regression	OR	3.48	1.31–9.23
Kruse 2009 [91]	Coronary heart disease	Age pensioner	Percent ratio***	RR	5.33	N/A
Smedegaard 2017 [97]	Myocardial infarction	Disability pension	Percent ratio***	PRR	4.00	N/A
Smedegaard 2017 [97]	Myocardial infarction	Pension	Percent ratio***	PRR	1.50	N/A

HR= hazard ratio, RR= relative risk ratio, PRR= prevalence rate ratio, OR= odds ratio, SHR= Sub distribution hazard ratio; *(CI95%= 95% confidence interval)*: N/A= not available, *** manually calculated.

2.4 Discussion

This systematic review of 27 studies found clear evidence that CVD is associated with higher exit from paid workforce, lower work performance and higher pension receipt from the government compared with those without CVD. The included studies were published in the last twenty years with populations from developed countries and the sample size ranged from a few thousand to several million. Most of the included studies were of medium quality and there was an equal proportion of cross-sectional and cohort studies. The definitions of exposures and outcomes reported in these studies were partly related to corresponding countries from where study participants were selected. The study types, analysis methods, exposure-outcome associations and adjustment variables in the included studies varied extensively. Hence, meta-analysis and pooled effect size estimation were not possible.

The evidence provided here is consistent with other reviews on the economic and employment effects of CVD [18, 70, 75, 76]. Similar to the current systematic review, the earlier reviews on employment and economic productivity [70], return to work [18], productivity losses [76] and presenteeism [75] have also indicated the adverse role of CVD. The challenge related to the methodological variation of the outcomes analysis, inconsistency in the definitions and measurement of outcomes as documented in the current systematic review was also found in previous systematic reviews [18, 75, 76]. However, unlike previous systematic reviews that included both qualitative and quantitative outcomes, the current review included only those studies that reported quantitative outcomes related to workforce participation of people with versus without CVD. The ways outcomes were defined and grouped in this systematic review also varied from those in previous systematic reviews. For example, in this systematic review, I have grouped outcomes such as, ‘retired’, ‘unemployed’, ‘exit from paid employment’ etc. into outcome groups related to ‘non-participation in paid work’ whereas Chaker et al. [70] grouped outcomes such as ‘unemployment’ , ‘sick leave’, ‘return to work’ etc. into ‘macro-economic productivity’. The primary justification of the ways the outcomes were categorised

in this review was that the categorisation was more specific in providing the estimates and conclusions around the important outcome of non-participation in the workforce. However, despite these differences in how outcomes were categorised and defined, the findings in this systematic review align with those reported in previous systematic reviews.

There are two main pathways through which CVD might lead to decreased workforce participation. The first is through diminished ability to fulfil job requirements, and the second is the preference to taking care of one's health over continuing paid work. Both mechanisms are corroborated by previous studies [106, 107]. Compared to people without CVD, the CVD survivors have reported having higher impaired physical and mental health, either of them adversely affecting fulfilling job requirements [108-110]. Second, people with CVD might choose to leave the paid workforce, fearing that participation in the workforce might deteriorate health conditions because of the work [111]. The disposition to leave paid workforce could also be because of the additional time needed to care for one's health, thus limiting the time to participate in the paid workforce, even though one has the physical and mental ability to work and is keen to participate in the workforce.

To the best of our knowledge, this is the first synthesis of existing empirical evidence on the association of workforce participation patterns and CVD compared with healthy controls. Due to variations in studies included, a meta-analysis could not be done, yet it is evident from these studies that workforce participation related outcomes are lower among people who have had a CVD event compared to those who have not. Though this systematic review adhered to PRISMA guidelines [79] and used a comprehensive search strategy, it had several limitations that are primarily related to included studies. First, there was heterogeneity in all domains of studies, and these encompassed exposures, outcomes, study designs, sources of the exposures and outcomes, data analyses methodologies and adjustment for potential confounders. Thus, it was not possible to properly compare CVD subtypes or to find vulnerable population subgroups. Second, this review did not find any studies from low and

middle-income countries, so findings from this review limit the generalisability of the results to low- and middle-income countries.

Some papers included in this systematic review were cross-sectional investigations which might have contributed to the limitation related to causal inference. In general, estimates of exposure-outcome relationships observed in cross-sectional studies are more than unrelated correlations, as they are based on hypothesis, apriori knowledge and adjustment for relevant confounders. However, the primary limitation of cross-sectional studies is that the temporal link between the outcome and the exposure cannot be determined because both are examined at the same time; they can provide clues about causal relationships but cannot be used for causal inference.

This systematic review demonstrated the positive association of CVD with non-participation in paid work, poor work performance and pension receipt. Different CVD subtypes and non-participation in paid work-related outcomes were investigated in some articles (such as Kouwenhoven-Pasmooi et al [90]). However, there was a lack of formal comparison with a control group without CVD and assessment of variation between CVD subtypes. Therefore, there was limited evidence on whether the relationship of CVD to workforce non-participation varied by CVD subtypes. Although not specifically examined in this systematic review, other studies have found that workforce participation is lower in people with greater physical functioning limitations [108]. This suggests that interventions to improve physical functioning limitations or to retrain people for less physically demanding roles may increase workforce participation following a CVD event [112]. Future research should involve large patient samples, include matched control groups, focus on different CVD subtypes, different population sub-groups based on sociodemographic and health-related factors, including physical functional limitations. Since the burden of CVD is increasing in low and middle-income countries [113] and no studies from these settings were available, it is suggested to

evaluate the association of CVD with workforce participation related outcomes in such settings. Given that CVD leads to further chronic conditions, it is recommended to investigate associations of CVD and workforce participation related outcomes over the life course rather than using a limited period only. CVD not only affects workforce participation but also the long-term financial situation, work ability and risk of poverty which could be improved substantially by participation in the workforce [69, 99, 114]. Therefore, the role of CVD in workforce non-participation over a longer period of time, including the productivity while at work and through absenteeism, could also be investigated to better understand the time-varying role of CVD over the course of life of people living with CVD.

2.5 Conclusion

In summary, the evidence from available studies indicates that people living with CVD are more likely to leave paid work, to perform poorly in paid work and to receive more government pension compared with people without CVD. Prior to the development of appropriate strategic interventions to enhance workforce participation and quality of life of those living with CVD, it is recommended to analyse the relationship between CVD and workforce non-participation across various CVD subtypes, and in different population sub-groups to identify whether certain groups of people are particularly vulnerable to work-related poor outcomes after a CVD event. Further research is also needed to elucidate what factors (such as physical functioning limitations) underpin this relationship of CVD to workforce non-participation.

CHAPTER 3 Systematic review on social interaction and CVD

3.0 Chapter summary

Social interaction is important for an individual's overall wellbeing and there is evidence that social interaction is low among CVD survivors whose numbers are increasing globally. However, there is very limited evidence on whether the level of social interaction differs between those with and without CVD, and whether having a CVD event results in a change in social interaction. The aim was to review literature that assessed the association of social interaction of people living with CVD compared to people without CVD. A systematic search of studies using PubMed, Scopus and Web of Science databases published until December 2019 was conducted. It was published as a protocol on the PROSPERO registration website (*https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020165442*). Eligible studies were those that compared social interaction in people with versus without CVD. Study characteristics, analysis methods and measures of association were extracted. Six articles with study populations from Europe, North and South America, and Australia were eligible to be included in this systematic review. All of them were cross-sectional investigations and in general, compared to people without CVD, people diagnosed with CVD had slightly fewer social activities and lesser levels of support. However, the evidence is small scale, does not account for different CVD subtypes, population subgroups, or physical disabilities. Further large-scale research is needed, especially to provide suitable guidance to CVD survivors and their care providers and the organisations which assist people living better with CVD.

The PROSPERO registration number: **CRD42020165442.**

3.1 Introduction

An increase in the proportion of people surviving a cardiovascular disease (CVD) event and improvement of life expectancy around the world [115] has led to a growing number and proportion of people living with CVD [61, 62]. The ability to interact with people in social settings is one of the person-centred outcomes that matter to individuals living with CVD and it is an indicator of overall wellbeing [116]. Different terms are used in the literature to describe social interaction, including social network, social connectedness, social capital, and social role. These terms are often used interchangeably even though they are derived from different social theories and relevant measurement constructs. However, instead of expanding the various conceptual aspects of social interaction, this chapter is primarily focused on those terminologies that broadly indicate the ability to interact with people in social settings as a person-centred outcome.

To understand just how essential social interaction is for humans, it is instructive to consider situations in which the opportunities for social interaction are lacking. For example, in prison settings, solitary confinement is perceived to be the ultimate punishment [117]. Current evidence suggests that healthy social interaction is one of the treatment objectives of those living with CVD [118] and thus it is important to understand the long-term effects of CVD survivorship on social interaction [45, 64].

There is a growing body of research demonstrating that people with CVD have increased disability [119] and different chronic conditions, including fatigue [65], cognitive deficits, anxiety, and depression [66, 67]. Such long-term effects of CVD may cause impairments that diminish ability or willingness for social interaction [18]. Many people living with CVD want to and are able to maintain healthy social life after diagnosis and treatment [72]. Previous studies have reported that higher social interaction reduces mortality [120], cognitive decline [121], the incidence of new CVD events [122] and improves the quality of life [123]. Recent systematic reviews of CVD and social interaction have shown that social interaction is

associated with reduced incident CVD [124], improvement in CVD recovery by reducing recovery time after acute CVD events like stroke [125], and inadequate social interaction is associated with increased hospital readmission in people with CVD [126]. However, these past reviews did not directly compare social interactions between people with and without CVD. There is also limited evidence on which population sub-groups are affected most.

A systematic review to summarise the literature on social interaction related outcomes amongst people with versus without CVD and identify knowledge gaps and directions for future research were conducted. This current literature review will enhance the understanding of the relationship of social interaction with different CVD sub-types. This will also provide stronger evidence base that might be informative to people living with CVD, their caregivers and the organisations that aim to support healthy aging in those with CVD.

3.2 Methods

3.2.1 Search strategy

We searched PubMed, Scopus and Web of Science until December 31, 2019, to identify articles evaluating the association between CVD and social interaction among adults. The search terms were developed in consultation with Australian National University (ANU) librarian (Rachel Karasick, Information Access Coordinator, Hancock Library, ANU, Australia) and included combinations of: ‘atherosclerosis’, ‘cardiocerebrovascular disease’, ‘cardiovascular disease’, ‘cardiovascular event’, ‘cerebral infarction’, ‘cerebrovascular attack’, ‘cerebrovascular disease’, ‘cerebrovascular disorder’, ‘coronary artery disease’, ‘coronary disease’, ‘coronary heart disease’, ‘heart attack’, ‘heart disease’, ‘heart failure’, ‘ischaemic heart disease’, ‘myocardial infarction’, ‘myocardial ischemia’, ‘myocardial ischaemia’, ‘peripheral arterial disease’, ‘stroke’ and ‘social engagement’, ‘social participation’, ‘social network’, ‘social integration’, ‘social contact’, ‘social visit’, ‘social isolation’, ‘social activity’, ‘social satisfaction’, ‘social consequence’, ‘social support’, ‘social support’, ‘communal

engagement'. The full search terms are presented in *Appendix 2 (Section S3.1).* There was no restriction on study year or language. Both cohort and cross-sectional studies were included but conference abstracts, case reports, case series, and qualitative studies were excluded. Studies were excluded if the exposure-outcome association of interest was not reported, or an appropriate comparator was not used. The study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guideline [79] (*Appendix 2: Table S3.2.1*), and registered in PROSPERO (CRD42020165442).

3.2.2 Data extraction and quality assessment

All citations identified through our search strategy were imported into EndNote version X8 (Thompson Reuters, New York, NY, USA) and Covidence (*https://www.covidence.org*). The title and abstracts of the identified articles and the full text were reviewed independently by two reviewers (Md Moustafa Kamal and I), with the final inclusion of studies decided through consensus. The data on the study characteristics of included studies were extracted. Data on the first author, year of publication, study design, surveillance period, geographical location, study setting (hospital or community), participant age (mean, median or range), per cent men, number of participants with CVD, number of participants in the comparison group, CVD type, outcomes and definition of outcomes, follow-up time (if any), analysis method, type of effect measures (e.g. HR, OR, etc), point estimates, 95% confidence interval (CI), adjustments/stratifications were extracted.

3.2.3 Quality assessment

The methodological quality of included studies was assessed by using the Newcastle-Ottawa Scale (NOS) adapted for cross-sectional [81] studies *(Appendix 1: Section S2.3).* This validated scoring scale assesses the quality of a study across three domains: selection of participants; comparability of study groups; and the ascertainment of outcomes of interest.

Another researcher (Md Moustafa Kamal) did the quality assessment independently, and we decided the final score of studies through consensus.

3.3 Results

3.3.1 Characteristics of the included studies

After removing duplicates, a total of 2724 studies across the three databases were identified. A after reviewing the title and abstract, 2708 of these were excluded. The full-text review eliminated 12 of the 18 remaining articles (*Appendix 2: Table S3.3.1, Table S3.3.2*), leaving six studies [34, 40, 56, 57, 102, 127] for inclusion in this systematic review (**Figure 3.1**). All included studies were cross-sectional, and among these, three studies were of high quality [34, 40, 127], two studies were of medium quality [56, 57], and one study [102] was of low quality (*Appendix 2: Table S3.4.1*).

The six studies included in this systematic review were from six countries (Australia, Brazil, France, Sweden, United Kingdom (UK) and the United States of America (USA)) with survey periods ranging from 1999 to 2015. All study samples were from community-based surveys (**Table 3.1).**

All studies reported outcomes according to individual CVD subtypes, and none reported on composite CVD. Most studies used self-reported CVD diagnosis and included several CVD subtypes such as stroke, ischaemic heart disease, heart failure and myocardial infarction (**Table 3.2**). The social interaction-related outcomes included in this review were reported using diverse measurement scales [128-137]. These outcomes were reported either as scores derived from social interaction related activities questionnaire (such as social functioning score [56]) or as binary categories. The binary categorisation of social interaction was based on either a single question (for example, social participation restriction (yes vs no) [40]) or on multiple questions (for example, use of Social Network and Social Support Scale (SOS) by Almerud et al. [127]). Though the reported social interaction related outcomes varied widely

from each other, they could be broadly categorised into two groups: (a) participation in social activities and (b) social support. Participation in social activities encompassed the outcomes that refer to a person's ability or willingness to participate in social activities, and social support comprised outcomes related to the extent of support available from a social network (**Table 3.2**).

The age of the participants ranged from 18 years to over 85 years old across the included studies. The number of participants included in the studies ranged from 51 to 232 303, and the percentage of men ranged from 0% to 69%. The number of participants in the CVD group was lower than those in the control group (**Table 3.3**).

Figure 3.1 PRISMA flow diagram of study selection in the systematic review on CVD and social interaction

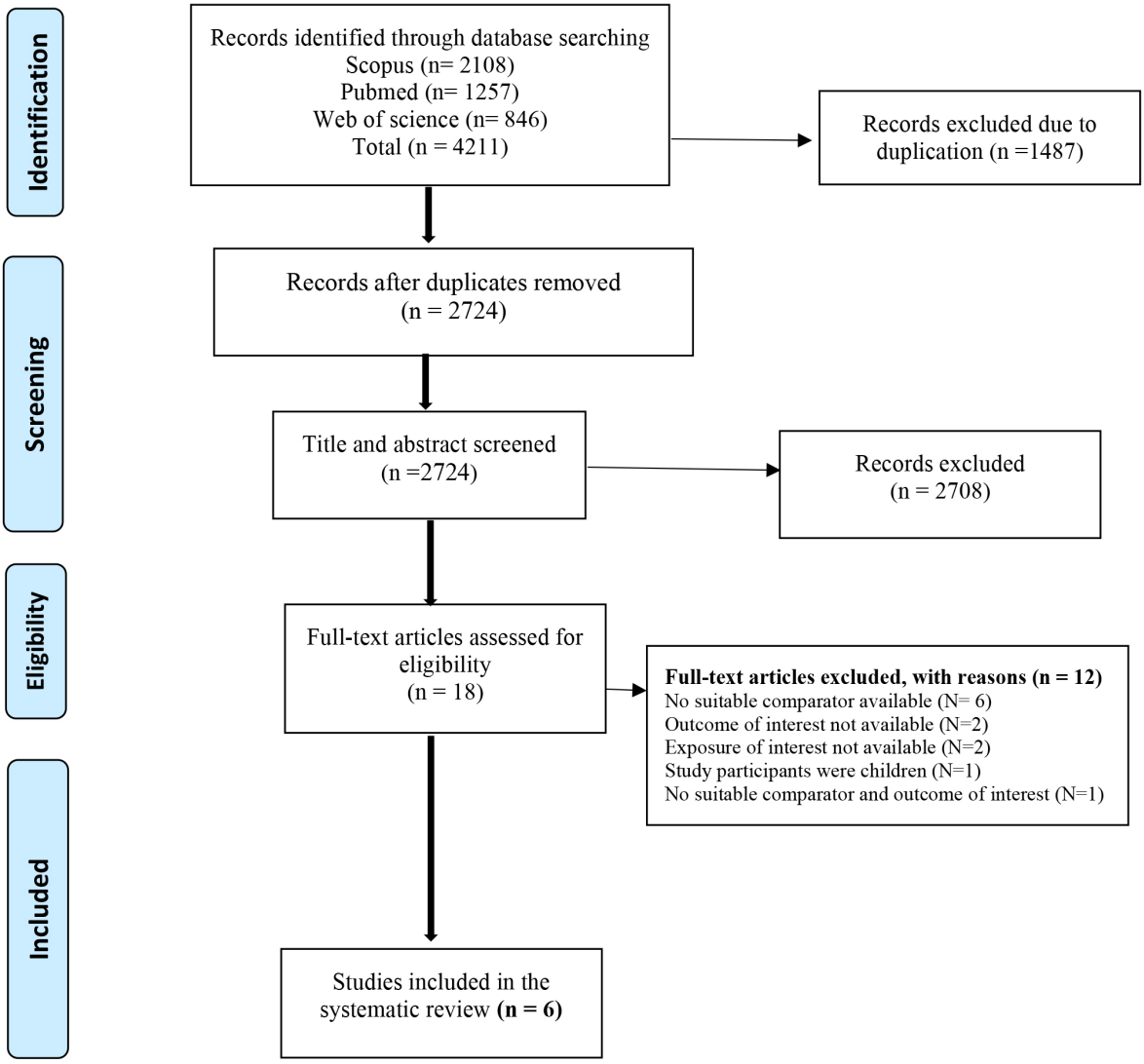


Table 3.1 Sources of data, survey year, publication year and countries of the study population in systematic review on CVD and social interaction

Study	Study Design	Surveillance period	Data Source**	Location**
Adamson 2004 [40]	Cross-sectional	1999-2001	The British Women's Heart and Health Study from 23 towns in England, Scotland and Wales.	UK
Almerud 2008 [127]	Cross-sectional	2003	Survey obtained from a university hospital, a central hospital, and a district hospital in the southern part of Sweden in 2003.	Sweden
Jorge 2017 [56]	Cross-sectional	2011-2012	Individuals aged 45 to 99 years, registered in the Family Doctor Program (PMF) of the city of Niterói, Rio de Janeiro State, Brazil	Brazil
McKenna 2009 [57]	Cross-sectional	N/A	A convenience survey to which participants responded after advertisements in local newspapers, flyers distributed through community organisations and local businesses and referrals from participants already involved in the study. Survey of a sample of people aged 65 years or older, living in Queensland, Australia	Australia
Mollon 2017 [34]	Cross-sectional	2015	Behavioral Risk Factor Surveillance System (BRFSS) survey	USA
Schnitzler 2019 [102]	Cross-sectional	2008-2009	Disability Health Survey that was administered in people's homes (DHH) in 2008 and in institutions (DHI) in 2009.	France

*N/A= Not available, **UK= United Kingdom, USA= The United States of America

Table 3.2 Exposures and their diagnosis methods, outcomes and their definitions and categorisation in systematic review on CVD and social interaction

Study References	Exposures	Exposure diagnosis	Outcomes	Definitions of outcomes	Categories
Adamson 2004 [40]	Stroke CHD	Self-report	Social participation restriction (yes vs no)	World Health Organisation (WHO) definition of 'participation restriction' which refers to problems an individual may experience in involvement in life situations related to social life [128].	***Social activities***
Almerud 2008 [127]	Acute coronary syndrome	Hospital admission	1. Social network and social support scale (SOS) (Binary: lower vs higher) 2. Medical outcomes study (MOS) social support survey score (Binary: lower vs higher)	1. Social Network and Social Support Scale (SOS): Emotional and practical support, homogeneity and approachability by means of 19 items with two or three response categories, with a score range from 19 (lowest) to 52 (highest), in the form of an additive scale [129]. Example includes 'I have persons nearby who care about how I manage', 'The persons in my social network know each other through me', etc followed by an ordinal scale level with three optional answers, 'Yes' 'Uncertain' and 'No', to the statements. 2. Medical Outcomes Study (MOS) Social Support Survey score: Emotional/informational, tangible, affectionate and positive social interaction by means of 19 items with five response categories, score range 1 (lowest) to 81 (highest), in the form of an additive scale [130]. One example of such question is "someone to health you if you were confined to bed" followed by five options: "None of the Time", "A Little of the Time", "some of the Time", "Most of the Time" and "All of the time".	***Social support***
Jorge 2017 [56]	Heart failure	Hospital admission	Social functioning score	The Portuguese version of Social functioning is obtained from Short-Form Health Survey (SF-36) questionnaire that measure the social interaction level [133]. Higher score indicates higher social interaction.	***Social activities***
McKenna 2009 [57]	Stroke	Self-report	1. Role as carer (yes vs no) 2. Role as home maintainer (yes vs no)	From the 'Role Checklist' [135] that asked the respondents to indicate whether they currently, previously or intend in the future to participate in the roles of student, worker, volunteer, carer, home maintainer, family member, friend,	***Social activities***

			3. Role as volunteer (yes vs no) 4. Role as friend (yes vs no) 5. Role as hobbyist/amateur (yes vs no) 6. Role as religious participant (yes vs no) 7. Role as Participant in organisations (yes vs no)	hobbyist/amateur, religious participant, participant in (any) organisations and other. Among these different roles, I considered seven roles (‘Carer’, ‘Home maintainer’, ‘volunteer’, ‘friend’, ‘hobbyist/amateur’, ‘religious participant’ and ‘participant in organisations’) as social activities.	
Mollon 2017 [34]	Myocardial infarction	Self-report	Activity limitations (yes vs no)	‘Activity limitation' component from health-related quality of life (HRQoL) Wilson and Cleary’s Health-Related Quality of Life Model questionnaire [136].	***Social activities***
Schnitzler 2019 [102]	Stroke	Self-report	1. Playing board games (yes vs no) 2. Going to concerts (yes vs no) 3. Going to the movie theatre (yes vs no) 4. Playing sports (yes vs no) 5. Going to the museum (yes vs no) 6. Using the telephone (yes vs no)	From the questionnaire that asked ‘‘In the past 12 months, have you been to play the board games?’’, with yes and no answers. Fifteen activities were included in this study: playing board games, going to concerts, going to the movie theatre, reading, listening to music, watching television, doing arts, knitting, tinkering, playing sports, going to the museum, using the telephone, using the computer, driving the car, and working [137]. Six activities were considered as outcome of interact because these activities involved interacting with other people in social settings.	***Social activities***

Table 3.3 Age and sample size of total, proportion of men, sample size in CVD and comparator groups in systematic review on CVD and social interaction

Study	Age	Total (n=)	% Men	CVD group (n=)	Comparator group (n=)
Adamson 2004 [40]	Range: 60–79 years	4219 for stroke 4242 for CHD	0%	131 for stroke, 694 for CHD	4088 for stroke, 3548 for CHD
Almerud 2008 [127]	Range: 18-74 years mean age was 66 years for patients, and 53 years for the controls	557	69% of total	241	316
Jorge 2017 [56]	Range: 46-99 years Mean (SD): 59.6 (10.4) years	633	39% for CVD group and 38.2% for control group	59	574
McKenna 2009 [57]	Mean (SD): 74.2 (7.8) years for stroke group, 75.0 (6.6) years for control group	218	69.6% for stroke group 41.5% for control group	23	195
Mollon 2017 [34]	Range: MI group: 50-64 years (38.29% of total) and others are ≥65 years No-MI group: 50-64 years (58.26% of total) and others are ≥65 years	Before matching: 232303 After matching: 66,916	Before matching: 63% for MI, 44.4% for control After matching: 62% for MI, 62.1% for control	Before matching: 18,891 After matching: 16,729	Before matching: 213,412 After matching: 50,187
Schnitzler 2019 [102]	Range: 19 years to >85 years	33,785	N/A	1,725	32,060

CHD=coronary heart disease, NR= Not reported, N/A: Not Available, MI= Myocardial infarction, SD= standard deviation

3.3.2 Association of social interaction and cardiovascular disease

Five studies [34, 40, 56, 57, 102] reported outcomes related to participation in social activities, with findings suggesting that people with CVD were less likely to participate in social activities compared to those without CVD. There was one study [40] that reported social interaction across two CVD subtypes (stroke and coronary heart disease), and the remaining studies examined only one CVD subtype such as heart failure [56], myocardial infarction [34] or stroke [57, 102]. The results from three studies [34, 40, 102] were minimally or extensively adjusted, and those from two studies [56, 57] were unadjusted and were reported as either scores or percentages. Three studies [34, 40, 56] reported only one type of social activity and the remaining two studies [57, 102] reported on multiple social activities. Although there was a large variation in the measures used for social interaction, the results were broadly consistent and in the same direction. For example, there was evidence that people with vs. without coronary heart disease (CHD) and with vs without myocardial infarction (MI) were more likely to have restricted social activities (OR for CHD: 2.04 [1.58-2.63]; OR for MI: 1.46 [1.34-2.59]) [34, 40]. Results from other studies were broadly consistent, showing greater social participation restriction in people with vs without stroke, although the results were not statistically significant ([OR= 1.49 (95% CI: 0.78-2.82)]) [40]. After adjustment for potential confounding, people who had a stroke event vs. those who had not were less likely to participate in specific social activities like going to concerts (OR=0.63 (95%CI: 0.47,0.84)), movie theatre (OR=0.69 (95%CI: 0.54, 0.88)), museum (OR=0.40 (95%CI: 0.30,0.53)), participating in sports (OR=0.41 (95%CI: 0.31,0.57)) or using phone (OR=0.21 (95%CI: 0.17,0.25)) [102]. However, it was not possible to combine and compare findings from two separate studies because of variation in social activity aspects, exposures-outcomes associations, types of studies, and different adjustment variables used in the analysis (**Table 3.4,** *Appendix 2: Table S3.4.2*).

One study [127] examined social support in people with versus without CVD. There were two social support scales for social support measurement, and they measured slightly different

aspects of social support. Though the analyses were adjusted for similar sociodemographic characteristics, the results varied depending on the measurement scales used to quantify the aspect of social support. The first scale measured emotional and practical support, and the analysis of its relationship with CVD has indicated that people with CVD were 17% more likely to report lower emotional and practical support ((OR=1.17 (95% CI:1.01-1.35)) compared with those without CVD. The examination of the relationship of CVD with second social support scale measuring emotional/informational, tangible, affectionate and positive social interaction has indicated that people with CVD had only 2% less likelihood to receive social support (OR=0.98 (95%CI: 0.97-0.99)) (**Table 3.4,** *Appendix 2: Table S3.4.2*).

Table 3.4 Effect size of social interaction in people with CVD in comparison to those without CVD

Study Reference	Exposure	Outcomes	Analysis	Measurement	Point estimate	95% CI
Adamson 2004 [40]	Stroke	Social participation restriction (yes vs no)	Multiple logistic regression	OR	1.49	0.78-2.82
Adamson 2004 [40]	Coronary Heart Disease	Social participation restriction (yes vs no)	Multiple logistic regression	OR	2.04	1.58-2.63
Almerud 2008 [127]	Acute Coronary Syndrome	Social network and social support scale (SOS) (lower vs higher)	Multiple logistic regression	OR	1.17	1.01–1.35
Almerud 2008 [127]	Acute Coronary Syndrome	Medical outcomes study (MOS) social support survey score (lower vs higher)	Multiple logistic regression	OR	0.98	0.97-0.99
Almerud 2008 [127]	Acute Coronary Syndrome	Sense of Coherence (SOC) Scale (lower vs higher)	Multiple logistic regression	OR	1.00	0.97-1.03
Jorge 2017 [56]	Heart Failure (HF)	Social functioning score** from SF-36 questionnaire (higher score indicates higher social interaction)	Non-parametric Mann-Whitney test (HF vs Control)	Mean (range)	87 (53-100) vs 100(62-100)	N/A
McKenna 2009 [57]	Stroke	Role as carer (yes vs no)	Chi-square test (stroke vs control)	Percent (%)	8.7% vs 34.9%	N/A
McKenna 2009 [57]	Stroke	Role as home maintainer (yes vs no)	Chi-square test (stroke vs control)	Percent (%)	78.3% vs 87.2%	N/A
McKenna 2009 [57]	Stroke	Role as volunteer (yes vs no)	Chi-square test (stroke vs control)	Percent (%)	21.7% vs 57.9%	N/A
McKenna 2009 [57]	Stroke	Role as friend (yes vs no)	Chi-square test (stroke vs control)	Percent (%)	87.0% vs 96.4%	N/A
McKenna 2009 [57]	Stroke	Role as hobbyist/amateur (yes vs no)	Chi-square test (stroke vs control)	Percent (%)	56.5% vs 75.4%	N/A
McKenna 2009 [57]	Stroke	Role as religious participant (yes vs no)	Chi-square test (stroke vs control)	Percent (%)	30.4% vs 43.1%	N/A
McKenna 2009 [57]	Stroke	Role as participant in organisations (yes vs no)	Chi-square test (stroke vs control)	Percent (%)	30.4% vs 65.5%	N/A
Mollon 2017 [34]	Myocardial infarction	Activity limitations (yes vs no)	Binary logistic regression	AOR	1.46	1.34-1.59

Schnitzler et al 2019 [102]	Stroke	Playing board games (yes vs no)	Logistic regression	OR	1.06	0.85–1.32
Schnitzler et al 2019 [102]	Stroke	Going to concerts (yes vs no)	Logistic regression	OR	0.63	0.47–0.84
Schnitzler et al 2019 [102]	Stroke	Going to the movie theatre (yes vs no)	Logistic regression	OR	0.69	0.54–0.88
Schnitzler et al 2019 [102]	Stroke	Playing sports (yes vs no)	Logistic regression	OR	0.41	0.31–0.57
Schnitzler et al 2019 [102]	Stroke	Going to the museum (yes vs no)	Logistic regression	OR	0.40	0.30–0.53
Schnitzler et al 2019 [102]	Stroke	Using the phone (yes vs no)	Logistic regression	OR	0.21	0.17–0.25

HF= Hear failure, AOR= Adjusted odds ratio, OR= Odds ratio, 95%CI= 95% confidence interval, *Difference is significant**,** ** higher score indicating higher social interaction, N/A= Not available

3.4 Discussion

This systematic review of six studies indicates that there is limited evidence that people with CVD have generally lower social interaction compared with people without CVD. All included studies were cross-sectional investigations, mostly of high quality, published in the last twenty years with populations from developed countries and with sample sizes ranging from less than one hundred to several hundred thousand. The definition of exposures and outcomes reported in these studies were partly related to the corresponding source of population. There was a large variation in the methods used for ascertaining social participation and support across the included studies. Despite this, the findings were generally consistent across different studies. However, those findings were somewhat limited in scope and size because of their focus on stroke and several types of coronary heart disease.

Earlier reviews have noted that there is a large variation in terms and measurements used for ascertaining social interaction [124-126, 138, 139]. These reviews have used various overarching terms to include the different dimensions of social interaction, based on conceptual frameworks used. For example, Choi et al. [139] have used ‘social capital’ as an overarching term and considered social support, social participation, civic participation, social networks, sense of community etc. as different dimensions of social capital. Although the terms used are different, all of them relate to the engagement of individuals with the society. My research focuses “social interaction” and “social isolation” as person-centred outcomes. It was difficult to draw direct comparisons due to differences in terminology, but the central concept remained the about one’s connection to society and the ability to engage.

Previous reviews have focused on the relationship of social interaction to CVD, finding that lower levels of social interaction are associated with an increased risk of having a CVD event and all-cause mortality [124-126, 138, 139]. The current systematic review is the first to consider the alternative direction of the relationship, examining the existing evidence for the relationship of change in social interaction following a CVD event. Taken together, the

available evidence from systematic reviews suggests the relationship between social interaction and CVD may be bi-directional. Higher levels of social interaction appear to be protective for CVD outcomes, while people who have had a CVD event show lower levels of social interaction than those without CVD. Various physiological mechanisms (such as autonomic dysregulation), psychological factors (such as depression), personality traits (such as low self-esteem), poor health behaviours (such as smoking) have been proposed to explain the relationship between lower levels of social interaction and adverse CVD outcomes [138, 139]. Several mechanisms have been suggested to explain lower levels of social interaction in people with CVD compared to those without. These include: deterioration of physical and psychological fitness impacting ability to participate in social activities [40, 56, 57]; loss of shared activities with friends [140, 141]; perception of social support and unhelpful responses from others [18, 142]; environmental barriers [143]; changing social desires [140, 141]; and personal choice driven by a change in perception of benefits and risks following a CVD event [127].

There are several strengths of this systematic review. This is the first synthesis of empirical evidence on social interaction of people with CVD compared with people without CVD. The second strength was that it was a comprehensive review and included multiple types of studies over a long period. The third strength is that this review adhered to PRISMA guidelines [79] and adopted a comprehensive search strategy, making it a high-quality synthesis of evidence.

This systematic review had several limitations that are related to the search period and diversity of the terminologies in the included studies. First, we have restricted the search for literature since 2000, and this review has not included the studies published before 2000. Second, there was a large amount of variation in the measures and terminologies used for social interaction. This resulted in difficulties synthesising the results since the terminologies reflected different social theories and relevant measurement constructs [117]. Third, there was diversity in all domains within included studies: exposures, outcomes, study designs, sources

of the exposures and outcomes, data analyses methodologies and adjustment for potential confounders. Thus, it was not possible to identify a CVD subtype whose association with social interaction is strongest. Fourth, it was not possible to find whether any sociodemographic or health-related factors play any role in the relationship of CVD to social interaction. Finally, there was not any study found in low and middle-income countries, thus findings from this review cannot be generalised to these settings.

Although this systematic review found consistent evidence that people with CVD have lower participation in social activities than those without CVD, all the studies were cross-sectional. It is not clear whether there is a causal relationship between CVD and decreased participation in social activities. We need longitudinal studies that investigate whether incident CVD is associated with changes in social interaction, including investigating whether this varies by CVD subtype. If longitudinal studies show associations between CVD events and change in social interaction, then studies that explore potential drivers of this relationship, such as physical functioning limitation, would be useful. This is particularly because the extent of physical disability differs by the type of CVD [108], and social interaction are affected by the extent of disability [144]. Therefore, it is suggested that future research should involve large patient samples, focus on different CVD subtypes, different population sub-groups based on sociodemographic and health-related factors, and physical disability. Studies are also needed in low and middle-income countries since the CVD burden is increasing in these countries [113] and differences in social support structures in these countries made it difficult to generalize the findings from higher-income countries in these settings [145].

3.5 Conclusion

Overall, there was consistent evidence in this systematic review that people with versus without CVD had lower participation in social activities. Only one study examined levels of social support with the direction of the findings varying by the type of scale used to measure

social support. Most included studies had small sample sizes, and none were longitudinal. Future studies are needed on the longitudinal relationship of CVD and social interaction, especially focusing on the role of different CVD subtypes, and different population characteristics, including the extent of physical disability.

CHAPTER 4 Data sources, research methods and ethics approval

4.0 Chapter summary

This chapter introduces the 45 and Up Study, and other linked datasets that are used to define exposures, outcomes, and other variables. Then it outlines the statistical methods and relevant issues required to address the gaps in knowledge as identified in chapters two and three. Particularly how the questionnaire items from the 45 and Up Study, and the hospitalisation codes are incorporated to define the relevant variables are briefly mentioned here. The statistical methods are described by the type of analyses conducted in different study designs as required to address the research questions in the remaining chapters of the thesis. Finally, two important issues (the representativeness of the 45 and Up Study and ethics approval) are briefly mentioned in the last two segments of this chapter.

4.1 Introduction

The 45 and Up Study [58] resource was used to address the research questions in this thesis. The 45 and Up Study is a large-scale dataset that includes longitudinal surveys linked to hospitalisation records and other administrative datasets, providing a valuable resource for examining associations between a large range of exposures and outcomes. The Sax Institute (www.saxinstitute.org.au) runs this study in collaboration with major partner Cancer Council NSW, and partners: the National Heart Foundation of Australia (NSW Division); NSW Ministry of Health; NSW Government Family & Community Services–Ageing, Carers and the Disability Council NSW; and the Australian Red Cross Blood Service.

In this section, the datasets used in this thesis were described, and the study variables (outcomes, main exposures, and other relevant variables) were defined. Then the representativeness of the 45 and Study was then briefly explored by comparing with other datasets.

4.2 Data sources

4.2.1 The 45 and Up Study baseline questionnaire

The 45 and Up Study from the Sax Institute is a population-based study of 267 153 people aged 45 and over in New South Wales (NSW), randomly sampled from the Medicare Australia database [58]. The Medicare database contains records for all Australian citizens and permanent residents, along with some temporary residents and refugees. Approximately 10% of the NSW general population in the target age range joined the study by completing a postal questionnaire distributed between 1 January 2006 and 31 December 2008; an additional 1.3% of participants joined the cohort without receiving an invitation by voluntarily contacting the study. Most participants were sampled in 2008 and the median baseline questionnaire date is February 2008. Persons aged 80 years and over and those living in rural areas were oversampled by a factor of two; all residents of remote areas were sampled. The response

rate to mailed invitations was estimated to be 18%, representing around 10% of the NSW population aged 45 years and older [58]. All participants provided consent for follow-up through linkage to a range of routinely collected data. A comparison of the 45 and Up Study with the NSW Population Health Survey found consistent exposure-outcome relationships between the two study populations [146] and the extent of representativeness of the 45 and Up Study is further explored in the latter part of this chapter.

The baseline questionnaire collected data on socio-demographic information, health behaviours, health status, medical history, and usage of medical services. Copies of the baseline and follow-up questionnaires are available on the study's website [147]. There were separate questionnaires for men and women, with three versions of each, with changes to some variables [147], but not those that I have used for addressing the research questions in my thesis. Questionnaire version 1 was completed by 13.9% of participants, version 2 by 1.0% of participants and version 3 by 85.1% of participants.

4.2.2 The 45 and Up Study follow-up questionnaire

The first two 45 and Up follow-up surveys were used in this thesis. The first survey was called 'Social, Economic and Environment Factors (SEEF) study', and the second survey was called, 'Wave 2'. Some participants took part in one of the surveys and some participants took part in both surveys. To maximise the number of people followed up and to allow for higher time intervals between baseline and follow-up in my study, the data from the two follow-up surveys were combined, and with priority to the later survey if two survey records were available for one participant. The initial purpose of the two surveys varied slightly but did not affect the essential variables required for defining outcomes and exposures in my studies (*Appendix 3: Table S4.1*).

The SEEF was a sub-study that gathered general demographic, health, and risk factor data, emphasising social, economic, and environmental factors. A total of 99,927 participants in the 45 and Up Study were invited to participate via a paper-based questionnaire, and 60337 participants had completed the SEEF survey (between January 2010 and April 2011) [148]. Participants were excluded from being sent the survey questionnaire if they had requested not be contacted further, had already been contacted for other sub-studies or were deceased (ascertained through linkages to death registries).

The Wave 2 follow-up survey questionnaires were circulated to eligible 45 and Up Study participants via printed questionnaire or online from January 2012 to December 2015, regardless of their participation in the SEEF survey. The conditions of exclusion from getting the survey questionnaire were the same as those for the SEEF survey. There were 142,548 participants who completed the Wave 2 questionnaire with 27,034 (41440 invited), 50,211 (86,250 invited), 28,670 (52,664 invited) and 36,633 (65,233 invited) completed in 2012, 2013, 2014 and 2015, respectively [149].

All variables derived from the baseline and follow-up questionnaires were self-reported, apart from the Accessibility Remoteness Index of Australia Plus (ARIA+) score which was derived for each participant's postcode of residence at the time of original recruitment as recorded by Medicare Australia. Australian Standard Geographical Classification (ASGC) Remoteness areas, based on enhanced measures of remoteness developed by the National Key Centre for Social Applications of Geographic Information Systems, categorises areas as 'major cities', 'inner regional', 'outer regional', 'remote' and 'very remote.' The ARIA+ index values are based on road distance from a locality to the closest service centre [150].

4.2.3 Data linkage

The baseline and follow-up datasets were probabilistically linked to other datasets by the NSW Centre for Health Record Linkage (CHeReL). Further details on the procedures are available on the CHeReL website (*https://www.cherel.org.au/master-linkage-key*). There are strict protocols for access. Users are not allowed to make data available – the data custodians and Sax institute do that subject to ethics and custodian approvals. I have used one dataset that records the 45 and Up Study participants' hospital admission records, one for the remoteness of residence of the participants, and four other datasets (**Figure 4.1**). I had full access to all relevant datasets. Data supporting the findings from this thesis are available from the Sax Institute, the NSW Department of Health and the Australian Bureau of Statistics, with data linkage conducted by the NSW CHeReL. Restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Researchers may apply for access to these data with the appropriate data custodian and ethics approvals. Information about data access and governance policies is available at: *https://www.saxinstitute.org.au/our-work/45-up-study/for-researchers/.*

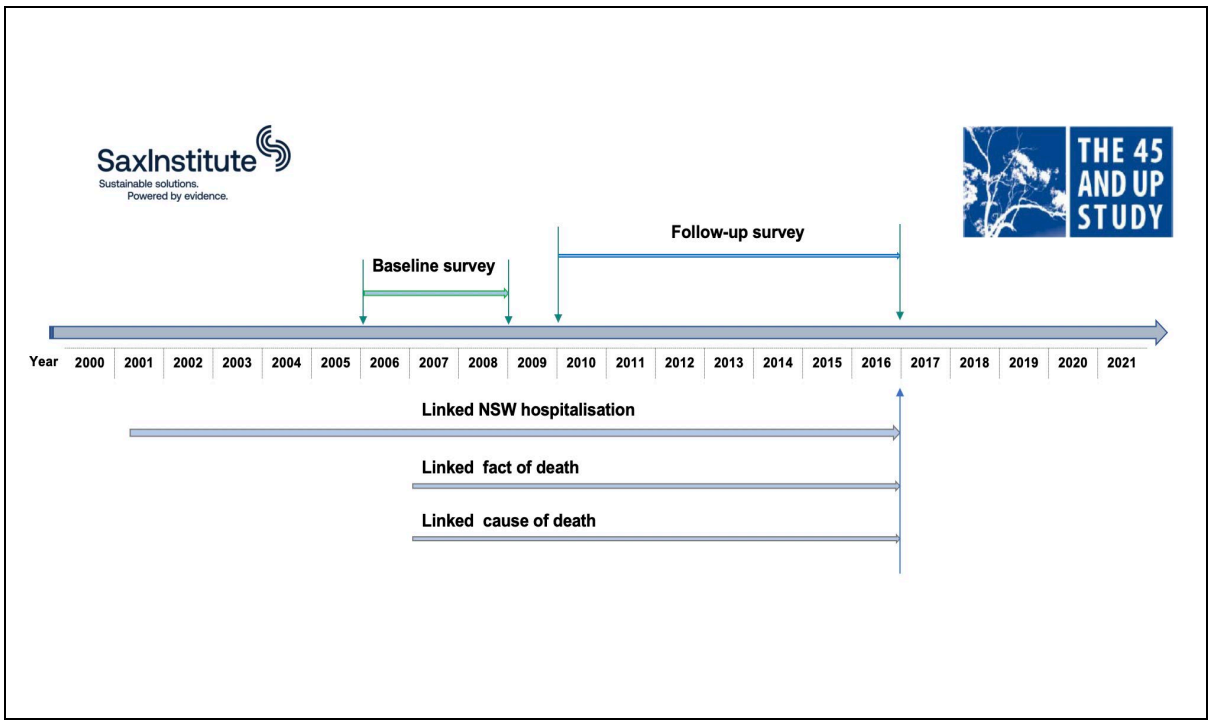
4.2.4 The NSW Admitted Patient Data Collection (APDC) data

Hospitalisation records of the study participants were from the NSW Admitted Patient Data Collection (APDC) that registers all inpatient separations (discharges, transfers, and deaths) from all public and private hospitals in NSW, as well as public multi-purpose services, private day procedure centres and public nursing homes. The dates of admission, transfer, discharge and death, and the records of primary and secondary diagnostic and procedures were used for determining the exposures and other relevant variables in the thesis. The NSW APDC data were probabilistically linked to the 45 and Up Study data through the CHeReL with false positive and negative rates of <0.5% and <0.1%, respectively.

4.2.5 The linked death data

Several death registrations datasets were used to capture deaths in the NSW and Australia. These registers include the NSW Register of Births, Deaths and Marriages (to provide the fact of death); the Australian Bureau of Statistics Cause of Death unit record files (to provide the cause of death) and the National Death Index (to provide fact and cause of death) up to the end of December 2015. These datasets were linked to the study participants and were used for the investigation of missing data and non-participation in the follow-up survey.

Figure 4.1 Datasets used in the thesis



4.3 Outcomes

4.3.1 Participation in workforce related outcomes

4.3.1.1 Workforce participation

Workforce participation is a binary outcome with two options (yes/no). This was based on responses to the following two questions: “What is your current work status?” and “About how

many hours each week do you usually spend doing the following - paid work, voluntary/unpaid work?". Those indicating valid non-zero paid hours/week (> 0 and <100) or work status as at least one of "In full time paid work", "In part time paid work", "Self-employed", "Partially retired" were classified as participating in the workforce; of the remaining participants, those indicating work status as "Doing unpaid work", "Completely retired/pensioner", "Studying", "Looking after home/family", "Disabled/sick", "Unemployed", "Other" were classified as not participating in the workforce *(Appendix 3: Table S4.2)*.

4.3.1.2 Paid work hours per week

Paid work hours/week is a count variable consisting of zero or non-zero positive integer values. It was defined based on responses to the following questions: "About how many hours each week do you usually spend doing the following? - paid work, voluntary/unpaid work". Zero or non-zero positive values less than 100 were considered valid paid hours per week. Further logical checks were applied with the workforce participation status variable derived from the question that asked, "What is your current work status?" *(Appendix 3: Table S4.2).*

4.3.1.3 Retirement

This is a binary outcome obtained from question number that asked 'If you are partially or completely retired, why did you retire?'. The question was followed by several options. Participants choosing any of the eight options ("Reached usual retirement age", "Lifestyle reasons", "To care for family members/friend", "Ill health", "Made redundant", "Could not find a job", "Other") were defined as 'retired' and those without any of these options were defined as 'not retired'.

4.3.1.4 Retirement due to ill health

Retirement due to ill health is a binary outcome with two options (yes/no) and it was defined from the question that asked 'If you are partially or completely retired, why did you retire?' and

following logical checks with workforce participation status. Participants not in the workforce were classified as “yes (retired due to ill health)” if they chose “ill health”, and otherwise as “no (retired for other reasons)” *(Appendix 3: Table S4.2).*

4.3.2 Social interaction related outcomes

4.3.2.1 Social isolation

Social isolation is the primary outcome (for the empirical analyses) related to social interaction in the thesis. Social isolation was derived from the Duke Social Support Index (DSSI) social interaction subscale score based on four social interaction components [151]. The four components were social visits per week, telephone contacts per week, social group meetings per week and the number of people to depend on. These were derived from two items from the 45 and Up Study survey questionnaire. The first questionnaire item asked: “How many times in the last week did you” a) “spend time with friends or family who do not live with you”, b) “talk to someone (friends, relatives or others) on the telephone”, and c) “go to meetings of social clubs, religious groups or other groups you belong to?”. The second questionnaire item asked, “How many people outside your home, but within one hour of travel, do you feel you can depend on or feel very close to?”.

The DSSI tool has been validated in older Australians and the definition of social isolation was based on previous recommendations [152, 153]. The DSSI components response options were non-negative integer values, and the values were re-coded as mentioned earlier [154] before summing the recoded values into a score that ranged from 4 to 12 (*Appendix 3: Table S4.3.1*). As recommended [153], all participants were divided into two groups, with the bottom 20% being classified as socially isolated and the remaining 80% being classified as not being socially isolated. Based on all study participants in the baseline survey, it was found that participants having a DSSI score of less than 8 were grouped as socially isolated. Hence,

those with a DSSI score of less than 8 in all surveys were grouped as socially isolated (*Appendix 3: Table S4.3*).

Previous studies have reported either the sum scores of DSSI [155-157] or separate components of the score [158-161] (*Appendix 3: Table S4.3.2*). Hence, to better reflect the different aspects of social activities, the individual components of DSSI were also investigated separately as follows.

4.3.2.2 Social visits per week

This is based on the question that asked: “How many times in the last week did you spend time with friends or family who do not live with you?”. The responses were recorded as non-negative integer values.

4.3.2.3 Telephone contacts per week

This is based on the question that asked: “How many times in the last week did you talk to someone (friends, relatives or others) on the telephone?”. The responses were recorded as non-negative integer values.

4.3.2.4 Social group meetings per week

This is based on the question that asked: “How many times in the last week did you go to meetings of social clubs, religious groups or other groups you belong to?”. The responses were recorded as non-negative integer values.

4.3.2.5 Number of people to depend on

This is based on the question that asked: “How many people outside your home, but within one hour of travel, do you feel you can depend on or feel very close to?”. The responses were recorded as non-negative integer values.

While studying the individual components of social interaction, those who had value more than [median + 3* (median absolute deviation)] of the corresponding social interaction components were defined as outliers [162], and the participations with outliers were excluded from the corresponding analysis. Each social interaction item was analysed as a binary variable (no social interaction versus other (i.e. one or more than one) social interaction), and the group with no social interaction was the category of interest in the main analysis. For example, in the case of social visits per week, the study participants with zero (i.e. no) social visits per week made up of the group having no social visit per week; and the remaining study participants having one or more than one social visits/week formed the other group. Such binary category was chosen because there is no validated scale of defining low social interaction for the social interaction components and the chosen categorisation identifies the group with relatively poorer social interaction levels.

4.4 Exposures

4.4.1 Cardiovascular disease (CVD) and incident CVD

Broadly, the main exposure of interest in the thesis was CVD, but its definition varied slightly depending on the type of investigation. CVD was defined from both the self-reported baseline questionnaire as well as from the hospital-recorded CVD to indicate any CVD ever diagnosed. The incident of CVD during the follow-up period was based on hospitalisation. There were some fatal CVD incidents and therefore those who die of incident CVD were not included in the analysis as there could be no follow-up measure.

Self-reported CVD was derived from the question that asked “Has a doctor EVER told you than you have: (if YES, please cross the box and give your age when the condition was first found)” followed by 16 different options related to various disease conditions. Participants

choosing yes to any of ‘heart disease’, ‘stroke’ and ‘blood clot (thrombosis)’ were categorised as having self-reported CVD.

Hospital-recorded CVD or CVD subtypes were ascertained by using the ICD-AM diagnosis codes in any diagnostic or procedure code fields in the linked hospital admissions data [23]. Participants were classified as having hospital-recorded CVD at baseline if they had at least one hospitalisation for CVD in the five-year window before the baseline survey. Since hospitalisations records were available from 2001 and the baseline survey started in 2006, a five-year window before baseline survey was chosen to ensure the uniform probability of identification of previous diagnoses from administrative data for all participants. Incident CVD or incident CVD subtypes were identified for the CVD free participants at the baseline after baseline survey but before corresponding participant’s follow-up survey date by using ICD-AM diagnosis codes (*Appendix 3: Table S4.4*).

4.4.2 CVD subtype and incident CVD subtype

I investigated five CVD subtypes which were defined based on hospitalisation records only. A participant with hospitalisation for a particular CVD subtype may or may not have had another type of CVD hospitalisation. The five CVD subtypes were (1) ischaemic heart disease (IHD) (ICD-AM codes: I20-I25), (2) myocardial infarction (MI) (ICD-AM codes: I21, I22 and I23), (3) cerebrovascular disease (ICD-AM codes: I61, I63, I64), (4) peripheral artery disease (PAD) (ICD-AM codes: I70-I74) and (5) Heart failure (HF) (ICD-AM codes: I50, I11.0, I13.0, I13.2). The ‘other CVD’ group comprised those participants with CVD who had self-reported CVD or any CVD codes other than the five CVD subtypes, as mentioned here, but it varied slightly depending on the type of studies.

4.5 Sociodemographic and health-related variables

4.5.1 Socio-demographic variables

Different sociodemographic and health variables known to be associated with outcomes [82, 92, 163-170] were included in the thesis. These variables were derived from the Medicare Australia database (age and sex), the NSW APDC records and the self-reported data from the 45 and Up Study [58].

4.5.1.1 Age

Age was obtained from the Medicare Australia database [58] and reported in years. Age of the study participants in the cross-sectional and longitudinal studies was derived at the corresponding participants' baseline and follow-up survey completion dates, respectively. Age of the participants was reported in years or in age-grouped which varied in various studies. There was variation in the age-group categories in different studies because of the number of available eligible study participants (Further details in chapters 5 and 6).

4.5.1.2 Sex

The variable sex was obtained from the Medicare Australia database [58], it was binary (men and women).

4.5.1.3 Region of residence

The remoteness of residence was derived from the mean ARIA+ score [150] and was categorised into three: major cities, inner regional and more remote areas.

4.5.1.4 Education

Education was derived from the 45 and Up Study baseline questionnaire that asked, "What is the highest qualification you have completed?". The question was followed by 6 options: (1) no school certificate or other qualifications, (2) school or intermediate certificate (or

equivalent), (3) higher school or leaving certificate (or equivalent), (4) trade/apprenticeship (e.g., hairdresser, chef), (5) certificate/diploma (e.g., childcare, technician) and (6) university degree or higher. The variable used in the final analysis was called 'Education'. It was categorised into (1) high school or less, (2) certificates/diploma/trade and (3) tertiary in reference to previously published paper [171].

4.5.1.5 Marital status

Marital status at baseline was derived from the 45 and Up Study baseline questionnaire that asked "What best describes your current situation? (please cross one box)". The question was followed by 6 options: (1) single, (2) married, (3) de facto/living with a partner, (4) widowed, (5) divorced and (6) separated. The variable used in the analysed was categorised into two: (1) married/defacto/ living with a partner, and (2) single/widowed/divorced/separated.

4.5.1.6 Country of birth

Country of birth was derived from the 45 and Up Study45 and Up Study baseline questionnaire that asked "In which country were you born?". The question was followed by 15 options: Australia, UK, Ireland, Italy, China, Greece, New Zealand, Germany, Lebanon, Philippines Netherlands, Vietnam, Malta, Poland and other (please specify). New Zealand citizens do not need a visa to live or work in Australia and have access to most of the same entitlements, including health and welfare, and opportunities as Australian citizens. Hence, Australian and New Zealand citizens were grouped as one category and participants from other countries were classified as others. The variable used in the final analysis was binary and categorised as: born in Australia/New Zealand (yes/no) like those published earlier [171].

4.5.1.7 Language spoken at home

Language spoken at home was derived from the 45 and Up Study45 and Up Study baseline questionnaire question that asked "Do you speak a language other than English at home" with

two options for answer: yes and no. The variable used in the final analysed was binary, categorised as ‘language spoken at home other than English (LOTE)’ (yes/no).

4.5.2 Health related variables

4.5.2.1 Body Mass Index (BMI)

Body Mass Index (BMI) was derived from two questions from the 45 and Up Study45 and Up Study baseline questionnaire. The first question asked, ‘How tall are you without shoes’ followed by 3 options to report in cm (centimetre), feet or inches. The next question asked, ‘About how much do you weigh?’ followed by 3 options to report in kg (Kilogram), stone or lbs (pound). For all participants, the weight was converted into kg and height was converted into meter (m) and the body mass index (BMI) was calculated as weight in kg divided by squared value of height in meter. Then BMI (kg/m^2) was categorised into 4 groups: (1) underweight (15-<18.5), (2) normal weight (18.5-<25), (3) overweight (25-<30) and (4) obese (30-50). A similar approach was considered for obtaining the BMI of the participants at the Wave 2 survey. Since the heights of the participants at the SEEF survey were not available, the corresponding heights of the participants at baseline were taken assuming that the participants did not gain or lose height during the survey intervals. Then the BMI of the participants were ascertained by considering the corresponding weight of the participants at the SEEF survey.

4.5.2.2 Alcohol consumption per week

Alcohol consumption per week at baseline is derived from the question that asked, “About how many alcoholic drinks do you have each week?” with the explanation of one drink by stating ‘a glass of wine, middy of beer of nip of spirits (put “0” if you do not drink or have less than one drink each week)’. The variable used in the final analysed was categorised into three groups: (1) non-drinkers (zero drinks per week), (2) moderate drinkers (>0-<15 drinks per

week), and (3) heavy drinkers (≥15 drinks per week)). The cut-points of alcohol consumption broadly reflect Australian guidelines on low-risk consumption [172].

4.5.2.3 Smoking status

The smoking status variable was derived from the question that asked, “Have you ever been regular smoker?” with two options: yes and no. Those who chose the yes option were directed to answer the question, “Are you a regular smoker now?” with two options, yes and no. From these questions, the smoking status of participants was categorised into three: (1) non-smoker, (2) past-smoker, and (3) Current smoker.

4.5.2.4 Comorbid disease: diabetes and cancer

The presence of diabetes and cancer status at baseline was derived from the question that asked “Has a doctor EVER told you than you have: (if YES, please cross the box and give your age when the condition was first found)” followed by sixteen different options related to various disease conditions. Participants choosing diabetes as yes was categorised as people with diabetes. Choosing yes for any of ‘skin cancer (not melanoma)’, ‘melanoma’, ‘prostate cancer (only in questionnaire for men) or breast cancer (only in questionnaire for women)’, ‘other cancer (type of cancer (please specify))’ was categorised as having cancer.

4.5.2.5 Comorbid disease: Osteoarthritis

Having osteoarthritis or not was a binary variable (yes/no). It was derived from the question that asked “In the last month have you been treated for: (if YES, please cross the box and give your age when the treatment started)”- followed by 13 different options related to various disease conditions. Participants choosing osteoarthritis as yes was categorised as having osteoarthritis and others were categorised into no.

4.5.2.6 Modified Charlson comorbidity index

The modified Charlson comorbidity index was adapted from the previously published coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data [173]. In this modified Charlson comorbidity index, ICD-10 AM codes were used and the codes for the four CVD-related disease conditions (myocardial infarction, congestive heart failure, peripheral vascular disease and cerebrovascular disease) were excluded, and the remaining 13 different disease conditions as recorded in the hospitalisation were considered for calculating the comorbidity index. These disease conditions were dementia, pulmonary disease, connective tissue disease-rheumatic disease, peptic ulcer disease, mild liver disease, diabetes without complications, diabetes with complications, paraplegia and hemiplegia, renal disease, cancer, moderate or severe liver disease, metastatic carcinoma and human immunodeficiency virus infection and acquired immune deficiency syndrome. Hospitalisations during 1 year before the follow-up survey were considered for each participant and a total weighted score was estimated by using the algorithm. Then the modified Charlson index was categorized into four groups: (1) No comorbidity (for those who had no recorded hospitalisations), (2) Minor comorbidity (for those who had hospitalisations and had a total weighted score of 0), (3) Moderate comorbidity (for those who had a total weighted score more than 0 but less than or equal to 2), and (4) Severe comorbidity (for those who had total weighted score more than 2).

4.5.2.7 Physical functioning limitations

Physical functioning was measured using the Medical Outcomes Score-Physical Functioning (MOS-PF) [174], which is equivalent to items from the physical functioning scale (PF-10) of the SF-36 health survey [175]. The PF-10 has been validated as a measure of physical functioning across a wide range of patient groups varying by age, sex, and comorbidities [176]. It consists of 10 questionnaire items in the baseline survey question number 28 and asks the study participants to choose one of the three choices ‘Yes, limited a lot’, ‘Yes, a little’ or ‘No, not limited at all’ in response to the question: “Does your health now limit you in any of

the following activities?" with a list of 10 activities as follows: (1) VIGOROUS activities (e.g running, strenuous sports); (2) MODERATE activities (e.g pushing a vacuum cleaner, playing golf); (3) Lifting or carrying shopping; (4) Climbing several flights of stairs; (5) Climbing one flights of stairs; (6) Walking one kilometer; (7) Walking half a kilometer; (8) Walking 100 metres; (9) Bending, kneeling or stooping; (10) Bathing or dressing yourself. For each item, participants who answered "yes, limited a lot," "yes, limited a little," or "no, not limited at all," had a score of 0, 50, or 100 respectively. An overall physical functioning score was calculated from the average of scores from all 10 items. Therefore, the PFL scores ranged from 0 to 100, where higher scores represented fewer limitations, and were grouped into four categories: no limitation (score of 100); minor limitation (score 90–<100); moderate limitation (60–<90); and severe limitation (score 0–<60) by using cut-points in reference to previous investigations [177] *(Appendix 3: Table S4.5).*

4.5.2.8 Psychological distress

The psychological distress was measured with the K10 [178] on the baseline questionnaire item that asked, 'During the past 4 weeks, about how often did you feel' followed by 10 different non-specific symptoms of distress. They were: (1) tired out for no good reason?, (2) nervous?, (3) so nervous that nothing could calm you down?, (4) hopeless?, (5) restless or fidgety?, (6) so restless that you could not sit still?, (7) depressed?, (8) that everything was an effort?, (9) so sad that nothing could cheer you up?, and (10) worthless?. There were five options for each of the questions: (1) none of the time, (2) a little of the time, (3) some of the time, (4) most of the time, and (5) all of the time. The scores range from 10 to 50 and higher scores can be used to indicate the increasing likelihood of the presence of a common mental disorder, including mood and anxiety disorders [179]. Since there are no universally agreed cut-points for the K10, I have used cut-points consistent with the Australian Bureau of Statistics reporting of psychological distress in the Australian population [180]: low (10- < 12), mild (12- < 16), moderate (16- < 22) and high (22–50) psychological distress.

4.5.2.9 Overall health and quality of health

The overall health and quality of health were obtained from the baseline question that asked 'In general, how would you rate your: overall health, quality of life' followed by five options: excellent, very good, good, fair, and poor. In the final analysis, either of the variables was categorised into three groups: (1) Excellent/Very high, (2) Good, and (3) Fair/poor.

4.5.3 Other variables

4.5.3.1 Follow-up period

The survey follow-up days were calculated by subtracting the baseline survey date from the corresponding follow-up survey date. Then it was grouped into four categories for reporting purposes (<5 year, 5-<6 year, 6-<8 year and >8 year).

4.5.3.2 Time since diagnosis of incident CVD

The date of incident CVD was recorded with the CVD diagnosis codes as mentioned earlier [23] and the days between the incident CVD and corresponding participants' follow-up survey date were calculated. Then the days were converted into years and categorised into 3 groups: Incident CVD diagnosed in <2-years, 2-<4-years, and ≥4-years considering the distribution of the people with incident CVD since time incident diagnosis.

4.5.3.3 Length of hospital stay

The length of hospital stay was derived from the hospitalisation admission and separation dates. The total length of stays was calculated by summing up all episodes of admission within a defined period. Finally, the length of hospital stays was categorised into 4 groups: (1) No hospital stays, (2) 1-10 days of hospital stays, (3) 11-30 days of hospital stays, and (4) More than 30 days of hospital admission.

4.6 Statistical methods

The statistical methods used in the thesis depended on the type of studies, nature of outcome variables, and the aims that addressed limitations of cohort study datasets used in the thesis. There were two types of studies (cross-sectional and longitudinal), and the outcomes were either categorical (binary) or count variables. Participants with missing values for the outcome of interest were excluded from the corresponding analysis. There were no missing data in the main exposure (CVD), age and sex. There were missing values of outcomes and other variables. The missing values of the variables used in model adjustments were grouped as a separate category. The sensitivity analysis considered the definition of exposures from hospitalisation records or self-reported survey, population subgroup of particular significance, presence of comorbid disease conditions or the ways (categorical or continuous) variables were used in the regression models. There were survey participants whose follow-up survey records were missing, and their missingness in the follow-up survey records might have some implications to overall effect sizes estimation which was done by non-missing follow-up survey participants only. I addressed this issue by comparing different characteristics of missing and non-missing participants derived from other linked datasets. Based on these contexts, the statistical methods in the thesis could be divided into 4 categories: (1) Descriptive statistics, (2) Cross-sectional analysis (3) Longitudinal analysis, and (4) Assessing the implication of non-participation in the follow-up survey.

4.6.1 Descriptive statistics

The descriptive statistics were used to summarise characteristics of the study population and distribution of the outcomes by exposures were reported. The summary statistics (mean, median) of the count or integer variables and the proportion in different categories of the categorical variables including missing numbers or proportions were reported. The results were presented either in the form of tables or in figures.

4.6.2 Cross-sectional analysis

The modified Poisson regression with robust error variance [181] was used to estimate prevalence ratios (PRs) for binary outcomes in relation to the exposures. A generalised linear model assuming a Poisson distribution and log link function was used to estimate the mean of count variables. The models were minimally adjusted but slightly varied depending on the types of outcomes. The PRs were also estimated separately within population subgroups; chi-square tests for heterogeneity were used to assess heterogeneity between subgroups. To examine the potential contribution of physical disability to the CVD-outcome associations, I have modelled the joint categorisation of CVD and physical disability on all binary outcomes.

4.6.3 Longitudinal analysis

The modified Poisson regression with robust error variance [181] was used to estimate risk ratios (RRs) for binary outcomes. The incident CVD, different incident CVD subtypes, different population sub-groups and physical functional limitations were considered while examining the relationship of exposures and both person-centred outcomes.

4.6.4 Assessing the implications of non-participation in the follow-up survey

There were four sequential steps of analyses for assessing the implication of missing data, and the statistical methods varied depending on the stages of analysis. I did the analyses with a case study from the thesis and used descriptive statistics to compare the characteristics of participants with non-missing versus missing follow-up participation in the first step. The variables were obtained either from the baseline survey or the hospitalisations records. Generalised linear models with robust error variance [181] were used to estimate the likelihood of non-participation in the follow-up survey in different population subgroups in the second step. Multiple imputations by chained equations [182] under missing at random (MAR) and missing not at random (MNAR) assumptions were used to impute the missing values in the third step. Then the generalised linear models with robust error variance [181] were used to

estimate the risk ratios (RRs) in the last step to compare values in the main versus sensitivity analyses.

4.7 Data analysis software

Analyses were carried out using SAS software version 9.4 and R version 3.5.2 and version 3.6.3 [183].

4.8 Comparison of the 45 and Up Study to representative health surveys

Since the response rate of the 45 and Up Study baseline survey is only 18%, the aim was to investigate its representativeness by comparing the responses rates, exposures, outcomes, and other relevant factors of the 45 and Up Study to other population-based contemporaneous surveys of the NSW and Australian populations. The median month of the 45 and Up Study baseline survey is February 2008 and the participants in the 45 and Up Study were older than or equal to 45 years old. Hence, only those surveys were considered that were conducted as close as possible to the median time and participants with a similar age range were possible to separate to compare their characteristics with the 45 and Up Study participants.

The first survey considered was the NSW Population Health Survey (2008) which was one of the annual health surveys conducted by the NSW Department of Health [184]. The outcomes and exposures in the thesis could not be compared with equivalent variables in the NSW Population Health Survey (2008). There were several variables comparable in both surveys. However, after restricting the age, only response rate and sex were comparable. Compared to the NSW Population Health Survey, the 45 and Up Study had a lower response rate (63% vs 18%) and had a higher proportion of men (40% vs 46%) [185]. The comparable exposures and outcomes in both surveys were not available. Then the National Health Survey (NHS) conducted between2007-2008 was explored for comparison with the 45 and Up Study.

The NHS (2007-08) was conducted by the Australian Bureau of Statistics and the results were weighted to population estimates for December 2007 [186]. Compared to the NHS (2007-08), the response rate was lower for the 45 and Up Study (94% vs 18%). The definition of one of the outcomes in the thesis (workforce participation in the 45 and Up Study) had similarity with one of the variables (employment) in the NHS (2007-08), but the comparison could not be done because of a lack of similarity in the set of conditions used in the definitions of the outcome in the thesis. Other outcomes and exposures in the thesis were not available to compare in the NHS (2007-08). Comparison of smoking status, alcohol consumption levels, obesity, and physical activity status of the participants in either survey was possible to some extent after stratification by age and sex. Such comparisons have indicated that the study participants of the 45 and Up Study were relatively healthier and had healthier lifestyle behaviours [185]. The possibility of a healthier cohort means that lower rates of CVD and higher rates of positive outcomes (such as being in the paid workforce) may be observed than in the NSW general population. It also implies that null associations should be interpreted with caution. Thus, the absolute estimates might not be representative. However, the relative estimates from the internal comparison in the 45 and Up Study could be considered valid and generalisable since the majority of observed associations in the 45 and Up Study were consistent with observations from the more representative NSW population health survey [146]. Another aspect of the source of the survey is missing data, like those in other cohort studies. The implication of missing data was explored with a case study from the thesis.

4.9 Ethics approval

Individuals gave written informed consent to take part in the study, including consent for linkage of their data to population health databases. The conduct of the 45 and Up Study was approved by the University of New South Wales Human Research Ethics Committee (HREC). Ethics approval for this project was obtained from the NSW Population and Health Services

Research Ethics Committee (Reference: HREC/12/CIPHS/31) and the Australian National University Human Research Ethics Committee (Reference: 2012/504).

CHAPTER 5 Empirical studies on the relationship of CVD to workforce participation

5.0 Chapter summary

This chapter presents two distinct but related studies that investigated the relationship of cardiovascular disease (CVD) and workforce participation by using the Sax Institute's 45 and Up Study and its linked datasets. To address the gaps in knowledge as identified in chapter two, these studies were conducted. The first study was a cross-sectional analysis that quantified workforce participation in 45-64-year-old men and women by comparing levels of non-participation in the workforce in people with CVD versus those without to understand the extent of the association. The second study was a longitudinal analysis that investigated the relationship between incident CVD and exit from the workforce to uncover the likely causal role of incident CVD on exit from the workforce.

The 45 and Up Study participants aged 45-64-year-old were examined in both studies. Workforce participation related outcomes were compared in people with versus without CVD in the first study. People who had no CVD and were in the workforce at baseline were followed up over time for comparing the exit from the workforce in those with versus without incident CVD during the follow-up period in the second study. Regression models were adjusted for sociodemographic variables in the first study. Then models were additionally adjusted for comorbidity in the second study. Both studies investigated variations according to CVD subtype, socio-demographic, and health factors, in particular, physical functioning limitations. Secondary outcomes included paid work hours per week, retirement, and retirement due to ill health.

Results in the first study (peer-reviewed publication in PLoS ONE [187]) indicated that most people aged 45-64 years old with and without CVD (60% vs 76%) were in the workforce, but after model adjustment, workforce non-participation was 36% higher with CVD compared to those without CVD. The second study showed that people with incident CVD versus those without had a 28% higher risk of exit from the workforce. The relationship of CVD to workforce

participation varied by CVD subtype and population characteristics in both cross-sectional and longitudinal results. Generally, workforce non-participation or exit from workforce were higher for those with cerebrovascular disease or heart failure compared to other types of CVD. Both workforce participation and exit from the workforce were much more strongly related to physical disability than to CVD diagnosis itself; among people without disability, levels of workforce participation were similar in people with and without CVD and poorer outcomes were observed in people with a severe disability regardless of CVD diagnosis.

Findings in this chapter enrich the current understanding of the relationship of CVD to workforce participation, particularly the likely consequences of incident CVD on exit from the workforce. The results on variation by CVD subtype and the role of physical disability are key novel contributions. The evidence generated is likely to be useful in informing CVD survivors, their care providers and organisations that help CVD survivors live a better quality of life with CVD.

5.1 Background

Mortality due to cardiovascular disease (CVD) is declining but CVD remains a leading contributor to the global burden of disease [62]. In Australia, CVD is the underlying cause of death in 27% of all deaths [188] and remains the second-largest contributor to the burden of disease [189]. With improving CVD survival, there is an increasing need to consider the consequences of living with CVD for individuals and society. An estimated 4.2 million adults aged 18 years and over in Australia had one or more CVD events in 2014–15 [190] and twenty-five per cent of people living with CVD reported being disabled to the extent that their core activities, including self-care, mobility, and communication are affected [191, 192], as is their ability to engage socially and take part in the workforce [193, 194]. The effect of CVD on workforce participation is of particular importance. It not only affects the overall health and financial well-being of the person living with CVD [50] but also has consequences for society given the substantial economic benefits of retaining people in the workforce [195], an increasingly important issue as the population ages.

The influence of CVD on workforce participation has been reported with outcomes such as the early exit from paid employment, unemployment status, partial or permanent work disability, receipt of disability pension, early retirement due to ill health and retirement pension, among others [82, 90, 91, 93, 196-198]. These cross-sectional and longitudinal studies, primarily set in Europe, have consistently shown that CVD is negatively associated with workforce participation, regardless of age, gender and geographical location. Studies within Australia have indicated that CVD is associated with lower productivity in work [41], lower income [49, 68, 114] and higher retirement due to ill-health [199]. However, there is limited evidence regarding the associations of workforce participation and CVD based on large-scale data in Australia. The available studies have lacked a direct comparison of outcomes in people with CVD to those in people without CVD. There is also limited evidence on people with specific subtypes of CVD and for population subgroups. I could not find any evidence

based on large-scale Australian studies regarding the change in workforce participation after incident CVD, and how these changes compare to those among people without CVD. There is also a lack of evidence on how workforce participation varies by incident CVD subtype, socio-demographic and health-related factors, particularly those that are associated with CVD [200] and workforce participation [201]. Among the people in the paid workforce, there is a lack of evidence on the longitudinal change of weekly paid work hours among the people with incident CVD compared to those without CVD. Among the people who had retired early, there is also a lack of evidence on how retirement due to ill health varies among those with incident CVD compared to those without CVD.

To address these gaps in knowledge, first, I aimed to understand the strength of association between CVD and workforce participation cross-sectionally in the first study. I have quantified workforce participation in a large population-based sample of 45-64-year-old men and women, comparing levels of non-participation in the workforce, hours of paid work per week, retirement and retirement due to ill-health, in those with versus without CVD, overall and according to CVD subtype including ischaemic heart disease (IHD) and its subgroup myocardial infarction (MI), cerebrovascular disease, heart failure (HF) and peripheral arterial disease (PAD). I have also aimed to examine whether the relationship between CVD and workforce non-participation varies in subgroups based on socio-demographic and health factors, and the extent to which co-existing physical functioning limitations might explain differences in workforce participation between those with and without CVD.

In the second study, the aim was to examine the likely causal role of incident CVD on exit from the workforce. Unlike the first study, this study was a longitudinal study that included only those participants who had no CVD at baseline, had been working at baseline and aged 45-<65 years at the follow-up survey. By comparing exit from the workforce at the follow-up survey in people with versus without incident CVD diagnosis during the follow-up period, I was

able to investigate the likely consequence on incident CVD on exit from workforce compared with those who had not developed CVD. I have also investigated the relationship by incident CVD subtype, population characteristics and physical disabilities like those in the first study. Finally, the aim was to study some secondary outcomes such as a longitudinal change in paid work hours per week and retirement due to ill health in people with versus without incident CVD to gather further evidence on the likely causal role of incident CVD to exit from the workforce.

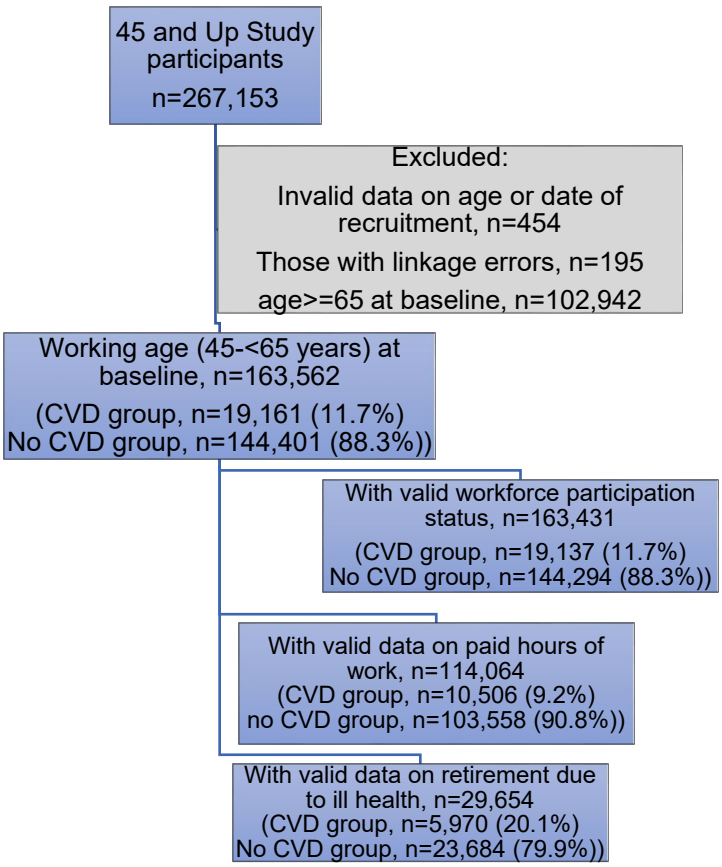
5.2 Workforce participation of working age older Australians with and without CVD

5.2.1 Materials and Methods

5.2.1.1 Study population and data sources

This is a cross-sectional investigation with study participants from the Sax Institute's 45 and Up Study [58] baseline questionnaire dataset which was probabilistically linked to several datasets including Medicare dataset and the NSW Admitted Patient Data Collection (APDC) datasets by the Centre for Health Record Linkage (CHeReL) [202]. The 45 and Up Study datasets were used to define outcomes, exposures, and other population characteristics. The Medicare datasets were used to define age and sex variables, the APDC datasets were used to define exposures from hospitalisations, and other linked datasets were used for logical checks of the linked datasets. The study population included only those participants who were of working age (45-<65 years old) at baseline; (n=163 562, 70 458 men, 93 104 women). There were no missing exposure data. However, after logical checking, there were missing data in outcomes that ranged from less than 0.1% to over 28%, and the number of study participants varied by the type outcomes (**Figure 5.1.1**).

Figure 5.1.1 Study design and flowchart for selection of participants for the association of CVD and workforce participation



5.2.1.2 Outcomes

The main outcome was non-participation in paid work (yes/no). Secondary outcomes were the number of paid hours of work per week (count), retirement (yes/no) and retirement due to ill-health (yes/no). These outcomes were defined based on responses recorded in the 45 and Up Study baseline questionnaire.

5.2.1.2.1 Main outcome

Workforce non-participation

The main outcome of interest in this investigation was workforce non-participation, and it was a binary variable with the detailed definition provided in section 4.3.1.1 in chapter 4 *(*Details in *Appendix 4: Section S5.1.1)*.

5.2.1.2.2 Secondary outcomes

Paid hours of work per week

Paid hours of work per week was defined as a count variable. Its definition was provided in section 4.3.1.2 in chapter 4. This outcome was studied only among the participants in the paid workforce. Those not in the workforce according to the main outcome definition were excluded from the analysis. Any value greater than or equal to 100 was invalidated and set to missing *(Details in Appendix 4: Section S5.1.1)*.

Retirement

Retirement was a binary outcome (yes/no) and its detailed definition was provided in section 4.3.1.3 in chapter 4. This outcome did not undergo further logical checks with another outcome variable, and it did not have any missing value.

Retired due to ill health

Retired due to ill health was a binary outcome (yes/no) and its definition was provided in section 4.3.1.3 in chapter 4. There were logical checks of this variable applied against workforce participation status (Table S5.1.2). Participants classified as 'being in the workforce' according to the main outcome definition were excluded. Retired due to ill health was examined only among the participants who had not been working in any form (Details in Appendix 4: Figure S5.1.4).

5.2.1.3 Exposures

CVD at baseline was defined as self-reported heart disease, stroke or blood clot on the baseline questionnaire, or at least one hospital admission in the five years before entering the study with a major CVD diagnosis, as identified in any diagnostic or a procedure code field [23]. A five-year window was used to ensure a uniform probability of identification of previous diagnoses from administrative data for all participants. The participants were categorised based on hospitalisations for the following CVD subtypes (yes/no): IHD (ICD-AM codes: I20-I25), MI (ICD-AM codes: I21, I22 and I23), cerebrovascular disease (ICD-AM codes: I61, I63, I64), PAD (ICD-AM codes: I70-I74) and HF (ICD-AM codes: I50, I11.0, I13.0, I13.2) *(Details in Appendix 3: Table S4.4).*

5.2.1.4 Other variables of interest

Sociodemographic variables included: age, sex, region of residence (categorised as major cities, inner regional and more remote, based on the mean Accessibility Remoteness Index of Australia Plus score [203]), marital status (categorised as married/defacto and single/widowed/divorced), education (categorised as tertiary, certificates/diploma/trade and high school or less), language other than English (LOTE) (yes/no) and born in Australia/New Zealand (yes/no). Health-related variables included: body mass index (BMI, kg/m^2)

categorised as underweight (15-<18.5), normal weight (18.5-<25), overweight (25-<30), obese (30-50); alcohol consumption (number of alcoholic drinks per week categorised as non-drinkers (zero drinks per week), moderate drinkers (>0-<15 drinks per week), heavy drinkers (≥15 drinks per week)); smoking status (non-smoker, past-smoker, current smoker); self-reported doctor-diagnosed diabetes/cancer/osteoarthritis (yes/no for each) and physical functioning limitations. The cut points of alcohol consumption broadly reflect the Australian guideline on low-risk consumption [172]. The degree of physical functioning limitations was assessed using the Medical Outcomes Study–Physical Functioning (MOS-PF) subscale which was based on 10 questionnaire items assessing varying levels of physical functioning [176]. Physical functioning limitations scores ranged from 0 to 100, where higher scores represented fewer limitations. The scores grouped the participants into four categories according to previous studies [177]: no limitation (score of 100); minor limitation (score 90–99); moderate limitation (60–89); and severe limitation (score 0–59) *(Appendix 3: Table S4.5*). These variables were included because of their associations with workforce participation [82, 92, 163-170, 204-207].

5.2.1.5 Statistical analysis

Descriptive statistics were used to summarise characterises of the study population and distribution of outcomes by CVD status. Modified Poisson regression with robust error variance [181] was used to estimate prevalence ratios (PRs) for binary outcomes: non-participation in the paid workforce, retirement, and retirement due to ill health. A generalised linear model (GLM) assuming a Poisson distribution and log link function was used to estimate the mean of paid work hours per week. As significant interaction by sex was not observed, the main models were adjusted for rather than stratified by sex. Models were sequentially adjusted, initially adjusting for age-group (5-year age bands) and sex [model 1], and then additionally adjusted for the region of residence and education [model 2]. Chi-square tests for heterogeneity were used to assess heterogeneity between subgroups. Participants with

missing values for the outcome of interest were excluded from the corresponding analysis. The analyses were carried out using SAS software version 9.4 and R version 3.5.2 [183].

5.2.1.6 Sensitivity analysis

Sources of CVD definition (self-reported or hospital admission) and presence of comorbid CVD conditions (from hospitalisation records only) were considered in the sensitivity analyses. These analyses were done to understand whether the effect sizes vary because of the way exposure was defined or because of multiple CVD subtypes diagnosis.

5.2.2 Results

5.2.2.1 Characteristics of the study participants

There were 163,562 study participants: 19,161 (11.7%) with CVD and 144,401 (88.3%) without CVD. There were 121,816 participants (74.5%) in the paid workforce, of whom 11,480 (9.4%) had CVD; and 155,723 participants (>95%) had valid paid work hours per week (i.e., ≥ 0 and <100). There were 43,397 participants who had retired, 29,654 retirees who had not been working in any form and 5,970 of whom had CVD (20.1%). The sociodemographic profile of participants with and without CVD was similar, except that the CVD group had higher proportions of men and older participants (**Table 5.1.1**). Participants with CVD had higher non-participation in work, lower paid-work hours per week and higher retirement due to ill health (**Figure 5.1.2**). Participants with CVD had a poorer health profile than those without CVD, with higher levels of smoking, obesity, comorbid diseases, and moderate/severe functional limitation (**Table 5.1.1**).

Figure 5.1.2 Workforce participation, paid work hours per week, retirement patterns according to CVD status, sex and age-group

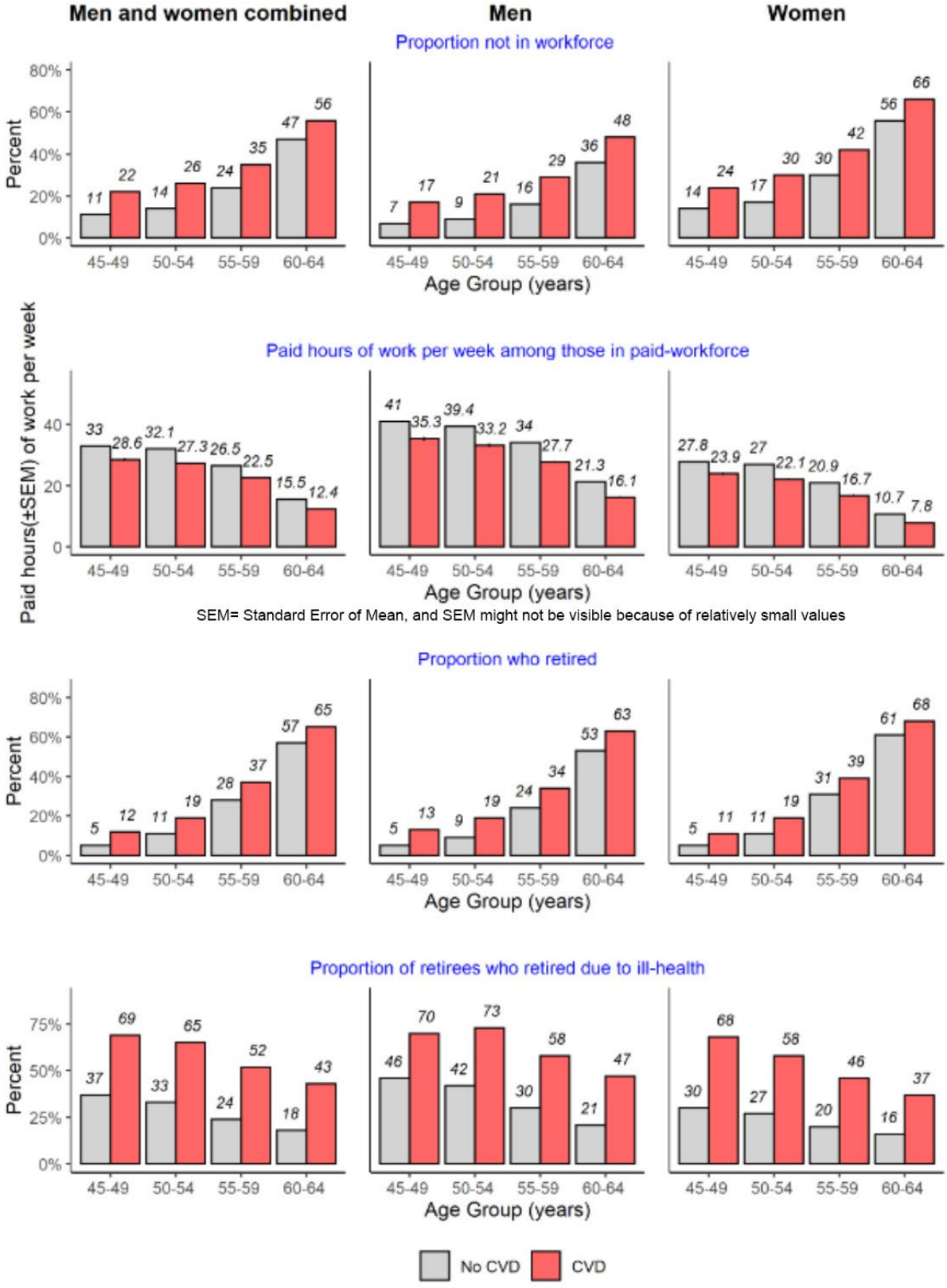


Table 5.1.1 Sociodemographic and health related characteristics of study participants

	People with CVD	People without CVD
Total participants (n = 163562)	19161	144401
Percentage (%)	11.7 (19161/ 163562)	88.3 (144401/ 163562)
Age (years)		
Mean (sd)	57.5 (5.18)	55.0 (5.38)
45-49	11.0 (2110)	22.7 (32759)
50-54	19.7 (3767)	27.1 (39173)
55-59	29.8 (5712)	27.5 (39733)
60-64	39.5 (7572)	22.7 (32736)
Sex		
Men	51.5 (9873)	42.0 (60585)
Women	48.5 (9288)	58.0 (83816)
Region of residence		
Major cities	49.5 (9477)	51.9 (75002)
Inner regional	36.1 (6911)	34.7 (50058)
More remote	12.4 (2370)	11.4 (16392)
Marital status		
single/widowed/separated	23.1 (4425)	20.1 (29042)
Married/defacto	76.3 (14613)	79.3 (114549)
Education attainment		
No school certificate	12.8 (2460)	7.8 (11225)
Certificate/diploma/trade	64.1 (12277)	62.3 (89897)
Tertiary	22.0 (4206)	29.0 (41853)
Language spoken at home other than English (Yes)	8.5 (1623)	10.0 (14443)
Country of birth in Australia/NZ	79.6 (15244)	78.0 (112655)
Alcohol consumption		
None (0 drink per week)	34.5 (6604)	28.9 (41680)
Moderate drinkers (1-14drinks per week)	48.2 (9237)	54.6 (78857)
Heavy drinkers (15 or more drinks per week)	15.6 (2988)	15.1 (21793)
Smoking status		
Current	10.7 (2046)	9.3 (13367)
Past	40.9 (7839)	33.0 (47590)
Never	48.0 (9194)	57.5 (82979)
BMI Category		
Underweight (15-<18.5)	0.9 (169)	0.9 (1369)
Normal weight (18.5-<25)	24.3 (4659)	34.7 (50047)
Overweight (25-<30)	36.3 (6959)	36.1 (52120)
Obese (30 to 50)	31.3 (6005)	21.6 (31159)
Medical History: Cancer: Yes	15.2 (2919)	10.7 (15416)
Medical History: Diabetes: Yes	14.4 (2753)	5.4 (7804)
Medical History: Osteoarthritis: Yes	4.8 (921)	2.8 (4026)
Physical functioning limitations		
No limitation	22.7 (4347)	41.7 (60166)
Minor limitation	24.6 (4714)	26.7 (38603)
Moderate limitation	24.2 (4645)	16.1 (23275)
Severe limitation	18.5 (3536)	6.1 (8812)

Note: % missing responses (CVD, No CVD): region of residence (2.1, 2); marital status (0.6, 0.6); education attainment (1.1, 1), country of birth (0.8, 0.8), alcohol per week (1.7, 1.4); smoking status (0.4, 0.3); BMI (7.1, 6.7); physical functioning limitations (10.0, 9.4). sd refers to standard deviation, NZ refers to New Zealand, BMI refers to Body Mass Index.

Table 5.1.2 Workforce participation, paid work hours per week, retirement patterns and physical functioning limitations among study participants

	People with CVD	**People without CVD**
Total N	19161	144401
In workforce*	**59.9** (11480)	**76.4** (110336)
In full time paid work	28.0 (5358)	38.8 (55971)
Self-employed	14.0 (2675)	17.3 (24913)
In part time paid work	15.4 (2950)	19.7 (28512)
Partially retired	6.8 (1297)	5.3 (7644)
Not in workforce	**40.0** (7657)	**23.5** (33958)
Doing unpaid work	5.8 (1102)	5.3 (7681)
Completely retired/pensioner	21.5 (4113)	12.3 (17729)
Studying	1.7 (319)	2.1 (3053)
Looking after home/family	9.9 (1902)	11.2 (16182)
Disabled/sick	14.9 (2859)	4.4 (6410)
Unemployed	3.8 (732)	3.1 (4502)
Other	2.0 (380)	1.7 (2419)
Paid hours of work (for those in workforce)		
N	10506	103558
Mean, SD	34.9, 15.6	35.9, 14.8
Median [inter quartile range]	38 [25, 45]	38 [26, 45]
Retirement reasons (among those who retired and not in the workforce)		
Total N	5970	23684
Retired due to ill health	53.0 (3166)	26.3 (6238)
Retired due to other reasons	47.0 (2804)	73.7 (17446)
Reached usual retirement age	7.9 (474)	12.2 (2896)
Lifestyle reasons	20.7 (1237)	32.4 (7684)
To care for family	10.9 (648)	14.9 (3537)
Made redundant	10.6 (630)	11.7 (2770)
Could not find a job	5.6 (332)	5.4 (1277)
Other	9.8 (584)	14.1 (3328)

One person might be in more than one category of sub-groups of those in workforce, not in workforce and retired due to other reasons. *% missing responses of workforce participation (Total, CVD, No CVD): (0.08, 0.13, 0.07).

5.2.2.2 CVD and non-participation in workforce

Overall, 60% of people with CVD were participating in the workforce, compared to 76% of people without CVD (**Figure 5.1.3**). Women and those of older age had higher non-participation regardless of CVD status. In every 5-year age bracket (45-<50 to 60-<65), non-participation was higher in men and women with CVD than without CVD **(Figure 5.1.2***).*

After adjusting for sociodemographic characteristics (age, sex, region of residence and education), workforce non-participation was 36% higher among people with any CVD compared to people without CVD [prevalence ratio (PR) = 1.36 (95% CI: 1.33-1.39)]. Workforce non-participation varied by CVD subtype, with PRs of 1.46 (95% CI: 1.41-1.50) for IHD and 1.92 (95% CI: 1.80-2.06) for cerebrovascular disease (**Figure 5.1.3**). Sensitivity analyses indicate that those with CVD hospitalisation had somewhat higher PRs of non-participation in the paid workforce compared to those with self-reported CVD only (*Appendix 4: Table S5.1.4*) and people with only one type of CVD had slightly lower PRs of non-participation in the paid workforce than those with more than one type of CVD (*Appendix 4: Table S5.1.5 and Table S5.1.6).*

5.2.2.2.1 CVD and workforce participation among population subgroups

Workforce participation was associated with a number of sociodemographic factors among both people with and without CVD, including age, marital status, education, country of birth, alcohol consumption, smoking status and having a medical history of osteoarthritis *(Appendix 4: Figures S5.1.5 and S5.1.6)*. When workforce participation was compared in people with and without CVD separately within subgroups based on sociodemographic and health-related factors, workforce non-participation remained higher among people with CVD compared to those without CVD, regardless of population subgroup. However, PRs were significantly higher among younger people, men, those who were not married/de facto, those without tertiary qualifications and those who were current smokers. Although the absolute crude

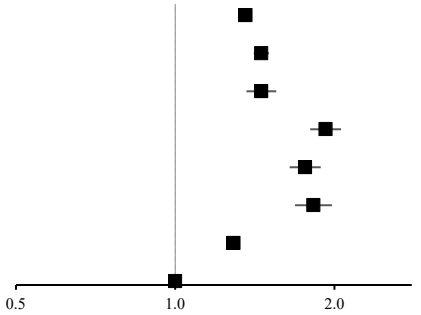
prevalence of workforce non-participation was higher in older compared to younger age groups (irrespective of CVD status), the relation of CVD and workforce non-participation became weaker with increasing age (**Figure 5.1.4**).

5.2.2.2.2 CVD, physical functioning limitations and workforce participation

Workforce participation was lower in those with greater physical functional limitations - among both those with and without CVD - but non-participation was higher among those with CVD in all sub-groups based on physical functioning limitations (**Figure 5.1.5**). Among participants with no physical functioning limitations, about one in 5 were not working - 21% of those with CVD and 16% of those without CVD; among participants with severe functioning limitations, 73% of those with CVD, and 60% of those without CVD, were not working. After adjustment for sociodemographic variables, compared to those without CVD and no functional limitations, participants without physical functional limitations but with CVD were 13% more likely to be out of the workforce (PR=1.13, 95% CI=1.07-1.20). Those with severe functioning limitations were 3 times as likely to be out of the workforce if they had CVD (PR= 2.91 (95% CI: 2.82-3.00)) and 2.7 times as likely if they did not have CVD (PR= 2.70 (95% CI: 2.63-2.77)) **(Figure 5.1.5).**

Figure 5.1.3 *Non-participation in the workforce:* Prevalence and adjusted prevalence ratios in people with and without CVD and according to hospitalisation for CVD subtypes

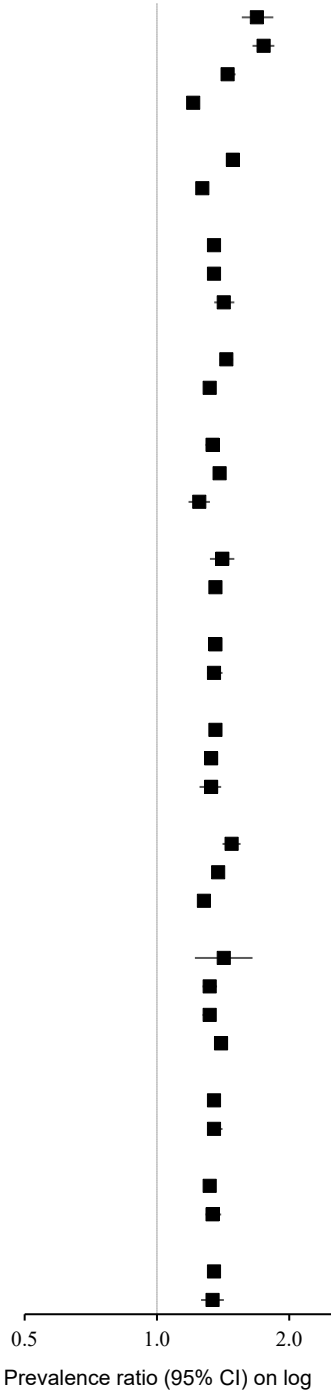
	Not in workforce % [n/N]	Prevalence ratio (95% CI)	
Total n/N	25.5 (41615/163431)	Model[1]	Model[2]
Any CVD [a]	40.0 (7657/19137)	1.43 (1.40-1.46)	1.36 (1.33-1.39)
Ischaemic heart disease [b]	43.0 (1979/4601)	1.57 (1.52-1.62)	1.46 (1.41-1.50)
Myocardial infarction [b]	40.1 (493/1229)	1.59 (1.49-1.70)	1.46 (1.36-1.55)
Cerebrovascular disease [b]	58.4 (409/700)	2.09 (1.96-2.24)	1.92 (1.80-2.06)
Peripheral arterial diseases [b]	56.5 (386/683)	1.95 (1.82-2.09)	1.76 (1.65-1.88)
Heart failure [b]	60.2 (266/442)	2.10 (1.94-2.27)	1.83 (1.68-1.98)
Other CVD [a]	37.8 (5053/13372)	1.34 (1.31-1.37)	1.29 (1.26-1.32)
No CVD (reference)	23.5 (33958/144294)	1	1



[1]Adjusted for age and sex. [2]Adjusted for age, sex, remoteness of residence and education.
[a] Based on self-report and hospital records [b]Based on hospital records only and regardless of presence of other CVD subtypes.
Effect sizes were estimated using 'no CVD' as the reference group.

Figure 5.1.4 *Non-participation in the workforce:* Prevalence and adjusted prevalence ratio of non-participation in the workforce in population subgroups based on socio-demographic and health related factors

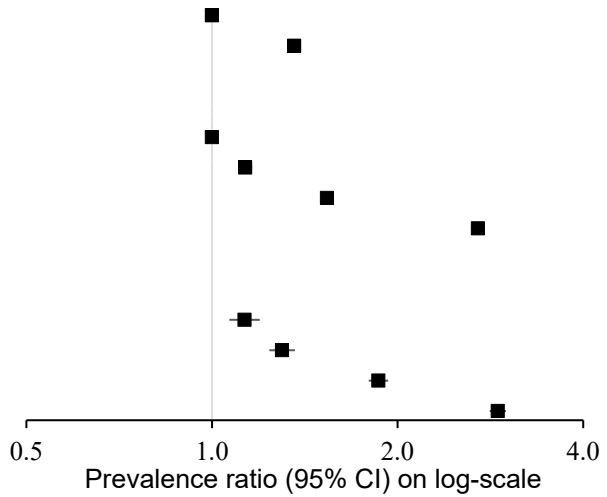
Factors and levels of the factors	Not in workforce % [n/N] CVD	No CVD	[1]PR (95% CI)	[1]PR (95% CI) of not in workforce of those with CVD compared to those without CVD	P-heterogeneity
Age group (years)					
45-49	21.5 (454/2108)	11.4 (3726/32749)	1.69 (1.56-1.84)		<0.0001
50-54	25.7 (968/3764)	13.7 (5350/39159)	1.75 (1.65-1.85)		
55-59	35.1 (2001/5706)	24.0 (9526/39698)	1.45 (1.40-1.51)		
60-64	56.0 (4234/7559)	47.0 (15356/32688)	1.21 (1.19-1.24)		
Sex					
Men	34.8 (3427/9859)	17.2 (10444/60551)	1.49 (1.44-1.54)		<0.0001
Women	45.6 (4230/9278)	28.1 (23514/83743)	1.27 (1.24-1.30)		
Region					
Major cities	36.7 (3478/9465)	21.8 (16331/74943)	1.35 (1.31-1.39)		0.2172
Inner regional	44.0 (3034/6902)	26.1 (13040/50027)	1.35 (1.31-1.39)		
More remote	43.1 (1021/2367)	24.9 (4075/16379)	1.42 (1.35-1.50)		
Marital status					
Not currently	49.8 (2198/4413)	28.0 (8130/29000)	1.44 (1.39-1.49)		<0.0001
Married/defacto	37.1 (5415/14602)	22.4 (25639/114484)	1.32 (1.29-1.35)		
Highest Education					
No school certificate	63.4 (1556/2455)	46.0 (5146/11196)	1.34 (1.29-1.38)		0.0013
Certificate/diploma/trade	41.1 (5039/12260)	25.0 (22488/89841)	1.39 (1.36-1.42)		
Tertiary	22.4 (943/4204)	13.9 (5824/41835)	1.25 (1.18-1.32)		
Language other than English					
Yes	41.8 (678/1621)	26.0 (3751/14422)	1.41 (1.32-1.50)		0.2953
No	39.8 (6979/17516)	23.3 (30207/129871)	1.36 (1.33-1.39)		
County of Birth					
Australia/NZ	39.6 (6035/15224)	23.0 (25858/112574)	1.36 (1.34-1.39)		0.7454
Others	41.2 (1553/3769)	25.4 (7838/30898)	1.35 (1.30-1.41)		
Alcohol consumption					
No drinkers	51.0 (3366/6597)	31.3 (13050/41644)	1.36 (1.32-1.39)		0.4987
Moderate drinkers	33.6 (3102/9228)	19.9 (15673/78804)	1.33 (1.29-1.37)		
Heavy drinkers	33.6 (1002/2980)	20.2 (4392/21784)	1.33 (1.25-1.40)		
Smoking status					
Current	52.6 (1076/2044)	30.4 (4059/13345)	1.48 (1.41-1.55)		<0.0001
Past	40.8 (3192/7827)	23.4 (11114/47559)	1.38 (1.34-1.42)		
Never	36.5 (3348/9184)	22.5 (18650/82926)	1.28 (1.25-1.32)		
BMI (kg/m2)					
Underweight (<18)	56.2 (95/169)	33.4 (456/1367)	1.42 (1.22-1.65)		0.0389
Normal weight (18–<25)	37.3 (1733/4650)	22.4 (11221/50018)	1.32 (1.27-1.37)		
Overweight Over weight	35.8 (2490/6947)	21.4 (11155/52081)	1.32 (1.27-1.36)		
Obese ((30+)	45.6 (2736/6003)	27.1 (8449/31132)	1.40 (1.36-1.45)		
Medical History: Cancer					
No	38.3 (6216/16224)	22.7 (29227/128889)	1.35 (1.33-1.38)		1.0000
Yes	49.5 (1441/2913)	30.7 (4731/15405)	1.35 (1.30-1.41)		
Medical History: Diabetes					
No	37.4 (6126/16389)	22.7 (31022/136501)	1.32 (1.29-1.34)		0.5136
Yes	55.7 (1531/2748)	37.7 (2936/7793)	1.34 (1.29-1.40)		
Medical History:					
No	38.7 (7053/18220)	23.0 (32236/140274)	1.35 (1.32-1.38)		0.8192
Yes	65.9 (604/917)	42.8 (1722/4020)	1.34 (1.26-1.42)		



[1]Adjusted for age, sex, remoteness of residence and education.

Figure 5.1.5 *Non-participation in the workforce*: Prevalence and adjusted prevalence ratios according to joint categories of physical functioning limitations and CVD

	Not in workforce % [n/N]	Prevalence ratio (95% CI) Model[1]	Model[2]
Without CVD	23.5 (33958/144294)	1	1
With CVD	40.0 (7657/19137)	1.43 (1.40-1.46)	1.36 (1.33-1.39)
No CVD and			
No limitations	15.8 (9501/60139)	1	1
Minor limitations	20.1 (7750/38587)	1.13 (1.10-1.16)	1.13 (1.10-1.16)
Moderate limitations	31.2 (7265/23256)	1.61 (1.57-1.65)	1.54 (1.50-1.58)
Severe limitations	59.6 (5243/8790)	3.03 (2.95-3.11)	2.70 (2.63-2.77)
CVD and			
No limitations	20.8 (904/4344)	1.15 (1.08-1.21)	1.13 (1.07-1.20)
Minor limitations	26.4 (1243/4712)	1.31 (1.25-1.38)	1.30 (1.24-1.36)
Moderate limitations	43.6 (2021/4637)	1.99 (1.92-2.07)	1.86 (1.80-1.93)
Severe limitations	73.1 (2578/3528)	3.33 (3.23-3.43)	2.91 (2.82-3.00)



[1]Adjusted for age and sex, [2]Further adjusted for remoteness of residence and education attainment. Those with 'no functional limitations and no CVD' were the reference group for estimating prevalence ratios (PR's) for non-participation in work according to joint categories of physical functioning limitations and CVD. CVD is based on both self-report and hospitalisation records. Physical functional limitations had scores ranged from 0 to 100, where higher scores represented fewer limitations, and were grouped into four categories: severe (0–<60); moderate (60-<90), minor (90-<100) and no (100) functional limitation.

5.2.2.3 CVD and weekly paid hours of work

Mean weekly working hours per week among those in paid work was lower for people with CVD than without CVD in both men and women in every 5-year age bracket (45-<50 to 60-<65) (**Figure 5.1.2**). After adjusting for sociodemographic characteristics, people with CVD worked 0.92 (95% CI: 0.82-1.02) fewer hours/week on average. This varied by CVD subtype, ranging from 0.62 (0.28-0.95) fewer hours/week for ischaemic heart disease to 3.40 (1.72-4.98) fewer hours/week for cerebrovascular disease (**Figure 5.1.6,** *Appendix 4: Tables S5.1.7 to S5.1.9*).

5.2.2.4 CVD and retirement

Of all participants, 42% of people with CVD had retired, compared to 25% of people without CVD (**Figure 5.1.7**). The retirement rate was higher in people with CVD than without CVD in both men and women in every 5-year age bracket (45-<50 to 60-<65) (**Figure 5.1.2**). After adjusting for sociodemographic characteristics, people with CVD had 25% higher likely (PR= 1.25, 95% CI: 1.23-1.28) to retire. This varied by CVD subtype, with PRs ranging from 1.28 (1.24-1.32) for IHD to 1.61 (1.51-1.72) for those with cerebrovascular disease (**Figure 5.1.7,** *Appendix 4: Tables S5.1.10 to S5.1.12*).

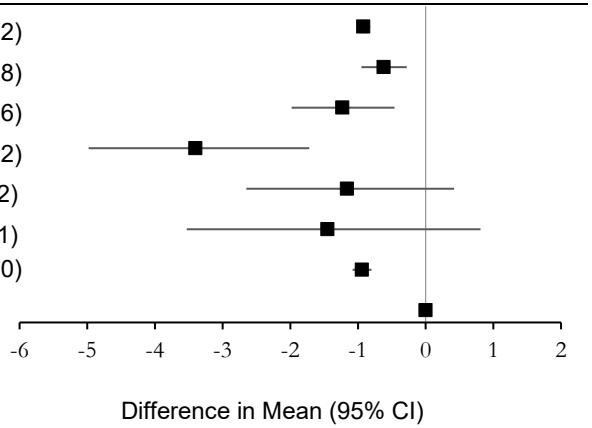
5.2.2.5 CVD and retirement due to ill health

Of the participants who had retired and who had not been in the workforce in any form, 53.0% of people with CVD had retired due to ill health, compared to 26.3% of people without CVD (**Figure 5.1.7)**. The rate of retirement due to ill health was higher among people with CVD than without CVD in both men and women in every 5-year age bracket (45-<50 to 60-<65) (**Figure 5.1.2**). After adjusting for sociodemographic characteristics, people with CVD were 88% more likely to retire due to ill-health compared to those of people without CVD (PR= 1.88, 95% CI: 1.82-1.94). This varied by CVD subtype, with PRs ranging from 2.08 (1.99-2.18) for those with

IHD to 2.62 (2.43-2.83) for those with heart failure (**Figure 5.1.7,** *Appendix 4: Tables S5.1.13 to S5.1.15*).

Figure 5.1.6 *Paid hours of work per week:* Means and adjusted mean differences in people with and without CVD and according to CVD subtypes among those in paid work

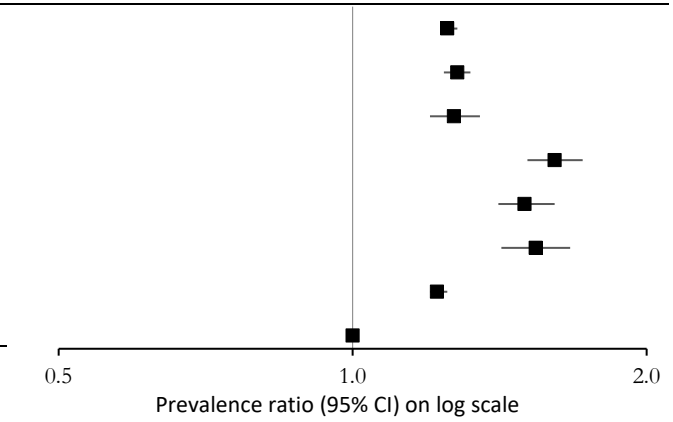
	Total N	Mean (95% CI)	Difference in Mean (95% CI)	
	114064		Model[1]	Model[2]
CVD [a]	10506	34.9 (34.6, 35.2)	-0.95 (-1.13, -0.77)	-0.92 (-1.02, -0.82)
Ischaemic heart disease [b]	2406	36.7 (36.0, 37.3)	-0.69 (-1.14, -0.23)	-0.62 (-0.95, -0.28)
Myocardial infarction [b]	679	36.9 (35.8, 38.1)	-1.50 (-2.38, -0.58)	-1.23 (-1.98, -0.46)
Cerebrovascular disease [b]	263	32.9 (31.0, 34.9)	-3.39 (-5.10, -1.57)	-3.40 (-4.98, -1.72)
Peripheral arterial diseases [b]	265	34.7 (32.7, 36.6)	-1.24 (-2.88, 0.49)	-1.16 (-2.65, 0.42)
Heart failure [b]	156	34.7 (32.0, 37.3)	-1.98 (-4.21, 0.42)	-1.45 (-3.53, 0.81)
Other CVD [a]	7612	34.5 (34.1, 34.8)	-0.95 (-1.18, -0.72)	-0.94 (-1.08, -0.80)
No CVD (reference)	103558	35.9 (35.8, 36.0)	0	0



[1]Adjusted for age and sex. [2]Adjusted for age, sex, remoteness of residence and education.
[a] Based on self-report and hospital records [b]Based on hospital records only and regardless of presence of other CVD subtypes.
Effect sizes were estimated using 'no CVD' as the reference group.

Figure 5.1.7 *Retirement:* Prevalence and adjusted prevalence ratios of retirement in people with and without CVD and according to CVD subtypes

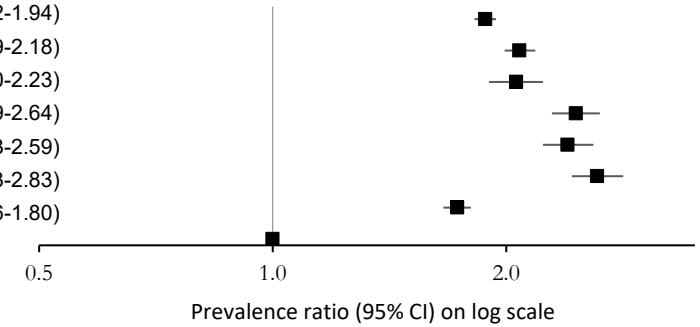
	Retired % (n/N)	Prevalence ratio (95% CI)	
Total n/N	26.5 (43397/163562)	**Model[1]**	**Model[2]**
CVD [a]	41.6 (7975/19161)	1.28 (1.25-1.30)	1.25 (1.23-1.28)
Ischaemic heart disease [b]	45.2 (2084/4609)	1.31 (1.27-1.35)	1.28 (1.24-1.32)
Myocardial infarction [b]	42.1 (518/1231)	1.31 (1.23-1.39)	1.27 (1.20-1.35)
Cerebrovascular disease [b]	55.9 (391/700)	1.66 (1.55-1.77)	1.61 (1.51-1.72)
Peripheral arterial diseases [b]	55.2 (378/685)	1.56 (1.46-1.66)	1.50 (1.41-1.61)
Heart failure [b]	56.8 (252/444)	1.63 (1.50-1.77)	1.54 (1.42-1.67)
Other CVD [a]	39.5 (5292/13387)	1.24 (1.21-1.26)	1.22 (1.20-1.25)
No CVD (reference)	24.5 (35422/144401)	1	1



Model[1]= Adjusted for age and sex, Model[2] = Further adjusted for remoteness of residence and education attainment. [a]Based on both self-reported survey and hospital records, [b]Based on hospital records only and regardless of other CVD diagnosis. Effect sizes were estimated using 'no CVD' as the reference group.

Figure 5.1.8 *Retirement due to ill health*: Prevalence and adjusted prevalence ratios in people with and without CVD and according to CVD subtypes among those who have retired and who had not been in paid workforce

	Retired due to ill health % (n/N)	Prevalence ratio (95% CI)	
Total n/N	31.7 (9404/29654)	Model[1]	Model[2]
CVD [a]	53.0 (3166/5970)	1.95 (1.89-2.01)	1.88 (1.82-1.94)
Ischaemic heart disease [b]	62.3 (992/1593)	2.19 (2.09-2.29)	2.08 (1.99-2.18)
Myocardial infarction [b]	63.8 (247/387)	2.16 (1.99-2.34)	2.06 (1.90-2.23)
Cerebrovascular disease [b]	72.9 (237/325)	2.50 (2.33-2.68)	2.46 (2.29-2.64)
Peripheral arterial diseases [b]	73.7 (233/316)	2.54 (2.36-2.72)	2.40 (2.23-2.59)
Heart failure [b]	81.9 (172/210)	2.82 (2.62-3.04)	2.62 (2.43-2.83)
Other CVD [a]	47.0 (1826/3883)	1.78 (1.71-1.85)	1.73 (1.66-1.80)
No CVD (reference)	26.3 (6238/23684)	1	1



Model[1]= Adjusted for age and sex, Model[2] = Adjusted for age-group, sex, remoteness of residence and education attainment. [a]Based on both self-reported survey and hospital records, [b]Based on hospital records only and regardless of other CVD diagnosis. Effect sizes were estimated using 'no CVD' as the reference group.

5.2.3 Study summary and limitations

In this large-scale cross-sectional Australian study, the results suggested that most people with CVD were doing paid work, but they were 36% more likely to be not participating in the workforce compared to those without CVD. These findings were observed across different types of CVD but with varying magnitudes, particularly those who had cerebrovascular disease were approximately two times more likely to not be participating in the workforce compared to those of people without CVD. Some sociodemographic groups, in particular, younger people and those not married or in a de facto relationship and current smokers with CVD, were more likely to not be participating in the workforce. Workforce participation was much more strongly related to physical disability than to CVD diagnosis itself, with poorer outcomes observed in people with severe disabilities regardless of CVD diagnosis. For example, people with CVD and severe physical disability were about three times more likely not in the paid workforce while those with CVD and no physical functioning limitations were around just as likely to be in paid work as those without CVD.

Secondary outcomes examined in this cross-sectional analysis also demonstrated the relation in the same direction. For example, among the working people, those with CVD had been working about one fewer hour per week on average than people who hadn't had a CVD. People with CVD were 25% and 88% more likely 'to retire' and 'to have retired due to ill health' than people without CVD.

The findings in this investigation have provided evidence on the extent of the associations, but they could not answer the likely causal role of CVD or CVD subtypes on exit from the workforce from these findings. Hence, a longitudinal investigation by selecting people who had no CVD at baseline and who had been working at baseline was conducted.

5.3 The relationship between incident CVD and exit from workforce over time among working age older Australians

5.3.1 Materials and Methods

5.3.1.1 Study design, settings and data sources

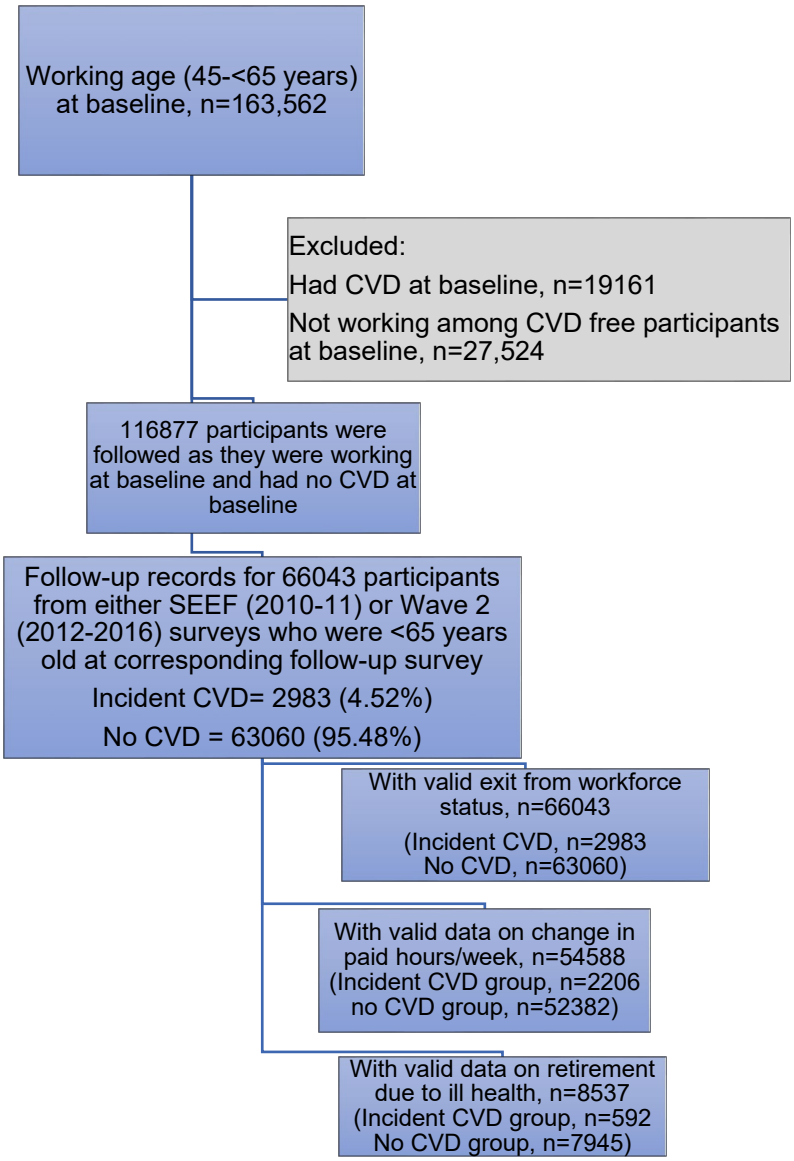
This is a longitudinal investigation with study participants from the 45 and Up Study baseline questionnaire and follow-up questionnaire which were probabilistically linked to NSW APDC by the CHeReL [202]. The 45 and Up Study follow-up surveys consisted of two surveys; first, the SEEF survey which was conducted between 01/01/2010 to 28/04/2011 with a study population of 31543 and second, the Wave 2 survey which was conducted between 18/12/2012 to 26/12/2016 with a study population of 66625 (*Appendix 4: Figure S5.2.1*). The NSW APDC records from the baseline to follow-up survey period were considered in the longitudinal analyses.

5.3.1.2 Study population and sample

Among the 163,562 people aged 45-64 in the baseline survey of the 45 and Up Study, 116,877 participants had no prior CVD admissions or no self-reported CVD and had been working at baseline. This study followed this cohort for the follow-up survey records. Participants aged less than 65 years old in the follow-up survey were included in the study. Among the potentially eligible participants, 24359 and 55439 participants filled out the ‘SEEF’ and ‘Wave 2’ surveys respectively and there were 13749 participants who had participated in both surveys. Those responding to at least one follow-up survey (from 01/01/2010 to 26/12/2016) were included, prioritising the survey response at ‘Wave 2’ for participants responding to both follow-up surveys. This strategy provided a longer follow-up time. After excluding those having missing or invalid follow-up data, there were 66043 participants included in the longitudinal study (*Appendix 4: Figure S5.2.1*). If the potentially eligible participants had completed neither ‘SEEF’ nor ‘Wave 2’ and were alive during the follow-up survey period, we considered these

participants as 'loss to follow-up' for the outcome. This issue was further explored in chapter seven of the thesis. Similar to cross-sectional analyses, the participants with missing outcome variables were excluded from the corresponding analysis. Therefore, the number of study participants varied by the outcome examined **(Figure 5.2.1**).

Figure 5.2.1 Study design and flowchart for selection of participants for the association of incident CVD and exit from workforce



*SEEF stands for Social, Economic and Environmental Factors and it is a survey for participants in the 45 and Up Study after baseline and WAVE 2 another survey for participants in the 45 and Up Study after SEEF survey.

5.3.1.3 Outcomes

The main outcome was 'exit from workforce' (both paid or self-employment) (yes/no) and the secondary outcomes were change in paid workhour per week and retirement due to ill health (yes/no). Exit from the workforce (yes/no) was measured at the follow-up survey, the change in paid hours was derived from baseline and follow-up survey, and retirement due to ill health was measured at the follow-up.

5.3.1.3.1 Main outcomes

Exit from workforce

Exit from workforce was the main outcome of interest in this investigation, and it was a binary variable with the detailed definition provided in section *5.2.1.2.2* of this chapter and section 4.3.1.1 in chapter 4 *(*Details in *Appendix 4: Section S5.1.1)*.

5.3.1.3.2 Secondary outcomes

Change in paid hours of work per week

Change in paid hours of work per week was based on baseline survey as well as follow up surveys (wave 2 and supplemented by SEEF survey) questions on paid hours of work per week. Some logical checking was done, similar to those mentioned in section *5.2.1.2.2* of this chapter.

Retirement due to ill health

Retired due to ill health at the follow-up survey was a binary outcome (yes/no) and its definition was provided in section 4.3.1.3 in chapter 4. Some logical checking was done, similar to those mentioned in section *5.2.1.2.2* of this chapter.

5.3.1.4 Exposures

The main exposure was non-fatal incident CVD between two surveys. The diagnoses were based on all diagnosis fields and procedures in APDC records after the baseline survey but prior to the corresponding follow-up surveys. Incident CVD was identified with ICD-10 AM as mentioned previously [23]. ICD-10 AM codes for incident CVD subtypes were incident IHD (I20-I25), incident MI (I21 and I22), incident cerebrovascular disease (I61, I63, I64), incident PAD (I70-I74) and incident HF (I50, I11.0, I13.0, I13.2) *(Appendix 3: Table S4.4)*. As participants could develop more than one CVD subtype, each CVD subtype was further stratified; for example, people with incident IHD between surveys were stratified as incident IHD only, incident IHD and other incident CVD conditions.

5.3.1.5 Sociodemographic factors of interest

Several sociodemographic variables of interest were included because previous studies have reported the association of these factors with CVD and paid workforce participation related to economic engagement [167-170, 207]. These variables were obtained from Medicare data (Age and sex), baseline or follow-up surveys of the 45 an Up Study, and the hospitalisation in between the surveys. Some variables included in the second study were the same as those in the first study of this chapter. These were the region of residence, education, language other than English (LOTE) and country of birth, which were obtained from the baseline survey. The variables obtained from the follow-up survey were doctor-diagnosed diseases such as diabetes/cancer/osteoarthritis, and physical functioning limitations [176, 208]. Categorisation of these variables was similar to those mentioned in '*section 5.2.1.4'* of this chapter, except for age which was grouped into three (<55 years, 55-<60 years, 60-<65 years). In contrast to four age groups in the first study, three age categories were done in this study because of the smaller number of participants in the 45-<50 years age group. Since the incident CVD is also associated with comorbidity [209], the level of comorbidity based on hospitalisation records one year prior to the follow-up survey period was also examined. The comorbidity was

estimated by using the modified Charlson's index (i.e. categorising comorbidities of patients based on non-CVD related ICD diagnosis codes in linked hospitalisations data) by using hospitalisation in APDC records [173]. The co-morbidity was grouped into four groups: no comorbidity, minor comorbidity, moderate comorbidity, severe comorbidity. Time since incident CVD diagnosis was obtained from the hospitalisation records during the follow-up survey and we grouped it into three categories: Incident CVD diagnosed in <2-years, 2-<4-years, and ≥4-years. Then the proportion of participants exiting the workforce according to time since incident CVD was described.

5.3.1.6 Statistical analysis

Descriptive statistics were used to summarise sociodemographic and health-related factors at follow up, stratified by exposure group (those with incident CVD vs those without CVD). The risk ratio (RR) for 'exit from workforce' and 'retirement due to ill health' were estimated by using modified Poisson regression, comparing people with incident CVD to those who do not develop CVD. Generalized linear model (GLM) assuming a Poisson distribution and log link function were used to estimate differences in change in paid work hours per week according to incident CVD status; people who do not develop CVD were used as the reference groups. Analyses initially adjusted for age-group at follow-up, sex and comorbidity index *(model 1*). Sequential models further adjusted for socioeconomic status, using education and remoteness of residence as proxies *(model 2).* In analyses pertaining to changes in hours of paid work, the number of hours of paid work at baseline was additionally adjusted.

The analyses were carried out by using SAS software version 9.4 and R version 3.5.2 [183].

5.3.1.7 Sensitivity analysis

The main exposure was defined based on hospitalisation records. To understand the role of incident CVD diagnoses in primary care (not resulting in hospitalisation), sensitivity analyses

considered self-reported CVD at follow-up in addition to records from hospitalisations. The second sensitivity analysis was carried out to understand the differences if the age (in years) of the participants in the follow-up survey were used as continuous variables instead of the age group as used in the main analysis.

5.3.2 Results

5.3.2.1 Characteristics of the study participants

A total of 66043 participants were included in the study; 4.52% (2983) experienced incident CVD hospitalisation and 63060 participants (95.48%) did not have a record of hospitalisation CVD during follow up (**Table 5.2.1)**. Among those who were working at the follow-up, 54597 (83.1%) participants had valid paid work hours/week (≥ 0 and <100) and among them 2206 (4%) had incident CVD and 52391 (96%) had no CVD (**Table 5.2.2)**. There were 8537 participants who retired and who had not been working at all. Among them, 592 (6.9%) had incident CVD and 7945 had no CVD (93.1%) (**Table 5.2.2)**. The sociodemographic profile of participants with and without CVD was similar, except among the CVD group, there were higher proportions of men and older participants. Participants with incident CVD had a poorer health profile than those without CVD, with higher levels of hospital recorded non-CVD comorbid diseases (**Table 5.2.1**). At baseline, everybody was in the paid workforce, but the number of hours of paid work for those with incident CVD was slightly higher. However, at follow-up, those with incident CVD had a higher proportion of exit from the workforce (26% vs 17%), slightly higher change in paid work hours per week (-4.7 vs -2.6), the higher proportion who retired due to ill health (40.4% vs 17.0%) and approximately similar paid work hour per week (**Table 5.2.2**). Workforce participation varied little according to time since incident CVD diagnosis, but retirement increased with time since diagnosis (**Table 5.2.3**). People with incident CVD had a higher exit from the workforce, higher decrease in paid workhour per week, and a higher proportion who retired due to ill health across all age and sex groups

except for women aged <55 years old in ‘change in paid work hour per week’ variable (**Figure 5.2.2**).

Table 5.2.1 Sociodemographic and health related characteristics of the participants in the study population at the follow-up period

	Follow-up survey participants N=66043	
	People with incident CVD, % (n/N)	**People without incident CVD, % (n/N)**
	At follow-up	At follow-up
Total N=66043	4.5 (2983/66043)	95.5 (63060/66043)
Age (years)		
Mean (sd)	59.9 (3.57)	58.4 (3.93)
<55	11.4 (339)	22.8 (14383)
55-60	32.8 (977)	36.7 (23153)
60-65	55.9 (1667)	40.5 (25524)
Sex		
Male	59.0 (1760)	41.6 (26256)
Female	41.0 (1223)	58.4 (36804)
Follow-up period		
<5 year	14.8 (442)	22.9 (14408)
5-6 year	37.6 (1122)	40.5 (25516)
6-8 year	32.5 (970)	27.3 (17234)
> 8 year	15.1 (449)	9.36 (5902)
Region of residence		
Major cities	51.9 (1548)	52.4 (33071)
Inner regional	34.8 (1039)	34.4 (21687)
More remote	11.3 (337)	11.0 (6910)
Marital status		
Married/defacto	64.6 (1927)	61.6 (38860)
Single/widowed/divorced	34.2 (1019)	37.6 (23718)
Education		
Tertiary	32.1 (958)	37.1 (23371)
Certificate/diploma/trade	62.6 (1838)	58.3 (36739)
Higher school or less	5.5 (163)	4.1 (2569)
Language Other Than English (Yes)	7.07 (211)	7.51 (4734)
Country of birth in Australia/NZ	84.3 (2507)	81.9 (51428)
Medical History: Cancer		
Yes	31.9 (951)	28.1 (17745)
Medical History: Diabetes		
Yes	12.5 (372)	5.6 (3509)
Medical History: Osteoarthritis		
Yes	13.3 (396)	10.6 (6697)
Modified Charlson Comorbidity Index		
No comorbidity	53.9 (1609)	80.8 (50934)
Minor comorbidity	30.6 (912)	17.0 (10723)
Moderate comorbidity	12.2 (365)	1.8 (1139)
Severe comorbidity	3.3 (97)	0.4 (264)

Note: % missing response (Total, CVD, no CVD): region of residence (2.2, 2.0, 2.2 marital status (0.8, 1.2, 0.8), education (0.6, 0.8, 0.6), language spoken at home (0.0, 0.0, 0.0), born in country (0.4, 0.3, 0.4), cancer (0.0, 0.0, 0.0), diabetes (0.8, 1.4, 0.7) and arthritis (0.0, 0.0, 0.0). The proportions are reported up to one decimal value and there might be some participants is missing, not necessarily zero in some categories. However, values less than 5 is not documented because of data privacy policy. The proportions are reported are column percentages.

Table 5.2.2 Workforce participation and retirement patterns in the participants at baseline according to CVD status in the follow up survey

	People with incident CVD, % (n/N)	People without incident CVD, %(n/N)
Baseline, N*	2983 (4.5%)	63060 (95.5%)
In workforce (N)	100 (2983)	100 (63060)
In full time paid work	56.1 (1673)	53.4 (33687)
Self-employed	22.7 (678)	20.7 (13080)
In part time paid work	21.8 (649)	26.6 (16784)
Partially retired	5.30 (158)	4.87 (3071)
Paid hours of work		
n	2983	63060
Mean, SD	38.1, 14.5	36.2, 14.4
Median [inter quartile range]	40 (17)	38 (17)
Follow-up		
In workforce	74.0 (2206)	83.1 (52392)
In full time paid work	47.7 (1052)	47.7 (24995)
Self-employed	22.1 (487)	21.4 (11193)
In part time paid work	23.9 (528)	28.2 (14793)
Partially retired	12.2 (270)	9.0 (4713)
Exit from workforce	26.0 (777)	16.9 (10668)
Doing unpaid work	9.0 (70)	10.1 (1075)
Completely retired/pensioner	63.4 (493)	65.0 (6937)
Studying	1.2 (9)	2.3 (248)
Looking after home/family	9.5 (74)	13.7 (1458)
Disabled/sick	19.3 (150)	7.9 (845)
Unemployed	9.4 (73)	11.8 (1263)
Other	2.3 (17)	4.2 (450)
Follow-up		
Retired *	6.93 (592)	93.1 (7945)
Retired due to ill health (among the retirees)	40.4 (239)	17.0 (1349)
Retired due to other reasons (among the retirees)	59.6 (353)	83.0 (6596)
Reached usual retirement age	26.9 (95	25.3 (1670/)
Lifestyle reasons	49.3 (174)	47.9 (3157)
To care for family member/friend	3.7 (13)	1.1 (73)
Made redundant	17.9 (63)	5.0 (327)
Could not find a job	4.3 (15)	4.9 (325)
Other	19.6 (69)	21.2 (1395)
Follow-up		
Paid hours of work (for those in workforce)		
n	2206	52391
Mean, SD	34.85, 15.55	34.48, 14.73
Median [inter quartile range]	38 (19, 43)	38 [18, 42]
Follow-up		
Change in paid hours of work (for those continuing in the workforce)		
n	2206	52391
Mean, SD	-4.68, 13.82	-2.60, 12.88
Median [inter quartile range]	-2 [-10,10]	0 [-8, 11]

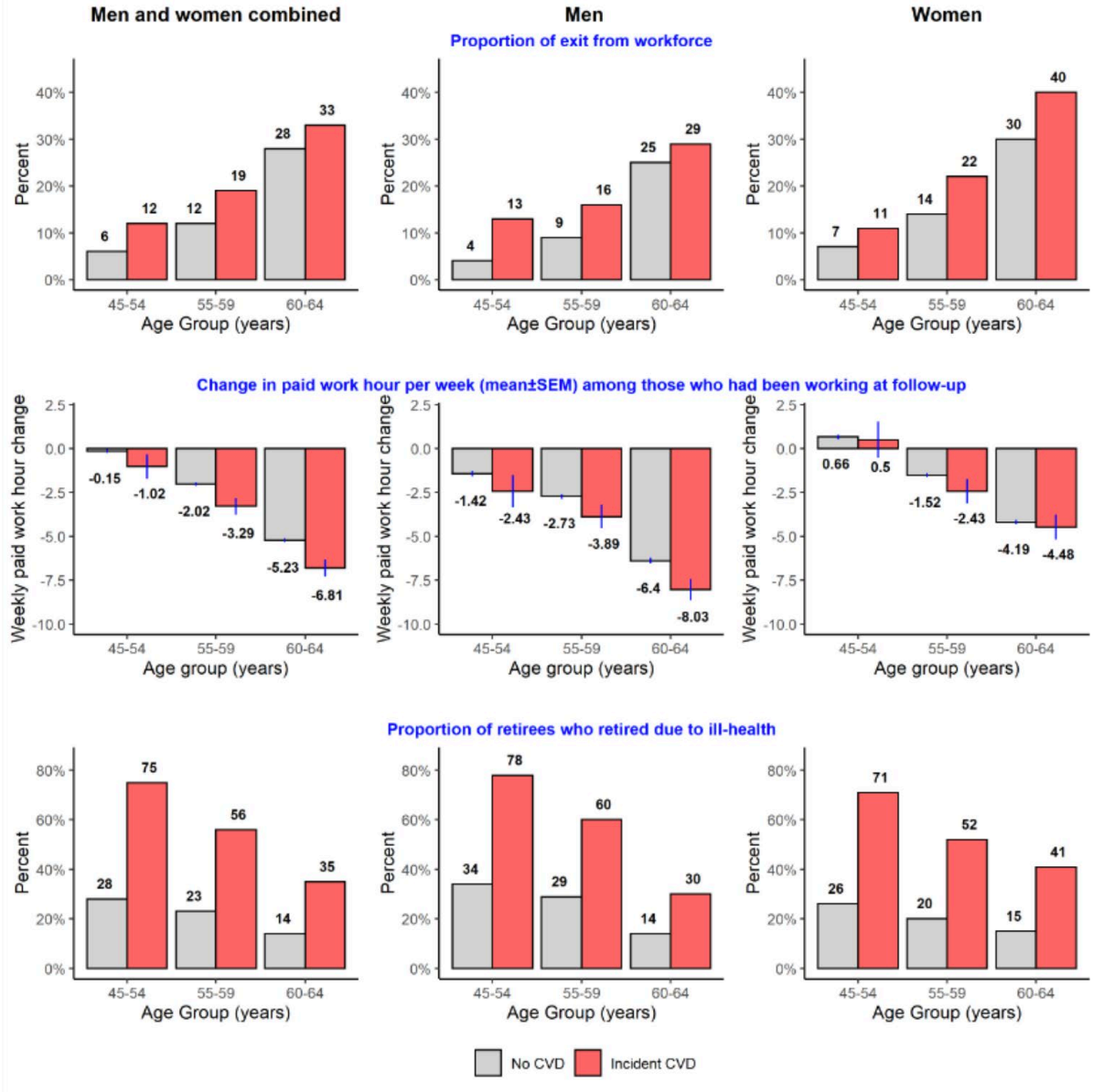
*Row percentage. Other proportions are reported are column percentages.

Table 5.2.3 Workforce participation and retirement patters according to time since incident CVD during follow up

	Incident CVD diagnosis period		
	< 2 year % (n/N)	2-<4 year % (n/N)	≥4 year % (n/N)
Total participants with CVD (N= 2983)	38.4 (1144/2983)	32.8 (979/2983)	28.8 (860/2983)
In workforce (N=2206)	76.5 (875/1144)	74.0 (724/979)	70.6 (607/860)
In full time paid work	49.1 (430/875)	47.2 (342/724)	46.1 (280/860)
Self-employed	21.6 (189/875)	22.5 (163/724)	22.2 (135/860)
In part time paid work	23.7 (207/875)	24.4 (177/724)	23.7 (144/860)
Partially retired	11.2 (98/875)	13.1 (95/724)	12.7 (77/860)
Exit from work (N=777)	23.5 (269/1144)	26.0 (255/979)	29.4 (253/860)
Doing unpaid work	8.2 (22/269)	10.2 (26/255)	8.7 (22/253)
Completely retired/pensioner	60.6 (163/269)	64.3 (164/255)	65.6 (166/253)
Studying*	-	-	-
Looking after home/family	10.4 (28/269)	11.8 (30/255)	6.3 (16/253)
Disabled/sick	21.6 (58/269)	17.3 (44/255)	19.0 (48/253)
Unemployed	8.6 (23/269)	10.2 (26/255)	9.5 (24/253)
Other*	-	-	-
Total retired (N=592)	31.8 (188/592)	32.8 (194/592)	35.5 (210/592)
Retired due to ill health (N= 239)	37.8 (71/188)	39.7 (77/194)	43.3 (91/210)
Retired due to other reasons (N=353)	62.2 (117/188)	60.3 (117/194)	56.7 (119/210)
Reached usual retirement age	29.1 (34/117)	27.4 (32/117)	24.4 (29/119)
Lifestyle reasons	41.9 (49/117)	52.1 (61/117)	53.8 (64/119)
To care for family member/friend*	-	-	-
Made redundant	19.7 (23/117)	15.4 (18/117)	18.5 (22/119)
Could not find a job*	-	-	-
Other	17.9 (21/117)	19.7 (23/117)	21.0 (25/119)
Paid hours of work (for those in workforce N= 2206)			
n	875	724	607
Mean, SD	34.9, 15.4	35.3, 15.4	34.3, 15.9
Median [inter quartile range]	38 ,21	38 ,16	38 ,22
Change in Paid hours of work (for those in workforce)			
n	875	724	607
Mean, SD	-4.1 ,12.9	-4.2 ,14.0	-6.0 ,14.9
Median [inter quartile range]	-2 ,10	0 ,11	-3 ,10

*Artificially made as missing because the number of observations in several categories were less than 5

Figure 5.2.2 Exit from workforce at follow up, change in number of hours of paid work per week and retirement patterns at follow up according to incident CVD status, sex and age-group



5.3.2.2 Exit from workforce after incident CVD

At follow up, 74% of people with incident CVD were participating in the workforce, compared to 83.1% of people without CVD (**Table 5.2.3**). The proportions of participants diagnosed with incident CVD were approximately similar during the follow-up period, regardless of the time since incident CVD diagnosis. However, among those with incident CVD, the workforce participation decreased with the increased diagnosis period **(Table 5.2.3)**.

Stratification by age group, sex and incident CVD indicated that women and those older participants had been less likely to be in the paid work regardless of incident CVD status (**Figure 5.2.2**). After adjusting for sociodemographic characteristics, people with incident CVD had a 28% higher risk of exit from the workforce (RR= 1.28 (95% CI: 1.20-1.36)). This varied by incident CVD subtype, with RRs ranging from 1.08 (95% CI: 0.79-1.46) for those with 'incident PAD only' to 2.27 (95% CI: 1.51-2.81) for those with 'cerebrovascular disease and other CVD conditions' (**Figure 5.2.3**).

The sensitivity analyses indicated that the risk of exit from the workforce was slightly declined if self-reported CVD was considered (*Appendix 4: Table S5.2.1*). Other sensitivity analyses indicated that the risk of exit from the workforce differed little, even if the age of the participants used in the model adjustment was a continuous variable (*Appendix 4: Table S5.2.2*).

5.3.3.2.1 Exit from workforce among population subgroups

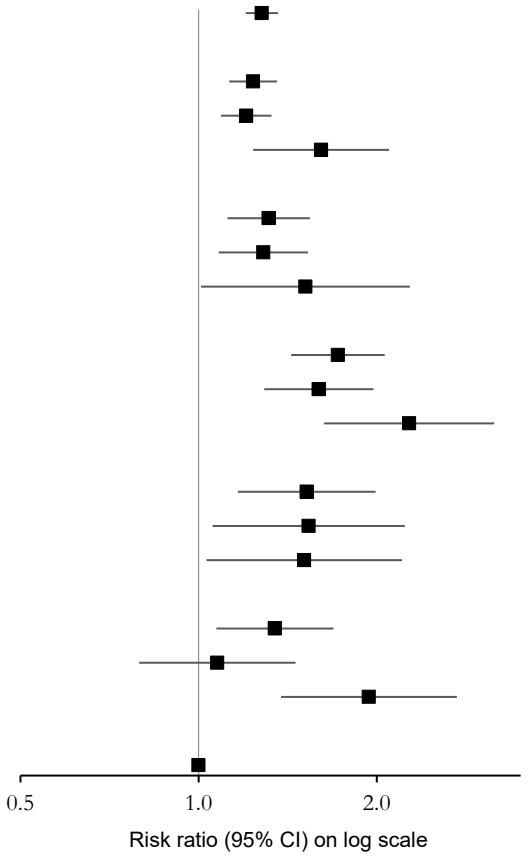
The risk of exit from the workforce was higher among people with incident CVD compared to those without CVD, regardless of population subgroup, as indicated by the consistently higher RRs across the different levels of the sociodemographic and health-related factors. However, there was variation in the effect size in relation to a range of characteristics, including age, sex and marital status **(Figure 5.2.4).**

5.3.3.2.2 Exit from workforce, physical functioning limitations and incident CVD

Exit from the workforce increased with the increased severity of the functional limitations for both groups but the extent of exit from workforce is higher for those with incident CVD in all sub-groups based on physical functioning limitations. About 87% of the people with no physical functioning limitations and no incident CVD had been working. However, with severe functioning limitations, only 54% and 64% of the people had been working from those with and without incident CVD, respectively. After adjustment for sociodemographic variables and comorbidity, compared to those without CVD and no functional limitations, participants without physical functional limitations but with CVD had a 16% higher risk for exit from the workforce but the risk was not statistically significant (RR=1.16, 95% CI= 0.97-1.38). However, those with severe functioning limitations had 2.6- and 2.3-times higher risk for exit from the workforce for those with incident CVD [RR= 2.57 (95% CI: 2.30-2.88)] and those without CVD (RR= 2.29 (95% CI: 2.17-2.43)) respectively (**Figure 5.2.5**).

Figure 5.2.3 *Exit from workforce:* Incidence of and adjusted risk ratios for exit from workforce in people with and without incident CVD and according to incident CVD subtypes

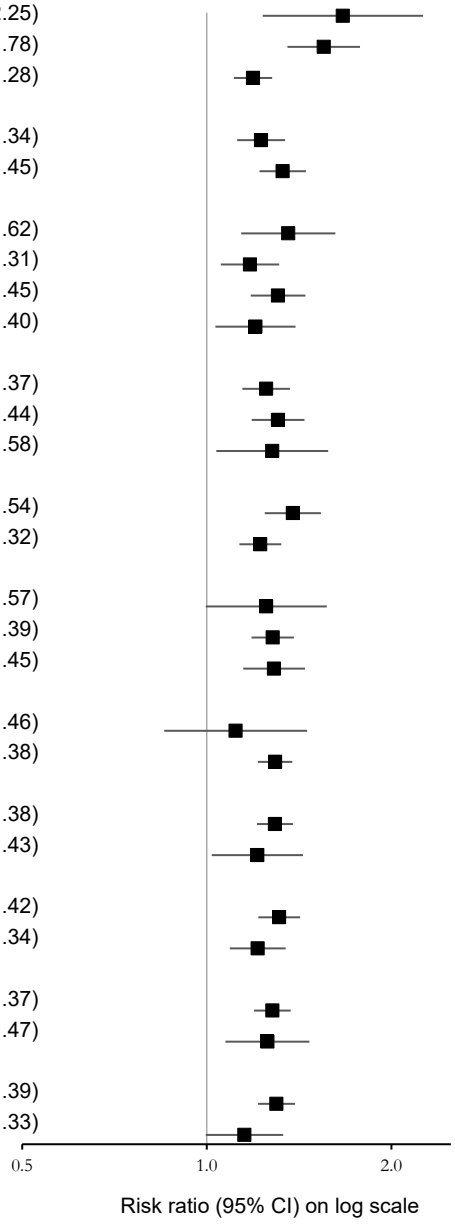
Total study participants (N = 66043)	Exit from workforce % (n/N)	Risk ratio (RR) (95% CI) of exit from workforce Model 1	Model 2
Overall	17.3(11445/66043)		
People with incident CVD during follow up	26.1(777/2983)	1.29(1.21-1.37)	1.28(1.20-1.36)
People with incident IHD	24.9(341/1372)	1.25(1.14-1.37)	1.24(1.13-1.36)
IHD only	24.0(305/1271)	1.22(1.10-1.34)	1.20(1.09-1.33)
IHD and other CVD conditions	35.6(36/101)	1.62(1.24-2.11)	1.61(1.24-2.10)
People with incident MI	25.7(109/424)	1.33(1.13-1.56)	1.31(1.12-1.54)
MI only	24.4(94/94)	1.30(1.09-1.55)	1.29(1.08-1.53)
MI only and other CVD conditions	39.5(15/38)	1.54(1.02-2.32)	1.52(1.01-2.27)
People with incident Cerebrovascular disease	35.2(75/213)	1.73(1.44-2.08)	1.72(1.43-2.06)
Cerebrovascular disease only	32.4(57/176)	1.61(1.30-2.00)	1.60(1.29-1.97)
Cerebrovascular disease and other CVD conditions	48.7(18/37)	2.27(1.63-3.16)	2.27(1.63-3.16)
People with incident HF	34.6(36/104)	1.55(1.18-2.02)	1.52(1.16-1.99)
HF only	35.9(19/53)	1.59(1.10-2.30)	1.53(1.06-2.23)
HF and other CVD conditions	33.3(17/51)	1.50(1.02-2.21)	1.51(1.03-2.21)
People with incident PAD	27.3(51/187)	1.36(1.09-1.71)	1.35(1.07-1.69)
PAD only	22.2(28/126)	1.09(0.81-1.48)	1.08(0.79-1.46)
PAD and other CVD conditions	37.7(23/61)	1.95(1.38-2.74)	1.94(1.38-2.73)
People without CVD (Reference)	16.9(10668/63060)	1	1



Model 1: age, sex, modified Charlson co-morbidity index adjusted; Model 2: age, sex, modified Charlson co-morbidity index, region of residence, education adjusted; RRs refers to risk ratio, IHD= ischaemic heart disease, MI= myocardial infarction, HF= heart failure, PAD= Peripheral arterial disease; Plot was drawn for model 2 with log-scale.

Figure 5.2.4 *Exit from workforce:* Incidence of and adjusted risk ratios for exit from workforce in people with and without incident CVD in a range of population subgroups based on sociodemographic and health related factors

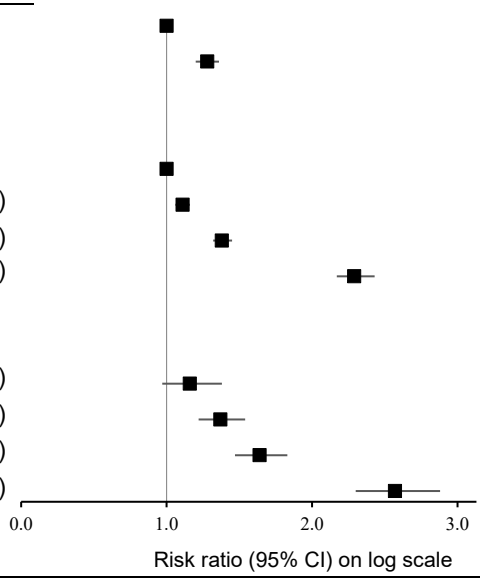
Factors and levels of the factors	Exit from workforce [% of total (n)]		[1]Risk ratio (95% CI) of exit from workforce of people with incident CVD compared to those without CVD	P-heterogeneity
	CVD	No CVD		
Age group (years)				
< 55 years	11.8 (40/339)	6.0 (861/14383)	1.67 (1.23-2.25)	0.0007
55-59	18.7 (183/977)	12.0 (2788/23153)	1.55 (1.35-1.78)	
60-64	33.2 (554/1667)	27.5 (7019/25524)	1.19 (1.11-1.28)	
Sex				
Men	23.4 (412/1760)	15.1 (3956/26257)	1.23 (1.12-1.34)	0.2047
Women	29.8 (365/1223)	18.2 (6712/36803)	1.33 (1.22-1.45)	
Follow-up time				
<5 year	23.1 (102/442)	14.1 (2027/14407)	1.36 (1.14-1.62)	0.3868
5-6 year	23.3 (261/1122)	16.2 (4123/25516)	1.18 (1.05-1.31)	
6-8 year	28.8 (279/970)	18.5 (3196/17235)	1.31 (1.18-1.45)	
>8 year	30.1 (135/449)	22.4 (1322/5902)	1.20 (1.03-1.40)	
Region				
Major cities	25.1 (389/ 1548)	16.8 (5572/33071)	1.25 (1.14-1.37)	0.8048
Inner regional	29.0 (301/1039)	18.0 (3912/21686)	1.31 (1.18-1.44)	
More remote	22.0 (74/337)	14.3 (989/6911)	1.28 (1.04-1.58)	
Marital status				
Not currently married/defacto	26.8 (273/1019)	16.4 (3883/23718)	1.38 (1.24-1.54)	0.0686
Married/defacto	25.7 (496/1927)	17.3 (6720/38859)	1.22 (1.13-1.32)	
Highest Education				
No school certificate	33.7 (55/163)	23.5 (604/2569)	1.25 (1.00-1.57)	0.9745
Certificate/diploma/trade	26.4 (486/1838)	17.4 (6410/36738)	1.28 (1.18-1.39)	
Tertiary	23.9 (229/958)	15.3 (3571/23371)	1.29 (1.15-1.45)	
Language other than English				
Yes	21.8 (46/211)	15.4 (728/4734)	1.11 (0.85-1.46)	0.2934
No	26.4 (731/2772)	17.0 (9940/58325)	1.29 (1.21-1.38)	
County of Birth				
Australia/NZ	26.6 (667/2507)	17.1 (8785/51428)	1.29 (1.21-1.38)	0.4829
Others	23.1 (108/467)	16.1 (1825/11356)	1.21 (1.02-1.43)	
Medical History: Cancer				
No	25.2 (512/2032)	15.8 (7167/45315)	1.31 (1.21-1.42)	0.2278
Yes	27.9 (265/951)	19.7 (3501/17744)	1.21 (1.09-1.34)	
Medical History: Diabetes				
No	25.1 (644/2568)	16.6 (9794/59084)	1.28 (1.19-1.37)	0.8320
Yes	33.3 (124/372)	22.8 (799/3509)	1.26 (1.07-1.47)	
Medical History: Osteoarthritis				
No	25.0 (648/2587)	16.0 (8990/56346)	1.30 (1.21-1.39)	0.1432
Yes	32.6 (129/396)	25.0 (1676/6697)	1.15 (1.00-1.33)	



[1]Adjusted for age-group, sex, modified Charlson co-morbidity index, region of residence, education

Figure 5.2.5 *Exit from workforce:* Incidence of and adjusted risk ratios for exit from workforce according to joint categories of physical functioning limitations and incident CVD

	Incident, % (n/N)	Risk ratio (95% CI) of exit from workforce	
		Model 1	Model 2
Without incident CVD	16.9 (10668/63060)	1	1
With incident CVD	26.0 (777/2983)	1.29 (1.21-1.37)	1.28 (1.2-1.36)
No CVD and			
No limitations	12.7 (2818/22278)	1	1
Minor limitations	15.6 (3426/21971)	1.11 (1.06-1.16)	1.11 (1.06-1.16)
Moderate limitations	20.6 (2812/13672)	1.39 (1.33-1.46)	1.38 (1.32-1.45)
Severe limitations	35.8 (1235/3446)	2.33 (2.20-2.47)	2.29 (2.17-2.43)
Incident CVD and			
No limitations	16.9 (106/626)	1.17 (0.98-1.39)	1.16 (0.97-1.38)
Minor limitations	21.5 (222/1032)	1.37 (1.21-1.54)	1.37 (1.22-1.54)
Moderate limitations	28.4 (237/834)	1.66 (1.48-1.85)	1.64 (1.47-1.83)
Severe limitations	46.5 (190/409)	2.62 (2.34-2.94)	2.57 (2.30-2.88)



[1]Adjusted for age-group, sex, modified Charlson co-morbidity index, [2]Further adjusted for remoteness of residence and education attainment. Those with 'no functional limitations and no CVD' were the reference group for estimating risk ratios (RR's) of exit from workforce according to joint categories of physical functioning limitations and incident CVD. Incident CVD is based on hospitalisation records only but people with no CVD had neither self-report and hospitalisation recorded CVD. Physical functional limitations had scores ranged from 0 to 100, where higher scores represented fewer limitations, and were grouped into four categories: severe (0–<60); moderate (60-<90), minor (90-<100) and no (100) functional limitation.

5.3.2.3 Change in number of paid hours of work per week after incident CVD

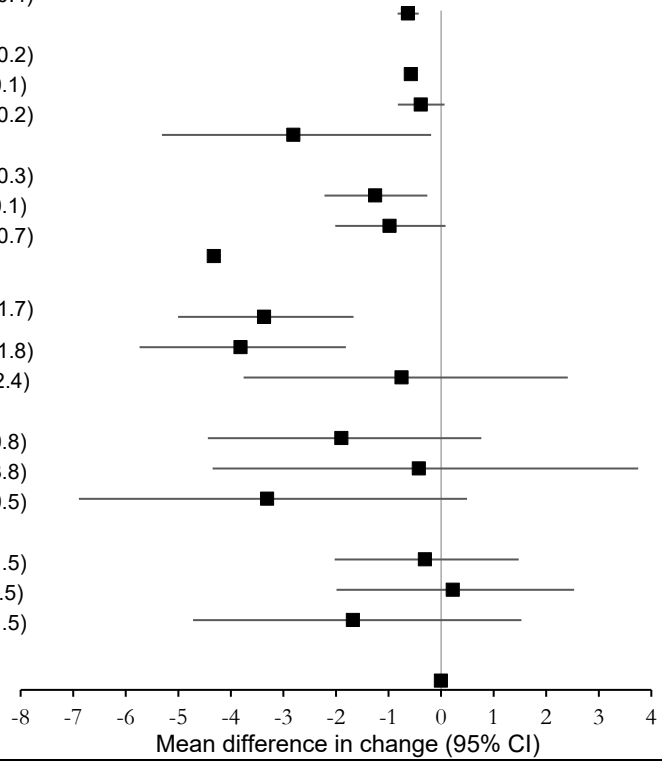
Overall, the change in weekly working hours per week among those doing paid work at the follow-up period was higher for those with incident CVD with a mean decrease of 4.7 and 2.6 work hours/week in those with and without incident CVD respectively (**Table 5.2.2**). Though the direction of change was broadly similar, the extent of change in paid work hours per week varied among those with and without incident CVD when stratified by age group and sex (**Figure 5.2.2**). Except for women aged <55years old, there was a decrease in paid hours of work per week among all groups stratified by age and sex (**Figure 5.2.2**). After adjusting for sociodemographic characteristics, people with incident CVD had a higher reduction of 0.6 (95% CI: 0.4, 0.8) paid hours of work per week on average compared to those without CVD. This varied by incident CVD subtypes, ranging from a reduction of 0.4 (95% CI: 0.1, 0.8) paid work hours per week on average for IHD only to 4.3 (95% CI: 0.7, 7.8) paid workhours /week on average for MI and other CVD conditions only (**Figure 5.2.6**).

5.3.2.4 Retirement due to ill health after incident CVD

Of the participants who had retired at follow-up, 40.4% of people with incident CVD had retired due to ill health, compared to 17.0% of people without CVD (**Table 5.2.2**). Stratification by age group and sex indicate a similar pattern of difference in people versus without incident CVD, but those with younger age had higher retirement due to ill health (**Figure 5.2.2**). After adjusting for sociodemographic characteristics, people with incident CVD had a 90% higher risk of retiring due to ill health with RR= 1.90 (95% CI: 1.70, 2.13). Such risk varied by incident CVD subtypes, with RRs ranging from 1.71 (1.43, 2.03) for those with incident 'IHD only' to 2.99 (95% CI: 1.93, 4.61) for those with incident HF only (**Figure 5.2.7**).

Figure 5.2.6 *Change in paid hours of work per week:* Baseline, follow-up paid work hour per week and difference in change in paid work hour per week in people with and without incident CVD, and according to incident CVD subtypes among those in paid work at the follow-up survey

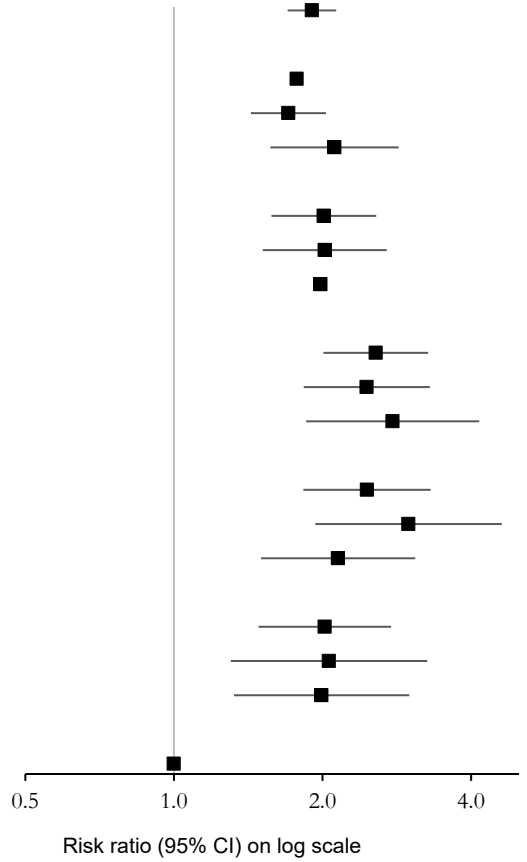
		Weekly paid work hour			Difference of change in weekly paid work hour compared to those without CVD	
	N	Baseline	Follow-up	Annual change	Model1	Model 2
		Mean	Mean	Mean	Mean (95%	Mean (95%
People with incident CVD during follow up	2206	39.5(14.1)	34.9(15.6)	-0.79	-0.6(-0.9, -0.4)	-0.6(-0.8, -0.4)
People with incident IHD	1031	40.4(13.4)	35.5(15.4)	-0.85	-0.6(-1.1, -0.1)	-0.6(-1.0, -0.2)
IHD only	966	40.3(13.3)	35.6(15.4)	-0.82	-0.4(-0.9,0.1)	-0.4(-0.8,0.1)
IHD and other CVD conditions	65	42.6(14.5)	34.3(14.3)	-1.36	-2.8(-5.4, -0.1)	-2.8(-5.3, -0.2)
People with incident MI	315	41.1(13.9)	35.3(14.9)	-0.89	-1.2(-2.3, -0.1)	-1.3(-2.2, -0.3)
MI only	292	41.3(13.4)	35.7(15.1)	-0.85	-0.9(-2.1,0.2)	-1.0(-2.0,0.1)
MI only and other CVD conditions	23	38.4(19.5)	30.4(12.3)	-1.42	-4.3(-7.9, -0.6)	-4.3(-7.8, -0.7)
People with incident Cerebrovascular disease	138	36.3(15.3)	30.1(15.4)	-1.02	-3.5(-5.3, -1.6)	-3.4(-5.0, -1.7)
Cerebrovascular disease only	119	36.5(15.6)	29.9(16.0)	-1.10	-4.0(-6.1, -1.8)	-3.8(-5.7, -1.8)
Cerebrovascular disease and other CVD	19	34.9(13.3)	31.6(12.1)	-0.55	-0.8(-3.9,2.5)	-0.7(-3.8, 2.4)
People with incident HF	68	42.0(16.6)	35.4(17.4)	-1.36	-1.7(-4.3,1.0)	-1.9(-4.4,0.8)
HF only	34	42.1(20.3)	36.3(19.8)	-1.07	-0.1(-4.1,4.0)	-0.4(-4.3,3.8)
HF and other CVD conditions	34	42.0(12.2)	34.5(15.1)	-1.65	-3.3(-7.0,0.7)	-3.3(-6.9,0.5)
People with incident PAD	136	36.6(16.7)	33.8(16.9)	-0.40	-0.2(-2.1,1.6)	-0.3(-2.0,1.5)
PAD only	98	35.1(16.3)	33.2(17.4)	-0.27	0.3(-2.0,2.7)	0.2(-2.0,2.5)
PAD and other CVD conditions	38	40.8(17.1)	35.4(15.7)	-0.73	-1.7(-4.8,1.6)	-1.7(-4.7,1.5)
People without CVD (Reference)	52382	37.1(14.0)	34.5(14.7)	-0.49	0	0



Model 1: age, sex, modified charlson co-morbidity index adjusted; Model 2: age, sex, modified charlson co-morbidity index, region of residence, education adjusted; RRs refers to risk ratio,IHD= ischaemic heart disease, MI= myocardial infarction, HF= heart failure, PAD= Peripheral arterial disease; plot was drawn for model 2 with log-scale.

Figure 5.2.7 *Retirement due to ill health:* Incidence of and adjusted risk ratios for retirement due to ill health in people with and without incident CVD, and according to incident CVD subtypes among those who have retired and who are not participating in workforce in any form

Subgroup Total retirees (N = 8537)	Retired due to ill health % (n/N)	Risk ratio (95% CI) of retirement due to ill health Model 1	 Model 2
Overall	18.6(1588/8537)		
People with incident CVD during follow up	40.4(239/592)	1.98(1.77, 2.22)	1.90 (1.70, 2.13)
People with incident IHD	40.1(103/257)	1.91(1.63, 2.24)	1.77 (1.52, 2.08)
IHD only	36.4(828/225)	1.84(1.53, 2.20)	1.71 (1.43, 2.03)
IHD and other CVD conditions	65.6(21/32)	2.27(1.71, 3.03)	2.12 (1.57, 2.85)
People with incident MI	47.4(37/78)	2.15(1.67, 2.77)	2.01 (1.58, 2.57)
MI only	42.4(28/66)	2.15(1.59, 2.90)	2.02 (1.51, 2.70)
MI only and other CVD conditions	75(9/12)	2.16(1.45, 3.22)	1.98 (1.33, 2.95)
People with incident Cerebrovascular disease	63.5(33/52)	2.58(2.02, 3.29)	2.56 (2.01, 3.27)
Cerebrovascular disease only	59.5(22/37)	2.50(1.88, 3.32)	2.46 (1.83, 3.30)
Cerebrovascular disease and other CVD conditions	73.3(11/15)	2.73(1.76, 4.22)	2.77 (1.85, 4.15)
People with incident HF	66.7(18/27)	2.70(2.05, 3.56)	2.46 (1.83, 3.31)
HF only	61.5(8/13)	2.98(1.86, 4.79)	2.99 (1.93, 4.61)
HF and other CVD conditions	71.4(10/14)	2.50(1.85, 3.39)	2.15 (1.50, 3.08)
People with incident PAD	48.8(21/43)	2.09(1.52, 2.87)	2.02 (1.48, 2.75)
PAD only	39.1(9/23)	2.00(1.25, 3.22)	2.06 (1.30, 3.26)
PAD and other CVD conditions	60(12/20)	2.15(1.41, 3.29)	1.99 (1.32, 3.00)
People without CVD (Reference)	17(1349/7945)	1	1



Model 1: age, sex, modified charlson co-morbidity index adjusted; Model 2: age, sex, modified charlson co-morbidity index, region of residence, education adjusted; RRs refers to risk ratio,IHD= ischaemic heart disease, MI= myocardial infarction, HF= heart failure, PAD= Peripheral arterial disease; plot was drawn for model 2 with log-scale.

5.3.3 Study summary on exit from workforce after incident CVD

In this large-scale longitudinal analysis on people living in Australia, people with incident CVD had a 29% higher risk to leave the paid workforce and approximately two times higher risk to have retired due to ill health than people without CVD. Although most people with incident CVD were doing paid work, they had a reduction of about two hours more per week on average than people who had not had an incident CVD. These findings were observed across different types of incident CVD but showed that the magnitude varied, with those who experienced more than one incident CVD had a higher risk to leave the paid workforce. For example, people with an incident cerebrovascular event and other CVD conditions had more than two times higher risk to leave paid workforce compared to those who had no CVD event. Some sociodemographic groups, in particular younger people, women, and those not married or in a de facto relationship had a higher risk to leave paid workforce following an incident CVD event. Physical disability was more prevalent among people with incident CVD, and it was strongly associated with a higher risk of exit from the workforce. People with incident CVD and severe physical disability had a 2.5 times higher risk to leave paid workforce while those with incident CVD and no physical disability had around just a similar risk (with ~5% difference) to leave the paid workforce as those without CVD.

5.4 Discussion

5.4.1 Results of this study in relation to other studies

The results presented in the cross-sectional and longitudinal analysis are consistent with those of previous international and Australian studies [39, 41, 53, 82, 83, 92, 94, 98-100]. No other study was found in Australia that has compared workforce participation in people with and without CVD using large-scale population data. The study results in this chapter are broadly comparable to studies set in Canada, Japan, and Europe, which have consistently shown that people with CVD are less likely to participate in the workforce than people without CVD [82, 95, 102]. It is somewhat difficult to compare the magnitude of the findings with these studies, given the variation in study design, the definition of workforce participation, case definition of CVD, and selection of the comparison population. For example, a cross-sectional investigation with a study population from 10 European countries found that people with stroke had an 11% higher odds of being unemployed [92] compared to those without stroke. A study with participants in France with stroke was 50% more likely to be out of the workforce [102]. The magnitude of the association between stroke and workforce participation from these European studies was lower than the 92% increase in odds of being out of the workforce for those with versus without cerebrovascular disease in this study.

No other study was found that reported workforce participation in absolute and relative terms among different population subgroups based on sociodemographic and health-related factors. Similar to a previous report [82], this study results indicate that women were more likely to be out of the paid workforce compared to men in absolute terms, but the magnitude of the relative association between CVD and workforce participation was greater among men than women. There was not any study available to compare results of these study findings that people with CVD who were single, had education less than tertiary education or were current smokers were more likely in absolute and relative terms to be out of the workforce compared to those without CVD. However, there were some studies to compare the secondary outcomes in this investigation but those varied by countries of the previously reported studies. For example, participants in Italy with MI had a 50% higher chance to

retire early [92], compared to 27% in the cross-sectional analysis of this chapter. Previous studies from 10 European countries have reported on the extent of early retirement of people with CVD subtypes, such as stroke [82] but the comparison could not be made due to variation in the definition of the CVD subtype as indicated in this study.

Like other studies published earlier, both studies in this chapter highlight the relatively high prevalence of workforce non-participation among people with CVD or higher risk of exit from the workforce after incident CVD. The stronger relationships in younger people in both studies are thus consistent with the idea that CVD is likely to be the driving force for exit from the workforce. The cohort studies in Europe and Canada provide evidence consistent with a causal explanation [90, 91, 93, 97, 103, 104, 108]. For example, one study from the Netherlands analysed various exit mechanisms from paid employment (such as, via unemployment benefits, via early retirement benefits etc.) and reported that in comparison to those without CVD, people with incident CVD were more likely to leave paid employment regardless of the exit mechanisms [108]. Nevertheless, the relationship between CVD and workforce participation, particularly when measured in terms of government benefits, is highly specific to the social welfare structure of the countries in which study participants live and work. In other studies, the risk of leaving employment increased with severe CVD subtypes such as coronary heart disease, stroke, and MI [90, 91, 93, 97, 103] which were also broadly similar to those reported in this investigation, especially participants living with multiple CVD subtype. Another underlying reason for higher workforce non-participation in people with CVD could be physical disability since physical functioning has been shown to decline following incident CVD [108].

The analyses in this analysis have demonstrated that people with existing as well as incident CVD had a high proportion with physical disabilities. This study has also indicated that those with higher physical functioning limitations had the highest probability of being out of the paid workforce and the highest risk of exit from the workforce after incident CVD. This key finding, that impaired physical

functioning is likely to be an important factor underpinning the difference in workforce participation rates or exit from workforce between those with and without CVD, has not been reported previously. However, it is consistent with the evidence from a European study reporting a relatively high proportion of people with CVD to leave the paid workforce via disability pension [101] compared to those without CVD. This may also explain the lower participation rates among people with cerebrovascular disease, peripheral artery disease and heart failure compared to those with ischemic heart disease. This is an important finding as cardiac rehabilitation programs help improve physical functional limitations [210] and hence may improve return to work.

5.4.2 Strength of the study

The strengths of this investigation are its large sample size, population-based nature, exposure classification by both record linkage and self-report, stratification of study groups on a variety of diverse exposures, and information on diversified factors. The next strength is reporting the outcomes based on CVD subtypes in a variety of ways in cross-sectional and longitudinal analysis. This investigation has quantified the risk of exit from the workforce after the incident of one or more types of CVD. In the majority of the cases, those with an incident CVD had hospitalisations for more than one type of CVD. Therefore, teasing out the role of a specific type of CVD was not possible. Hence, the implications are that those diagnosed with CVD, regardless of the type of CVD, require additional support to continue taking part in the paid workforce.

5.4.3 Limitation of the study

The limitation of this study includes the non-representativeness of some estimates, lack of categories of work and unavailability of the precise date of exit from the workforce and their associations with incident CVD. The absolute estimates of the outcomes reported in this study may not represent that in the general population but the PRs, RRs, the mean differences or change in mean differences-based on internal comparisons, such as those described here, are generalisable and remain valid in non-representative studies [146]. Workforce participation, as mentioned in this investigation, has

potential limitations because of the way workforce participation was defined. For example, both full-time and part-time work comprised workforce participation, and thus this might have over-estimated the workforce participation. The types of works people were engaged in [211] could not be reported because of the unavailability of such aspects of information in the survey questionnaires. Given the absence of qualitative aspects of workforce participation, this pragmatic definition was considered as a valuable population-level indicator. Availability of the types of works people was engaged in would have been valuable in better understanding the observed workforce participation patterns.

Representativeness could be another limitation of the study. The study population was randomly sampled from a whole-of-population database and included ~ 10% of the entire population in the target age group and the response rate was ~18%, consistent with cohort studies of this nature. Generally, participants in cohort studies are healthier than the general population [212]. Though I could not find a comparable age group similar to ours for the prevalence of CVD in Australia, the workforce participation rate in this study was 9% higher (74.6% vs 65.2%) than that reported for Australia for the same age group during the same period (2007-08) by the Australian Bureau of Statistics [213, 214]. Hence, while our absolute estimates of CVD prevalence and workforce participation may not be directly representative, PRs which are based on internal comparisons are still likely to be generalisable [146].

Another limitation, especially relevant for the second study, is that many potentially eligible participants did not take part in the follow-up survey. The implication of such non-participation (i.e., missingness) is further explored in chapter seven of the thesis.

5.4.4 Novel contribution of the findings

This large-scale population-based cross-sectional study with linkage to hospital records allowed comparison of workforce non-participation in people with and without CVD, within the population subgroups and across CVD subtypes enabling a comprehensive comparative description of

workforce participation in individuals living with CVD in the community. Then longitudinal investigation by considering these factors provided a comprehensive result on the likely causal role of incident CVD on exit from the workforce. This is thus the first in Australia to report a wide variety of workforce participation related outcomes maintaining the control participants who had no CVD. The association of non-participation according to joint categories of physical functioning limitations and CVD is also newer evidence from large-scale population-level data in Australia.

To the best of our knowledge, this is the first study that followed CVD free working-age older people in Australia longitudinally and reported exit from the workforce according to incident CVD and its subtypes in a variety of ways. Though one recent study with the working-age population from Canada has reported that the difference of workforce participation of people with incident CVD and control participants widen with an increasing period after incident CVD [104], the likely causal associations as presented here is substantially newer.

5.4.5 Interpretation of the findings

The cross-sectional results show that most people with CVD were still in the paid workforce but people who have experienced a CVD event, especially those with physical disabilities, were more vulnerable to not being in the workforce or had the highest risk of exit from the workforce compared to their counterparts. Similar associations with CVD were observed for paid hours of work per week among those who had been working, retirement among all study participants and retirement due to ill health among retirees who had not been working in any form. It was found in the longitudinal analysis that the risk of exit from the workforce after incident CVD is higher compared to those of people who had not developed CVD. Compared to those without CVD, a higher risk of exit from the workforce was observed for different incident CVD subtypes, and among different population sub-groups. The risk of exit from the workforce was relatively higher for people who had had a stroke, heart failure or peripheral vascular disease, who were in their 50s. Physical disability was a key factor in exit from the workforce both for those with and without incident CVD.

Such evidence might not have direct implications in clinical practice, but the evidence generated through the systematic sequential investigations in this chapter could be used to inform people with CVD, management and care of people living with CVD and in modelling CVD outcomes and costs. These results of this investigation will help those with CVD to understand better how the workforce participation related outcomes look like for them compared to those in people without CVD. The evidence generated in the thesis might be reassuring to people following a CVD event, particularly those with reasonable physical functioning. It may also provide motivation for those rehabilitation program participants who are keen to re-enter the workforce [215]. Therefore, the immediate course of action might be to disseminate the findings to people living with CVD or other stakeholders, such as the Australian Heart Foundation, which informs and educates the public and assists people with CVD.

The findings show that even though some of the severe types of CVD had higher non-participation, most people with one incident CVD had multiple CVD incidents subsequently. This implies that people with any type of CVD hospitalisation requires support for participation in work and contributes to the economy instead of premature retirement and drawing pension. To improve the management and care of the people living with CVD, relevant stakeholders might consider the findings in this thesis. The role of physical disability, CVD subtypes in exit from the workforce as found in the thesis, might help mathematical modelling for projecting CVD outcomes.

Given the importance of paid work for mental health and the overall economy [49], initiatives or programs aiming to help people with CVD or other major illnesses remain or re-enter the workforce could help lessen this gap. The results underpin the importance of rehabilitation and suggest encouraging employment among older persons should integrate consideration of the role of chronic disease, including CVD.

Several studies could be conducted in future regarding the relationship between CVD and workforce participation. One such study might involve the role of types of works (such as technical knowledge-

based or manual labour-based work etc.). Different types of works require different physical and mental strengths, which might be affected by CVD differently. Finding the type of work affected most might help to provide additional support to people engaged in those works. Another study might investigate the relationship between incident CVD with the exit from the workforce with the study participants who had the exact date of exit from the workforce. Though the second study had the exact date of incident CVD, it did not have the exact date of exit from the workforce. Future studies with such information might help generate newer evidence on the likely causal role of incident CVD with higher accuracy. Both the first and second studies of this chapter investigated the primary outcomes (workforce non-participation or exit from workforce) considering both as binary variables. However, changes in work status might be multidirectional, such as changes in the types of work, changes in the amount of work. Hence, a study might longitudinally assess such a pattern of changes in workforce participation of those with versus without incident CVD over a long period. This will help understand the extent to which the exit from the paid workforce is similar or dissimilar to those with or without CVD. All the above-mentioned future studies might provide further evidence for the improvement of the financial conditions of those living with CVD and the society they live in.

CHAPTER 6 Empirical studies on the relationship of CVD to social interaction

6.0 Chapter summary

This chapter presents two related but separate investigations that examined the relationship between cardiovascular disease (CVD) and social interaction by using the Sax Institute's 45 and Up Study and its linked datasets. These studies were conducted to address the gaps in knowledge as identified in chapter three. The first investigation was a cross-sectional analysis that quantified social isolation in Australian men and women aged 45 years and above, comparing levels of social interaction in people with versus without CVD to understand the extent of the association. The second investigation was a longitudinal study that examined the likely causal role of incident CVD in becoming socially isolated.

The 45 and Up Study participants aged 45-year-old and above were examined in both studies. Social isolation, derived from the Duke Social Support Index subscale based on four items (social visits per week, telephone contacts per week, social group meetings per week, and the number of people to depend on), was compared in people with versus without CVD in the first study. The participants who had no CVD at baseline and were not socially isolated at baseline were followed overtime for the second study. The eligible participants were then investigated, comparing social isolation in people with versus without incident CVD during the follow-up period. Regression models in both studies were adjusted for sociodemographic variables. The roles of the CVD subtype, population characteristics and physical disability were investigated in both studies.

In the first study, there were 266,504 study participants, with 21.4% having CVD. People with CVD were 5% more likely than people without CVD to be socially isolated. The second study included 101,833 participants and 8.9% had incident CVD. The analyses showed that people with incident CVD had almost similar likelihood to be socially isolated compared with those without CVD. The relationship of CVD to social isolation varied slightly by CVD subtype in both studies. Generally, social isolation was higher for those living with cerebrovascular disease compared to other types of CVD. The magnitude but not the direction of results varied by population characteristics. Social

isolation in both studies was much more strongly related to physical disability than to CVD diagnosis itself, with poorer outcomes observed in people with severe disabilities regardless of CVD diagnosis.

Results in this chapter enrich the current understanding of the relationship of CVD to social interaction, particularly the likely consequences of incident CVD on becoming socially isolated. The findings on variation by CVD subtype and the role of physical disability are key novel contributions. The evidence generated might be useful to inform CVD survivors, their caregivers and organisation like the Australian Heart Foundation that inform and educate the public and assist people with CVD.

6.1 Background

Social interaction is an important component for social wellbeing regardless of the presence of chronic diseases like cardiovascular disease (CVD) [216]. Participation in social activities is also one of the indicators of disease recovery and it plays a role in the reduction of mortality and improvement of quality of life [217, 218]. Recently, there is an increasing need to understand the consequence of CVD on social interaction, at least for two reasons. First, there is an increasing number and proportion of people surviving a CVD event due to improvement of medical treatment and life expectancy around the world [61, 62, 115]. Second, modern society has experienced an increased prevalence of loneliness and social isolation in general [219, 220]. A significant proportion of people living with CVD are disabled to the extent that their core activities, including their ability to engage in social activities, are affected [191, 192]. Inadequate participation in social activities by people with CVD might affect the social wellbeing of a person as well as impact negatively the functioning of a society like that in Australia where it is projected to have more people living with CVD in the next several decades [50].

Participation in social and civic activities after CVD has been examined in some earlier studies. Social interaction related outcomes in these studies have been reported with various terms such as social networks, social integration, social participation, social participation restriction, social support, social support outcomes etc. Broadly, these investigations have indicated that those with CVD had more restrictions on participation in social activities [118], fewer social networks [221-223] and lower social activity [224] in general. There were also some studies that compared social interaction in people with versus without CVD, which showed that people with CVD had lower social interaction compared to those without CVD in general [34, 40, 56, 57, 102, 127]. The evidence on social interaction in people with versus without CVD is small scale and does not report variations across different subtypes of CVD. There was not any study available that investigated the role of population characteristics, particularly physical disability, for the relationship of CVD to social interaction.

To address these gaps in knowledge, particularly those identified in chapter three, the aim was to understand the strength of association between CVD and both social isolation and no social interaction- cross-sectionally in the first study. Social isolation was quantified by using the 45 and Up Study, comparing levels of social isolation in people with versus without CVD, overall and according to CVD subtypes including ischaemic heart disease (IHD) and its subgroup myocardial infarction (MI), cerebrovascular disease, heart failure (HF) and peripheral arterial disease (PAD). I have also aimed to examine whether the relationship between CVD and social isolation varies in subgroups based on socio-demographic and health factors, and the extent to which co-existing physical functioning limitations might explain differences in social isolation between those with and without CVD.

The second study aimed to examine the likely causal role of incident CVD on social isolation. Unlike the first study, this study was a longitudinal study that included only those participants who had no CVD at baseline and who were not socially isolated at the baseline. By comparing the social isolation in the follow-up survey, I was able to investigate the likely consequence of incident CVD in becoming socially isolated compared with those who had not developed CVD. In addition, I also examined the relationship across five incident CVD subtypes and in various population subgroups, including by the joint categorization of incident CVD and physical disability.

6.2 Social interaction of middle-aged and older Australians with and without CVD

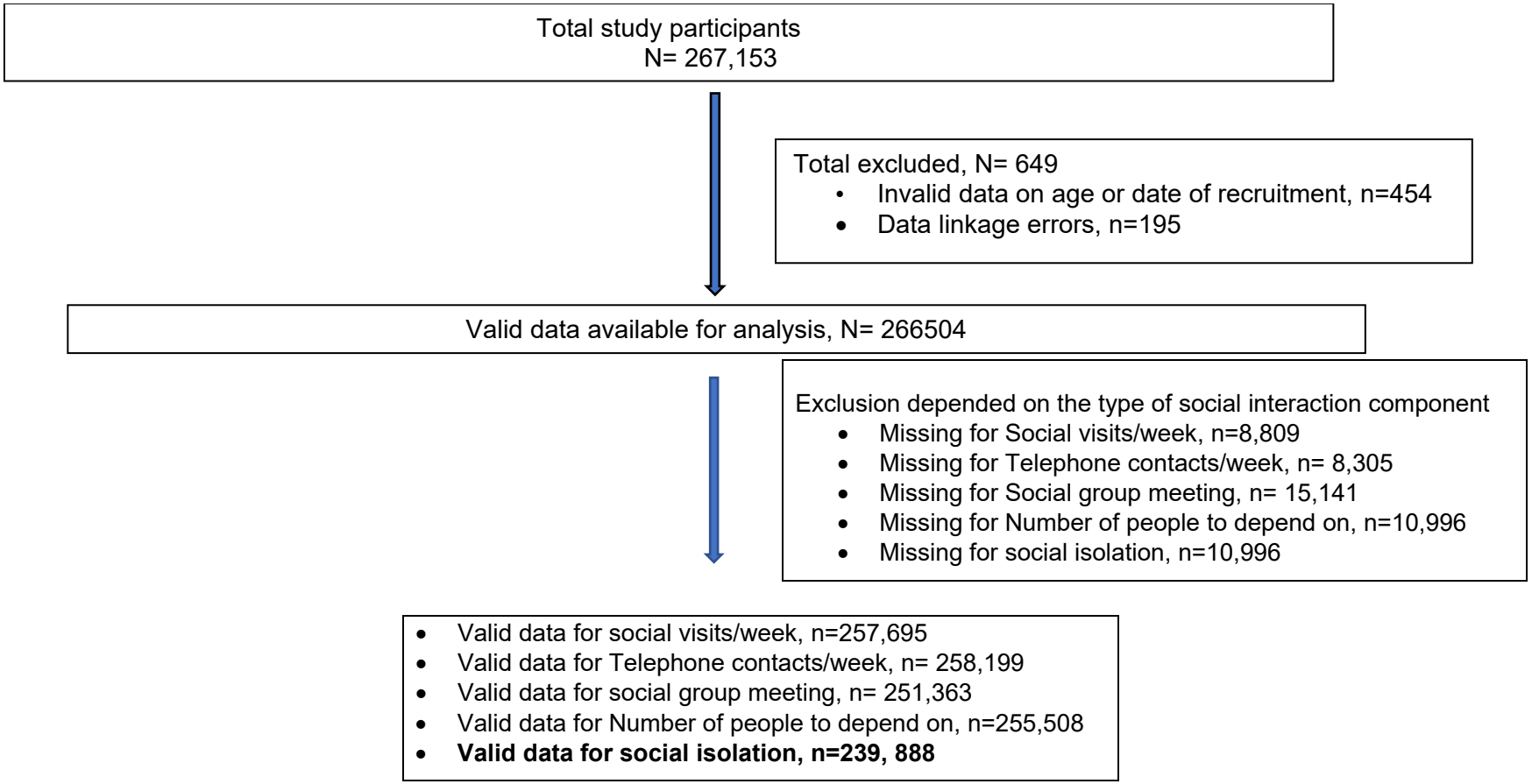
6.2.1 Materials and Methods

6.2.1.1 Study population and data sources

This is a cross-sectional investigation with study participants from the Sax Institute's 45 and Up Study [58] baseline questionnaire dataset which was probabilistically linked to several datasets including the Medicare dataset and the NSW Admitted Patient Data Collection (APDC) datasets by the Centre for Health Record Linkage (CHeReL) [202]. The 45 and Up Study datasets were used to define outcomes, exposures, and other population characteristics. The Medicare datasets were used to define age and sex variables, the APDC datasets were used to define exposures from hospitalisations, and other linked datasets were for logical checks of the linked datasets. Further details are provided in chapter 4.

The study population in this cross-section investigation of the relationship of CVD and social isolation included all participants aged 45 years and above at baseline survey (n=266504, 123616 men, 142888 women). There were no missing exposure data but there were missing data in outcomes that ranged from less than 3.1% to more than 5.7%, and the number of study participants varied by the types of outcomes (**Figure 6.1.1**).

Figure 6.1.1 Flowchart for selection of participants for the association of CVD and social isolation



6.2.1.2 Outcomes

Social isolation is the primary outcome related to social interaction in the thesis. Social isolation was derived from the Duke Social Support Index (DSSI) social interaction subscale score based on four social interaction components [151]. The four components were social visits per week, telephone contacts per week, social group meetings per week and the number of people to depend on. These were derived from two items from the 45 and Up Study survey questionnaire. The first questionnaire item asked: “How many times in the last week did you” a) “spend time with friends or family who do not live with you”, b) “talk to someone (friends, relatives or others) on the telephone”, and c) “go to meetings of social clubs, religious groups or other groups you belong to?”. The second questionnaire item asked, “How many people outside your home, but within one hour of travel, do you feel you can depend on or feel very close to?”.

The DSSI tool has been validated in older Australians, the DSSI score calculation method was mentioned earlier, and the definition of social isolation was based on previous recommendations [152, 153]. The DSSI components response options were non-negative integer values, and the values were re-coded as mentioned earlier [154] prior to summing the recoded values into a score that ranged from 4 to 12 (*Appendix 5: Table S6.1.1*). As recommended [153], all participants were divided into two groups, with the bottom 20% being classified as socially isolated and the remaining 80% being classified as not being socially isolated. Based on all study participants in the baseline survey, I found that participants having a DSSI score of less than 8 were grouped as socially isolated. Hence, those with a DSSI score less than 8 were grouped as socially isolated (*Appendix 3: Table S4.3, Appendix 5: Table S6.1.1*).

Previous studies have reported either the sum scores of DSSI [155-157] or separate components of the score [158-161]. Hence, to better reflect the different aspects of social activities, I have also investigated individual components of DSSI separately. While studying the individual components, those who had values more than [median + 3* (median absolute deviation)] of the corresponding social interaction were defined as outliers [162] and the observations with outliers were excluded from the corresponding analysis. Each of the social interaction items were analysed as a binary variable (no social interaction versus other social interaction) and the group with no social interaction component was the category of interest in the main analysis (Further details in Chapter 4).

6.2.1.3 Exposures

Baseline CVD was defined as self-reported heart disease, stroke or blood clot on the baseline questionnaire, or at least one hospital admission in the five years before entering the study with a CVD diagnosis code, as identified in any diagnostic or a procedure code fields (*details in Appendix: 3)* [23]. A five-year window was used to ensure a uniform probability of identification of previous diagnoses from administrative data for all participants. I also categorised participants based on hospitalisations for the following CVD subtypes (yes/no): IHD (ICD-AM codes: I20-I25), MI (ICD-AM codes: I21, I22 and I23), cerebrovascular disease (ICD-AM codes: I61, I63, I64), PAD (ICD-AM codes: I70-I74) and HF (ICD-AM codes: I50, I11.0, I13.0, I13.2) *(Appendix 3: Table S4.4)*.

6.2.1.4 Other variables of interest

Sociodemographic variables included: age (categorised as 45-<55, 55-<65, 65-<75, 75-75+ years), sex (men and women), region of residence (categorised as major cities, inner regional and more remote, based on the mean Accessibility Remoteness Index of Australia Plus score [203]), marital status (categorised as married/de facto and single), education (categorised as tertiary, certificates/diploma/trade and high school or less), language other than English

(LOTE) (yes/no) and born in Australia/New Zealand (yes/no), participation in the paid workforce (yes/no). Health-related variables included body mass index (BMI, kg/m^2) categorised as underweight (15-<18.5), normal weight (18.5-<25), overweight (25-<30), obese (30 to 50); alcohol consumption (number of alcoholic drinks per week categorised as non-drinkers (zero drinks per week), moderate drinkers (0<-<15 drinks per week), heavy drinkers (≥15 drinks per week)); smoking status (non-smoker, past-smoker, current smoker); diagnosis of diabetes/cancer/osteoarthritis (yes/no for each) and physical functioning limitations. The cut-points of alcohol consumption broadly reflect the Australian guideline on low-risk consumption [172]. The degree of physical functioning limitations was assessed using the Medical Outcomes Study–Physical Functioning (MOS-PF) subscale which was based on 10 questionnaire items assessing varying levels of physical functioning [176]. The physical functioning limitations scores ranged from 0 to 100, where higher scores represented fewer limitations, and were grouped into four categories in reference to previous studies [177]: no limitation (score of 100); minor limitation (score 90–99); moderate limitation (60–89); and severe limitation (score 0–59) (*Appendix 3: Table S4.5*). These variables were selected due to their relevance to social interactions and CVD [45, 161, 225-227].

6.2.1.5 Statistical analysis

Descriptive statistics were used to summarise the characteristics of the study population and the distribution of outcomes by CVD status. Modified Poisson regression with robust error variance [181] was used to estimate prevalence ratios (PRs) for social isolation (yes versus no) and for no social interaction (yes versus no) for all four interaction items in relation to CVD. All models were adjusted by age group (10-year age bands), sex, region of residence and education. The PRs for social isolation were also estimated separately within population subgroups; chi-square tests for heterogeneity were used to assess heterogeneity between subgroups. To examine the potential contribution of physical functioning to the CVD-social isolation relationship, I estimated PRs for social isolation in joint categorises of CVD and

physical functioning limitations. In this analysis, the group with no CVD and no physical functioning limitations was the reference group and the models were adjusted for age-group, sex, region of residence and education. Participants with missing values for the outcome were excluded from the corresponding analysis. There were no missing data on the main exposure (CVD status), age or sex. Missing values for the factors used in the model adjustments were included in the analysis as separate categories.

Analysis was carried out using SAS software version 9.4 and R version 3.5.2 [183].

6.2.1.6 Sensitivity analysis

To investigate the potential contribution of CVD subtype and physical disability, a sensitivity analysis was conducted, and it was done in two steps. In the first step, the proportion of participants in each joint category of physical functional limitations and CVD subtype were calculated. Then in the second step, the PRs of 'no social interaction' for all social interaction component outcomes were estimated considering group with no CVD and no physical functioning limitations as the reference group, adjusting for age-group, sex, region of residence and education.

6.2.2 Results

6.2.2.1 Characteristics of the study participants

There were 266 504 study participants, 57 097 (21.4%) with CVD and 209 407 (78.6%) without CVD. The sociodemographic profile of participants with and without CVD was similar, except that the CVD group had higher proportions of men (25.8% versus 17.6%) and older participants. Participants with CVD had a poorer health profile than those without CVD, with higher levels of smoking, obesity, comorbid diseases, and moderate/severe functional limitation (**Table 6.1.1,** *Appendix 5: Table S6.1.2*). Stratification by CVD status shows that social visits/week, telephone contacts/week, social group meetings/week and the number of

people to depend on were also similar for both men and women (*Appendix 5: Figure S6.1.1, S6.1.2*). Most commonly, people had ≥3 social visits per week, 2 to 5 telephone contacts per week, 1 to 2 social group meetings per week, ≥3 people to depend on and DSSI score in between 7 and 9 (**Table 6.1.2,** *Table S6.1.3*).

Table 6.1.1 Sociodemographic and Health related characteristics of participants with CVD in the study population

	CVD	**No CVD**
	% (n)	% (n)
Percentage (%)	21.4	78.6
(n/N)	(57097/266504)	(209407/266504)
Age (years)		
mean (sd)	70.0 (11.03)	60.7 (10.35)
Age group (years)		
45-<55	10.3 (5877)	34.4 (71932)
55-<65	23.3 (13284)	34.6 (72469)
65-<75	29.7 (16939)	19.6 (40990)
≥75	36.8 (20997)	11.5 (24016)
Sex		
Men	55.9 (31899)	43.8 (91717)
Women	44.1 (25198)	56.2 (117690)
Region		
Major cities	53.5 (30551)	51.8 (108500)
Inner regional	34.1 (19494)	34.9 (73186)
More remote	10.7 (6135)	11.3 (23691)
Marital status		
Not currently married/defacto	30.0 (17156)	23.2 (48677)
Married/defacto	69.2 (39517)	76.2 (159537)
Highest Education		
No school certificate	16.5 (9407)	10.4 (21821)
Certificate/diploma/trade	64.6 (36892)	63.3 (132462)
Tertiary	16.5 (9400)	24.9 (52063)
Language other than English		
Yes	91.3 (52142)	90.2 (188945)
No	8.7 (4953)	9.8 (20461)
County of Birth		
Australia/NZ	76.8 (43878)	76.8 (160852)
Others	21.9 (12525)	22.4 (46910)
Working		
Yes	71.8 (41003)	41.7 (87408)
No	27.9 (15955)	58.1 (121748)
Alcohol consumption		
No drinkers	37.9 (21618)	30.9 (64719)
Moderate drinkers	46.5 (26564)	52.8 (110523)
Heavy drinkers	12.8 (7295)	14.4 (30132)
Smoking status		
Current	5.7 (3279)	7.6 (16014)
Past	43.2 (24659)	34.2 (71533)
Never	50.7 (28953)	57.9 (121215)
BMI (kg/m2)		
Underweight (<18)	1.3 (768)	1.1 (2327)
Normal weight (18–<25)	30.0 (17153)	35.1 (73544)
Overweight Over weight (25–<30)	36.8 (20993)	36.4 (76315)
Obese ((30–30+)	23.0 (13157)	20.0 (41834)
Medical History: Cancer (Yes)	22.7 (12980)	14.0 (29391)
Medical History: Diabetes (Yes)	16.3 (9302)	7.0 (14586)
Medical History: Osteoarthritis (Yes)	9.3 (5311)	4.8 (10017)
Physical functioning limitations		
No limitation	12.3 (7023)	34.2 (71720)
Minor limitation	19.5 (11151)	26.4 (55216)
Moderate limitation	26.9 (15341)	19.1 (39979)
Severe limitation	24.5 (13973)	8.0 (16654)

BMI: Body Mass Index, Missing: [CVD, No CVD]: [%(n), %(n)]: region [1.6 (917), 1.9 (4030)], marital status [0.7 (424), 0.6 (1193)], education [2.4 (1398), 1.5 (3061)], Country of birth [1.2 (694), 0.8 (1645)], alcohol drinking per week [2.8 (1620), 1.9 (4033)], smoking status [0.4 (206), 0.3 (645)], BMI [8.8 (5026), 7.3 (15387)], physical functioning limitations [16.8 (9609), 12.3 (25838)].

Table 6.1.2 Categories of social visits per week, telephone talk per week, social group meeting per week and number of people to depend on according to frequencies among those with and without CVD

	CVD	**No CVD**
Total	57097	209407
	% (n/N)	% (n/N)
Social visits/week		
Min, median, max	0, 3, 100	0, 3, 100
0	11.1 (6357)	9.7 (20386)
1-2	24.5 (13983)	28.2 (58998)
≥ 3	59.5 (33994)	59.2 (123977)
Telephone talks/week		
Min, median, max	0, 4, 480	0, 4, 500
0	5.2 (2952)	4.0 (8350)
1-5	52.5 (29973)	54.8 (114713)
≥6	37.7 (21522)	38.5 (80689)
Social group meetings/week		
Min, median, max	0, 1, 50	0, 1, 50
0	37.9 (21613)	42.2 (88332)
1-2	50.0 (28539)	48.8 (102277)
≥ 3	5.0 (2853)	3.7 (7749)
Number of people to depend on		
Min, median, max	0, 5, 1000	0, 5, 1000
0	6.3 (3574)	6.3 (13237)
1-2	18.8 (10727)	17.4 (36467)
≥3	69.5 (39671)	72.5 (151832)
Duke Social support subscale Index (DSSI) score		
Min, median, max	4,9,12	4,9,12
4-6	8.3 (4732)	8.2 (17261)
7-9	43.4 (24779)	47.4 (99256)
10-12	35.4 (20235)	35.1 (73616)

*The missing values [Total, CVD, No CVD: %(n), %(n), %(n)] for social visits per week, telephone talks per week, social group meetings per week and number of people to depend on and DSSI were [3.3 (8809), 4.8 (2763), 2.9 (6046)], [3.1 (8305), 4.6 (2650), 2.7 (5655)], [5.7 (15141), 7.2 (4092), 5.3 (11049)], [4.1(10996), 5.5 (3125), 3.8 (7871)] and [10.0 (26616), 12.9 (7351), 9.2 (19265)] respectively.

6.2.2.2 CVD and social interactions

6.2.2.2.1 Overall and according to CVD subtype

Overall, 19% of people with CVD were socially isolated, compared to similar proportions (19%) of people without CVD. Men and those of younger age had higher levels of social isolation regardless of CVD status (**Figure 6.1.2).**

After adjusting for sociodemographic characteristics (age, sex, region of residence and education), social isolation was 5% higher among people with any CVD compared to people without CVD [prevalence ratio (PR) = 1.05 (95% CI: 1.03-1.07)]. Social isolation varied by CVD subtype, with PRs of 1.05 (95% CI: 1.02-1.09) for IHD and 1.32 (95% CI: 1.24-1.41) for heart failure (**Figure 6.1.3**). Four social interaction components that investigated 'the likelihood of zero social interaction' also showed the weak association between CVD and social interaction (**Figure 6.1.3,** *Appendix 5: Figure S6.1.2, Figure S6.1.3*).

Sensitivity analyses indicate that those with CVD hospitalisation had somewhat higher PRs of social isolation compared to those with self-reported CVD only (*Figure S6.1.4*) and people with only one type of CVD had slightly lower PRs of social isolation than those with over one type of CVD (*Appendix 5: Figure S6.1.5).*

6.2.2.2.2 Within sociodemographic subgroups

Social isolation was associated with several sociodemographic factors among both people with and without CVD, including education and smoking status *(Figure S6.1.6a, Figure S6.1.6b, Figures S6.1.7a to S6.1.10b)*. When social isolation was compared in people with and without CVD separately within subgroups based on sociodemographic and health-related factors, social isolation remained slightly higher among people with CVD compared to those without CVD, regardless of the population subgroup. However, PRs were significantly higher among women and those who were not married/de facto. Although the absolute crude

prevalence of social isolation was higher in younger compared to older age groups (irrespective of CVD status), the relation between CVD and social isolation became slightly stronger with increasing age (**Figure 6.1.4**). The associations were also mostly like individual social interaction components *(Appendix 5: Figure S6.1.11, Figure S6.1.12).*

6.2.2.2.3 According to physical functioning limitations

Overall, 24% of participants with CVD had severe physical disabilities, compared to 8% of people without CVD (**Table 6.1.1**). Social isolation was higher in those with greater physical functional limitations - among both those with and without CVD - but social isolation was slightly lower among those with CVD in all sub-groups based on physical functioning limitations (**Figure 6.1.6**). Among participants with no physical functioning limitations, about one in 5 were socially isolated - 17% of those with CVD and 18% of those without CVD; among participants with severe functioning limitations, 24% of those with CVD, and 25% of those without CVD, were socially isolated. After adjustment for sociodemographic variables, compared to those without CVD and no functional limitations, participants without physical functional limitations but with CVD had a similar likelihood of social isolation (PR=1.00, 95%CI=0.94-1.06). Those with severe functioning limitations had a 56% higher likelihood of social isolation if they had CVD [PR= 1.56 (95% CI: 1.51-1.63)] as well as if they did not have CVD [PR= 1.56 (95% CI: 1.51-1.63)] **(Figure 6.1.5).** The associations were mostly similar to individual social interaction components *(Appendix 5: Figure S6.1.13).*

Among CVD subtypes, those with cerebrovascular disease and heart failure had the highest proportion with severe physical disabilities, and the proportions were 39% and 51%, respectively *(Appendix 5: Table S6.1.5).* After adjusting for sociodemographic characteristics (age-group, sex, region of residence and education) and analysis across all CVD subtypes and physical functioning limitations sub-groups indicated that those with severe physical functioning limitations and cerebrovascular disease and heart failure had a consistently higher

likelihood to belong to people with no social interaction components (*Appendix 5:* Figures: *S6.1.14 to S6.1.18)*.

Figure 6.1.2 *Social isolation:* Proportion of participants with social isolation according to age-group, sex and CVD status

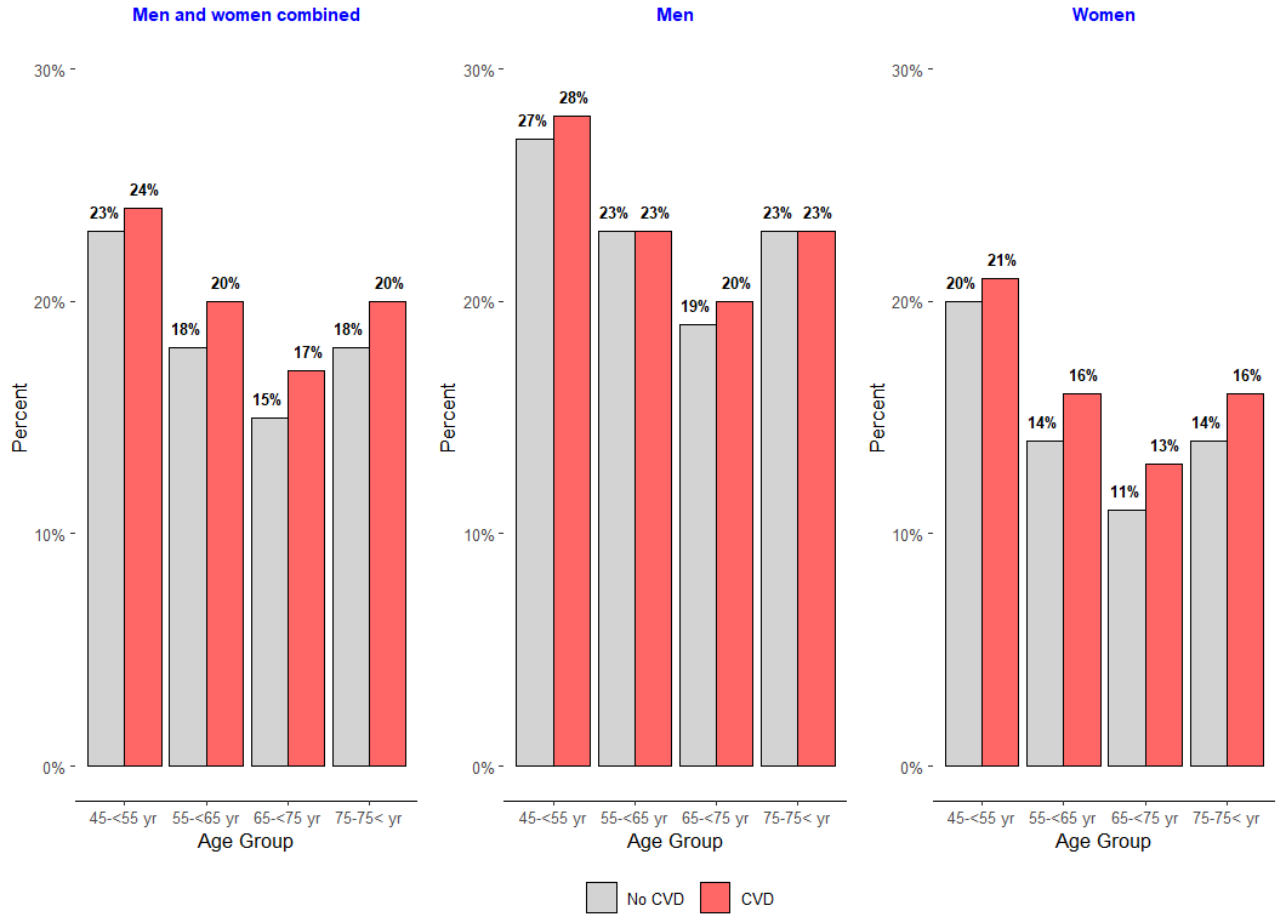


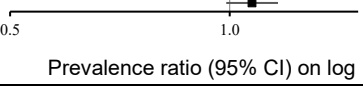
Figure 6.1.3 *Social isolation and no social interaction*: Prevalence and adjusted prevalence ratios of social isolation and no social interaction in people with and without CVD and according to hospitalisation for CVD subtypes

		[1]PR (95% CI) of social isolation and no social interaction components	
	% (n/N)		
Social isolation			
Any CVD [a]	19.6 (9731/49746)	1.05 (1.03-1.07)	
Ischaemic heart disease	20.4 (2973/14605)	1.05 (1.02-1.09)	
Myocardial infarction	22.5 (784/3479)	1.13 (1.06-1.20)	
Cerebrovascular disease	24.3 (673/2772)	1.27 (1.19-1.36)	
Peripheral arterial diseases	21.7 (673/3105)	1.13 (1.06-1.21)	
Heart failure	25.2 (715/2842)	1.32 (1.24-1.41)	
Other CVD	18.8 (5785/30838)	1.03 (1.00-1.05)	
No CVD [a] (reference)	19.1 (36315/190142)	1	
No social visit/week			
Any CVD [a]	11.7 (6357/54334)	1.08 (1.05-1.11)	
Ischaemic heart disease	12.7 (2055/16127)	1.12 (1.07-1.17)	
Myocardial infarction	14.0 (539/3854)	1.20 (1.11-1.30)	
Cerebrovascular disease	15.3 (477/3109)	1.34 (1.23-1.46)	
Peripheral arterial diseases	14.5 (502/3460)	1.24 (1.14-1.35)	
Heart failure	16.6 (540/3244)	1.42 (1.31-1.54)	
Other CVD	10.8 (3599/33412)	1.03 (1.02-1.07)	
No CVD (reference)	10.0 (20383/203361)	1	
No telephone contacts/week			
Any CVD [a]	5.4 (2945/54447)	1.07 (1.02-1.12)	
Ischaemic heart disease	6.2 (1001/16143)	1.08 (1.01-1.15)	
Myocardial infarction	7.3 (282/3861)	1.24 (1.10-1.38)	
Cerebrovascular disease	8.6 (266/3108)	1.47 (1.30-1.65)	
Peripheral arterial diseases	7.6 (265/3496)	1.25 (1.11-1.41)	
Heart failure	8.1 (263/3255)	1.36 (1.20-1.53)	
Other CVD	4.8 (1593/33486)	1.03 (0.97-1.08)	
No CVD [a] (reference)	4.1 (8317/203752)	1	
No social-group meeting/week			
Any CVD [a]	40.8 (21612/53005)	1.04 (1.03-1.05)	
Ischaemic heart disease	41.7 (6540/15697)	1.07 (1.05-1.09)	
Myocardial infarction	44.4 (1665/3752)	1.11 (1.07-1.15)	
Cerebrovascular disease	43.6 (1321/3028)	1.16 (1.11-1.20)	
Peripheral arterial diseases	44.1 (1493/3385)	1.18 (1.13-1.22)	
Heart failure	47.4 (1485/3131)	1.30 (1.25-1.35)	
Other CVD	39.8 (12990/32619)	1.01 (0.99-1.02)	
No CVD [a] (reference)	44.5 (88324/198358)	1	
No people to depend on			
Any CVD [a]	6.6 (3574/53972)	1.07 (1.03-1.11)	
Ischaemic heart disease	6.6 (1061/16041)	1.05 (0.99-1.12)	
Myocardial infarction	7.6 (291/3825)	1.17 (1.05-1.31)	
Cerebrovascular disease	7.4 (229/3104)	1.22 (1.07-1.39)	
Peripheral arterial diseases	5.9 (205/3454)	0.97 (0.85-1.11)	
Heart failure	7.3 (237/3233)	1.23 (1.09-1.40)	
Other CVD	6.6 (2201/33132)	1.08 (1.03-1.13)	
No CVD [a] (reference)	6.6 (13237/201536)	1	
			PR (95% CI) on log scale

Exposures were based on hospital records only otherwise specified, [a] Based on self-report and hospital records. Effect sizes were estimated using 'no CVD' as the reference group. [1]Adjusted for age-group, sex, region of residence and education.

Figure 6.1.4 *Social isolation:* Prevalence and adjusted prevalence ratios of social isolation in people with and without CVD in population subgroups based on socio-demographic and health related factors

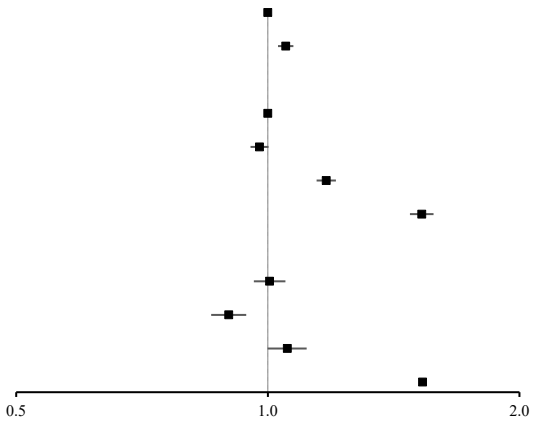
Factors and levels of the factors	Social isolation % [n/N] CVD	No CVD	[1]PR (95% CI)	[1]PR (95% CI) of social isolation of those with CVD compared to people without CVD	P-heterogeneity
Age group (years)					
45-<55	24.1 (1320/5471)	22.9 (15367/67118)	1.01 (0.97-1.06)		0.137
55-<65	20.0 (2419/12122)	17.9 (11927/66630)	1.04 (1.00-1.08)		
65-<75	17.0 (2523/14874)	15.0 (5487/36555)	1.06 (1.02-1.11)		
≥75-	20.4 (3523/17279)	18.4 (3645/19839)	1.06 (1.02-1.11)		
Sex					
Men	22.7 (6321/27873)	23.5 (19581/83442)	1.02 (0.99-1.04)		<0.001
Women	15.8 (3464/21873)	15.8 (16845/106700)	1.10 (1.06-1.14)		
Region					
Major cities	18.5 (4913/26617)	18.4 (18082/98508)	1.03 (1.00-1.07)		0.201
Inner regional	20.3 (3475/17096)	19.5 (13003/66682)	1.06 (1.02-1.09)		
More remote	23.4 (1221/5223)	21.3 (4535/21265)	1.10 (1.03-1.16)		
Marital status					
Not currently married/defacto	20.7 (3016/14569)	19.7 (8539/43276)	1.09 (1.05-1.13)		<0.001
Married/defacto	19.2 (6700/34862)	19.0 (27660/145873)	1.03 (1.01-1.06)		
Highest Education					
No school certificate	24.8 (1921/7736)	23.8 (4365/18310)	1.09 (1.03-1.14)		0.302
Certificate/diploma/trade	18.9 (6109/32374)	18.7 (22536/120362)	1.05 (1.03-1.08)		
Tertiary	17.1 (1484/8673)	18.3 (9008/49242)	0.98 (0.93-1.03)		
Language other than English					
Yes	27.7 (1139/4107)	26.8 (4744/17718)	1.05 (0.99-1.11)		0.339
No	18.9 (8646/45638)	18.4 (31682/172423)	1.06 (1.03-1.08)		
County of Birth					
Australia/NZ	18.2 (7001/38399)	17.6 (25849/146824)	1.08 (1.05-1.11)		0.316
Others	24.5 (2660/10842)	24.5 (10285/42028)	1.01 (0.96-1.04)		
Alcohol consumption					
No drinkers	22.8 (4270/18728)	22.3 (13049/58460)	1.05 (1.02-1.09)		0.020
Moderate drinkers	16.9 (3957/23456)	17.1 (17275/101237)	1.00 (0.97-1.03)		
Heavy drinkers	19.5 (1275/6545)	19.8 (5484/27747)	1.03 (0.98-1.10)		
Smoking status					
Current	31.2 (892/2855)	27.7 (3984/14382)	1.12 (1.05-1.19)		0.003
Past	21.6 (4656/21516)	20.1 (13078/65192)	1.06 (1.03-1.10)		
Never	16.6 (4194/25230)	17.5 (19231/110029)	1.00 (0.97-1.04)		
BMI (kg/m2)					
Underweight (<18)	23.7 (152/641)	25.1 (514/2048)	0.93 (0.79-1.10)		0.086
Normal weight (18–<25)	20.0 (2998/15019)	19.0 (12733/66938)	1.03 (1.00-1.07)		
Overweight Over weight	18.4 (3392/18431)	18.6 (13007/69858)	1.05 (1.01-1.08)		
Obese ((30+)	20.6 (2401/11628)	19.9 (7622/38225)	1.07 (1.03-1.12)		
Medical History: Cancer					
No	19.9 (7630/38432)	19.5 (31896/163668)	1.05 (1.02-1.07)		0.324
Yes	19.0 (2155/11314)	17.1 (4530/26474)	1.08 (1.02-1.13)		
Medical History: Diabetes					
No	19.1 (8008/41848)	19.0 (33624/177284)	1.04 (1.01-1.06)		0.510
Yes	22.5 (1777/7898)	21.8 (2802/12858)	1.04 (0.99-1.10)		
Medical History: Osteoarthritis					
No	19.8 (8965/45210)	19.3 (35009/181319)	1.05 (1.02-1.07)		0.116
Yes	18.1 (820/4536)	16.1 (1417/8823)	1.07 (0.99-1.16)		



[1]Adjusted for age, sex, remoteness of residence and education.

Figure 6.1.5 *Social isolation:* Prevalence and adjusted prevalence ratios of social isolation according to joint categories of physical functioning limitations and CVD

	% [n/N]	Prevalence ratio of social isolation
Without CVD	19.1 (36315/190142)	1
With CVD	19.6 (9731/49746)	1.05 (1.03-1.07)
No CVD and		
No limitations	18.5 (12235/66100)	1
Minor limitations	17.1 (8810/51521)	0.98 (0.95-1.00)
Moderate limitations	19.2 (7152/37047)	1.18 (1.14-1.21)
Severe limitations	25.2 (3764/14947)	1.53 (1.48-1.58)
CVD and		
No limitations	17.8 (1131/6345)	1.00 (0.95-1.06)
Minor limitations	15.2 (1560/10232)	0.90 (0.85-0.94)
Moderate limitations	17.1 (2378/13931)	1.05 (1.01-1.10)
Severe limitations	24.5 (3005/12256)	1.53 (1.48-1.59)



[1]Adjusted for age and sex, [2]Further adjusted for remoteness of residence and education attainment. Those with 'no functional limitations and no CVD' were the reference group for estimating prevalence ratios (PR's) for social isolation and no social interaction according to joint categories of physical functioning limitations and CVD. CVD is based on both self-report and hospitalisation records. Physical functional limitations had scores ranged from 0 to 100, where higher scores represented fewer limitations, and were grouped into four categories: severe (0–<60); moderate (60-<90), minor (90-<100) and no (100) functional limitation.

6.2.3 Study summary

In this large population-based cross-sectional study from Australia, it was found that people with CVD were around 5% more likely than those without to be socially isolated. Among different CVD subtypes, people living with cerebrovascular disease and heart failure had a higher likelihood of social isolation than other CVD subtypes. The slightly higher probability of social isolation among people with CVD was evident regardless of age group, sex, and sociodemographic and health-related characteristics. Importantly, severe physical disability was strongly associated with social isolation. In people without severe physical disabilities, social participation in those with and without CVD was broadly similar. However, people with severe physical disabilities, regardless of CVD status, were about 53% more likely than those without CVD and without physical disability to be socially isolated.

This investigation has provided evidence on the extent of the associations, but the likely causal role of CVD or CVD subtypes could not be answered from this investigation. Hence, a longitudinal study was conducted by following CVD-free cohort study participants who were not socially isolated at baseline, and then by investigating social isolation in those people with incident CVD compared with those who had not developed CVD during the follow-up period.

6.3 The relationship between incident CVD and social isolation over time among older Australians

6.3.1 Materials and Methods

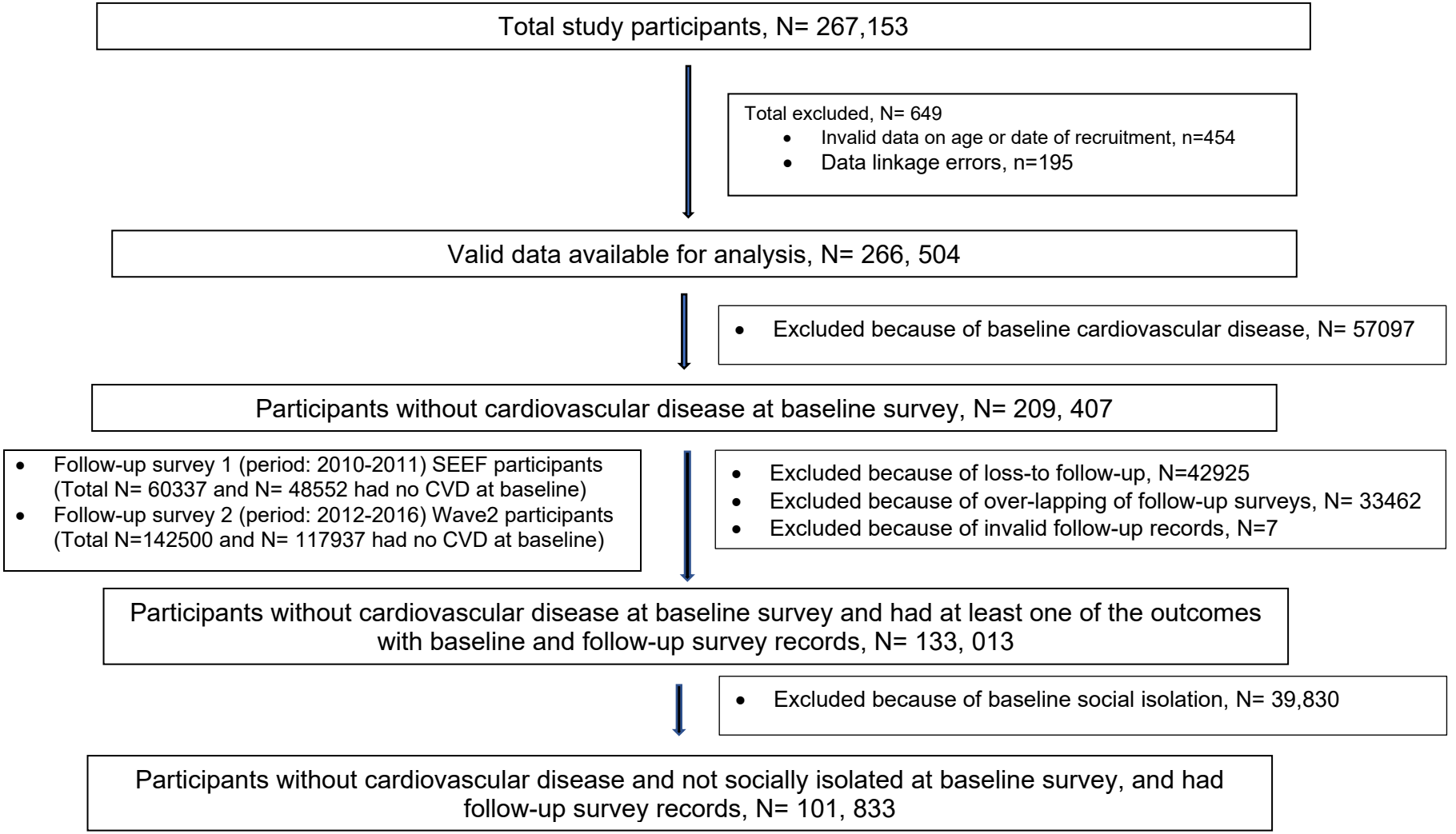
6.3.1.1 Study design, settings, and data sources

This is a longitudinal investigation with study participants from the 45 and Up Study baseline questionnaire and follow-up questionnaire which were probabilistically linked to NSW APDC by the CHeReL [202]. The baseline survey was conducted between 1 January 2006 to 31 December 2008. The first follow-up survey was SEEF conducted between 2010 to 2011 and the second follow-up survey (Wave2) was conducted between 2012 to 2016. There was the prioritisation of outcomes from Wave2 if one participant had outcomes in both follow-up surveys. This was being done to accommodate higher time intervals between baseline and follow-up surveys. Those participants were selected if they had no CVD at baseline and who were not socially isolated at baseline (**Figure 6.2.1**). Further details of the data source are provided in Chapter 4.

6.3.1.2 Outcomes

Social isolation was the outcome that was measured using the Duke Social Support Index (DSSI) social interaction subscale having four social interaction components [151]. The DSSI components were from two items in the 45 and Up Study follow-up survey questionnaire, like those in the baseline survey. Response options were non-negative integer values and summarised to a score of 4 to 12 [152, 153]. It classified participants with DSSI score less than eight at follow up survey as socially isolated. Further details are in the section *6.2.1.2* above.

Figure 6.2.1 Flowchart for selection of participants for the relationship between incident CVD and social isolation over time



6.3.1.3 Exposures

Participants were classified as having an incident CVD diagnosis if they had a record in the APDC database after baseline survey and before follow-up survey of the corresponding participants. For the definition of incident CVD and sub-types of incident CVD, the ICD-10 AM codes were used. The codes for incident IHD (ICD-AM codes: I20-I25), incident MI (ICD-AM codes: I21, I22 and I23), incident cerebrovascular disease (ICD-AM codes: I61, I63, I64), incident PAD (ICD-AM codes: I70-I74) and incident HF (ICD-AM codes: I50, I11.0, I13.0, I13.2 was slightly modified as mentioned previously [23] *(Appendix 3: Table S4.4)*.

6.3.1.4 Sociodemographic factors of interest

Several sociodemographic variables of interest were included because previous studies have reported the association of these factors with CVD and social interaction related outcomes [45, 161, 225-227]. These variables were obtained from Medicare data (age and sex), baseline or follow-up surveys of the 45 an Up Study, and the hospitalisation in between the surveys. Some variables included in the second study were like those in the first study of this chapter. These are the region of residence, education, language other than English (LOTE) and country of birth, which were obtained from the baseline survey. The variables obtained from the follow-up survey were doctor-diagnosed diseases such as diabetes/cancer/osteoarthritis, and physical functioning limitations [176, 208]. Exactly similar methods were used for the categorisation of the variables as mentioned in section 6.2.1 of this chapter. Time since incident CVD diagnosis was obtained from the hospitalisation records during the follow-up survey and was grouped into three categories: < 2 years, 2 - <4 years, ≥4 years.

6.3.1.5 Statistical analysis

The demographic characteristics of the study population by incident CVD status (participants who developed incident CVD or did not develop CVD during follow up) were presented as numbers and proportions. Besides summary statistics (minimum, median, maximum) for the

DSSI score, summary statistics (mean, median) were also presented for each of the 4 social interaction measures by incident CVD status—number of telephone contacts in the last week, number of times spent with friends/family in the last week, number of social, religious or other group meetings attended in the last week, number of people outside the home that the participant can depend on.

Modified Poisson regression with robust error variance [181] was used to estimate risk ratios (RRs) for social isolation (yes versus no) in relation to incident CVD. All models were adjusted by age at the follow-up survey (10-year age bands), sex, region of residence and education.

The RRs for social isolation were also estimated separately within population subgroups; chi-square tests for heterogeneity were used to assess heterogeneity between subgroups. To examine the potential contribution of physical disability to the incident CVD-social isolation relationship, I modelled the joint categorisation of incident CVD and physical disability on social isolation. In this analysis, the group with no CVD and no physical functioning limitations was the reference group and the models were adjusted for age-group at the follow-up survey, sex, region of residence and education. Participants with missing values for the outcome were excluded from the corresponding analysis. There were no missing data on the main exposure (CVD status), age or sex. Missing values for the factors used in the model adjustments were included in the analysis as separate categories.

Analyses were carried out using SAS software version 9.4 and R version 3.5.2 [183].

6.3.1.6 Sensitivity analysis

The first sensitivity analysis was conducted to investigate the potential contribution of CVD obtained from self-reported follow-up in the definition of incident CVD. The second sensitivity

analysis considered age variables as a continuous variable instead of a categorical variable, as was done in the main analysis.

6.3.2 Results

6.3.2.1 Characteristics of the study participants

There were 101833 study participants, 9082 (8.9%) developed incident CVD during follow up and 92751 (91.1%) did not develop CVD. The sociodemographic profile of participants with and without incident CVD was similar, except that the incident CVD group had higher proportions of men and older participants. Those with incident CVD had a higher proportion with severe functional limitations and had doctor-diagnosed cancer, diabetes, and osteoarthritis (**Table 6.2.1**). Descriptive values of social interaction at baseline, follow-up, and the proportions of participants in various categories among those with and without incident CVD did not vary as well (**Table 6.2.2**).

Table 6.2.1 Characteristics of the study participants according to incident CVD during follow up

	*People with incident CVD % (n)	*People without CVD % (n)
Overall[1], N=101833	8.9 (9082)	91.1 (92751)
Age (years) [2]	72.5 (9.74)	65.4 (9.11)
Age-group at follow-up (years)		
45-<55	2.8 (253)	12.1 (11242)
55-<65	21.7 (1973)	41.0 (38001)
65-<75	34.8 (3163)	31.3 (29072)
≥75	41.7 (3693)	15.6 (14436)
Sex		
Male	55.7 (5063)	39.5 (36607)
Female	44.3 (4019)	60.5 (56144)
Region of residence		
Major cities	53.1 (4822)	51.1 (47383)
Inner regional	34.9 (3166)	35.9 (33269)
More remote	10.3 (931)	11.1 (10265)
Marital status		
Not married/de facto	35.7 (3244)	35.5 (32824)
Married/de facto	62.9 (5711)	63.7 (59086)
Education attainment		
Tertiary	24.0 (2177)	30.3 (28123)
Certificate/diploma/trade	65.8 (5966)	62.1 (57575)
Higher school or less	9.1 (831)	6.8 (6291)
Language Other Than English (Yes)	5.5 (497)	6.3 (5879)
Country of birth (Australia/NZ)	81.2 (7375)	80.7 (74887)
Alcohol consumption		
None	33.6 (3050)	29.2 (27098)
Moderate drinkers	51.2 (4653)	55.7 (51706)
Heavy drinkers	12.7 (1151)	13.3 (12365)
Smoking status		
Current	2.6 (236)	3.8 (3553)
Past	39.7 (3609)	33.3 (30890)
Never	56.6 (5134)	62.1 (57613)
BMI		
Underweight	1.2 (110)	1.1 (982)
Normal weight	27.5 (2496)	32.5 (30121)
Overweight	35.8 (3250)	33.8 (31305)
Obese	21.7 (1973)	19.1 (17739)
Physical functional limitation		
No limitation	10.6 (960)	26.3 (24349)
Minor limitation	25.6 (2321)	33.0 (30619)
Moderate limitation	32.6 (2962)	26.4 (24523)
Severe limitation	24.2 (2201)	10.0 (9236)
Medical History: Cancer (Yes)	47.3 (4296)	37.7 (34946)
Medical History: Diabetes (Yes)	13.8 (1249)	7.9 (7308)
Medical History: Osteoarthritis (Yes)	23.7 (2154)	17.1 (15850)

Column percentages unless indicated otherwise, [1]Row percentage, [2]Mean (standard deviation), Missing : [Incident CVD, No CVD]: [%(n), %(n)]: region [1.8 (163), 2.0 (1834)], marital status [1.4 (127), 0.9 (841)], education [1.2 (108), 0.8 (762)], other than English spoken at home [0.0 (0), 0.0 (N/A)], Country of birth [0.7 (66), 0.6 (521)], alcohol drinking per week [2.5 (228), 2.0 (2388)], smoking status [1.1 (103), 0.7 (695)], BMI [13.8 (1253), 13.6 (12604)], cancer [0.0 (0), 0.0 (N/A)], diabetes [1.3 (118), 0.8 (724)] , arthritis [0.0 (N/A), 0.0 (32)], physical functioning limitations [7.0 (638), 4.3 (4024)].

Table 6.2.2 Duke's social support index score and its components at follow up by incident CVD during follow up

Social isolation and social interaction components	People with incident CVD, % (N)	People without CVD, % (N)
*Total Participants, N= 101833	8.9 (9082)	91.1 (92751)
Duke Social Support Index (DSSI) score		
Baseline (min, med, max)	8, 10, 12	8, 9, 12
Follow-up (min, med, max)	4, 9, 12	4, 9, 12
4-6	3.9 (357)	3.9 (3580)
7-9	43.7 (3964)	46.8 (43394)
10-12	41.8 (3795)	41.5 (38458)
Social visits per week		
Baseline (min, med, max)	0, 4, 100	0, 4, 100
Follow-up (min, med, max)	0, 4, 99	0, 4, 100
0	5.7 (519)	5.0 (4655)
1-2	23.7 (2150)	25.1 (23257)
>=3	66.8 (6063)	67.5 (62645)
Telephone contacts/week		
Baseline (min, med, max)	0,6, 400	0, 5, 500
Follow-up (min, med, max)	0, 5, 99	0, 5, 160
0	3.1 (281)	2.5 (2279)
1-5	53.2 (4834)	54.2 (50310)
>=6	39.6 (3598)	40.8 (37808)
Social group meetings/week		
Baseline (min, med, max)	0, 1, 40	0, 1, 50
Follow-up (min, med, max)	0, 1, 60	0, 1, 99
0	33.8 (3069)	37.9 (35126)
1-2	36.6 (3327)	36.9 (34254)
>=3	22.8 (2067)	20.0 (18536)
Number of people to depend on		
Baseline (min, med, max)	0, 6, 1000	0, 6, 1000
Follow-up (min, med, max)	0, 5, 99	0, 6, 1000
0	3.0 (274)	3.0 (2793)
1-2	15.8 (1432)	15.2 (14058)
>=3	77.8 (7064)	79.5 (73728)

*Missing values (total, incident CVD and no CVD) at follow-up [%(n)] for DSSI score [8.1 (8285), 10.6 (966), 7.9 (7319)], social visits per week [2.5 (2544), 3.9 (350), 2.4 (2194)], Telephone contacts/week [2.7 (2723), 4.1 (369), 2.5 (2354)], Social group meetings/week [5.4 (5449), 6.8 (619), 5.2 (4830)], and Number of people to depend on at follow-up [2.4 (2484), 3.4 (312), 2.3 (2172)].

Table 6.2.3 *Becoming socially isolated:* Proportion of people who became socially isolated according to time since incident CVD occurrence

Groups based on time since incident CVD diagnosis	**Proportions with social isolation**
	% (n/N)
No CVD [a]	11.9 (10181/85432)
Total incident CVD diagnosed prior to follow-up survey	12.4 (1010/8116)
Incident CVD diagnosed in < 2 years	11.4 (344/3023)
Incident CVD diagnosed in 2-<4 years	13.0 (326/2514)
Incident CVD diagnosed in ≥4 years	13.2 (340/2579)

[a] Based on self-report and hospital records, and others are based on hospitalisation records, CVD= Cardiovascular disease.

6.3.2.2 Social isolation after incident CVD

6.3.2.2.1 Overall and according to incident CVD subtype

Overall, 12% of people with and without incident CVD were socially isolated. The proportion of women with social isolation was lower compared with that in men in most age groups. The proportion of participants diagnosed with incident CVD was approximately similar during the follow-up period, regardless of the time since incident CVD diagnosis. However, among those with incident CVD, the social isolation did not vary much with the increased diagnosis period (**Table 6.2.3**). The proportions varied slightly by incident CVD status and those having incident CVD status had slightly higher social isolation across most age groups and the effect of age seems to be non-linear (**Figure 6.2.2**). After adjusting for sociodemographic characteristics (age, sex, region of residence and education), the risk of social isolation was not significantly different overall, in those with incident CVD versus those without [risk ratio (RR) = 1.07 (95% CI: 1.00-1.13)]. Social isolation varied by CVD subtype with RRs ranging from 1.02 (0.93-1.11) for IHD to 1.20 (0.97-1.47) for HF. However, RR's were non-signification for all CVD subtypes except for cerebrovascular disease which had a RR of 1.43 (1.22-1.69) (**Figure 6.2.3**).

Sensitivity analyses show that considering self-reported CVD in the definition of incident CVD, those with incident CVD had an almost similar risk of social isolation compared to those defined from incident CVD recorded from hospitalisations only (*Appendix 5: Table S6.2.1).* The second sensitivity analysis indicated that the magnitude of associations remained similar if age was considered as a continuous variable in the model adjustments (*Appendix 5: Table S6.2.2*).

6.3.2.2.2 According to population subgroups

When social isolation was compared in people with and without incident CVD separately within subgroups based on sociodemographic and health-related factors, the risk of social isolation was slightly higher among people with incident CVD compared to those without CVD in some

population subgroups, but most of the associations were not statistically significant. For example, the RRs were slightly higher among older people, women and those having osteoarthritis. Although the absolute crude prevalence of social isolation was higher in current smokers compared to past other groups (irrespective of CVD status), the relation between incident CVD and social isolation was not statistically significant (**Figure 6.2.4**).

6.3.2.2.3 According to physical functioning limitations

Overall, 25% of participants with incident CVD had severe physical disabilities, compared to 10% of people without CVD (**Table 6.2.1,** *Table S6.1.5*). Social isolation was higher in those with greater physical functional limitations - among both those with and without CVD - but social isolation was slightly lower among those with CVD in sub-groups with no, minor and moderate physical disability (**Figure 6.2.5**). Among participants with no physical functioning limitations, about one in 10 were socially isolated - 10% of those with CVD and 12% of those without CVD; among participants with severe physical disabilities, 15% of those with incident CVD, and 16% of those without CVD were socially isolated. After adjustment for sociodemographic variables, compared to those without CVD and no functional limitations, participants without physical functional limitations but with incident CVD did not have a significantly different risk of social isolation with RR 0.89 (95% CI=0.73-1.09). Those with severe physical disabilities had a 63% higher risk for social isolation if they had incident CVD (RR= 1.63 (95% CI: 1.45-1.82)) and 66% higher risk if they had not been diagnosed with CVD (RR= 1.66 (95% CI: 1.55-1.76)) (**Figure 6.2.5**).

Figure 6.2.2 *Becoming socially isolated:* Proportion of participants becoming socially isolated according to age-group, sex and incident CVD status

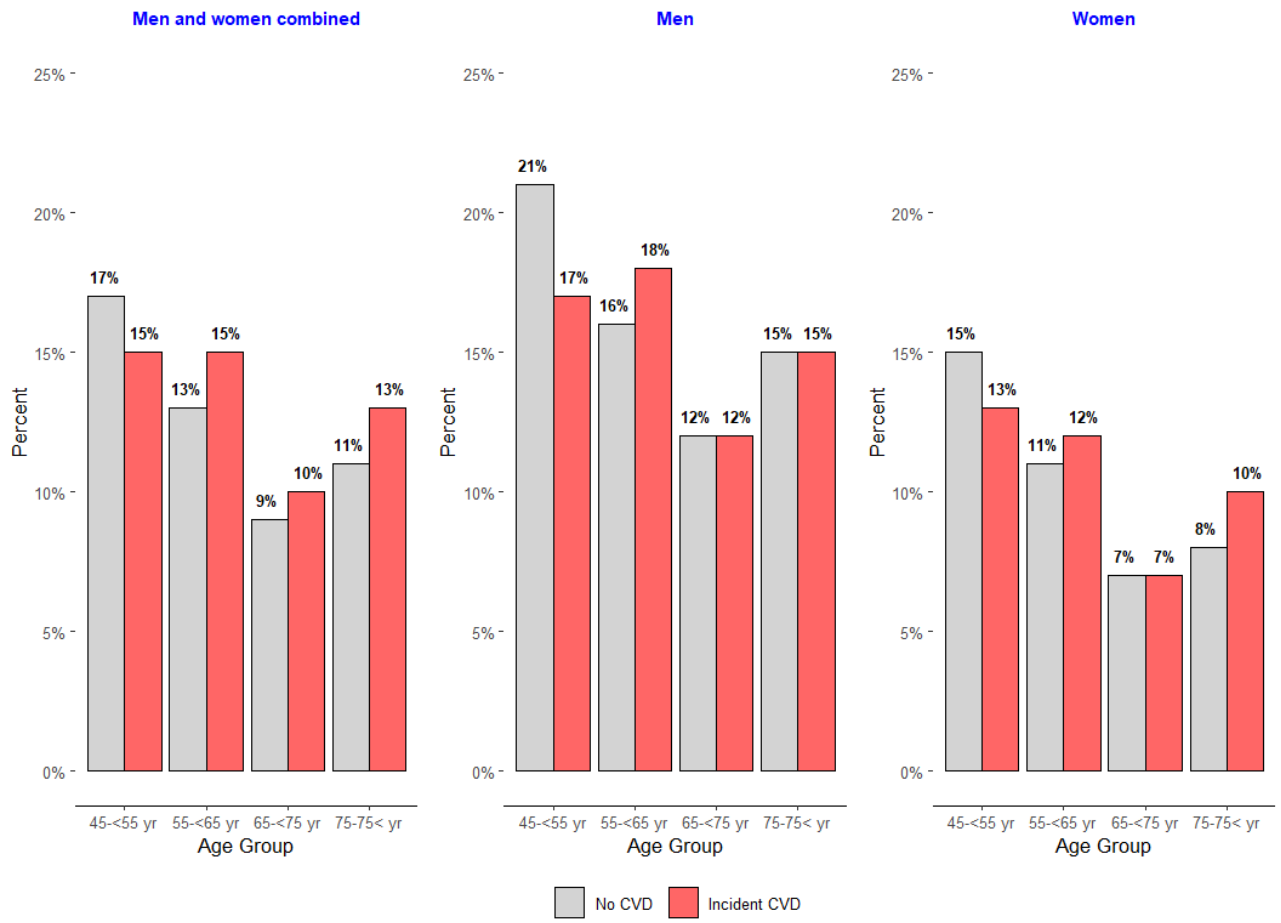
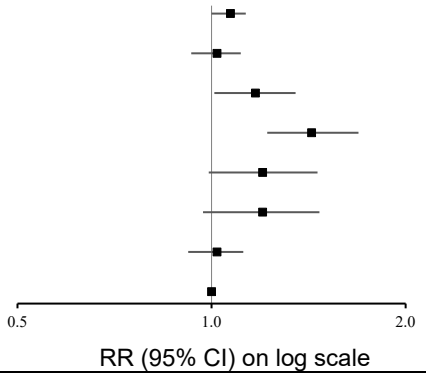


Figure 6.2.3 *Becoming socially isolated:* Incidence of and adjusted risk ratios for becoming socially isolated according to incident CVD and its subtypes

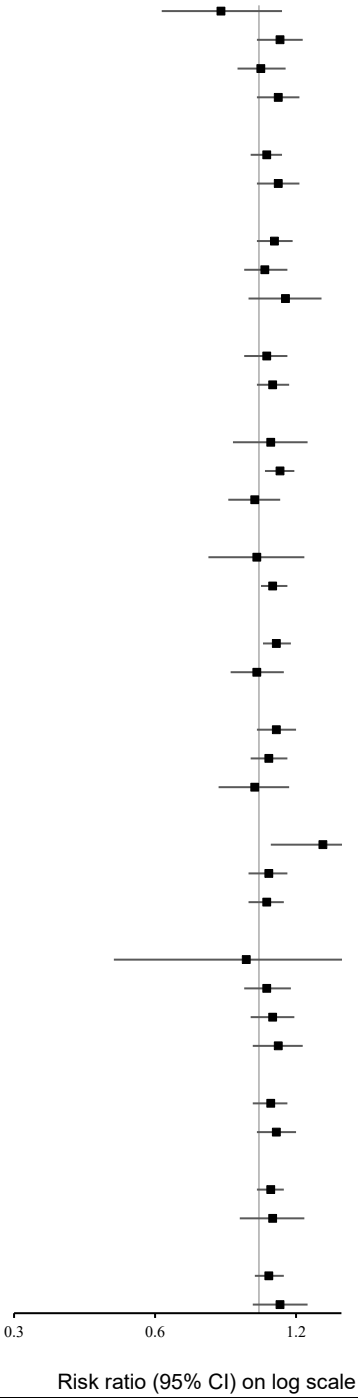
Incident CVD and incident CVD subtype	Social isolation % (n/N)	[1]RR (95% CI) of developing social isolation
Any incident CVD [a]	12.4 (1010/8116)	1.07 (1.00-1.13)
Ischaemic heart disease [a]	12.2 (449/3678)	1.02 (0.93-1.11)
Myocardial infarction [a]	14.6 (159/1091)	1.17 (1.01-1.35)
Cerebrovascular disease [a]	16.6 (122/736)	1.43 (1.22-1.69)
Peripheral arterial diseases [a]	14.0 (89/637)	1.20 (0.99-1.46)
Heart failure [a]	14.2 (78/550)	1.20 (0.97-1.47)
Other incident CVD [a]	11.5 (362/3137)	1.02 (0.92-1.12)
No CVD (reference) [b]	11.9 (10181/85432)	1



[a] Based-on hospital records only, [b]Based on self-report and hospital records. Effect sizes were estimated using 'no CVD' as the reference group. [1]Adjusted for age-group, sex, region of residence and education.

Figure 6.2.4 *Becoming socially isolated:* Incidence of and adjusted risk ratios for becoming socially isolated in people with and without incident CVD in population subgroups based on socio-demographic and health related factors

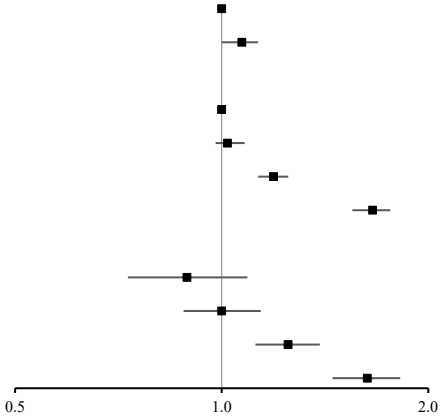
Factors and levels of the factors	Social isolation % [n/N] Incident CVD	No CVD	[1]RR (95% CI)	[1]RR (95% CI) of becoming socially isolated of those with incident CVD compared to those without CVD	P-heterogeneity
Age group (years)					
45-<55	15.1 (36/239)	16.9 (1786/10556)	0.83 (0.62-1.12)		0.051
55-<65	15.5 (283/1828)	12.9 (4621/35713)	1.11 (0.99-1.24)		
65-<75	9.9 (284/2882)	9.0 (2395/26697)	1.01 (0.90-1.14)		
75-75+	12.9 (407/3167)	11.1 (1379/12466)	1.10 (0.99-1.22)		
Sex					
Men	14.7 (665/4534)	15.0 (5064/33787)	1.04 (0.96-1.12)		0.151
Women	9.6 (345/3582)	9.9 (5117/51645)	1.10 (0.99-1.22)		
Region					
Major cities	12.4 (536/4322)	11.8 (5154/43758)	1.08 (0.99-1.18)		0.021
Inner regional	12.1 (340/2816)	11.8 (3607/30624)	1.03 (0.93-1.15)		
More remote	14.4 (119/828)	12.8 (1193/9354)	1.14 (0.95-1.36)		
Marital status					
Not currently	12.1 (346/2871)	12.5 (3775/30128)	1.04 (0.93-1.15)		0.921
Married/defacto	12.5 (641/5144)	11.5 (6301/54589)	1.07 (0.99-1.16)		
Highest Education					
No school certificate	15.9 (112/705)	15.7 (853/5429)	1.06 (0.88-1.27)		0.561
Certificate/diploma/trade	12.6 (669/5294)	11.8 (6217/52724)	1.11 (1.03-1.19)		
Tertiary	10.8 (220/2030)	11.3 (3020/26626)	0.98 (0.86-1.11)		
Language other than English					
Yes	15.2 (67/440)	15.8 (842/5328)	0.99 (0.78-1.25)		0.388
No	12.3 (943/7676)	11.7 (9339/80103)	1.07 (1.01-1.15)		
County of Birth					
Australia/NZ	12.0 (789/6582)	11.3 (7825/68981)	1.09 (1.02-1.17)		0.547
Others	14.4 (213/1480)	14.4 (2310/15988)	0.99 (0.87-1.13)		
Alcohol consumption					
No drinkers	14.3 (387/2709)	13.7 (3393/24813)	1.09 (0.99-1.20)		0.161
Moderate drinkers	11.3 (476/4198)	10.8 (5182/47962)	1.05 (0.96-1.15)		
Heavy drinkers	12.1 (127/1049)	12.7 (1451/11451)	0.98 (0.82-1.16)		
Smoking status					
Current	23.5 (51/217)	18.1 (587/3249)	1.37 (1.06-1.76)		0.566
Past	13.6 (438/3209)	12.8 (3647/28422)	1.05 (0.95-1.15)		
Never	11.0 (505/4609)	11.1 (5879/53184)	1.04 (0.95-1.13)		
BMI (kg/m2)					
Underweight (<18)	11.6 (10/86)	13.3 (118/887)	0.94 (0.49-1.79)		0.950
Normal weight (18–<25)	12.5 (280/2247)	11.4 (3193/27939)	1.04 (0.93-1.17)		
Overweight Over weight	11.8 (349/2955)	11.5 (3355/29059)	1.07 (0.96-1.19)		
Obese ((30+)	13.7 (246/1792)	13.1 (2153/16472)	1.10 (0.97-1.24)		
Medical History: Cancer					
No	13.1 (560/4270)	12.8 (6795/53230)	1.06 (0.97-1.15)		0.840
Yes	11.7 (450/3846)	10.5 (3386/32202)	1.09 (0.99-1.20)		
Medical History: Diabetes					
No	12.0 (828/6894)	11.7 (9176/78120)	1.06 (0.99-1.13)		0.383
Yes	14.7 (164/1117)	13.7 (910/6633)	1.07 (0.91-1.25)		
Medical History: Osteoarthritis					
No	12.6 (779/6181)	12.2 (8620/70941)	1.05 (0.98-1.13)		0.001
Yes	11.9 (231/1935)	10.8 (1558/14463)	1.11 (0.97-1.27)		



[1]Adjusted for age, sex, remoteness of residence and education.

Figure 6.2.5 *Becoming socially isolated:* Incidence of and adjusted risk ratios for becoming socially isolated according to joint categories of physical functioning limitations and incident CVD

	Development of social isolation % [n/N]	Risk ratio of development of social isolation
Without CVD	11.9 (10181/85432)	1
With incident CVD	12.4 (1010/8116)	1.07 (1.00-1.13)
No incident CVD and		
No limitations	11.6 (2623/22645)	1
Minor limitations	11.0 (3158/28666)	1.02 (0.98-1.08)
Moderate limitations	11.8 (2674/22735)	1.19 (1.13-1.25)
Severe limitations	15.9 (1323/8345)	1.66 (1.55-1.76)
Incident CVD and		
No limitations	10.1 (89/883)	0.89 (0.73-1.09)
Minor limitations	10.7 (231/2154)	1.00 (0.88-1.14)
Moderate limitations	12.3 (334/2716)	1.25 (1.12-1.39)
Severe limitations	15.2 (292/1923)	1.63 (1.45-1.82)



[1]Adjusted for age, sex, remoteness of residence and education, [2]Further adjusted for remoteness of residence and education attainment. Those with 'no functional limitations and no CVD' were the reference group for estimating prevalence ratios (PR's) for social isolation and no social interaction according to joint categories of physical functioning limitations and CVD. CVD is based on both self-report and hospitalisation records. Physical functional limitations had scores ranged from 0 to 100, where higher scores represented fewer limitations, and were grouped into four categories: severe (0–<60); moderate (60-<90), minor (90-<100) and no (100) functional limitation.

6.3.3 Summary of findings in the longitudinal investigation

In this longitudinal study, I found that the risk of social isolation was mostly similar regardless of experiencing incident CVD. Overall, the risk of becoming socially isolated was not significantly higher after incident CVD, but it varied slightly across different incident CVD subtypes and population subgroups. Those with the incident cerebrovascular disease had a slightly higher risk of social isolation compared to other CVD subtypes. However, people having severe physical disabilities had a higher risk of becoming socially isolated, whether one had incident CVD or not. The analyses indicated that the group with the highest risk for social isolation consisted of people with severe physical disabilities, regardless of incident CVD status.

6.4 Discussion of the findings

6.4.1 Results of the study in relation to other studies

This large-scale, population-based investigation is the first in Australia and the most comprehensive study so far in the analyses of the associations between social isolation and CVD. This large-scale population-based study with linkage to hospital records allowed comparison of social isolation and social interaction components in people with and without CVD, across CVD subtypes and within the population subgroups enabling a comprehensive comparative description of social interaction in individuals living with CVD in the community. Social isolation according to joint categories of physical disability and CVD is also newer evidence in Australia. This is also the only study in Australia reporting social isolation after incident CVD among participants who were not socially isolated and who had no CVD at baseline survey and considered the role of CVD subtypes and physical disability.

There was one Australian study [57] that compared different social roles in people with versus without stroke. The study was a community-based investigation with a small population size (n=218) that reported outcomes only in percentages, and without adjustments for any other variables. The overall findings in the previously published study [57] and that in the cross-sectional investigation in this chapter were broadly similar, that is people with CVD had slightly lower social roles or higher social isolation compared to those in people without CVD. However, it was not possible to compare the magnitudes of findings because of variations in social interaction outcomes definition. The findings in this Chapter are also comparable to studies set in other countries like those in Brazil, France, Sweden, the United Kingdom (UK), and the United States of America (USA) which have consistently shown that people with CVD are less likely to take part in social interaction than people without CVD [34, 40, 56, 102, 127]. However, it is difficult to compare the magnitude of the findings in this investigation with the previously published studies, given the variation in study design, the definition of social interaction, case definition of CVD, and selection of the comparison population. For example,

a cross-sectional investigation with a study population from the USA [34] found that people with myocardial infarction had 46% higher odds of having social activity limitations compared to people without CVD. Whereas, in the cross-sectional analyses of this chapter, it was found that people with myocardial infarction had a 13% higher chance to be socially isolated compared to those without CVD. Another study from France [102] has shown that people with stroke were 79% less likely to use a phone than the participants without stroke. This study demonstrated that people with stroke had a 47% higher likelihood of having no telephone contacts/week.

There was not any other study found that reported social isolation or social interaction components in absolute and relative terms among different population subgroups based on sociodemographic and health-related factors. The cross-sectional results indicate men were more likely to have no social interaction compared to women in absolute terms, but the magnitude of the relative association between CVD and social isolation was greater among women than men. There was not any other study found to compare the findings that people with CVD who were born in Australia or New Zealand, current smokers, had a medical history of osteoarthritis were more likely in absolute and relative terms to be socially isolated compared to those without CVD.

There was not any longitudinal investigation available that investigated the likely causal role of CVD in social isolation. While this study, like others, highlights a higher prevalence of social isolation among people with CVD, we should not assume that CVD is the cause without additional evidence. A key finding that impaired physical functioning is likely to be an important factor underpinning the difference in social isolation between those with and without CVD has not been reported previously. However, it is consistent with the idea that a relatively high proportion of people with CVD have physical disabilities [101] compared to those without CVD. This may also explain the higher social isolation among people with cerebrovascular disease and heart failure compared to those with other less severe types of CVD. This is an

important finding for cardiac rehabilitation programs. Earlier studies have shown that these programs help improve physical functioning despite having low participation rates in such programs [210]. The evidence generated in this thesis regarding the role of physical disability in social isolation might be useful to promote the importance of participation in cardiac rehabilitation programs and as well as to improve participation in social activities.

6.4.2 Strengths of the investigation

This population-based study had several strengths. The first one is its comprehensive comparative nature of describing social interaction in individuals living with versus without CVD. The cross-sectional study with a large sample size enabled comparisons across CVD subtypes and within the population subgroups based on different social-demographic and health-related factors. An investigation of the associations on multiple time points is the next strength. I was able to use questionnaire data collected at two time points, including repeated measures of social isolation, thus allowing me to ascertain both magnitudes of the association between CVD to social isolation as well as the likely consequential role of incident CVD in social isolation. The third strength is using linked administrative data to define exposure and other variables more reliably. Using questionnaires linked to administrative data facilitated the assessment of sociodemographic and health-related factors with virtually complete and objectively measured incident CVD status. Administrative data allowed me to exclude people with prior CVD and independently measure incident CVD with virtually complete follow-up. The fourth strength is the availability of follow-up data to define different variables. Prospective questionnaire data allowed assessment of sociodemographic and health-related risk factors often not available when using administrative data. The fifth strength is investigating over one outcome related to social interaction. The large-scale nature of the study allowed us to capture a relatively large number of outcome events over a relatively short period.

6.4.3 Limitation of the investigation

Even with this large sample, there were some limitations related to study population representativeness, availability of fewer social interaction components, and selection bias. This study population was randomly sampled from a whole-of-population database and included ~ 10% of the entire population in the target age group and the response rate was ~18%, consistent with cohort studies of this nature. Generally, participants in cohort studies are healthier than the general population [212]. The study included only community-dwelling adults and those elders who had been transferred to special care settings have not been included in this study, which might induce bias.

No other study was found that reported the prevalence of CVD in Australia for the comparable age group similar to that investigated in the study. Hence, we could not compare the prevalence of CVD in this study with those from other nationally representative Australian studies. We also could not find other studies from Australia to compare the magnitude of social isolation as reported in the thesis to validate the findings. Hence, while the absolute estimates of CVD prevalence and social isolation may not be representative of that in the general population the PRs or RRs based on internal comparisons, such as those described here, have been shown to be generalisable and remain valid in non-representative studies [146]. Findings of the consistency of the relative estimates in a wide variety of population subgroups also support the validity of the relative findings. Social isolation and social interaction components, as mentioned in this investigation, have potential limitations because of the way they were defined. For example, social visits per week did not distinguish between the direction and purpose of the visits. The study participants might spend time with friends or family members who do not live with them because the participants went out to visit friends or family for social purposes. Alternatively, the study participants might be too ill to go out and thus spend time with friends or family members who came to see the study participants because of their illness. Given the absence of individual-level in-depth interviews on social isolation and social interaction, the pragmatic categorisation of social isolation and interaction

components as used in this investigation could be considered as a valuable population-level indicator. Like most population-based cohort studies, the 45 and Up Study sample is healthier than the general population [58] and the incident CVD rate was slightly higher among those who had not completed the follow-up questionnaire compared to those who did. However, the participants did not differ much in terms of sociodemographic variables, whether they had completed the follow-up survey or not. Loss to follow-up from nonparticipation in the follow-up survey has been shown to have minimal impact on effect estimates [228], and relative effect estimates are expected to remain valid in the absence of confounding and effect modification [146, 229]. However, I cannot exclude the bias in the estimate that might arise from that loss to follow-up. Had there been all participants' data available, it would have been possible that the findings of this study were an underestimate of the associations between incident CVD and social isolation. Despite the large sample size, it was observed to have few outcome events in some exposure groups, limiting the precision of the estimates. The longitudinal investigation had a study sample restricted to participants who completed two questionnaires, and thus it cannot be ruled out that loss to follow-up biased the estimates. This issue was addressed later in the thesis (Chapter Seven).

6.4.4 Interpretation of the findings

Since this study was conducted with data collected before the widespread use of social media, the results of this investigation have significant implications for healthy ageing for those living with CVD and for people and the organisations that care and assist people with CVD to have meaningful ageing. Social interaction and the concept of social isolation, as defined and operationalized in the thesis, embraced the diversity of terminologies that have been used in previous investigations to indicate the person-centred outcomes related to social wellbeing. The terminologies used in the thesis were partly driven by the data resource, and the primary outcome variable (social isolation) was the most appropriate terminology for the measurement of social wellbeing related person-centred outcomes. Since the analysis results from various terminologies used in the thesis and those mentioned in earlier papers broadly supported each

other, there were not any specific implications of the focus because of the chosen terminologies in the thesis. These results of this investigation will help people with CVD to understand better how the social isolation or social interaction looks like for them compared to those in people without CVD. Social interactions are important for older people [230] and the World Health Organisation (WHO) recognises the ability to participate in societal activities as one of the direct consequences of health [231]. The slight increase of social isolation or reduction in the level of social interaction as found in this thesis might help dispel the depressive view of living with CVD. The findings in the thesis will provide a positive view of social isolation status or social interaction level of people with CVD to their family members and friends. This will help minimise the negative perspective of people on the extent of social isolation of people with CVD and thus might help increase higher social interaction among people with CVD.

A key finding in the thesis is that physical disability was a key factor underpinning the difference in social isolation or social interaction components between those with and without CVD. This is similar to previous investigations that used a different measurement tool for social interaction and disability and reported an inverse relationship between social interaction and disability [232]. Thus, the findings in this chapter are consistent with the previously reported results that a greater disability can restrict social interaction and increase social isolation [233-235]. This may also explain the slightly higher social isolation among people with a more severe type of CVD subtypes, such as cerebrovascular disease and heart failure. This is an important finding, as cardiac rehabilitation programs help improve physical functional limitations [210] and might reduce social isolation.

Findings in this chapter on the large-scale evidence on the relationship of CVD to social isolation will contribute to a better understanding of the quality of life of people living with CVD. The results might help identify the group of CVD survivors who need social support more compared to others and might inform carers to design better care models for improving the

quality of life of the patients. The findings might also inform the community support programs, such as the ‘Seniors Connected Program’, ‘Community Visitors Scheme’. in Australia, that receive government funding to address the social isolation [236]. For example, the ‘Seniors Connected Program’ includes a phone support service delivered by ‘Friends for Good’. This service offers older Australians an opportunity to call and have a free, anonymous, friendly chat with a volunteer over the phone [237]. The findings in the thesis might be informative to this program and organisations like the Australian Heart Foundation to identify and inform the vulnerable people with CVD and to incentivise the discussion to update its strategy to reach out to the vulnerable people to offer its service.

Further studies incorporating the quality (e.g., using in-depth interviews) and nature (e.g., interactions with family/carers versus others, social media use) of social interaction are likely to enable a better understanding of the relationship between social interaction and CVD diagnosis.

CHAPTER 7 Implication of missing data

7.0 Chapter summary

This Chapter describes missing data, a common problem in cohort studies, and the implication of missing data with a case study, 'The relationship between incident CVD and exit from workforce overtime among working-age older Australians', taken from Chapter five. This investigation was done to examine possible bias because of non-participation in the follow-up surveys. The sequential steps of the investigation were: (1) exploring patterns of missing data in the context of thesis, (2) examining the factors associated with missing outcome data at follow-up survey, (3) applying 'multiple imputations' to impute the missing values, and (4) estimating relative risk ratio (RR) of exiting workforce with multiply imputed data to compare it to the complete case analysis. Descriptive statistics were used for step one, generalised linear models in steps two and four, and multiple imputations by 'chained equation' with both missing at random (MAR) and missing not at random (MNAR) assumptions in step three.

While exploring the missing data, it was found that the proportion of missing data for exposures, outcomes and confounding variables ranged from 0% to less than 10% in the cross-sectional analyses. In the longitudinal analyses, the proportions of missing values for the exposure and confounding variables were mostly similar to those in the cross-sectional analyses, but those for outcome variables were substantially higher (~33%). The primary reason for a higher proportion of missing outcomes in the longitudinal analyses was non-participation in the follow-up survey. While investigating different factors associated with non-participation in the follow-up survey, it was found that the participants with relatively unfavourable health conditions at baseline, and those who developed CVD during follow-up, had a slightly higher non-participation rate in the follow-up survey. The age and sex adjusted prevalence ratios (PR's) of non-participation in the follow-up survey were also higher among those having adverse health conditions, but the PR of non-participation did not vary by CVD hospitalisation during the follow-up period. After applying 'multiple imputations', I found that compared to the complete case analysis, the point estimates did not change materially, and

the precision did not improve substantially, as the confidence interval widths were similar. Hence, the main analysis could be considered valid.

7.1 Background

7.1.1 Missing data and multiple imputations

Epidemiological studies typically aim to quantify the association between exposure and outcome in the population and selection bias is a key consideration when making conclusions about the target population using a study sample [238]. Cohort studies tend to be non-representative of the target population (healthier and more health-conscious). However, representativeness is not necessarily required for reliable estimates of relative risk based on internal comparisons, although biases can occur if selection depends on both the exposure and outcome [146]. Furthermore, in prospective studies, selection into baseline is unlikely to introduce bias as participants are enrolled before they experience the outcome. In cohort studies with more than one wave of follow up, retention of subjects may be differentially related to exposure and outcome, and this has a similar effect that can bias the results. This phenomenon (i.e., non-participation in the follow-up survey) results in missing data [146, 238, 239]. According to Rubin [240, 241], missing data can be categorised into three types based on missing data mechanism: (i) missing completely at random (MCAR), where the probability of data being missing does not depend on any observed or unobserved data; (ii) missing at random (MAR), where the probability of missing data is conditional on the observed data but does not depend on any unobserved data; or (iii) missing not at random (MNAR), the probability of data being missing depends on unobserved data. The missing data mechanisms are generally conceptual and cannot be verified by using statistical tests [242].

Though there is nothing that can replace actual data, finding ways to deal with missing data is an active area of research and several conceptual frameworks have been proposed to deal with missing data [243, 244]. These methods include but are not limited to, multiple imputations, listwise or case deletion, pairwise deletion, mean substitution, regression imputation, last observation carried forward, maximum likelihood and expectation-maximization [243]. Among these different methods for missing data analysis, I have applied

a widely used statistical method called ‘multiple imputations’ [245] to impute the missing data because of its increasing popularity. ‘Multiple imputations’ is a two-step process whereby missing data are imputed multiple times and the resulting estimates of the parameter (s) of interest are combined across the completed datasets. Broadly there are two approaches for carrying out multiple imputations- Multiple imputations with chained equations (MICE), and multivariate normal imputation (MVNI). The former uses a series of regression models to impute missing values, cycling through the variables with missingness [182] and the latter uses a Markov Chain Monte Carlo algorithm to obtain imputed values assuming a multivariate normal distribution for all variables subject to missing data [246]. A greater number of imputations is generally suggested to reduce noise from the imputation. However, because of a little gain in precision from running more imputations compared with the computation time required, it is suggested to increase the number of iterations close to the proportion of missingness [247].

7.1.2 Things to consider before multiple imputations

Multiple imputations could be a superior technique [248] to complete case analysis, but there is an increasing body of evidence that suggests that multiple imputations might introduce bias if not carried out appropriately [242, 249]. Therefore, it is suggested to consider several important issues related to missing data, especially to investigate whether multiple imputations are likely to be more feasible and to produce better results (in terms of reducing bias or improving precision) than complete case analysis. These issues are whether there was a known reason for missing data, whether the missing at random was a plausible assumption, whether there are variables that are correlated with the incomplete variables, the type of the variables that contain missing data, and the extent of missingness in the dataset [242, 250, 251]. Examining these issues help to assess which assumption (among MCAR, MAR, and MNAR) is plausible, identify variables that could be used to impute/predict the missing value [252], or whether multiple imputations can introduce bias from the ill-fitting model [253]. Since in most cases, multiple imputations are carried out with MAR assumption, it is also suggested

to conduct multiple imputations with MNAR assumption as a sensitivity analysis in those cases [254].

7.1.3 Missing data in the context of the thesis

The 45 and Up Study [58] datasets and its linked datasets to conduct four studies. Missing data mechanism and proportion of missing data differed in these studies depending on the study design, outcome, exposure, and covariates. Four primary outcomes and nine secondary outcome variables (all relating to workforce participation and social interaction) examined in this thesis were derived from responses to survey questions. The proportion of missing outcome data varied, with <0.1% to 10.0% in cross-sectional analyses and 33.1% to 42.9% longitudinal analyses for potentially eligible study participants (**Table 7.1**).

The main exposure in the cross-sectional studies is existing CVD and that in the longitudinal studies is incident CVD. The existing CVD in the cross-sectional study was based on both self-reported survey and hospitalisation records, the incident CVD for the longitudinal study was primarily based on linked hospitalisation records (although some sensitivity analyses included self-reported CVD from survey response as well). There was no missing data for existing CVD or incident CVD since complete hospitalisation records are available for all participants through data linkage, even for those who did not respond to the follow-up survey. Two variables (age and sex) used for statistical model adjustments were derived from the Medicare dataset, and there was no missing data for these either. Other covariates used in regression models had no missing data (as they were either derived from linked hospitalisations) or had small proportions of missing data (~0.1%). Missing data in these covariates were modelled as a separate category in regression models. Therefore, their impacts on cross-sectional analyses were deemed to be minimal. However, the proportion of missing outcome data was notably high in longitudinal studies, which is the primary interest of discussion in this chapter.

The proportions of missing outcome data among potentially eligible participants in baseline and follow-up surveys differed substantially. In cross-sectional analyses, missing outcome data stems from non-response or invalid responses to specific questions on the baseline survey and were within less than 0.01% to 13.3%. However, in longitudinal analyses, missing outcome data proportions were substantially higher due to cohort attrition because of non-participation, besides missing/invalid response to survey questionnaire items among those who take part (<0.01% to 14.8%) (*Appendix 6: Figure S7.1.1*). For the longitudinal analyses, a key advantage of the datasets used in the thesis is that even for those who did not take part in the follow-up survey, information on exposure variables and several other key variables that could be potential predictors of the missing outcome were available through linked data. Such auxiliary variables provided an excellent opportunity to deal with missing outcome data while applying multiple imputations for imputing missing data.

7.1.4 Outline of investigations assessing the impact on of missing data

The patterns of missing outcome data were described with a case study (The relationship between incident CVD and exit from workforce overtime among working-age older Australians). Multiple imputations under MAR and MNAR assumptions were applied to impute the missing values, the effect sizes were estimated by using imputed datasets, and the results were compared to those provided in Chapter 5. As the outcome (exit from the paid workforce) is not relevant for participants who died before completing the follow-up survey and had a 100% probability of non-participation in the follow-up survey, the study was conditioned on survival at 1897 days (i.e., 5.2 years), the median time between the baseline and follow-up surveys, or participation in the follow-up survey.

Table 7.1 Summary of study designs, primary outcomes and exposures, the covariates and missing data among potentially eligible participants

Study No.	Study designs	Analyses Components	Variables	Potentially eligible participants (N)	Missing data % (n)
1	**Cross-sectional**	*Outcomes*	Workforce participation	**163562**	**0.1 (131)**
		Exposures	CVD	163562	0 (0)
		Covariates	Age	163562	0 (0)
			Sex	163562	0 (0)
			Region of residence	163562	2.1 (3352)
			Education	163562	1.0 (1644)
2	**Longitudinal**	*Outcomes*	Exit from workforce[1]	**118232**	**33.1 (39074)**
		Exposures	Incident CVD	118232	0 (0)
		Covariates	Age	118232	0 (0)
			Sex	118232	0 (0)
			Region of residence	118232	2.0 (2398)
			Education	118232	0.9 (1057)
			Comorbidity	118232	0 (0)
3	**Cross-sectional**	*Outcomes*	Social isolation[2]	**266504**	**10.0 (26616)**
		Exposures	CVD	266504	0 (0)
		Covariates	Age	266504	0 (0)
			Sex	266504	0 (0)
			Region of residence	266504	1.9 (4947)
			Education	266504	1.7 (4459)
4	**Longitudinal**	*Outcomes*	Social isolation[5]	**163405**	**42.9 (70117)**
		Exposures	Incident CVD	163405	0 (0)
		Covariates	Age	163405	0 (0)
			Sex	163405	0 (0)
			Region of residence	163405	1.9 (3024)
			Education	163405	1.3 (2128)

[1]Among those who had been working at baseline and whose workforce participation status at baseline were unknown, [2]Composite variable based on other four social interaction components.

7.2 Methods

7.2.1 Data resources and study population

The investigation of the exit from paid workforce included only those participants from the 45 and Up Study [58] aged less than 65 years old at the time of resurvey. For the participants who did not take part in the resurvey, a pseudo-follow-up period of 1897 days (i.e., 5.2 years) from the corresponding baseline survey dates were applied. This period represents the observed median time interval between the two surveys. Then, the age of the participants in the follow-up survey was defined as the age at the date of the actual or pseudo-follow-up survey. The participants aged 65 years and over at actual or pseudo-follow-up survey date, and those who had died before the follow-up survey were excluded. After applying these exclusion conditions, 123,106 participants were potentially eligible for study inclusion. Then these participants were characterised according to loss to follow-up participation status in relation to CVD, age and hospitalisation status at baseline and follow-up surveys.

7.2.2 Outcomes

The outcome was the exit from the workforce, and it was obtained from the follow-up survey of the 45 and Up Study [58]. Further detail on the condition of definition was provided in Chapter 5.

7.2.3 Exposures

The primary exposure was incident CVD status diagnosed in between baseline and actual or pseudo-follow-up period, according to the CVD codes reported earlier [23]. However, baseline CVD status was considered for characterising the potentially eligible participants.

7.2.4 Confounding factors

The adjustment variables were at follow-up survey grouped into three (<55year, 55-<60year, 60-<65year), sex (men, women), region of residence, education, and comorbidity index.

Region of residence was categorised as major cities, inner regional and more remote, it was based on the mean Accessibility Remoteness Index of Australia Plus score [203]. The comorbidity of the participants was estimated by using the modified Charlson index (i.e. categorising comorbidities of patients based on non-CVD related ICD diagnosis codes in linked hospitalisations data) by using index admission in APDC records one year before the follow-up survey [173].

7.2.5 Prognostic variables

Twenty-three variables were initially considered as prognostic variables for the outcome (exit from the workforce at the follow-up). These were incident CVD, age, sex, region, education, workforce participation status at baseline, country of birth, language spoken at home, body mass index, alcohol drinking per week, smoking status, comorbid cancer, comorbid diabetes, comorbid arthritis, physical functional limitations, psychological distress, quality of life, quality of health, comorbidity index, total hospitalisations from baseline to the follow-up survey, total hospitalisations 1 year prior to the follow-up survey, CVD hospitalisation 1 year before the follow-up survey, and total CVD hospitalisation from baseline to follow-up survey. Further details of the definition of the variables are provided in Chapter 4.

7.2.6 Statistical analysis

Descriptive statistics were used to estimate the number and proportions for different conditions of survey participation and health characteristics. The potentially eligible participants were grouped into four groups (No CVD at baseline or at the follow-up survey, incident CVD at the follow-up survey only, CVD at baseline survey only, CVD both at baseline and follow-up survey), and for the baseline CVD status, both self-reported CVD status at baseline survey, and hospitalisation records 5-year before baseline survey were considered.

Missing data characterisation

Descriptive statistics were used to estimate the proportions and crude prevalence ratios (PRs) of missing outcome data (yes versus no) in the follow-up survey. The modified Poisson regression with robust error variance [181] was used to estimate adjusted PRs for missing outcome data (yes versus no) within different population subgroups, and the group with a favourable health condition was considered as the reference group. The models were adjusted for age group and sex only and estimated adjusted PRs.

Prognostic variables for multiple imputations

A higher Pearson Correlation Coefficients to identify the variables related to the outcome variable (exit from the workforce). Then the ranking of the variables based on the Pearson correlation coefficient was prepared.

Multiple imputations

MICE was used for the imputation of missing variables under the MAR assumption [182]. Ten variables were included in the multiple imputation models. The included variables were those that were used in the regression model adjustment in the main analyses and the other five variables with higher Pearson correlation coefficients (absolute values greater than 0.066) in relation to outcome variables (exit from the workforce). Finally, the included prognostic variables in the multiple imputations were age-group, sex, remoteness of residence, education, comorbidity index, workforce participation status at baseline, physical functional limitations, self-rated quality of life, self-rated health, and hospitalisations in one year before the survey. Since there were about 33% missing data in the follow-up study, I have adopted thirty-five-times imputations.

As sensitivity to the sensitivity analysis under the MAR assumption, multiple imputations under the MNAR assumption have been conducted by using the delta method [255, 256]. The

pattern-mixture model approach was used to multiple imputations under the MNAR assumption; a shift parameter delta =1 was applied to the logit function values for the exit from the workforce at follow up.

Effect size estimation with datasets having imputed values

The datasets with imputed values as, mentioned above, were then used to estimate the risk ratios of exit from the workforce in people with versus without incident CVD. The modified Poisson regression with robust error variance [181] was used to estimate risk ratios (RRs) for exit from the workforce (yes versus no) and people without CVD were the reference group. The RRs of the exiting workforce were adjusted for age group, sex, remoteness of residence, education, and comorbidity index. The effect sizes were combined by Rubin's rule [257]. The results were then compared to those mentioned in Chapter 5, where the RRs were estimated for complete cases by using similar regression models with the same adjustment variables and reference group.

7.3 Results

7.3.1 Study population and missing outcome data

There were 123096 participants who were alive and aged less than 65 years old at the follow-up survey, 66.7% (n=82146) filled out the follow-up survey. The follow-up participation rate varied slightly by CVD status at baseline and follow-up survey, with slightly higher participation observed in people with no CVD at baseline or in the follow-up survey, and a slightly lower participation rate was among people with CVD both at baseline and follow-up survey (**Figure 7.1**).

Characterisation of potentially eligible participants by CVD status stratified by age and hospitalisation indicates that the participants differ slightly by CVD status. In the case of age-based stratification, the highest proportion of participants belonged to the group aged 55-<65

years of baseline age and the group aged 60-<65 years of the follow-up age across all groups based on CVD status. Similarly, the lowest proportion of participants belonged to the group aged 45-<50 years of baseline age and aged <55 years of the follow-up age across all groups by CVD status. The proportions of participants by hospitalisation status both 1 year prior to baseline and follow-up survey had almost identical distributions in all groups by CVD status (**Figure 7.2**).

These findings indicate that people were almost similar in their age and hospitalisation records regardless of CVD status either before or after the baseline survey. This is also supported by overall attrition of follow-up participation because similar reasons such as death (*Appendix 6: Figure S7.1.1*) and by a similar pattern of participation after baseline survey or not being diagnosed with incident CVD and observed a similar pattern of participation rate regardless of existing CVD status at baseline survey (*Appendix 6: Table S7.2.1*). The proportion of missing values was near to negligence for the baseline outcome of interest and the participants varied little by population characteristics *(Appendix 6: Table S7.3.1).* Therefore, no further statistical treatments were pursued for baseline outcome variable and the subsequent analysis only focused on the implication of missing values for outcome variable in the follow-up survey.

7.3.2 Characteristics of participants by missing outcome data

There were 118232 participants who were potentially eligible for inclusion in the study (**Figure 7.3**). These participants had no CVD at baseline, aged <65 at follow-up and whose work status was not non-participation in work (i.e., either they had been working or had work status missing). There were 33% outcomes missing in the follow-up surveys (**Table 7.2**). These participants had a higher proportion of men, education status ‘no school certificate’, country of birth other than Australia/New Zealand, language spoken at home other than English, obese, current smoker, having severe functional limitations, high psychological distress and poor/fair quality of life and health. The hospitalisation patterns in between baseline and follow-

up surveys were mostly similar regardless of participation status. Stratification by incident CVD status shows that the loss to participation in the follow-up survey group had a slightly higher proportion of people with incident CVD (5.1% vs 4.7%) and had slightly higher proportions with unfavourable health conditions *(Appendix 6: Table S7.4.1).*

7.3.3 Factors associated with missing outcome data

Correlation coefficient matrix of outcome (exit from the workforce) and other twenty-three variables showed that work status at baseline, age of the participants and physical disability were the top three factors associated with exit from workforce missing data *(Appendix 6: Table S7.5.1).* Investigation of the missing outcome data in different population sub-groups indicated that proportions of missing outcome data varied by population subgroups. The age and sex adjusted PRs of missing outcome data in different population subgroups based on socio-demographic variables have shown that younger people (aged 55-60 years) had over than 50% higher likelihood of non-participation in the follow-up survey (PR = 1.51 (95% CI 1.48-1.54)) compared to people aged 60-<65 years. People with the education of 'no school certificate' had more than two times higher likelihood of non-participation (PR = 2.02 (95% CI 1.96-2.07)) in the follow-up survey **(Table 7.3).**

Health-related factors were also related to loss to take part in the follow-up survey, particularly people with poorer health conditions had a higher likelihood of loss to take part in the follow-up survey. This is significant for obese person [PR=1.21 (1.18-1.24)], current smokers (PR = 1.50 (95% CI 1.47-1.54)), people with severe physical disabilities (PR = 1.47 (95% CI 1.43-1.51)), high psychological distress (PR = 1.66 (95% CI 1.60-1.72)), poor/fair quality of life (PR = 1.61 (95% CI 1.58-1.65)) and health (PR = 1.55 (95% CI 1.51-1.59)) **(Table 7.3).**

The missing outcome data due to the loss to participate in the follow-up survey did not vary much by hospitalisation records. Four different variables were estimated to address sickness, hospitalisation numbers during the baseline to follow-up, or one-year prior to the follow-up

survey. There was not any trend in the likelihood of missing outcome data due to the loss to take part in the follow-up survey (**Table 7.3**).

7.3.4 Multiple imputations

The evidence in the above analysis suggests that the study participants with poor health status were more likely to be missing in the follow-up survey. However, it was not strongly supported by the hospitalisation records of the participants, from baseline survey to actual/pseudo-follow-up dates. Had there been a higher sickness among those not participating in the follow-up survey, there would have been higher hospitalisation records among those who had not participated in the follow-up survey compared to those who had taken part in the follow-up survey. In fact, there was a little difference in the hospitalisation records of those with versus without follow-up survey participation. Therefore, poorer health status was unlikely to be associated with selection in the follow-up survey. Though there was not any systematic data missingness, it cannot be said either that the data were missing under the MCAR assumption. However, MAR could be a plausible assumption [241] because there was very little variation in the hospitalisation records among those with versus without follow-up survey participation. Alternatively, if non-participation in the follow-up survey is suspected to depend on unobserved values, neither standard multiple imputations nor complete case analysis will be appropriate [258].

Since the variables that are predictors of missing variables could be used to impute the missing values [252], a wide range of variables were initially considered. Then it was found that most of the correlations were very weak. Eventually only those variables that were either strongly correlated with outcome variables or used in the regression model adjustment were used in the imputation models [242].

In this case study, there were 30% to 40% outcome variables were missing. Therefore, multiple imputations under MAR assumption were used to investigate missing data and the

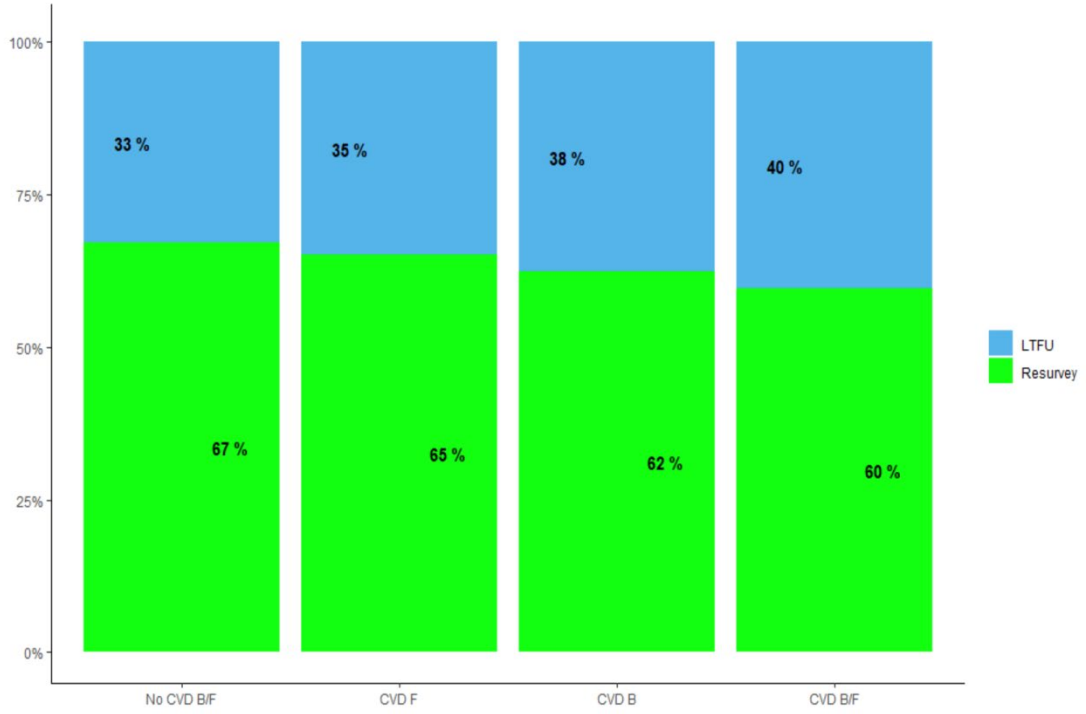
analysis was followed by a supplemented sensitivity analysis under MNAR assumption using the delta method [259]. The shift parameters were used for the six variables which were either outcome variables or those that were strongly related to outcome (*Appendix 6*: *Table S7.6.1*). The results were then compared with those from the complete case analyses.

7.3.5 Comparison of results from Chapter 5 and after multiple imputations

Overall, 26% of people with incident CVD exited the workforce, compared to 17% of people without CVD (**Figure 5.2**). After imputations, the proportions of participants with incident CVD exited workforce ranged from 20% to 26%, compared to 13% to 17% people without CVD (*Table S7.7.1*).

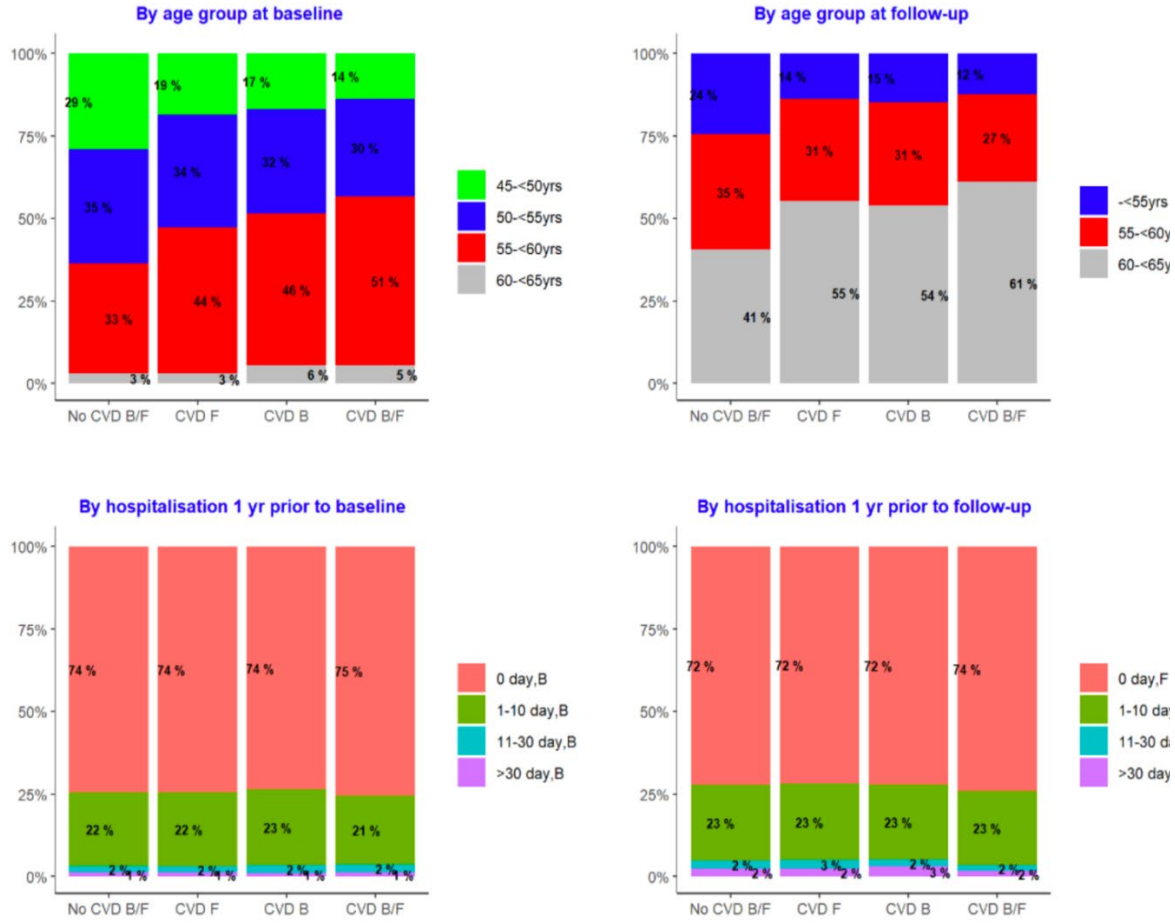
After adjusting for age, sex, region of residence, education and comorbidity, people with incident CVD had a RR of 1.28 (95% CI: 1.20-1.36) for exiting the workforce for complete case analyses. However, under both MAR and MNAR assumptions, the risk of exiting the workforce attenuated slightly with the RR of 1.19 (1.12-1.27) and 1.23 (1.15-1.32) respectively. Thus, the results show that regardless of the missing data assumption, missing data did not materially affect the strength of association between incident CVD to exit from the workforce (**Figure 7.4**).

Figure 7.1 The numbers and proportions of resurvey and loss to follow-up among participants* who were alive at the time of follow-up survey according to cardiovascular status at baseline and follow-up surveys*



*Total eligible participants, n= 123106, CVD= cardiovascular disease, LTFU= Loss to follow-up, F= Follow-up survey, B= Baseline survey, No CVD B/F = No CVD at baseline or follow-up survey (n=112520), CVD F= Incident CVD (n= 5712), CVD B= previous CVD at baseline (n= 3482), CVD B/F= CVD at both baseline and follow-up surveys (n=1392).

Figure 7.2 The proportions of participants at the time of follow-up survey in different groups by cardiovascular disease status at baseline and follow-up survey stratified by age and hospitalisation records*



*Total eligible participants, n= 123106, CVD= cardiovascular disease, F= Follow-up survey, B= Baseline survey, No CVD B/F = No CVD at baseline or follow-up survey (n=112520), CVD F= Incident CVD (n= 5712), CVD B= previous CVD at baseline (n= 3482), CVD B/F= CVD at both baseline and follow-up surveys (n=1392).

Figure 7.3 Flowchart for selection of participants in the missing outcome data at the follow-up survey

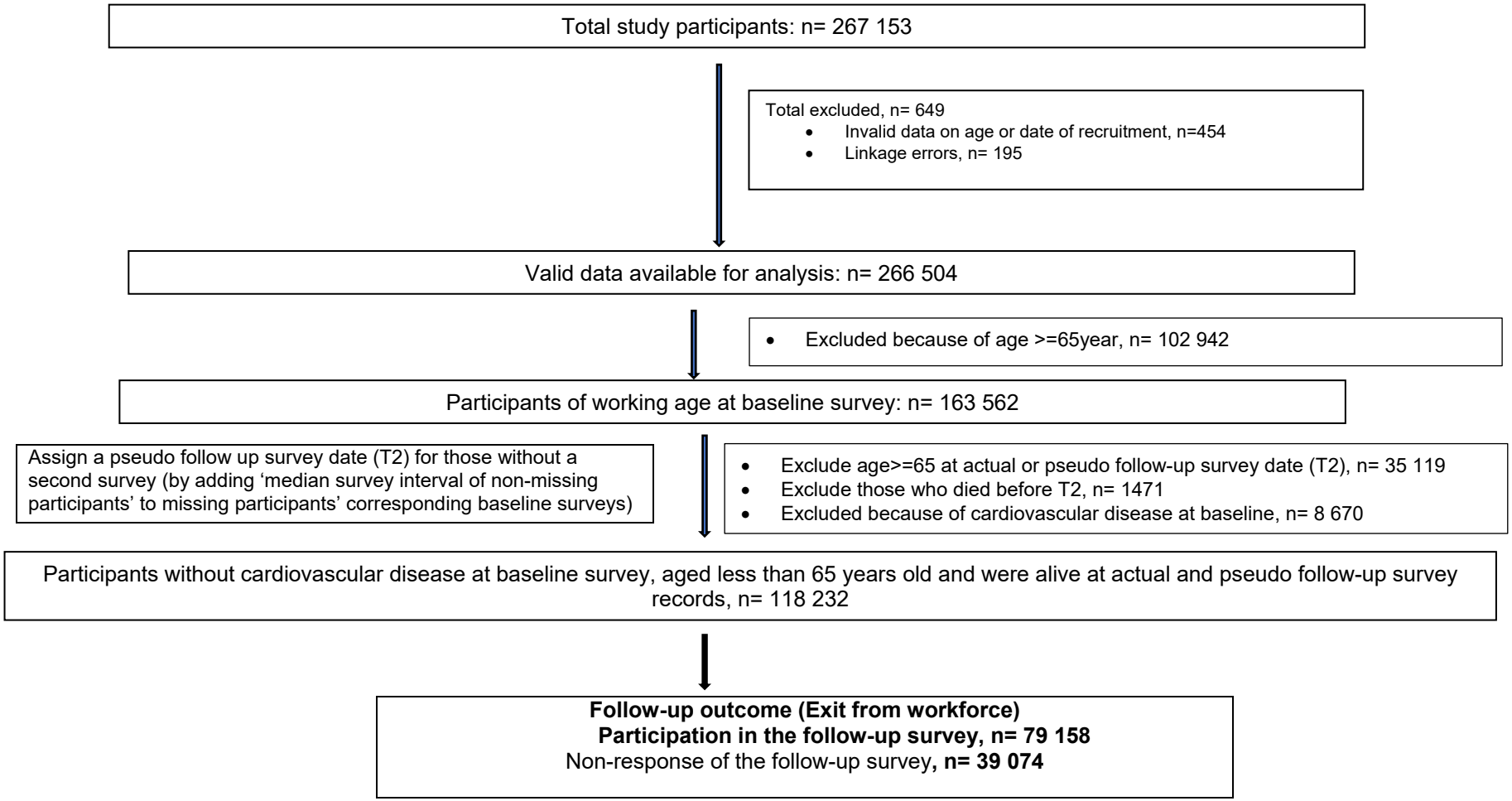


Table 7.2 *Missing data:* Proportions, and crude and adjusted prevalence ratios of outcome (exit from workforce) missing data at follow-up survey according to sociodemographic factors and health related characteristics

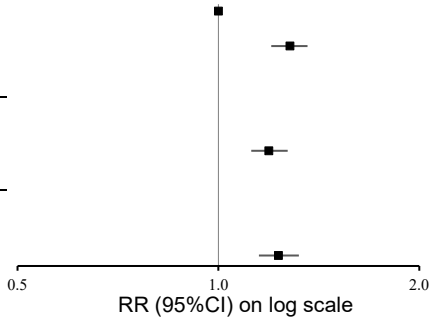
				Missing data	
	Overall missing data % (n/N)*	**Follow-up work status missing group****	**Follow-up work status non-missing group****	**Crude PR*****	**PR (95%CI) #**
Total participants n = 118232	**33.1 (3974/118232)**	**n= 39074**	**n= 79158**		
Age at follow-up (mean, sd)		57.8, 4.1	58.8, 4.0		
Age-group at follow-up					
< 55 year	42.0 (11894/28348)	30.4 (11894)	20.8 (16454)	1.50	1.51 (1.48-1.54)
55-<60 year	33.0 (13538/40977)	34.6 (13538)	34.7 (27439)	1.18	1.19 (1.16-1.21)
60-<65 year	27.9 (13642/48907)	34.9 (13642)	44.6 (35265)	1.00	1
Sex					
Men	34.8 (16798/48320)	43.0 (16798)	39.8 (31522)	1.09	1.10 (1.08-1.12)
Women	31.9 (22276/69912)	57.0 (22276)	60.2 (47636)	1.00	1
Region					
Missing	30.8 (738/2398)	1.9 (738)	2.1 (1660)	0.90	0.90 (0.85-0.96)
Major cities	34.3 (21295/62004)	54.5 (21295)	51.4 (40709)	1.00	0.92 (0.90-0.93)
Inner regional	31.3 (12689/40564)	32.5 (12689)	35.2 (27875)	0.91	0.96 (0.94-0.99)
More remote	32.8 (4352/13266)	11.1 (4352)	11.3 (8914)	0.96	1
Education					
Missing value	48.7 (515/1057)	1.3 (515)	0.7 (542)	1.94	1.96 (1.84-2.09)
No school certificate	48.9 (4199/8593)	10.7 (4199)	5.6 (4394)	1.94	2.02 (1.96-2.07)
Certificate/diploma/trade	34.9 (25343/72695)	64.9 (25343)	59.8 (47352)	1.39	1.40 (1.37-1.42)
Tertiary	25.1 (9017/35887)	23.1 (9017)	33.9 (26870)	1.00	1
Country of birth					
Missing	41.1 (255/621)	0.7 (255)	0.5 (366)	1.32	1.34 (1.22-1.48)
Australia/NZ	31.1 (29047/93519)	74.3 (29047)	81.4 (64472)	1.00	1.31 (1.29-1.33)
Other	40.6 (9772/24092)	25.0 (9772)	18.1 (14320)	1.31	1
Language spoken at home other than English					
Missing	N/A	0.0 (0)	0.0 (*)	0.00	N/A
0. No	31.0 (32908/106043)	84.2 (32908)	92.4 (73135)	1.00	1
1. Yes	50.6 (6166/12188)	15.8 (6166)	7.6 (6022)	1.63	1.60 (1.57-1.63)
Body Mass Index (BMI)$					
Missing	38.7 (3075/7951)	7.9 (3075)	6.2 (4876)	1.27	1.28 (1.24-1.32)
Underweight (15 to <18.5)	35.7 (412/1155)	1.1 (412)	0.9 (743)	1.18	1.17 (1.09-1.27)
Healthy weight (18.5 to <25)	30.4 (12560/41379)	32.1 (12560)	36.4 (28819)	1.00	1
Overweight (25 to <30)	32.3 (13512/41851)	34.6 (13512)	35.8 (28339)	1.06	1.06 (1.03-1.08)
Obese (30 to 50)	36.7 (9515/25896)	24.4 (9515)	20.7 (16381)	1.21	1.21 (1.18-1.24)
Alcohol drinking per week					
Missing	50.5 (808/1599)	2.1 (808)	1.0 (791)	1.66	1.66 (1.58-1.75)
None	37.4 (12842/34356)	32.9 (12842)	27.2 (21514)	1.23	1.24 (1.22-1.27)
1-14	30.5 (19772/64824)	50.6 (19772)	56.9 (45052)	1.00	1
15 or more	32.4 (5652/17453)	14.5 (5652)	14.9 (11801)	1.06	1.03 (1.00-1.05)
Smoking					
Missing	47.7 (190/398)	0.5 (190)	0.3 (208)	1.56	1.53 (1.38-1.70)
Current smoker	47.6 (5563/11693)	14.2 (5563)	7.7 (6130)	1.56	1.50 (1.47-1.54)
Past smoker	32.9 (12489/37925)	32.0 (12489)	32.1 (25436)	1.08	1.07 (1.05-1.09)
Never smoker	30.5 (20832/68216)	53.3 (20832)	59.9 (47384)	1.00	1
Cancer					
No	33.1 (35422/106916)	90.7 (35422)	90.3 (71494)	1.00	1
Yes	32.3 (3652/11316)	9.3 (3652)	9.7 (7664)	0.97	1.01 (0.99-1.04)
Diabetes					
No	32.7 (36686/112352)	93.9 (36686)	95.6 (75666)	1.00	1
Yes	40.6 (2388/5880)	6.1 (2388)	4.4 (3492)	1.24	1.28 (1.24-1.32)
Arthritis					
No	33.1 (38187/115489)	97.7 (38187)	97.7 (77302)	1.00	1

Yes	32.3 (887/2743)	2.3 (887)	2.3 (1856)	0.98	1.08 (1.02-1.14)
Physical functioning limitations					
Missing	42.0 (4345/10350)	11.1 (4345)	7.6 (6005)	1.34	1.39 (1.36-1.43)
No limitation (100)	31.4 (16309/51879)	41.7 (16309)	44.9 (35570)	1.00	1
Minor limitation (90 to <100)	29.5 (9085/30841)	23.3 (9085)	27.5 (21756)	0.94	0.96 (0.94-0.98)
Moderate limitation (60 to <90)	34.4 (6243/18123)	16.0 (6243)	15.0 (11880)	1.10	1.15 (1.12-1.18)
Severe limitation (0 to <60)	43.9 (3092/7039)	7.9 (3092)	5.0 (3947)	1.40	1.47 (1.43-1.51)
Psychological distress (K-10 score)					
Missing	45.4 (2399/5286)	6.1 (2399)	3.6 (2887)	1.49	1.56 (1.51-1.61)
Low (10- < 12)	30.4 (24945/82040)	63.8 (24945)	72.1 (57095)	1.00	1
Mild (12- < 16)	34.6 (7148/20650)	18.3 (7148)	17.1 (13502)	1.14	1.12 (1.09-1.14)
Moderate (16- < 22)	41.9 (3070/7329)	7.9 (3070)	5.4 (4259)	1.38	1.35 (1.31-1.38)
High (22–50)	51.7 (1512/2927)	3.9 (1512)	1.8 (1415)	1.70	1.66 (1.60-1.72)
Quality of life					
Missing	44.0 (1910/4342)	4.9 (1910)	3.1 (2432)	1.52	1.53 (1.48-1.59)
Excellent/Very Good	28.9 (22411/77664)	57.4 (22411)	69.8 (55253)	1.00	1
Good	38.6 (10502/27226)	26.9 (10502)	21.1 (16724)	1.28	1.32 (1.30-1.35)
Poor/Fair	47.2 (4251/9000)	10.9 (4251)	6.0 (4749)	1.57	1.61 (1.58-1.65)
Quality of health					
Missing	43.8 (1322/3021)	3.4 (1322)	2.1 (1699)	1.52	1.53 (1.47-1.59)
Excellent/Very Good	28.7 (19697/68578)	50.4 (19697)	61.8 (48881)	1.00	1
Good	36.6 (12863/35104)	32.9 (12863)	28.1 (22241)	1.34	1.26 (1.24-1.29)
Poor/Fair	45.0 (5192/11529)	13.3 (5192)	8.0 (6337)	1.64	1.55 (1.51-1.59)
CCI index 1 year prior to follow-up survey					
None	33.5 (31475/93965)	80.6 (31475)	78.9 (62490)	1.00	1
Minor	30.2 (6252/20689)	16.0 (6252)	18.2 (14437)	0.90	0.92 (0.90-0.94)
Moderate	37.5 (1059/2824)	2.7 (1059)	2.2 (1765)	1.12	1.16 (1.10-1.21)
Severe	38.2 (288/754)	0.7 (288)	0.6 (466)	1.14	1.19 (1.08-1.30)
Total hospitalisations 1 year prior to follow-up survey					
No hospitalisation	33.0 (28156/85386)	72.1 (28156)	72.3 (57230)	1.00	1
1-10-day hospitalisations	33.2 (9004/27136)	23.0 (9004)	22.9 (18132)	1.01	1.01 (0.99-1.03)
11-30-day hospitalisations	32.4 (903/2785)	2.3 (903)	2.4 (1882)	0.98	0.98 (0.93-1.04)
>30-day hospitalisations	34.6 (1011/2925)	2.6 (1011)	2.4 (1914)	1.05	1.05 (1.00-1.10)
CVD hospitalisation 1-year prior to follow-up survey					
No hospitalisation	33.1 (37257/112717)	95.3 (37257)	95.3 (75460)	1.00	1
1-10-day hospitalisations	33.1 (1165/3515)	3.0 (1165)	3.0 (2350)	1.00	1.00 (0.97-1.03)
11-30-day hospitalisations	31.7 (336/1060)	0.9 (336)	0.9 (724)	0.96	0.96 (0.92-1.00)
>30-day hospitalisations	33.6 (316/940)	0.8 (316)	0.8 (624)	1.02	0.98 (0.94-1.02)
Total CVD hospitalisation baseline to follow-up survey					
No hospitalisation	33.1 (32597/98394)	83.4 (32597)	83.1 (65797)	1.00	1
1-10-day hospitalisations	33.2 (3585/10801)	9.2 (3585)	9.1 (7216)	1.00	1.00 (0.96-1.05)
11-30-day hospitalisations	31.8 (1347/4242)	3.4 (1347)	3.7 (2895)	0.96	0.97 (0.88-1.05)
>30-day hospitalisations	32.2 (1545/4795)	4.0 (1545)	4.1 (3250)	0.97	1.02 (0.93-1.11)

*Row percentage, **Column percentage, ***PR=Prevalence ratio, #Adjusted for age-group at follow-up and sex, $Kilogram/meter square, NZ=New Zealand, CCI= Charlson comorbidity index, CVD= cardiovascular disease

Figure 7.4 *Exit from workforce:* Adjusted risk ratios of exiting workforce at follow-up survey estimated by main analysis, and that under missing at random (MAR) assumption and missing not at random (MNAR) assumption

	RR (95% CI) ** of exit from workforce
Main analysis [a]	
No CVD	1
Incident CVD (complete case analysis)	1.28 (1.20-1.36)
Missing at random (MAR) assumption [b]	
Incident CVD (35 imputations)	1.19 (1.12-1.27)
Missing not at random (MNAR) assumption [b]	
Incident CVD (35 imputations)	1.23 (1.15-1.32)



[a] Total number of participants were 63043, [b] The number eligible participants varied slightly in each iteration since the eligible participants depended on baseline workforce participation status whose missing values were imputed in resulting in slight variable number of eligible people. Further details in the supplementary *Table S7.7.1;* **CVD**= Cardiovascular disease, **Adjusted for age-group at follow-up, sex, comorbidity index, region and education

7.4 Discussion

The reason for missing outcome data because of non-participation in the follow-up survey is not known but based on the linked hospitalisation records it appears that participation and non-participation in the follow-up survey do not differ much in their hospitalisation records. However, from the baseline self-administered survey, it was found that the participants with missing outcome data had relatively higher unfavourable health conditions compared with non-missing outcome participants, and the proportions of missing outcome data differed in people with different sociodemographic and health-related characteristics. After analysing missingness patterns in the follow-up survey, it was found that MAR is a reasonable assumption for imputing the missing values by using 'multiple imputations'. Since there was substantial missing outcome data (>30%), it was decided to consider the MNAR assumption for missing data imputations in the sensitivity analysis. In both imputation processes, several important correlated variables were used in the imputation models. Then effect sizes were estimated, and the results were combined by Rubin's law [257]. The RR of exiting the workforce, estimated after thirty-five iterations of imputations of missing data, have indicated that compared to the complete case analysis, the point estimates did not change materially. The precision did not improve substantially either, since the confidence interval widths were broadly similar. Hence, the main analysis in the thesis could be considered valid and robust.

It cannot be measured to what extent multiple imputations reduced bias and improved precision since the missing outcome variable was imputed. Many sociodemographic variables are incorporated in the multiple imputations for missing data estimations, but not enough biological or pathological variables obtain from primary care about diagnosed health conditions and clinical measures of health (e.g., blood pressure, blood tests etc.). Thus, it is possible that there was some gain in reducing bias. However, there was not much improvement in the precision given those similar widths of confidence intervals after multiple imputations compared with the main analysis. In reference to prior literature [240, 260], a sensitivity analysis under the MNAR assumption was also conducted. The results also

supported the main analysis as well as those obtained under the MAR assumption. Hence, based on this systematic analysis and other relevant literature [212], it could be broadly stated that the relative estimates as reported in this thesis were robust and are likely to be generalisable.

The STROBE guidelines [261], aimed at improving the quality of reporting of observational studies, recommend the reporting of methods used to address missing data as a standard practice. However, reporting and handling of missing data continue to be a problem, especially in cohort studies with repeated measurements [262]. The quality of data collected and the availability of the predictor/auxiliary variables are key considerations in multiple imputations [242]. Large-scale data linkage involving routinely collected datasets increases access to comprehensive a range of information such as hospitalisations and mortality. However, health behaviours (e.g. smoking, physical activity) or measures of well-being (e.g. quality of life, physical functioning) are generally not captured in such data sources. Access to a standardised set of information about health behaviours, well-being and functions would allow a more detailed exploration of changes in health, functioning, and person-centred outcomes.

CHAPTER 8 Conclusion

8.0 Thesis context

The research presented in this thesis occurred within the context of a large and increasing burden of CVD globally and an increasing number of the population living with CVD [12]. The survivors of CVD and their carers want to know how the health of people with CVD is likely to differ from their counterparts without CVD [10, 18, 20]. A number of national organisations that monitor trends in disease rates over time, such as the Australian Institute of Health and Welfare and the National Heart Foundation of Australia, use person-centred outcomes as indicators to describe health and the performance of health care [263]. However, there is very limited evidence on person-centred outcomes of people living with CVD.

Given this context, this thesis aimed was to inform and improve CVD survivorship by generating reliable large-scale evidence on person-centred outcomes in people with versus without CVD. In this thesis, two important person-centred outcomes – workforce participation and social interaction were examined. They are understudied but of high significance for the financial and social wellbeing of an individual living with CVD, as well as the community more generally [264].

The preceding chapters of this thesis have presented research on the association of CVD with workforce participation and social interaction. The sequential steps for detailed investigation were describing the background on CVD and person-centred outcomes (specifically workforce participation and social interaction), synthesising available evidence and identifying gaps in knowledge, describing methods and resources to address the gaps in knowledge; generating newer evidence addressing the gaps and finally interpreting the findings. In this final chapter, the main findings and contributions to knowledge arising from the thesis were summarised, the findings in the context of the evidence to date were considered and the evidence was used to identify strategies to improve the overall health and wellbeing of people with CVD, as well

as their caregivers and community. This Chapter is concluded by briefly discussing the strengths and limitations of the findings in this thesis and suggestions for future research.

8.1 Summary of key findings

Twenty-seven articles were identified in a systematic review comparing workforce-participation-related outcomes in people with versus without CVD, and the evidence consistently shows that people with CVD have lower participation in the workforce compared with people without CVD. However, most studies have been small scale, and there is limited information on the likely magnitude of the effect of CVD on workforce participation in the contemporary Australian setting, how workforce participation varies according to CVD subtype, and by population characteristics, particularly by physical disability.

Based on data from the largest Australian cohort study, the 45 and Up Study, my research showed that although most people aged 45-64 years were in paid work, around 40% of people with CVD were not participating compared to 24% of people without CVD. After adjustment for population characteristics (age, sex, region of residence and education), the prevalence ratio (PR) of workforce non-participation was 1.36 (95%CI: 1.33-1.39) in people with versus without CVD. Workforce non-participation was greater for all CVD subtypes, with PRs of 1.92 (1.80-2.06) in those with cerebrovascular disease and 1.80 (1.68-1.98) in those with heart failure, compared to people without CVD. The strength but not the direction of association between CVD and non-participation in the workforce varied in different population subgroups, and people aged 50-54 years old had a greater likelihood of non-participation (PR 1.75, 1.65-1.85) compared to other age groups.

Severe physical disability was more prevalent among working-age people with versus without CVD (18.5% vs 6.1%), and when restricted to those without physical disability, workforce non-participation was also slightly higher in people with CVD versus without CVD (21% vs 16%).

After adjusting for sociodemographic characteristics, physical disability was much more strongly associated with non-participation in the workforce than CVD itself, and those with CVD and physical disability had the highest likelihood for non-participation in the workforce. For example, compared to people without CVD and no physical disability, people with severe functioning limitations were 3 times as likely to be out of the workforce if they had CVD (PR 2.91, 2.82–3.00) and 2.7 times as likely if they did not have CVD (PR 2.70, 2.63–2.77).

Longitudinal analyses also supported the findings in my cross-sectional analyses. Overall, 4.5% of working-age people experienced an incident CVD event over a median five-year follow-up period, and 26% of people with incident CVD exited the workforce compared to 17% of those who had not developed CVD. After adjustment for population characteristics (age, sex, region of residence and education) and comorbidity, the risk ratio (RR) of exiting the workforce was 1.28 (1.20-1.36) in people with incident CVD compared to people who had not developed CVD. Similar to the cross-sectional results, I observed a greater risk of exiting the workforce for all incident CVD subtypes examined and, in all population sub-groups investigated.

People with versus without incident CVD had more hospital-recorded comorbidity (3.3% vs 0.4%) and self-reported severe physical disability (13.7% vs 5.5%). The findings in the longitudinal investigations supported the cross-sectional results that physical disability was much more strongly associated with exit from the workforce than CVD itself, and those with incident CVD and physical disability had the highest risk for exit from the workforce.

The secondary outcomes also supported the findings on the relationship of CVD to workforce non-participation, and incident CVD to exit from the workforce, including across all CVD subtypes. For example, compared to people without CVD, people with CVD had a PR of 1.88 (1.82-1.94) for retirement due to ill health, and for people with newly diagnosed CVD, the RR for retirement due to ill health was 1.90 (1.70-2.13). However, for those in the workforce,

people with CVD worked on average just 0.9 (1.0, 0.8) hours less per week than people without CVD, and the average reduction in weekly paid work hour among people with incident CVD was just 0.6 (0.4, 0.8) hours greater compared to people who had not developed CVD.

The second systematic review identified six articles that compared social interaction related outcomes in people with versus without CVD, with evidence showing people with CVD have lower social interaction compared with people without CVD. The studies were mostly set in Europe and America but included one Australian study [57] which was a small-scale descriptive study. The review demonstrated that there is limited information on the magnitude of the relationship of CVD to social interaction in the contemporary Australian setting, and how the relationship varies according to CVD subtype, and by population characteristics, including physical disability.

In the cross-sectional study, the proportion of people aged 45 years and older reporting social isolation was 20% vs 19% in people with vs without CVD. After adjustment for population characteristics (age, sex, region of residence, and education), the likelihood of social isolation in people with CVD was 5% higher (PR 1.05 (1.03-1.07)) compared with people without CVD. The magnitude of the relationship varied by CVD subtype, but the direction of association was mostly similar across all CVD subtypes investigated, and people with cerebrovascular disease and heart failure had a relatively greater likelihood of social isolation than other CVD subtypes. For example, after adjustment for similar population characteristics as in the main analysis, the PRs of social isolation were 1.27 (1.19-1.36) for people with cerebrovascular disease and 1.32 (1.24-1.41) for people with heart failure, compared to people without CVD. The relationships of CVD to social isolation in most population subgroups were similar to main analyses in terms of magnitude and directions of associations.

Severe physical disability was more prevalent among people aged 45 years and older with versus without CVD (24.5% vs 8.0%), and when restricted to those without physical disability,

there were similar levels of social isolation in people with and without CVD (18% vs 19%). After adjusting for sociodemographic characteristics, physical disability was much more strongly associated with social isolation than CVD itself, and the presence of CVD in people with a severe disability made little difference. After adjustment for sociodemographic variables, compared to those without CVD and no functional limitations, participants with a severe physical disability had a 53% higher likelihood of social isolation for both people with and without CVD.

Longitudinal analyses with follow-up survey records showed mostly non-significant relationships though there was a small but significant relationship between CVD and social isolation in the cross-sectional analyses. Among people who had no CVD and who were not socially isolated at baseline, 9% of people were diagnosed with incident CVD over a median 5-year follow-up period, and similar proportions of people with versus without incident CVD (12% vs 12%) were socially isolated at the follow-up survey. After adjustment for population characteristics (age, sex, education, and region of residence), it was found that the risk of social isolation was 7% (RR 1.07 (1.00-1.13)) higher in people with incident CVD than those without CVD but the association was not statistically significant. The magnitude of risk for social isolation varied slightly by different incident CVD subtypes and population characteristics but was weak and not statistically significant in most instances. People with versus without incident CVD had more self-reported severe physical disability (24.8% vs 10.4%). Similar to the cross-sectional analyses, the findings from the longitudinal analyses also show that social isolation is much more strongly related to physical disability than to incident CVD, and those with a severe physical disability had the highest risk for social isolation regardless of incident CVD status.

While conducting the longitudinal analyses in Chapters 5 and 6, it was found that one-third of the participants among the potentially eligible participants had not completed the follow-up survey. To demonstrate the implications of such non-participation, a case study from the thesis

was examined, with findings indicating non-participation in the follow-up survey did not materially affect the relative effect size estimates. The findings indicate that younger participants and those with relatively adverse health at the baseline survey were more likely to not participate in the follow-up survey. For example, compared to people aged 60-<65 years old, the PRs of non-participation in the follow-up survey were 1.51(1.48-1.54), and 1.19 (1.16-1.21) for people aged <55years and 55-<60years, respectively. Compared to people with no physical disability, the PRs of non-participation in the follow-up survey among those with moderate and severe physical disability were 1.15 (1.12-1.18) and 1.47 (1.43-1.51), respectively. Using health condition variables derived from the linked hospitalisation records during the follow-up period also showed that loss to participation in the follow-up survey increased with increased comorbidity. For example, compared with participants with no comorbidity, the PRs of loss to the follow-up due to non-participation in the second surveys were 0.92 (0.90-0.94), 1.12 (1.10-1.21) and 1.19 (1.08-1.30) for participants with minor, moderate, and severe comorbidity in 1 year before the follow-up survey, respectively. After applying “multiple imputations” [245], a widely used statistical method, to impute the missing values, it was found that non-participation in the follow-up survey did not materially affect the relative estimates. Hence, the findings in the thesis might be considered robust and the relative estimates, such as RR in the thesis, could be generalised externally, under the assumption of no confounding or effect modification.

8.2 Contribution to knowledge

This thesis adds to the limited literature on the relationship of CVD to workforce participation and social interaction, particularly in Australia. It has generated new evidence on the relationship of CVD to both person-centred outcomes by considering major CVD subtypes and population characteristics, including the likely role of physical disability.

The primary contribution of the thesis is the creation of evidence on the relationship of CVD to both person-centred outcomes across five major CVD subtypes: ischaemic heart disease (and its subtype myocardial infarction), cerebrovascular disease; peripheral arterial disease, and heart failure. Though earlier studies [39, 40, 82, 89, 90, 92, 95, 104] had reported on such relationships across multiple CVD subtypes both cross-sectionally and longitudinally, there was no comprehensive approach to examine which of the CVD subtypes and sociodemographic groups had the stronger relationships. What this thesis contributes to is generating large-scale evidence to address the gaps in knowledge by examining both the magnitude and likely causal role of five major CVD subtypes to both person-centred outcomes by using a large-scale survey linked to administrative datasets. Studying the relationship of CVD to both person-centred outcomes in different population subgroups based on various socio-demographic and health factors is another important contribution of the thesis. Earlier studies have described both person-centred outcomes by limited population characteristics such as sex [56, 82, 85], but what this thesis contributes to is an analysis of the relationships across a wide range of sociodemographic and health-related characteristics. Availability of many population variables in the 45 and Up Study survey datasets and the data linkage to the hospitalisation records provided such an opportunity to generate a wide range of variables. The consistent findings across different population subgroups in both cross-sectional and longitudinal analyses for both person-centred outcomes supported the main findings although the magnitude of association varied substantially. Thus, this thesis contributes to identifying several population sub-groups where the effect of CVD on workforce participation and social interaction was greater than for other population subgroups.

A major contribution of this thesis is the investigation of the relationship of CVD to workforce participation and social interaction by joint categorisation of CVD and physical disability, and findings on the likely role of physical disability in explaining the relationship of CVD to both person-centred outcomes. It is known that physical disability is more prevalent among people with CVD [30] than those without CVD and physical disability plays an important role in exit

from the workforce and reduction of social interaction [28, 29]. The findings in the thesis confirmed that physical disability is more prevalent in people with CVD and provided novel evidence — that physical disability is much more strongly related to workforce participation and social interaction than CVD itself. This thesis demonstrated that if participants were restricted to those without physical disability workforce participation and social interaction related adverse outcomes were mostly similar in people with versus without CVD. The findings across all cross-sectional and longitudinal studies have indicated that people with CVD and physical disability were the most vulnerable group needing support more than others to continue work or participate in social activities.

Another important contribution of the thesis is quantifying the relationship of CVD to workforce participation and social interaction by providing supporting evidence through additional analyses on secondary outcomes related to both person-centred outcomes across different CVD subtypes. There is some prior evidence on the relationship of CVD and secondary workforce participation outcomes including retirement [82], early retirement [89], retirement due to ill health [96], overall work impairment [94], and receipt of a disability pension [97]. This thesis generated new evidence by investigating the relationship of retirement due to ill health and hours of paid work per week across major CVD subtypes with findings that supported the primary results on the relationship between CVD and workforce participation. Earlier studies on the relationship of CVD to social interaction reported different social activities such as going to the movies, using the telephone, etc. [40, 56, 265]. What this thesis adds to the existing literature is the examination of the relationship of CVD and its subtypes to various social activities that covered multiple aspects of social interaction and provided a broader view of social activities in addition to the primary relationship of CVD to social isolation. To the best of my knowledge, no other studies have provided such detailed analyses on the relation of CVD to workforce participation and social interaction among people living with CVD.

The final contribution of the thesis is utilising the benefits of linked datasets to examine the implications of loss to follow-up due to non-participation. Almost all cohort studies have missing data on participants in follow-up surveys but not all cohort studies have access to administrative datasets to study the implications of missing data in this way. Because of the availability of a wide range of population characteristics in the survey data and access to records in other linked data, it was possible to characterise the participants who had versus had not participated in the follow-up survey in detail. The results of the examination indicated that the non-participation in the follow-up survey did not materially affect the relative estimates in the thesis, thus indicating the robustness of the findings of the thesis.

8.3 Implications of the findings

The large-scale quantitative evidence presented in this thesis has implications for people with CVD and their caregivers and the organisations that inform and assist people with CVD, quantitative modelling of the consequences of CVD, and future research.

Qualitative data indicate that people living with CVD value the opportunity to continue with work and see such participation as contributing to social and economic wellbeing [18]. Studies have also reported that participation in paid work and having meaningful social interaction increase the quality of life [266, 267]. The finding in this thesis, based on participants in the 45 and Up Study, that despite an elevated risk of exiting the workforce most working-age people with CVD continue in paid work is likely to be informative for people living with CVD, their caregivers, and organisation like the Australian Heart Foundation that inform and assist people with CVD to lead a better quality life. Having large-scale contemporary evidence on positive outcomes for most people is likely to be encouraging for people going through the process of diagnosis, care, and rehabilitation. The central roles of age and physical disability–regardless of the cause–in influencing workforce participation should provide further information to tailor

advice and expectations. The likelihood of people with incident CVD having similar levels of social interaction as those without CVD should also help to avoid unrealistic negative expectations related to the social interaction of life post-diagnosis, at the same time as helping to identify and support those who are most at risk.

Although participation in the paid workforce remained high following a CVD event, findings from the systematic review suggested that people with CVD had higher levels of presenteeism or absenteeism than those without CVD, and empirical data generated in Chapter 5 showed an increased risk of leaving the workforce after a CVD event, especially for those with physical disabilities. Although the exact reasons underpinning absenteeism and the risk of leaving the workforce were out of scope for this thesis, these findings support the need for flexible return to work strategies for people with chronic conditions, such as CVD.

The quantitative findings from this thesis on workforce participation following a CVD event will also inform mathematical simulations, currently being developed, of the population health impacts and costs of CVD across the Australian population. Such mathematical models are commonly used to inform disease-specific policy and practice around the world. CVD microsimulation models have been developed for multiple countries including the USA and UK [268]. Most of the existing models focus on the direct health outcomes (hospitalisations and deaths) and costs (DALYs or indirect costs) of CVD [269-271], but integrating quantitative information on the risks of exit from the workforce, changes in social interaction and the role of physical functioning will allow the development of richer models which include outcomes which are important to patients.

Although there was no statistically significant difference in social isolation between those with and without CVD, it was found that people with incident CVD and physical disabilities had more than 60% higher risk of being socially isolated compared with those without CVD and no physical disabilities. This finding might be informative to the people with CVD and the

organisations or government programs that aim to improve the social wellbeing of the people living in the communities in general. Higher community activities, such as social events for sharing CVD survivorship experience, might help improve CVD survivorship among older people, given the general increase in social isolation in recent times [272] and particularly among those with physical disabilities. The findings in the thesis might be informative to the community support programs that address social isolation via national or regional programs. One such program is called the ‘Seniors Connected Program’ and it provides older Australians with an opportunity to call and have a free, anonymous, friendly chat with a volunteer over the phone [237]. The findings in the thesis indicate that people with physical disabilities have a higher risk of being socially isolated might be informative to identify the vulnerable Australians and to promote the offerings of the ‘Seniors Connected Program’ among them.

There are several avenues for future research that can be explored. For example, it is currently not clear what factors are contributing to people leaving the workforce or to absenteeism and presenteeism in the workplace following a CVD event. To guide return to work policies, future cohort studies which follow people after a CVD event and examine the role of factors such as type of work and level of workplace and family/social support would be beneficial. Future research on the relationship of CVD to social interaction might consider subjective social support and the younger people (aged less than 45 years old) who have slightly different patterns of social interaction compared with older people [225]. Further details are provided in the ‘8.5 Future research directions’ section of this chapter.

8.4 Strengths and limitations of the thesis

The strengths and limitations of the individual studies in the thesis have been examined in the relevant Chapters. Here, an overview of the important strengths and limitations of the research is presented.

A major strength of the analyses was that relatively large-scale datasets, including linked administrative datasets, were used. The availability of such datasets provided the opportunity to conduct the research project in a way that capitalised on the relative and complementary strengths of each dataset. For example, the 45 and Up Study datasets contained outcome variables and a wide range of population characteristics at baseline and follow-up survey periods. The linkage of the datasets to the hospitalisation records allowed to identify incident CVD cases without relying on self-reported data only. It also allowed the generation of several variables to objectively characterise certain health characteristics of study participants, which is typically not possible in studies not linked to administrative data. The linked hospitalisation datasets provided the opportunity to assess bias because of non-participation in the follow-up survey of the 45 and Up Study.

There are also some key limitations to the research conducted in the thesis. One important limitation is the unavailability of a precise date of the exit from the workforce. Though the date of incident CVD event was available, the exact date of exit from the workforce was not available limiting the ability to conclude the likely causal role of incident CVD in exit from the workforce as investigated in the thesis. Another limitation is that workforce participation status is defined as a binary variable (yes versus no). The 45 and Up Study did not include any further information on the type of work or any qualitative aspects of workforce participation. The thesis has assessed the workforce participation status as a binary variable, and it has not investigated the nature of work [211] or alternative measures of productivity at work, such as ‘presenteeism’[105].

A key limitation of the social interaction outcomes examined is that they tell us nothing about the quality of the social interaction. For example, a patient who has had a stroke may get more visits from family members so that they can support the patient, but the person with the stroke may have communication difficulties as a result of the stroke [273]. Therefore, even with more

numbers of visitors from the social circles, the patient may still feel socially isolated. This aspect of quality of social interaction is thus not necessarily reflected in the numbers provided by the survey participants. Another key limitation of social interaction measurement in the thesis is not accounting for the social interaction that happens via digital platforms. The findings in the thesis might be robust considering the primary mood of social interaction among older people at the time of data collection. However, the advent of digital platforms for social interaction and their widespread uses among the adult population may necessitate the use of measures that account for newer forms of social interaction [274].

The relationship between incident CVD and exit from the workforce might play out differently depending on one's type of job, ability to work and support available. The findings in the thesis are based on data from Australia, a high-income country; even though the relationship between CVD and physical disability is likely to be generalisable [275], these findings may not be directly applicable to low and middle-income countries. As part of the government's social welfare policy, Australia has a wide range of support and community services available, including income support payments for unemployed people [276] and 'Disability Employment Services' to help employers recruit and retain employees with disability [277]. However, such social security and financial support are not always available in low and middle-income countries, and even if these are available, there are substantial access barriers [278]. People being forced to remain in the workforce to maintain their income would weaken the observed association between incident CVD and exit from the workforce, where as any employer discrimination against people with health issues is likely to contribute to a stronger relationship between incident CVD and exit from the workforce. The findings on the association of CVD and social interaction might also not be generalisable to low and middle-income countries because social interaction varies across different countries and cultures [279].

The study population investigated in the thesis was randomly sampled from a whole-of-population database and included ~10% of the entire population in the target age group and the response rate was ~18%, consistent with cohort studies of this nature. Generally, participants in cohort studies are healthier than the general population [212]. This notion is supported by the 9% (74.6% vs 65.2%) higher workforce participation rate in the study population than that reported by the Australian Bureau of Statistics for Australians in the same age group during the same period (2007–08) [213, 280]. As to the representativeness of the study population with respect to social isolation, there was not any comparable Australian data found to validate the findings. Since the findings in the cross-sectional and longitudinal analyses supported each other, it might be stated that though the rate of workforce participation, exit from the workforce, social isolation, and social interaction components may not be directly representative, the PRs and RRs which were based on internal comparisons, are still likely to be generalisable [146].

8.5 Future research directions

Throughout different Chapters of the thesis, it has been indicated where there are opportunities for future research. On a broader scale, the results presented in this thesis reaffirm the need for well-designed observational studies and careful interpretation of findings, including with full respect to the limitations and potential for bias within each study. Given the ongoing reliance on observational studies in this area of research, there may never be studies sufficiently free of bias that allows us to establish, with a high degree of certainty, whether there is a direct independent association of CVD to workforce participation and social interaction.

The findings presented here also highlight that research investigations seeking to understand the association of CVD with workforce participation and social interaction should be done with

practical implications in mind. What is, and has always been, clear is that CVD can be a debilitating condition. The emphasis should be on generating evidence, which from a practical point of view, can be used to guide strategies to prevent tertiary CVD risk factors among people with CVD. The evidence generated in this thesis, together with previous findings, indicates that there may be practical advantages to viewing CVD as a marker for elevated exit from the workforce or poor social interaction, and people with physical disabilities as the vulnerable population. However, which strategies are likely to effectively support individuals with physical disabilities to lower their risk, and to what extent these interventions are scalable and cost-effective needs further investigation. Continuing preoccupation with establishing or questioning the existence of a direct causal association may serve only to detract from these productive lines of research.

Keeping in mind the above-mentioned principles, future research on the relationship of CVD to workforce participation might consider the role of types of jobs and younger age (less than 45 years old). The association of CVD with different types of paid work based on occupations (such as skilled-based work or labour-intensive work) or types of employment (such as full-time, part-time) [281] was not investigated in the thesis. Physical disability increases the risk of exit from the workforce, as found in the thesis, but the physical fitness requirement varies according to the type of job as well. Investigating the type of job and CVD might help identify population sub-groups needing more support to return to work. The study in this thesis was restricted to examining the relationship of CVD to workforce participation in mid-aged and older people. Given the higher relative risk of exit from the workforce among the younger age group after incident CVD, as found in the thesis, it is important to understand the long-term effect of CVD among working-age people who are less than 45 years old. Since workforce participation status does not directly indicate the quality of work performance, future studies might investigate the association of CVD and the outcomes indicating work performance, such as absenteeism, presenteeism, and reduced productivity. Since there is an increasing opportunity of nationally linked data Australia, such as Multi-Agency Data Integration Project

(MADIP) [282], in the future, it is suggested looking into other important person-centred outcomes - such as, financial implications of CVD by linking hospital and social security data. From the nationally linked data, it is possible to record CVD and other chronic diseases that required hospitalisations as well as detailed information on the social benefits such as unemployed payments received by the working-age people. Hence, one future study might investigate the relationship of CVD and other chronic diseases to unemployed payments received by the working-age people in Australia [276]. Such investigation will be directly generalisable for national estimates as well largely addressing the issue of missing data for longitudinal analyses.

Since growing evidence in young adults shows that trends in incident CVD have been increasing over the past few decades [283], future research on the relationship of CVD to social interaction might consider subjective social support and the younger people, aged less than 45 years old. Though social interaction components were used from one validated scale, it was not possible to distinguish between subjective social support one needed and social interaction one voluntarily avoids or participates in. Previous studies have indicated subjective social support measurements are strongly associated with subjective well-being [284], and therefore generating large-scale robust evidence on the relationship of CVD to social support might inform programs that aim for better social wellbeing. Previous studies have indicated that social interaction patterns are different in younger compared with older people [225] and the analyses conducted in the thesis involved only people aged 45 and older. Hence, understanding the relation of CVD to social interaction and the likely change of social interaction after a CVD event in younger people might generate evidence that might be useful for long-term care-plan for younger people who have survived a CVD event.

8.6 Conclusion

While 60% of working-age people with CVD in this study continued to undertake paid work, non-participation in the workforce was 36% higher in people with versus without CVD. Over a median 5-year follow-up period, 4.5% of working-age people developed CVD, and these individuals had a 28% higher risk of exiting the workforce compared to people who had not been diagnosed with CVD. While similar proportions (~20%) of people with and without CVD were socially isolated, after adjusting for population characteristics, people with existing CVD had a slightly higher (5%) likelihood for social isolation. However, by following people who were without CVD and not socially isolated at baseline, I found that there was not any meaningful difference in becoming socially isolated in people with incident CVD compared to those who had not developed CVD during the follow-up period.

The relationship of CVD to workforce participation varied across different CVD subtypes and different population sub-groups, and it was relatively higher for people who had had a stroke or heart failure, and those who were aged less than 55 years. The strength and the direction of association between CVD and social interaction varied also slightly across different CVD subtypes or different population sub-groups. Physical disability was a key factor for the relationships of CVD to workforce participation and social interaction. It was more prevalent among people with CVD compared with those without CVD, and after restricting to the participants without physical disability, there were mostly similar levels of adverse outcomes for workforce participation and social interaction in people with and without CVD. Physical disability was much more strongly associated with workforce non-participation, exit from the workforce, social isolation, and no social interaction than CVD itself in all instances. The greater the physical disability, the greater the risk of adverse outcomes for both person-centred outcomes.

The findings throughout the thesis, particularly those across different CVD subtypes and the role of physical disability, are likely to be informative for people with CVD, their care providers,

and for organisations and programs that aim for healthy and successful ageing for those living with CVD. They also underpin those programs that encourage greater social activity among older persons should integrate consideration of the role of chronic disease, including CVD.

APPENDICES

Appendix 1 Supplementary material Chapter 2

S2.1 Full search strategies for the systematic review on CVD and workforce participation

I have searched for studies in PubMed, SCOPUS and Web of Science databases until December 31, 2019, with no limitations on year or language of publication. Different terms such as CVD [269] or 'heart disease'[285] are used to indicate unspecified CVD. Cerebrovascular disease, stroke, coronary heart disease (CHD), myocardial infarction (MI), peripheral arterial disease (PAD), venous thromboembolism (VTE) are major subtypes of CVD [23, 62, 286, 287]. The phrase 'workforce participation' is broadly meant to include 'labour force participation', 'work performance at work', 'whether people are receiving pension due early retirement because of illness or other reasons' and 'miscellaneous'. The working age population is defined as those aged 15 to 64 years but it might vary because of jurisdictions [288]. Therefore, the search strings are as follows.

S2.1.1 PubMed Search string

("atherosclerosis"[All Fields] OR "atherosclerosis"[MeSH Terms] OR "cardiocerebrovascular disease"[All Fields] OR "cardiovascular disease"[All Fields] OR "cardiovascular event"[All Fields] OR "cerebral infarction"[All Fields] OR "cerebral infarction"[MeSH Terms] OR "cerebrovascular attack"[All Fields] OR "cerebrovascular disease"[All Fields] OR "cerebrovascular disorder"[All Fields] OR "coronary artery disease"[All Fields] OR "coronary artery disease"[MeSH Terms] OR "coronary disease"[All Fields] OR "coronary disease"[MeSH Terms] OR "coronary heart disease"[All Fields] OR "heart attack"[All Fields] OR "heart disease"[All Fields] OR "heart failure"[All Fields] OR "heart failure"[MeSH Terms] OR "ischaemic heart disease"[All Fields] OR "ischemic heart disease"[All Fields] OR "myocardial infarction"[All Fields] OR "myocardial infarction"[MeSH Terms] OR "myocardial ischemia"[All Fields] OR "myocardial ischemia"[MeSH Terms] OR "myocardial ischaemia"[All Fields] OR "peripheral arterial disease"[All Fields] OR "peripheral arterial disease"[MeSH Terms] OR "stroke"[All Fields] OR "stroke"[MeSH Terms])
AND
("absenteeism"[All Fields] OR "absenteeism"[MeSH Terms] OR "disability pension"[All Fields] OR "early retirement"[All Fields] OR "employment"[All Fields] OR "employment"[MeSH Terms] OR "unemployment"[All Fields] OR "unemployment"[MeSH Terms] OR "labor force participation"[All Fields] OR "labour force participation"[All Fields] OR "return to work "[All Fields] OR "return to work "[MeSH Terms] OR "sick leave"[All Fields] OR "sick leave"[MeSH Terms] OR (subsidized[All Fields] AND job[All Fields]) OR (subsidized[All Fields] AND ("salaries and fringe benefits"[MeSH Terms] OR ("salaries"[All Fields] AND "fringe"[All Fields] AND "benefits"[All Fields]) OR "salaries and fringe benefits"[All Fields] OR "salary"[All Fields])) OR "workforce participation"[All Fields] OR "working hour"[All Fields] OR "occupation"[All Fields] OR "vocation"[All Fields] OR "work resumption"[All Fields])
AND
("Cohort Studies"[All Fields] OR "Cohort Studies"[MeSH Terms] OR "Cross-Sectional Studies"[All Fields] OR "Cross-Sectional Studies"[MeSH Terms] OR "Follow-Up Studies"[All Fields] OR "Follow-Up Studies"[MeSH Terms] OR "Hazard Ratio"[All Fields] OR "Odds Ratio"[All Fields] OR "Odds Ratio"[MeSH Terms] OR "Case-Control Studies"[All Fields] OR "Case-Control Studies"[MeSH Terms] OR "Longitudinal Studies"[All Fields] OR "Longitudinal Studies"[MeSH Terms] OR "Prospective"[All Fields])
AND
"humans"[MeSH Terms]
AND
("1900/01/01"[PDAT] : "2019/12/31"[PDAT])

S2.1.2 Scopus search string

(TITLE-ABS-KEY ("atherosclerosis" OR "cardiocerebrovascular disease" OR "cardiovascular disease" OR "cardiovascular event" OR "cerebral infarction" OR "cerebrovascular attack" OR "cerebrovascular disease" OR "cerebrovascular disorder" OR "coronary artery disease" OR "coronary disease" OR "coronary heart disease" OR "heart attack" OR "heart disease" OR "heart failure" OR "ischaemic heart disease" OR "ischemic heart disease" OR "myocardial infarction" OR "myocardial ischemia" OR "myocardial ischaemia" OR "peripheral arterial disease" OR "stroke"))
AND
(TITLE-ABS-KEY ("absenteeism" OR "disability pension" OR "early retirement" OR "employment" OR "unemployment" OR "labor force participation" OR "labour force participation" OR "return to work " OR "sick leave" OR "subsidized job" OR "subsidized salary" OR "workforce participation" OR "working hour" OR "occupation" OR "vocation" OR "work resumption"))
AND
(TITLE-ABS-KEY ("Cohort Studies" OR "cross-sectional studies" OR "case-control studies" OR "prospective" OR "Follow-Up Studies" OR "Longitudinal Studies" OR "odds ratio" OR "Hazard ratio"))
AND
PUBYEAR < 2020
AND
(LIMIT-TO (DOCTYPE , "ar"))

S2.1.3 Web of Science search string

S/L	Search Terms
#1	TS = ("atherosclerosis" OR "cardiocerebrovascular disease" OR "cardiovascular disease" OR "cardiovascular event" OR "cerebral infarction" OR "cerebrovascular attack" OR "cerebrovascular disease" OR "cerebrovascular disorder" OR "coronary artery disease" OR "coronary disease" OR "coronary heart disease" OR "heart attack" OR "heart disease" OR "heart failure" OR "ischaemic heart disease" OR "ischemic heart disease" OR "myocardial infarction" OR "myocardial ischemia" OR "myocardial ischaemia" OR "peripheral arterial disease" OR "stroke") Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=1900-2019
#2	TS= ("absenteeism" OR "disability pension" OR "early retirement" OR "employment" OR "unemployment" OR "labor force participation" OR "labour force participation" OR "return to work " OR "sick leave" OR "subsidized job" OR "subsidized salary" OR "workforce participation" OR "working hour" OR "occupation" OR "vocation" OR "work resumption") Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=1900-2019
#3	TS= ("prospective" OR "odds ratio" OR "Hazard ratio" OR "Follow-Up Studies" OR "Longitudinal Studies" OR "cross-sectional studies" OR "case-control studies" OR "Cohort Studies") Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=1900-2019
#4	#3 AND #2 AND #1 Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=1900-2019

The final search result is the serial number #4.

S2.2 PRISMA assessment checklist for systematic review on CVD and workforce participation

Table S2.2.1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) assessment checklist for systematic review on CVD and workforce participation

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	16
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	17
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	18
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	19
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	20
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	19-20
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	19
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	19
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	19-20
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	20
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	20
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or	21

		outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	20
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	20
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	21
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	21
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	21
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	21
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	21-36
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	21
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	37
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	39
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	40
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

N/A= Not applicable. The PRISMA assessment checklist is from Moher et al., 2019 [79]. For more information, visit: **www.prisma-statement.org**.

S2.3 Newcastle-Ottawa Scale

S2.3.1 Newcastle - Ottawa quality assessment scale for cohort studies

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort
   a) truly representative of the average _____ (describe) in the community ✵
   b) somewhat representative of the average _____ in the community ✵
   c) selected group of users eg nurses, volunteers
   d) no description of the derivation of the cohort

2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ✵
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview ✵
   c) written self report
   d) no description

4) Demonstration that outcome of interest was not present at start of study
   a) yes ✵
   b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for _____ (select the most important factor) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome
   a) independent blind assessment ✵
   b) record linkage ✵
   c) self report
   d) no description

2) Was follow-up long enough for outcomes to occur
   a) yes (select an adequate follow up period for outcome of interest) ✵
   b) no

3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for ✵
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ✵
   c) follow up rate < ____% (select an adequate %) and no description of those lost
   d) no statement

Reference:

Wells GA, S.B., O'Connell D, Peterson J, Welch V, Losos M, Tugwell P,. *The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. [cited 2019 30 Janurary, 2019].

S2.3.2 Newcastle - Ottawa quality assessment scale for cross-sectional studies

Selection: (Maximum 5 stars)

1) Representativeness of the sample:
a) Truly representative of the average in the target population. ✸ (all subjects or random sampling)
b) Somewhat representative of the average in the target population. ✸ (non-random sampling)
c) Selected group of users.
d) No description of the sampling strategy.

2) Sample size:
a) Justified and satisfactory. ✸
b) Not justified.

3) Non-respondents:
a) Comparability between respondents and non-respondents characteristics is established, and the response rate is satisfactory. ✸
b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.
c) No description of the response rate or the characteristics of the responders and the non-responders.

4) Ascertainment of the exposure (risk factor):
a) Validated measurement tool. ✸✸
b) Non-validated measurement tool, but the tool is available or described. ✸
c) No description of the measurement tool.

Comparability: (Maximum 2 stars)

1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.
a) The study controls for the most important factor (select one). ✸
b) The study control for any additional factor. ✸

Outcome: (Maximum 3 stars)

1) Assessment of the outcome:
a) Independent blind assessment. ✸✸
b) Record linkage. ✸✸
c) Self report. ✸
d) No description.
2) Statistical test:
a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). ✸
b) The statistical test is not appropriate, not described or incomplete.

Reference:

Herzog R, Álvarez-Pasquin MJ, Díaz C, Del Barrio JL, Estrada JM, Gil Á. Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review. BMC Public Health. 2013 Feb 19;13:154. doi: 10.1186/1471-2458-13-154. PubMed PMID: 23421987

S2.4 Excluded studies after full text review for systematic review on CVD and workforce participation

Table S2.4.1 List of studies excluded from the systematic review on CVD and workforce participation with reasons for exclusion

Ref	Study	Reasons for exclusion
1	Abdin 2016	Separate estimates for people of working age not included
2	Abramson 1992	Exposure of interest was not available
3	Andersen 2016	Exposure of interest was not available
4	Arndt 2005	Exposure-outcome association of interest is not available
5	Banefelt 2016	Participants had pre-existing disease conditions, since the study population already has hyperlipidaemia
6	Butt 2018	Appropriate comparator was not available
7	Buzina 1970	Outcome of interest was not available
8	CadyJr 1986	Outcome of interest was not available
9	Callander 2016	Outcome of interest was not available
10	Cay 1973	Appropriate comparator was not available
11	Chen 2007	Outcome of interest was not available
12	Crossland 2005	Exposure of interest was not available
13	Du 2013	Appropriate comparator was not available
14	Duijts 2017	Exposure-outcome association of interest is not available
15	Ervasti 2015	Exposure-outcome association of interest is not available
16	Fleischmann 2018	Separate estimates for people of working age not included
17	Fu 2019	Separate estimates for people of working age not included
18	Geyer 2009	Appropriate comparator was not available
19	Gharasi-Manshadi 2018	Appropriate comparator was not available
20	Goossens 1966	Appropriate comparator was not available
21	Hällberg 2009	Appropriate comparator was not available
22	Hewitt 2009	Exposure of interest was not available
23	Huffman 2011	Exposure-outcome association of interest is not available, Not specifically working age people, No comparator;
24	Juvani 2014	Exposure-outcome association of interest is not available
25	Kamphuis 2002	Exposure-outcome association of interest is not available
26	Karan 2014	Exposure-outcome association of interest is not available
27	Kark 2009	Participants had pre-existing disease conditions (out of interest. Here those with high bp is compared with those normal
28	Lallukka 2018	Exposure-outcome association of interest is not available
29	Lederer 2001	Exposure-outcome association of interest is not available
30	Li 2019	Exposure of interest was not available
31	Lie 1975	Appropriate comparator was not available
32	Mäntyniemi 2012	Exposure-outcome association of interest is not available
33	Maruthappu 2015	Exposure-outcome association of interest is not available
34	Maslow 2011	Exposure of interest was not available
35	McCarthy 2012	Exposure-outcome association of interest is not available
36	Meraya 2016	Exposure-outcome association of interest is not available
37	Nwaru 2017	Exposure of interest was not available

38	O'Neil 2012	Separate estimates for people of working age not included
39	Phillips 2018	Exposure-outcome association of interest is not available
40	Pit 2010	Exposure of interest was not available
41	Polvinen 2014	Exposure-outcome association of interest is not available
42	Polvinen 2018	Exposure-outcome association of interest is not available
43	Scharn 2019	Exposure of interest was not available
44	Schofield 2013	Outcome of interest was not available
45	Tatli 2019	Outcome of interest was not available
46	Ubalde-Lopez 2017	Exposure-outcome association of interest is not available
47	Vedin 1975	Exposure-outcome association of interest is not available
48	Virtanen 2017	Exposure-outcome association of interest is not available
49	vonBondorff 2015	Appropriate comparator was not available
50	Vuong 2015	Exposure-outcome association of interest is not available
51	Wang 2018	Appropriate comparator was not available
52	Whitney 1968	Outcome of interest was not available

Table S2.4.2 References for excluded studies from the systematic review on CVD and workforce participation

1. Abdin, E., et al., *Days out of role due to mental and physical conditions: Results from the Singapore mental health study.* PLoS One, 2016. **11**(2).
2. Abramson, J.H., et al., *WORK HEALTH RELATIONSHIPS IN MIDDLE-AGED AND ELDERLY RESIDENTS OF A JERUSALEM COMMUNITY.* 1992. **34**(7): p. 747-755.
3. Andersen, I., et al., *Increasing illness among people out of labor market - A Danish register-based study.* Social Science and Medicine, 2016. **156**: p. 21-28.
4. Arndt, V., et al., *Construction work and risk of occupational disability: A ten year follow up of 14 474 male workers.* Occup Environ Med, 2005. **62**(8): p. 559-566.
5. Banefelt, J., et al., *Work productivity loss and indirect costs associated with new cardiovascular events in high-risk patients with hyperlipidemia: estimates from population-based register data in Sweden.* Eur J Health Econ, 2016. **17**(9): p. 1117-1124.
6. Butt, J.H., et al., *Return to the workforce following coronary artery bypass grafting: A Danish nationwide cohort study.* Int J Cardiol, 2018. **251**: p. 15-21.
7. Buzina, R., et al., *Coronary heart disease in seven countries. V. Five-year follow-up in Dalmatia and Slavonia.* Circulation, 1970. **41**(4 Suppl): p. I40-51.
8. Cady Jr, L.D., P.C. Thomas, and S. Arzemanian, *A case-control study of major coronary events.* J Cardiopulm Rehabil, 1986. **6**(8): p. 302-306.
9. Callander, E.J. and D.J. Schofield, *The risk of falling into poverty after developing heart disease: a survival analysis.* BMC Public Health, 2016. **16**: p. 10.
10. Cay, E.L., et al., *Return to work after a heart attack.* J Psychosom Res, 1973. **17**(3): p. 231-43.
11. Chen, J.D., et al., *Job categories and acute ischemic heart disease: a hospital-based, case-control study in Taiwan.* Am J Ind Med, 2007. **50**(6): p. 409-14.
12. Crossland, D.S., et al., *Employment and advice regarding careers for adults with congenital heart disease.* Cardiol Young, 2005. **15**(4): p. 391-5.
13. Du, C.L., et al., *Workplace justice and psychosocial work hazards in association with return to work in male workers with coronary heart diseases: a prospective study.* Int J Cardiol, 2013. **166**(3): p. 745-7.
14. Duijts, S.F.A., et al., *Cancer and heart attack survivors' expectations of employment status: results from the English Longitudinal Study of Ageing.* BMC Public Health, 2017. **17**(1): p. 640.
15. Ervasti, J., et al., *Return to work after depression-related absence by employees with and without other health conditions: a cohort study.* Psychosom Med, 2015. **77**(2): p. 126-35.
16. Fleischmann, M., et al., *Can favourable psychosocial working conditions in midlife moderate the risk of work exit for chronically ill workers? A 20-year follow-up of the Whitehall II study.* Occup Environ Med, 2018. **75**(3): p. 183-190.
17. Fu, R., et al., *How do cardiovascular diseases harm labor force participation? Evidence of nationally representative survey data from Japan, a super-aged society.* PLoS ONE, 2019. **14**(7).
18. Geyer, S., et al., *Chances of employment in women and men after surgery of congenital heart disease: comparisons between patients and the general population.* Congenit Heart Dis, 2009. **4**(1): p. 25-33.
19. Gharasi-Manshadi, M., M. Meskarpour-Amiri, and P. Mehdizadeh, *Lost productivity among military personnel with cardiovascular disease.* J R Army Med Corps, 2018. **164**(4): p. 235-239.
20. Goossens, A. and R. Messin, *Initial results of a prospective epidemiologic cardiovascular study in a population of Belgian employees (Brussels).* Malattie cardiovascolari, 1966. **7**(2): p. 173-205.
21. Hällberg, V., et al., *Retention of work capacity after coronary artery bypass grafting. A 10-year follow-up study.* Journal of Cardiothoracic Surgery, 2009. **4**.
22. Hewitt, S. and S. Graff-Iversen, *Risk factors for cardiovascular diseases and diabetes in disability pensioners aged 40--42 years: a cross-sectional study in Norway.* Scand J Public Health, 2009. **37**(3): p. 280-6.

23. Huffman, M.D., et al., *A cross-sectional study of the microeconomic impact of cardiovascular disease hospitalization in four low- and middle-income countries.* PLoS One, 2011. **6**(6).
24. Juvani, A., et al., *Effort-reward imbalance as a risk factor for disability pension: the Finnish Public Sector Study.* 2014. **40**(3): p. 266-277.
25. Kamphuis, M., et al., *Employment in adults with congenital heart disease.* Arch Pediatr Adolesc Med, 2002. **156**(11): p. 1143-8.
26. Karan, A., M. Engelgau, and A. Mahal, *The household-level economic burden of heart disease in India.* Trop Med Int Health, 2014. **19**(5): p. 581-91.
27. Kark, M. and F. Rasmussen, *High systolic blood pressure increases the risk of obtaining a disability pension because of cardiovascular disease: a cohort study of 903 174 Swedish men.* Eur J Cardiovasc Prev Rehabil, 2009. **16**(5): p. 597-602.
28. Lallukka, T., et al., *Trends in diagnosis-specific work disability before and after stroke: A longitudinal population-based study in Sweden.* J Am Heart Assoc, 2018. **7**(1).
29. Lederer, P., D. Weltle, and A. Weber, *Illness-related premature unfitness for work among civil servants in Bavaria - An evaluation in the social medical field.* Gesundheitswesen, 2001. **63**(8-9): p. 509-513.
30. Li, X., et al., *Effects of health status on work exit and absenteeism among the older working population in China: A secondary analysis of a cohort sample.* BMJ Open, 2019. **9**(9).
31. Lie, K.I., et al., *Prospective study of 1-year survival and resumption of work following myocardial infarct.* Ned Tijdschr Geneeskd, 1975. **119**(48): p. 1890-1893.
32. Mäntyniemi, A., et al., *Job strain and the risk of disability pension due to musculoskeletal disorders, depression or coronary heart disease: A prospective cohort study of 69 842 employees.* Occup Environ Med, 2012. **69**(8): p. 574-581.
33. Maruthappu, M., et al., *Unemployment, government healthcare spending, and cerebrovascular mortality, worldwide 1981-2009: an ecological study.* Int J Stroke, 2015. **10**(3): p. 364-71.
34. Maslow, G.R., et al., *Growing up with a chronic illness: Social success, educational/vocational distress.* Journal of Adolescent Health, 2011. **49**(2): p. 206-212.
35. Mc Carthy, V.J.C., I.J. Perry, and B.A. Greiner, *Age, job characteristics and coronary health.* Occupational Medicine, 2012. **62**(8): p. 613-619.
36. Meraya, A.M. and U. Sambamoorthi, *Chronic Condition Combinations and Productivity Loss Among Employed Nonelderly Adults (18 to 64 Years).* J Occup Environ Med, 2016. **58**(10): p. 974-978.
37. Nwaru, C.A., et al., *Chronic diseases as predictors of labour market attachment after participation in subsidised reemployment programme: A 6-year follow-up study*. J Epidemiol Community Health, 2017. **71**(11): p. 1101-1106.
38. O'Neil, A., et al., *Co-morbid depression is associated with poor work outcomes in persons with cardiovascular disease (CVD): a large, nationally representative survey in the Australian population.* BMC Public Health, 2012. **12**: p. 47.
39. Phillips, J. and K. Radford, *RETURN TO WORK AFTER STROKE - PROSPECTIVE SIX-YEAR FOLLOW-UP.* British Journal of Occupational Therapy, 2018. **81**: p. 68-69.
40. Pit, S.W., et al., *Health problems and retirement due to ill-health among Australian retirees aged 45-64 years.* Health Policy, 2010. **94**(2): p. 175-81.
41. Polvinen, A., et al., *The contribution of major diagnostic causes to socioeconomic differences in disability retirement.* Scandinavian Journal of Work, Environment and Health, 2014. **40**(4): p. 353-360.
42. Polvinen, A., et al., *Working while on a disability pension in Finland: Association of diagnosis and financial factors to employment.* Scand J Public Health, 2018. **46**(19_suppl): p. 74-81.
43. Scharn, M., et al., *Influence of chronic diseases on societal participation in paid work, volunteering and informal caregiving in Europe: A 12-year follow-up study.* Journal of Epidemiology and Community Health, 2019. **73**(2): p. 136-141.
44. Schofield, D., et al., *The personal and national costs of CVD: Impacts on income, taxes, government support payments and GDP due to lost labour force participation.* Int J Cardiol, 2013. **166**(1): p. 68-71.
45. Tatli, I.Y. and B.S. Akel, *A controlled study analyzing the temporal activity patterns of individuals with stroke compared to healthy adults.* British Journal of Occupational Therapy, 2019. **82**(5): p. 288-295.
46. Ubalde-Lopez, M., et al., *The effect of multimorbidity on sickness absence by specific diagnoses.* Occup Med (Lond), 2017. **67**(2): p. 93-100.

47. Vedin, A. and C. Wilhelmsson, *ANGINA PECTORIS, HYPERTENSION, DECOMPENSATION AND RETURN TO WORK DURING TWO YEARS' FOLLOW-UP.* Acta Med Scand, 1975. **197**(575 S): p. 25-30.
48. Virtanen, M., et al., *Work disability before and after a major cardiovascular event: a ten-year study using nationwide medical and insurance registers.* Scientific Reports, 2017. **7**: p. 8.
49. Vuong, T.D., F. Wei, and C.J. Beverly, *Absenteeism due to Functional Limitations Caused by Seven Common Chronic Diseases in US Workers.* J Occup Environ Med, 2015. **57**(7): p. 779-84.
50. von Bondorff, M.B., et al., *Early life origins of all-cause and cause-specific disability pension: findings from the Helsinki Birth Cohort Study.* PLoS One, 2015. **10**(4): p. e0122134.
51. Wang, M., et al., *Trajectories and characteristics of work disability before and after acute myocardial infarction.* Heart, 2018. **104**(4): p. 340-348.
52. Whitney, L.H., *Coronary heart disease among men in the Bell System.* J Occup Med, 1968. **10**(1): p. 4-20.

S2.5 Additional results

Table S2.5.1 Quality assessment of cohort studies of the systematic review on CVD and workforce participation

STUDY	Selection				Comparability		Outcome		Total score	Overall quality*
	Representativeness of the Exposed Cohort	Selection of the Non-Exposed Cohort	Ascertainment of Exposure	Demonstration That Outcome of Interest Was Not Present at Start of Study	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Was Follow-Up Long Enough for Outcomes to Occur	Adequacy of Follow Up of Cohorts		
Brækkan 2016 [84]	2	1	1	1	2	1	1	1	9	High
deBoer 2018 [85]	1	1	0	1	2	0	1	1	7	Medium
Ervasti 2016 [86]	1	1	0	1	2	1	1	0	7	Medium
Feigl et al 2019 [103]	1	1	0	1	2	0	1	1	7	Medium
Garland et al 2019 [104]	1	1	1	1	2	1	1	1	9	High
Hemingway 2007 [87]	1	1	0	0	2	1	1	1	7	Medium
Holland 2009 [52]	1	1	1	1	2	1	1	0	8	High
Jespersen 2013 [88]	1	1	1	1	2	1	1	0	8	High
Kang 2015 [89]	1	1	0	1	2	0	1	0	6	Medium
Kouwenhoven-Pasmooij 2016 [90]	1	1	1	1	2	0	1	0	7	Medium
Kruse 2009 [91]	1	1	1	1	2	1	1	0	8	High
Maaijwee 2014 [93]	1	1	1	0	2	1	1	0	7	Medium
Oude Hengel et al 2019 [101]	1	1	0	0	2	0	1	1	6	Medium
Smedegaard 2017 [68]	1	1	1	1	2	1	1	0	8	High

******The study* ***'Overall quality'*** is '***High'***, if the New Castle Ottawa score (NOS) is more than 80% of the highest possible score (10) and *study* ***'Overall quality'*** is '**medium'** if the NOS is 60-80% of the highest possible score

Table S2.5.2 Quality assessment of cross-sectional studies of the systematic review on CVD and workforce participation

STUDY	**Selection**				**Comparability**	**outcome**		**Total score**	**Overall quality***
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure (risk factor)	Comparability	Assessment of the outcome	Statistical test		
Alavinia 2008 [82]	1	1	0	1	2	1	1	7	Medium
Anesetti-Rothermel 2011 [39]	1	1	0	1	2	1	1	7	Medium
Bielecky 2015 [83]	1	1	0	1	2	1	1	7	Medium
Holden 2011 [41]	0	1	0	2	1	1	1	6	Medium
Johansen 1999 [53]	1	1	0	1	1	1	1	6	Medium
LiRanzi 2013 [92]	1	1	0	1	2	1	1	7	Medium
Marrett 2013 [94]	1	1	0	1	2	1	0	6	Medium
Nakaya 2016 [95]	1	1	0	1	2	1	1	7	Medium
Pit 2013 [96]	1	1	0	1	2	1	1	7	Medium
Schnitzler et al 2019 [102]	1	1	0	1	1	1	1	6	Medium
Stein 2006 [98]	1	1	0	1	2	1	1	7	Medium
vandenBerg 2017 [99]	0	1	0	1	2	1	1	6	Medium
Zhang 2016 [100]	1	1	0	1	2	1	1	7	Medium

***The study **'Overall quality'** is '**High'**, if the New Castle Ottawa score (NOS) is more than 80% of the highest possible score (10) and study **'Overall quality'** is '**medium'** if the NOS is 60-80% of the highest possible score

Table S2.5.3 Study outcomes, outcomes category and method of outcomes diagnosis of the systematic review on CVD and workforce participation

Study Reference	Outcomes reported	Outcomes category	Outcomes diagnosis methods
Alavinia 2008 [82]	Homemaker	Miscellaneous	Survey_self-report
Alavinia 2008 [82]	Retired	Non-participation in paid workforce related	Survey_self-report
Alavinia 2008 [82]	Unemployed	Non-participation in paid workforce related	Survey_self-report
Anesetti-Rothermel 2011 [39]	Disability days	Work performance related	Survey_self-report
Bielecky 2015 [83]	Presenteeism	Work performance related	Survey_self-report
Brækkan 2016 [84]	Work-related disability_dateOfDP	Pension related	Registry_Norwaygian National Insurance Administration Database
deBoer 2018 [85]	Exit from paid employment	Non-participation in paid workforce related	Survey_self-report
Ervasti 2016 [86]	Disabiliy pension_All-cause disability pension	Pension related	Registry_Sickness Allowance Register records of sickness absence
Feigl et al 2019 [103]	Employment	Non-participation in paid workforce related	Survey_self-report
Feigl et al 2019 [103]	Additional Days missed/year	Non-participation in paid workforce related	Survey_self-report
Feigl et al 2019 [103]	Additional hours missed/weak	Non-participation in paid workforce related	Survey_self-report
Feigl et al 2019 [103]	Intention to retire early	Non-participation in paid workforce related	Survey_self-report
Garland et al 2019 [104]	Working	Non-participation in paid workforce related	Hospital registry
Hemingway 2007 [87]	Sickness absence_Medically certified spells (> 3 days) of sickness absence	Work performance related	Registry_employers' registers
Holden 2011 [41]	Absenteeism	Work performance related	Survey_self-report
Holden 2011 [41]	Presenteeism	Work performance related	Survey_self-report

Holland 2009 [52]	Likelihood of leaving employment	Non-participation in paid workforce related	Registry_Longitudinal Population Register on Education, Income and Work (LOUISE)
Jespersen 2013 [88]	Disability pension	Pension related	Registry_Copenhegen heart study
Jespersen 2013 [88]	Premature exit from workforce	Non-participation in paid workforce related	Registry_Copenhegen heart study
Johansen 1999 [53]	Employed	Participation in paid workforce related	Survey_self-report
Johansen 1999 [53]	Not employed because illness/disability	Non-participation in paid workforce related	Survey_self-report
Johansen 1999 [53]	Not employed because retired	Non-participation in paid workforce related	Survey_self-report
Kang 2015 [89]	Early retirement	Non-participation in paid workforce related	Survey_self-report
Kouwenhoven-Pasmooij 2016 [90]	Disability pension	Pension related	Survey_self-report
Kouwenhoven-Pasmooij 2016 [90]	Early retirement	Non-participation in paid workforce related	Survey_self-report
Kouwenhoven-Pasmooij 2016 [90]	Homemaker/other	Miscellaneous	Survey_self-report
Kouwenhoven-Pasmooij 2016 [90]	Unemployment	Non-participation in paid workforce related	Survey_self-report
Kruse 2009 [91]	Age pensioner_percent ratio	Pension related	Registry_Copenhegen heart study (DANCOS)
Kruse 2009 [91]	Early retired_Percent ratio	Non-participation in paid workforce related	Registry_Copenhegen heart study (DANCOS)
Kruse 2009 [91]	Risk of labour market withdrawal	Non-participation in paid workforce related	Registry_Copenhegen heart study (DANCOS)
Kruse 2009 [91]	Unemployment_Percent ratio	Non-participation in paid workforce related	Registry_Copenhegen heart study (DANCOS)
LiRanzi 2013 [92]	Early retirement	Non-participation in paid workforce related	Survey_self-report
Maaijwee 2014 [93]	Unemployment_From disability pension data	Non-participation in paid workforce related	Registry_Follow-Up of TIA and stroke patients and Unelucidated Risk factor Evaluation (FUTURE)
Maaijwee 2014 [93]	Unemployment_Full or partial	Non-participation in paid workforce related	Registry_Follow-Up of TIA and stroke patients and Unelucidated Risk factor Evaluation (FUTURE)

Maaijwee 2014 [93]	Unemployment_Full or partial (2typesofstroke)	Non-participation in paid workforce related	Registry_Follow-Up of TIA and stroke patients and Unelucidated Risk factor Evaluation (FUTURE)
Marrett 2013 [94]	Absenteeism	Work performance related	Survey_self-report
Marrett 2013 [94]	Overall work impairment	Work performance related	Survey_self-report
Marrett 2013 [94]	Presenteeism	Work performance related	Survey_self-report
Nakaya 2016 [95]	Unemployment	Non-participation in paid workforce related	Survey_self-report
Oude Hengel et al 2019 [101]	Exit from paid employment by Disability benefits	Non-participation in paid workforce related	Survey_self-report
Oude Hengel et al 2019 [101]	Exit from paid employment by Unemployment benefits	Non-participation in paid workforce related	Survey_self-report
Oude Hengel et al 2019 [101]	Exit from paid employment by Early retirement benefits	Non-participation in paid workforce related	Survey_self-report
Oude Hengel et al 2019 [101]	Exit from paid employment by Economically inactive	Non-participation in paid workforce related	Survey_self-report
Pit 2013 [96]	Fully retired_due to ill health	Non-participation in paid workforce related	Survey_self-report
Pit 2013 [96]	Partly retired_due to ill health	Non-participation in paid workforce related	Survey_self-report
Schnitzler et al 2019 [102]	Working	Non-participation in paid workforce related	Survey_self-report
Smedegaard 2017 [68]	Disability pension	Pension related	Registry_DREAM database Denmark
Smedegaard 2017 [68]	Early retirement	Non-participation in paid workforce related	Registry_DREAM database Denmark
Smedegaard 2017 [68]	Pension	Pension related	Registry_DREAM database Denmark
Smedegaard 2017 [68]	Sick leave	Work performance related	Registry_DREAM database Denmark
Smedegaard 2017 [68]	Subsidized job	Pension related	Registry_DREAM database Denmark
Smedegaard 2017 [68]	Unemployment	Non-participation in paid workforce related	Registry_DREAM database Denmark
Smedegaard 2017 [68]	Working	Participation in paid workforce related	Registry_DREAM database Denmark
Stein 2006 [98]	Work absence	Work performance related	Survey_self-report
vandenBerg 2017 [99]	Sick leave (25-365 days)	Work performance related	Self_reported
Zhang 2016 [100]	Absent work days due to any health problems	Work performance related	Survey_self-report

Table S2.5.4 Exposures and diagnosis methods

Study Reference	Exposures reported	Exposure diagnosis methods
Alavinia 2008 [82]	Heart Attack	Survey self-report
Alavinia 2008 [82]	Stroke	Survey self-report
Anesetti-Rothermel 2011 [39]	Heart disease	Survey self-report
Anesetti-Rothermel 2011 [39]	Stroke	Survey self-report
Bielecky 2015 [83]	Heart disease	Survey self-report
Brækkan 2016 [84]	Venous thromboembolism	Hospital registry
deBoer 2018 [85]	Cardiovascular disease	Survey self-report
Ervasti 2016 [86]	Heart or cerebrovascular disease	Hospital registry
Feigl et al 2019 [103]	Heart disease	Survey self-report
Garland et al 2019 [104]	Acute myocardial infarction	Hospital registry
Garland et al 2019 [104]	Cardiac arrest	Hospital registry
Garland et al 2019 [104]	Stroke	Hospital registry
Hemingway 2007 [87]	Angina	Self-reported
Holden 2011 [41]	Cardiovascular disease	Survey self-report
Holland 2009 [52]	Ischaemic heart disease	Hospital registry
Jespersen 2013 [88]	Angiographically normal	Hospital registry
Jespersen 2013 [88]	Angiographically diffuse	Hospital registry
Johansen 1999 [53]	Heart disease	Survey self-report
Kang 2015 [89]	Cardiovascular disease	Survey self-report
Kang 2015 [89]	Cerebrovascular disease	Survey self-report
Kouwenhoven-Pasmooij 2016 [90]	Heart disease	Survey self-report
Kouwenhoven-Pasmooij 2016 [90]	Stroke	Survey self-report
Kruse 2009 [91]	Coronary heart disease	Hospital registry
LiRanzi 2013 [92]	Angina pectoris	Survey self-report
LiRanzi 2013 [92]	Myocardial infarction	Survey self-report
LiRanzi 2013 [92]	Stroke	Survey self-report
Maaijwee 2014 [93]	Stroke (TIA, ischemic stroke, or intracerebral haemorrhage)	Hospital registry
Maaijwee 2014 [93]	Stroke (ischemic stroke, or intracerebral haemorrhage)	Hospital registry
Marrett 2013 [94]	Peripheral arterial disease	Survey self-report
Nakaya 2016 [95]	Myocardial infarction	Survey self-report
Nakaya 2016 [95]	Stroke	Survey self-report
Oude Hengel et al 2019 [101]	Cardiovascular disease	Survey self-report
Pit 2013 [96]	Heart disease	Survey self-report

Pit 2013 [96]	Stroke	Survey self-report
Schnitzler et al 2019 [102]	Stroke	Survey self-report
Smedegaard 2017	Myocardial infarction	Hospital registry
Stein 2006 [98]	Heart disease	Survey self-report
vandenBerg 2017 [99]	Cardiovascular disease	Self-reported
Zhang 2016 [100]	Heart disease	Survey self-report

S2.6 PROSPERO Registration document

Citation

Muhammad Shahdaat Bin Sayeed, Angus McLure, Ellie Paige, Grace Joshy, Rosemary J Korda, Emily Banks. Workforce participation following cardiovascular disease: protocol for a systematic review and meta-analysis. PROSPERO 2019 CRD42019119356 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019119356

Review question [1 change]

How does participation in paid work in people of working age who have survived a major cardiovascular disease (CVD) event compare with those who have not had a CVD?

Searches [1 change]

We will search for quantitative studies in PubMed, Scopus and Web of Science databases. We will restrict our search to human studies only up to December 31, 2018. The search terms for CVD will be developed in accordance with the Medical Subject Headings (MeSH) thesaurus using a combination of keywords such as 'atherosclerosis' , 'cardiocerebrovascular disease' , 'cardiovascular disease' , 'cardiovascular event' , 'cerebral infarction' , 'cerebrovascular attack' , 'cerebrovascular disease' , 'cerebrovascular disorder' , 'coronary artery disease' , 'coronary disease' , 'coronary heart disease' , 'heart attack' , 'heart disease' , 'heart failure' , 'ischaemic heart disease' , 'ischemic heart disease' , 'myocardial infarction' , 'myocardial ischemia' , 'myocardial ischaemia' , 'peripheral arterial disease' and 'stroke'. The search term for workforce participation will be 'workforce participation', 'labour force participation', 'labor force participation', 'return to work' 'work resumption', 'employment', 'occupation', 'vocation', 'sick leave', 'disability pension', 'unemployment', 'early retirement', 'absenteeism', 'working hour', 'subsidized salary' and 'subsidized job'.

Types of study to be included

Retrospective and prospective cohort studies and cross-sectional studies will be included. Case reports, case series, and qualitative studies as well as conference abstracts that do not provide sufficient information will be excluded.

Condition or domain being studied [1 change]

The condition being studied is participation in paid workforce following CVD events. Here CVD event could be one type of CVD e.g. stroke, myocardial infarction or broad terms such heart disease etc. We will include studies reporting paid employment (both full-time and part-time) and/or self-employment. Other related terms such as labour force participation and relevant outcomes such as sick leave disability pension receipt following CVD events will also be included.

Participants/population

The study population will be working-age people. Studies that include subjects beyond working age in respective jurisdictions or do not exclusively mention those in working age will be excluded.

Intervention(s), exposure(s) [1 change]

The exposed group will be people who survive a CVD event.

Comparator(s)/control [1 change]

The comparison group will be people who have not had a recorded CVD event.

Context [1 change]

Studies conducted with participants from hospitals or community settings without geographical restriction and

time of the study will be included.

Main outcome(s) [1 change]

Paid workforce participation after a CVD event.

Additional outcome(s)

Sick leave, disability pension, paid hours etc.

Data extraction (selection and coding)

All citations identified through our search strategy will be imported into EndNote version X8 (Thompson Reuters, New York, NY, USA). Then they will be imported in required format to import into Covidence (https://www.covidence.org). The title and abstracts of the identified articles will be assessed independently by two reviewers, with final inclusion of studies to be decided through consensus. Differences will be resolved by discussion with a third author. If the title and abstract of a paper appear relevant, the full text of the paper will be reviewed independently by two reviewers, with differences resolved by discussion. Data will be extracted from eligible studies by two independent reviewers, and information will be collated in a Microsoft Excel 2016 spreadsheet.

We will extract data on study characteristics and outcomes from each paper. The following information will be extracted from each paper:

First author

Year of publication

Journal name

Type of study (cross-sectional, cohort)

Geographical location (country, area of residence, WHO region)

Study settings (hospital or community)

Study period

Age of the participants

Percent Male/Female

Study participation rate

Number of patients with MI

Number of people in comparison group

MI type

Outcomes

Follow-up time

Analysis method

Effect measures (e.g. HR, OR, etc)

Adjustment/Stratifications

Results (other)

Conflicts of interest

Comments or Notes

We will follow the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guideline (Moher et al. 2009).

Risk of bias (quality) assessment [1 change]

We will assess the methodological quality of the included studies, including the risk of bias in the selection of the study groups and outcome ascertainment using the Newcastle-Ottawa Scale or ROBIN-I methods depending on the study types.

Strategy for data synthesis

Data extracted from selected studies will be presented in tables. We will undertake the descriptive statistical analyses of the extracted data using R and use a Bayesian random-effects meta-analysis model to obtain pooled estimates of rates or proportions across studies for the outcomes of interest if meta-analysis is possible. This model assumes that there is heterogeneity of true effect sizes (e.g. post-MI), and our goal will be to estimate the measure of this value.

Analysis of subgroups or subsets

Depending on data availability, we intend to perform a subgroup analysis to assess whether participation in paid workforce varies by different characteristics, for example by sex or age group.

Contact details for further information

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Organisational affiliation of the review

Australian National University
http://rsph.anu.edu.au/

Review team members and their organisational affiliations [1 change]

Mr Muhammad Shahdaat Bin Sayeed. Australian National University
Mr Angus McLure. Australian National University
Dr Ellie Paige. Australian National University
Dr Grace Joshy. Australian National University
Assistant/Associate Professor Rosemary J Korda. Australian National University
Professor Emily Banks. Australian National University

Type and method of review

Systematic review

Anticipated or actual start date

01 December 2018

Anticipated completion date

15 March 2019

Funding sources/sponsors

Australian Government Research Training Program Stipend Scholarship

Conflicts of interest

Language

English

Country
Australia

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Humans; Myocardial Infarction

Date of registration in PROSPERO
07 January 2019

Date of first submission
11 December 2018

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
07 January 2019
30 January 2019

Appendix 2 Supplementary material Chapter 3

S3.1. Full search strategies

I searched for studies in PubMed, SCOPUS and Web of Science databases until December 31, 2019, with no limitations on year or language of publication. Different terms such as CVD [269] or 'heart disease'[285] are used to indicate unspecified CVD. cerebrovascular disease, stroke, coronary heart disease (CHD), myocardial infarction (MI), peripheral arterial disease (PAD), venous thromboembolism (VTE) are major subtypes of CVD [23, 62, 286, 287]. By social interaction the following terms are indicated: "social engagement", "social participation" "social network" "social integration" "social contact" "social visit" "social isolation" "social activity" "social satisfaction" "social consequence" "social support" "social support" [All Fields] and "communal engagement".

S3.1.1 PubMed Search string

((((((("Atherosclerosis"[All Fields] OR "Atherosclerosis"[MeSH Terms] OR "cardiocerebrovascular disease"[All Fields] OR "cardiocerebrovascular disease"[MeSH Terms] OR "cardiovascular disease"[All Fields] OR "cardiovascular disease"[MeSH Terms] OR "cardiovascular event"[All Fields] OR "cardiovascular event"[MeSH Terms] OR "cerebral infarction"[All Fields] OR "cerebral infarction"[MeSH Terms] OR "cerebrovascular attack"[All Fields] OR "cerebrovascular attack"[MeSH Terms] OR "cerebrovascular disease"[All Fields] OR "cerebrovascular disease"[MeSH Terms] OR "cerebrovascular disorder"[All Fields] OR "cerebrovascular disorder"[MeSH Terms] OR "Coronary Disease"[All Fields] OR "Coronary Disease"[MeSH Terms] OR "coronary artery disease"[All Fields] OR "coronary artery disease"[MeSH Terms] OR "coronary heart disease"[All Fields] OR "coronary heart disease"[MeSH Terms] OR "heart attack" [All Fields] OR "heart attack" [MeSH Terms] OR "heart disease" [All Fields] OR "heart disease" [MeSH Terms] OR "heart failure" [All Fields] OR "heart failure" [MeSH Terms] OR "ischemic heart disease"[All Fields] OR "ischemic heart disease"[MeSH Terms] OR "myocardial infarction"[All Fields] OR "myocardial infarction"[MeSH Terms] OR "Myocardial Ischemia"[All Fields] OR "Myocardial Ischemia"[MeSH Terms] OR "stroke"[All Fields] OR "stroke"[MeSH Terms] OR "peripheral arterial disease"[All Fields] OR "peripheral arterial disease"[MeSH Terms])))
AND
("social engagement" [All Fields] OR "social participation" [All Fields] OR "social network" [All Fields] OR "social integration" [All Fields] OR "social contact" [All Fields] OR "social visit" [All Fields] OR "social isolation" [All Fields] OR "social activity" [All Fields] OR "social satisfaction" [All Fields] OR "social consequence" [All Fields] OR "social support" [All Fields] OR "loneliness" [All Fields] OR "communal engagement" [All Fields] OR "social engagement" [MeSH Terms] OR "social participation" [MeSH Terms] OR "social network" [MeSH Terms] OR "social integration" [MeSH Terms] OR "social contact" [MeSH Terms] OR "social visit" [MeSH Terms] OR "social isolation" [MeSH Terms] OR "social activity" [MeSH Terms] OR "social satisfaction" [MeSH Terms] OR "social consequence" [MeSH Terms] OR "social support" [MeSH Terms] OR "loneliness" [MeSH Terms] OR "communal engagement" [MeSH Terms])
AND
(("Cohort Studies"[Mesh Terms] "Cohort Studies"[All Fields] OR
"case-control studies"[MeSH Terms] OR "case-control studies"[All Fields] OR
"cross-sectional studies"[MeSH Terms] OR "cross-sectional studies"[All Fields] OR
"Follow-Up Studies"[MeSH Terms] OR "Follow-Up Studies"[All Fields] OR
"Hazard ratio"[MeSH Terms] OR "Hazard ratio"[All Fields] OR
"odds ratio"[MeSH Terms] OR "odds ratio"[All Fields] OR
"prospective"[MeSH Terms] OR "prospective"[All Fields])))

AND
"humans"[MeSH Terms]
AND
("2000/01/01"[PDAT] : "2019/12/31"[PDAT])

S3.1.2 Scopus search string

(TITLE-ABS-KEY ("atherosclerosis" OR "cardiocerebrovascular disease" OR "cardiovascular disease" OR "cardiovascular event" OR "cerebral infarction" OR "cerebrovascular attack" OR "cerebrovascular disease" OR "cerebrovascular disorder" OR "coronary artery

disease" OR "coronary disease" OR "coronary heart disease" OR "heart attack" OR "heart disease" OR "heart failure" OR "ischaemic heart disease" OR "ischemic heart disease" OR "myocardial infarction" OR "myocardial ischemia" OR "myocardial ischaemia" OR "peripheral arterial disease" OR "stroke"))
AND
(TITLE-ABS-KEY ("social engagement" OR "social participation" OR "social network" OR "social integration" OR "social contact" OR "social visit" OR "social isolation" OR "social activity" OR "social satisfaction" OR "social consequence" OR "social support" OR "loneliness" OR "communal engagement")) AND (TITLE-ABS-KEY ("Cohort Studies" OR "cross-sectional studies" OR "case-control studies" OR "prospective" OR "Follow-Up Studies" OR "Longitudinal Studies" OR "odds ratio" OR "Hazard ratio"))
AND
PUBYEAR < 2020
AND
(LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUBYEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000))

S3.1.3 Web of Science search string

S/L	Search Terms
#1	TS = ("atherosclerosis" OR "cardiocerebrovascular disease" OR "cardiovascular disease" OR "cardiovascular event" OR "cerebral infarction" OR "cerebrovascular attack" OR "cerebrovascular disease" OR "cerebrovascular disorder" OR "coronary artery disease" OR "coronary disease" OR "coronary heart disease" OR "heart attack" OR "heart disease" OR "heart failure" OR "ischaemic heart disease" OR "ischemic heart disease" OR "myocardial infarction" OR "myocardial ischemia" OR "myocardial ischaemia" OR "peripheral arterial disease" OR "stroke") Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=2000-2019
#2	TS= (“social engagement” or “social participation” or “social network” or “social integration” or “social contact” or “social visit” or “social isolation” or “social activity” or “social satisfaction” or “social consequence” or “social support” or “loneliness” or “communal engagement”) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=2000-2019
#3	TS= ("prospective" OR "odds ratio" OR "Hazard ratio" OR "Follow-Up Studies" OR "Longitudinal Studies" OR "cross-sectional studies" OR "case-control studies" OR "Cohort Studies") Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=2000-2019
#4	#3 AND #2 AND #1 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=2000-2019

The final search result is the serial number #4.

S3.2 PRISMA assessment checklist for the systematic review on CVD and social interaction

Table S3.2.1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) assessment checklist for systematic review on CVD and social interaction

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	42
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	43
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	44
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	45
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	46
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	45-46
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	45
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	45
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	45-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	46
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	N/A
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	46
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	46

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	46
Section/topic	#	Checklist item	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	46
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	49
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	47-48
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	47
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	47-56
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	47
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	58
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	59-60
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	61
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

N/A= Not applicable. The PRISMA assessment checklist is from Moher et al., 2019 [79]. For more information, visit: **www.prisma-statement.org**.

S3.3 Excluded studies after full text review

Table S3.3.1 List of studies excluded from the systematic review on CVD and social interaction with reasons for exclusion

Study	Reasons for exclusion
1. Byles 2015	No suitable comparator and outcome of interest
2. Cai 2019	No suitable comparator available
3. Chau 2009	No suitable comparator available
4. Christensen 2008	Outcome of interest not available
5. Cooper 2014	Exposure of interest not available
6. Cooper 2015	Exposure of interest not available
7. Floud 2015	Expected exposure and outcome of interest not available
8. Lo 2014	Participants were not adults
9. Maunder 2015	No suitable comparator available
10. Zhang 2017	No suitable comparator available
11. Zhang 2018	No suitable comparator available
12. Griffith 2017	No suitable comparator available

Table S3.3.2 References for excluded studies from the systematic review on CVD and social interaction

1. Byles JE, Francis JL, Chojenta CL, Hubbard IJ. Long-term survival of older australian women with a history of stroke. Journal of Stroke and Cerebrovascular Diseases. 2015;24(1):53-60.
2. Cai Y, Towne SD, Bickel CS. Multi-level factors associated with social participation among stroke survivors: China's health and retirement longitudinal study (2011–2015). International Journal of Environmental Research and Public Health. 2019;16(24).
3. Chau JPC, Thompson DR, Twinn S, Chang AM, Woo J. Determinants of participation restriction among community dwelling stroke survivors: A path analysis. Bmc Neurology. 2009;9:49.
4. Christensen U, Kriegbaum M, Hougaard CO, Mortensen OS, Diderichsen F. Contextual factors and social consequences of incident disease. European Journal of Public Health. 2008;18(5):454-9.
5. Cooper CL, Phillips LH, Johnston M, Radlak B, Hamilton S, McLeod MJ. Links between emotion perception and social participation restriction following stroke. Brain injury. 2014;28(1):122-6.
6. Cooper CL, Phillips LH, Johnston M, Whyte M, MacLeod MJ. The role of emotion regulation on social participation following stroke. The British journal of clinical psychology. 2015;54(2):181-99.
7. Floud S, Balkwill A, Canoy D, Reeves GK, Green J, Beral V, et al. Social participation and coronary heart disease risk in a large prospective study of UK women. European Journal of Preventive Cardiology. 2015;23(9):995-1002.
8. Lo W, Gordon A, Hajek C, Gomes A, Greenham M, Perkins E, et al. Social competence following neonatal and childhood stroke. Int J Stroke. 2014;9(8):1037-44.
9. Maunder RG, Nolan RP, Park JS, James R, Newton G. Social support and the consequences of heart failure compared with other cardiac diseases: The contribution of support received within an attachment relationship. Archives of cardiovascular diseases. 2015;108(8-9):437-45.
10. Zhang L, Sui M, Yan T, You L, Li K, Gao Y. A study in persons later after stroke of the relationships between social participation, environmental factors and depression. Clinical rehabilitation. 2017;31(3):394-402.
11. Zhang L, Yan T, You L, Gao Y, Li K, Zhang C. Functional activities and social participation after stroke in rural China: a qualitative study of barriers and facilitators. Clinical rehabilitation. 2018;32(2):273-83.
12. Griffith LE, Raina P, Levasseur M, Sohel N, Payette H, Tuokko H, et al. Functional disability and social participation restriction associated with chronic conditions in middle-aged and older adults. J Epidemiol Community Health. 2017;71(4):381-9.

S3.4 Additional results

Table S3.4.1 Quality assessment of the included studies in systematic review on CVD and social interaction

STUDY	Selection				Comparability	Outcome		Total score*	% of Maximum score	Overall quality
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure (risk factor)	Comparability	Assessment of the outcome	Statistical test			
Adamson 2004 [40]	1	1	-	1	2	1	1	7	70	High
Almerud 2008 [127]	1	1	-	2	1	1	1	7	70	High
Jorge 2017 [56]	1	-	-	2	1	1	1	6	60	Medium
McKenna 2009 [57]	1	-	-	1		1	1	4	40	Medium
Mollon 2017 [34]	1	1	-	1	2	1	1	7	70	High
Schnitzler 2019 [102]	1	1	-	1	1	1	1	6	60	Low

*The possible maximum score was 10

Table S3.4.2 Adjustment variables and presence of sub-group analysis in the systematic review on CVD and social interaction

Study Reference	Adjustment variables	Sub-group
Adamson 2004 [40]	Age, social class, body mass index, smoking and alcohol intake	
Adamson 2004 [40]	Age, social class, body mass index, smoking and alcohol intake	
Almerud 2008 [127]	Age, sex, marital status and educational level	
Almerud 2008 [127]	Age, sex, marital status and educational level	
Almerud 2008 [127]	Age, sex, marital status and educational level	
Jorge 2017 [56]	N/A	Total subject
Jorge 2017 [56]	N/A	Men only
Jorge 2017 [56]	N/A	Women only
Jorge 2017 [56]	N/A	Age (45 to 59 years)
Jorge 2017 [56]	N/A	Age (60 to 99 years)
McKenna 2009 [57]		
Mollon 2017 [34]	marital status, education, employment, annual famil income, insurance status, usual source of care, region and metropolitan living status	
Schnitzler 2019 [102]	age and sex	

N/A= Not available.

S3.5 PROSPERO Registration document

Citation

Muhammad Shahdaat Bin Sayeed, Md Moustafa Kamal. Social interactions following cardiovascular disease: protocol for a systematic review and meta-analysis. PROSPERO 2020 CRD42020165442 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020165442

Review question [1 change]

How do social interactions in people who have survived a major cardiovascular disease (CVD) event compare with those who do not have CVD?

Searches

We will search for quantitative studies in PubMed, Scopus and Web of Science databases. We will restrict our search to human studies only up to December 31, 2019. The search terms for CVD will be developed in accordance with the Medical Subject Headings (MeSH) thesaurus (where applicable) using a combination of keywords such as 'atherosclerosis' , 'cardiocerebrovascular disease' , 'cardiovascular disease' , 'cardiovascular event' , 'cerebral infarction' , 'cerebrovascular attack' , 'cerebrovascular disease' , 'cerebrovascular disorder' , 'coronary artery disease' , 'coronary disease' , 'coronary heart disease' , 'heart attack' , 'heart disease' , 'heart failure' , 'ischaemic heart disease' , 'ischemic heart disease' , 'myocardial infarction' , 'myocardial ischemia' , 'myocardial ischaemia' , 'peripheral arterial disease' and 'stroke'. The search term for workforce participation will be 'social engagement', 'social participation', 'social network', 'social integration', 'social contact', 'social visit', 'social isolation', 'social activity', 'social satisfaction', 'social consequence', 'social support', 'loneliness' and 'communal engagement'.

Types of study to be included

Retrospective and prospective cohort studies and cross-sectional studies will be included. Case reports, case series, and qualitative studies, as well as conference abstracts that do not provide sufficient information, will be excluded.

Condition or domain being studied [1 change]

The condition being studied is social interactions following CVD events. Here CVD event could be one type of CVD e.g. stroke, myocardial infarction or broad terms such heart disease etc. We will include studies reporting social interactions following CVD events.

Participants/population

The study population will be people regardless of age.

Intervention(s), exposure(s)

The exposed group will be people who survive a CVD event.

Comparator(s)/control

The comparison group will be people who have not had a recorded CVD event.

Context

Studies conducted with participants from hospitals or community settings without geographical restriction and time of the study will be included.

Main outcome(s) [1 change]

The primary outcome will be social interactions after a CVD event.

Measures of effect

The outcomes after CVD events

Additional outcome(s) [1 change]

Relevant outcomes related to social interactions.

Measures of effect

From 2000 to 2020

Data extraction (selection and coding)

All citations identified through our search strategy will be imported into EndNote version X8 (Thompson Reuters, New York, NY, USA) and then into Covidence (https://www.covidence.org). The title and abstracts of the identified articles will be assessed independently by two reviewers, with final inclusion of studies to be decided through consensus. Differences will be resolved by discussion with a third author. If the title and abstract of a paper appear relevant, the full text of the paper will be reviewed independently by two reviewers, with differences resolved by discussion. Data will be extracted from eligible studies by two independent reviewers, and information will be collated in a Microsoft Excel 2016 spreadsheet.

We will extract data on study characteristics and outcomes from each paper. The following information will be extracted from each paper:

First author

Year of publication

Journal name

Type of study (cross-sectional, cohort)

Geographical location (country, area of residence, WHO region)

Study settings (hospital or community)

Study period

Age of the participants

Percent Male/Female

Study participation rate

Number of patients with CVD

Number of people in comparison group

CVD type

Outcomes

Follow-up time

Analysis method

Effect measures (e.g. HR, OR, etc)

Adjustment/Stratifications

Results (other)

Conflicts of interest

Comments or Notes

We will follow the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guideline.

Risk of bias (quality) assessment

We will assess the methodological quality of the included studies, including the risk of bias in the selection of the study groups and outcome ascertainment using the Newcastle-Ottawa Scale.

Strategy for data synthesis

Data extracted from selected studies will be presented in tables. We will undertake the descriptive statistical analyses of the extracted data using R and use a Bayesian random-effects meta-analysis model to obtain pooled estimates of rates or proportions across studies for the outcomes of interest if meta-analysis is possible. This model assumes that there is heterogeneity of true effect sizes (e.g. post-CVD), and our goal will be to estimate the measure of this value.

Analysis of subgroups or subsets [1 change]

Depending on data availability, we intend to perform a subgroup analysis to assess whether social interaction varies by different characteristics, for example by sex or age group.

Contact details for further information

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Review team members and their organisational affiliations [1 change]

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Epidemiologic, Prevention, Systematic review

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Language

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Stage of review [1 change]

Review Completed not published

Subject index terms status
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Cardiovascular Diseases; Humans; Research Design; Social Interaction

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Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Revision note
Some terminologies were updated, a co-author was included

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
28 April 2020
16 November 2021

Appendix 3 Supplementary material Chapter 4

S4.1 The questionnaire items for the baseline and follow-up surveys

The variables used in the thesis were primarily derived from the 45 and Up Study baseline or follow-up questionnaires. Though most of these variables were obtained from one question but some depended on multiple questions in the questionnaires or in combination with other datasets (*Table S4.1*). These resulted in missing-ness of the variables and classification of a participant in apparently conflicting categories. This issue was addressed in multiple ways including sensitivity analysis and multiple imputations.

Table S4.1 The questionnaire items and question number in the baseline and follow-up survey questionnaires used to define the outcomes, exposures and other relevant factors

	BASELINE ITEM	FOLLOW-UP ITEM	
Questionnaire/derived items	**2006-09**	**SEEF**	**Wave 2**
Outcome 1			
Work status	Q47	Q62	Q41
Hours of paid work/week	Q49	Q63	Q43
Retirement and reason for	Q48	Q64	Q42
Outcome 2			
Social interactions/week	Q55	Q71	Q48
Number of people can depend on	Q56	Q72	Q49
Exposure definition component			
Ever told had heart disease	Q24	Q37	Q22
Ever told had blood clot	Q24	Q37	Q22
Ever told had stroke	Q24	Q37	Q22
Other relevant variables of interest			
Age	Derived[1]	Derived[1]	Derived[1]
Sex	Form[2]	Q3	Form[2]
Region of Residence	From geocodes[3]	From geocodes[3]	From geocodes[3]
Education	Q5		
Country of birth	Q9		
Language spoken at home	Q10		
Marital status	Q14	Q19	Q9
Height	Q3	N/A	Q3
Weight	Q4	Q12	Q4
Body mass index (BMI, kg/m^2)	Derived from Q3	Derived from Q3	Derived from
Alcohol consumption	Q12	Q8	Q7
Smoking status	Q11	Q4, Q5, Q6, Q7	Q5
Cancer	Q24	Q37	Q22
Diabetes	Q24	Q37	Q22
Osteoarthritis	Q25	Q38	Q23
Physical functional limitation	Q28	Q44	Q37
Psychological distress	Q57	Q48	Q51
Overall health	Q31	Q30	Q38
Quality of health	Q31	Q30	Q38

[1]Age is derived from Medicare data, [2]Gender is determined from the questionnaire version completed (men or women), [3]Broad level geography is based on geocoded location of residence data, N/A= Not available, Q= Question number in the corresponding survey, SEEF= Social, Economic and Environment Factors.

S4.2 Defining workforce participation related outcomes from questionnaire responses

Table S4.2 Workforce participation, retirement, and retirement due to ill health

The main outcome of interest was non-participation in paid work (yes/no). We also reported on paid work hours/week among those in paid work, retirement of all working age participants (yes/no), and retirement due to ill-health (yes/no) among the retirees who were not in the workforce. The outcomes as mentioned in this investigation are based on the 3 questions in the 45 and Up Study [58] as follows:

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

Question 48: If you are partially or completely retired, why did you retire?

- ◊ Reached usual retirement age
- ◊ To care for family members/friend
- ◊ Made redundant
- ◊ Other
- ◊ Lifestyle reasons
- ◊ Ill health
- ◊ Made redundant
- ◊ Could not find a job

Question 49: About how many HOURS each week do you usually spend doing the following:

hours per week

		paid work

- **Paid hours of work per week**

This is a count variable consisting of zero or non-zero positive values obtained from question number 49 in the 45 and Up Study. Those having more than value more than 100 or negative values as recorded in the survey were considered as invalid and hence considered missing in the survey.

- **Workforce participation**

This is a binary outcome obtained from question number 47 and 49 in the 45 and Up Study generating two options: yes versus no. Those indicating valid paid hours (≥ 0 and <100) or work status (current work status as at least one of “In full time paid work”, “In part time paid work”, “Self-employed”, “Partially retired”) were classified as participating in the workforce, and others (“Doing unpaid work”, “Completely retired/pensioner”, “Studying”, “Looking after home/family”, “Disabled/sick”, “Unemployed”, “Other”) were classified as not participating in the workforce. The steps of defining workforce participation were as follows:

1. Participants were considered to be in paid work if:

1.1. Number of hours of paid work hours is valid (0 to <100) OR

1.2. Reported being in full time paid work, in part time paid work, self-employed or partially retired.

2. Participants were considered to be not in paid work if:

2.1. Number of hours of paid work hours per week is zero (0) or missing (but not invalid) AND
2.2. Not reported being in fulltime paid work, part time paid work, self-employed or partially retired
3. People who are not paid for work automatically received zero (0) for paid work hour per week
4. For those who are in "paid" category and entered 0 as paid work hour per week, their paid work status was accepted, and weekly paid work hours were invalidated
5. For those who are in "not paid" category and entered valid paid work hours per week, their paid work status was changed, and weekly paid work hours were accepted when the weekly paid work hours were larger than 0.

- **Retirement due to ill health**

This is a binary outcome with two options (yes/no) and it was defined from question that asked 'If you are partially or completely retired, why did you retire?' and following logical checks with workforce participation status. The binary definition of retirement and workforce participation status resulted in some participants who had been categorised as both 'retirees' and 'participating in paid workforce'. Hence, to indicate those who had retired and not participating in the paid workforce, the participants who had been defined as participating in the workforce among the retirees were excluded. Then among the retirees who had not been working, reasons for retirement were classified as binary outcome: 'retirement due to ill health' and 'retirement due to other reasons' ("Reached usual retirement age", "Lifestyle reasons", "To care for family member/friend", "Made redundant", "Could not find a job", "Other").

Reference

1. Banks, E., et al., *Cohort profile: the 45 and Up Study.* Int J Epidemiol, 2008. **37**(5): p. 941-7.

S4.3 Defining social interaction related outcomes from questionnaire responses

Table S4.3.1 Duke social support index (DSSI) social interaction subscale questions and coding

Question	Short name of the variable	Original response*	Recoding*
How many TIMES in the LAST WEEK did you: spend time with friends or family who do not live with you?	Social visits per week	Mean of 4.4 Min 0 Median 3 Max 100	1=None 2=Once or twice 3=Three or more times
How many TIMES in the LAST WEEK did you: talk to someone (friends, relatives or others) on the telephone?	Telephone contacts per week	Mean of 6.7 Min 0 Median 1 Max 500	1=None or once 2=Two to five times 3=Six or more times
How many TIMES in the LAST WEEK did you: go to meetings of social clubs, religious groups or other groups you belong to?	Social group meetings per week	Mean of 1.5 Min 0 Median 1 Max 50	1=None or once 2=Two to five times 3=Six or more times
How many people outside your home, but within one hour of travel, do you feel you can depend on or feel very close to?	Number of people to depend on	Mean of 7.1 Min 0 Median 5 Max 1000	1=None 2=1-2 people 3=More than 2 people
All four questions above	Social isolation	Mean of 8.8 Min 4 Median 9 Max 12	Summation of the above four values and those having score less than 8 were defined as socially isolated

*For the original responses provided in fractional values were converted into nearest integer values prior to recoding and Dukes social support index score calculation

Table S4.3.2 Social interaction subscale questions and coding

Study [references]	Definition of Social interaction
Korda et al., 2017 [155]	Measured by using Duke social support index (DSSI) score which was calculated as continuous value according to earlier publication [289].
Howe et al. 2010 [156]	Measured by using Duke social support index (DSSI) score which was calculated as continuous value as suggested earlier [289]
Pachana et al. 2008 [157]	Measured by using Duke social support index (DSSI) score which was calculated as continuous value.
Feng et al. 2017 [158]	As count variables as they are reported in the survey instead of modification as done elsewhere, such as [157].
Feng et al. 2016 [159]	As count variables as they are reported in the survey instead of modification as done elsewhere, such as [157].
Phongasavan et al., 2013 [160]	Individual components were reported. The components were reported as either 4 or 2 categories.
Macniven et al. 2016 [290]	Binary category but any in any consistent patterns. These categories are follows: • 0–3 vs 4 + Times last week with friends, family (do not live with) • 0 vs 1 Times last week at social clubs, other groups meetings • 0–3 vs 4 + People outside home, within 1 h travel can depend on.
Feng et al. 2013 [291]	They divided into four quartile and reported as low, low to moderate, moderate to high and high.
Vajdic et al., 2019 [292]	Grouped into four categories: None, 1-2, 3-8, >9

S4.4 ICD-10 AM codes for CVD hospitalization records

Table S4.4 Codes for CVD selection from hospitalization records

A. CVD includes those with either ICD-10-AM codes or coronary procedures codes as follows

1. *ICD-10-AM codes*

I11-I13
120-I25
I26-I28
I34-36,
I42
I44
I46-I51
I61-I67
I69
I70-I77
I80

G45
G46

2. *Coronary procedure codes*

*Percutaneous coronary interventions;
35304-00, 35305-00, 35304-01, 35305-01,35310-00, 35310-01, 35310-02,35310-03, 35310-04, 35310-05, 38300-00, 38303-00, 38306-00, 38306-01, 38306-02, 38306-03, 38306-05
*Coronary artery bypass grafting;
38497-00 to 38497-07
38500-00 to 38500-04
38503-00, 38503-01
90201-01 to 90201-03,
*Heart transplant:
90205-00, 90205-01
*Cardiac defibrillator implants:
38524-00, 38521-01, 38521-02, 38521-03, 38393-00
*Valve replacement, repair or reconstruction:
38456-10, 38483-00, 38270-01, 38480-00, 38481-00, 38488-00, 38488-01, 38489-00, 38489-01,38456-15, 38653-04, 38475-02, 38477-02,38487-00, 38485-01, 38270-02, 38480-01, 38481-01, 38475-00, 38477-00,38488-02, 38488-03, 38489-02,38485-00, 38456-16, 38653-05, 38456-11, 38480-02, 38481-02, 38475-01, 38477-01,38488-04, 38488-05,38489-03, 38456-17, 38653-06, 38456-01, 38270-03, 38488-06, 38488-07, 38489-04, 38489-05, 38456-18, 38653-07
*pacemaker insertion:
38281-00, 38281-01, 38281-02, 38281-03, 38281-04, 38281-05, 38281-06, 38281-07,38281-08, 38281-09, 38281-10, 38281-11, 38281-12, 38281-13, 38353-00
*Carotid endarterectomy:
33500-00

B. CVD Subtypes codes

1. Ischaemic heart disease based on ICD-10-AM codes:
   I20-I25
2. Cerebrovascular disease based on ICD-10-AM codes:
   I61-I67, I69
3. Myocardial infarction based on ICD-10-AM codes:
   I22-I23
4. Heart Failure based on ICD-10-AM codes:
   I50
5. Peripheral Arterial Disease based on ICD-10-AM codes:
   I70-I74, I77

C. Other CVD

Includes those who had self-reported CVD from the 45 and Up Study survey or had any ICD-10-AM codes or coronary procedures codes as mentioned in **A** as above except those as mentioned in **B** as above.

S4.5 Defining physical functional and categorization from questionnaire responses

Table S4.5 The physical functional limitations calculation and categorisation

Physical functioning was measured using the Medical Outcomes Score-Physical Functioning (MOS-PF)[174], which is equivalent to items from the physical functioning scale (PF-10) of the SF-36 health survey[175]. The PF-10 has been validated as a measure of physical functioning across a wide range of patient groups varying by age, sex, and comorbidities [176]. It consists of 10 questionnaire items and asks the study participants to choose one of the three choices 'Yes, limited a lot', 'Yes, a little' or 'No, not limited at all' in response to the question:

"Does your health now limit you in any of the following activities?" with a list of 10 activities as follows:

1. VIGOROUS activities (e.g running, strenuous sports)
2. MODERATE activities (e.g pushing a vacuum cleaner, playing golf)
3. Lifting or carrying shopping
4. Climbing several flights of stairs
5. Climbing one flights of stairs
6. Walking one kilometre
7. Walking half a kilometre
8. Walking 100 metres
9. Bending, kneeling or stooping
10. Bathing or dressing yourself

For each item, participants answer "yes, limited a lot," "yes, limited a little," or "no, not limited at all," had score of 0, 50, or 100 respectively. An overall physical functioning score was calculated from the average of scores from all 10 items. Therefore, the PFL scores ranged from 0 to 100, where higher scores represented fewer limitations, and were grouped into four categories: no limitation (score of 100); minor limitation (score 90–<100); moderate limitation (60–<90); and severe limitation (score 0–<60). Such cut-off values were chosen in refence to previously published research [4-6]

Reference

1. Stewart AL, Ware JE. Measuring functioning and well-being: the medical outcomes study approach: duke university Press; 1992.
2. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992 Jun;30(6):473-83. PMID: 1593914
3. Haley SM, McHorney CA, Ware JE Jr. Evaluation of the MOS SF-36 physical functioning scale (PF-10): I. Unidimensionality and reproducibility of the Rasch item scale. J Clin Epidemiol. 1994 Jun;47(6):671-84. doi: 10.1016/0895-4356(94)90215-1. PMID: 7722580

4. Gubhaju L, Banks E, MacNiven R, McNamara BJ, Joshy G, Bauman A, Eades SJ. Physical Functional Limitations among Aboriginal and Non-Aboriginal Older Adults: Associations with Socio-Demographic Factors and Health. PLoS One. 2015 Sep 30;10(9):e0139364. doi: 10.1371/journal.pone.0139364. PMID: 26422239

5. Zhang Y, Joshy G, Glass K, Banks E. Physical functional limitations and psychological distress in people with and without colorectal cancer: findings from a large Australian study. J Cancer Surviv. 2020 Dec;14(6):894-905. doi: 10.1007/s11764-020-00901-y. Epub 2020 Jul 2. PMID: 32613443

6. Gardiner PA, Reid N, Gebel K, Ding D. Sitting Time and Physical Function in Australian Retirees: An Analysis of Bidirectional Relationships. J Gerontol A Biol Sci Med Sci. 2018 Nov 10;73(12):1675-1681. doi: 10.1093/gerona/gly008. PMID: 29408975

Appendix 4 Supplementary material Chapter 5

Empirical studies on the relationship of CVD to workforce participation in middle-aged Australians

S5.1 Workforce participation of working age older Australians with and without CVD

S5.1.1 Steps of selecting participants at baseline for different outcomes

The depth of the analysis as presented in this paper required to select whole or portions of the participants which were broadly mentioned in four stages. The study participants selected in stage 1 were used for presenting the characteristics of the study participants. The number of participants used in the final exposure-outcome association analysis varied and it depended on the corresponding outcomes. The stages and the number of participants in respective analysis are as follows:

- **Stage 1:** Identifying eligible study participants who were aged less than 65 years old. There were 163562 participants finally selected who were used for describing the characteristics of the study participants (*Figure S5.1.1).*
- **Stage 2:** Getting the study participants who had non-missing workforce participation status to investigate the association of CVD and workforce participation status by considering CVD subtypes, population sub-groups and physical functioning limitations. There were 131 participants with missing workforce participation status. They were excluded and the final analysis that investigated the association of CVD and workforce participation status included 163431 participants (*Figure S5.1.1*).
- **Stage 3:** Divide the study participants into two groups and continue further investigations in those groups separately. We have divided into two groups based on workforce participation status (*Table S5.1.1*) and investigated paid work hour per week in those who had been working (and had valid paid work hour per week) and retired due to ill health in those who had not been working (and had valid record of retirement).
    - *Group 1:* Getting the participants who had been working and had valid weekly paid work hour. Then the associations of CVD and paid work hours per week among the selected participants were investigated. The final analysis that studied the association of CVD and paid work hours per week included 114064 participants (*Figure S5.1.2*).
    - *Group 2:* Getting the participants who had not been working and had valid retirement due to ill-health record as outcome. Then the association of CVD and retirement due to ill health among the selected participants who had not working in any form were studied. The final

analysis that investigated the association of CVD and paid work hour per week included 114064 participants (*Figure S5.1.2*).

- **Stage 4:** The final analysis was to investigate the association of CVD and retirement. There were some conflictions after cross-tabulation of workforce participation status and retirement. For example, 11961 participants were grouped as both 'Not in paid workforce' and 'Not retired' category, and 13645 participants were grouped as both 'In paid workforce' and 'retired' (*Table S5.1.2*). However, we have not considered this apparent conflicting issue while investigating the association of CVD and retirement. Since there was no missing data for retirement, the final analysis that investigated the association of CVD and retirement included 163562 participants (*Table S5.1.3*).

Figure S5.1.1 Flowchart for selection of participants included in the analysis to estimate the effect size for the association of CVD and workforce participation status

Steps	Study participants selection steps	CVD	No CVD	Total	Comments
1	Eligible participants from the 45 and Up Study who were <65 years old	n= 19161	n= 144401	n= 163562	
2	Participants having missing workforce participation status	n= 24	n= 107	n= 131	Excluded
3	Participants having valid workforce participation status	n= 19137	n= 144294	n= 163431	Finally included

Table S5.1.1 The study participants number based on workforce participation-based classification

Groups	Workforce participation status	Number of participants
Group 1	In workforce	N= 121816
Group 2	Not in workforce	N= 41615
Total participants		N= 163431

Figure S5.1.2 Flowchart for selection of participants included in the analysis to estimate the effect size for the association of CVD and paid work hour per week

Steps	Study participants	CVD group	No CVD group	Total	Comments
1	Eligible participants from the 45 and Up Study who were <65 years old and working	n=11480	n=110336	n= 121816	
2	Participants having missed paid work hours per week	n=972	n=6736	n= 7708	Excluded
3	Participants having more than or equal to 100 hours of work per week. We defined these outliers and thus considered missing	n=2	n=42	n= 44	Excluded
4	Participants having valid paid work hours per week	n= 10506	n= 103558	n= 114064	Finally included

Figure S5.1.3 Flowchart for selection of participants included in the analysis to estimate the effect size for the association of CVD and retirement due to ill health

Steps	Study participants	CVD group	No CVD group	Total	Comment
1	Eligible participants from the 45 and Up Study who were <65 years old and not working	n= 7657	n= 33958	n= 41615	
2	Participants who had been grouped as 'not retired'. This is because retired and workforce participation status were defined based on different questions sets. Since the same person being 'not in work' and 'not retired' is conflicting, we have considered these as invalid/missing.	n=1687	n=10274	n= 11961	Excluded
3	Participants having valid record on retirement due to ill health or not	n= 5970	n= 23684	n= 29654	Finally included

Table S5.1.2 The number of participants according to participating in the workforce and retirement

Workforce participation status	Retirement status		Total
	Not retired	Retired	
Not in paid workforce	n= 11961	n= 29654	n= 41615
In Paid workforce	n= 108171	n= 13645	n= 121816
Missing	n= 33	n= 98	n= 131
Total	n= 120165	n= 43397	n= 163562

Table S5.1.3 The number of participants according to CVD and retirement status

	CVD	No CVD	Total
Not Retired	n= 11186	n= 108979	n= 120165
Retired	n= 7975	n= 35422	n= 43397
Total	n= 19161	n= 144401	n= 163562

S5.1.2 Sensitivity analyses for non-participation in the workforce

Non-participation in the workforce: Sensitivity analysis I

Table S5.1.4 Non-participation in the workforce: Prevalence and adjusted prevalence ratios according to CVD status according to hospitalisation

Hospital recorded CVD only (excluding those with self-reported CVD) [c]	39.6 (1302/3285)	1.43 (1.37-1.49)	1.34 (1.29-1.40)
Self-reported CVD only (excluding those with hospitalisation recorded CVD) [c]	37.6 (3937/10478)	1.33 (1.30-1.36)	1.28 (1.25-1.31)
Both self-reported and hospitalisation recorded CVD [c]	45.0 (2418/5374)	1.63 (1.59-1.68)	1.53 (1.48-1.58)
Main analysis CVD [c]	40.0 (7657/19137)	1.43 (1.40-1.46)	1.36 (1.33-1.39)
No self-reported or hospital recorded CVD [c] (Ref)	23.5 (33958/144294)	1	1

[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a]Based on hospital admission only, [b] Based on self-report only, [c] Based on both self-report and hospital admission

Non-participation in the workforce: Sensitivity analysis II

Table S5.1.5 Non-participation in the workforce: Prevalence and adjusted prevalence ratios according to CVD status excluding those with multiple CVD subtypes

	Not in workforce % [n/N]	**Prevalence ratio (95% CI)**	
Total n/N	25.5 (41615/163431)	**Model[1]**	**Model[2]**
CVD [a]	40.0 (7657/19137)	1.43 (1.40-1.46)	1.36 (1.33-1.39)
Ischaemic heart disease only b	41.8 (1260/3017)	1.49 (1.42-1.55)	1.39 (1.34-1.45)
Myocardial infarction only b	36.1 (382/1059)	1.45 (1.35-1.57)	1.34 (1.24-1.44)
Cerebrovascular disease only b	55.0 (280/509)	1.99 (1.83-2.16)	1.85 (1.70-2.01)
Peripheral arterial diseases only b	52.1 (214/411)	1.81 (1.65-1.98)	1.66 (1.52-1.82)
Heart failure only b	49.7 (91/183)	1.77 (1.52-2.05)	1.51 (1.29-1.75)
No CVD (reference)	23.5 (33958/144294)	1	1

[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a] Based on self-report and hospital records [b]Based on hospital records only and participants with CVD subtypes other than the named particular type of CVD subtype were excluded. Effect sizes were estimated using 'no CVD' as the reference group.

Non-participation in the workforce: Sensitivity analysis III

Table S5.1.6 Non-participation in the workforce: Prevalence and adjusted prevalence ratios according to different CVD-subtype in combination defined based on hospitalisation records

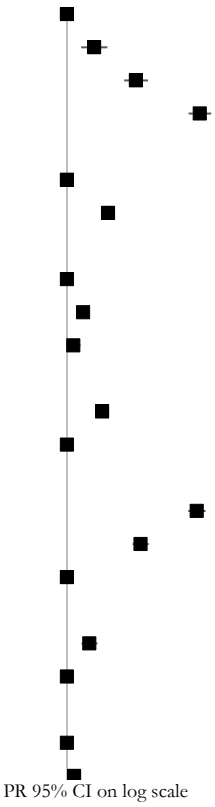
	Not in workforce % [n/N]	Prevalence ratio (95% CI)	
		Model[1]	Model[2]
IHD and Cerebrovascular disease combined [a]	65.7 (94/143)	2.33(2.05-2.64)	2.09 (1.82-2.40)
IHD and HF combined [a]	69.2 (164/237)	2.35 (2.14-2.57)	2.07(1.89-2.27)
IHD, HF and PAD combined [a]	81.3 (26/32)	2.55(2.14-3.05)	2.12 (1.77-2.55)
Stroke and HF combined [a]	84.4 (27/32)	2.95 (2.48-3.50)	2.62 (2.18-3.16)
IHD, Cerebrovascular disease and PAD combined [a]	66.7 (16/24)	2.10 (1.56-2.82)	2.10 (1.50-2.94)
Main analysis CVD [b]	40.0 (7657/19137)	1.43 (1.40-1.46)	1.36 (1.33-1.39)
No self-reported or hospital recorded CVD [b] (Ref)	23.5 (33958/144294)	1	1

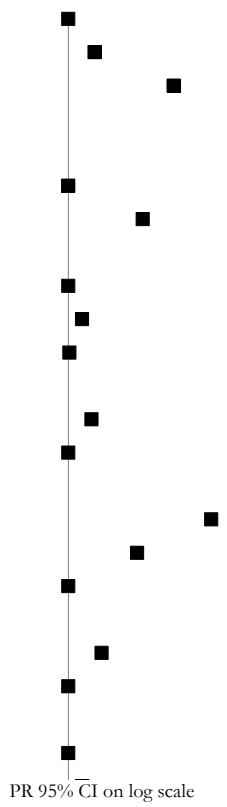
[*]Combination of different subtypes were reported where sufficient numbers were available.
[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a]Hospital admission only, [b] both self-report and hospital admission, IHD= Ischaemic heart disease, HF= Heart failure, PAD= Peripheral arterial disease

S5.1.3 Factors associated with non-participation in the workforce

Figure S5.1.5 Relation of sociodemographic factors to non-participation in the workforce among those with and without CVD

	CVD			No CVD			P-interaction
	Not in paid workforce			Not in paid workforce			
	% (n)	[1]Prevalence ration (95% CI)		% (n)	[1]Prevalence ration (95% CI)		
Age group (years)							
45-50	21.5 (454)	1		11.4 (3726)	1		<0.0001
50-55	25.7 (968)	1.22 (1.11-1.34)		13.7 (5350)	1.20 (1.15-1.24)		
55-60	35.0 (2001)	1.64 (1.51-1.79)		24.0 (9526)	2.05 (1.98-2.13)		
60-65	55.9 (4234)	2.60 (2.40-2.82)		46.9 (15356)	3.95 (3.82-4.07)		
Sex							
Men	34.7 (3427)	1		17.2 (10444)	1		<0.0001
Women	45.5 (4230)	1.34 (1.30-1.39)		28.1 (23514)	1.66 (1.63-1.70)		
Region							
Major cities	36.7 (3478)	1		21.8 (16331)	1		0.7981
Inner regional	43.9 (3034)	1.12 (1.08-1.16)		26.0 (13040)	1.10 (1.08-1.12)		
More remote	43.1 (1021)	1.05 (0.99-1.10)		24.9 (4075)	1.01 (0.98-1.04)		
Marital status							
Not currently married/defacto	49.7 (2198)	1.29 (1.24-1.33)		28.0 (8130)	1.17 (1.15-1.20)		<0.0001
Married/defacto	37.1 (5415)	1		22.4 (25639)	1		
Highest Education							
No school certificate	63.3 (1556)	2.55 (2.39-2.71)		45.8 (5146)	2.66 (2.57-2.74)		<0.0001
Certificate/diploma/trade	41.0 (5039)	1.70 (1.60-1.80)		25.0 (22488)	1.60 (1.56-1.64)		
Tertiary	22.4 (943)	1		13.9 (5824)	1		
Language other than English							
Yes	41.8 (678)	1.18 (1.11-1.24)		26.0 (3751)	1.25 (1.22-1.29)		0.1075
No	39.8 (6979)	1		23.2 (30207)	1		
County of Birth							
Australia/NZ	39.6 (6035)	1		23.0 (25858)	1		0.0054
Others	41.2 (1553)	1.05 (1.01-1.10)		25.3 (7838)	1.10 (1.08-1.12)		

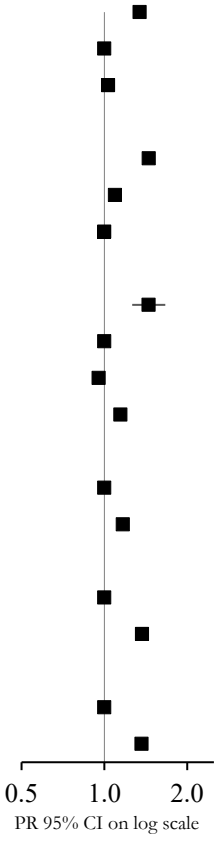


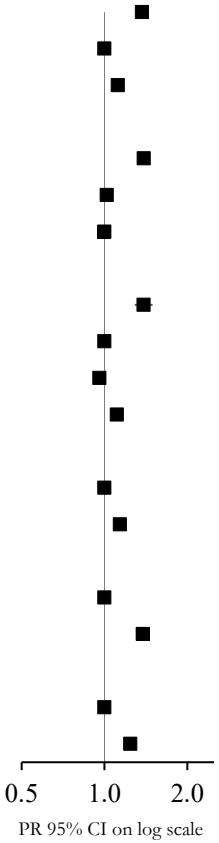


[1]Adjusted for age, sex, remoteness of residence and education.

Figure S5.1.6 Relation of health-related factors to non-participation in the workforce in those with and without CVD

	CVD		No CVD		P-interaction
	Not in paid workforce		Not in paid workforce		
	% (n)	[1]Prevalence ration (95% CI)	% (n)	[1]Prevalence ration (95% CI)	
Alcohol consumption					
No drinkers	51.0 (3366)	1.34 (1.30-1.39)	31.3 (13050)	1.37 (1.34-1.40)	0.5358
Moderate drinkers	33.6 (3102)	1	19.9 (15673)	1	
Heavy drinkers	33.5 (1002)	1.03 (0.98-1.09)	20.2 (4392)	1.12 (1.09-1.15)	
Smoking status					
Current	52.6 (1076)	1.45 (1.38-1.52)	30.4 (4059)	1.39 (1.35-1.43)	0.0039
Past	40.7 (3192)	1.09 (1.06-1.13)	23.4 (11114)	1.02 (1.00-1.04)	
Never	36.4 (3348)	1	22.5 (18650)	1	
BMI (kg/m2)					
Underweight (<18)	56.2 (95)	1.45 (1.26-1.66)	33.3 (456)	1.39 (1.29-1.49)	0.3785
Normal weight (18–<25)	37.2 (1733)	1	22.4 (11221)	1	
Overweight Over weight (25–<30)	35.8 (2490)	0.95 (0.91-1.00)	21.4 (11155)	0.96 (0.94-0.98)	
Obese ((≥ 30)	45.6 (2736)	1.14 (1.10-1.20)	27.1 (8449)	1.11 (1.09-1.14)	
Medical History: Cancer					
No	38.3 (6216)	1	22.7 (29227)	1	0.2351
Yes	49.4 (1441)	1.17 (1.12-1.22)	30.7 (4731)	1.14 (1.11-1.17)	
Medical History: Diabetes					
No	37.3 (6126)	1	22.7 (31022)	1	<0.0001
Yes	55.6 (1531)	1.37 (1.32-1.42)	37.6 (2936)	1.38 (1.34-1.42)	
Medical History: Osteoarthritis					
No	38.7 (7053)	1	23.0 (32236)	1	0.0168
Yes	65.6 (604)	1.37 (1.30-1.44)	42.8 (1722)	1.24 (1.20-1.29)	





[1]Adjusted for age, sex, remoteness of residence and education.

S5.1.4 Sensitivity analyses for Paid hours of work per week

Paid hours of work per week: Sensitivity analysis I

Table S5.1.7 Paid hours of work per week: Means and mean differences according to CVD status where CVD was defined based on hospitalisation records and self-reported survey

	Total N	Mean (95% CI)	Difference in Mean (95% CI)	
			Model[1]	Model[2]
Hospital recorded CVD (regardless of self-reported CVD) [a]	4522	35.8 (35.3, 36.2)	-0.95 (-1.26, -0.64)	-0.90 (-1.11, -0.69)
Self-reported CVD (regardless of hospitalisation recorded CVD) [b]	8686	34.8 (34.5, 35.1)	-1.01 (-1.22, -0.80)	-0.98 (-1.11, -0.86)
Hospital recorded CVD only (excluding those with self-reported CVD) [c]	1820	35.6 (34.9, 36.2)	-0.68 (-1.21, -0.14)	-0.64 (-1.05, -0.22)
Self-reported CVD only (excluding those with hospitalisation recorded CVD) [c]	5984	34.3 (33.9, 34.7)	-0.96 (-1.23, -0.68)	-0.95 (-1.12, -0.77)
Both self-reported and hospitalisation recorded CVD [c]	2702	35.9 (35.3, 36.5)	-1.14 (-1.57, -0.70)	-1.08 (-1.39, -0.76)
Main analysis CVD [c]	10506	34.9 (34.6, 35.2)	-0.95 (-1.13, -0.77)	-0.92 (-1.02, -0.82)
No self-reported or hospital recorded CVD [c] (Ref)	103558	35.9 (35.8, 36.0)	0	0

[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education. [a]Based on hospital admission only, [b] Based on self-report only, [c] Based on both self-report and hospital admission

Paid hours of work per week: Sensitivity analysis II

Table S5.1.8 Paid hours of work per week: Means and mean differences according to CVD status among those in paid work excluding those with multiple CVD subtypes

	Total N	Mean (95% CI)	Difference in Mean (95% CI)	
Total N	114064		**Model[1]**	**Model[2]**
CVD [a]	10506	34.9 (34.6, 35.2)	-0.95 (-1.13, -0.77)	-0.92 (-1.02, -0.82)
Ischaemic heart disease only b	1613	36.7 (35.9, 37.4)	-0.26 (-0.83, 0.33)	-0.29 (-0.74, 0.17)
Myocardial infarction only b	625	37.0 (35.8, 38.2)	-1.53 (-2.46, -0.57)	-1.23 (-2.02, -0.41)
Cerebrovascular disease only b	210	32.7 (30.6, 34.9)	-3.40 (-5.28, -1.39)	-3.34 (-5.08, -1.47)
Peripheral arterial diseases only b	179	33.9 (31.4, 36.4)	-1.76 (-3.86, 0.50)	-1.81 (-3.75, 0.30)
Heart failure only b	82	35.4 (31.5, 39.3)	-1.06 (-4.27, 2.52)	-0.62 (-3.72, 2.85)
No CVD (reference)	103558	35.9 (35.8, 36.0)	0	0

Model[1]= Adjusted for age and sex, Model[2] = Further adjusted for remoteness of residence and education attainment. [b]Based on hospital records only and participants with CVD subtypes other than the named particular type of CVD subtype were excluded, Effect sizes were estimated using 'no CVD' as the reference group.

Paid hours of work per week: Sensitivity analysis III

*Table S5.1.9 Paid hours of work per week**: Means and mean differences according to different CVD-subtype in combination defined based on hospitalisation records

	Total N	Mean (95% CI)	Difference in Mean (95% CI)	
			Model[1]	Model[2]
IHD and Cerebrovascular disease combined [a]	43	34.1 (28.3, 40.0)	-2.88 (-7.58, 2.66)	-3.37 (-7.99, 2.14)
IHD and HF combined [a]	64	33.5 (29.5, 37.5)	-3.24 (-6.57, 0.50)	-2.66 (-5.75, 0.82)
Main analysis CVD [c]	10506	34.9 (34.6, 35.2)	-0.95 (-1.13, -0.77)	-0.92 (-1.02, -0.82)
No self-reported or hospital recorded CVD [c] (Ref)	103558	35.9 (35.8, 36.0)	0	0

*Combination of different subtypes were reported where sufficient numbers were available.
[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a]Hospital admission only, [b] both self-report and hospital admission, IHD= Ischaemic heart disease, HF= Heart failure

S5.1.5 Sensitivity analyses for Retirement

Retirement: Sensitivity analysis I

Table S5.1.10 Retirement: Prevalence and adjusted prevalence ratios according to CVD status where CVD was defined based on hospitalisation records and self-reported survey

	Retired % [n/N]	**Prevalence ratio (95% CI)**	
		Model[1]	**Model[2]**
Hospital recorded CVD (regardless of self-reported CVD) [a]	44.3 (3840/8670)	1.32 (1.29-1.35)	1.30 (1.27-1.33)
Self-reported CVD (regardless of hospitalisation recorded CVD) [b]	42.2 (6691/15873)	1.29 (1.27-1.31)	1.27 (1.24-1.29)
Hospital recorded CVD only (excluding those with self-reported CVD) [c]	39.1 (1284/3288)	1.21 (1.16-1.26)	1.18 (1.14-1.23)
Self-reported CVD only (excluding those with hospitalisation recorded CVD) [c]	39.4 (4135/10491)	1.24 (1.21-1.27)	1.22 (1.19-1.25)
Both self-reported and hospitalisation recorded CVD [c]	47.5 (2556/5382)	1.39 (1.35-1.43)	1.36 (1.32-1.40)
Main analysis CVD [c]	41.6 (7975/19161)	1.28 (1.25-1.30)	1.25 (1.23-1.28)
No self-reported or hospital recorded CVD [c] (Ref)	24.5 (35422/144401)	1	1

[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a]Based on hospital admission only, [b] Based on self-report only, [c] Based on both self-report and hospital admission

Retirement: Sensitivity analysis II

Table S5.1.11 Retirement: Prevalence and adjusted prevalence ratios according to CVD status excluding those with multiple CVD subtypes

	Retired % [n/N]	**Prevalence ratio (95% CI)**	
Total n/N	26.5 (43397/163562)	**Model[1]**	**Model[2]**
CVD [a]	41.6 (7975/19161)	1.28 (1.25-1.30)	1.25 (1.23-1.28)
Ischaemic heart disease only b	44.1 (1332/3021)	1.26 (1.21-1.31)	1.24 (1.19-1.29)
Myocardial infarction only b	40.1 (425/1061)	1.27 (1.19-1.36)	1.24 (1.16-1.32)
Cerebrovascular disease only b	52.1 (265/509)	1.60 (1.47-1.74)	1.56 (1.44-1.69)
Peripheral arterial diseases only b	50.9 (209/411)	1.49 (1.36-1.63)	1.45 (1.33-1.59)
Heart failure only b	48.4 (89/184)	1.50 (1.29-1.75)	1.41 (1.21-1.65)
No CVD (reference)	24.5 (35422/144401)	1	1

[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a] Based on self-report and hospital records [b]Based on hospital records only and participants with CVD subtypes other than the named particular type of CVD subtype were excluded. Effect sizes were estimated using 'no CVD' as the reference group.

Retirement: Sensitivity analysis-III

Table S5.1.12 Retirement:* Prevalence and adjusted prevalence ratios according to different CVD-subtype in combination defined based on hospitalisation records

	Retired % [n/N]	Prevalence ratio (95% CI)	
		Model[1]	Model[2]
IHD and Cerebrovascular disease combined [a]	66.4 (95/143)	1.81 (1.61-2.03)	1.73 (1.53-1.95)
IHD and HF combined [a]	64.7 (154/238)	1.72 (1.57-1.89)	1.65 (1.50-1.81)
IHD, HF and PAD combined [a]	75.8 (25/33)	1.86 (1.53-2.25)	1.74 (1.44-2.11)
Stroke and HF combined [a]	78.1 (25/32)	2.10 (1.71-2.58)	1.99 (1.61-2.46)
IHD, Cerebrovascular disease and PAD combined [a]	75.0 (18/24)	1.80 (1.51-2.14)	1.80 (1.51-2.15)
Main analysis CVD [b]	41.6 (7975/19161)	1.28 (1.25-1.30)	1.25 (1.23-1.28)
No self-reported or hospital recorded CVD [b] (Ref)	24.5 (35422/144401)	1	1

[*]Combination of different subtypes were reported where sufficient numbers were available.
[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a]Hospital admission only, [b] both self-report and hospital admission, IHD= Ischaemic heart disease, HF= Heart failure, PAD= Peripheral arterial disease

S5.1.6 Sensitivity analyses for Retirement due to ill health

Retirement due to ill health: Sensitivity analysis I

Table S5.1.13 Retirement due to ill health: Prevalence and adjusted prevalence ratios according to CVD status where CVD was defined based on hospitalisation records and self-reported survey

	Retirement due to ill health **% [n/N]**	**Prevalence ratio (95% CI)**	
		Model[1]	**Model[2]**
Hospital recorded CVD (regardless of self-reported CVD) [a]	59.6 (1758/2952)	2.11 (2.04-2.19)	2.02 (1.95-2.10)
Self-reported CVD (regardless of hospitalisation recorded CVD) [b]	53.5 (2669/4990)	1.97 (1.90-2.03)	1.90 (1.84-1.97)
Hospital recorded CVD only (excluding those with self-reported CVD) [c]	50.7 (497/980)	1.85 (1.73-1.97)	1.76 (1.65-1.87)
Self-reported CVD only (excluding those with hospitalisation recorded CVD) [c]	46.7 (1408/3018)	1.78 (1.70-1.86)	1.73 (1.66-1.81)
Both self-reported and hospitalisation recorded CVD [c]	63.9 (1261/1972)	2.24 (2.15-2.33)	2.15 (2.07-2.24)
Main analysis CVD [c]	53.0 (3166/5970)	1.95 (1.89-2.01)	1.88 (1.82-1.94)
No self-reported or hospital recorded CVD [c] (Ref)	26.3 (6238/23684)	1	1

[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a]Based on hospital admission only, [b] Based on self-report only, [c] Based on both self-report and hospital admission

Retirement due to ill health: Sensitivity analysis II

Table S5.1.14 Retirement due to ill health: Prevalence and adjusted prevalence ratios according to CVD status excluding those with multiple CVD subtypes

	Retirement due to ill health **% [n/N]**	**Prevalence ratio (95% CI)**	
Total n/N	31.7 (9404/29654)	**Model[1]**	**Model[2]**
CVD [a]	53.0 (3166/5970)	1.95 (1.89-2.01)	1.88 (1.82-1.94)
Ischaemic heart disease only b	57.6 (583/1013)	2.05 (1.94-2.17)	1.95 (1.85-2.07)
Myocardial infarction only b	60.9 (185/304)	2.06 (1.88-2.26)	1.98 (1.80-2.17)
Cerebrovascular disease only b	69.4 (152/219)	2.38 (2.17-2.61)	2.35 (2.14-2.57)
Peripheral arterial diseases only b	68.0 (119/175)	2.34 (2.11-2.59)	2.20 (1.98-2.45)
Heart failure only b	77.1 (54/70)	2.71 (2.38-3.08)	2.51 (2.19-2.88)
No CVD (reference)	26.3 (6238/23684)	1	1

[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a] Based on self-report and hospital records [b]Based on hospital records only and participants with CVD subtypes other than the named particular type of CVD subtype were excluded. Effect sizes were estimated using 'no CVD' as the reference group

Retirement due to ill health: Sensitivity analysis III

Table S5.1.15 Retirement due to ill health:* Prevalence and adjusted prevalence ratios according to different CVD-subtype in combination defined based on hospitalisation records

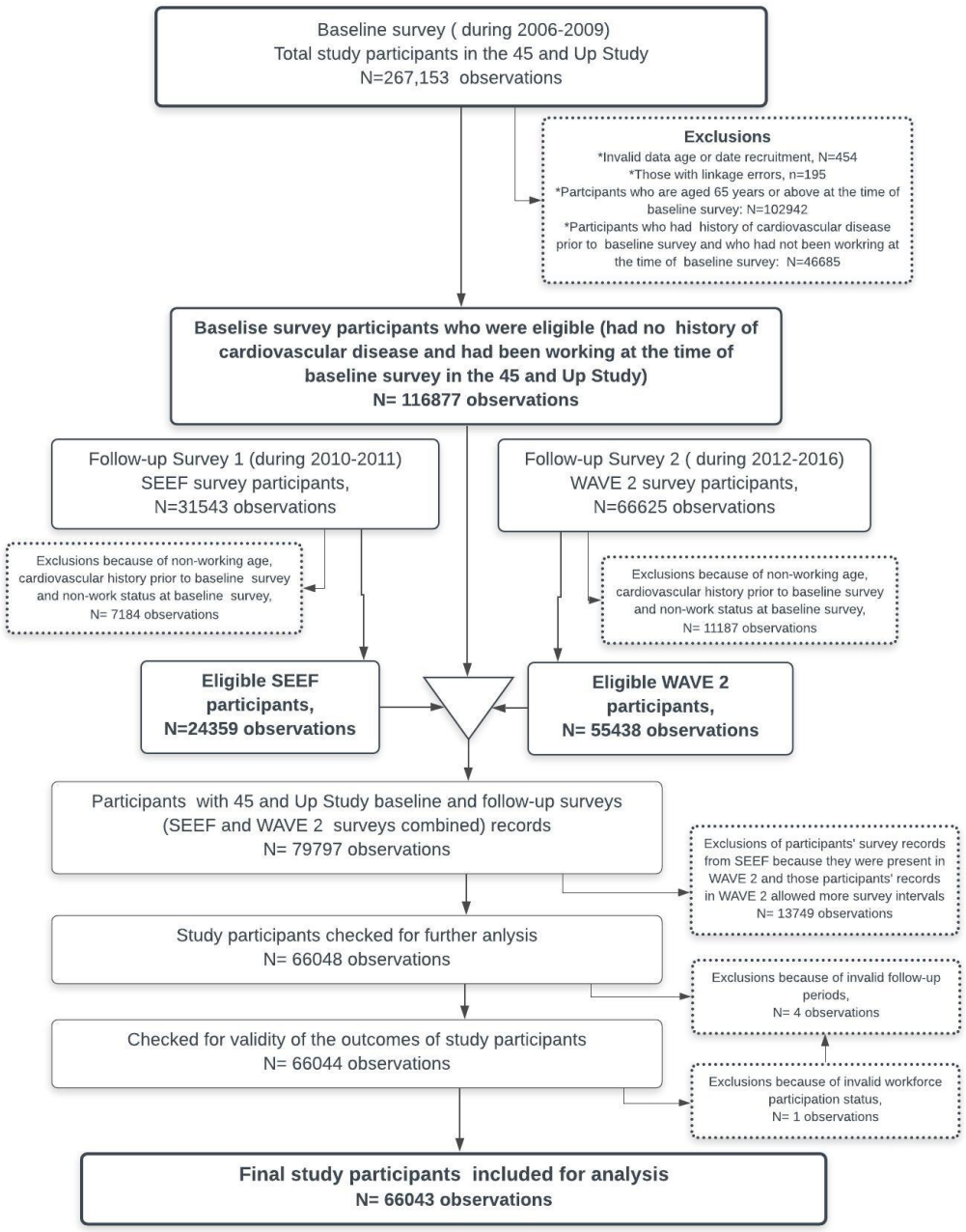
	Retirement due to ill health **% [n/N]**	**Prevalence ratio (95% CI)**	
		Model[1]	**Model[2]**
IHD and Cerebrovascular disease combined [a]	82.3 (65/79)	2.73 (2.44-3.05)	2.68 (2.37-3.03)
IHD and HF combined [a]	83.5 (111/133)	2.88 (2.63-3.15)	2.67 (2.43-2.94)
IHD, HF and PAD combined [a]	95.5 (21/22)	3.45 (3.06-3.89)	3.24 (2.81-3.74)
Stroke and HF combined [a]	91.3 (21/23)	3.02 (2.58-3.53)	2.91 (2.46-3.44)
IHD, Cerebrovascular disease and PAD combined [a]	86.7 (13/15)	3.08 (2.50-3.79)	3.23 (2.54-4.10)
Main analysis CVD [b]	53.0 (3166/5970)	1.95 (1.89-2.01)	1.88 (1.82-1.94)
No self-reported or hospital recorded CVD [b] (Ref)	26.3 (6238/23684)	1	1

[*]Combination of different subtypes were reported where sufficient numbers were available.
[1]Adjusted for age and sex. [2]Further adjusted for remoteness of residence and education.
[a]Hospital admission only, [b] both self-report and hospital admission, IHD= Ischaemic heart disease, HF= Heart failure, PAD= Peripheral arterial disease

S5.2 The relationship between incident CVD and exit from workforce over time among working age Australians

S5.2.1 Study participants selection on exit from workforce after incident CVD

Figure S5.2.1 Expanded study participants selection in longitudinal analyses on CVD and exit from workforce



*SEEF stands for Social, Economic and Environmental Factors and it is a survey for participants in the 45 and Up Study after baseline and WAVE 2 another survey for participants in the 45 and Up Study after SEEF survey.

S5.2.2 Exit from workforce: Sensitivity analysis I

Considering source of incident CVD definition

Table S5.2.1 Exit from workforce: Incidence of and adjusted risk ratios for exit from workforce in people with and without incident CVD by considering source of follow-up incident CVD definition

	Exit from workforce % [n/N]	**Risk ratio (RR) (95% CI)** [1]
Main Analysis (Only Hospital records)		
CVD	26.1 (777 / 2983)	1.28 (1.20-1.36)
No CVD	16.9 (10668 / 63060)	1
Self-report + Hospital records		
CVD	24.4 (1414 / 5803)	1.25 (1.19-1.32)
No CVD	16.7 (10031 /60240)	1

[1]Adjusted for age, sex, remoteness of residence, education and morbidity index.

S5.2.3 Exit from workforce: Sensitivity analysis II

Considering age variable variably in the adjusted regression model

Table S5.2.2 Exit from workforce: Incidence of and adjusted risk ratios for exit from workforce in people with and without incident CVD by considering age as categorical and continuous variable in the regression model

	Exit from workforce % [n/N]	**Risk ratio (RR) (95% CI)***
Main analysis		
No CVD (Reference)	16.9 (10668 / 63060)	1
All participants with incident CVD[1]	26.1 (777 / 2983)	1.28 (1.20-1.36)
All participants with incident CVD[2]	26.1 (777 / 2983)	1.25 (1.18-1.34)

[*1]Adjusted for age-group (45-<55, 55-<60, 60-<65 year) at follow-up, sex, region of residence, education, and comorbidity

[*2]Adjusted for age in year at follow-up as continuous variable, sex, region of residence, education, and comorbidity

Appendix 5 Supplementary material Chapter 6

Empirical studies on the relationship of CVD to social interaction in middle-aged Australian

S6.1 Social interaction of middle-aged and older Australians with and without CVD

S6.1.1 Exploring Duke social support index (DSSI) social interaction subscale and defining social isolation

Table S6.1.1 Duke social support index (DSSI) social interaction subscale questions and coding

Distribution of the social	**Original response***
Social visits per week	Mean of 4.4 Min 0 Median 3 Max 100
Telephone contacts per week	Mean of 6.7 Min 0 Median 1 Max 500
Social group meetings per week	Mean of 1.5 Min 0 Median 1 Max 50
Number of people to depend on	Mean of 7.1 Min 0 Median 5 Max 1000
DSSI score**	Mean of 8.8 Min 4 Median 9 Max 12

*Based on baseline survey of the 45 and Up Study and mean values were up to one decimal values, and Dukes social support index score calculation, ** Summation of recoded values of four social interaction components

S6.1.2 Characteristics of participants stratified by sex

Table S6.1.2 Sociodemographic and Health related characteristics of participants with CVD in the study population

	People with CVD % (n)**		**People without CVD** % (n)**	
	Men	Women	Men	Women
Total men=123616	n= 31899	n=25198	n= 91717	n= 117690
Total women= 142888				
Percentage (%)*	25.8	17.6	74.2	82.4
Age (years)				
mean (sd)	70.5 (10.47)	69.4 (11.67)	61.4 (10.38)	60.2 (10.30)
Age group (years)				
45-<55	8.2 (2628)	12.9 (3249)	31.4 (28790)	36.7 (43142)
55-<65	22.7 (7245)	24.0 (6039)	34.7 (31795)	34.6 (40674)
65-<75	31.0 (9873)	28.0 (7066)	21.3 (19578)	18.2 (21412)
75-75+	38.1 (12153)	35.1 (8844)	12.6 (11554)	10.6 (12462)
Region				
Major cities	54.4 (17338)	52.4 (13213)	52.6 (48198)	51.2 (60302)
Inner regional	33.6 (10719)	34.8 (8775)	34.2 (31372)	35.5 (41814)
More remote	10.5 (3345)	11.1 (2790)	11.2 (10297)	11.4 (13394)
Marital status				
Not currently married/defacto	21.9 (6980)	40.4 (10176)	17.9 (16377)	27.4 (32300)
Married/defacto	77.2 (24617)	59.1 (14900)	81.2 (74495)	72.3 (85042)
Education				
No school certificate	14.5 (4621)	19.0 (4786)	9.5 (8741)	11.1 (13080)
Certificate/diploma/trade	64.1 (20438)	65.3 (16454)	62.1 (56947)	64.2 (75515)
Tertiary	19.0 (6068)	13.2 (3332)	26.9 (24635)	23.3 (27428)
Language other than English				
Yes	90.5 (28857)	92.4 (23285)	89.6 (82181)	90.7 (106764)
No	9.5 (3041)	7.6 (1912)	10.4 (9535)	9.3 (10926)
County of Birth				
Australia/NZ	74.8 (23847)	79.5 (20031)	75.2 (69012)	78.0 (91840)
Others	24.0 (7666)	19.3 (4859)	23.9 (21957)	21.2 (24953)
Working				
Yes	69.2 (22064)	75.2 (18939)	37.3 (34226)	45.2 (53182)
No	30.6 (9762)	24.6 (6193)	62.6 (57392)	54.7 (64356)
Alcohol consumption				
No drinkers	27.9 (8895)	50.5 (12723)	21.5 (19720)	38.2 (44999)
Moderate drinkers	50.3 (16043)	41.8 (10521)	52.4 (48017)	53.1 (62506)
Heavy drinkers	19.6 (6255)	4.1 (1040)	24.7 (22643)	6.4 (7489)
Smoking status				
Current	5.8 (1839)	5.7 (1440)	8.3 (7580)	7.2 (8434)
Past	53.9 (17187)	29.7 (7472)	41.2 (37763)	28.7 (33770)
Never	40.0 (12748)	64.3 (16205)	50.2 (46073)	63.8 (75142)
BMI (kg/m2)				
Underweight (<18)	0.8 (250)	2.1 (518)	0.6 (519)	1.5 (1808)
Normal weight (18–<25)	28.1 (8962)	32.5 (8191)	29.0 (26624)	39.9 (46920)
Overweight Over weight (25–<30)	41.9 (13352)	30.3 (7641)	44.7 (41000)	30.0 (35315)
Obese ((30–30+)	21.8 (6954)	24.6 (6203)	19.6 (17962)	20.3 (23872)
Medical History: Cancer (Yes)	24.3 (7766)	20.7 (5214)	14.6 (13396)	13.6 (15995)
Medical History: Diabetes (Yes)	18.0 (5737)	14.1 (3565)	8.5 (7788)	5.8 (6798)
Medical History: Osteoarthritis (Yes)	4.1 (1292)	15.9 (4019)	1.6 (1454)	7.3 (8563)
Physical functioning limitations				
No limitation	12.9 (4118)	11.5 (2905)	36.1 (33130)	32.8 (38590)
Minor limitation	23.3 (7434)	14.8 (3717)	29.4 (26983)	24.0 (28233)
Moderate limitation	28.0 (8933)	25.4 (6408)	17.5 (16086)	20.3 (23893)
Severe limitation	20.8 (6650)	29.1 (7323)	6.6 (6075)	9.0 (10579)

*row proportions among men or women, **column proportions, BMI: Body Mass Index, Men missing [%(n)]: 1.9% (2347) for region, 0.9% (1147) for marital status, 1.8% (2166) for education, 0.9% (1134) for country of birth, 0.1% (172) for workforce participation status, 1.7% (2043) for alcohol drink/week, 0.3% (426) for smoking status, 6.5% (7993) for BMI, 11.5% (14207) for physical functioning limitations (PFL). Women missing [%(n)]: 1.8% (2600) for region, 0.3% (470) for marital status, 1.6% (2293) for education, 0.8 (1205) for country of birth, 0.2% (218) for workforce participation status, 2.5% (3610) missing for alcohol/week, 0.3% (425) for smoking, 8.7% (12420) for BMI, 14.9% (21240) for PFL.

Table S6.1.3 Categories of social visits per week, telephone contacts per week, social group meeting per week and number of people to depend on according to frequencies among those with and without CVD

	People with CVD*		**People without CVD****	
	Men	**Women**	**Men**	**Women**
Social interaction components	% (n) N= 31 899	% (n) N= 25 198	% (n) N= 91 717	% (n) N= 117 690
Social visits/week				
Min, median, max	0, 3, 100	0, 4, 100	0, 3, 100	0, 3, 100
0	12.8 (4076)	9.1 (2281)	12.2 (11161)	7.8 (9225)
1-2	25.9 (8269)	22.7 (5714)	30.7 (28114)	26.2 (30884)
≥ 3	56.6 (18066)	63.2 (15928)	54.3 (49774)	63.0 (74203)
Telephone contacts/week				
Min, median, max	0, 5, 480	0, 5, 330	0, 4, 500	0, 4, 500
0	7.1 (2267)	2.7 (685)	6.2 (5650)	2.3 (2700)
1-5	56.5 (18011)	47.5 (11962)	58.5 (53619)	51.9 (61094)
≥6	31.7 (10101)	45.3 (11421)	32.4 (29724)	43.3 (50965)
Social group meetings/week				
Min, median, max	0, 1, 50	0, 1, 50	0, 1, 50	0, 1, 50
0	40.1 (12804)	35.0 (8809)	44.4 (40738)	40.4 (47594)
1-2	47.7 (15212)	52.9 (13327)	46.5 (42677)	50.6 (59600)
≥ 3	5.0 (1602)	5.0 (1251)	3.9 (3566)	3.6 (4183)
Number of people to depend on				
Min, median, max	0, 5, 1000	0, 4, 1000	0, 5, 1000	0, 5, 720
0	6.9 (2196)	5.5 (1378)	7.7 (7019)	5.3 (6218)
1-2	18.1 (5777)	19.6 (4950)	17.1 (15638)	17.7 (20829)
≥3	69.5 (22160)	69.5 (17511)	71.4 (65457)	73.4 (86375)
Duke Social support subscale Index (DSSI) score				
Min, median, max	4, 9, 12	4, 9, 12	4, 9, 12	4, 9, 12
4-6	9.9 (3153)	6.3 (1579)	10.6 (9743)	6.4 (7518)
7-9	46.5 (14839)	39.4 (9940)	50.6 (46406)	44.9 (52859)
10-12	31.0 (9881)	41.1 (10354)	29.8 (27293)	39.4 (46323)

*The missing values [%(n)] for CVD group [men, women] in social visits per week, telephone contacts per week, social group meeting per week, number of people to depend on and DSSI score were [4.6% (1488), 5.1% (1275)]; [4.8% (1520), 4.4% (1130)]; [7.1% (2281), 7.2% (1811)]; [5.5% (1766), 5.4% (1359)] and [12.6% (4026), 13.2% (3325)] respectively.

**The missing values [%(n)] for no CVD group [men, women] in social visits per week, telephone contacts per week, social group meeting per week , number of people to depend on and DSSI score were [2.9% (2668), 2.9% (3378)]; [3.0% (2724), 2.5% (2931)]; [5.2% (4736), 5.4% (6313)]; [3.9% (3603), 3.6% (4268)] and [9.0% (8275), 9.3% (10990)] respectively.

Figure S6.1.1 Cumulative frequencies and percentages of the four different social interaction components in men and women with and without CVD

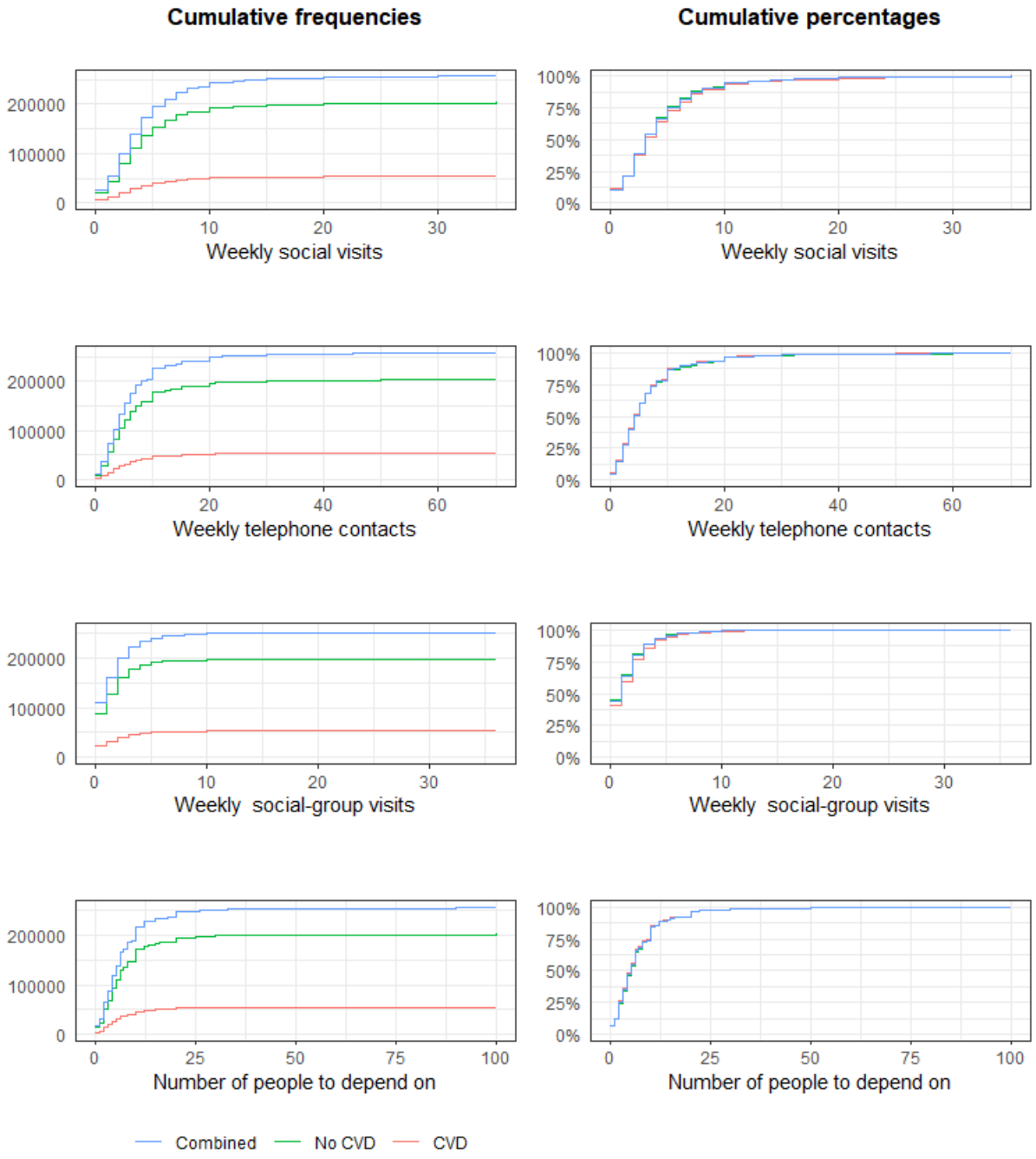


Figure S6.1.2 Distribution of the four different social interaction components in men and women with and without CVD

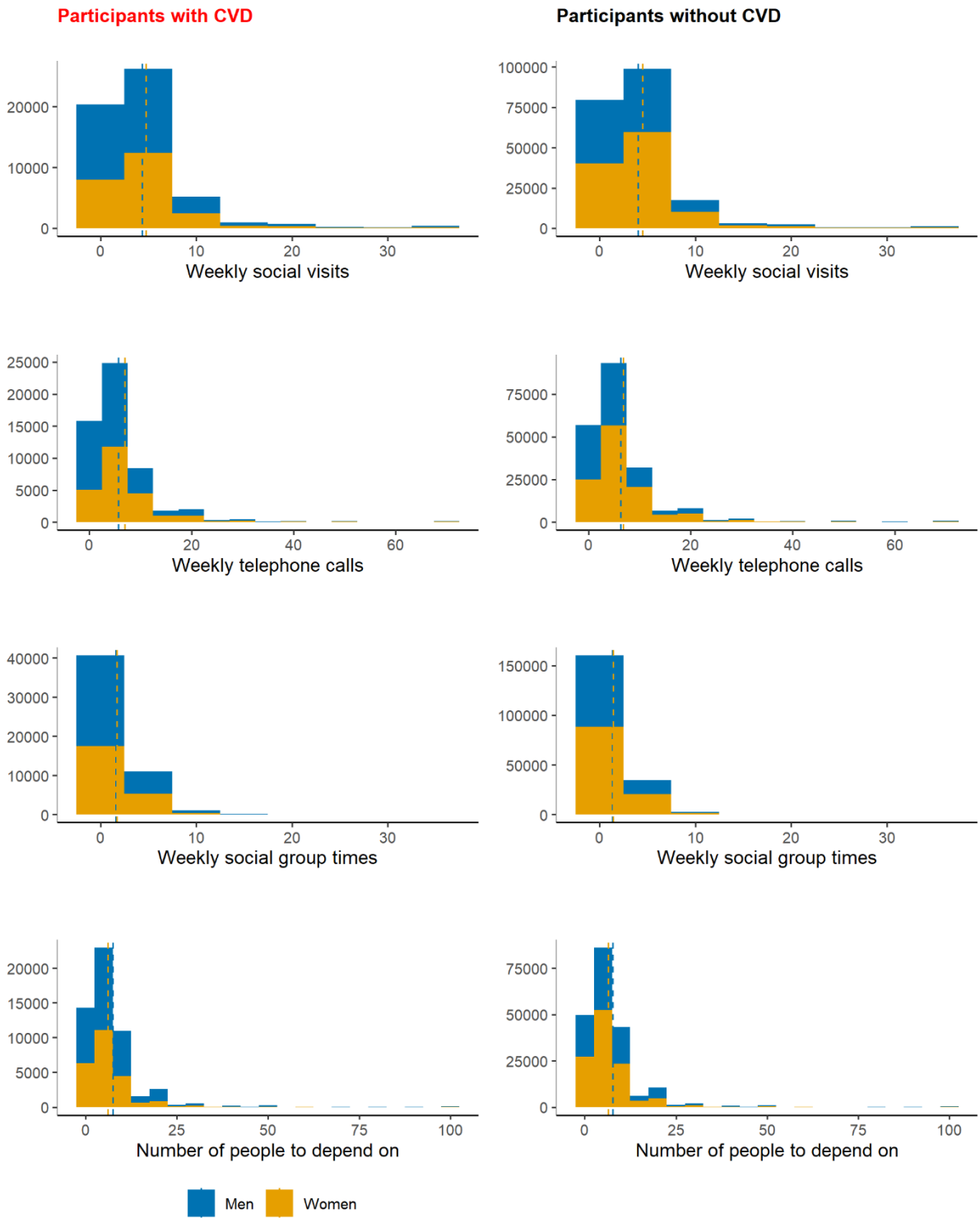
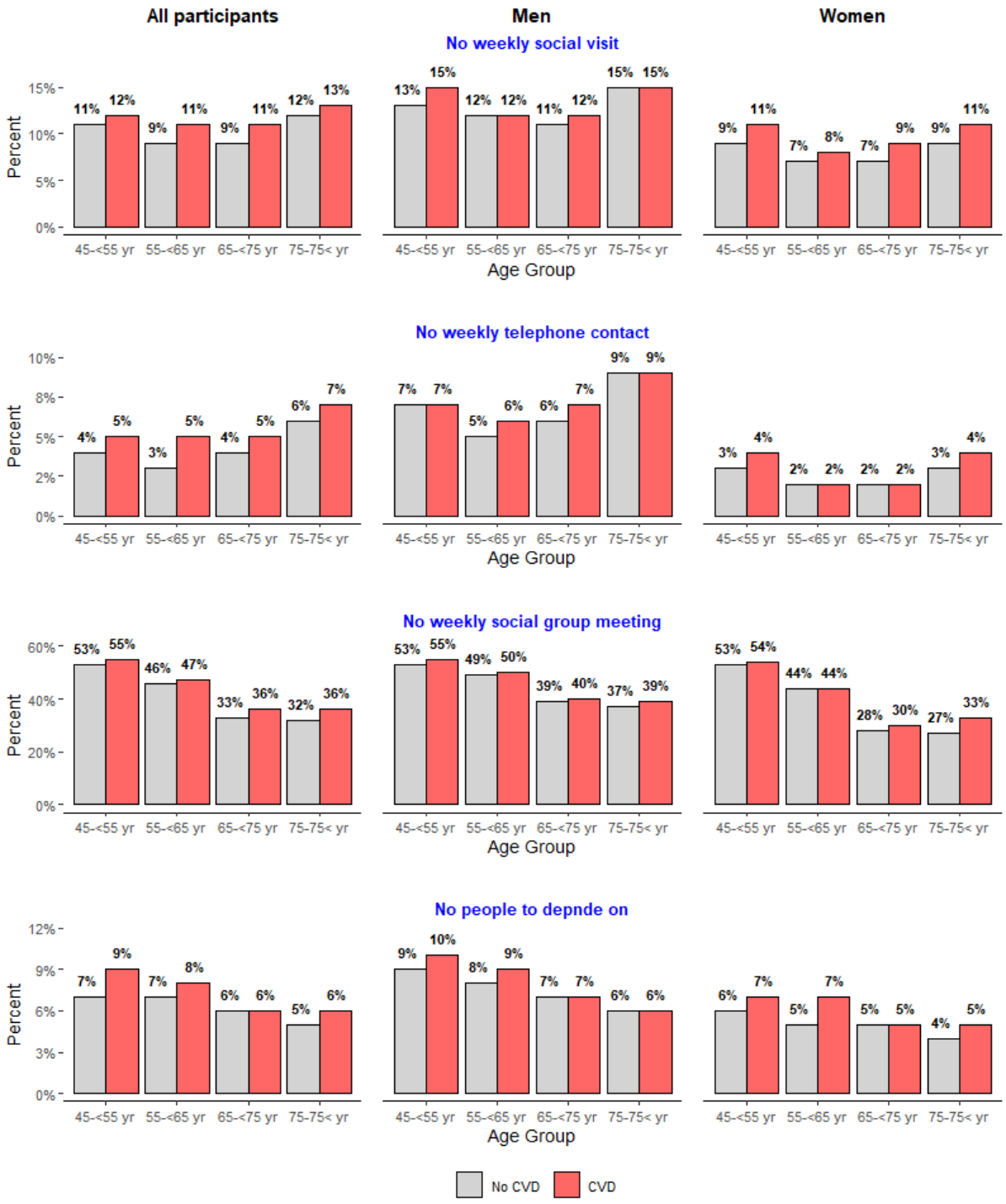


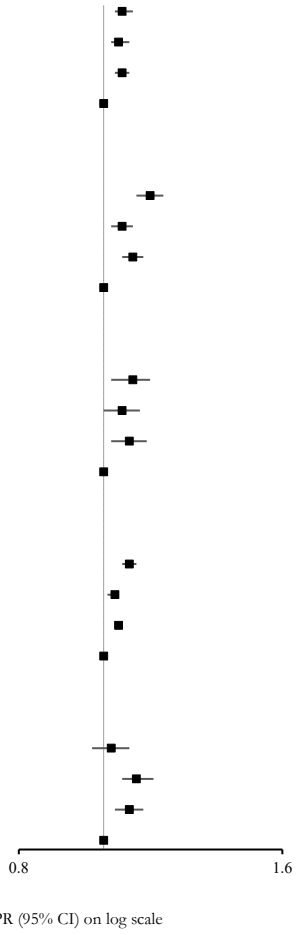
Figure S6.1.3 Proportion of participants with no social interaction according to age-group, sex and CVD status



S6.1.3 Sensitivity analysis I: Stratifying by those who were defined by hospitalization and self-report

Figure S6.1.4 Social isolation and no social interaction: Prevalence of and adjusted prevalence ratios (PRs) for social isolation and no social interaction among population based on self-reported and hospitalisation records definition

		[1]PR (95% CI) of
	% (n/N)	social isolation or no social interaction
Social isolation		
CVD defined by hospital admission only	20.1 (5379/26762)	1.05 (1.03-1.08)
CVD defined by self-report only	19.5 (7894/40554)	1.04 (1.02-1.07)
CVD (*Main analysis*) [a]	19.6 (9731/49746)	1.05 (1.03-1.07)
No CVD [a] (Reference)	19.1 (36315/190142)	1
No social visits/week		
CVD defined by hospital admission only	12.6 (3734/29559)	1.13 (1.09-1.17)
CVD defined by self-report only	11.4 (5011/43984)	1.05 (1.02-1.08)
CVD (*Main analysis*) [a]	11.7 (6357/54334)	1.08 (1.05-1.11)
No CVD [a] (Reference)	10.0 (20383/203361)	1
No telephone contacts/week		
CVD defined by hospital admission only	5.9 (1754/29600)	1.08 (1.02-1.13)
CVD defined by self-report only	5.3 (2329/44098)	1.05 (1.00-1.10)
CVD (*Main analysis*) [a]	5.4 (2945/54447)	1.07 (1.02-1.12)
No CVD [a] (Reference)	4.1 (8317/203752)	1
No social group meetings/week		
CVD defined by hospital admission only	41.4 (11908/28760)	1.07 (1.05-1.09)
CVD defined by self-report only	40.6 (17433/42975)	1.03 (1.01-1.04)
CVD (*Main analysis*) [a]	40.8 (21612/53005)	1.04 (1.03-1.05)
No CVD [a] (Reference)	44.5 (88324/198358)	1
No people-to-depend on		
CVD defined by hospital admission only	6.4 (1876/29387)	1.02 (0.97-1.07)
CVD defined by self-report only	6.8 (2950/43693)	1.09 (1.05-1.14)
CVD (*Main analysis*) [a]	6.6 (3574/53972)	1.07 (1.03-1.11)
No CVD [a] (Reference)	6.6 (13237/201536)	1

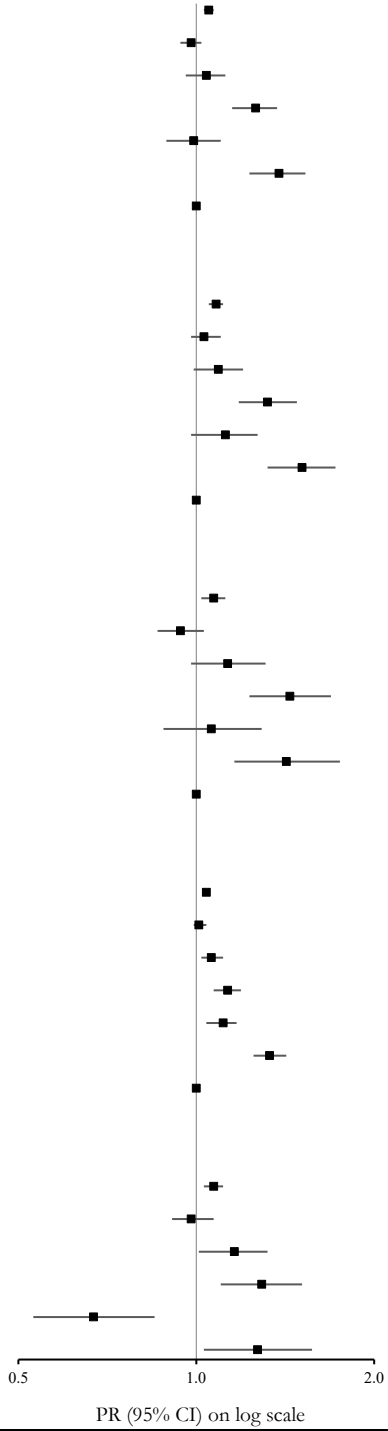


[a] Based on self-report and hospital records. Effect sizes were estimated using 'no CVD' as the reference group. [1]Adjusted for age-group, sex, region of residence and education

S6.1.4 Sensitivity analysis-II: Considering a particular CVD subtype only by excluding those having multiple CVD subtypes and CVD procedures

Figure S6.1.5 No social interaction: Prevalence of and adjusted prevalence ratios (PRs) for social isolation in people with and without CVD by considering comorbid CVD subtypes

		[1]PR (95% CI) of no social interaction components
	% (n/N)	
Social isolation		
CVD [a]	19.6 (9731/49746)	1.05 (1.03-1.07)
Ischaemic heart disease only [b]	18.7 (1630/8711)	0.98 (0.94-1.02)
Myocardial infarction only [b]	20.9 (524/2510)	1.04(0.96-1.12)
Cerebrovascular disease only [b]	23.8 (382/1605)	1.26 (1.15-1.37)
Peripheral arterial diseases only [b]	18.8 (270/1438)	0.99 (0.89-1.10)
Heart failure only [b]	25.8 (246/954)	1.38 (1.23-1.53)
No CVD (reference)	19.1 (36315/190142)	1
No social visits/week		
CVD [a]	11.7 (6357/54334)	1.08 (1.05-1.11)
Ischaemic heart disease only [b]	11.5 (1096/9529)	1.03 (0.98-1.10)
Myocardial infarction only [b]	12.6 (348/2766)	1.09 (0.99-1.20)
Cerebrovascular disease only [b]	14.8 (264/1787)	1.32 (1.18-1.48)
Peripheral arterial diseases only [b]	12.7 (202/1587)	1.12 (0.98-1.27)
Heart failure only [b]	17.3 (185/1069)	1.51 (1.32-1.72)
No CVD (reference)	10.0 (20383/203361)	1
No telephone contacts/week		
CVD [a]	5.4 (2945/54447)	1.07 (1.02-1.12)
Ischaemic heart disease only [b]	5.2 (495/9542)	0.94 (0.86-1.03)
Myocardial infarction only [b]	6.5 (180/2761)	1.13 (0.98-1.31)
Cerebrovascular disease only [b]	7.9 (141/1778)	1.44 (1.23-1.69)
Peripheral arterial diseases only [b]	6.1 (97/1603)	1.06 (0.88-1.29)
Heart failure only [b]	7.8 (85/1083)	1.42 (1.16-1.75)
No CVD (reference)	4.1 (8317/203752)	1
No social group meetings/week		
CVD [a]	40.8 (21612/53005)	1.04 (1.03-1.05)
Ischaemic heart disease only [b]	39.8 (3701/9305)	1.01 (0.99-1.04)
Myocardial infarction only [b]	43.3 (1165/2689)	1.06 (1.02-1.11)
Cerebrovascular disease only [b]	43.2 (757/1753)	1.13 (1.07-1.19)
Peripheral arterial diseases only [b]	42.2 (657/1557)	1.11 (1.04-1.17)
Heart failure only [b]	48.9 (510/1043)	1.33 (1.25-1.42)
No CVD (reference)	44.5 (88324/198358)	1
No people to depend on		
CVD [a]	6.6 (3574/53972)	1.07 (1.03-1.11)
Ischaemic heart disease only [b]	6.1 (583/9485)	0.98 (0.91-1.07)
Myocardial infarction only [b]	7.7 (210/2736)	1.16 (1.01-1.32)
Cerebrovascular disease only [b]	7.8 (140/1789)	1.29 (1.10-1.51)
Peripheral arterial diseases only [b]	4.1 (65/1586)	0.67 (0.53-0.85)
Heart failure only [b]	7.5 (81/1079)	1.27 (1.03-1.57)
No CVD (reference)	6.6 (13237/201536)	1



.,[a] Based on self-report and hospital records, [b]Based on hospital records only and without any other CVD subtypes. Effect sizes were estimated using 'no CVD' as the reference group. [1]Adjusted for age, sex, region of residence and education attainment.

S6.1.5 Supplement analysis I: Factors associated with social isolation and no social interaction

Figure S6.1.6a Relation of sociodemographic factors with social isolation

Social isolation		**CVD**	CVD	CVD		No CVD	No CVD	**No CVD**	**P-inter**
		% (n)	**PR 95% CI**	**PR 95% CI**		% (n)	PR 95% CI	PR 95% CI	
Age group (years)									
45-<55		10.1 (2113)	1			9.3 (2237)	1		>0.05
55-<65		13.2 (777)	0.81 (0.74-0.88)			12.2 (8752)	0.81 (0.78-0.83)		
65-<75		11.0 (1462)	0.67 (0.62-0.73)			10.0 (7269)	0.66 (0.63-0.68)		
75-75+		9.1 (1547)	0.80 (0.74-0.86)			8.3 (3408)	0.79 (0.76-0.83)		
Sex									
Men		8.6 (2165)	1			8.7 (10223)	1		>0.05
Women		11.7 (3734)	0.70 (0.67-0.74)			12.5 (11443)	0.68 (0.66-0.70)		
Region									
Major cities		12.9 (1218)	1			12.4 (2714)	1		<0.05
Inner regional		11.1 (1905)	1.12 (1.06-1.18)			11.1 (5379)	1.13 (1.09-1.16)		
More remote		10.0 (3949)	1.36 (1.26-1.46)			10.1 (16134)	1.24 (1.19-1.28)		
Marital status									
Not currently married/defacto		9.9 (3668)	1.22 (1.16-1.29)			10.1 (13377)	1.19 (1.15-1.22)		>0.05
Married/defacto		9.1 (852)	1			10.1 (5241)	1		
Highest Education									
No school certificate		11.1 (1905)	1.69 (1.55-1.83)			9.6 (10439)	1.51 (1.45-1.58)		<0.05
Certificate/diploma/trade		10.0 (3949)	1.19 (1.11-1.28)			10.8 (7911)	1.08 (1.05-1.11)		
Tertiary		12.9 (1218)	1			11.9 (2828)	1		
Language other than English									
Yes		10.0 (5232)	1.46 (1.42-1.47)			10.0 (18904)	1.47 (1.45-1.48)		>0.05
No		13.5 (667)	1			13.5 (2762)	1		
County of Birth									
Australia/NZ		10.0 (5232)	1			9.6 (15383)	1		>0.05
Others		13.5 (667)	1.39 (1.31-1.46)			13.0 (6112)	1.47 (1.43-1.51)		
				0.5 1.0 2.0				0.5 1.0 2.0	
				PR (95% CI) on log scale				PR (95% CI) on log scale	

[1]Adjusted for age, sex, region of residence and education

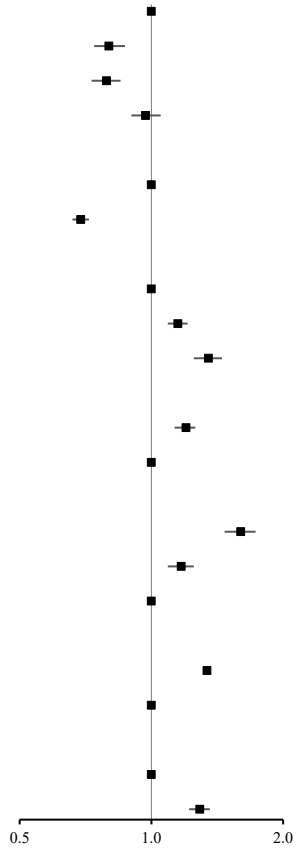
Figure S6.1.6b Relation of health-related factors with social isolation

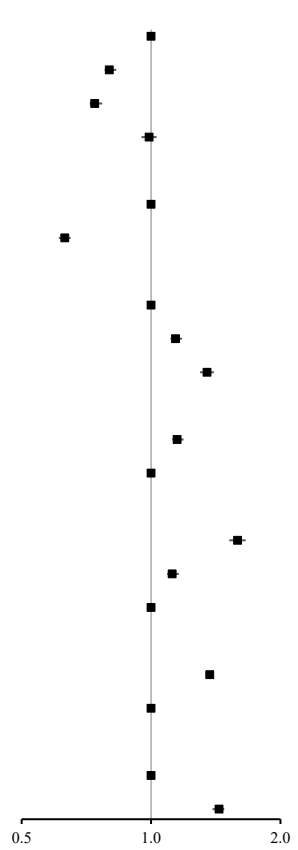
Social isolation		**CVD**	CVD	CVD		No CVD	No CVD	**No CVD**	**P-int.**
		% (n)	**PR 95% CI**	**PR 95% CI**		% (n)	PR 95% CI	PR 95% CI	
Alcohol consumption									
No drinkers		12.2 (2640)	1.48 (1.40-1.56)			12.4 (8001)	1.44 (1.40-1.48)		>0.05
Moderate drinkers		10.6 (771)	1			10.6 (3194)	1		
Heavy drinkers		8.7 (2318)	1.07 (0.99-1.16)			9.1 (10092)	1.00 (0.96-1.04)		
Smoking status									
Current		17.6 (577)	1.83 (1.68-1.99)			15.7 (2508)	1.52 (1.46-1.58)		<0.05
Past		11.5 (2831)	1.25 (1.18-1.31)			10.9 (7826)	1.11 (1.08-1.14)		
Never		8.5 (2463)	1			9.3 (11236)	1		
BMI (kg/m2)									
Underweight (<18)		14.2 (109)	1.41 (1.18-1.68)			13.8 (321)	1.47 (1.33-1.63)		>0.05
Normal weight (18–<25)		11.2 (1468)	1			11.1 (4640)	1		
Overweight Over weight (25–<30)		10.8 (1854)	0.83 (0.78-0.88)			10.2 (7484)	0.91 (0.88-0.94)		
Obese ((30–30+)		9.4 (1976)	0.97 (0.91-1.04)			10.0 (7659)	1.02 (0.98-1.05)		
Medical History: Cancer									
No		10.3 (4552)	1.01 (0.95-1.07)			10.5 (18858)	0.96 (0.92-1.00)		<0.05
Yes		10.4 (1347)	1			9.6 (2808)	1		
Medical History: Diabetes									
No		10.1 (4805)	1.17 (1.10-1.24)			10.2 (19903)	1.21 (1.16-1.27)		>0.05
Yes		11.8 (1094)	1			12.1 (1763)	1		
Medical History: Osteoarthritis									
No		10.4 (5367)	1.13 (1.03-1.23)			10.4 (20778)	1.07 (1.00-1.14)		<0.05
Yes		10.0 (532)	1			8.9 (888)	1		
				0.5 1.0 2.0				0.5 1.0 2.0	
				PR (95% CI) on log scale				PR (95% CI) on log scale	

[1]Adjusted for age, sex, region of residence and education.

Figure S6.1.7a Relation of sociodemographic factors with 'no social visits per week'

No social visits/week	CVD	CVD	CVD	No CVD	No CVD	No CVD	P-inter
	% (n)	PR 95% CI	PR 95% CI	% (n)	PR 95% CI	PR 95% CI	
Age group (years)							
45-<55	12.2 (715)	1		10.7 (7694)	1		>0.05
55-<65	10.2 (1358)	0.80 (0.74-0.87)		9.0 (6493)	0.80 (0.78-0.83)		
65-<75	10.3 (1743)	0.79 (0.73-0.85)		8.6 (3537)	0.74 (0.72-0.77)		
75-75+	12.1 (2541)	0.97 (0.90-1.05)		11.1 (2659)	0.99 (0.95-1.03)		
Sex							
Men	12.8 (4076)	1		12.2 (11160)	1		<0.05
Women	9.1 (2281)	0.69 (0.66-0.72)		7.8 (9223)	0.63 (0.61-0.65)		
Region							
Major cities	10.2 (3128)	1		8.9 (9643)	1		>0.05
Inner regional	11.7 (2275)	1.15 (1.09-1.21)		10.1 (7424)	1.14 (1.11-1.18)		
More remote	13.8 (845)	1.35 (1.25-1.45)		12.1 (2876)	1.35 (1.30-1.40)		
Marital status							
Not currently married/defacto	12.0 (2058)	1.20 (1.13-1.26)		10.4 (5039)	1.15 (1.12-1.19)		>0.05
Married/defacto	10.7 (4235)	1		9.5 (15192)	1		
Highest Education							
No school certificate	14.1 (1324)	1.60 (1.47-1.73)		12.8 (2800)	1.59 (1.52-1.66)		>0.05
Certificate/diploma/trade	10.6 (3925)	1.17 (1.09-1.25)		9.6 (12661)	1.12 (1.09-1.16)		
Tertiary	9.4 (882)	1		8.7 (4548)	1		
Language other than English							
Yes	10.9 (5670)	1.34 (.-.)		9.5 (17884)	1.37 (.-.)		>0.05
No	13.9 (687)	1		12.2 (2499)	1		
County of Birth							
Australia/NZ	10.5 (4607)	1		9.0 (14513)	1		>0.05
Others	13.2 (1650)	1.29 (1.22-1.36)		12.1 (5683)	1.44 (1.39-1.48)		

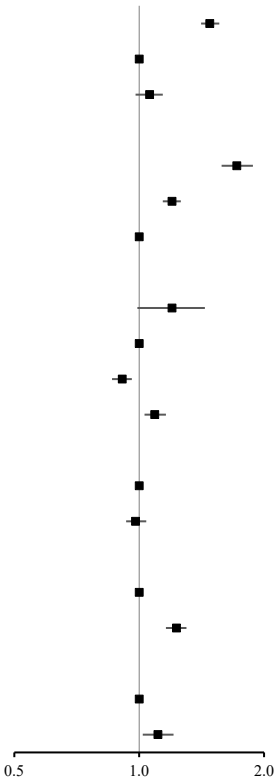




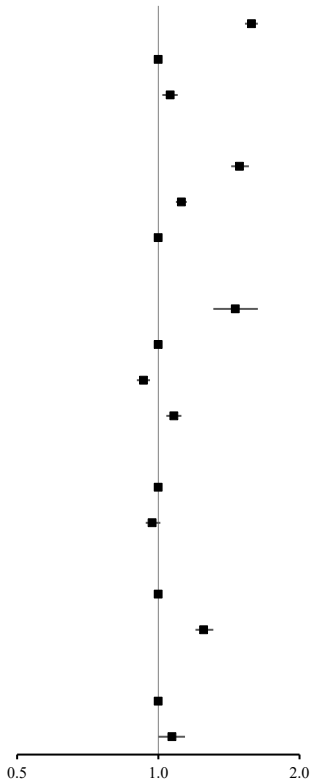
[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.7b Relation of health-related factors with 'no social visits per week'

No social visits/week	**CVD** **% (n)**	CVD **PR 95% CI**	CVD **PR 95% CI**	No CVD % (n)	No CVD PR 95% CI	**No CVD** PR 95% CI	**P-int.**
Alcohol consumption							
No drinkers	13.2 (2849)	1.48 (1.41-1.56)		12.2 (7878)	1.58 (1.53-1.63)		>0.05
Moderate drinkers	9.4 (2491)	1		8.1 (8997)	1		
Heavy drinkers	11.0 (802)	1.06 (0.98-1.14)		10.2 (3076)	1.06 (1.02-1.10)		
Smoking status							
Current	17.1 (561)	1.72 (1.58-1.88)		14.3 (2287)	1.49 (1.43-1.56)		<0.05
Past	12.3 (3045)	1.20 (1.14-1.26)		10.5 (7521)	1.12 (1.09-1.15)		
Never	9.4 (2717)	1		8.7 (10496)	1		
BMI (kg/m2)							
Underweight (<18)	13.0 (100)	1.20 (0.99-1.44)		12.9 (301)	1.46 (1.31-1.63)		>0.05
Normal weight (18–<25)	11.1 (1909)	1		9.3 (6842)	1		
Overweight Over weight (25–<30)	10.4 (2187)	0.91 (0.86-0.96)		9.5 (7232)	0.93 (0.90-0.96)		
Obese ((30–30+)	12.0 (1574)	1.08 (1.01-1.15)		10.7 (4467)	1.08 (1.04-1.12)		
Medical History: Cancer							
No	11.1 (4900)	1		9.8 (17598)	1		>0.05
Yes	11.2 (1457)	0.98 (0.93-1.04)		9.5 (2785)	0.97 (0.94-1.01)		
Medical History: Diabetes							
No	10.7 (5102)	1		9.5 (18572)	1		>0.05
Yes	13.5 (1255)	1.23 (1.16-1.30)		12.4 (1811)	1.25 (1.20-1.31)		
Medical History: Osteoarthritis							
No	11.1 (5771)	1		9.8 (19503)	1		>0.05
Yes	11.0 (586)	1.11 (1.02-1.21)		8.8 (880)	1.07 (1.00-1.14)		



PR (95% CI) on log scale

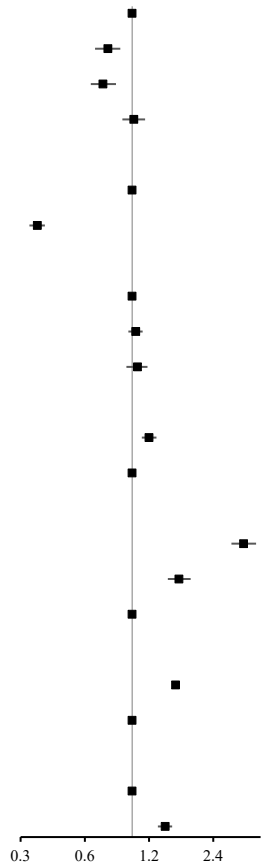


PR (95% CI) on log scale

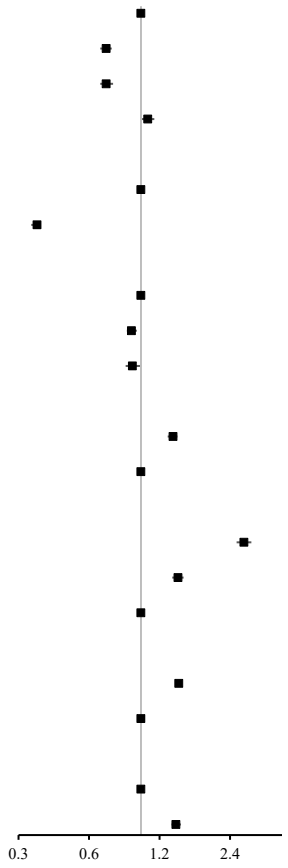
[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.8a Relation of sociodemographic factors with 'no telephone contacts per week'

No telephone contacts/week	**CVD**	CVD	CVD	No CVD	No CVD	**No CVD**	**P-int**
	% (n)	**PR 95% CI**	**PR 95% CI**	% (n)	PR 95% CI	PR 95% CI	
Age group (years)							
45-<55	5.0 (295)	1		4.3 (3082)	1		<0.05
55-<65	4.4 (582)	0.77 (0.67-0.88)		3.3 (2390)	0.71 (0.67-0.75)		
65-<75	4.5 (770)	0.73 (0.64-0.84)		3.6 (1491)	0.71 (0.67-0.76)		
75-75+	6.2 (1298)	1.02 (0.90-1.15)		5.6 (1354)	1.07 (1.01-1.14)		
Sex							
Men	7.1 (2262)	1		6.1 (5627)	1		>0.05
Women	2.7 (683)	0.36 (0.33-0.39)		2.3 (2690)	0.36 (0.34-0.37)		
Region							
Major cities	5.0 (1537)	1		4.1 (4447)	1		<0.05
Inner regional	5.3 (1027)	1.04 (0.96-1.12)		3.8 (2768)	0.91 (0.87-0.96)		
More remote	5.6 (343)	1.06 (0.94-1.18)		4.0 (951)	0.92 (0.86-0.99)		
Marital status							
Not currently married/defacto	5.4 (920)	1.20 (1.11-1.30)		4.7 (2292)	1.37 (1.30-1.43)		<0.05
Married/defacto	5.1 (1999)	1		3.7 (5941)	1		
Highest Education							
No school certificate	8.7 (815)	3.33 (2.92-3.81)		6.8 (1493)	2.75 (2.56-2.96)		>0.05
Certificate/diploma/trade	4.7 (1720)	1.66 (1.47-1.88)		3.9 (5122)	1.44 (1.36-1.52)		
Tertiary	3.1 (289)	1		2.9 (1511)	1		
Language other than English							
Yes	4.9 (2552)	1.60 (.-.)		3.8 (7150)	1.45 (.-.)		>0.05
No	7.9 (393)	1		5.7 (1167)	1		
County of Birth							
Australia/NZ	4.7 (2043)	1		3.6 (5798)	1		>0.05
Others	6.8 (850)	1.43 (1.32-1.54)		5.1 (2414)	1.41 (1.35-1.48)		



PR (95% CI) on log scale

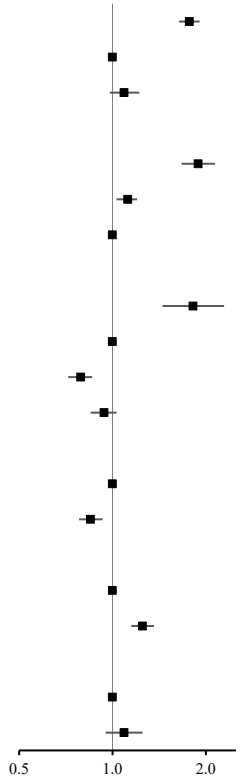


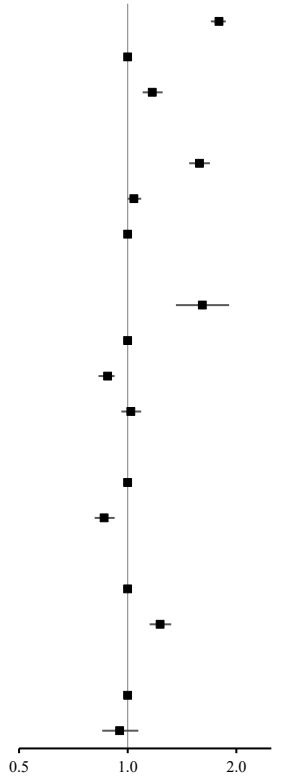
PR (95% CI) on log scale

[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.8b Relation of health-related factors with 'no telephone contacts per week'

No telephone contacts/week	**CVD** **% (n)**	CVD **PR 95% CI**	CVD **PR 95% CI**	No CVD % (n)	No CVD PR 95% CI	**No CVD** PR 95% CI	**P-int**
Alcohol consumption							
No drinkers	6.4 (1382)	1.77 (1.64-1.91)		5.0 (3267)	1.79 (1.70-1.87)		<0.05
Moderate drinkers	4.0 (1066)	1		3.1 (3379)	1		
Heavy drinkers	5.3 (390)	1.09 (0.98-1.22)		4.8 (1447)	1.17 (1.10-1.25)		
Smoking status							
Current	9.1 (298)	1.89 (1.67-2.14)		6.6 (1049)	1.58 (1.48-1.69)		<0.05
Past	5.9 (1450)	1.12 (1.03-1.20)		4.3 (3061)	1.04 (1.00-1.09)		
Never	4.1 (1181)	1		3.4 (4160)	1		
BMI (kg/m2)							
Underweight (<18)	9.1 (70)	1.82 (1.45-2.29)		5.5 (128)	1.61 (1.36-1.91)		<0.05
Normal weight (18–<25)	5.5 (942)	1		3.7 (2727)	1		
Overweight Over weight (25–<30)	4.7 (977)	0.79 (0.72-0.86)		3.9 (2955)	0.88 (0.83-0.92)		
Obese ((30–30+)	5.2 (680)	0.94 (0.85-1.03)		4.2 (1772)	1.02 (0.96-1.09)		
Medical History: Cancer							
No	5.2 (2316)	1		4.0 (7249)	1		>0.05
Yes	4.8 (629)	0.85 (0.78-0.93)		3.6 (1068)	0.86 (0.81-0.92)		
Medical History: Diabetes							
No	4.9 (2325)	1		3.9 (7523)	1		>0.05
Yes	6.7 (620)	1.25 (1.15-1.36)		5.4 (794)	1.23 (1.15-1.32)		
Medical History: Osteoarthritis							
No	5.2 (2715)	1		4.0 (8026)	1		
Yes	4.3 (230)	1.09 (0.95-1.25)		2.9 (291)	0.95 (0.85-1.07)		>0.05

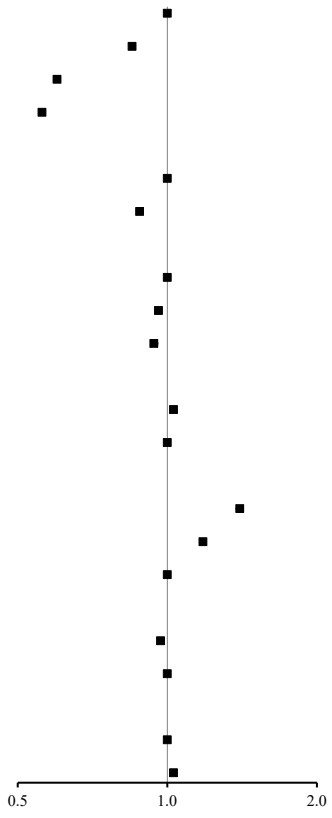


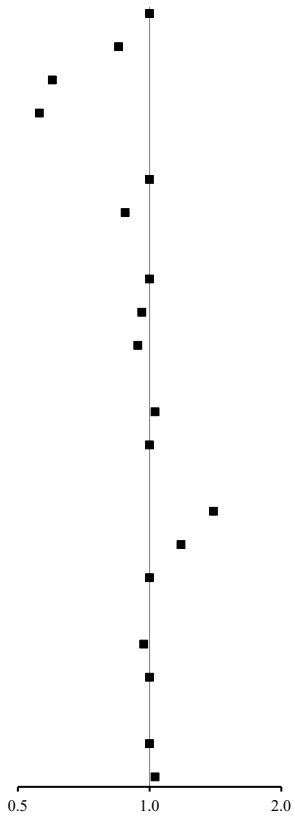


[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.9a Relation of sociodemographic factors with 'no social group meetings per week'

No social group meetings/week	**CVD**	CVD	CVD	No CVD	No CVD	**No CVD**	**P-int**
	% (n)	**PR 95% CI**	**PR 95% CI**	% (n)	PR 95% CI	PR 95% CI	
Age group (years)							
45-<55	52.4 (3082)	1		51.0 (36718)	1		<0.05
55-<65	44.7 (5942)	0.84 (0.81-0.86)		43.9 (31796)	0.85 (0.84-0.86)		
65-<75	33.7 (5706)	0.63 (0.61-0.65)		31.4 (12876)	0.60 (0.59-0.61)		
75-75+	32.8 (6882)	0.62 (0.60-0.64)		28.9 (6934)	0.56 (0.55-0.57)		
Sex							
Men	40.1 (12803)	1		44.4 (40734)	1		
Women	35.0 (8809)	0.83 (0.81-0.85)		40.4 (47590)	0.88 (0.87-0.89)		<0.05
Region							
Major cities	37.6 (11499)	1		42.7 (46313)	1		<0.05
Inner regional	37.8 (7376)	0.97 (0.95-0.99)		41.7 (30483)	0.96 (0.95-0.97)		
More remote	39.0 (2395)	1.00 (0.96-1.03)		41.1 (9732)	0.94 (0.93-0.96)		
Marital status							
Not currently married/defacto	37.1 (6357)	1.05 (1.03-1.08)		41.0 (19953)	1.03 (1.02-1.05)		>0.05
Married/defacto	38.2 (15108)	1		42.6 (67899)	1		
Highest Education							
No school certificate	43.3 (4076)	1.46 (1.41-1.51)		44.6 (9725)	1.40 (1.37-1.42)		<0.05
Certificate/diploma/trade	37.3 (13755)	1.16 (1.12-1.19)		42.8 (56649)	1.18 (1.16-1.19)		
Tertiary	35.1 (3303)	1		40.0 (20826)	1		
Language other than English							
Yes	37.8 (19684)	1.05 (1.01-1.09)		42.3 (79921)	0.97 (.-.)		<0.05
No	38.9 (1927)	1		41.1 (8403)	1		
County of Birth							
Australia/NZ	37.6 (16515)	1		42.3 (67971)	1		<0.05
Others	38.8 (4862)	1.05 (1.03-1.08)		42.1 (19760)	1.03 (1.01-1.04)		

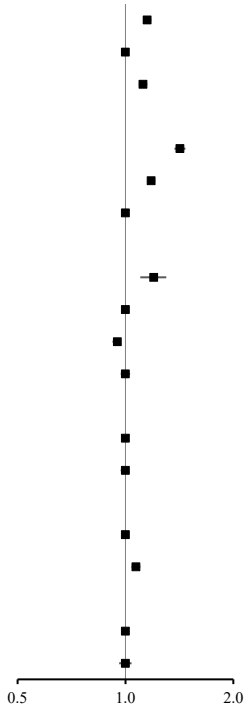




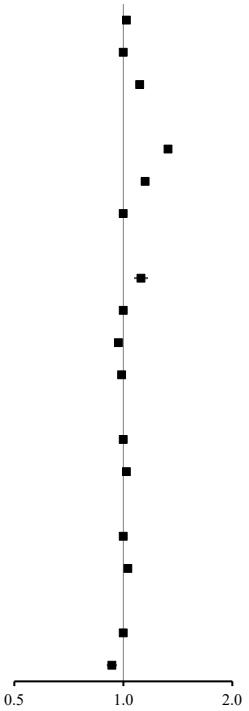
[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.9b Relation of health-related factors with 'no social group meetings per week'

No social group meetings/week	**CVD % (n)**	CVD **PR 95% CI**	CVD **PR 95% CI**	No CVD % (n)	No CVD PR 95% CI	**No CVD** PR 95% CI	**P-int**
Alcohol consumption							
No drinkers	39.8 (8614)	1.15 (1.13-1.18)		41.6 (26927)	1.02 (1.01-1.03)		<0.05
Moderate drinkers	35.4 (9395)	1		41.4 (45773)	1		
Heavy drinkers	42.6 (3110)	1.12 (1.09-1.15)		47.8 (14411)	1.11 (1.09-1.12)		
Smoking status							
Current	55.2 (1811)	1.42 (1.37-1.47)		56.7 (9081)	1.33 (1.32-1.35)		<0.05
Past	40.7 (10046)	1.18 (1.15-1.21)		44.9 (32102)	1.15 (1.13-1.16)		
Never	33.4 (9670)	1		38.7 (46851)	1		
BMI (kg/m2)							
Underweight (<18)	42.1 (323)	1.20 (1.10-1.30)		44.2 (1029)	1.12 (1.07-1.17)		<0.05
Normal weight (18–<25)	37.2 (6379)	1		41.9 (30808)	1		
Overweight Over weight (25–<30)	36.9 (7748)	0.95 (0.92-0.97)		41.9 (31978)	0.97 (0.96-0.98)		
Obese ((30–30+)	40.8 (5368)	1.00 (0.97-1.03)		43.9 (18385)	0.99 (0.98-1.00)		
Medical History: Cancer							
No	38.2 (16874)	1		42.6 (76702)	1		>0.05
Yes	36.5 (4738)	1.00 (0.97-1.02)		39.5 (11622)	1.02 (1.00-1.03)		
Medical History: Diabetes							
No	37.4 (17892)	1		42.3 (82362)	1		<0.05
Yes	40.0 (3720)	1.07 (1.04-1.10)		40.9 (5962)	1.03 (1.01-1.05)		
Medical History: Osteoarthritis							
No	38.2 (19805)	1		42.6 (85011)	1		<0.05
Yes	34.0 (1807)	1.00 (0.96-1.04)		33.1 (3313)	0.93 (0.90-0.96)		



PR (95% CI) on log scale

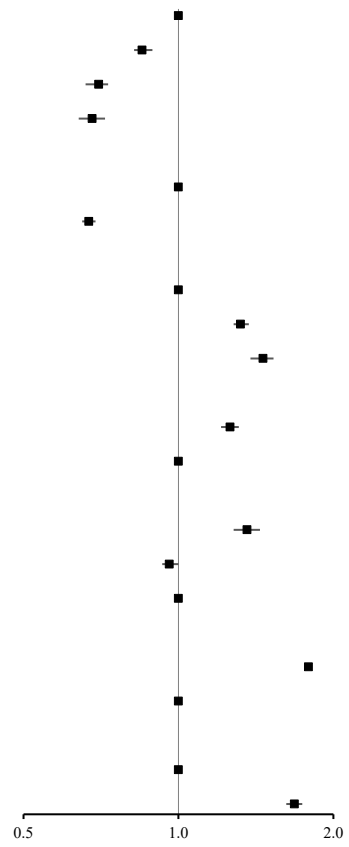


PR (95% CI) on log scale

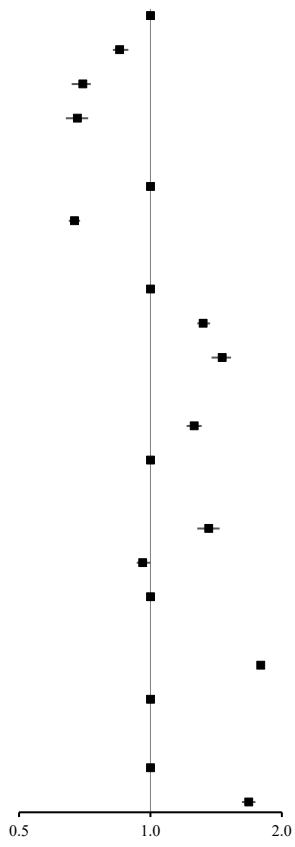
[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.10a Relation of sociodemographic factors with 'no people to depend on'

No people to depend on	**CVD**	CVD	CVD	No CVD	No CVD	**No CVD**	**P-int**
	% (n)	**PR 95% CI**	**PR 95% CI**	% (n)	PR 95% CI	PR 95% CI	
Age group (years)							
45-<55	8.4 (492)	1		7.3 (5217)	1		>0.05
55-<65	7.4 (988)	0.86 (0.78-0.96)		6.4 (4621)	0.85 (0.82-0.89)		
65-<75	5.9 (995)	0.68 (0.61-0.75)		5.4 (2204)	0.70 (0.66-0.73)		
75-75+	5.2 (1099)	0.65 (0.58-0.72)		5.0 (1195)	0.68 (0.64-0.72)		
Sex							
Men	6.9 (2196)	1		7.7 (7019)	1		<0.05
Women	5.5 (1378)	0.76 (0.71-0.81)		5.3 (6218)	0.67 (0.65-0.69)		
Region							
Major cities	5.2 (1592)	1		5.4 (5832)	1		>0.05
Inner regional	7.3 (1431)	1.38 (1.28-1.48)		7.1 (5191)	1.32 (1.28-1.37)		
More remote	7.9 (487)	1.48 (1.34-1.64)		7.9 (1869)	1.46 (1.38-1.53)		
Marital status							
Not currently married/defacto	6.7 (1145)	1.24 (1.16-1.34)		7.0 (3395)	1.26 (1.21-1.31)		>0.05
Married/defacto	6.1 (2407)	1		6.1 (9747)	1		
Highest Education							
No school certificate	7.0 (660)	1.20 (1.08-1.34)		7.8 (1702)	1.36 (1.28-1.44)		>0.05
Certificate/diploma/trade	6.0 (2220)	0.98 (0.90-1.07)		6.0 (7960)	0.96 (0.93-1.00)		
Tertiary	6.4 (602)	1		6.5 (3366)	1		
Language other than English							
Yes	5.9 (3100)	1.86 (.-.)		6.0 (11316)	1.79 (.-.)		>0.05
No	9.6 (474)	1		9.4 (1921)	1		
County of Birth							
Australia/NZ	5.7 (2504)	1		5.7 (9120)	1		>0.05
Others	8.3 (1034)	1.60 (1.49-1.71)		8.5 (3985)	1.68 (1.62-1.74)		



PR (95% CI) on log scale

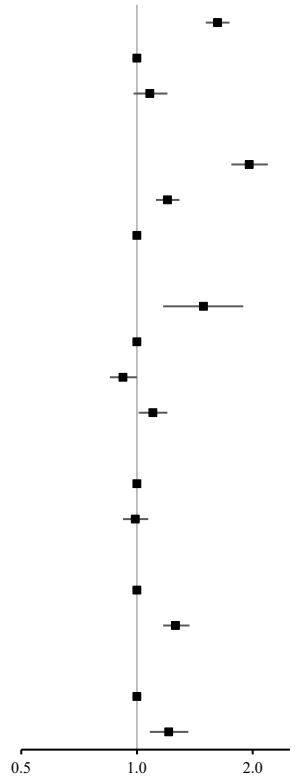


PR (95% CI) on log scale

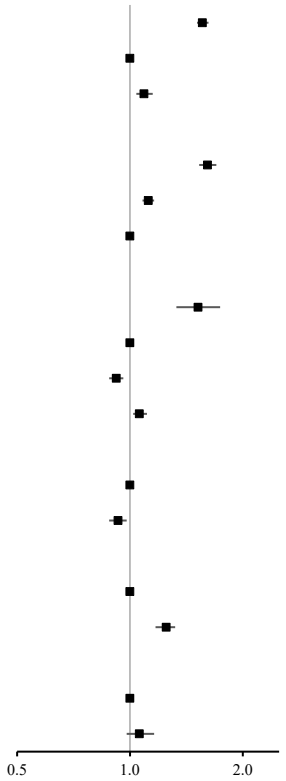
[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.10b Relation of health-related factors with 'no people to depend on'

No people to depend on	**CVD**	CVD	CVD	No CVD	No CVD	**No CVD**	**P-intert**
	% (n)	**PR 95% CI**	**PR 95% CI**	% (n)	PR 95% CI	PR 95% CI	
Alcohol consumption							
No drinkers	7.6 (1640)	1.62 (1.51-1.74)		7.7 (4997)	1.56 (1.51-1.62)		>0.05
Moderate drinkers	5.1 (1361)	1		5.4 (5918)	1		
Heavy drinkers	6.3 (460)	1.08 (0.98-1.20)		6.9 (2070)	1.09 (1.04-1.15)		
Smoking status							
Current	11.8 (388)	1.96 (1.76-2.19)		10.1 (1613)	1.61 (1.53-1.70)		<0.05
Past	6.7 (1659)	1.20 (1.12-1.29)		6.7 (4780)	1.12 (1.08-1.16)		
Never	5.2 (1512)	1		5.6 (6786)	1		
BMI (kg/m2)							
Underweight (<18)	8.3 (64)	1.49 (1.17-1.89)		8.6 (199)	1.52 (1.33-1.74)		>0.05
Normal weight (18–<25)	5.9 (1020)	1		6.1 (4487)	1		
Overweight Over weight (25–<30)	5.9 (1235)	0.92 (0.85-1.00)		6.1 (4660)	0.92 (0.88-0.96)		
Obese ((30–30+)	7.3 (957)	1.10 (1.01-1.20)		7.0 (2930)	1.06 (1.02-1.11)		
Medical History: Cancer							
No	6.3 (2792)	1		6.4 (11576)	1		>0.05
Yes	6.0 (782)	0.99 (0.92-1.07)		5.7 (1661)	0.93 (0.88-0.98)		
Medical History: Diabetes							
No	6.0 (2873)	1		6.2 (12126)	1		>0.05
Yes	7.5 (701)	1.26 (1.17-1.37)		7.6 (1111)	1.25 (1.17-1.32)		
Medical History: Osteoarthritis							
No	6.3 (3243)	1		6.4 (12711)	1		<0.05
Yes	6.2 (331)	1.21 (1.08-1.36)		5.3 (526)	1.06 (0.98-1.16)		



PR (95% CI) on log scale



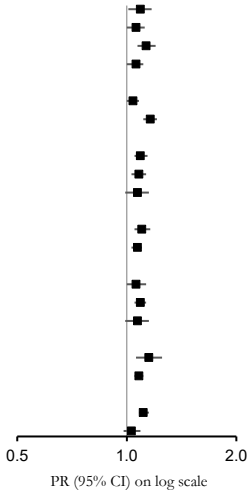
PR (95% CI) on log scale

[1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.11 No social interaction: Prevalence of and adjusted prevalence ratios (PRs) for no social interaction among population subgroups based on socio-demographic factors

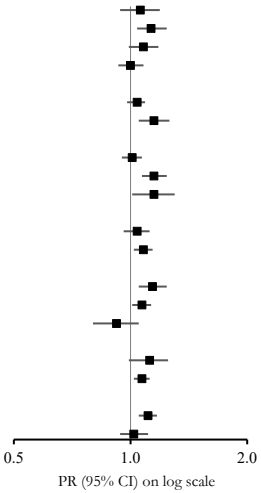
a: No social visits/week

	CVD	No CVD	*PR (95% CI)	P-heterogeneity
Age group (years)				
45-<55	12.4 (715/5765)	10.9 (7694/70619)	1.09 (1.01-1.17)	0.3422
55-<65	10.5 (1358/12932)	9.2 (6493/70881)	1.06 (1.00-1.12)	
65-<75	10.7 (1743/16222)	8.9 (3537/39537)	1.13 (1.07-1.20)	
75-75+	13.1 (2541/19415)	11.9 (2659/22324)	1.06 (1.00-1.11)	
Sex				
Men	13.4 (4076/30411)	12.5 (11160/89049)	1.04 (1.00-1.08)	0.0002
Women	9.5 (2281/23923)	8.1 (9223/114312)	1.16 (1.11-1.21)	
Region				
Major cities	10.8 (3128/29054)	9.2 (9643/105315)	1.09 (1.05-1.14)	0.9014
Inner regional	12.2 (2275/18602)	10.4 (7424/71248)	1.08 (1.03-1.13)	
More remote	14.6 (845/5792)	12.6 (2876/22873)	1.07 (0.99-1.15)	
Marital status				
Not currently	12.8 (2058/16054)	10.8 (5039/46628)	1.10 (1.05-1.16)	0.3639
Married/defacto	11.2 (4235/37900)	9.8 (15192/155625)	1.07 (1.03-1.10)	
Highest Education				
No school certificate	15.1 (1324/8744)	13.6 (2800/20536)	1.06 (1.00-1.13)	0.7187
	11.1 (3925/35268)	9.8 (12661/128863)	1.09 (1.05-1.13)	
Tertiary	9.6 (882/9145)	8.9 (4548/51311)	1.07 (0.99-1.15)	
Language other than				
Yes	14.9 (687/4614)	12.8 (2499/19497)	1.15 (1.06-1.25)	0.1571
No	11.4 (5670/49719)	9.7 (17884/183863)	1.08 (1.05-1.11)	
County of Birth				
Australia/NZ	11.0 (4607/41824)	9.3 (14513/156579)	1.11 (1.08-1.15)	0.0176
Others	13.8 (1650/11918)	12.5 (5683/45299)	1.03 (0.98-1.09)	



b: No telephone contacts/week

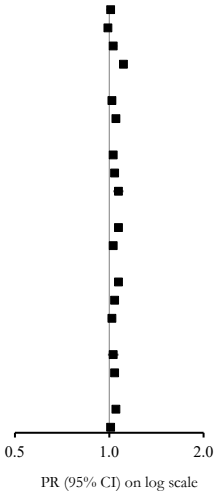
	CVD	No CVD	*PR (95% CI)	P-heterogeneity
Age group (years)				
45-<55	5.1 (295/5758)	4.4 (3082/70662)	1.06 (0.94-1.19)	0.2089
55-<65	4.5 (582/12932)	3.4 (2390/70953)	1.13 (1.04-1.24)	
65-<75	4.7 (770/16285)	3.8 (1491/39664)	1.08 (0.99-1.18)	
75-75+	6.7 (1298/19472)	6.0 (1354/22473)	1.00 (0.93-1.08)	
Sex				
Men	7.4 (2262/30379)	6.3 (5627/88993)	1.04 (0.98-1.09)	0.0619
Women	2.8 (683/24068)	2.3 (2690/114759)	1.15 (1.05-1.26)	
Region				
Major cities	5.3 (1537/29054)	4.2 (4447/105399)	1.01 (0.95-1.07)	0.0141
Inner regional	5.5 (1027/18692)	3.9 (2768/71385)	1.15 (1.07-1.24)	
More remote	5.9 (343/5820)	4.1 (951/23023)	1.15 (1.01-1.30)	
Marital status				
Not currently	5.7 (920/16136)	4.9 (2292/46742)	1.04 (0.96-1.12)	0.4364
Married/defacto	5.3 (1999/37941)	3.8 (5941/155903)	1.08 (1.02-1.14)	
Highest Education				
No school certificate	9.3 (815/8770)	7.3 (1493/20560)	1.14 (1.05-1.24)	0.0307
	4.9 (1720/35345)	4.0 (5122/129166)	1.07 (1.01-1.13)	
Tertiary	3.2 (289/9156)	2.9 (1511/51359)	0.92 (0.80-1.05)	
Language other than				
Yes	8.5 (393/4601)	6.0 (1167/19527)	1.12 (0.99-1.25)	0.4761
No	5.1 (2552/49845)	3.9 (7150/184224)	1.07 (1.02-1.12)	
County of Birth				
Australia/NZ	4.9 (2043/41973)	3.7 (5798/156876)	1.11 (1.05-1.17)	0.0947
Others	7.2 (850/11877)	5.3 (2414/45373)	1.02 (0.94-1.11)	



b

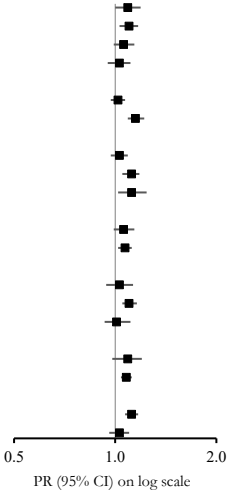
c: No social group meetings

	CVD	No CVD	*PR (95% CI)	P-heterogeneity
Age group (years)				
45-<55	54.6 (3082/5641)	53.2 (36718/69064)	1.01 (0.98-1.03)	<0.001
55-<65	47.1 (5942/12605)	46.1 (31796/68955)	0.99 (0.97-1.01)	
65-<75	36.1 (5706/15811)	33.4 (12876/38550)	1.03 (1.01-1.06)	
75-75+	36.3 (6882/18948)	31.8 (6934/21789)	1.11 (1.08-1.14)	
Sex				
Men	43.2 (12803/29618)	46.8 (40734/86981)	1.02 (1.00-1.04)	0.0377
Women	37.7 (8809/23387)	42.7 (47590/111377)	1.05 (1.03-1.07)	
Region				
Major cities	40.6 (11499/28331)	45.1 (46313/102672)	1.03 (1.02-1.05)	0.1638
Inner regional	40.5 (7376/18194)	43.9 (30483/69510)	1.04 (1.02-1.06)	
More remote	42.6 (2395/5616)	43.6 (9732/22329)	1.07 (1.03-1.11)	
Marital status				
Not currently	40.6 (6357/15658)	43.8 (19953/45546)	1.07 (1.04-1.09)	0.0070
Married/defacto	40.8 (15108/36991)	44.7 (67899/151752)	1.03 (1.01-1.04)	
Highest Education				
No school certificate	48.2 (4076/8454)	49.2 (9725/19751)	1.07 (1.04-1.10)	0.0632
Certificate/diploma/trade	40.0 (13755/34415)	45.1 (56649/125482)	1.04 (1.02-1.05)	
Tertiary	36.7 (3303/9002)	41.2 (20826/50589)	1.02 (0.99-1.05)	
Language other than				
Yes	43.2 (1927/4459)	44.4 (8403/18939)	1.03 (0.99-1.07)	0.6361
No	40.5 (19684/48544)	44.5 (79921/179418)	1.04 (1.03-1.05)	
County of Birth				
Australia/NZ	40.4 (16515/40846)	44.5 (67971/152728)	1.05 (1.03-1.06)	0.0076
Others	42.0 (4862/11575)	44.7 (19760/44196)	1.01 (0.99-1.04)	



d: No people to depend on

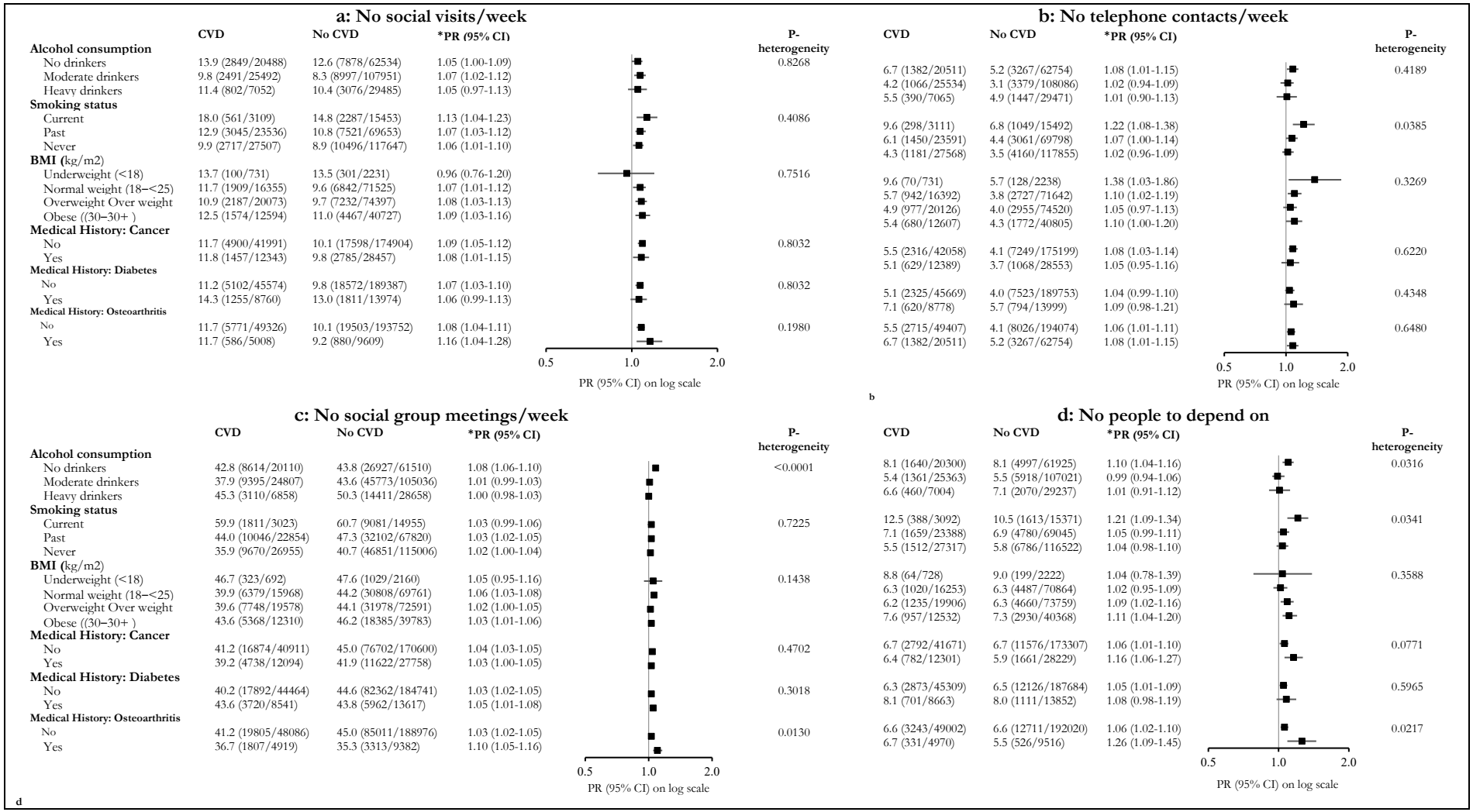
	CVD	No CVD	*PR (95%	P-heterogeneity
Age group (years)				
45-<55	8.6 (492/5718)	7.5 (5217/69973)	1.09 (1.00-1.19)	0.5976
55-<65	7.7 (988/12829)	6.6 (4621/70216)	1.10 (1.03-1.17)	
65-<75	6.2 (995/16051)	5.6 (2204/39152)	1.06 (0.99-1.14)	
75-75+	5.7 (1099/19374)	5.4 (1195/22195)	1.03 (0.95-1.11)	
Sex				
Men	7.3 (2196/30133)	8.0 (7019/88114)	1.02 (0.97-1.07)	0.0016
Women	5.8 (1378/23839)	5.5 (6218/113422)	1.15 (1.09-1.22)	
Region				
Major cities	5.5 (1592/28855)	5.6 (5832/104350)	1.03 (0.97-1.09)	0.1022
Inner regional	7.7 (1431/18515)	7.4 (5191/70568)	1.12 (1.05-1.18)	
More remote	8.5 (487/5738)	8.2 (1869/22729)	1.12 (1.02-1.24)	
Marital status				
Not currently	7.1 (1145/16061)	7.3 (3395/46445)	1.06 (0.99-1.14)	0.8279
Married/defacto	6.4 (2407/37543)	6.3 (9747/153997)	1.07 (1.02-1.12)	
Highest Education				
No school certificate	7.6 (660/8716)	8.4 (1702/20372)	1.03 (0.94-1.13)	0.1761
Certificate/diploma/trade	6.3 (2220/35010)	6.2 (7960/127674)	1.10 (1.05-1.16)	
Tertiary	6.6 (602/9069)	6.6 (3366/50864)	1.01 (0.93-1.11)	
Language other than				
Yes	10.5 (474/4507)	10.1 (1921/19031)	1.09 (0.98-1.20)	0.8670
No	6.3 (3100/49464)	6.2 (11316/182504)	1.08 (1.04-1.12)	
County of Birth				
Australia/NZ	6.0 (2504/41641)	5.9 (9120/155408)	1.12 (1.07-1.17)	0.0437
Others	8.8 (1034/11731)	8.9 (3985/44660)	1.03 (0.96-1.10)	



d

*Prevalence ratio, adjusted for age-group, sex, region of residence and education

Figure S6.1.12 No social interaction: Prevalence of and adjusted prevalence ratios (PRs) for no social interaction among population subgroups based on health-related factors

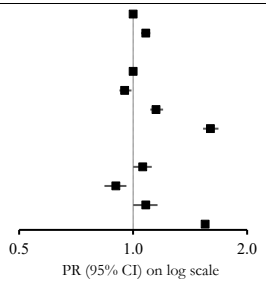


*Prevalence ratio, adjusted for age-group, sex, region of residence and education

Figure S6.1.13 No social interaction: Prevalence of and adjusted prevalence ratios (PRs) for no social interaction according to joint categories of CVD and physical functioning limitations

a: No social visits/week

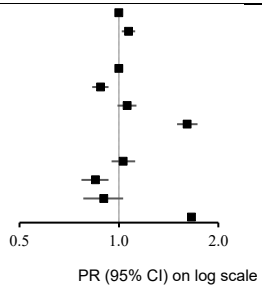
	% (n/N)	[1]PR (95% CI)
Without CVD	11.7 (6357/54334)	1
With CVD	10.0 (20383/203361)	1.08 (1.05-1.11)
No CVD and		
No limitations	9.3 (6543/70200)	1
Minor limitations	8.7 (4719/54282)	0.95 (0.92-0.99)
Moderate limitations	10.2 (3997/39175)	1.15 (1.11-1.20)
Severe limitations	14.6 (2340/16053)	1.60 (1.53-1.68)
CVD and		
No limitations	10.1 (685/6807)	1.06 (0.98-1.14)
Minor limitations	8.6 (932/10857)	0.90 (0.84-0.96)
Moderate limitations	10.2 (1514/14892)	1.08 (1.02-1.14)
Severe limitations	14.7 (1962/13338)	1.55 (1.47-1.63)



a

b: No telephone contacts/week

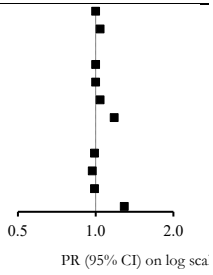
	% (n/N)	[1]PR (95% CI)
Without CVD	4.1 (8317/203752)	1
With CVD	5.4 (2945/54447)	1.07 (1.02-1.12)
No CVD and		
No limitations	3.8 (2686/70247)	1
Minor limitations	3.3 (1811/54312)	0.88 (0.83-0.93)
Moderate limitations	3.9 (1533/39244)	1.06 (0.99-1.13)
Severe limitations	6.4 (1026/16114)	1.61 (1.50-1.73)
CVD and		
No limitations	4.4 (299/6811)	1.03 (0.92-1.16)
Minor limitations	3.8 (417/10893)	0.85 (0.77-0.94)
Moderate limitations	4.0 (603/14907)	0.90 (0.82-0.98)
Severe limitations	7.6 (1021/13351)	1.66 (1.54-1.79)



b

c: No social group meetings/week

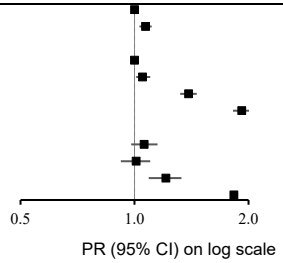
	% (n/N)	[1]PR (95% CI)
Without CVD	44.5 (88324/198358)	1
With CVD	40.8 (21612/53005)	1.04 (1.03-1.05)
No CVD and		
No limitations	46.3 (31686/68405)	1
Minor limitations	43.4 (23066/53163)	1.00 (0.99-1.01)
Moderate limitations	43.0 (16550/38474)	1.04 (1.02-1.05)
Severe limitations	48.6 (7644/15731)	1.18 (1.16-1.20)
CVD and		
No limitations	42.2 (2796/6622)	0.99 (0.96-1.02)
Minor limitations	37.9 (4048/10671)	0.97 (0.94-0.99)
Moderate limitations	37.0 (5402/14598)	0.99 (0.97-1.01)
Severe limitations	47.4 (6205/13088)	1.29 (1.26-1.31)



c

d: No people to depend on

	% (n/N)	[1]PR (95% CI)
Without CVD	6.6 (13237/201536)	1
With CVD	6.6 (3574/53972)	1.07 (1.03-1.11)
No CVD and		
No limitations	5.9 (4086/69584)	1
Minor limitations	5.9 (3170/53755)	1.05 (1.01-1.10)
Moderate limitations	7.2 (2773/38757)	1.39 (1.32-1.46)
Severe limitations	9.7 (1545/15911)	1.92 (1.82-2.04)
CVD and		
No limitations	5.9 (400/6755)	1.06 (0.96-1.17)
Minor limitations	5.4 (578/10772)	1.01 (0.93-1.10)
Moderate limitations	5.9 (866/14729)	1.21 (1.12-1.30)
Severe limitations	8.5 (1122/13254)	1.83 (1.71-1.95)



d

[1]Adjusted for age-group, sex, region of residence and education. Effect sizes were estimated using 'no CVD and No limitations' as the reference group.

S6.1.6 Supplementary analysis II: CVD subtypes and physical functional limitation

Table S6.1.5 CVD and CVD subtypes along with physical functioning limitations

	CVD	*Ischaemic heart disease*	*Myocardial infarction*	*Cerebrovascular disease*	*Peripheral arterial diseases*	*Heart failure*	**No CVD**
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
Physical functioning limitations							
No limitations	12.3 (7023)	8.9 (1529)	9.6 (392)	6.4 (214)	4.7 (175)	2.0 (70)	34.2 (71720)
Minor limitations	19.5 (11151)	17.7 (3031)	17.5 (719)	10.0 (336)	11.2 (418)	5.8 (208)	26.4 (55216)
Moderate limitations	26.9 (15341)	26.2 (4479)	25.1 (1032)	22.0 (739)	23.8 (891)	18.1 (645)	19.1 (39979)
Severe limitations	24.5 (13973)	28.4 (4853)	29.1 (1194)	38.9 (1306)	38.4 (1435)	50.6 (1804)	8.0 (16654)

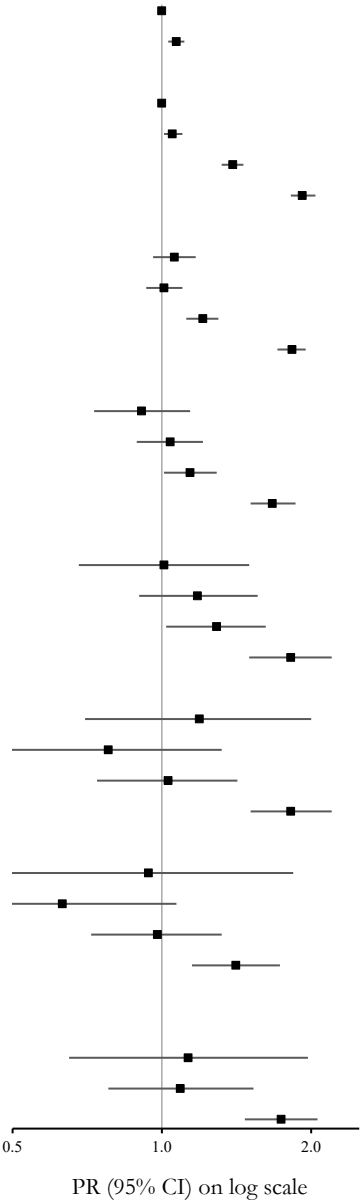
Figure S6.1.14 Social isolation: Prevalence of and adjusted prevalence ratios according to joint categories of CVD subtypes and physical functioning limitations

	Social isolation	**[1]PR (95% CI) of social isolation**	
	% (n/N)	PR (95% CI)	
Without CVD (Reference)	19.2 (36426/190142)	1	
With CVD [a]	19.7 (9785/49746)	1.05 (1.03-1.07)	
No CVD and			
No limitations (Reference)	18.6 (12265/66100)	1	
Minor limitations	17.1 (8832/51521)	0.98 (0.95-1.00)	
Moderate limitations	19.4 (7172/37047)	1.17 (1.14-1.21)	
Severe limitations	25.3 (3782/14947)	1.53 (1.48-1.58)	
CVD [a] and			
No limitations	17.9 (1136/6345)	1.00 (0.95-1.06)	
Minor limitations	15.3 (1569/10232)	0.90 (0.86-0.94)	
Moderate limitations	17.2 (2391/13931)	1.06 (1.01-1.10)	
Severe limitations	24.6 (3017/12256)	1.53 (1.48-1.59)	
Ischaemic heart disease [b] and			
No limitations	17.5 (236/1352)	0.93 (0.83-1.05)	
Minor limitations	14.9 (415/2777)	0.84 (0.77-0.92)	
Moderate limitations	17.7 (714/4025)	1.04 (0.97-1.11)	
Severe limitations	24.8 (1040/4191)	1.48 (1.40-1.57)	
Myocardial infarction [b] and			
No limitations	21.5 (74/344)	1.08 (0.88-1.32)	
Minor limitations	15.0 (99/658)	0.81 (0.67-0.97)	
Moderate limitations	19.6 (181/922)	1.10 (0.96-1.25)	
Severe limitations	26.4 (270/1024)	1.56 (1.41-1.73)	
Cerebrovascular disease [b] and			
No limitations	20.7 (39/188)	1.15 (0.87-1.52)	
Minor limitations	14.7 (44/300)	0.85 (0.65-1.11)	
Moderate limitations	18.6 (123/661)	1.11 (0.95-1.30)	
Severe limitations	28.3 (317/1119)	1.69 (1.54-1.86)	
Peripheral arterial diseases [b] and			
No limitations	20.1 (30/149)	1.19 (0.87-1.63)	
Minor limitations	14.9 (56/376)	0.86 (0.68-1.10)	
Moderate limitations	17.4 (137/787)	1.02 (0.88-1.19)	
Severe limitations	24.7 (304/1231)	1.45 (1.31-1.60)	
Heart failure [b] and			
No limitations	16.4 (9/55)	0.90 (0.49-1.66)	
Minor limitations	19.4 (35/180)	1.09 (0.81-1.47)	
Moderate limitations	19.2 (108/563)	1.15 (0.97-1.36)	
Severe limitations	26.4 (400/1514)	1.59 (1.46-1.73)	
			0.4 0.8 1.6
			PR (95% CI) on log scale

,[a] Based on self-report and hospital records, [b]Based on hospital records only and without any other CVD subtypes. Effect sizes were estimated using 'no CVD and No limitations' as the reference group. [1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.15 No social visits per week: Prevalence of and adjusted prevalence ratios according to joint categories of CVD subtypes and physical functioning limitations

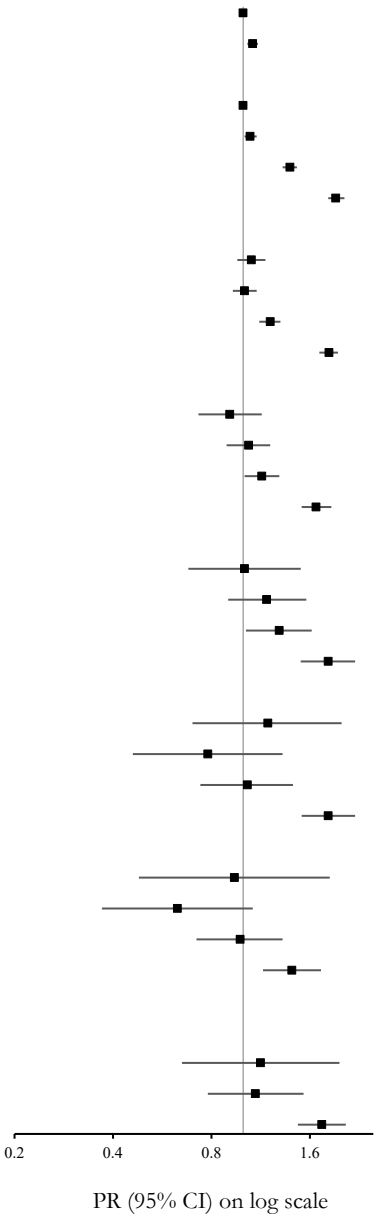
	No social visits/week	**[1]PR (95% CI) of no social visits/week**
	% (n/N)	PR (95% CI)
Without CVD (Reference)	11.7 (6357/54334)	1
With CVD [a]	10.0 (20383/203361)	1.08 (1.05-1.11)
No CVD and		
No limitations (Reference)	9.3 (6543/70200)	1
Minor limitations	8.7 (4719/54282)	0.95 (0.92-0.99)
Moderate limitations	10.2 (3997/39175)	1.15 (1.11-1.20)
Severe limitations	14.6 (2340/16053)	1.60 (1.53-1.68)
CVD [a] and		
No limitations	10.1 (685/6807)	1.06 (0.98-1.14)
Minor limitations	8.6 (932/10857)	0.90 (0.84-0.96)
Moderate limitations	10.2 (1514/14892)	1.08 (1.02-1.14)
Severe limitations	14.7 (1962/13338)	1.55 (1.47-1.63)
Ischaemic heart disease [b] and		
No limitations	10.8 (158/1468)	1.06 (0.91-1.23)
Minor limitations	8.5 (250/2937)	0.85 (0.75-0.96)
Moderate limitations	10.5 (453/4325)	1.05 (0.96-1.15)
Severe limitations	15.6 (718/4602)	1.56 (1.45-1.68)
Myocardial infarction [b] and		
No limitations	13.4 (50/374)	1.24 (0.95-1.60)
Minor limitations	8.2 (57/692)	0.79 (0.62-1.02)
Moderate limitations	12.1 (119/987)	1.17 (0.98-1.38)
Severe limitations	16.4 (186/1131)	1.63 (1.42-1.86)
Cerebrovascular disease [b] and		
No limitations	14.4 (30/208)	1.46 (1.05-2.04)
Minor limitations	8.0 (26/327)	0.80 (0.55-1.15)
Moderate limitations	10.8 (77/713)	1.09 (0.88-1.35)
Severe limitations	18.1 (224/1240)	1.78 (1.58-2.02)
Peripheral arterial diseases [b] and		
No limitations	9.6 (16/166)	1.01 (0.64-1.61)
Minor limitations	10.9 (43/393)	1.08 (0.81-1.43)
Moderate limitations	11.7 (100/853)	1.15 (0.96-1.39)
Severe limitations	16.8 (227/1355)	1.63 (1.44-1.84)
Heart failure [b] and		
No limitations	12.7 (8/63)	1.24 (0.65-2.39)
Minor limitations	14.9 (29/194)	1.41 (1.01-1.97)
Moderate limitations	14.5 (89/614)	1.43 (1.18-1.74)
Severe limitations	15.6 (264/1688)	1.54 (1.37-1.72)



.,[a] Based on self-report and hospital records, [b]Based on hospital records only and without any other CVD subtypes. Effect sizes were estimated using 'no CVD and No limitations' as the reference group. [1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.16 No telephone contacts per week: Prevalence of and adjusted prevalence ratios according to joint categories of CVD subtypes and physical functioning limitations

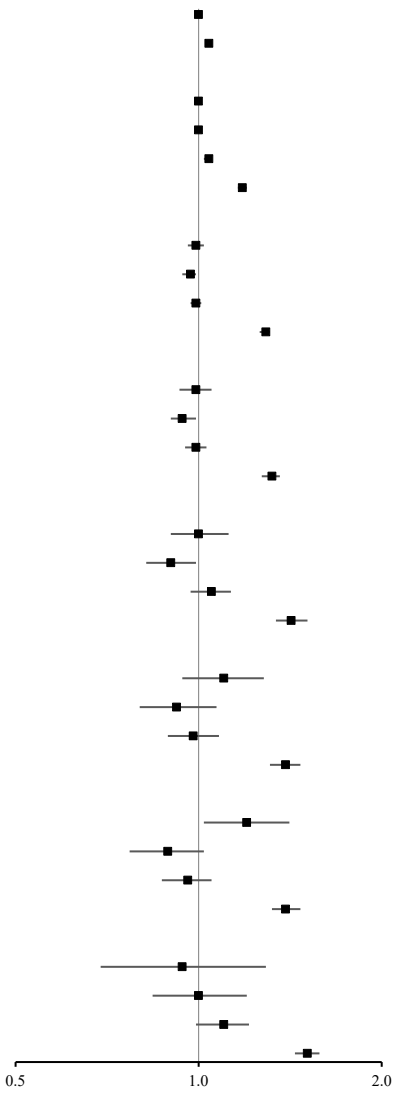
	No telephone contacts/week	**[1]PR (95% CI) of no telephone contacts/week**
	% (n/N)	PR95%CI
Without CVD (Reference)	4.1 (8317/203752)	1
With CVD [a]	5.4 (2945/54447)	1.07 (1.02-1.12)
No CVD and		
No limitations (Reference)	3.8 (2686/70247)	1
Minor limitations	3.3 (1811/54312)	0.88 (0.83-0.93)
Moderate limitations	3.9 (1533/39244)	1.06 (0.99-1.13)
Severe limitations	6.4 (1026/16114)	1.61 (1.50-1.73)
CVD [a] and		
No limitations	4.4 (299/6811)	1.03 (0.92-1.16)
Minor limitations	3.8 (417/10893)	0.85 (0.77-0.94)
Moderate limitations	4.0 (603/14907)	0.90 (0.82-0.98)
Severe limitations	7.6 (1021/13351)	1.66 (1.54-1.79)
Ischaemic heart disease [b] and		
No limitations	5.2 (76/1466)	1.03 (0.82-1.29)
Minor limitations	4.5 (133/2946)	0.88 (0.74-1.05)
Moderate limitations	4.7 (205/4331)	0.92 (0.80-1.06)
Severe limitations	7.8 (360/4599)	1.50 (1.35-1.68)
Myocardial infarction [b] and		
No limitations	6.4 (24/373)	1.17 (0.80-1.73)
Minor limitations	4.7 (33/696)	0.89 (0.64-1.25)
Moderate limitations	4.8 (48/991)	0.90 (0.69-1.19)
Severe limitations	9.3 (105/1131)	1.78 (1.47-2.14)
Cerebrovascular disease [b] and		
No limitations	6.4 (13/204)	1.27 (0.75-2.15)
Minor limitations	2.2 (7/325)	0.43 (0.21-0.89)
Moderate limitations	5.2 (37/714)	1.02 (0.74-1.39)
Severe limitations	12.0 (148/1231)	2.27 (1.94-2.66)
Peripheral arterial diseases [b] and		
No limitations	6.0 (10/166)	1.30 (0.72-2.36)
Minor limitations	2.7 (11/403)	0.51 (0.28-0.91)
Moderate limitations	5.0 (43/856)	0.94 (0.70-1.25)
Severe limitations	9.6 (131/1367)	1.74 (1.47-2.06)
Heart failure [b] and		
No limitations	-	-
Minor limitations	6.6 (13/197)	1.22 (0.72-2.07)
Moderate limitations	4.9 (30/617)	0.93 (0.66-1.32)
Severe limitations	8.0 (134/1681)	1.50 (1.27-1.78)



[a] Based on self-report and hospital records, [b]Based on hospital records only and without any other CVD subtypes. Effect sizes were estimated using 'no CVD and No limitations' as the reference group. [1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.17 No social group meetings per week: Prevalence of and adjusted prevalence ratios according to joint categories of CVD subtypes and physical functioning limitations

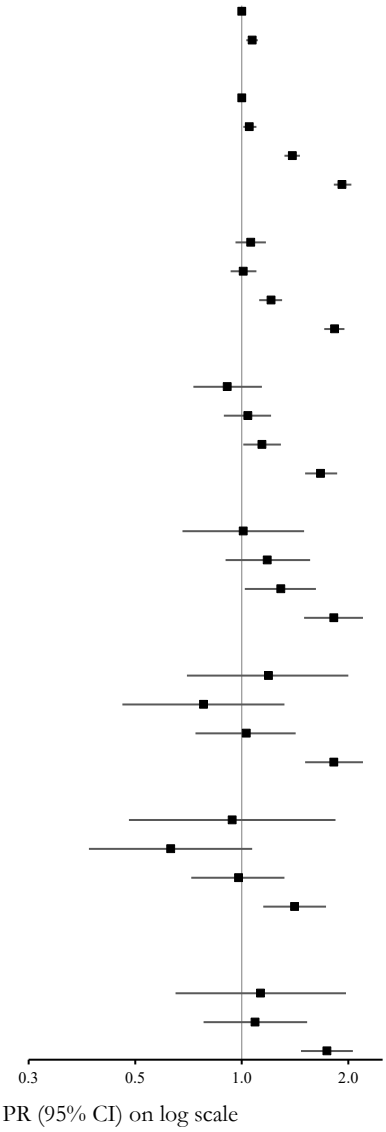
	No social group meetings/week	**[1]PR (95% CI) of no social group meetings/week**
	% (n/N)	PR95%CI
Without CVD (Reference)	44.5 (88324/198358)	1
With CVD [a]	40.8 (21612/53005)	1.04 (1.03-1.05)
No CVD and		
No limitations (Reference)	46.3 (31686/68405)	1
Minor limitations	43.4 (23066/53163)	1.00 (0.99-1.01)
Moderate limitations	43.0 (16550/38474)	1.04 (1.02-1.05)
Severe limitations	48.6 (7644/15731)	1.18 (1.16-1.20)
CVD [a] and		
No limitations	42.2 (2796/6622)	0.99 (0.96-1.02)
Minor limitations	37.9 (4048/10671)	0.97 (0.94-0.99)
Moderate limitations	37.0 (5402/14598)	0.99 (0.97-1.01)
Severe limitations	47.4 (6205/13088)	1.29 (1.26-1.31)
Ischaemic heart disease [b] and		
No limitations	42.4 (601/1419)	0.99 (0.93-1.05)
Minor limitations	37.1 (1071/2886)	0.94 (0.90-0.99)
Moderate limitations	37.3 (1582/4240)	0.99 (0.95-1.03)
Severe limitations	48.4 (2182/4509)	1.32 (1.27-1.36)
Myocardial infarction [b] and		
No limitations	44.3 (162/366)	1.00 (0.90-1.12)
Minor limitations	37.0 (253/683)	0.90 (0.82-0.99)
Moderate limitations	41.1 (398/969)	1.05 (0.97-1.13)
Severe limitations	52.4 (580/1107)	1.42 (1.34-1.51)
Cerebrovascular disease [b] and		
No limitations	46.0 (91/198)	1.10 (0.94-1.28)
Minor limitations	35.0 (112/320)	0.92 (0.80-1.07)
Moderate limitations	35.6 (250/702)	0.98 (0.89-1.08)
Severe limitations	50.5 (608/1203)	1.39 (1.31-1.47)
Peripheral arterial diseases [b] and		
No limitations	48.1 (76/158)	1.20 (1.02-1.41)
Minor limitations	33.6 (133/396)	0.89 (0.77-1.02)
Moderate limitations	34.7 (291/838)	0.96 (0.87-1.05)
Severe limitations	51.1 (679/1329)	1.39 (1.32-1.47)
Heart failure [b] and		
No limitations	39.3 (24/61)	0.94 (0.69-1.29)
Minor limitations	37.9 (72/190)	1.00 (0.84-1.20)
Moderate limitations	38.9 (231/594)	1.10 (0.99-1.21)
Severe limitations	53.4 (883/1653)	1.51 (1.44-1.58)



[a] Based on self-report and hospital records, [b]Based on hospital records only and without any other CVD subtypes. Effect sizes were estimated using 'no CVD and No limitations' as the reference group. [1]Adjusted for age, sex, region of residence and education attainment

Figure S6.1.18 No people to depend on: Prevalence of and adjusted prevalence ratios according to joint categories of CVD subtypes and physical functioning limitations

	No people to depend on	**[1]PR (95% CI) of No people to depend on**
	% (n/N)	PR95%CI
Without CVD (Reference)	6.6 (13237/201536)	1
With CVD [a]	6.6 (3574/53972)	1.07 (1.03-1.11)
No CVD and		
No limitations (Reference)	5.9 (4086/69584)	1
Minor limitations	5.9 (3170/53755)	1.05 (1.01-1.10)
Moderate limitations	7.2 (2773/38757)	1.39 (1.32-1.46)
Severe limitations	9.7 (1545/15911)	1.92 (1.82-2.04)
CVD [a] and		
No limitations	5.9 (400/6755)	1.06 (0.96-1.17)
Minor limitations	5.4 (578/10772)	1.01 (0.93-1.10)
Moderate limitations	5.9 (866/14729)	1.21 (1.12-1.30)
Severe limitations	8.5 (1122/13254)	1.83 (1.71-1.95)
Ischaemic heart disease [b] and		
No limitations	5.3 (77/1452)	0.91 (0.73-1.14)
Minor limitations	5.6 (164/2920)	1.04 (0.89-1.21)
Moderate limitations	5.8 (247/4285)	1.14 (1.01-1.29)
Severe limitations	7.9 (365/4593)	1.67 (1.51-1.86)
Myocardial infarction [b] and		
No limitations	6.3 (23/367)	1.01 (0.68-1.50)
Minor limitations	6.8 (47/695)	1.18 (0.90-1.56)
Moderate limitations	6.8 (67/979)	1.29 (1.02-1.62)
Severe limitations	8.7 (98/1130)	1.82 (1.50-2.20)
Cerebrovascular disease [b] and		
No limitations	6.4 (13/203)	1.19 (0.70-2.00)
Minor limitations	4.0 (13/327)	0.78 (0.46-1.32)
Moderate limitations	4.9 (35/709)	1.03 (0.74-1.42)
Severe limitations	8.6 (106/1228)	1.82 (1.51-2.20)
Peripheral arterial diseases [b] and		
No limitations	4.8 (8/166)	0.94 (0.48-1.84)
Minor limitations	3.2 (13/404)	0.63 (0.37-1.07)
Moderate limitations	4.8 (41/850)	0.98 (0.72-1.32)
Severe limitations	6.8 (91/1339)	1.41 (1.15-1.73)
Heart failure [b] and		
No limitations	-	-
Minor limitations	6.2 (12/195)	1.13 (0.65-1.97)
Moderate limitations	5.3 (32/607)	1.09 (0.78-1.53)
Severe limitations	8.0 (133/1668)	1.74 (1.47-2.06)



[a] Based on self-report and hospital records, [b]Based on hospital records only and without any other CVD subtypes. Effect sizes were estimated using 'no CVD and No limitations' as the reference group. [1]Adjusted for age, sex, region of residence and education attainment

S6.2 The relationship between incident CVD and social isolation over time among older Australians

S6.2.1 Sensitivity analysis I: Becoming socially isolated considering source of incident CVD definition

Table S6.2.1 Becoming socially isolated: Incidence of and adjusted risk ratios for becoming socially isolated by considering source of follow-up incident CVD definition

	Social isolation	
	Frequency % (n)	*RR (95%CI)
Social isolation		
No CVD	11.9 (9766)	1
Incident CVD [1] (main analysis)	12.4 (1010)	1.07 (1.00-1.13)
Incident CVD [2] (sensitivity analysis)	12.4 (1425)	1.06 (1.01-1.12)

*Adjusted for age group at follow-up, sex, region, education, No CVD is the reference Group, [1]defined from hospital admission only, [2]defined from both self-reported survey at follow-up as well as hospital admissions.

S6.2.2. Sensitivity analysis II: Becoming socially isolated considering age as continuous variable in the adjusted regression model

Table S6.2.2 Becoming socially isolated: Incidence of and adjusted risk ratios for becoming socially isolated by considering age as grouped and continuous variable in the regression models

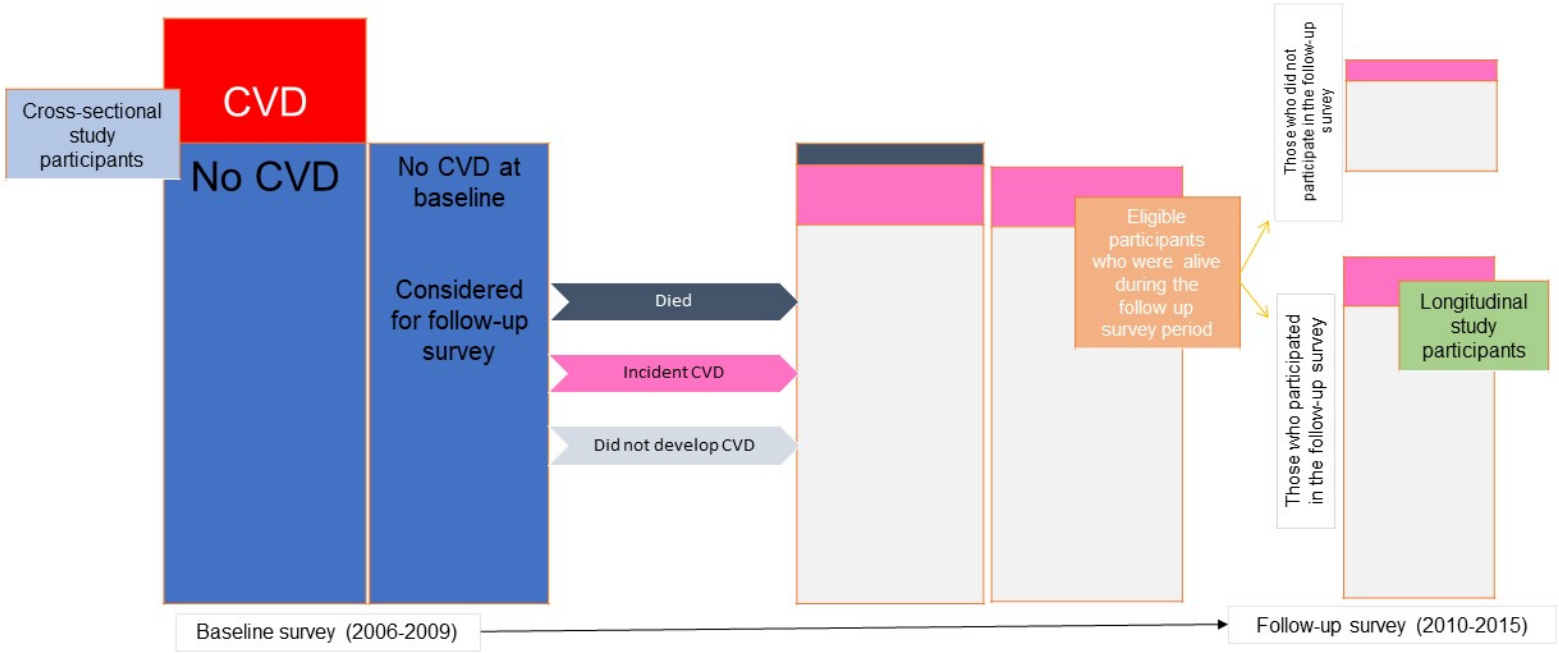
	Social isolation	
	Frequency % (n)	*RR (95%CI)
Social isolation		
No CVD (Reference)	11.9 (9766)	1
Incident CVD [1] (main analysis)	12.4 (1010)	1.07 (1.00-1.13)
Incident CVD [2] (sensitivity analysis)	12.4 (1010)	1.06 (1.02-1.11)

*Adjusted risk ratio and no CVD is the reference
[1]Adjusted for age-group (45-<55, 55-<65, 65-<75, 75- 75+ year) at follow-up, sex, region of residence and education.
[2]Adjusted for age at follow-up as continuous variable in year, sex, region of residence and education.

Appendix 6 Supplementary material Chapter 7

S7.1 Overview of missing data for the potentially eligible participants due to non-participation in the follow-up survey

Figure S7.1.1 The study participants in the baseline survey and their participation or non-participation in the follow-up survey



CVD= Cardiovascular disease (The figure is not necessarily drawn to the exact proportions and the number participants differed based on the outcome considered).

S7.2 Characteristics of participation in the follow-up survey by baseline CVD status

Over the 11-year follow-up period, the proportion of participants who died after baseline survey was higher in people with CVD compared with those without CVD at baseline (11% vs 3.3%). The proportion of participants who took part in the follow-up survey was lower in people with versus without CVD at baseline (58.6% vs 66.4%). However, if the proportion of participants who died in between the baseline survey were considered, I did not find much difference in the proportions of participants with missing data at the follow-up survey among people with versus without CVD (30.4% vs 30.3%) *(Table S7.2.1).*

Table S7.2.1 The proportion of people filling out the survey according to time after baseline survey and cardiovascular status at baseline

		Follow-up period (F)*											
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**Total**
CVD at baseline	Eligible for follow-up (n)	8670	8576	8478	7776	7647	6369	4659	4120	3472	2821	2660	
	Deaths (n)	94	94	98	84	107	101	105	126	108	25	16	**11.0% (968/8670)**
	Filled second survey (n)	0	4	604	45	1171	1609	434	522	543	136	12	
	Percent (%) **	0.0%	0.0%	7.0%	0.5%	13.5%	18.6%	5.0%	6.0%	6.3%	1.6%	0.1%	**58.6 % (5080/8670)**
	Total missing												**30.4% (2632/8670)**
No CVD at baseline	Eligible for follow-up (n)	154892	154561	154061	143295	142201	119708	86775	75915	63767	50079	47368	
	Deaths (n)	331	413	456	488	521	573	634	659	639	201	120	**3.3% (5035/154892)**
	Filled second survey (n)	0	87	10310	606	21972	32360	10226	11489	13049	2510	247	
	Percent (%) ***	0.0%	0.1%	6.7%	0.4%	14.2%	20.9%	6.6%	7.4%	8.4%	1.6%	0.2%	**66.4% (102856/154892)**
	Total missing												**30.3% (47001/154892)**
	CVD hospitalisation	1786	2025	2102	2374	2697	2833	2989	3129	2590	834	443	

*F1 to F11 are follow-up period calculated by adding multiple of 365.25 to participants' baseline survey. For example, F1=baseline surveydate+365.25, F2= baseline surveydate+2*365.25, F11= baseline surveydate+11*365.25 etc. * Percent of 8670; ***percent of 154 892.

S7.3 Characteristics of participants by baseline outcome missing

There were only 60 participants (<1%) whose workforce participation status is missing at baseline out of 118,232 potentially eligible participants who had no CVD at baseline and who were aged less than 65 years old at the follow-up survey *(Table S7.3.1).* The group with missing outcome was slightly younger cohort, did not vary by sex. The missing participants had relatively higher proportion in who were younger aged 45-49 years old, had no school certificate as educational qualification but did not vary by sex, region of residence or sickness status as indicated by the number of hospitalisation records *(Table S7.3.1).*

Table S7.3.1 Characteristics of people with missing workforce participation status at baseline

	Eligible participants at baseline	**Missing group (baseline work status)**	**Non-missing group (baseline work status)**
	Percent (frequency/total)	**Percent (frequency/total)**	**Percent (frequency/total)**
Participants (n)	118232	60	118172
Age (Mean, sd)	53.0, 4.2	54.8, 4.1	53.0, 4.2
Age group at baseline			
45-49	28.6 (33824/118232)	58.3 (35/60)	33.7 (39809/118172)
50-54	34.6 (40935/118232)	**	3.1 (3628/118172)
55-59	33.7 (39844/118232)	40.0 (24/60)	40.9 (48296/118172)
60-64	3.1 (3629/118232)	60.0 (36/60)	59.1 (69876/118172)
Sex			
Men	40.9 (48320/118232)	40.0 (24/60)	40.9 (48296/118172)
Women	59.1 (69912/118232)	60.0 (36/60)	59.1 (69876/118172)
Region			
Missing	2.0 (2398/118232)	**	2.0 (2396/118172)
Major city	52.4 (62004/118232)	60.0 (36/60)	52.4 (61968/118172)
Inner city	34.3 (40564/118232)	28.3 (17/60)	34.3 (40547/118172)
More remote	11.2 (13266/118232)	**	11.2 (13261/118172)
Education			
No school certificate	7.3 (8593/118232)	30.0 (18/60)	7.3 (8575/118172)
Certificate/diploma/trade	61.5 (72695/118232)	45.0 (27/60)	61.5 (72668/118172)
Tertiary	30.4 (35887/118232)	20.0 (12/60)	30.4 (35875/118172)
Missing	0.9 (1057/118232)	**	0.9 (1054/118172)
Hospitalisation records between baseline and T2[#]			
No hospitalisation	31.5 (37246/118232)	23.3 (14/60)	31.5 (37232/118172)
1-10-day hospitalisations	48.0 (56696/118232)	56.7 (34/60)	47.9 (56662/118172)
11-30-day hospitalisations	9.2 (10870/118232)	10.0 (6/60)	9.2 (10864/118172)
>30-day hospitalisations	11.4 (13420/118232)	10.0 (6/60)	11.4 (13414/118172)

sd= standard deviation, [#]Actual or pseudo follow-up date calculated based on median follow-up period, **number of participants less than 10

S7.4 Characteristics of participants by follow-up outcome missing

Table S7.4.1 Sociodemographic and health-related characteristics of participants derived from self-reported survey at baseline or hospitalisation records between baseline and follow-up survey stratified by incident CVD status

	Incident CVD group		**No CVD group**	
	Follow-up work status **missing group** % (n/N)	Follow-up work status **non-missing group** % (n/N)	Follow-up work status **missing group** % (n/N)	Follow-up work status **non-missing group** % (n/N)
Total participants n = 118232	**5.1 (1993/39074)**	**4.7 (3719/79158)**	**94.9 (37081/39074)**	**95.3 (75439/79158)**
Participants in each group	1993	3719	37081	75439
Age at follow-up (mean, sd) * ¥	59.2, 3.9	60.1, 3.6	57.8, 4.1	58.7, 4.0
Age-group at follow-up * ¥				
< 55 year	18.6 (371)	11.1 (412)	31.1 (11523)	21.3 (16042)
55-60 year	32.7 (652)	30.2 (1124)	34.8 (12886)	34.9 (26315)
60-65 year	48.7 (970)	58.7 (2183)	34.2 (12672)	43.9 (33082)
Sex				
Men	58.0 (1156)	55.6 (2069)	42.2 (15642)	39.0 (29453)
Women	42.0 (837)	44.4 (1650)	57.8 (21439)	61.0 (45986)
Region				
Missing	1.7 (34)	1.9 (70)	1.9 (704)	2.1 (1590)
Major cities	52.5 (1047)	50.4 (1873)	54.6 (20248)	51.5 (38836)
Inner regional	33.4 (665)	35.9 (1334)	32.4 (12024)	35.2 (26541)
More remote	12.4 (247)	11.9 (442)	11.1 (4105)	11.2 (8472)
Education				
Missing value	1.6 (31)	0.9 (34)	1.3 (484)	0.7 (508)
No school certificate	15.8 (315)	7.5 (280)	10.5 (3884)	5.5 (4114)
Certificate/diploma/trade	64.4 (1284)	62.9 (2339)	64.9 (24059)	59.7 (45013)
Tertiary	18.2 (363)	28.7 (1066)	23.3 (8654)	34.2 (25804)
Country of birth				
Missing	0.8 (16)	0.3 (12)	0.6 (239)	0.5 (354)
Australia/New Zealand	78.2 (1558)	83.5 (3106)	74.1 (27489)	81.3 (61366)
Other	21.0 (419)	16.2 (601)	25.2 (9353)	18.2 (13719)
Language spoken at home other than English				
Missing				
No	86.9 (1732)	92.8 (3450)	84.1 (31176)	92.4 (69685)
Yes	13.1 (261)	7.2 (269)	15.9 (5905)	7.6 (5753)
Body mass index (BMI)				
Missing	9.9 (197)	6.9 (255)	7.8 (2878)	6.1 (4621)
Underweight (15 to <18.5)	0.6 (12)	0.6 (24)	1.1 (400)	1.0 (719)
Healthy weight (18.5 to <25)	20.2 (402)	24.8 (922)	32.8 (12158)	37.0 (27897)
Overweight (25 to <30)	35.9 (716)	37.8 (1404)	34.5 (12796)	35.7 (26935)
Obese (30 to 50)	33.4 (666)	30.0 (1114)	23.9 (8849)	20.2 (15267)
Alcohol drinks per week				
Missing	2.9 (57)	1.3 (47)	2.0 (751)	1.0 (744)
None	35.8 (713)	28.1 (1045)	32.7 (12129)	27.1 (20469)
1-14	45.0 (897)	51.5 (1915)	50.9 (18875)	57.2 (43137)
15 or more	16.4 (326)	19.1 (712)	14.4 (5326)	14.7 (11089)
Smoking				
Missing	1.0 (19)	0.3 (13)	0.5 (171)	0.3 (195)
Current smoker	20.0 (399)	11.9 (441)	13.9 (5164)	7.5 (5689)
Past smoker	34.2 (682)	35.0 (1301)	31.8 (11807)	32.0 (24135)
Never smoker	44.8 (893)	52.8 (1964)	53.8 (19939)	60.2 (45420)
Cancer				
No	89.6 (1785)	88.9 (3308)	90.7 (33637)	90.4 (68186)
Yes	10.4 (208)	11.1 (411)	9.3 (3444)	9.6 (7253)
Diabetes				
No	85.1 (1696)	90.3 (3360)	94.4 (34990)	95.8 (72306)
Yes	14.9 (297)	9.7 (359)	5.6 (2091)	4.2 (3133)

Arthritis				
No	96.6 (1925)	97.0 (3606)	97.8 (36262)	97.7 (73696)
Yes	3.4 (68)	3.0 (113)	2.2 (819)	2.3 (1743)
Physical functioning limitations				
Missing	12.8 (256)	8.8 (328)	11.0 (4089)	7.5 (5677)
No limitation (100)	28.9 (576)	34.0 (1265)	42.4 (15733)	45.5 (34305)
Minor limitation (90 to <100)	21.6 (430)	27.5 (1021)	23.3 (8655)	27.5 (20735)
Moderate limitation (60 to <90)	19.5 (388)	20.1 (747)	15.8 (5855)	14.8 (11133)
Severe limitation (0 to <60)	17.2 (343)	9.6 (358)	7.4 (2749)	4.8 (3589)
Psychological distress (K-10 score)				
Missing	7.7 (153)	4.7 (173)	6.1 (2246)	3.6 (2714)
Low (10- < 12)	56.7 (1131)	66.9 (2488)	64.2 (23814)	72.4 (54607)
Mild (12- < 16)	18.8 (375)	18.5 (689)	18.3 (6773)	17.0 (12813)
Moderate (16- < 22)	11.1 (221)	7.3 (272)	7.7 (2849)	5.3 (3987)
High (22–50)	5.7 (113)	2.6 (97)	3.8 (1399)	1.7 (1318)
Quality of life				
Missing	6.7 (134)	3.4 (127)	4.8 (1776)	3.1 (2305)
Excellent/Very Good	45.8 (912)	60.7 (2256)	58.0 (21499)	70.3 (52997)
Good	29.8 (594)	25.9 (962)	26.7 (9908)	20.9 (15762)
Poor/Fair	17.7 (353)	10.1 (374)	10.5 (3898)	5.8 (4375)
Quality of health				
Missing	4.1 (82)	2.3 (87)	3.3 (1240)	2.1 (1612)
Excellent/Very Good	36.7 (732)	47.9 (1780)	51.1 (18965)	62.4 (47101)
Good	34.8 (693)	34.7 (1292)	32.8 (12170)	27.8 (20949)
Poor/Fair	24.4 (486)	15.1 (560)	12.7 (4706)	7.7 (5777)
Charlson Comorbidity index (CCI) 1 year prior to follow-up survey*				
None	48.7 (971)	52.7 (1960)	82.3 (30504)	80.2 (60530)
Minor	34.1 (680)	36.4 (1355)	15.0 (5572)	17.3 (13082)
Moderate	11.7 (234)	7.8 (290)	2.2 (825)	2.0 (1475)
Severe	5.4 (108)	3.1 (114)	0.5 (180)	0.5 (352)
Total hospitalisations 1 year prior to follow-up survey*				
No hospitalisation	70.5 (1406)	72.5 (2696)	72.1 (26750)	72.3 (54534)
1-10-day hospitalisations	24.0 (478)	22.8 (849)	23.0 (8526)	22.9 (17283)
11-30-day hospitalisations	2.6 (51)	2.6 (98)	2.3 (852)	2.4 (1784)
>30-day hospitalisations	2.9 (58)	2.0 (76)	2.6 (953)	2.4 (1838)
CVD hospitalisation 1-year prior to follow-up survey*				
No hospitalisation	94.7 (1888)	95.5 (3552)	95.4 (35369)	95.3 (71908)
1-10-day hospitalisations	3.5 (69)	2.9 (108)	3.0 (1096)	3.0 (2242)
11-30-day hospitalisations	1.0 (20)	0.9 (33)	0.9 (316)	0.9 (691)
>30-day hospitalisations	0.8 (16)	0.7 (26)	0.8 (300)	0.8 (598)
Total CVD hospitalisation baseline to follow-up survey*				
No hospitalisation	81.9 (1632)	80.9 (3010)	83.5 (30965)	83.2 (62787)
1-10-day hospitalisations	9.7 (194)	10.8 (402)	9.1 (3391)	9.0 (6814)
11-30-day hospitalisations	4.5 (90)	4.1 (154)	3.4 (1257)	3.6 (2741)
>30-day hospitalisations	3.9 (77)	4.1 (153)	4.0 (1468)	4.1 (3097)

* A pseudo-follow-up survey date which was given to those who were lost in the follow-up survey. It was obtained after adding median follow-up days of the non-missing participants to the baseline survey date. ¥age at actual or pseudo follow-up date, sd= standard deviation,

S7.5 Correlation coefficients of the predictors with the outcome missing data

Table S7.5.1 Correlation coefficient values of the different variables in associated with workforce exit missing data

Variables	Correlation coefficient*
Exit from workforce at the follow-up survey	1
Workforce participation status at baseline survey	0.53158
Age at actual/pseudo follow-up survey	-0.29186
Physical disability	-0.21096
Self-rated overall health rating	-0.14445
Education	0.13622
Overall quality of life	-0.13013
Sex	-0.08946
Charlson comorbidity index	-0.06872
Diabetes status at follow-up	-0.06583
Alcoholic drinks per week	0.0653
Osteoarthritis status at follow-up	-0.06006
Marital status in the follow-up	0.05378
Incident CVD status	-0.05052
Died	-0.04935
Cancer status at follow-up	-0.04845
BMI category	-0.0428
Smoking status	0.0308
Region of residence	-0.01649
Language spoken at home	0.00535
Total days of hospital stay for with incident CVD from baseline to follow-up survey	0.00474
Total days of hospital stay for with incident CVD during 1 year prior to follow-up survey	-0.00466
Total days of hospital stay during 1 year prior to follow-up survey	0.0023
Total days of hospital stay for with incident CVD during follow-up survey	0.00088

*Pearson correlation coefficient estimated by individual variables and exit from workforce variable

S7.6 Shift parameter delta values under the MNAR assumption

Table S7.6.1 Shift parameter delta values for six variables imputed under the MNAR assumption

Variables	Delta values*
Exit from workforce at the follow-up survey	1
Workforce participation status at baseline survey	1
Physical disability	3
Self-rated overall health rating	2
Education	2
Overall quality of life	2

*A shift parameter delta was applied to the logit function values for the variables with higher rank based on the correlation coefficient values with exit from workforce.

S7.7 Exit from workforce under MAR and MNAR assumption

Table S7.7.1 Exit from workforce: Incidence of exit from workforce in people with and without incident CVD in each imputed dataset

Imputation number	Incident CVD status	Exit from workforce % (n/Total)[1]	
		MAR assumption*	MNAR assumption**
1	No CVD	16.3 (15186/92889)	13.5 (12581/92898)
1	Incident CVD	23.7 (1047/4410)	20.2 (893/4410)
2	No CVD	16.4 (15232/92891)	13.7 (12694/92902)
2	Incident CVD	24.4 (1076/4410)	20.2 (892/4410)
3	No CVD	16.3 (15132/92892)	13.6 (12591/92901)
3	Incident CVD	24.1 (1062/4410)	20.6 (907/4410)
4	No CVD	16.3 (15186/92895)	13.6 (12605/92900)
4	Incident CVD	23.7 (1046/4410)	20.4 (899/4410)
5	No CVD	16.3 (15152/92889)	13.6 (12590/92894)
5	Incident CVD	23.9 (1053/4410)	20.7 (913/4410)
6	No CVD	16.3 (15105/92893)	13.5 (12536/92903)
6	Incident CVD	24.3 (1071/4410)	20.7 (913/4410)
7	No CVD	16.3 (15184/92892)	13.6 (12644/92901)
7	Incident CVD	23.9 (1056/4410)	20.5 (904/4410)
8	No CVD	16.2 (15092/92887)	13.5 (12563/92897)
8	Incident CVD	24.2 (1069/4410)	20.5 (906/4410)
9	No CVD	16.3 (15177/92889)	13.6 (12661/92899)
9	Incident CVD	24.6 (1083/4409)	20.9 (923/4409)
10	No CVD	16.3 (15173/92888)	13.6 (12614/92896)
10	Incident CVD	24.5 (1079/4409)	20.7 (914/4410)
11	No CVD	16.5 (15304/92889)	13.6 (12660/92895)
11	Incident CVD	23.9 (1053/4410)	20.7 (915/4410)
12	No CVD	16.4 (15253/92886)	13.6 (12668/92897)
12	Incident CVD	24.3 (1070/4410)	20.5 (903/4410)
13	No CVD	16.4 (15206/92888)	13.5 (12575/92896)
13	Incident CVD	23.8 (1051/4410)	20.5 (904/4410)
14	No CVD	16.4 (15264/92892)	13.6 (12657/92902)
14	Incident CVD	23.7 (1043/4408)	20.3 (893/4409)
15	No CVD	16.4 (15239/92887)	13.6 (12626/92896)
15	Incident CVD	23.5 (1035/4410)	20.2 (889/4410)
16	No CVD	16.5 (15299/92891)	13.6 (12653/92899)
16	Incident CVD	24.5 (1081/4410)	20.8 (916/4410)
17	No CVD	16.3 (15119/92884)	13.5 (12526/92892)
17	Incident CVD	23.7 (1046/4410)	20.6 (907/4410)
18	No CVD	16.3 (15133/92886)	13.6 (12605/92893)
18	Incident CVD	23.9 (1054/4410)	20.6 (907/4410)
19	No CVD	16.3 (15182/92885)	13.6 (12619/92890)
19	Incident CVD	23.7 (1046/4408)	20.4 (900/4410)
20	No CVD	16.4 (15238/92888)	13.6 (12649/92895)
20	Incident CVD	24.6 (1083/4409)	20.4 (898/4409)
21	No CVD	16.4 (15227/92893)	13.6 (12594/92901)
21	Incident CVD	24.4 (1076/4410)	20.6 (910/4410)
22	No CVD	16.3 (15173/92890)	13.6 (12599/92901)
22	Incident CVD	23.8 (1049/4410)	20.2 (891/4410)
23	No CVD	16.3 (15185/92887)	13.5 (12562/92892)
23	Incident CVD	24.4 (1075/4410)	20.7 (915/4410)

24	No CVD	16.5 (15301/92890)	13.7 (12717/92897)
24	Incident CVD	23.8 (1050/4409)	20.0 (884/4409)
25	No CVD	16.5 (15301/92891)	13.7 (12719/92898)
25	Incident CVD	23.4 (1034/4410)	20.4 (899/4410)
26	No CVD	16.4 (15258/92891)	13.6 (12624/92899)
26	Incident CVD	23.8 (1051/4409)	20.5 (902/4409)
27	No CVD	16.3 (15144/92897)	13.6 (12593/92903)
27	Incident CVD	24.1 (1064/4410)	20.8 (918/4410)
28	No CVD	16.3 (15182/92888)	13.6 (12611/92899)
28	Incident CVD	24.0 (1059/4410)	20.3 (897/4410)
29	No CVD	16.4 (15203/92889)	13.6 (12656/92900)
29	Incident CVD	24.9 (1100/4410)	21.1 (929/4410)
30	No CVD	16.3 (15150/92887)	13.5 (12565/92894)
30	Incident CVD	24.2 (1069/4409)	21.1 (931/4409)
31	No CVD	16.4 (15213/92888)	13.5 (12582/92901)
31	Incident CVD	24.0 (1059/4410)	20.7 (914/4410)
32	No CVD	16.4 (15230/92893)	13.6 (12624/92898)
32	Incident CVD	24.1 (1064/4410)	20.6 (907/4410)
33	No CVD	16.4 (15205/92891)	13.6 (12593/92900)
33	Incident CVD	23.7 (1045/4409)	20.4 (898/4409)
34	No CVD	16.4 (15199/92892)	13.6 (12643/92896)
34	Incident CVD	24.2 (1069/4410)	20.5 (906/4410)
35	No CVD	16.3 (15100/92885)	13.5 (12525/92894)
35	Incident CVD	24.1 (1065/4410)	20.7 (915/4410)

[1]Only those participants were included who had been working at baseline and who had no CVD at baseline. This resulted in variable number of potentially eligible person in each imputation because the missing values for workforce participation at baseline were imputed resulting in possibility of being at work or not at work in each imputation stage. *Multiple imputation with missing at random assumption, **Multiple imputation with missing not at random assumption.

REFERENCES

1. National Heart, Lung, Blood Institute. *Know the differences: cardiovascular disease, heart disease, coronary heart disease [accessed on 21 Feb 2021 from webpage https://www.nhlbi.nih.gov/sites/default/files/media/docs/Fact_Sheet_Know_Diff_Design.508_pdf.pdf]*. 2019.
2. Roth, G.A., et al., *Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study.* J Am Coll Cardiol, 2020. **76**(25): p. 2982-3021.
3. WHO, *World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions.* Lancet Glob Health, 2019. **7**(10): p. e1332-e1345.
4. Australian Bureau of Statistics. *National Health Survey 2017-18, (https://www.abs.gov.au/statistics/health/health-conditions-and-risks/national-health-survey-first-results/latest-release) last accessed 27 June 2021.*
5. Australian Institute of Health and Welfare (AIHW). *Cardiovascular disease. Cat. no. CVD 83. Canberra: AIHW. Viewed 27 June 2021, https://www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium.*
6. Australian Institute of Health and Welfare (AIHW). *Australian Burden of Disease Study: impact and causes of illness and death in Australia 2015. Cat. no. BOD 22. Canberra: AIHW. doi:10.25816/5ebca2a4fa7dc*. 2019.
7. Heart Foundation, *Heart Foundation Australia HeartWatch Survey June 2020 (https://www.heartfoundation.org.au/health-professional-tools/Interactive-Heart-Map-Australia) accessed 27June 2021.*
8. Heart Foundation, *Key Statistics: Cardiovascular Disease (Statistics and information on Cardiovascular disease in Australia) (https://www.heartfoundation.org.au/activities-finding-or-opinion/key-stats-cardiovascular-disease last accessed 27 June 2021).* 2021.
9. Clark, E.G. and H.R. Leavell, *Preventive Medicine for the Doctor in His Community: An Epidemiological Approach*. 1965: McGraw-Hill.
10. Katz, D.L., et al., *Jekel's Epidemiology, Biostatistics and Preventive Medicine*. 2013: Elsevier Health Sciences.
11. Lucan, S.C., *Coronary artery disease prevention: as easy as 1, 2, 3?* American Family Physician, 2010. **82**(10): p. 1167.
12. Mensah, G.A., et al., *Decline in Cardiovascular Mortality: Possible Causes and Implications.* Circ Res, 2017. **120**(2): p. 366-380.
13. United Nations, *World Population Ageing 2019: highlights (ST/ESA/SER. A/430).* Department of Economic and Social Affairs, Population Division, 2019.
14. Reynolds, I., R.L. Page, and R.S. Boxer, *Cardiovascular health and healthy aging*, in *Healthy Aging*. 2019, Springer. p. 31-51.
15. PCA, *Productivity Commission Australia, An Ageing: Preparing for the Future.* Canberra: Commision Research Paper Overview, 2013.
16. Chan, Y.-K., et al., *Current and projected burden of heart failure in the Australian adult population: a substantive but still ill-defined major health issue.* BMC Health Services Research, 2016. **16**(1): p. 501.
17. Tulloch, H., et al., *Learning a new way of living together: a qualitative study exploring the relationship changes and intervention needs of patients with cardiovascular disease and their partners.* BMJ Open, 2020. **10**(5): p. e032948.
18. Daniel, K., et al., *What are the social consequences of stroke for working-aged adults? A systematic review.* Stroke, 2009. **40**(6): p. e431-40.

19. Nordfonn, O.K., I.M. Morken, and A.M. Lunde Husebø, *A qualitative study of living with the burden from heart failure treatment: Exploring the patient capacity for self-care.* Nurs Open, 2020. **7**(3): p. 804-813.

20. Checa, C., et al., *Living with advanced heart failure: A qualitative study.* PLOS ONE, 2020. **15**(12): p. e0243974.

21. Halatchev, I.G., J.R. McDonald, and W.-C. Wu, *A patient-centred, comprehensive model for the care for heart failure: the 360° heart failure centre.* Open Heart, 2020. **7**(2): p. e001221.

22. Kim, D.H. and M.W. Rich, *Patient-Centred Care of Older Adults With Cardiovascular Disease and Multiple Chronic Conditions.* Can J Cardiol, 2016. **32**(9): p. 1097-107.

23. Joshy, G., et al., *Categorising major cardiovascular disease hospitalisations from routinely collected data.* Public Health Res Pract, 2015. **25**(3): p. e2531532.

24. Waters, A.-M., et al., *Latest statistics on cardiovascular disease in Australia.* Clin Exp Pharmacol Physiol, 2013. **40**(6): p. 347-356.

25. Shipley, J., et al., *The personal and social experiences of community-dwelling younger adults after stroke in Australia: a qualitative interview study.* BMJ Open, 2018. **8**(12): p. e023525.

26. Petrea, R.E., et al., *Gender differences in stroke incidence and poststroke disability in the Framingham heart study.* Stroke, 2009. **40**(4): p. 1032-7.

27. Beauchamp, M.K., et al., *Predictive validity and responsiveness of patient-reported and performance-based m easures of function in the Boston RISE study.* J Gerontol A Biol Sci Med Sci, 2015. **70**(5): p. 616-22.

28. Umberson, D., R. Crosnoe, and C. Reczek, *Social Relationships and Health Behavior Across Life Course.* Annu Rev Sociol, 2010. **36**: p. 139-157.

29. Australian Institute of Health and Welfare (AIHW). *People with disability in Australia. Cat. no. DIS 72. Canberra: AIHW. Last acccessed, 28 February 2021, https://www.aihw.gov.au/reports/disability/people-with-disability-in-australia.* 2020.

30. Australian Institute of Health and Welfare (AIHW). *Chronic conditions and disability 2015, ISBN: 978-1-76054-433-1, Cat. no: CDK 8*. 2018, AIHW: Canberra.

31. Zhang, Y., et al., *Physical functional limitations and psychological distress in people with and without colorectal cancer: findings from a large Australian study.* J Cancer Surviv, 2020. **14**(6): p. 894-905.

32. Joshy, G., et al., *Disability, psychological distress and quality of life in relation to cancer diagnosis and cancer type: population-based Australian study of 22,505 cancer survivors and 244,000 people without cancer.* BMC Medicine, 2020. **18**(1): p. 372.

33. Haley, W.E., et al., *Quality of life after stroke: a prospective longitudinal study.* Qual Life Res, 2011. **20**(6): p. 799-806.

34. Mollon, L. and S. Bhattacharjee, *Health related quality of life among myocardial infarction survivors in the United States: a propensity score matched analysis.* Health Qual Life Outcomes, 2017. **15**(1): p. 235.

35. Hegeman, J.M., et al., *Effect of chronic somatic diseases on the course of late-life depression.* Int J Geriatr Psychiatry, 2017. **32**(7): p. 779-787.

36. Jorgensen, T.S., et al., *Incidence of Depression After Stroke, and Associated Risk Factors and Mortality Outcomes, in a Large Cohort of Danish Patients.* JAMA Psychiatry, 2016. **73**(10): p. 1032-1040.

37. Lee, Y., W.-S. Kim, and N.-J. Paik, *Gender differences in physical activity and health-related behaviors among stroke survivors: data from the 5th Korea National Health and Nutrition Examination Survey.* Topics in Stroke Rehabilitation, 2017. **24**(5): p. 381-387.

38. O'Donnell, J., et al., *Self-reported and objectively measured physical activity in people with and without chronic heart failure: UK Biobank analysis.* Open Heart, 2020. **7**(1): p. e001099.

39. Anesetti-Rothermel, A. and U. Sambamoorthi, *Physical and mental illness burden: disability days among working adults.* Popul health manag, 2011. **14**(5): p. 223-30.

40. Adamson, J., D.A. Lawlor, and S. Ebrahim, *Chronic diseases, locomotor activity limitation and social participation in older women: cross sectional survey of British Women's Heart and Health Study.* Age Ageing, 2004. **33**(3): p. 293-8.

41. Holden, L., et al., *Which health conditions impact on productivity in working Australians?* J Occup Environ Med, 2011. **53**(3): p. 253-257.

42. Byles, J.E., et al., *Long-term survival of older australian women with a history of stroke.* Journal of Stroke and Cerebrovascular Diseases, 2015. **24**(1): p. 53-60.

43. Granville, G. and M. Evandrou, *Older men, work and health.* Occup Med (Lond), 2010. **60**(3): p. 178-83.

44. Payne, S. and L. Doyal, *Older women, work and health.* Occup Med (Lond), 2010. **60**(3): p. 172-7.

45. Umberson, D. and J.K. Montez, *Social relationships and health: a flashpoint for health policy.* J Health Soc Behav, 2010. **51 Suppl**: p. S54-66.

46. Australian Bureau of Statistics*, Labour Statistics: Concepts, Sources and Methods. no : 6102.0.55.001 - Feb2018 accessed on 24 Feb 2021 from https://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/6102.0.55.001Main+Features1Feb%202018?OpenDocument).* 2018.

47. Şahan, C., et al., *Changes in Employment Status after Myocardial Infarction among Men.* Balkan Med J, 2016. **33**(4): p. 419-25.

48. Sharma, T., M. Bamford, and D. Dodman, *Person-centred care: an overview of reviews.* Contem Nurse, 2015. **51**(2-3): p. 107-120.

49. Schofield, D., et al., *The personal and national costs of CVD: Impacts on income, taxes, government support payments and GDP due to lost labour force participation.* Int J Cardiol, 2013. **166**(1): p. 68-71.

50. Goodman, N., *The impact of employment on the health status and health care costs of working-age people with disabilities.* LEAD Center Policy Brief, 2015.

51. Schuring, M., et al., *The effects of ill health on entering and maintaining paid employment: evidence in European countries.* J Epidemiol Community Health, 2007. **61**(7): p. 597-604.

52. Holland, P., et al., *Socioeconomic inequalities in the employment impact of ischaemic heart disease: a longitudinal record linkage study in Sweden.* Scand J Public Health, 2009. **37**(5): p. 450-8.

53. Johansen, H., *Living with heart disease--the working-age population.* Health Rep, 1999. **10**(4): p. 33-45(eng); 31.

54. Boundless, *'Social interaction' in 'Sociology' (https://socialsci.libretexts.org/@go/page/8023) ,disseminated via the Open Education Resource (OER) LibreTexts Project (https://LibreTexts.org) . Last accessed on 26 Februrary 2021 and the content is licensed by CC BY-NC-SA 3.0.* 2021.

55. Boundless, *'Types of social interaction' in 'Sociology' (https://socialsci.libretexts.org/@go/page/7590) ,disseminated via the Open Education Resource (OER) LibreTexts Project (https://LibreTexts.org) . Last accessed on 26 Februrary 2021 and the content is licensed by CC BY-NC-SA 3.0.* 2021.

56. Jorge, A.J.L., et al., *Evaluation of Quality of Life in Patients with and without Heart Failure in Primary Care.* Arq Bras Cardiol, 2017. **109**(3): p. 248-252.

57. McKenna, K., et al., *Comparison of time use, role participation and life satisfaction of older people after stroke with a sample without stroke.* Aust Occup Ther J, 2009. **56**(3): p. 177-88.

58. Banks, E., et al., *Cohort profile: the 45 and up study.* Int J Epidemiol, 2008. **37**(5): p. 941-7.

59. Joshy, G., et al., *Impact of loss to follow-up in cohort studies on estimates of 10 well-established exposure and outcome relationships*, in *Australian Statistical Society and New Zealand Statistical Association Conference, 05-09 July 2021*.

60. Thandrayen, J., et al., *Workforce participation in relation to cancer diagnosis, type and stage: Australian population-based study of 163,556 middle-aged people.* J Cancer Surviv, 2021.

61. O'Flaherty, M., I. Buchan, and S. Capewell, *Contributions of treatment and lifestyle to declining CVD mortality: why have CVD mortality rates declined so much since the 1960s?* Heart, 2013. **99**(3): p. 159-62.

62. Roth, G.A., et al., *Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015.* J Am Coll Cardiol, 2017. **70**(1): p. 1-25.

63. Pilipiec, P., W. Groot, and M. Pavlova, *The Effect of an Increase of the Retirement Age on the Health, Well-Being, and Labor Force Participation of Older Workers: a Systematic Literature Review.* J Popul Ageing, 2020.

64. Doyle, Y., et al., *Meeting the challenge of population ageing.* BMJ. 2009. **339**: p. b3926.

65. Eckhardt, A.L., et al., *Fatigue in the presence of coronary heart disease.* Nurs Res, 2014. **63**(2): p. 83-93.

66. Jha, M.K., et al., *Screening and Management of Depression in Patients With Cardiovascular Disease: JACC State-of-the-Art Review.* J Am Coll Cardiol, 2019. **73**(14): p. 1827-1845.

67. Deckers, K., et al., *Coronary heart disease and risk for cognitive impairment or dementia: Systematic review and meta-analysis.* PLoS One, 2017. **12**(9): p. e0184244.

68. Schofield, D.J., et al., *Labour force participation and the influence of having CVD on income poverty of older workers.* Int J Cardiol, 2012. **156**(1): p. 80-3.

69. Schofield, D., et al., *The long term financial impacts of CVD: Living standards in retirement.* Int J Cardiol, 2012. **155**(3): p. 406-408.

70. Chaker, L., et al., *The global impact of non-communicable diseases on macro-economic productivity: a systematic review.* Eur J Epidemiol, 2015. **30**(5): p. 357-95.

71. Hegewald, J., et al., *Interventions to support return to work for people with coronary heart disease.* Cochrane Database Syst Rev, 2019. **3**: p. CD010748.

72. Tornbom, K., J. Lundalv, and K.S. Sunnerhagen, *Long-term participation 7-8 years after stroke: Experiences of people in working-age.* PLoS One, 2019. **14**(3): p. e0213447.

73. Wolfenden, B. and M. Grace, *Returning to work after stroke: a review.* Int J Rehabil Res, 2009. **32**(2): p. 93-7.

74. Ferrie, J.E., M. Virtanen, and M. Kivimaki, *The healthy population-high disability paradox.* Occup Environ Med, 2014. **71**(4): p. 232-3.

75. Vaughan Dickson, V., *Presenteeism among older workers (≥ 45 years) with coronary heart disease: An integrative literature review.* Open Public Health Journal, 2013. **6**: p. 31-41.

76. Gordois, A.L., et al., *Productivity losses associated with cardiovascular disease: a systematic review.* Expert Rev Pharmacoecon Outcomes Res, 2016. **16**(6): p. 759-769.

77. Ilmarinen, J.E., Occup Environ Med. *AGING WORKERS.* 2001. **58**(8): p. 546-546.

78. Cooke, M, *Policy changes and the labour force participation of older workers: evidence from six countries.* Can J Aging. 2006. **25**(4): p. 387-400.

79. Moher, D., et al., *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.* PLOS Medicine, 2009. **6**(7): p. e1000097.

80. Wells GA, S.B., O'Connell D, Peterson J, Welch V, Losos M, Tugwell P,. *The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. [website: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp cited 2019 30 Janurary, 2019].

81. Herzog, R., et al., *Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review.* BMC Public Health, 2013. **13**: p. 154.

82. Alavinia, S.M. and A. Burdorf, *Unemployment and retirement and ill-health: a cross-sectional analysis across European countries.* Int Arch Occup Environ Health, 2008. **82**(1): p. 39-45.

83. Bielecky, A., et al., *The impact of co-morbid mental and physical disorders on presenteeism.* Scand J Work Environ Health, 2015. **41**(6): p. 554-64.

84. Brækkan, S.K., et al., *Venous thromboembolism and subsequent permanent work-related disability.* J Thromb Haemost, 2016. **14**(10): p. 1978-1987.

85. de Boer, A., et al., *Employment status transitions in employees with and without chronic disease in the Netherlands.* Int J Public Health, 2018. **63**(6): p. 713-722.

86. Ervasti, J., et al., *Health- and work-related predictors of work disability among employees with a cardiometabolic disease - A cohort study.* J Psychosom Res, 2016. **82**: p. 41-47.

87. Hemingway, H., et al., *Outcome of stable angina in a working population: the burden of sickness absence.* Eur J Cardiovasc Prev Rehabil, 2007. **14**(3): p. 373-9.

88. Jespersen, L., et al., *Symptoms of angina pectoris increase the probability of disability pension and premature exit from the workforce even in the absence of obstructive coronary artery disease.* Eur Heart J, 2013. **34**(42): p. 3294-3303.

89. Kang, M.Y., C.G. Yoon, and J.H. Yoon, *Influence of illness and unhealthy behavior on health-related early retirement in Korea: Results from a longitudinal study in Korea.* J Occup Health, 2015. **57**(1): p. 28-38.

90. Kouwenhoven-Pasmooij, T.A., et al., *Cardiovascular disease, diabetes and early exit from paid employment in Europe; the impact of work-related factors.* Int J Cardiol, 2016. **215**: p. 332-7.

91. Kruse, M., et al., *Short and long-term labour market consequences of coronary heart disease: a register-based follow-up study.* Eur J Cardiovasc Prev Rehabil, 2009. **16**(3): p. 387-91.

92. Li Ranzi, T., A. d'Errico, and G. Costa, *Association between chronic morbidity and early retirement in Italy.* Int Arch Occup Environ Health, 2013. **86**(3): p. 295-303.

93. Maaijwee, N., et al., *Long-term increased risk of unemployment after young stroke A long-term follow-up study.* Neurology, 2014. **83**(13): p. 1132-1138.

94. Marrett, E., M.D. DiBonaventura, and Q. Zhang, *Burden of peripheral arterial disease in Europe and the United States: A patient survey.* Health Qual Life Outcomes, 2013. **11**(1).

95. Nakaya, N., et al., *Unemployment risk among individuals undergoing medical treatment for chronic diseases.* Occup Med (Lond), 2016. **66**(2): p. 143-9.

96. Pit, S.W., et al., *Partial and complete retirement due to ill-health among mature age Australians.* Public Health, 2013. **127**(6): p. 561-71.

97. Smedegaard, L., et al., *Return to Work and Risk of Subsequent Detachment From Employment After Myocardial Infarction: Insights From Danish Nationwide Registries.* J Am Heart Assoc, 2017. **6**(10).

98. Stein, M.B., et al., *Does co-morbid depressive illness magnify the impact of chronic physical illness? A population-based perspective.* Psychol Med, 2006. **36**(5): p. 587-96.

99. van den Berg, S., A. Burdorf, and S.J.W. Robroek, *Associations between common diseases and work ability and sick leave among health care workers.* Int Arch Occup Environ Health, 2017. **90**(7): p. 685-693.

100. Zhang, W., C. McLeod, and M. Koehoorn, *The relationship between chronic conditions and absenteeism and associated costs in Canada.* Scand J Work Environ Health, 2016. **42**(5): p. 413-22.

101. Oude Hengel, K., et al., *Educational inequalities in the impact of chronic diseases on exit from paid employment among older workers: a 7-year prospective study in the Netherlands.* Occup Environ Med, 2019. **76**(10): p. 718-725.

102. Schnitzler, A., et al., *Participation in work and leisure activities after stroke: A national study.* Ann Phys Rehabil Med, 2019. **62**(5): p. 351-355.

103. Feigl, A.B., et al., *The short-term effect of BMI, alcohol use, and related chronic conditions on labour market outcomes: A time-lag panel analysis utilizing European SHARE dataset.* PLoS One, 2019. **14**(3): p. e0211940.

104. Garland, A., et al., *Effects of cardiovascular and cerebrovascular health events on work and earnings: a population-based retrospective cohort study.* Cmaj, 2019. **191**(1): p. E3-e10.

105. Hemp, P., *Presenteeism: at work-but out of it.* Harvard business review, 2004. **82**(10): p. 49-58.

106. Jeon, Y.H., et al., *Economic hardship associated with managing chronic illness: a qualitative inquiry.* BMC Health Serv Res, 2009. **9**: p. 182.

107. Chirikos, T.N., *The Relationship between Health and Labor Market Status.* 1993. **14**(1): p. 293-312.

108. Kucharska-Newton, A., et al., *Cardiovascular Disease and Patterns of Change in Functional Status Over 15 Years: Findings From the Atherosclerosis Risk in Communities (ARIC) Study.* J Am Heart Assoc, 2017. **6**(3).

109. Butterworth, P., K.M. Kiely, and P. Timmins, *The role of psychosocial work factors in the decision to retire early. Canberra: Safe Work Australia*. 2017.

110. Munir, F., et al., *Work factors related to psychological and health-related distress among employees with chronic illnesses.* J Occup Rehabil, 2007. **17**(2): p. 259-77.

111. Zhang, T., et al., *Predictors of smoking relapse after percutaneous coronary intervention in Chinese patients.* J Clin Nurs, 2018. **27**(5-6): p. e951-e958.

112. Oguzoglu, U., *Severity of Work Disability and Work.* Economic Record, 2011. **87**(278): p. 370-383.

113. Yeates, K., et al., *A Global Perspective on Cardiovascular Disease in Vulnerable Populations.* Can J Cardiol, 2015. **31**(9): p. 1081-93.

114. Callander, E.J. and D.J. Schofield, *The risk of falling into poverty after developing heart disease: a survival analysis.* BMC Public Health, 2016. **16**: p. 570.

115. Foreman, K.J., et al., *Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories.* Lancet, 2018. **392**(10159): p. 2052-2090.

116. Sandstrom, G.M. and E.W. Dunn, *Social Interactions and Well-Being:The Surprising Power of Weak Ties.* Pers Soc Psychol Bull, 2014. **40**(7): p. 910-922.

117. Jetten, J., S.A. Haslam, and C. Haslam, *The case for a social identity analysis of health and well-being.* The social cure: Identity, health and well-being, 2012: p. 3-19.

118. Skolarus, L.E., et al., *Understanding stroke survivorship: expanding the concept of poststroke disability.* Stroke, 2014. **45**(1): p. 224-30.

119. Kleipool, E.E., et al., *Frailty in Older Adults with Cardiovascular Disease: Cause, Effect or Both?* Aging Dis, 2018. **9**(3): p. 489-497.

120. Ramsay, S., et al., *Social engagement and the risk of cardiovascular disease mortality: results of a prospective population-based study of older men.* Ann Epidemiol, 2008. **18**(6): p. 476-83.

121. Tse, T., et al., *Increased work and social engagement is associated with increased stroke specific quality of life in stroke survivors at 3 months and 12 months post-stroke: a longitudinal study of an Australian stroke cohort.* Top Stroke Rehabil, 2017. **24**(6): p. 405-414.

122. Floud, S., et al., *Social participation and coronary heart disease risk in a large prospective study of UK women.* Eur J Prev Cardiol, 2016. **23**(9): p. 995-1002.

123. Mendes de Leon, C.F., et al., *The effect of a psychosocial intervention and quality of life after acute myocardial infarction: the Enhancing Recovery in Coronary Heart Disease (ENRICHD) clinical trial.* J Cardiopulm Rehabil, 2006. **26**(1): p. 9-13; quiz 14-5.

124. Chin, B. and S. Cohen, *Review of the Association Between Number of Social Roles and Cardiovascular Disease: Graded or Threshold Effect?* Psychosom Med, 2020. **82**(5): p. 471-486.

125. Elloker, T. and A.J. Rhoda, *The relationship between social support and participation in stroke: A systematic review.* Afr J Disabil, 2018. **7**.

126. Heidari Gorji, M.A., A. Fatahian, and A. Farsavian, *The impact of perceived and objective social isolation on hospital readmission in patients with heart failure: A systematic review and meta-analysis of observational studies.* Gen Hosp Psychiatry, 2019. **60**: p. 27-36.

127. Almerud, S., et al., *Acute coronary syndrome: social support and coping ability on admittance.* Br J Nurs, 2008. **17**(8): p. 527-31.

128. WHO and WHOStaff, *International classification of functioning, disability and health: ICF*. 2001: World Health Organization.

129. Hildingh, C. and B. Fridlund, *Patient participation in peer support groups after a cardiac event.* Br J Nurs, 2001. **10**(20): p. 1357-63.

130. Sherbourne, C.D. and A.L. Stewart, *The MOS social support survey.* Soc Sci Med, 1991. **32**(6): p. 705-14.

131. Langius, A. and H. Björvell, *The Salutogenic Model and the Use of the Sense of Coherence Scale in Nursing Research—A Methodological Report.* Vård i Norden, 1996. **16**(1): p. 28-32.

132. Whiteneck, G. and M.P. Dijkers, *Difficult to measure constructs: conceptual and methodological issues concerning participation and environmental factors.* Arch Phys Med Rehabil, 2009. **90**(11 Suppl): p. S22-35.

133. Ciconelli, R.M., et al., *Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36).* Rev bras reumatol, 1999. **39**(3): p. 143-50.

134. Bedell, G.M., *Developing a follow-up survey focused on participation of children and youth with acquired brain injuries after discharge from inpatient rehabilitation.* NeuroRehabilitation, 2004. **19**(3): p. 191-205.

135. Oakley, F., et al., *The Role Checklist: Development and empirical assessment of reliability.* The Occupational Therapy Journal of Research, 1986. **6**(3): p. 157-170.

136. Wilson, I.B. and P.D. Cleary, *Linking clinical variables with health-related quality of life: a conceptual model of patient outcomes.* JAMA, 1995. **273**(1): p. 59-65.

137. Palazzo, C., et al., *Respective contribution of chronic conditions to disability in France: results from the national Disability-Health Survey.* PLoS One, 2012. **7**(9).

138. Lett, H.S., et al., *Social support and coronary heart disease: epidemiologic evidence and implications for treatment.* Psychosom Med, 2005. **67**(6): p. 869-78.

139. Choi, M., et al., *Social capital, mortality, cardiovascular events and cancer: a systematic review of prospective studies.* Int J Epidemiol, 2014. **43**(6): p. 1895-920.

140. Parr, S., et al., *Social exclusion of people with marked communication impairment following stroke (https://www.jrf.org.uk/report/social-exclusion-people-marked-communication-impairment-following-stroke, access data: May 20, 2021).* Joseph Rowntree Foundation Findings, 2004. **814**.

141. Northcott, S. and K. Hilari, *Why do people lose their friends after a stroke?* Int J Lang Commun Disord, 2011. **46**(5): p. 524-34.

142. Scott, C.L., et al., *Emotion processing and social participation following stroke: study protocol.* BMC Neurol, 2012. **12**: p. 56.

143. Meulenkamp, T., et al., *People with activity limitations' perceptions of their health condition and their relationships with social participation and experienced autonomy.* BMC Public Health, 2019. **19**(1): p. 1536.

144. Andrew, M.K., et al., *Social and Societal Implications of Frailty, Including Impact on Canadian Healthcare Systems.* J Frailty Aging, 2018. **7**(4): p. 217-223.

145. Shillingford, J.P., *The social and economic consequences of cardiovascular disease and the need for heart foundations to promote research.* Eur Heart J, 1987. **8**(suppl_F): p. 11-13.

146. Mealing, N.M., et al., *Investigation of relative risk estimates from studies of the same population with contrasting response rates and designs.* BMC Med Res Methodol, 2010. **10**(1): p. 26.

147. Sax Institute. *Sax Institute Questionnaires (https://www.saxinstitute.org.au/our-work/45-up-study/questionnaires/ ,last accessed, 22 May 2021)*. 2020 [cited 2020 17/11/2020].

148. Banks, E., *The 45 and Up Study update (https://www.slideshare.net/SaxInstitute/the-45-and-up-study-update, accessed 20 May 2021).* 2016.

149. Sax Institute, *The 45 and Up Study | Data Book – Wave 2 (First follow-up),May 2021 (https://www.saxinstitute.org.au/wp-content/uploads/W2-databook-May2021.pdf, last accessed 20May 2021).* 2021.

150. Australian Institute of Health and Welfare *(*AIHW*). Rural, regional and remote health: A guide to remoteness classifications Cat. no. PHE 53. Canberra: AIHW.* 2004. **53**.

151. George, L.K., et al., *Social support and the outcome of major depression.* Br J Psychiatry, 1989. **154**(4): p. 478-485.

152. Koenig, H.G., et al., *Abbreviating the Duke Social Support Index for use in chronically ill elderly individuals.* Psychosomatics, 1993. **34**(1): p. 61-9.

153. Goodger, B., et al., *Assessment of a short scale to measure social support among older people.* Aust N Z J Public Health, 1999. **23**(3): p. 260-5.

154. Barr, M., et al., *Social isolation and health service use in the Central and Eastern Sydney area, CPHCE, UNSW For further information, please contact Centre for Primary Health Care and Equity (CPHCE).* 2020.

155. Korda, R.J., et al., *Variation in readmission and mortality following hospitalisation with a diagnosis of heart failure: prospective cohort study using linked data.* BMC Health Serv Res, 2017. **17**(1): p. 220.

156. Howe, C., L.R. Matthews, and R. Heard, *Work to retirement: A snapshot of psychological health in a multicultural Australian population.* Work, 2010. **36**(2): p. 119-27.

157. Pachana, N.A., et al., *Responsiveness of the Duke Social Support sub-scales in older women.* Age Ageing, 2008. **37**(6): p. 666-72.

158. Feng, X. and T. Astell-Burt, *Impact of a type 2 diabetes diagnosis on mental health, quality of life, and social contacts: a longitudinal study.* BMJ Open Diabetes Res Care, 2017. **5**(1): p. e000198.

159. Feng, X. and T. Astell-Burt, *What types of social interactions reduce the risk of psychological distress? Fixed effects longitudinal analysis of a cohort of 30,271 middle-to-older aged Australians.* J Affect Disord, 2016. **204**: p. 99-102.

160. Phongsavan, P., et al., *Age, gender, social contacts, and psychological distress: findings from the 45 and up study.* J Aging Health, 2013. **25**(6): p. 921-43.

161. Chiew, M., et al., *A cross-sectional exploration of smoking status and social interaction in a large population-based Australian cohort.* Soc Sci Med, 2012. **75**(1): p. 77-86.

162. Leys, C., et al., *Detecting outliers: Do not use standard deviation around the mean, use absolute deviation around the median.* J Exp Soc Psychol, 2013. **49**(4): p. 764-766.

163. Blake, H.L., et al., *The relationship between spoken English proficiency and participation in higher education, employment and income from two Australian censuses.* Int J Speech Lang Pathol, 2018. **20**(2): p. 202-215.

164. Jørgensen, M.B., et al., *Alcohol consumption and labour market participation: a prospective cohort study of transitions between work, unemployment, sickness absence, and social benefits.* Eur J Epidemiol. 2019. **34**(4): p. 397-407.

165. Norrbäck, M., et al., *The association of mobility disability and obesity with risk of unemployment in two cohorts from Sweden.* BMC Public Health, 2019. **19**(1): p. 347.

166. Webber, D.A. and M.J. Bjelland, *The Impact of Work-Limiting Disability on Labor Force Participation.* Health Econ. 2015. **24**(3): p. 333-352.

167. Majeed, T., et al., *Work after age 65: A prospective study of Australian men and women.* Australas J Ageing, 2017. **36**(2): p. 158-164.

168. Majeed, T., et al., *A gendered approach to workforce participation patterns over the life course for an Australian baby boom cohort.* J Vocat Behav, 2015. **87**: p. 108-122.

169. Korda, R.J., et al., *Socioeconomic variation in incidence of primary and secondary major cardiovascular disease events: an Australian population-based prospective cohort study.* Int J Equity Health, 2016. **15**(1): p. 189.

170. Paige, E., et al., *Socioeconomic variation in absolute cardiovascular disease risk and treatment in the Australian population.* Prev Med, 2018. **114**: p. 217-222.

171. Welsh, J., et al., *Psychological distress and medication use for secondary prevention of cardiovascular events: Evidence from a large-scale population-based cohort study*. J Psychosom Res, 2019. 124: p. 109748.

172. NHMRC, *Australian guidelines to reduce health risks from drinking alcohol / National Health and Medical Research Council*, ed. H. National and C. Medical Research. 2009, Canberra: National Health and Medical Research Council.

173. Quan, H., et al., *Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data.* Med Care, 2005. **43**(11): p. 1130-9.

174. Stewart, A.L. and J.E. Ware, *Measuring functioning and well-being: the medical outcomes study approach*. 1992: duke university Press.

175. Ware Jr, J.E. and C.D. Sherbourne, *The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection.* Medical care, 1992: p. 473-483.

176. Haley, S.M., C.A. McHorney, and J.E. Ware, *Evaluation of the mos SF-36 physical functioning scale (PF-10): I. Unidimensionality and reproducibility of the Rasch Item scale.* J Clin Epidemiol, 1994. **47**(6): p. 671-684.

177. Gubhaju, L., et al., *Physical Functional Limitations among Aboriginal and Non-Aboriginal Older Adults: Associations with Socio-Demographic Factors and Health.* PLoS One, 2015. **10**(9): p. e0139364.

178. Kessler, R.C., et al., *Short screening scales to monitor population prevalences and trends in non-specific psychological distress.* Psychol Med, 2002. **32**(6): p. 959-976.

179. Andrews, G. and T. Slade, *Interpreting scores on the Kessler psychological distress scale (K10).* Aust N Z J Public Health, 2001. **25**(6): p. 494-497.

180. Australian Bureau of Statistics, *Information Paper: Use of the Kessler Psychological Distress Scale in ABS Health Surveys, Australia, 2007–08, in Cat. No. 4817.0.55.001, Australian Bureau of Statistics (ABS), Canberra (2012)*. 2012.

181. Zou, G., *A modified poisson regression approach to prospective studies with binary data.* Am J Epidemiol, 2004. **159**(7): p. 702-706.

182. Raghunathan, T.E., et al., *A multivariate technique for multiply imputing missing values using a sequence of regression models.* Survey methodology, 2001. **27**(1): p. 85-96.

183. Team, R.C., *R: A language and environment for statistical computing.* 2013.

184. CER, *(Centre for Epidemiology Research), 2008 Report on adult health from the New South Wales population health survey*. 2009, NSW Department of Health Sydney.

185. Sarich, P., *Alcohol Consumption and Cancer Incidence and Mortality in Australia: A Prospective Cohort Analysis of the New South Wales 45 and Up Study.* 2018.

186. Australian Bureau Of Statistics*, National Health Survey: Summary of Results 2007-2008.* Canberra, Australian Bureau of Statistics, 2009.

187. Bin Sayeed, M.S., et al., *Cardiovascular disease subtypes, physical disability and workforce participation: A cross-sectional study of 163,562 middle-aged Australians.* PLOS ONE, 2021. **16**(4): p. e0249738.

188. Australian Institute of Health and Welfare*. Cardiovascular disease. Cat. no. CVD 83. Canberra: AIHW. Viewed 26 August 2021, https://www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium.* 2020.

189. Australian Institute of Health and Welfare (AIHW), *Australian health expenditure—demographics and diseases: hospital admitted patient expenditure 2004–05 to 2012–13*, in *HEALTH AND WELFARE EXPENDITURE SERIES*. 2017, AIHW: Australia.

190. Australian Institute of Health and Welfare (AIHW), *Cardiovascular health compendium. Web report. Last updated 22 DEC 2017.* 2017.

191. Australian Institute of Health and Welfare *(*AIHW*). Australia's health 2016. Australia's health series no. 15.Cat. no. AUS 199. Canberra: AIHW. 2016.* 2016.

192. Jonsson, B., *Measurement of health outcome and associated costs in cardiovascular disease.* Eur Heart J, 1996. **17 Suppl A**: p. 2-7.

193. AIHW, *Australian Institute of Health and Welfare 2009. Chronic disease and participation in work. Cat. no. PHE 109. Canberra: AIHW.* 2009.

194. Price, A.E., *Heart disease and work.* Heart, 2004. **90**(9): p. 1077-84.

195. AustralianNetworkonDisability, *The economic benefits of increasing employment for people with disability, Commissioned by the Australian Network on Disability (AND), retrieved December 8, 2019*. 2011, Australian Network on Disability (AND): https://www.and.org.au/data/Conference/DAE_Report_8May.pdf.

196. Virtanen, M., et al., *The joint contribution of cardiovascular disease and socioeconomic status to disability retirement: A register linkage study.* Int J Cardiol, 2017. **230**: p. 222-227.

197. Nwaru, C.A., et al., *Chronic diseases as predictors of labour market attachment after participation in subsidised re-employment programme: a 6-year follow-up study.* J Epidemiol Community Health, 2017. **71**(11): p. 1101-1106.

198. Mittendorfer-Rutz, E., et al., *Synergistic effect between ischaemic heart disease and common mental disorders and the risk of premature exit from the labour market: a nationwide register based study from Sweden.* Eur Heart J, 2018. **39**(7): p. 578-585.

199. Paradise, M.B., et al., *The impact of gender on early ill-health retirement in people with heart disease and depression.* Aust N Z J Psychiatry, 2012. **46**(3): p. 249-56.

200. Britton, A., et al., *Limitations to functioning and independent living after the onset of coronary heart disease: what is the role of lifestyle factors and obesity?* Eur J Public Health, 2012. **22**(6): p. 831-5.

201. Australian Institute of Health Welfare *(*AIHW*,), People with disability in Australia*. 2019, AIHW: Canberra.

202. Irvine, K., R. Hall, and L. Taylor, *Centre for Health Record Linkage: expanding access to linked population data for NSW and the ACT, Australia.* Int J Popul Data Sci, 2019. **4**(2).

203. Australian Institute of Health and Welfare (AIHW). *Rural, regional and remote health: A guide to remoteness classifications.* 2004. AIHW cat. no. PHE **53**.

204. Jung, Y., et al., *The Effects of Employment Conditions on Smoking Status and Smoking Intensity: The Analysis of Korean Labor & Income Panel 8th–10th Wave.* PLOS ONE, 2013. **8**(2): p. e57109.

205. Sidorchuk, A., et al., *Employment status and psychological distress in a population-based cross-sectional study in Sweden: the impact of migration.* BMJ Open, 2017. **7**(4): p. e014698.

206. Kikuchi, H., et al., *Social participation among older adults not engaged in full- or part-time work is associated with more physical activity and less sedentary time.* Geriatr Gerontol Int, 2017. **17**(11): p. 1921-1927.

207. Schofield, D., et al., *Costs of being a carer: labour force participation and lost earnings among older working-aged Australians.* Aust N Z J Public Health, 2013. **37**(2): p. 192-3.

208. Hays R, L.H., Spritzer K, et al, *Item response theory analyses of physical functioning items in the medical outcomes study.* Medical Care, 2007. **45**: p. S32-8.

209. Kendir, C., et al., *Cardiovascular disease patients have increased risk for comorbidity: A cross-sectional study in the Netherlands.* Eur J Gen Pract, 2018. **24**(1): p. 45-50.

210. Audelin, M.C., P.D. Savage, and P.A. Ades, *Exercise-based cardiac rehabilitation for very old patients (> or =75 years): focus on physical function.* J Cardiopulm Rehabil Prev, 2008. **28**(3): p. 163-73.

211. International Labour Office, *International Standard Classification of Occupations 2008 (ISCO-08): Structure, group definitions and correspondence tables. 2012*: International Labour Office.

212. Ramirez-Santana, M., *Limitations and biases in cohort studies . Available from: https://www.intechopen.com/books/cohort-studies-in-health-sciences/limitations-and-biases-in-cohort-studies doi: 10.5772/intechopen.74324*. 2018: IntechOpen.

213. Australian Bureau of Statistics (ABS)*. Labour force, Australia, May 2008. Cat. no. 6202.0. 2008.* 2008.

214. Australian Institute of Health and Welfare (AIHW*). Cardiovascular disease: Australian facts 2011. Cardiovascular disease series. Cat. no. CVD 53. Canberra: AIHW. 2011.* 2011.

215. Australian Heart Foundation. Mental health and heart disease (https://www.heartfoundation.org.au/heart-health-education/mental-health-and-heart-disease), (accessed on 18 December 2021).

216. Jette AM, Field MJ. *The Future of Disability in America. Washington, DC: The National Academies Press. https://doi.org/10.17226/11898.*, in *The Future of Disability in America*.

217. Holt-Lunstad, J., T.B. Smith, and J.B. Layton, *Social relationships and mortality risk: a meta-analytic review.* PLoS Med, 2010. **7**(7): p. e1000316.

218. Mookadam, F. and H.M. Arthur, *Social Support and Its Relationship to Morbidity and Mortality After Acute Myocardial Infarction: Systematic Overview.* Arch Intern Med, 2004. **164**(14): p. 1514-1518.

219. Xia, N. and H. Li, *Loneliness, Social Isolation, and Cardiovascular Health.* Antioxid Redox Signal, 2018. **28**(9): p. 837-851.

220. Holt-Lunstad, J. and T.B. Smith, *Loneliness and social isolation as risk factors for CVD: implications for evidence-based patient care and scientific inquiry.* Heart, 2016. **102**(13): p. 987-989.

221. Northcott, S., J. Marshall, and K. Hilari, *What Factors Predict Who Will Have a Strong Social Network Following a Stroke?* J Speech Lang Hear Res, 2016. **59**(4): p. 772-83.

222. Northcott, S., S.P. Hirani, and K. Hilari, *A Typology to Explain Changing Social Networks Post Stroke.* Gerontologist, 2018. **58**(3): p. 500-511.

223. Chang, S.C., et al., *Social Integration and Reduced Risk of Coronary Heart Disease in Women: The Role of Lifestyle Behaviors.* Circ Res, 2017. **120**(12): p. 1927-1937.

224. Welin, C.L., A. Rosengren, and L.W. Wilhelmsen, *Social relationships and myocardial infarction: a case-control study.* J Cardiovasc Risk, 1996. **3**(2): p. 183-90.

225. Zhaoyang, R., et al., *Age differences in adults' daily social interactions: An ecological momentary assessment study.* Psychol Aging, 2018. **33**(4): p. 607-618.

226. Deaux, K. and B. Major, *Putting gender into context: An interactive model of gender-related behavior.* Psychological review, 1987. **94**(3): p. 369.

227. Brueckner, J.K. and A.G. Largey, *Social interaction and urban sprawl.* J. Urban Econ, 2008. **64**(1): p. 18-34.

228. Joshy, G., et al., *Impact of loss to follow-up on estimates of well-established exposure and health outcome relationships*, in *Proceedings of the 40th Annual Conference of theInternational Society for Clinical Biostatistics 2019, Leuven, Belgium.* 2019.

229. Rothman, K.J., J.E. Gallacher, and E.E. Hatch, *Why representativeness should be avoided.* Int J Epidemiol, 2013. **42**(4): p. 1012-4.

230. Adams, K.B., S. Leibbrandt, and H. Moon, *A critical review of the literature on social and leisure activity and wellbeing in later life.* Ageing Soc, 2011. **31**(4): p. 683-712.

231. WHO, *World Health Organization: The world health report 2008: primary health care now more than ever:* 2008: World Health Organization.

232. Mendes de Leon, C.F., T.A. Glass, and L.F. Berkman, *Social Engagement and Disability in a Community Population of Older Adults: The New Haven EPESE.* Am J Epidemiol, 2003. **157**(7): p. 633-642.

233. Rimmer, J.H., et al., *Accessibility of Health Clubs for People with Mobility Disabilities and Visual Impairments.* Am J Public Health, 2005. **95**(11): p. 2022-2028.

234. Everard, K.M., et al., *Relationship of Activity and Social Support to the Functional Health of Older Adults.* J Gerontol B Psychol Sci Soc Sci, 2000. **55**(4): p. S208-S212.

235. Etman, A., et al., *Do lifestyle, health and social participation mediate educational inequalities in frailty worsening?* Eur J Public Health, 2014. **25**(2): p. 345-350.

236. Australian Institute of Health and Welfare. *Social isolation and loneliness*. (https://www.aihw.gov.au/reports/australias-welfare/social-isolation-and-loneliness-covid-pandemic. 2021) (accessed on 18 December 2021).

237. Australian Government Department of Social Services, *Seniors Connected Program* (https://www.dss.gov.au/communities-and-vulnerable-people-programs-services/seniors-connected-program ; accessed on 22 January, 2022).

238. Coggon, D., G. Rose, and D. Barker, *Chapter 4. Measurement error and bias, in Epidemiology for the uninitiated (https://www.bmj.com/about-bmj/resources-readers/publications/epidemiology-uninitiated/4-measurement-error-and-bias)*.

239. LaMorfe, W., *Boston University School of Public Health website: https://sphweb.bumc.bu.edu/otlt/mph-modules/ep/ep713_bias/ep713_bias3.html#headingtaglink_1*

240. Little, R.J. and D.B. Rubin, *Statistical analysis with missing data*. Vol. 793. 2019: John Wiley & Sons.

241. Van Buuren, S., *Flexible imputation of missing data*. 2018: CRC press.

242. Lee, K.J. and J.B. Carlin, *Recovery of information from multiple imputation: a simulation study.* Emerg Themes Epidemiol, 2012. **9**(1): p. 1-10.

243. Kang, H., *The prevention and handling of the missing data.* Korean J Anesthesiol, 2013. **64**(5): p. 402-6.

244. Carpenter, J.R. and M. Smuk, *Missing data: A statistical framework for practice.* Biom J. 2021. **63**(5): p. 915-947.

245. Klebanoff, M.A. and S.R. Cole, *Use of Multiple Imputation in the Epidemiologic Literature.* Am J Epidemiol, 2008. **168**(4): p. 355-357.

246. Schafer, J.L., *Analysis of incomplete multivariate data*. 1997: CRC press.

247. Schafer, J.L. and M.K. Olsen, *Multiple imputation for multivariate missing-data problems: A data analyst's perspective.* Multivariate Behav Res, 1998. **33**(4): p. 545-571.

248. Molenberghs, G. and M. Kenward, *Missing data in clinical studies*. Vol. 61. 2007: John Wiley & Sons.

249. von Hippel, P.T., *Should a Normal Imputation Model be Modified to Impute Skewed Variables?* Sociol Methods Res, 2013. **42**(1): p. 105-138.

250. Lee, K.J., et al., *Multiple imputation for missing data in a longitudinal cohort study: a tutorial based on a detailed case study involving imputation of missing outcome data.* Int J Soc Res Methodol, 2016. **19**(5): p. 575-591.

251. Galimard, J.-E., et al., *Heckman imputation models for binary or continuous MNAR outcomes and MAR predictors.* BMC Med Res Methodol. 2018. **18**(1): p. 1-13.

252. Graham, J.W., *Missing data: Analysis and design*. 2012: Springer Science & Business Media.

253. Rubin, D.B., *Multiple imputation after 18+ years.* J Am Stat Assoc, 1996. **91**(434): p. 473-489.

254. Carpenter, J.R., M.G. Kenward, and I.R. White, *Sensitivity analysis after multiple imputation under missing at random: a weighting approach.* Stat Methods Med Res, 2007. **16**(3): p. 259-75.

255. SASInstituteInc., *SAS Institute Inc. 2015. (Chapter 75: The MI Procedure) SAS/STAT® 14.1 User's Guide. Cary, NC: SAS Institute Inc.* 2015.

256. Berglund, P. and S.G. Heeringa, *Multiple imputation of missing data using SAS*. 2014: SAS Institute.

257. Marshall, A., et al., *Comparison of techniques for handling missing covariate data within prognostic modelling studies: a simulation study.* BMC Med Res Methodol, 2010. **10**(1): p. 1-16.

258. Rubin, D.B., *Multiple imputation for survey nonresponse*. 1987, New York: Wiley.

259. Cro, S., et al., *Sensitivity analysis for clinical trials with missing continuous outcome data using controlled multiple imputation: a practical guide.* Stat Med, 2020. **39**(21): p. 2815-2842.

260. Carpenter, J. and M. Kenward, *Multiple imputation and its application*. 2012: John Wiley & Sons.

261. Vandenbroucke, J.P., et al., *Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration*. PLoS Med, 2007. 4(10): p. e297.

262. Karahalios, A., et al., *A review of the reporting and handling of missing data in cohort studies with repeated assessment of exposure measures*. BMC Med Res Methodol. 2012. 12(1): p. 96.

263. Australian Institute of Health and Welfare (AIHW), *Australia's health performance framework. (last accessed June 3, 2021)*. 2021; Available from: https://www.aihw.gov.au/reports-data/indicators/australias-health-performance-framework.

264. OECD, *How's Life? 2020: Measuring Well-being, OECD Publishing, Paris, https://doi.org/10.1787/9870c393-en.* 2020.

265. Schnitzler, A., et al., *Participation in work and leisure activities after stroke: A national study.* Ann Phys Rehabil Med, 2019. **62**(5): p. 351-355.

266. Ra, Y.-A. and W.H. Kim, *Impact of employment and age on quality of life of individuals with disabilities: A multilevel analysis.* Rehabil Couns Bull, 2016. **59**(2): p. 112-120.

267. Datta, D., P.P. Datta, and K.K. Majumdar, *Role of social interaction on quality of life.* National J Med Res, 2015. **5**(4): p. 290-292.

268. Lay-Yee, R. and G. Cotterell, *The role of microsimulation in the development of public policy, in Policy Practice and Digital Science*. 2015, Springer. p. 305-320.

269. Global Burden of Cardiovascular Diseases Collaboration, *The Burden of Cardiovascular Diseases Among US States, 1990-2016The Burden of Cardiovascular Diseases Among US States, 1990-2016The Burden of Cardiovascular Diseases Among US States, 1990-2016.* JAMA Cardiol, 2018. **3**(5): p. 375-389.

270. Schofield, D., et al., *The indirect costs of ischemic heart disease through lost productive life years for Australia from 2015 to 2030: results from a microsimulation model*. BMC Public Health, 2019. 19(1): p. 802.

271. Virani, S.S., et al., *Heart Disease and Stroke Statistics - 2020 Update: A Report From the American Heart Association*. Circulation, 2020. 141(9): p. e139-e596.

272. Nicholson, N.R., *A Review of Social Isolation: An Important but Underassessed Condition in Older Adults.* J Prim Prev, 2012. **33**(2): p. 137-152.

273. Mukherjee, D., et al., *The Cognitive, Emotional, and Social Sequelae of Stroke: Psychological and Ethical Concerns in Post-Stroke Adaptation*. Top Stroke Rehabil., 2006. 13(4): p. 26-35.

274. Haz, L., et al. *Digital Platforms as Means of Social Interaction: Threats and Opportunities in Online Affective Relationships. 2019*. Cham: Springer International Publishing.

275. Wang, C., et al., *Risk-Attributable Burden of Ischemic Heart Disease in 137 Low- and Middle-Income Countries From 2000 to 2019*. J Am Heart Assoc, 2021. 10(19): p. e021024.

276. Australian Institute of Health and Welfare. *Unemployment and parenting income support payments [Internet].* Canberra: Australian Institute of Health and Welfare, 2021 [January 26, 2022]. Available from: https://www.aihw.gov.au/reports/australias-welfare/unemployment-and-parenting-income-support-payments.

277. Department of Social Services (Australian Government), *Disability Employment Services to help employers recruit and retain employees with disability* (https://www.dss.gov.au/sites/default/files/documents/09_2014/emloyers_guide_to_employing_someone_with_disability_0.pdf). 2014.

278. Thorpe, J., et al., *Income security during periods of ill health: a scoping review of policies, practice and coverage in low-income and middle-income countries*. BMJ Glob Health, 2020. 5(6): p. e002425.

279. Fokkema, T., et al., *Cross-National Differences in Older Adult Loneliness*. J Psychol, 2012. 146(1-2): p. 201-228.

280. Australian Institute of Health and Welfare (AIHW). *Cardiovascular disease: Australian facts 2011. Cardiovascular disease series. Cat. no. CVD 53. Canberra: AIHW. 2011.*

281. Australian Bureau of Statistics, *Characteristics of Employment, Australia (https://www.abs.gov.au/statistics/labour/earnings-and-work-hours/characteristics-employment-australia).* 2020.

282. Australian Bureau of Statistics*. Multi-Agency Data Integration Project (MADIP), ABS Website, accessed 22 July 2021.*

283. Andersson, C. and R.S. Vasan, *Epidemiology of cardiovascular disease in young individuals.* Nat Rev Cardiol, 2018. **15**(4): p. 230-240.

284. Gülaçtı, F., *The effect of perceived social support on subjective well-being.* Procedia Soc Behav Sci, 2010. **2**(2): p. 3844-3849.

285. Canada, S. *Canadian Community Health Survey - Annual Component (CCHS) [Internet]*. 2014; Available from: http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3226.

286. WHO. *Cardiovascular diseases (CVDs)*. 2017 [cited 2019 18 February]; Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).

287. Benjamin, E.J., et al., *Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association.* Circulation, 2018. **137**(12): p. e67-e492.

288. OECD. *Working age population (indicator)*. 2019 [cited 2019 18/02].

289. Powers, J.R., et al., *Assessment of the abbreviated Duke Social Support Index in a cohort of older Australian women*. Australas J Ageing, 2004. 23(2): p. 71-76.

290. Macniven, R., et al., *Physical activity, healthy lifestyle behaviors, neighborhood environment characteristics and social support among Australian Aboriginal and non-Aboriginal adults*. Prev Med Rep, 2016. 3: p. 203-10.

291. Feng, X., et al., *Do social interactions explain ethnic differences in psychological distress and the protective effect of local ethnic density? A cross-sectional study of 226 487 adults in Australia.* BMJ Open, 2013. 3(5): p. e002713].

292. Vajdic, C.M., et al., *Demographic, social and lifestyle risk factors for cancer registry-notified cancer of unknown primary site (CUP).* Cancer Epidemiol, 2019. 60: p. 156-161].