

Understanding the Role of Loneliness in Population Health Outcomes and Health Care Utilisation

Neta HaGani

MSW

A thesis with publications submitted in fulfilment of the requirements
for the degree of Doctor of Philosophy



THE UNIVERSITY OF
SYDNEY

School of Public Health

Faculty of Medicine and Health

The University of Sydney

October 2024

This research reported in this thesis was supported by the award of a Research
Training Program scholarship to the PhD Candidate

In dedication and memory of my grandmother Frida Levi

מוקדש לסבתי פרידה לוי, יהי זכרה ברוך

STATEMENT OF ORIGINALITY

This is to certify that to the best of my knowledge, the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes. I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

I confirm that I served as the principal contributor to the conceptual framework that forms the foundation of this thesis. Additionally, I took the lead in conducting the analysis and drafting all publications incorporated in this work. Detailed author contributions are detailed in Chapters 3-6.

Signature:

Name: Neta HaGani

Date: 15 June 2024

In our capacity as supervisors overseeing the candidature upon which this thesis is built, we can verify the accuracy of the authorship attribution statements provided in Chapters 3-6.

Signature:

Name: Ding Ding

Date: 15 June 2024

Signature:

Name: Ben J Smith

Date: 15 June 2024

Signature:

Name: Philip J Clare

Date: 15 June 2024

Signature:

Name: Dafna Merom

Date: 15 June 2024

ACKNOWLEDGEMENTS

My PhD journey would not be possible without the help of others. I would like to acknowledge my family, friends, supervisors, colleagues and fellow students, for supporting me throughout my PhD. It truly does take a village. First, I am immensely grateful to the **Faculty of Medicine and Health at the University of Sydney** for awarding me the RTP scholarship. This opportunity is invaluable to me, and I deeply appreciate your confidence in my abilities. Receiving this scholarship has made it possible for me to pursue my PhD, for which I am eternally thankful.

I am deeply thankful to my supervisory team **Melody Ding, Dafna Merom, Ben Smith, and Philip Clare** for their guidance and support. I appreciate your willingness to share your expertise, your patience, and respect throughout my educational journey. Thank you for being accessible and accommodating the challenges of long-distance supervision during the COVID-19 pandemic. Your support has been invaluable. I would like to extend a special thanks to **Melody Ding and Dafna Merom**. You are truly my mentors and role models, inspiring me both professionally and personally as strong, successful, uncompromising women in academia. Your dedication to providing incredible opportunities and doing everything within your power to ensure my success has not gone unnoticed. Thank you for going above and beyond, especially in making me feel at home and building a social network for me even before my arrival, which significantly impacted my experience. I would also like to acknowledge my honorary supervisor **Gil Merom** for your kind support and advice, for the soft landing you and Dafna provided me and especially for the amazing sushi!

Susan, Lucy and Daniel, my PhD gang! Thank you for always being there to encourage, to offer a kind word or a piece of practical advice. I also want to express my deep appreciation to my colleagues from the Prevention Research Collaboration, specifically **PH, Lisa, Bronwyn, Binh, Fiona, Tracy, Nicole, Karen, Karine, Becky, Zoe and Robert**. Thank you for welcoming me into your research group, making me feel at home, and becoming my work family. I couldn't have asked for a better place to pursue my PhD. I would also like to extend my gratitude to the **Charles Perkins Centre** for creating enriching academic learning and social opportunities for students. Your support has been instrumental in my development and experience as a researcher.

I would also like to express my greatest appreciation to my supervisors, mentors and colleagues at the University of Haifa and Rambam Health Care Campus, **Manfred Green**,

Orna Baron-Epel, Riki Tesler, Roni Gaglin, Ilana Duvdevani, Carmit-Noa Shpigelman, Miri Cohen and Mika Moran. Thank you for giving me my start in research, for your support in my PhD process, and your mentorship, guidance and friendship!

Above all, I want to express my deepest gratitude to my supportive and loving family. To my **mom, Pnina**, who has consistently been there for me, always willing to do anything to ensure my happiness, and to my brother and sister, **Oren and Maya**, thank you for your unwavering support and belief in me. I am also grateful to my extended family, **Nahum, Noa, Ilil, Goni, Tomer and Yosi** for their continuous support and acceptance. Your encouragement has been a cornerstone of my journey. A special acknowledgement to my grandmother, **Frida Levi**, a real-life wonder woman who has been my role model for my entire life and has encouraged me to follow my dreams even though they were different from hers.

Lastly, I want to express my gratitude to my friends back home, **Riki, Michal, Liat, Sivan, Sima and Shvat**. Your encouragement and unwavering belief in me have meant the world. To my sisters from other misters, **Elisa and Bruna**, thank you for your support, for offering valuable perspectives on life, and for ensuring I never felt alone. Your presence has been a source of strength and comfort throughout my journey.

Thank you

TABLE OF CONTENTS

STATEMENT OF ORIGINALITY	ii
ACKNOWLEDGEMENTS.....	iii
TABLE OF CONTENTS	v
ABBREVIATIONS.....	xi
ABSTRACT.....	xii
CHAPTER 1: Introduction and review of the literature	1
1.1. Preface- the rise of social wellbeing research.....	1
1.2. Psychosocial constructs	1
1.2.1. Distinguishing between psychosocial constructs.....	4
1.2.2. Loneliness as a social construct	5
1.2.3. Measuring loneliness	6
1.3. Loneliness prevalence and trends	8
1.4. Loneliness determinants.....	10
1.4.1. Individual-level determinants of loneliness	10
1.4.2. Society-level determinants of loneliness	14
1.4.3. Environment-level determinants of loneliness.....	16
1.5. The effect of loneliness on individuals' health and its economic consequences.....	17
1.5.1. Association of loneliness with health and wellbeing outcomes.....	17
1.5.2. The economic implications of loneliness.....	19
1.6. Intervention and prevention strategies	20
1.6.1. Psychosocial interventions – types and effectiveness.....	20
1.6.2. The effect of social interventions on individuals' health	22
1.7. Appendices.....	24
Appendix 1.7.1. 20-item UCLA Loneliness Scale (36).....	24
Appendix 1.7.2. 11-item de-Jong Gierveld Loneliness Scale (34).....	25
1.8. References.....	27
CHAPTER TWO: Theoretical framework and research overview	52
2.1. Thesis rational.....	52
2.2. Theoretical framework.....	55
2.3. Purpose and outline of the current thesis	56
2.3.1. Thesis outline	57

2.4. References.....	59
CHAPTER THREE: The effect of retirement on loneliness: A longitudinal comparative analysis across Australia, China, and the United States.....	62
3.1. Preface to the chapter.....	62
3.2. Research dissemination.....	62
3.3. Author attribution statement	63
3.4. Paper in published format	63
3.5. Appendices.....	71
3.6. Concluding summary for this chapter and knowledge gained from this study.....	102
CHAPTER FOUR: Loneliness and long-term health-related quality of life: A latent class analysis among middle-aged and older Australian women.....	103
4.1. Preface to the chapter.....	103
4.2. Research dissemination.....	103
4.3. Author attribution statement	103
4.4. Manuscript	105
4.5. References.....	117
4.6. Appendices.....	134
4.7. Concluding summary for this chapter and knowledge gained from this study.....	161
CHAPTER FIVE: Loneliness and all-cause mortality in middle-aged Australian women: A causal inference analysis of longitudinal data	162
5.1. Preface to the chapter.....	162
5.2. Research dissemination.....	162
5.3. Author attribution statement	162
5.4. Manuscript	164
5.5. References.....	177
5.6. Appendices.....	187
5.7. Concluding summary for this chapter and knowledge gained from this study.....	215
CHAPTER SIX: Health care utilization following interventions to improve social well-being: A systematic review and meta-analysis	216
6.1. Preface to the chapter.....	216
6.2. Research dissemination.....	216
6.3. Author attribution statement	217
6.4. Paper in published format	217
6.5. Appendices.....	235

6.6.	Concluding summary for this chapter and knowledge gained from this study.....	277
CHAPTER 7: Discussion.....		278
7.1.	Overview	278
7.1.	Thesis key findings and significance	279
7.2.	Determinants and outcomes of loneliness from a social-ecological perspective...	283
7.2.1.	Individual-level determinants and outcomes of loneliness.....	283
7.2.2.	Social and community level determinants of loneliness.....	286
7.3.	Implications for health professionals and policymakers.....	291
7.4.	Methodological strengths and limitations.....	292
7.5.	Directions for future research	294
7.6.	Conclusions.....	296
7.7.	References.....	297
APPENDICES		310
Appendix 1. Additional publications.....		310

LIST OF TABLES

Chapter 1

Table 1. Summary of common psychosocial constructs used in research	3
---	---

Chapter 3

Tables included in the paper published in the Journal of Epidemiology and Community Health

Table 1 Baseline characteristics of participants in Australia (2008), China (2011) and the USA (2008–2010)	67
--	----

Chapter 4

Table 1. Baseline characteristics of participants- The Australian Longitudinal Study of Women's Health (ALSWH) 1946-51 cohort (waves 1-2; n = 13, 714)	125
--	-----

Table 2. Multivariate multinomial logistic regression predicting latent class membership using baseline predictors	127
--	-----

Table 3. Multivariate multinomial linear regression predicting latent class membership using baseline predictors (Beta coefficients, 95%CI): Data fully adjusted, adjusted only for sociodemographic characteristics and unadjusted	130
---	-----

Chapter 5

Table 1. Baseline characteristics of participants: The Australian Longitudinal Study of Women's Health (ALSWH) 1946-51 cohort (waves 1-2; n = 11,412).....	183
--	-----

Chapter 7

Table 1. Summary of the key findings from the thesis chapters according to the theoretical framework of loneliness and associated health outcomes	280
---	-----

LIST OF FIGURES

Chapter 1

Figure 1. Measures of social constructs placed on the two dimensions of structure versus function and subjectivity versus objectivity (Valtorta et al (21)).....5

Figure 2. Age distribution of loneliness in 2014 (n = 1,278) and 2018 (n = 1,162) in the United States (US): General Social Survey Waves (64)9

Chapter 2

Figure 1. Theoretical framework of loneliness, social isolation, and associated health outcomes. A guiding framework developed by the National Academies of Sciences, Engineering, and Medicine (NASEM) on the Health and Medical Dimensions of Social Isolation and Loneliness in Older Adults 2020 (25).55

Figure 2. The thesis outline according to the theoretical framework of loneliness, social isolation, and associated health outcomes (25).....58

Chapter 3

Figures included in the paper published in The Journal of Epidemiology and Community Health

Figure 1. Adjusted marginal prevalence of loneliness according to retirement status in Australia, China and the USA. CHARLS, China Health and Retirement Longitudinal Study; HILDA, Household, Income and Labour Dynamics in Australia; HRS, Health and Retirement Study.....67

Figure 2. Adjusted marginal prevalence of loneliness according to the nature of retirement in Australia and the USA. HILDA, Household, Income and Labour Dynamics in Australia; HRS, Health and Retirement Study.67

Figure 3. Associations between the adjusted marginal prevalence of loneliness and retirement according to social engagement status in Australia, China and the USA. CHARLS, China Health and Retirement Longitudinal Study; HILDA, Household, Income and Labour Dynamics in Australia; HRA, Health and Retirement Study.....68

Figure 4. Adjusted marginal prevalence of loneliness among urban participants in Australia, China and the USA. CHARLS, China Health and Retirement Longitudinal Study; HILDA, Household, Income and Labour Dynamics in Australia; HRS, Health and Retirement Study.....68

Chapter 4

Figure 1. Probabilities of loneliness for each loneliness class over time.....133

Chapter 5

Figure 1. Risk of all-cause mortality (1 Jan 2001 to 31 Dec 2021) according to the total number of waves of experiencing loneliness185

Figure 2. All-cause mortality according to the number of consecutive waves of experiencing loneliness.....	186
--	-----

Chapter 6

Figures included in the paper published in JAMA Network Open

Figure 1. Flowchart of Identification of Studies Via Databases and Registers.....	222
Figure 2. Pooled 95%CI Odds Ratio of the Association of Psychosocial Interventions With Health Care Utilization.....	224
Figure 3. Pooled 95%CI Standardized Mean Difference of the Association of Psychosocial Interventions With Health Care Utilization.....	225
Figure 4. Pooled 95%CI Standardized Mean Difference of the Association of Psychosocial Interventions With Social Support.....	226
Figure 5. Pooled 95%CI Standardized Mean Difference of the Association of Psychosocial Interventions With Loneliness.....	227

Chapter 7

Figure 1. Number of studies on loneliness across time (7).....	278
--	-----

ABBREVIATIONS

ALSWH	Australian longitudinal study of women’s health
BMI	Body mass index
CBT	Cognitive behavioural therapy
CES-D	Centre for epidemiological studies depression
CHARLS	China health and retirement longitudinal study
CI	Confidence interval
COVID-19	Coronavirus disease 2019
DAG	Directed acyclic graph
ER	Emergency room
GP	General practitioner
HCU	Health care utilisation
HILDA	Household, Income and Labour Dynamics in Australia
HIV	Human immunodeficiency virus
HRQoL	Health-related quality of life
HRS	Health and retirement study
IPTW	Inverse probability of treatment weights
LCA	Latent class analysis
MSM	Marginal structural models
OR	Odds ratio
RCT	Randomised control trial
RR	Relative risk
SD	Standard deviation
SES	Socioeconomic status
SMD	Standardised mean difference
UCLA	University of California, Los Angeles
UK	United Kingdom
US	United States
WHO	World Health Organization

ABSTRACT

Loneliness, shaped by biological, personal, and environmental factors, is increasingly recognised for its impact on health. Despite extensive literature, causal evidence linking loneliness, its determinants, and health outcomes remains limited. This thesis investigates the independent long-term effect of loneliness on health and mortality while exploring community and societal factors that influence loneliness. It also examines the potential for intervention and prevention to reduce loneliness and alleviate its economic impact. **Chapter 3** includes a study of cross-country comparisons to understand the causal effect of retirement on loneliness across cultures with similarities and differences in macro-level determinants. **Chapter 4** identified longitudinal trajectories of loneliness among middle-aged and Australian women and examined predictors of these trajectories and their associations with health-related quality of life (HRQoL). **Chapter 5** explored the causal effects of persistent and chronic loneliness on mortality among Australian women, estimated using targeted maximum likelihood estimation. Finally, **Chapter 6** involved a systematic review and meta-analysis of the effect of psychosocial interventions on healthcare utilisation and social well-being. Altogether, our research indicates that loneliness determinants may vary depending on cultural norms and geographical regions. Additionally, long-term patterns of loneliness are negatively associated with HRQoL and increase the risk of mortality. Finally, our findings reveal that psychosocial interventions can increase social well-being and simultaneously decrease healthcare utilisation across different population groups and countries. These findings imply that loneliness is a significant social determinant of health with serious health and economic implications. Therefore, addressing social health should be prioritised from a public health standpoint, on par with the prevention of physical and mental health issues.

CHAPTER 1: Introduction and review of the literature

1.1. Preface- the rise of social wellbeing research

Research on social well-being, i.e., psychosocial constructs such as loneliness, social isolation, and social support, has witnessed significant growth over the past three decades (1). In its early days, loneliness and social isolation were perceived as personal failures to adapt to societal demands. Consequently, research on social well-being was initially limited, and public discourse around the topic was fueled by stigma and prejudice (2, 3). The surge in research on social well-being may be attributable to social changes such as urbanisation and globalisation, an increase in life expectancy, declining birth rates and family size in much of the developed world (1, 3). These trends have been identified as potential causes and contributing factors to a decline in social well-being and simultaneously, to a rise in physical and mental health conditions (3). Moreover, the growing awareness of the interconnectedness of social well-being and health has fueled research efforts to identify patterns and pathways of these associations (2, 3). The ongoing efforts to deconstruct the stigma surrounding social well-being have fostered legitimate discussions and greater exposure to this important topic (2). However, only in recent years, social connection (and its absence in the form of loneliness and isolation) has been recognised as a public health concern (4). Researchers across diverse disciplines have also come to acknowledge the therapeutic effect of social well-being on overall health, offering a solution to challenges faced by economies and healthcare systems (5-7). This chapter will define and review the current literature on loneliness as a psychosocial construct, and its importance to the health and well-being of individuals and societies worldwide. It will highlight the gaps in research and measurement of loneliness and will employ models to study the cause-and-effect relationships with health outcomes. Finally, this chapter will discuss psychosocial interventions' efficacy in improving physical, mental and social well-being and their importance in regulating health systems.

1.2. Psychosocial constructs

Psychosocial constructs of social well-being encompass a spectrum of experiences, both positive and negative, within the social realm (8). Some constructs reflect more positive aspects like social support, social relationships, and social engagement, emphasising the enriching and supportive aspects of interpersonal interactions. Conversely, some constructs characterise the negative dimensions of social well-being such as loneliness and social isolation, highlighting the potential challenges and adverse effects on social well-being

associated with social disconnection (9). Below are examples of the most common social constructs that are used to describe social well-being and frequently employed in research. These constructs are summarised in **Table 1**.

Social support

Social support refers to the assistance, comfort, and encouragement that individuals receive from their social connections, such as friends, family, peers, or community members (10). Social support can be classified into four types: emotional support, which involves offering empathy, love, and care; instrumental support, which includes the provision of direct aid and services; informational support, which entails giving advice and information; and appraisal support, which consists of providing constructive feedback and affirmation (11).

Social network

A social network refers to a structured pattern of relationships, interactions, or connections among individuals or groups. These connections can be interpersonal, involving friends, family, colleagues, and acquaintances, and they may extend to virtual platforms. Social networks provide a framework for communication, support, and the exchange of information. This includes both the quantitative features like network size, degree, and density, as well as the qualitative aspects such as network intensity and directionality (12).

Social engagement/ participation

Social engagement refers to active participation, involvement, or interaction within social activities, networks, or communities (13). It involves the extent to which individuals connect with others, contribute to social interactions, and play roles in social settings. Social engagement encompasses various forms of involvement, such as participating in conversations, joining group activities, volunteering, attending events, and maintaining relationships (14).

Social capital

Social capital refers to the collective experience and value of social networks, relationships, and shared norms within a community or society. It includes personal, interpersonal and community social resources (15), representing the trust, cooperation, and resources that individuals or groups accumulate through their social interactions and connections (16).

Social isolation

Social isolation refers to a state in which an individual lacks social connections or engagement with others. It is characterised by a significant reduction in social interactions, limited contact with friends, family, or community, and a sense of detachment from social networks (17). Social isolation can be either voluntary, as a personal choice to limit social interactions, or involuntary, arising from external factors such as geographical remoteness, health conditions, or societal circumstances (18).

Loneliness

Loneliness is a subjective, negative emotional response to a perceived discrepancy between a person's desired and actual social relationships. It involves a feeling of isolation, where an individual experiences a sense of being alone or lacking meaningful connections with others (19). Loneliness is not solely determined by the number of social contacts one has but is more about the perceived quality and satisfaction derived from those connections (20). Some researchers went a step further and defined different types of loneliness such as social, emotional, instrumental and existential (18). Social loneliness refers to the absence of a broader social network and connections, capturing a sense of isolation from the wider community; Emotional loneliness refers to the longing for deep, meaningful emotional connections and intimacy; instrumental loneliness revolves around the perception of lacking practical assistance or tangible support; existential loneliness involves a profound sense of being fundamentally alone or disconnected from the core of existence, encompassing a more philosophical or spiritual aspect (9).

Table 1. Summary of common psychosocial constructs used in research

Psychosocial Constructs	Definition
Social Support	The network of assistance, comfort, encouragement, information and feedback received from social connections, encompasses emotional and practical aid that contributes to well-being and resilience.
Social Network	A structured pattern of relationships, interactions, or connections among individuals or groups, that forms a complex web of social relationships and influences social identity.
Social Engagement	Participation, involvement, or interaction within social activities, networks, or communities, that reflects the extent to which individuals connect with others and contribute to social interactions.

Social Capital	The collective experience and value of social networks, relationships, and shared norms within a community or society, that fosters cooperation, trust, and mutual support.
Social Isolation	A significant reduction in social interactions and limited contact with friends, family, or community (can be voluntary).
Loneliness	A feeling of discrepancy between the observed and expected levels of different relationships and connections with others.

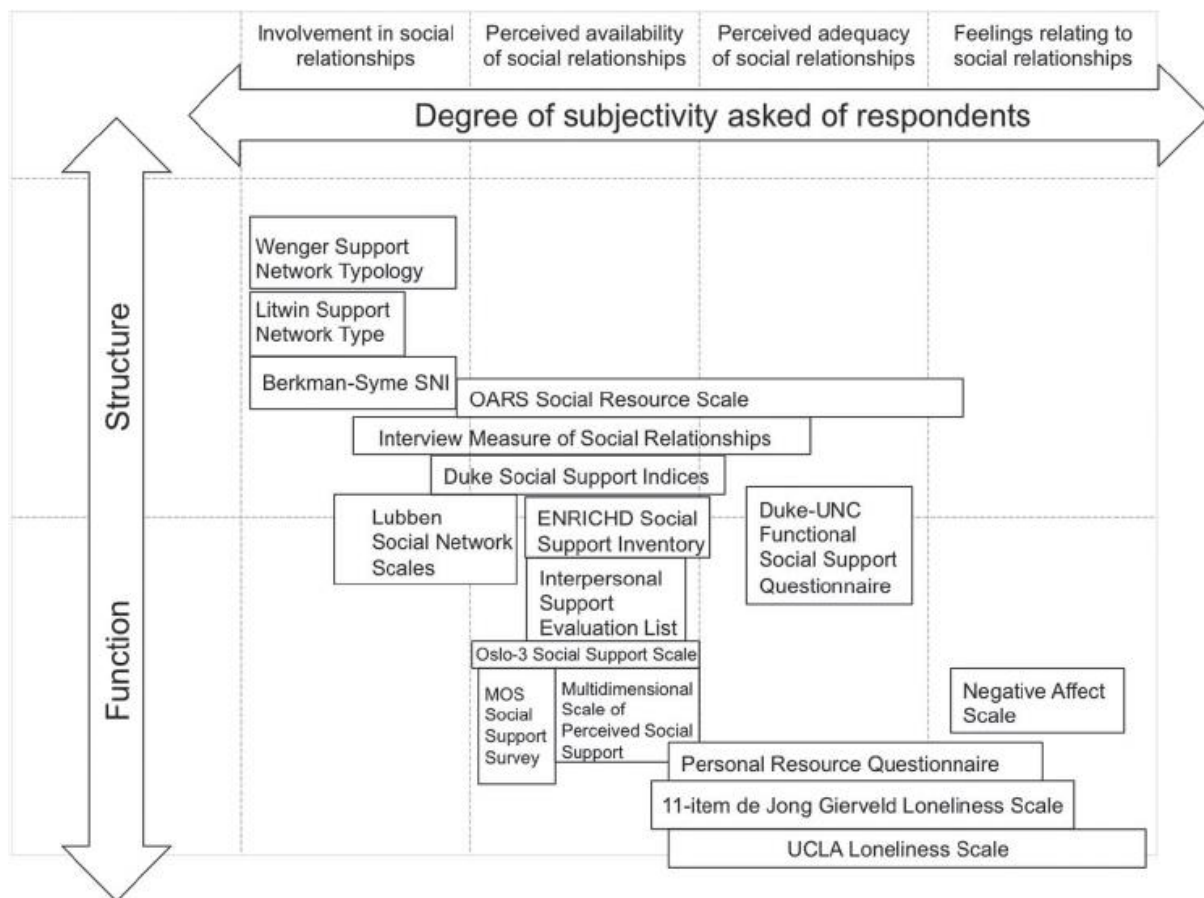
1.2.1. Distinguishing between psychosocial constructs

There is an overlap between a number of the psychosocial constructs presented in **Table 1**, and because of this researchers may occasionally employ these terms vaguely and interchangeably (21). A classification of these psychosocial constructs was conducted by Valtorta et al (2016) to better delineate the constructs and to assist researchers in choosing the right measure for a specific purpose (21). This classification distinguishes two dimensions across which social structures or concepts can range (22). The first is structure versus function. On the one end of this dimension are constructs that emphasise the structure of social networks/ relationships/ connections, i.e., how many social connections are there from each category (family, friends, colleges etc), the modes of communication (face-to-face, phone, email, social media) and the frequency of the relationship (daily, weekly, monthly etc). On the other side of this dimension are social constructs that emphasise the functionality of the social network/relationship/connections, i.e., describe the emotional, social and instrumental uses of social constructs (23). The second dimension considers the level of objectivity versus subjectivity of the social constructs. For example, constructs that tend to refer to quantitative aspects of relationships, i.e., the number of interactions and the frequency of these interactions, tend to be more objective (24), while constructs that emphasise satisfaction, perceptions, and feelings about the interactions, are more subjective (25).

Figure 1 places widely used measures of each construct shown in **Table 1** along the range of those two dimensions. Horizontally, lies the objectivity vs. subjectivity dimension and vertically is the structure vs. function dimension. For example, loneliness describes feelings towards social connections and measures of this construct are therefore placed on the subjectivity end of the spectrum. It refers to the emotional, social and instrumental functions of social support and is therefore placed on the functionality end of the spectrum. Social

networks and social isolation, emphasise quantitative aspects of social interactions such as the number of interactions and frequencies, therefore, measures of these constructs are placed on the end of the objectivity and structure dimensions. Notably, most of the measures tend to be centrally located in the middle of those two dimensions and address aspects from several sides of the spectrums.

Figure 1. Measures of social constructs placed on the two dimensions of structure versus function and subjectivity versus objectivity (Valtorta et al (21))



1.2.2. Loneliness as a social construct

All of the social constructs described above have been examined by observational as well as intervention studies (26-28). However, both the constructs of loneliness and social isolation have been continuously used in the literature to represent critical elements of social well-being, with loneliness representing the subjective experience and social isolation the more objective experience (18). They were found to be highly correlated, although individuals can experience loneliness while still having many and frequent social interactions, and vice versa (18, 20). The subjective emotions and perspectives of individuals play a significant role in their overall well-being and can influence their future health behaviours and social

interactions (29). Loneliness represents the lack of satisfaction of social connections, engagements, and support. It reflects the desire and need for more support and more positive interactions with others (18). Therefore, it is often being referred to as an important risk factor and a social determinant of health (30).

1.2.3. Measuring loneliness

Several measures have been developed over the years and are now commonly used to assess loneliness in different studies (31). Studies employing these measures have aimed to determine the prevalence, determinants and health implications associated with loneliness, and to evaluate the efficacy of psychosocial interventions (26, 32, 33). Some of the instruments include a battery of items to create a summary score of loneliness (34), while others include a one-item instrument that directly asks about the frequency of experiencing loneliness (35). While there are several multi-item instruments for measuring loneliness, the two that are widely recognised and used in both research and clinical settings are the University of California, Los Angeles (UCLA) Loneliness Scale (36, 37) and the de Jong Gierveld Loneliness Scale (31).

The UCLA Loneliness Scale

The UCLA Loneliness Scale has a full (20 items) (36) and a validated abbreviated version (3 items) (37). The full measure comprehensively addresses different dimensions of loneliness, including social, emotional, and relational aspects and includes a response to different statements such as “I have nobody to talk to”; “My social relationships are superficial” and “No one really knows me well”. The statements are measured on a scale of 0-3 (never-often) (36). The abbreviated measure refers to the frequency of feeling a lack of companionship, feeling left out and feeling isolated, on a scale of 1-3 (hardly ever, some of the time and often) (37) (**Appendix 1.1**).

de Jong Gierveld Loneliness Scale

The de Jong Gierveld Loneliness Scale offers a distinction between emotional and social loneliness. Similar to the UCLA scale, it has a full (34) and an abbreviated version (38). The original long scale includes 11 items on a 0-3 scale (none of the time - all of the time), with items reflecting different experiences such as: “I miss having a really close friend”; “There are enough people I feel close to”; “I often feel rejected”. The abbreviated version includes six selected items from the original scale with answers: “yes”, “more or less”, and “no” (**Appendix 1.2**).

Single-item instruments

There are several single-item measures for loneliness, which refer to the frequency of experiencing loneliness during a particular period (39-41). The loneliness item derived from the Centre for Epidemiologic Studies Depression Scale (CES-D) (35) is the most common item being used (33). It includes the item: “During the past week how often have you felt lonely?” The item is on a 4-point Likert scale: 1. ‘Rarely or none of the time (less than 1 day)’, 2. ‘Some or a little of the time (1-2 days)’, 3. ‘Occasionally or a moderate amount of time (3-4 days)’, 4. ‘Most or all of the time (5-7 days)’. The single-item loneliness measures are often re-categorised as binary variables with the two lower categories, categorised as “not lonely”, while the two upper categories are considered as “lonely” (42). However, there is no official cutoff point for this measure, and it appears that individuals categorised as "lonely" based on cut-off scores from multi-item scales may not align with those identified as "lonely" using cut-off scores from single-item measures (43, 44). This raises questions about whether single-item scores adequately capture the complexity of the construct in the same manner as scores from multi-item scales (45). The lack of a clear-cut definition of who is considered lonely has led to confusion in both the single and multi-item scales. This ambiguity may have contributed to the notable variability and inconsistency observed in loneliness prevalence and its associated outcomes (9, 33).

Although all instruments have undergone validation processes, with a moderate-high correlation between single and multi-item measures (39, 46, 47), there is still a discussion regarding the efficacy of single-item versus multi-item loneliness measurement scales (45). The advantages of one-item measures include their brevity, which mitigates the risk of participant fatigue, and their direct inquiry into loneliness, enhancing validity and reliability. However, single-item scales may overlook nuances in the experience of loneliness, such as distinguishing between emotional and social loneliness (40, 45). Additionally, the societal stigma surrounding loneliness may deter individuals from admitting their feelings, potentially introducing cultural bias (40). For example, gender differences in loneliness, commonly attributed to men hesitating to admit their loneliness due to societal norms surrounding masculinity, almost disappeared and were even reversed when using an indirect loneliness measure (48). While opinions vary on the preference for one-item or multi-item measures, both direct and indirect approaches have their merits. The United Kingdom (UK) Office of National Statistics has suggested that in situations where time or resource constraints dictate

the use of only one measure, opting for a direct inquiry specifically addressing loneliness is advisable (41).

Since loneliness is a subjective feeling and it can vary across ages, genders, and cultures, it is challenging to capture it across different populations (49-51). The subjective nature of self-reporting introduces an inherent limitation, as individuals may perceive and express loneliness differently (52). Cultural differences and social desirability can influence how loneliness is understood and communicated (52, 53). There is a high level of stigma that surrounds loneliness that may be more prominent in populations where mental and social health is not usually discussed openly (53). Despite these limitations, previous research has sought to identify loneliness's prevalence and trends across ages and countries. The next section will detail these findings on loneliness prevalence and explore its trajectories across different time and age groups, analysing how various contributors of loneliness may have influenced these trajectories.

1.3. Loneliness prevalence and trends

Loneliness differs globally and according to age, making it challenging to provide a singular estimate applicable universally. However, in a recent meta-analysis that estimated loneliness among adults across Europe, adults in Eastern European countries reported the highest levels of loneliness, while Northern European countries reported the lowest among countries with usable data (33). In a longitudinal study of Australian population-based data between the years 2014-2018, 34% of Australian adults experienced loneliness, with 21% experiencing episodic loneliness and 13% experiencing chronic loneliness (54).

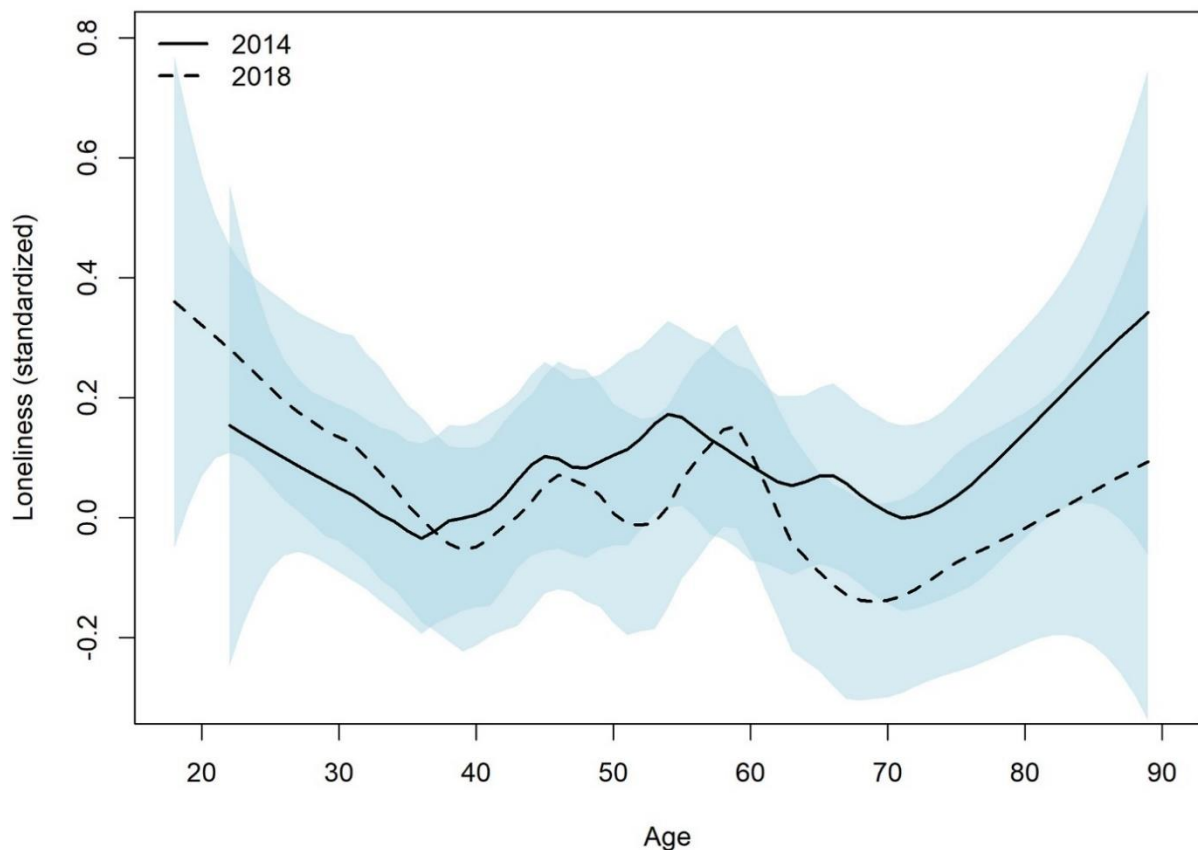
The trajectory of loneliness over time is debated. While it's evident that factors associated with objective social isolation, such as living alone and time spent alone, have risen over the past fifty years, it remains less certain whether loneliness has also increased during this time (55, 56). Most of the evidence on loneliness trends comes from cross-temporal meta-analyses. The evidence suggests a small increase in loneliness over time among young adults across countries such as the US and China (57, 58), although this evidence is mixed, with other studies showing opposite trends (59). Increases in loneliness have also been identified among older adults in China (60), however, these were found to be not significant in a worldwide meta-analysis (58). Although meta-analyses provide significant insights into loneliness trends, they may be prone to biases due to potential exclusions of data that do not meet inclusion criteria. On the other hand, individual studies often rely on

convenience samples with low response rates, limiting their representativeness to the broader population (61-63).

There is a lack of population-based studies on temporal trends in loneliness and there are only two studies that provide data from a longitudinal design, both from the US (64, 65). One study showed a decrease in loneliness among adults ages 50 and above from 20.1% in 1998 to 15.5% in 2018 (65). The second longitudinal study showed an increasing loneliness trend among young adults and a decreasing trend among older adults in the US between the years 2014-2018 (64). In addition, this study revealed a shift in loneliness trends between older and younger adults. In 2014 loneliness was most prevalent among the oldest-old demographic (ages 80-90) and least common among young adults (ages 20-30). However, observations from 2018 suggest that older adults, particularly those aged 70-90, now experience lower levels of loneliness, while younger adults face heightened rates of loneliness (64) (**Figure 2**). Given the absence of current studies from other countries on loneliness trends, it is challenging to determine whether this pattern is specific to the US or reflects a global trend.

Figure 2. Age distribution of loneliness in 2014 (n = 1,278) and 2018 (n = 1,162) in the United States (US): General Social Survey Waves (64)

Loneliness Distribution in 2014 and 2018



1.4. Loneliness determinants

Loneliness stems from a complex interplay of biological, personal, social and environmental factors. This section will outline the various determinants and mechanisms of loneliness according to the levels (individual, society, environmental) at which they occur.

1.4.1. Individual-level determinants of loneliness

Loneliness is an inherent feeling that is rooted in basic human existence. However, loneliness has been associated with several personal characteristics such as age, gender, marital and socioeconomic status (SES) and risky health behaviours. Additionally, loneliness is associated with life transitions and adversities such as illness and disability, retirement and more. Here I describe some of the more prominent individual-level determinants of loneliness.

Biological mechanisms and genetic predisposition

From an evolutionary standpoint, social connections and group living have provided survival advantages. As such, the human brain has evolved to prioritise social interactions (66). The brain has a specialised network known as the social brain network, which includes regions

like the prefrontal cortex, amygdala, insula, and anterior cingulate cortex (67). These areas are involved in social cognition, empathy, and emotional regulation (68). Loneliness is associated with altered activity in these brain regions including the dysregulation of cortisol and neurotransmitters like dopamine and serotonin. Additionally, it is associated with increased levels of pro-inflammatory cytokines (69). This brain activity is meant to trigger a biological stress response to encourage individuals to seek social connections for protection and support (66). But while loneliness is an adaptive function for short-term survival, in the modern world it may be experienced over a long period of time, therefore having long-term consequences on health and well-being (70, 71).

There is evidence to suggest that genetics may also play a role in individuals' susceptibility to loneliness (72) with heritability estimated between 14%-55% (73, 74). The genetic predisposition to loneliness is further supported by personality traits associated with cognition, perception, regulation, communication, and attachment, which have been found to predict loneliness and shape the experience of social (dis)connectedness (75). Individuals who display chronic loneliness may have a predisposed hypersensitivity to social exclusion, which in turn may lead to social isolation and exacerbate loneliness (76, 77). There are ongoing discussions about whether and to what extent loneliness should be conceptualised as a trait, as it shares similarities in heritability, stability, and change across the lifespan, similar to other broader personality traits (49). However, while broader personality traits and loneliness are interconnected, none of these relationships are notably strong enough to determine that loneliness is a trait (58). In addition, the effect of epigenetic factors on loneliness heritability, i.e., socio-environmental influences (diet, SES, area pollution etc..) that can affect how the body interprets and responds to DNA sequences, remains unclear (78).

Age

Apart from genetics, other personal characteristics such as age have been associated with loneliness (79). Although loneliness can be experienced at any age, research has focused on several age groups that may be more prone to loneliness than others (80). Older adults have been targeted for many years as the focus of loneliness research, especially due to the loss of social networks and the increase in chronic illnesses and disability during old age, which are both strongly associated with loneliness (81). However, more recent research has shown not only that loneliness does not increase with age (82), but younger adults have similar and even higher loneliness rates (50, 64, 83). The surge in loneliness among young adults is attributed

to mounting social pressures, including the challenges of navigating relationships, academic achievements, and identity formation, which have intensified over the past two decades, partly due to advancements in technology and social media (84-88). Both younger and older adults experience many formative life transitions that may contribute to heightened loneliness during adjustment periods. For younger adults, these may include puberty and leaving home and for older adults, these may include retirement, empty nest syndrome, and health changes (89-91). However, it has been suggested that the rise of loneliness among young adults may reflect generational differences in norms, including shifts in stigma and heightened emotional awareness (50).

Gender

There is conflicting evidence regarding the association between gender and loneliness. On the one hand, there is evidence that women are at increased risk of experiencing loneliness compared to men (51, 92, 93), which is consistent with the gender imbalance in other mental health risks such as depression and anxiety (94). In Australia, between the years 2001-2019 the pooled prevalence of loneliness among women aged 15-85 was 18.8%, compared to 16.1% in men, according to a single-item direct loneliness measure (95). The gender difference in loneliness is mostly explained by the greater vulnerability among women to health problems and disability (96). In addition, women have longer life spans and therefore may experience more occurrences of widowhood and living alone (97, 98). Other factors that may influence this association are potentially social and behavioural. Women's socialisation is focused more strongly on investing in and maintaining social ties (99), therefore they may display higher sensitivity to interpersonal relationships and may be more willing to admit they are lonely (100). Conversely, there is some evidence that men suffer from higher loneliness due to lower social connections and engagements compared to women (50, 101). The high stigma about loneliness may lead to underestimation of loneliness prevalence among men. There is evidence that studies that found higher or comparable loneliness rates between genders may have provided anonymity, such as online surveys, thus enabling participants to openly admit their genuine feelings (50), further proving the potential bias in the association between gender and loneliness.

Relationship status

One's relationship status is described as the strongest, most consistent predictor of loneliness (102). Most of the evidence on the association between relationship status and living situation

was obtained from older adults since old age is linked to singlehood (103). There is an indication that older adults who are in a relationship and/or who reside with others may experience lower levels of loneliness compared to those who are not in a relationship (104). However, while a fulfilling relationship between two healthy individuals is likely to prevent loneliness and enhance overall well-being, an unhappy relationship or a relationship that is filled with physical, financial or emotional stressors can lead to heightened feelings of loneliness, as evidenced by prior research (105). In addition, some factors such as social engagement, social capital, religiosity and gender were found to modify the association between relationship status and loneliness (103). For example, men, regardless of age, tend to invest fewer resources in their social networks, leaving them more vulnerable and with less emotional support when their relationship status changes (106, 107). In addition, some research has revealed that older individuals who have never been married exhibit less loneliness compared to those who have recently become single (103). Becoming divorced or widowed and losing a partner is an abrupt life change, which can significantly affect self-perception and mental well-being (107). However, long-term never-married individuals may develop social skills and circles, rendering them more resilient to loneliness compared to widowed, divorced, and separated older adults (108, 109).

Socio-economic status (SES)

Social determinants, such as income, education, access to resources and social support, play crucial roles in loneliness and health-related outcomes (101, 110). Population-based research from European countries like Denmark and The Netherlands shows that individuals in the lowest income bracket or living in deprived neighbourhoods often experience significantly higher levels of loneliness compared to those in the highest income group or the broader population (111, 112). This socioeconomic gap could be attributed to financial difficulties which may contribute to a sense of isolation as individuals struggle with meeting their expenses (113). In addition, individuals from lower socio-economic backgrounds may have limited access to social resources, such as community facilities and recreational activities, which may restrict social participation and engagement (114, 115). SES was also found to play a moderating role in the relationship between loneliness and health outcomes in a nationally representative Danish Health and Morbidity Survey (112). This could be due to individuals from lower SES backgrounds having fewer resources to manage loneliness and its associated health effects, which can intensify existing disparities (116). Additionally, residing

in economically disadvantaged areas with limited access to health and well-being resources may contribute to both loneliness and poor health (80).

1.4.2. Society-level determinants of loneliness

Society-level determinants of loneliness refer to factors beyond the personal characteristics of an individual. They include the norms, culture, religion, area SES, community characteristics, policies or any other factors present in the wider societal context in which individuals interact (102). These determinants may have a direct influence on loneliness (80). For example, the cohesiveness of a community and the social engagement opportunities it provides may affect individuals' experiences of loneliness (117). Alternatively, these factors can have an indirect effect on loneliness, for example, societal norms and culture may shape attitudes towards older adults, women, or other social minorities, influencing individuals' perceptions of themselves and their social surroundings, ultimately affecting levels of loneliness (118).

Country income level

There is an indication that loneliness is more prevalent in high-income compared to low-income countries (33). In previous cross-country analyses among European countries, it was found that the lowest prevalence of loneliness was consistently observed in high-income Northern European countries and the highest in low-middle-income Eastern European countries (33, 119). Low and middle-income countries may face challenges related to economic disparities, inadequate social infrastructure, and limited access to mental health services (102, 120). Loneliness and social isolation can then be exacerbated in these countries due to factors such as poverty, lack of community resources, and insufficient support systems (121).

It was also found that loneliness is higher in countries with higher levels of economic inequalities (122). Country-level economic inequality directly influences different aspects of life, including education, employment opportunities, income levels, access to healthcare, and social connections, thereby amplifying the number of individuals experiencing poverty (123), all of which may increase loneliness (101, 124). However, while higher-income countries may generally have more resources to invest in social programs and support systems, the prevalence of loneliness can still vary (82). In high-income countries, factors such as urbanisation, technological advancements, and changes in social structures can still contribute to increased feelings of loneliness (80).

Cultural and social norms

Cultural and social norms play a significant role in the way loneliness is experienced, manifested and reported (80, 125). For example, social norms regarding gender roles may influence the way different genders experience and express loneliness. Women's socialisation is focused more strongly on investing and maintaining social ties (99), therefore they may display higher sensitivity to interpersonal relationships compared to men (100). Deviations from these traditional social norms such as being single, identifying as nonbinary or having a physical/mental disability, have been found to increase loneliness (79, 126).

The most prominent cultural aspect examined in relation to loneliness is the individualism-collectivism spectrum. Individualistic cultures emphasise self-reliance, autonomy, and independent living away from family ties, whereas collectivistic cultures prioritise the needs of the family and community and reciprocal caregiving within the social unit (127, 128). Loneliness may be more prevalent in individualistic cultures because of factors such as increased single-households and distant relationships, as well as a heightened awareness of loneliness within these societies (50). However, there is an indication that individuals from collectivistic cultures experience higher levels of loneliness compared to individualistic cultures according to a study conducted across European countries (129, 130). This may be attributed to greater expectations from family and community to provide support, which may not always be met, leading to feelings of relationship dissatisfaction and loneliness despite the presence of strong social ties (130). Moreover, in individualistic cultures, the evolving concept of family is becoming more inclusive and less dependent on biological connections. As a result, individuals in these cultures may still find support and alleviate loneliness through diverse social networks and relationships (127). Therefore, the notion that increasing individualism automatically heightens the risk of loneliness in a population is not straightforward.

Community cohesiveness

The social dynamics within a community can significantly affect individuals' well-being (131). In communities characterised by strong cohesiveness, residents often benefit from supportive social networks, access to shared resources, and opportunities for community engagement (131). However, changes in work and lifestyle over the past decades have been associated with lower levels of volunteering, religious participation and engagement in neighbourhood activities (132, 133). In addition, the optimal community characteristics that contribute to cohesiveness and connectedness have been found to be less common in

disadvantaged neighbourhoods where there are fewer resources and where people have less time to socialise due to longer working hours and longer commute times (133).

Policies and regulations

Similar to SES, policies and regulations that affect social welfare, health, housing, employment, transportation, education etc, can shape the experience of loneliness within a society (134). For example, social welfare policies, such as accessible healthcare and social assistance programs, may contribute to reducing loneliness by providing individuals with a sense of security and support (135). Affordable housing initiatives also play a role in fostering stable communities, contributing to a sense of belonging and connection (136, 137). Policies that invest in recreational facilities, community centres, and social support networks create opportunities for people to engage in shared activities, fostering the development of meaningful relationships (134).

1.4.3. Environment-level determinants of loneliness

Environment-level determinants include country-level attributes such as geographical attributes or the built environment features. These factors may influence and interact with both the societal and individual level factors. For example, the built environment might intersect with age, constraining older adults' walkability due to broken sidewalks, inadequate green spaces, or a lack of nearby commercial centres in residential areas (138).

Geographic remoteness

Literature shows the differences in physical, mental and social well-being between residents of different regions according to the level of area remoteness (139-141). Residents of rural areas frequently face socio-economic disadvantages compared to their urban counterparts, including limited access to healthcare services that result in poorer health outcomes (142, 143). In Australia for example, ischemic heart disease morbidity was disproportionately higher and lifestyle behaviours associated with cancer incidence and mortality such as smoking, risky alcohol intake and low fruit and vegetable intake were poorer in regional and remote areas compared to major cities (144, 145). Rural authorities are also generally underfunded compared to urban areas and there is often a shortage of skilled workers, including health professionals (146). These health inequalities between rural and urban residents can potentially lead to lower social engagement and loneliness. However, research indicates that loneliness may not necessarily be more prevalent in rural areas and could even be lower compared to urban areas (147, 148). A UK longitudinal study between 2006-2014

revealed that it is not the remoteness of an area but rather its level of deprivation that influences loneliness in rural and urban areas (149). Another study from the US conducted in 2017-2018 suggested that expectations from perceived isolation may be the reason for urban residents reporting more loneliness compared to rural residents. While some degree of isolation is anticipated in rural settings, navigating feelings of isolation in vibrant urban environments could pose a greater challenge (147).

The built environment

Similar to area remoteness, the built environment, i.e., the human-made physical surroundings in which people live, work, and interact (150), has been a recent topic for discussion in the context of loneliness and other social constructs (151). As reported by a systematic review, the built environment was found to play an important role in shaping social connections and mitigating loneliness within communities (152). Well-designed urban planning, including accessible public spaces and pedestrian-friendly areas, can foster opportunities for social interaction and community engagement, and increase the sense of safety and social cohesion, thus, reducing the likelihood of loneliness and social isolation (138, 151, 153). Conversely, poorly planned urban spaces, lack of green areas, and disconnected infrastructure were found to contribute to feelings of loneliness and alienation (154, 155).

1.5. The effect of loneliness on individuals' health and its economic consequences

Similar to loneliness determinants, the effect of loneliness extends across multiple dimensions: individual, social, and environmental. However, the majority of direct consequences are at the individual level, particularly concerning physical health and mental well-being. It is these health-related outcomes of loneliness that ripple outward, impacting broader circles, including the social and economic implications of elevated rates of disconnection within communities and workplaces.

1.5.1. Association of loneliness with health and wellbeing outcomes

Loneliness has been found to be associated with various aspects of an individual's well-being, encompassing physical, mental and social health, quality of life, and even mortality (32, 156). Physically, loneliness was found to be associated with the incidence of several health conditions such as diabetes, heart disease, stroke, cancer and even premature death (32, 157, 158). A systematic review that examined the risk of loneliness on the incidence of coronary heart disease and stroke found a 29% higher risk of heart disease and 32% higher risk of

stroke among lonely individuals (158). Loneliness has also been found to be associated with a 23% increased risk for prostate cancer and a 10% risk for total cancer incidence after adjustments for lifestyle and health-related covariates (157).

Prolonged loneliness may also impair cognitive function and lead to difficulties in concentration and decision-making (159) and to cognitive disorders such as dementia (160). Longitudinal studies have provided evidence that loneliness can predict accelerated cognitive decline, even after adjustments for sociodemographic characteristics, health, mental health and social isolation (159, 161). Mentally, loneliness was found to be associated with severe mental health outcomes such as depression, anxiety, stress, bipolar disorder and schizophrenia (162-164). Notably, longitudinal research has found that loneliness at baseline predicted subsequent increased levels of depression, anxiety, poorer global mental health and heightened risk of an eating disorder (165).

The physical, mental and social ramifications of loneliness were found to play a role in mortality rates, with studies showing loneliness predicts an average of a 26% increased likelihood of mortality (166-169). However, across studies, findings are mixed as to whether loneliness independently predicts mortality risk after adjusting for initial health status, health behaviours, depression, and social isolation (170), with a significant attenuation of effect in the models that adjust for these factors (168, 171).

As described in **Section 1.4.1** the mechanism of the association between loneliness and different health outcomes is assumed to be through an evolutionary biological stress response which can be both the cause and the result of loneliness (172, 173). It is assumed that a biological stress response to loneliness may contribute to inflammation (174, 175) making individuals more vulnerable to conditions such as cardiovascular diseases, certain types of cancer and early mortality (157, 175, 176). In addition, a number of studies have found that loneliness is associated with unhealthy behaviours such as smoking, physical inactivity and poor diet, which also increases susceptibility to adverse health outcomes and premature death (173, 177, 178). In a public health survey among older adults ages 65-102, high perceived stress, daily smoking, physical inactivity and poor sleep duration were significant mediators in the association between loneliness and health outcomes such as cardiovascular disease, diabetes and migraine (179). Finally, it is suggested that individuals facing loneliness are less socially engaged and have a smaller social network. Therefore, they lack the necessary support system that could prevent a health condition from deteriorating, thereby contributing to impaired health and early mortality (180, 181).

It should be acknowledged that there is a growing body of evidence indicating that the relationships between loneliness and health outcomes are bidirectional (156, 182). While loneliness can contribute to the worsening of health outcomes (183), poor health and risky behaviours can also lead to increased loneliness due to challenges in fulfilling different social roles (184, 185). For example, loneliness may be the result of poor mental health due to difficulties in socialising and the stigma that surrounds mental disorders (186). Similarly, loneliness has been found to increase over time in longitudinal research conducted among older adults with chronic illness (187). There appears to be a reciprocal relationship between loneliness and health outcomes, forming a detrimental cycle where the effects of loneliness on health exacerbate feelings of loneliness, leading to additional health challenges (188).

1.5.2. The economic implications of loneliness

Despite the known health effects of loneliness, the economic implications of loneliness were not considered until recently, with evidence limited almost entirely to older adults and no studies conducted on adolescents or younger adults (189). However, there is an indication that the physical, mental, and social consequences of loneliness among older adults are associated with higher healthcare use and costs (190, 191). There is also evidence that older adults experiencing loneliness often seek medical care to deal with their lack of social connections, contributing to excess healthcare utilisation and increased costs (190, 192). However, the association between loneliness and healthcare use is not straightforward. While there is some evidence of increased inpatient care and use of general practitioners (GPs) among lonely individuals (193, 194), other studies have reported no effect on ambulatory care use (190) and a decrease in Medicare spending (195). Observed decreases in healthcare utilisation may be indicative of more available supports and resources that would enable individuals to access outpatient and preventive services (9). Lower usage of ambulatory and preventive care may in turn have a flow-on effect of higher rates of inpatient care among lonely individuals (196, 197).

A review of the economic implications of loneliness among older adults found only three studies. Among them, two identified increased healthcare expenses linked to loneliness, however, the third study found lower costs associated with loneliness but higher costs associated with social isolation (189). Although there is some information on the direct healthcare cost of loneliness, there is a paucity of data on the indirect cost of loneliness such as that related to productivity losses (189). Loneliness has been found to be associated with reduced job satisfaction, worse worker–manager relationships and elevated burnout (198). A

report issued by the New Economics Foundation for the UK National Commission on loneliness found the cost of loneliness to non-private employers to be £2.5 billion per year and £2.10 billion per year for private employers. The primary excess costs of loneliness stemmed from increased sickness absence, employees' caring responsibilities, loss of productivity and increased turnover (199).

1.6. Intervention and prevention strategies

With the increasing global recognition of the health consequences of loneliness, along with its financial implications on healthcare systems, loneliness has emerged as a significant public health concern. Consequently, various prevention and intervention strategies have been proposed spanning various activities, formats, and delivery methods across different organisations including hospitals, clinics, and social and community organisations (200, 201).

1.6.1. Psychosocial interventions – types and effectiveness

Psychosocial interventions aim to address social needs and challenges and can be used in a variety of settings and disciplines, including health care, educational or community settings (202). Some psychosocial interventions aim at improving loneliness and other social constructs such as social engagement, support and networking (200), while others use the benefits of psychosocial interventions in alleviating loneliness, to improve health outcomes and reduce healthcare utilisation and costs (203-205).

One-on-one interventions

Psychosocial one-on-one interventions assist individuals better understand their social relationships, improve communication, and increase individuals' social networks by connecting them with services in the community (206, 207). The effectiveness of psychosocial one-on-one interventions lies in their individualised nature (208). By focusing on the unique needs and circumstances of each person, these interventions can be tailored, promoting a sense of empowerment and facilitating meaningful changes in individuals' social life (200). The confidentiality of these interventions also encourages a trusting relationship between patients and health professionals, fostering a supportive environment for personal growth and healing (209). There are many forms of psychosocial one-on-one interventions. For example, therapeutic modalities can be used including cognitive-behavioural therapy (CBT), psychodynamic therapy, or mindfulness approaches, depending on the goals and preferences of the individual (206). One-on-one interventions may also include coaching, mentoring or peer support. For example, peer-support interventions include mentors with

lived experience of a social or medical condition (such as a psychiatric illness, addiction, etc..) and can provide support to people with the same condition to overcome the condition and maintain a healthy lifestyle (210).

Group interventions

Psychosocial group interventions are also commonly used to target loneliness. These interventions refer to therapeutic approaches that involve a group of individuals with similar concerns or challenges participating in activities or discussions led by a trained facilitator. The group environment not only facilitates connections with others but also provides a platform for practising interpersonal interactions (211, 212). Similar to one-on-one interventions, group interventions focus on the psychosocial aspects of well-being, aiming to address issues such as mental health, interpersonal relationships, and personal development (213). Common forms of psychosocial group interventions are support groups, where individuals facing similar challenges gather to share experiences and provide mutual support (211, 214). Other common forms are similar to one-on-one interventions only the intervention is delivered in a group mode (200). For example, peer support, psychoeducational groups, CBT groups, life skills groups and expressive therapy groups that utilise creative activities like art, music, or drama therapy (215). Some groups use physical activity as a form of bonding while implementing other life skills such as persistence, resilience, overcoming challenges and a healthy lifestyle (216, 217). Group interventions were found to be effective in developing interpersonal skills, and emotional support, and in creating a sense of community and belongingness, contributing to overall well-being and mental health (26, 214, 218).

There isn't conclusive evidence of the efficacy of one-on-one vs. group interventions (219). Since there is high variability of interventions and measurement instruments, and since loneliness is a result of multivariate contributors, it is difficult to eliminate all other influences to determine which type of intervention is more efficient in alleviating loneliness. Therefore, many interventions include both group and one-on-one activities (220). These multi-component interventions were also found to be effective in alleviating loneliness (219).

Use of technology and online psychosocial interventions

Using technology in group or one-on-one psychosocial interventions has become a common method in these types of interventions, especially since the Coronavirus disease (COVID-19) pandemic (221). These platforms can include using teletherapy services that provide

counselling and therapy sessions remotely or online support groups where individuals facing similar challenges can connect and share experiences remotely (221). In addition, social media platforms are used to disseminate information, raise awareness, and foster peer support (222). Community and health professionals utilise online platforms to share resources and facilitate online communities dedicated to mental health and well-being (221). Other methods include mobile applications that can deliver psychoeducational content, self-help tools, and reminders for coping strategies directly to users' smartphones. Features like mood tracking, mindfulness exercises, or cognitive-behavioural therapy modules empower individuals to manage their mental health proactively (223, 224). In addition, artificial intelligence (AI) is being used in the form of social robots to increase social support and reduce loneliness (225). These robots are designed to interact with users in ways that simulate human-like communication and empathy, offering emotional and instrumental support, such as playing games, sharing news and information, or helping with daily tasks (226). Interventions that incorporate technology were found effective in alleviating loneliness in most studies and reviews, especially as technology improved over the years (220, 227). One systematic review found significant results in 3 out of 4 studies examined (220) and another review found the use of technology interventions was effective even in different settings (one-on-one and group) and among both community-dwellers and institutionalised older adults (228).

1.6.2. The effect of social interventions on individuals' health

According to numerous systematic reviews, psychosocial interventions were found to have significant effects on physical health outcomes such as blood pressure, immune response and mortality (7, 229-231), as well as on the well-being and quality of life of people with chronic illnesses such as diabetes, and arthritis (232, 233). Psychosocial interventions were also found effective in improving health behaviours such as diet, exercise, sexual health, disease management, retention in care and substance use (27, 234, 235). In addition, psychosocial interventions were found to have a profound effect on various mental health conditions such as anxiety disorders, depression, post-traumatic stress disorder (PTSD), and schizophrenia (236-238), by assisting individuals in maintaining stability and resilience and by increasing treatment adherence (236, 239). Similarly, psychosocial interventions were found effective in improving cognitive functioning in individuals with cognitive impairments or disorders such as dementia, traumatic brain injury, and neurodevelopmental disorders (240) and in maintaining cognitive health and preventing cognitive decline in healthy individuals (241). However, the evidence is mixed, with some systematic reviews showing a moderate effect

(241) and others showing only effect on some cognitive functions such as memory but not others such as executive functioning (242). Many of the interventions that have been researched and identified as highly effective were either physical activity-based such as aerobic exercise and walking programs, or cognition-based including reminiscence therapy (241, 243). Therefore, despite the presence of strong evidence supporting the efficacy of psychosocial interventions in improving health outcomes, the evidence has been inconsistent, with some systematic reviews showing no- to little effect and others showing limited effect over time (210, 236, 244-246).

1.7. Appendices

Appendix 1.7.1. 20-item UCLA Loneliness Scale (36)

INSTRUCTIONS: Indicate how often each of the statements below is descriptive of you.

O indicates “I often feel this way”; S indicates “I sometimes feel this way”; R indicates “I rarely feel this way”; N indicates “I never feel this way”

1. I am unhappy doing so many things alone O S R N
2. I have nobody to talk to O S R N
3. I cannot tolerate being so alone O S R N
4. I lack companionship O S R N
5. I feel as if nobody really understands me O S R N
6. I find myself waiting for people to call or write O S R N
7. There is no one I can turn to O S R N
8. I am no longer close to anyone O S R N
9. My interests and ideas are not shared by those around me O S R N
10. I feel left out O S R N
11. I feel completely alone O S R N
12. I am unable to reach out and communicate with those around me O S R N
13. My social relationships are superficial O S R N
14. I feel starved for company O S R N
15. No one really knows me well O S R N
16. I feel isolated from others O S R N
17. I am unhappy being so withdrawn O S R N
18. It is difficult for me to make friends O S R N
19. I feel shut out and excluded by others O S R N
20. People are around me but not with me O S R N

Scoring: Make all O's =3, all S's =2, all R's =1, and all N's =0. Keep scoring continuous.

Appendix 1.7.2. 11-item de-Jong Gierveld Loneliness Scale (34)

		None of the time	Rarely	Some of the time	Often	All of the time
1	There is always someone I can talk to about my day-to-day problems					
2	I miss having a really close friend					
3	I experience a general sense of emptiness					
4	There are plenty of people I can lean on when I have problems					
5	I miss the pleasure of the company of others					
6	I find my circle of friends and acquaintances too limited					
7	There are many people I can trust completely					
8	There are enough people I feel close to					
9	I miss having people around me					
10	I often feel rejected					
11	I can call on my friends whenever I need them					

Processing the scale data manually

Step 1

Count the neutral and positive answers ("more or less", "yes", or "yes!") on items 2, 3, 5, 6, 9, 10. This is the *emotional loneliness score*.

Count the missing values (i.e., no answer) on items 2, 3, 5, 6, 9, 10. This is the *missing emotional loneliness score*.

Count the neutral and negative ("no!", "no", or "more or less") answers on items 1, 4, 7, 8, 11. This is the *social loneliness score*.

Count the missing values (i.e., no answer) on items 1, 4, 7, 8, 11. This is the *missing social loneliness score*.

Step 2

Compute the total *loneliness score* by taking the sum of the *emotional loneliness score* and the *social loneliness score*.

Step 3

The *emotional loneliness score* is valid only if the *missing emotional loneliness score* equals 0. The *social loneliness score* is valid only if the *missing social loneliness score* equals 0.

The total *loneliness score* is valid only if the sum of the *missing emotional loneliness score* and the *missing social loneliness score* equals 0 or 1.

Step 4

If desired, the total *loneliness score* can be categorized into four levels: *not lonely* (score 0, 1 or 2), *moderate lonely* (score 3 through 8), *severe lonely* (score 9 or 10), and *very severe lonely* (score 11).

1.8. References

1. Ciolfi ML. Historical Perspectives on the Research of Social Isolation, Loneliness, and Social Support. In: Kaye LW, Singer CM, editors. New York: Springer Publishing Company; 2018. p. 17-34.
2. Killeen C. Loneliness: an epidemic in modern society. *J Adv Nurs*. 1998;28(4):762-70.
3. Burnett C. The Historical Roots of Loneliness. *Vulcan Historical Review* [Internet]. 2023 [cited 2024 2 June]; 27:[14 p.]. Available from: <https://digitalcommons.library.uab.edu/cgi/viewcontent.cgi?article=1135&context=vulcan>.
4. Ozawa-de Silva C, Parsons M. Toward an anthropology of loneliness. *Transcult Psychiatry*. 2020;57(5):613-22.
5. Seemann A. The Psychological Structure of Loneliness. *Int J Environ Res Public Health*. 2022;19(3):1061.
6. Eccles AM, Qualter P. Review: Alleviating loneliness in young people – a meta-analysis of interventions. *Child and Adolescent Mental Health*. 2021;26(1):17-33.
7. Farver-Vestergaard I, Danielsen JTT, Løkke A, Zachariae R. Psychosocial intervention in chronic obstructive pulmonary disease: meta-analysis of randomized controlled trials. *Psychosom Med*. 2022;84(3):347-58.
8. Pearce E, Birken M, Pais S, Tamworth M, Ng Y, Wang J, et al. Associations between constructs related to social relationships and mental health conditions and symptoms: an umbrella review. *BMC Psychiat*. 2023;23(1):652.
9. National Academies of Sciences Engineering & Medicine, Division of Behavioral Social Sciences Education Health & Medicine, Division Board on Behavioral Cognitive Sensory Sciences, Board on Health Sciences Policy, Committee on the Health Medical, Dimensions of Social Isolation Loneliness in Older Adults. *Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System*. Washington (DC): National Academies Press (US); 2020.

10. Hupcey JE. Clarifying the social support theory-research linkage. *J Adv Nurs*. 1998;27(6):1231-41.
11. Heaney CA, Israel BA. Social networks and social support. In: Karen G, Barbara KR, K. Viswanath, editors. *Health behavior and health education: Theory, research, and practice*. 4. San Francisco, CA: Jossey-Bass; 2008. p. 189-210.
12. Mitchell JC. The concept and use of social networks. In: Mitchell JC, editor. *Social Networks in Urban Situations: Analyses of Personal Relationships in Central African Towns*. Manchester: Manchester University Press; 1969. p. 1–50.
13. Levasseur M, Richard L, Gauvin L, Raymond É. Inventory and analysis of definitions of social participation found in the aging literature: Proposed taxonomy of social activities. *Soc Sci Med*. 2010;71(12):2141-9.
14. Van Ingen E. Social participation revisited: Disentangling and explaining period, life-cycle and cohort effects. *Acta Sociologica*. 2008;51(2):103-21.
15. Portes A. Social capital: Its origins and applications in modern sociology. *Annu Rev Sociol*. 1998;24(1):1-24.
16. Putnam RD. *Bowling alone: The collapse and revival of American community*: Simon and schuster; 2000.
17. Zavaleta D, Samuel K, Mills C. *Social isolation: A conceptual and measurement proposal*: Oxford Poverty & Human Development Initiative (OPHI); 2014.
18. de Jong-Gierveld J, Van Tilburg TG, Dykstra PA. Loneliness and social isolation. In: Perlman D, Vangelisti A, editors. *The Cambridge handbook of personal relationships*: Cambridge University Press; 2006. p. 485-500.
19. Peplau LA, Perlman D. Perspectives on Loneliness. In: Letitia AP, Daniel P, editors. *Loneliness: A sourcebook of current theory, research, and therapy*: John Wiley & Sons; 1982. p. 1-19.
20. Wang J, Lloyd-Evans B, Giacco D, Forsyth R, Nebo C, Mann F, Johnson S. Social isolation in mental health: a conceptual and methodological review. *Soc Psychiatry Psychiatr Epidemiol*. 2017;52(12):1451-61.

21. Valtorta NK, Kanaan M, Gilbody S, Hanratty B. Loneliness, social isolation and social relationships: what are we measuring? A novel framework for classifying and comparing tools. *BMJ Open*. 2016;6(4).
22. Due P, Holstein B, Lund R, Modvig J, Avlund K. Social relations: network, support and relational strain. *Soc Sci Med*. 1999;48(5):661-73.
23. Cohen S. Social relationships and health. *Am Psychol*. 2004;59(8):676.
24. Lubben JE. Assessing social networks among elderly populations. *Fam Community Health*. 1988;11(3):42-52.
25. Ikeda A, Iso H, Kawachi I, Yamagishi K, Inoue M, Tsugane S. Social support and stroke and coronary heart disease: the JPHC study cohorts II. *Stroke*. 2008;39(3):768-75.
26. Bessaha ML, Sabbath EL, Morris Z, Malik S, Scheinfeld L, Saragossi J. A Systematic Review of Loneliness Interventions Among Non-elderly Adults. *Clin Soc Work J*. 2020;48(1):110-25.
27. Hunter RF, de la Haye K, Murray JM, Badham J, Valente TW, Clarke M, Kee F. Social network interventions for health behaviours and outcomes: A systematic review and meta-analysis. *PLoS Med*. 2019;16(9):e1002890.
28. Kelly ME, Duff H, Kelly S, McHugh Power JE, Brennan S, Lawlor BA, Loughrey DG. The impact of social activities, social networks, social support and social relationships on the cognitive functioning of healthy older adults: a systematic review. *Syst Rev*. 2017;6(1):259.
29. Ferrer RA, Mendes WB. Emotion, health decision making, and health behaviour. *Psychol Health*. 2018;33(1):1-16.
30. World Health Organization. Social Isolation and Loneliness2024 [cited 2024 15 March]. Available from: <https://www.who.int/teams/social-determinants-of-health/demographic-change-and-healthy-ageing/social-isolation-and-loneliness>.
31. Simo N, Godaert L, Villeneuve R, Dartigues JF, Teguo MT, Dramé M. Tools for assessing social isolation and feelings of loneliness in older adults: a systematic review. *Geriatr Psychol Neuropsychiatr Vieil*. 2023;21(2):241-50.

32. Wang F, Gao Y, Han Z, Yu Y, Long Z, Jiang X, et al. A systematic review and meta-analysis of 90 cohort studies of social isolation, loneliness and mortality. *Nat Hum Behav.* 2023;7(8):1307-19.
33. Surkalim DL, Luo M, Eres R, Gebel K, van Buskirk J, Bauman A, Ding D. The prevalence of loneliness across 113 countries: systematic review and meta-analysis. *BMJ.* 2022;376:e067068.
34. de Jong-Gierveld J, Kamphuis F. The development of a Rasch-type loneliness scale. *Appl Psych Meas.* 1985;9(3):289-99.
35. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Appl Psych Meas.* 1977;1:385-401.
36. Russell DW. UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure. *J Pers Assess.* 1996;66(1):20-40.
37. Hughes ME, Waite LJ, Hawkey LC, Cacioppo JT. A Short Scale for Measuring Loneliness in Large Surveys: Results From Two Population-Based Studies. *Res Aging.* 2004;26(6):655-72.
38. Gierveld JDJ, Tilburg TV. A 6-item scale for overall, emotional, and social loneliness: Confirmatory tests on survey data. *Res Aging.* 2006;28(5):582-98.
39. Reinwarth AC, Ernst M, Krakau L, Brähler E, Beutel ME. Screening for loneliness in representative population samples: Validation of a single-item measure. *PloS One.* 2023;18(3):e0279701.
40. Badcock J, Lim M. A Guide to Measuring Loneliness for Community Organizations2021 [cited 2024 2 June]. Available from: https://endingloneliness.com.au/wp-content/uploads/2021/08/A-Guide-to-Measuring-Loneliness-for-Community-Organisations_Ending-Loneliness-Together.pdf.
41. Office for National Statistics. Measuring loneliness: guidance for use of the national indicators on surveys2018 [cited 2024 2 June]. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing/methodologies/measuringlonelinessguidanceforuseofthenationalindicatorsonsurveys>.

42. Kotwal AA, Cenzer IS, Waite LJ, Smith AK, Perissinotto CM, Hawkley LC. A single question assessment of loneliness in older adults during the COVID-19 pandemic: A nationally-representative study. *J Am Geriatr Soc.* 2022;70(5):1342-5.
43. Eccles AM, Qualter P, Madsen KR, Holstein BE. Loneliness in the lives of Danish adolescents: Associations with health and sleep. *Scand J Public Health.* 2020;48(8):877-87.
44. Shiovitz-Ezra S, Ayalon L. Use of direct versus indirect approaches to measure loneliness in later life. *Res Aging.* 2012;34(5):572-91.
45. Mund M, Maes M, Drewke PM, Gutzeit A, Jaki I, Qualter P. Would the Real Loneliness Please Stand Up? The Validity of Loneliness Scores and the Reliability of Single-Item Scores. *Assessment.* 2022;30(4):1226-48.
46. Peplau L, Perlman, D, Russell, Daniel. The measurement of loneliness. In: Peplau L, Perlman, D, editor. *Loneliness: A Sourcebook of Current Theory, Research and Theory*: John Wiley & Sons; 1982. p. 81-104.
47. Nicolaisen M, Thorsen K. Who are lonely? Loneliness in different age groups (18-81 years old), using two measures of loneliness. *Int J Aging Hum Dev.* 2014;78(3):229-57.
48. Maes M, Qualter P, Vanhalst J, Van den Noortgate W, Goossens L. Gender differences in loneliness across the lifespan: A meta-analysis. *Eur J Personality.* 2019;33(6):642-54.
49. Mund M, Freuding MM, Möbius K, Horn N, Neyer FJ. The Stability and Change of Loneliness Across the Life Span: A Meta-Analysis of Longitudinal Studies. *Pers Soc Psychol Rev.* 2019;24(1):24-52.
50. Barreto M, Victor C, Hammond C, Eccles A, Richins MT, Qualter P. Loneliness around the world: Age, gender, and cultural differences in loneliness. *Pers Individ Dif.* 2021;169:110066.
51. Nicolaisen M, Thorsen KJ. Gender Differences in Loneliness Over Time: A 15-Year Longitudinal Study of Men and Women in the Second Part of Life. *Int J Aging Hum Dev.* 2023;98(1):103-32.

52. Heu LC, Hansen N, van Zomeren M, Levy A, Ivanova TT, Gangadhar A, Radwan M. Loneliness across cultures with different levels of social embeddedness: A qualitative study. *Pers Relationship*. 2021;28(2):379-405.
53. Heu LC, van Zomeren M, Hansen N. Does loneliness thrive in relational freedom or restriction? The culture-loneliness framework. *Rev Gen Psychol*. 2021;25(1):60-72.
54. Lim MH, Manera KE, Owen KB, Phongsavan P, Smith BJ. The prevalence of chronic and episodic loneliness and social isolation from a longitudinal survey. *Sci Rep*. 2023;13(1):12453.
55. Snell KDM. The rise of living alone and loneliness in history. *Soc Hist*. 2017;42(1):2-28.
56. Anttila T, Selander K, Oinas T. Disconnected lives: trends in time spent alone in Finland. *Soc Indic Res*. 2020;150:711-30.
57. Xin S, Xin Z. Birth cohort changes in Chinese college students' loneliness and social support: One up, as another down. *Int J Behav Dev*. 2016;40(5):398-407.
58. Buecker S, Mund M, Chwastek S, Sostmann M, Luhmann M. Is loneliness in emerging adults increasing over time? A preregistered cross-temporal meta-analysis and systematic review. *Psychol Bull*. 2021;147(8):787.
59. Clark DMT, Loxton NJ, Tobin SJ. Declining loneliness over time: Evidence from American colleges and high schools. *Pers Soc Psychol Bull*. 2015;41(1):78-89.
60. Yan Z, Yang X, Wang L, Zhao Y, Yu L. Social change and birth cohort increase in loneliness among Chinese older adults: A cross-temporal meta-analysis, 1995–2011. *Int Psychogeriatr*. 2014;26(11):1773-81.
61. Rebecca AM, Sebastian T, Roy TS, Winston RL, John M, Donald E. Nease, Jr., et al. Loneliness in Primary Care Patients: A Prevalence Study. *Ann Fam Med*. 2019;17(2):108.
62. Igbokwe CC, Ejeh VJ, Agbaje OS, Umoke PIC, Iweama CN, Ozoemena EL. Prevalence of loneliness and association with depressive and anxiety symptoms among retirees in Northcentral Nigeria: a cross-sectional study. *BMC Geriatr*. 2020;20(1):153.

63. Rahman MS, Rahman MA, Rahman MS. Prevalence and determinants of loneliness among older adults in Bangladesh. *Int J Emerg Trend Socl Sci*. 2019;5(2):57-64.
64. Hawkley LC, Buecker S, Kaiser T, Luhmann M. Loneliness from young adulthood to old age: Explaining age differences in loneliness. *Int J Behav Dev*. 2020;46(1):39-49.
65. Surkalim DL, Clare PJ, Eres R, Gebel K, Bauman A, Ding D. Have Middle-Aged and Older Americans Become Lonelier? 20-Year Trends From the Health and Retirement Study. *J Gerontol B Psychol Sci Soc Sci*. 2023;78(7):1215-23.
66. Cacioppo JT, Cacioppo S. Loneliness in the modern age: An evolutionary theory of loneliness (ETL). *Adv Expl Soc Psychol*. 2018;58:127-97.
67. Johnson MH, Griffin R, Csibra G, Halit H, Farroni T, de Haan M, et al. The emergence of the social brain network: evidence from typical and atypical development. *Dev Psychopathol*. 2005;17(3):599-619.
68. Kim MJ, Sul S. On the relationship between the social brain, social connectedness, and wellbeing. *Front Psychiatry*. 2023;14:1112438.
69. Cacioppo S, Capitanio JP, Cacioppo JT. Toward a neurology of loneliness. *Psychol Bull*. 2014;140(6):1464.
70. Martín-María N, Caballero FF, Miret M, Tyrovolas S, Haro JM, Ayuso-Mateos JL, Chatterji S. Differential impact of transient and chronic loneliness on health status. A longitudinal study. *Psychol Health*. 2020;35(2):177-95.
71. Roddick CM, Chen FS. Effects of Chronic and State Loneliness on Heart Rate Variability in Women. *Ann Behav Med*. 2021;55(5):460-75.
72. Waaktaar T, Torgersen S. Genetic and environmental causes of variation in perceived loneliness in young people. *Am J Med Genet B*. 2012;159(5):580-8.
73. Goossens L, Van Roekel E, Verhagen M, Cacioppo JT, Cacioppo S, Maes M, Boomsma DI. The genetics of loneliness: Linking evolutionary theory to genome-wide genetics, epigenetics, and social science. *Perspect Psychol Sci*. 2015;10(2):213-26.

74. Gao J, Davis LK, Hart AB, Sanchez-Roige S, Han L, Cacioppo JT, Palmer AA. Genome-wide association study of loneliness demonstrates a role for common variation. *Neuropsychopharmacol.* 2017;42(4):811-21.
75. Ernst M, Brähler E, Kruse J, Kampling H, Beutel ME. Does loneliness lie within? Personality functioning shapes loneliness and mental distress in a representative population sample. *J Affect Disorders Rep.* 2023;12:100486.
76. van Roekel E, Verhagen M, Engels RCME, Scholte RHJ, Cacioppo S, Cacioppo JT. Trait and State Levels of Loneliness in Early and Late Adolescents: Examining the Differential Reactivity Hypothesis. *J Clin Child Adolescent Psychol.* 2018;47(6):888-99.
77. Vanhalst J, Soenens B, Luyckx K, Van Petegem S, Weeks MS, Asher SR. Why do the lonely stay lonely? Chronically lonely adolescents' attributions and emotions in situations of social inclusion and exclusion. *J Pers Soc Psychol.* 2015;109(5):932-48.
78. Distel MA, Rebollo-Mesa I, Abdellaoui A, Derom CA, Willemsen G, Cacioppo JT, Boomsma DI. Familial Resemblance for Loneliness. *Behav Genet.* 2010;40(4):480-94.
79. Luhmann M, Hawkley LC. Age differences in loneliness from late adolescence to oldest old age. *Devl Psychol.* 2016;52(6):943.
80. Luhmann M, Buecker S, Rüsberg M. Loneliness across time and space. *Nat Rev Psychol.* 2023;2(1):9-23.
81. Taube E, Kristensson J, Sandberg M, Midlöv P, Jakobsson U. Loneliness and health care consumption among older people. *Scand J Caring Sci.* 2015;29(3):435-43.
82. Chawla K, Kunonga TP, Stow D, Barker R, Craig D, Hanratty B. Prevalence of loneliness amongst older people in high-income countries: A systematic review and meta-analysis. *PloS One.* 2021;16(7):e0255088.
83. Pyle E, Evans D. Loneliness-what characteristics and circumstances are associated with feeling lonely. Newport: Office for National Statistics [Internet]. 2018 [cited 2024 2 June]. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing/articles/lonelinesswhatcharacteristicsandcircumstancesareassociatedwithfeelinglonely/2018-04-10>.

84. Sundqvist A, Hemberg J. Adolescents' and young adults' experiences of loneliness and their thoughts about its alleviation. *Int J Adolescence Youth*. 2021;26(1):238-55.
85. Medaris A. Gen Z adults and younger millennials are “completely overwhelmed” by stress[cited 2024 2 June]. Available from: <https://www.apa.org/topics/stress/generation-z-millennials-young-adults-worries#:~:text=Young%20adults%20in%20America%20like,Stress%20in%20America%20survey%20found>.
86. Nowland R, Necka EA, Cacioppo JT. Loneliness and social internet use: pathways to reconnection in a digital world? *Perspect Psychol Sci*. 2018;13(1):70-87.
87. Primack BA, Shensa A, Sidani JE, Whaite EO, yi Lin L, Rosen D, et al. Social media use and perceived social isolation among young adults in the US. *Am J Prev Med*. 2017;53(1):1-8.
88. Hosozawa M, Cable N, Yamasaki S, Ando S, Endo K, Usami S, et al. Predictors of chronic loneliness during adolescence: a population-based cohort study. *Child Adol Psych Men*. 2022;16(1):107.
89. Segel-Karpas D, Ayalon L, Lachman ME. Loneliness and depressive symptoms: the moderating role of the transition into retirement. *Aging Ment Health*. 2018;22(1):135-40.
90. Korzhina Y, Hemberg J, Nyman-Kurkiala P, Fagerström L. Causes of involuntary loneliness among adolescents and young adults: An integrative review. *Int J Adolescence Youth*. 2022;27(1):493-514.
91. Phillips DM, Finkel D, Petkus AJ, Muñoz E, Pahlen S, Johnson W, et al. Longitudinal analyses indicate bidirectional associations between loneliness and health. *Aging Ment Health*. 2023;27(6):1217-25.
92. Pagan R. Gender and Age Differences in Loneliness: Evidence for People without and with Disabilities. *Int J Environ Res Public Health*. 2020;17(24).
93. Dong X, Chen R. Gender differences in the experience of loneliness in U.S. Chinese older adults. *J Women Aging*. 2017;29(2):115-25.

94. McQuaid RJ, Cox SML, Ogunlana A, Jaworska N. The burden of loneliness: Implications of the social determinants of health during COVID-19. *Psy Res.* 2021;296:113648.
95. Kung CSJ, Kunz JS, Shields MA. Economic Aspects of Loneliness in Australia. *Aus Econ Rev.* 2021;54(1):147-63.
96. Gordon EH, Hubbard RE. Do sex differences in chronic disease underpin the sex-frailty paradox? *Mech Ageing Dev.* 2019;179:44-50.
97. Dahlberg L, Andersson L, McKee KJ, Lennartsson C. Predictors of loneliness among older women and men in Sweden: A national longitudinal study. *Aging Ment Health.* 2015;19(5):409-17.
98. World Health Organization. Mental health of older adults- fact sheets 2017 [updated 20 October 2023]. Available from: <https://www.who.int/news-room/fact-sheets/detail/mental-health-of-older-adults#:~:text=Mental%20health%20and%20well-being%20are%20as%20important%20in,60%20and%20over%20suffer%20from%20a%20mental%20disorder.>
99. Pinquart M, Sorensen S. Influences on loneliness in older adults: A meta-analysis. *Basic Appl Soc Psych.* 2001;23(4):245-66.
100. Rokach A. The effect of gender and culture on loneliness: A mini review. *Emerg Sci J.* 2018;2(2):59-64.
101. Hutten E, Jongen EMM, Hajema K, Ruiter RAC, Hamers F, Bos AER. Risk factors of loneliness across the life span. *J Soc Pers Relat.* 2021;39(5):1482-507.
102. Barjaková M, Garneró A, d'Hombres B. Risk factors for loneliness: A literature review. *Soc Sci Med.* 2023;334:116163.
103. Kislev E. Aging, marital status, and loneliness: Multilevel analyses of 30 countries. *Res Ageing Soc Policy.* 2022;10(1):77-103.
104. Zuo S, Lin L, Chen S, Wang Z, Tian L, Li H, Xu Y. Influencing factors of loneliness among older adults in China: a systematic review and meta-analysis. *Psychogeriatrics.* 2023;23(1):164-76.

105. Ayalon L, Shiovitz-Ezra S, Palgi Y. Associations of loneliness in older married men and women. *Aging Ment Health*. 2013;17(1):33-9.
106. Kislev E. Happiness, post-materialist values, and the unmarried. *J Happiness Stud*. 2018;19:2243-65.
107. Štípková M. Marital status, close social network and loneliness of older adults in the Czech Republic. *Aging Soc*. 2021;41(3):671-85.
108. Band-Winterstein T, Manchik-Rimon C. The Experience of Being an Old Never-Married Single: A Life Course Perspective. *Int J Aging Hum Dev*. 2014;78(4):379-401.
109. Buss C, Casper WJ, Marquardt DJ, Roberto KJ. The Hidden Family Lives of Single Adults Without Dependent Children. In: Allen. TD, Eby LT, editors. *The Oxford Handbook of Work and Family*: Oxford University Press; 2016. p. 182–95.
110. de Jong Gierveld J, Keating N, Fast JE. Determinants of Loneliness among Older Adults in Canada. *Can J Aging*. 2015;34(2):125-36.
111. Bosma H, Jansen M, Schefman S, Hajema KJ, Feron F. Lonely at the bottom: a cross-sectional study on being ill, poor, and lonely. *Pub Health*. 2015;129(2):185-7.
112. Algren MH, Ekholm O, Nielsen L, Ersbøll AK, Bak CK, Andersen PT. Social isolation, loneliness, socioeconomic status, and health-risk behaviour in deprived neighbourhoods in Denmark: A cross-sectional study. *Popul Health*. 2020;10:100546.
113. Drost MA, Snyder AR, Betz M, Loibl C. Financial strain and loneliness in older adults. *Appl Econ Lett*. 2022:1-4.
114. Cohen-Mansfield J, Hazan H, Lerman Y, Shalom V. Correlates and predictors of loneliness in older-adults: a review of quantitative results informed by qualitative insights. *Int Psychogeriatr*. 2016;28(4):557-76.
115. Domènech-Abella J, Mundó J, Lara E, Moneta MV, Haro JM, Olaya B. The role of socio-economic status and neighborhood social capital on loneliness among older adults: evidence from the Sant Boi Aging Study. *Soc Psychiatry Psychiatr Epidemiol*. 2017;52(10):1237-46.

116. Macdonald SJ, Nixon J, Deacon L. 'Loneliness in the city': examining socio-economics, loneliness and poor health in the North East of England. *Pub Health*. 2018;165:88-94.
117. Fong P, Cruwys T, Robinson SL, Haslam SA, Haslam C, Mance PL, Fisher CL. Evidence that loneliness can be reduced by a whole-of-community intervention to increase neighbourhood identification. *Soc Sci Med*. 2021;277:113909.
118. Rokach A. Loneliness of the marginalized. *Open J Depress*. 2014;3:147-53.
119. Yang K, Victor C. Age and loneliness in 25 European nations. *Aging Soc*. 2011;31(8):1368-88.
120. Akhter-Khan SC, van Es W, Prina M, Lawrence V, Piri I, Rokach A, et al. Experiences of loneliness in lower- and middle-income countries: A systematic review of qualitative studies. *Soc Sci Med*. 2024;340:116438.
121. de Jong Gierveld J, Tesch-Römer C. Loneliness in old age in Eastern and Western European societies: Theoretical perspectives. *Eur J Ageing*. 2012;9:285-95.
122. Tapia-Muñoz T, Staudinger UM, Allel K, Steptoe A, Miranda-Castillo C, Medina JT, Calvo E. Income inequality and its relationship with loneliness prevalence: A cross-sectional study among older adults in the US and 16 European countries. *PloS One*. 2022;17(12):e0274518.
123. Granados JAT. Health at advanced age: social inequality and other factors potentially impacting longevity in nine high-income countries. *Maturitas*. 2013;74(2):137-47.
124. Morrish N, Medina-Lara A. Does unemployment lead to greater levels of loneliness? A systematic review. *Soc Sci Med*. 2021;287:114339.
125. Barreto M, van Breen J, Victor C, Hammond C, Eccles A, Richins MT, Qualter P. Exploring the nature and variation of the stigma associated with loneliness. *J Soc Pers Relat*. 2022;39(9):2658-79.
126. Heu LC. The Loneliness of the Odd One Out: How Deviations From Social Norms Can Help Explain Loneliness Across Cultures. *Perspect Psychol Sci*. 2023;17456916231192485.

127. Santos HC, Varnum MEW, Grossmann I. Global increases in individualism. *Psychol Sci.* 2017;28(9):1228-39.
128. Cheng AW, Rizkallah S, Narizhnaya M. Individualism vs. collectivism. In: Carducci. BJ, Nave. CS, Mio. JS, Riggio RE, editors. *The Wiley Encyclopedia of Personality and Individual Differences: Clinical, Applied, and Cross-Cultural Research: Wiley Online Library*; 2020. p. 287-97.
129. Fokkema T, De Jong Gierveld J, Dykstra PA. Cross-national differences in older adult loneliness. *J Psychol.* 2012;146(1-2):201-28.
130. Swader CS. Loneliness in Europe: Personal and societal individualism-collectivism and their connection to social isolation. *Soc Forces.* 2019;97(3):1307-36.
131. Kearns A, Whitley E, Tannahill C, Ellaway A. Loneliness, social relations and health and well-being in deprived communities. *Psychol Health Med.* 2015;20(3):332-44.
132. Dietz N, Grimm Jr RT. *Where Are America's Volunteers?* 2018.
133. Weston G, Zilanawala A, Webb E, Carvalho LA, McMunn A. Long work hours, weekend working and depressive symptoms in men and women: findings from a UK population-based study. *J Epidemiol Community Health.* 2019;73(5):465-74.
134. Wigfield A, Turner R, Alden S, Green M, Karania VK. Developing a new conceptual framework of meaningful interaction for understanding social isolation and loneliness. *Soc Policy Soc.* 2022;21(2):172-93.
135. Nyqvist F, Nygård M, Scharf T. Loneliness amongst older people in Europe: a comparative study of welfare regimes. *Eur J Ageing.* 2019;16(2):133-43.
136. Szabo A, Allen J, Alpass F, Stephens C. Loneliness, socio-economic status and quality of life in old age: the moderating role of housing tenure. *Aging Soc.* 2019;39(5):998-1021.
137. Ornelas J, Martins P, Zilhão MT, Duarte T. Housing First: An ecological approach to promoting community integration. *Eur J Homeless.* 2014;8(1):29-56.

138. Cao Q, Dabelko-Schoeny HI, White KM, Choi M-S. Age-friendly communities and perceived disconnectedness: the role of built environment and social engagement. *J Aging Health*. 2019;32(9):937-48.
139. Abshire DA, Graves JM, Amiri S, Williams-Gilbert W. Differences in loneliness across the rural-urban continuum among adults living in Washington State. *J Rural Health*. 2022;38(1):187-93.
140. Sun J, Lyu S. Social participation and urban-rural disparity in mental health among older adults in China. *J Affect Disorders*. 2020;274:399-404.
141. Loccoh Eméfah C, Joynt Maddox Karen E, Wang Y, Kazi Dhruv S, Yeh Robert W, Wadhera Rishi K. Rural-Urban Disparities in Outcomes of Myocardial Infarction, Heart Failure, and Stroke in the United States. *J Am Coll Cardiol*. 2022;79(3):267-79.
142. Quashie NT, Pothisiri W. Rural-urban gaps in health care utilization among older Thais: The role of family support. *Arch Gerontol Geriatr*. 2019;81:201-8.
143. Nicole V, Theodore JI, Matthew MD. Worsening Rural-Urban Gap in Hospital Mortality. *J Am Board Fam Med*. 2017;30(6):816.
144. Alston L, Allender S, Peterson K, Jacobs J, Nichols M. Rural Inequalities in the Australian Burden of Ischaemic Heart Disease: A Systematic Review. *Heart Lung Circ*. 2017;26(2):122-33.
145. Goodwin BC, Rowe AK, Crawford-Williams F, Baade P, Chambers SK, Ralph N, Aitken JF. Geographical disparities in screening and cancer-related health behaviour. *Int J Environ Res Public Health*. 2020;17(4):1246.
146. Summers-Gabr NM. Rural–urban mental health disparities in the United States during COVID-19. *Psychol Trauma*. 2020;12(S1):S222-S4.
147. Repke MA, Ipsen C. Differences in social connectedness and perceived isolation among rural and urban adults with disabilities. *Disabil Health J*. 2020;13(1):100829.
148. Abshire DA, Graves JM, Amiri S, Williams-Gilbert W. Differences in Loneliness Across the Rural-Urban Continuum Among Adults Living in Washington State. *J Rural Health*. 2022;38(1):187-93.

149. Victor CR, Pikhartova J. Lonely places or lonely people? Investigating the relationship between loneliness and place of residence. *BMC Pub Health*. 2020;20(1):778.
150. Roof K, Oleru N. Public health: Seattle and King County's push for the built environment. *J Environ Health*. 2008;71(1):24-7.
151. Dinnissen NM. Combating Loneliness Through The Built Environment [Master]: Eindhoven University of Technology; 2023.
152. Bower M, Kent J, Patulny R, Green O, McGrath L, Teesson L, et al. The impact of the built environment on loneliness: A systematic review and narrative synthesis. *Health Place*. 2023;79:102962.
153. Engel L, Chudyk AM, Ashe MC, McKay HA, Whitehurst DGT, Bryan S. Older adults' quality of life – Exploring the role of the built environment and social cohesion in community-dwelling seniors on low income. *Soc Sci Med*. 2016;164:1-11.
154. Buecker S, Ebert T, Götz FM, Entringer TM, Luhmann M. In a lonely place: Investigating regional differences in loneliness. *Soc Psychol Pers Sci*. 2021;12(2):147-55.
155. Domenech-Abella J, Mundo J, Leonardi M, Chatterji S, Tobiasz-Adamczyk B, Koskinen S, et al. Loneliness and depression among older European adults: The role of perceived neighborhood built environment. *Health Place*. 2020;62:102280.
156. Park C, Majeed A, Gill H, Tamura J, Ho RC, Mansur RB, et al. The Effect of Loneliness on Distinct Health Outcomes: A Comprehensive Review and Meta-Analysis. *Psy Res*. 2020;294:113514.
157. Kraav S-L, Lehto SM, Kauhanen J, Hantunen S, Tolmunen T. Loneliness and social isolation increase cancer incidence in a cohort of Finnish middle-aged men. A longitudinal study. *Psy Res*. 2021;299:113868.
158. Valtorta NK, Kanaan M, Gilbody S, Ronzi S, Hanratty BJ. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. *Heart*. 2016;102(13):1009-16.

159. Donovan NJ, Wu Q, Rentz DM, Sperling RA, Marshall GA, Glymour MM. Loneliness, depression and cognitive function in older US adults. *Int J Geriatr Psych.* 2017;32(5):564-73.
160. Holwerda TJ, Deeg DJ, Beekman AT, Van Tilburg TG, Stek ML, Jonker C, Schoevers RA. Feelings of loneliness, but not social isolation, predict dementia onset: results from the Amsterdam Study of the Elderly (AMSTEL). *J Neurol Neurosurg Ps.* 2014;85(2):135-42.
161. Shankar A, Hamer M, McMunn A, Steptoe A. Social isolation and loneliness: relationships with cognitive function during 4 years of follow-up in the English Longitudinal Study of Ageing. *Psychosom Med.* 2013;75(2):161-70.
162. Erzen E, Çikrikci Ö. The effect of loneliness on depression: A meta-analysis. *Int J Soc Psych.* 2018;64(5):427-35.
163. Domènech-Abella J, Mundó J, Haro JM, Rubio-Valera M. Anxiety, depression, loneliness and social network in the elderly: Longitudinal associations from The Irish Longitudinal Study on Ageing (TILDA). *J Affect Disorders.* 2019;246:82-8.
164. Michalska da Rocha B, Rhodes S, Vasilopoulou E, Hutton P. Loneliness in psychosis: a meta-analytical review. *Schizophrenia bull.* 2018;44(1):114-25.
165. Richardson T, Elliott P, Roberts R. Relationship between loneliness and mental health in students. *J Pub Mental Health.* 2017;16(2):48-54.
166. Beller J. Loneliness and mortality: The moderating effect of positive affect. *Appl Psychol Health Well Being.* 2023;15(1):49-65.
167. Lara E, Moreno-Agostino D, Martín-María N, Miret M, Rico-Urbe LA, Olaya B, et al. Exploring the effect of loneliness on all-cause mortality: Are there differences between older adults and younger and middle-aged adults? *Soc Sci Med.* 2020;258:113087.
168. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect Psychol Sci.* 2015;10(2):227-37.

169. Rico-Uribe LA, Caballero FF, Martín-María N, Cabello M, Ayuso-Mateos JL, Miret M. Association of loneliness with all-cause mortality: A meta-analysis. *PloS One*. 2018;13(1):e0190033.
170. Ong AD, Uchino BN, Wethington E. Loneliness and Health in Older Adults: A Mini-Review and Synthesis. *Gerontol*. 2016;62(4):443-9.
171. Hakulinen C, Pulkki-Råback L, Virtanen M, Jokela M, Kivimäki M, Elovainio M. Social isolation and loneliness as risk factors for myocardial infarction, stroke and mortality: UK Biobank cohort study of 479 054 men and women. *Heart*. 2018;104(18):1536-42.
172. Campagne DM. Stress and perceived social isolation (loneliness). *Arch Gerontol Geriat*. 2019;82:192-9.
173. Christiansen J, Larsen FB, Lasgaard M. Do stress, health behavior, and sleep mediate the association between loneliness and adverse health conditions among older people? *Soc Sci Med*. 2016;152:80-6.
174. Smith KJ, Gavey S, Riddell NE, Kontari P, Victor C. The association between loneliness, social isolation and inflammation: A systematic review and meta-analysis. *Neurosci Biobehav R*. 2020;112:519-41.
175. Brown EG, Gallagher S, Creaven AM. Loneliness and acute stress reactivity: A systematic review of psychophysiological studies. *Psychophysiology*. 2018;55(5):e13031.
176. Pourriyahi H, Yazdanpanah N, Saghaideh A, Rezaei N. Loneliness: An Immunometabolic Syndrome. *Int J Environ Res Public Health*. 2021;18(22):12162.
177. Philip KEJ, Bu F, Polkey MI, Brown J, Steptoe A, Hopkinson NS, Fancourt D. Relationship of smoking with current and future social isolation and loneliness: 12-year follow-up of older adults in England. *Lancet Reg Health Eur*. 2022;14.
178. Hanna K, Cross J, Nicholls A, Gallegos D. The association between loneliness or social isolation and food and eating behaviours: A scoping review. *Appetite*. 2023;191:107051.

179. Christiansen J, Larsen FB, Lasgaard M. Do stress, health behavior, and sleep mediate the association between loneliness and adverse health conditions among older people? *Soc Sci Med*. 2016;152:80-6.
180. Spiers G, Matthews F, Moffatt S, Barker R, Jarvis H, Stow D, et al. Impact of social care supply on healthcare utilisation by older adults: a systematic review and meta-analysis. 2019;48(1):57-66.
181. McFarlane WR. Family Interventions for Schizophrenia and the Psychoses: A Review. *Fam Process*. 2016;55(3):460-82.
182. Singer C. Health effects of social isolation and loneliness. *J Aging Life Care*. 2018;28:4-8.
183. Christiansen J, Lund R, Qualter P, Andersen CM, Pedersen SS, Lasgaard M. Loneliness, social isolation, and chronic disease outcomes. *J Annals Behavioral Medicine*. 2021;55(3):203-15.
184. Westergaard ML, Lau CJ, Allesøe K, Andreasen AH, Jensen RH. Poor social support and loneliness in chronic headache: Prevalence and effect modifiers. *Cephalalgia*. 2021;41(13):1318-31.
185. Ansari S, Muhammad T, Dhar M. How Does Multi-Morbidity Relate to Feeling of Loneliness among Older Adults? Evidence from a Population-Based Survey in India. *J Pop Ageing*. 2023;16(1):45-66.
186. Meltzer H, Bebbington P, Dennis MS, Jenkins R, McManus S, Brugha TS. Feelings of loneliness among adults with mental disorder. *Soc Psychiatry Psychiatr Epidemiol*. 2013;48:5-13.
187. Barlow MA, Liu SY, Wrosch C. Chronic illness and loneliness in older adulthood: The role of self-protective control strategies. *Health Psychol*. 2015;34(8):870-9.
188. Ahmed M, Cerda I, Maloof M. Breaking the vicious cycle: The interplay between loneliness, metabolic illness, and mental health. *Front Psych*. 2023;14.

189. Mihalopoulos C, Le LK-D, Chatterton ML, Bucholc J, Holt-Lunstad J, Lim MH, Engel L. The economic costs of loneliness: a review of cost-of-illness and economic evaluation studies. *Soc Psychiatry Psychiatr Epidemiol*. 2020;55(7):823-36.
190. Valtorta NK, Moore DC, Barron L, Stow D, Hanratty B. Older adults' social relationships and health care utilization: a systematic review. *Am J Public Health*. 2018;108(4):e1-e10.
191. Fulton L, Jupp B. Investing to tackle loneliness: a discussion paper. 2015.
192. Gerst-Emerson K, Jayawardhana J. Loneliness as a public health issue: the impact of loneliness on health care utilization among older adults. *Am J Public Health*. 2015;105(5):1013-9.
193. Hawker M, Romero-Ortuno R. Social Determinants of Discharge Outcomes in Older People Admitted to a Geriatric Medicine Ward. *J Frailty Aging*. 2016;5(2):118-20.
194. Sirois FM, Owens J. A meta-analysis of loneliness and use of primary health care. *Health Psychol Rev*. 2023;17(2):193-210.
195. Shaw JG, Farid M, Noel-Miller C, Joseph N, Houser A, Asch SM, et al. Social isolation and Medicare spending: Among older adults, objective isolation increases expenditures while loneliness does not. *J Aging Health*. 2017;29(7):1119-43.
196. Doshmangir L, Khabiri R, Jabbari H, Arab-Zozani M, Kakemam E, Gordeev VS. Strategies for utilisation management of hospital services: a systematic review of interventions. *Globalization Health*. 2022;18(1):53.
197. Holt-Lunstad J, Smith TB. Loneliness and social isolation as risk factors for CVD: implications for evidence-based patient care and scientific inquiry. *BMJ*. 2016;102(13):987-9.
198. Bryan BT, Andrews G, Thompson KN, Qualter P, Matthews T, Arseneault L. Loneliness in the workplace: a mixed-method systematic review and meta-analysis. *Occup Med*. 2023;73(9):557-67.
199. Jeffrey K, Abdallah S, Michaelson J. The cost of loneliness to UK employers. London: New Economics Foundation [Internet]. 2017 [cited 2024 3 June 2024]. Available from: <https://neweconomics.org/2017/02/cost-loneliness-uk-employers>.

200. Morrish N, Choudhury S, Medina-Lara A. What works in interventions targeting loneliness: a systematic review of intervention characteristics. *BMC Pub Health*. 2023;23(1):2214.
201. Masi CM, Chen H-Y, Hawkley LC, Cacioppo JT. A meta-analysis of interventions to reduce loneliness. *Pers Soc Psychol Rev*. 2011;15(3):219-66.
202. Chatterjee HJ, Camic PM, Lockyer B, Thomson LJM. Non-clinical community interventions: a systematised review of social prescribing schemes. *Arts Health*. 2018;10(2):97-123.
203. Mosher CE, Winger JG, Given BA, Shahda S, Helft PR. A systematic review of psychosocial interventions for colorectal cancer patients. *Support Care Cancer*. 2017;25(7):2349-62.
204. Veazie S, Gilbert J, Winchell K, Paynter R, Guise J-M. Addressing social isolation to improve the health of older adults: a rapid review. Agency for Healthcare Research and Quality (US); 2019.
205. Dieng M, Cust AE, Kasparian NA, Mann GJ, Morton RL. Economic evaluations of psychosocial interventions in cancer: a systematic review. *Psycho-Oncol*. 2016;25(12):1380-92.
206. Käll A, Bäck M, Welin C, Åman H, Bjerkander R, Wänman M, et al. Therapist-Guided Internet-Based Treatments for Loneliness: A Randomized Controlled Three-Arm Trial Comparing Cognitive Behavioral Therapy and Interpersonal Psychotherapy. *Psychother Psychosom*. 2021;90(5):351-8.
207. Yanguas J, Pinazo-Henandis S, Tarazona-Santabalbina FJ. The complexity of loneliness. *Acta Biomed*. 2018;89(2):302-14.
208. Kotwal AA, Fuller SM, Myers JJ, Hill D, Tha SH, Smith AK, M Perissinotto C. A peer intervention reduces loneliness and improves social well-being in low-income older adults: A mixed-methods study. *J Am Geriatr Soc*. 2021;69(12):3365-76.

209. Cohen-Mansfield J, Hazan H, Lerman Y, Shalom V, Birkenfeld S, Cohen R. Efficacy of the I-SOCIAL intervention for loneliness in old age: Lessons from a randomized controlled trial. *J Psychiat Res*. 2018;99:69-75.
210. Fuhr DC, Salisbury TT, De Silva MJ, Atif N, van Ginneken N, Rahman A, Patel V. Effectiveness of peer-delivered interventions for severe mental illness and depression on clinical and psychosocial outcomes: a systematic review and meta-analysis. *Soc Psychiatry Psychiatr Epidemiol*. 2014;49(11):1691-702.
211. Vickery A. 'It's made me feel less isolated because there are other people who are experiencing the same or very similar to you': Men's experiences of using mental health support groups. *Health Soc Care Community*. 2022;30(6):2383-91.
212. Hempel R, Vanderbleek E, Lynch TR. Radically open DBT: Targeting emotional loneliness in Anorexia Nervosa. *Eat Disord*. 2018;26(1):92-104.
213. Committee on Developing Evidence-Based Standards for Psychosocial Interventions for Mental Disorders, Board on Health Sciences Policy, Institute of Medicine. In: England MJ, Butler AS, Gonzalez ML, editors. *Psychosocial Interventions for Mental and Substance Use Disorders: A Framework for Establishing Evidence-Based Standards*. Washington (DC): National Academies Press (US); 2015.
214. Brunelli AA, Murphy GC, Athanasou JA. Effectiveness of Social Support Group Interventions for Psychosocial Outcomes: A Meta-analytic Review. *Aust J Rehab Counsell*. 2016;22(2):104-27.
215. Cleveland R. *Art Therapy Used as a Tool to Improve Loneliness, Social Connectedness, and Well-Being with Older Adults [Master]*. California, United States: Notre Dame de Namur University; 2018.
216. Bartlett H, Warburton J, Lui C-W, Peach L, Carroll M. Preventing social isolation in later life: findings and insights from a pilot Queensland intervention study. *Aging Soc*. 2013;33(7):1167-89.
217. Shvedko AV, Thompson JL, Greig CA, Whittaker AC. Physical Activity Intervention for Loneliness (PAIL) in community-dwelling older adults: a randomised feasibility study. *Pilot Feasibil Stud*. 2020;6:1-15.

218. Pinks D, Warren-James M, Katsikitis M. Does a peer social support group intervention using the cares skills framework improve emotional expression and emotion-focused coping in paramedic students? *Aust Emerg Care*. 2021;24(4):308-13.
219. Hogan BE, Linden W, Najarian B. Social support interventions: Do they work? *Clin Psychol Rev*. 2002;22(3):381-440.
220. Poscia A, Stojanovic J, La Milia DI, Duplaga M, Grysztar M, Moscato U, et al. Interventions targeting loneliness and social isolation among the older people: An update systematic review. *Expl Gerontol*. 2018;102:133-44.
221. Ye Z, Li W, Zhu R. Online psychosocial interventions for improving mental health in people during the COVID-19 pandemic: A systematic review and meta-analysis. *J Affect Disorders*. 2022;316:120-31.
222. Oser TK, Oser SM, Parascando JA, Hessler-Jones D, Sciamanna CN, Sparling K, et al. Social Media in the Diabetes Community: a Novel Way to Assess Psychosocial Needs in People with Diabetes and Their Caregivers. *Curr Diabetes Rep*. 2020;20(3):10.
223. Konrath S. Positive technology: Using mobile phones for psychosocial interventions. In: Yan Z, editor. *Encyclopedia of mobile phone behavior*: IGI Global; 2015. p. 871-97.
224. Champion L, Economides M, Chandler C. The efficacy of a brief app-based mindfulness intervention on psychosocial outcomes in healthy adults: A pilot randomised controlled trial. *PloS One*. 2018;13(12):e0209482.
225. Loveys K, Fricchione G, Kolappa K, Sagar M, Broadbent E. Reducing patient loneliness with artificial agents: design insights from evolutionary neuropsychiatry. *J Med Internet Res*. 2019;21(7):e13664.
226. Robinson NL, Cottier TV, Kavanagh DJ. Psychosocial health interventions by social robots: systematic review of randomized controlled trials. *J Med Internet Res*. 2019;21(5):e13203.
227. Jarvis MA, Padmanabhanunni A, Chipps J. An Evaluation of a Low-Intensity Cognitive Behavioral Therapy mHealth-Supported Intervention to Reduce Loneliness in Older People. *Int J Environ Res Public Health*. 2019;16(7):1305.

228. Cohen-Mansfield J, Perach R. Interventions for alleviating loneliness among older persons: a critical review. *Am J Health Promot.* 2015;29(3):e109-e25.
229. Scott-Sheldon LAJ, Gathright EC, Donahue ML, Balletto B, Feulner MM, DeCosta J, et al. Mindfulness-Based Interventions for Adults with Cardiovascular Disease: A Systematic Review and Meta-Analysis. *Ann Behav Med.* 2020;54(1):67-73.
230. Shields GS, Spahr CM, Slavich GM. Psychosocial Interventions and Immune System Function: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Psychiat.* 2020;77(10):1031-43.
231. Smith TB, Workman C, Andrews C, Barton B, Cook M, Layton R, et al. Effects of psychosocial support interventions on survival in inpatient and outpatient healthcare settings: A meta-analysis of 106 randomized controlled trials. *PLoS Med.* 2021;18(5):e1003595.
232. Pascoe MC, Thompson DR, Castle DJ, Jenkins ZM, Ski CF. Psychosocial Interventions and Wellbeing in Individuals with Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Front Psychol.* 2017;8.
233. Santos EJJ, Duarte C, Marques A, Cardoso D, Apóstolo J, da Silva JAP, Barbieri-Figueiredo M. Effectiveness of non-pharmacological and non-surgical interventions for rheumatoid arthritis: an umbrella review. *JBIC Database System Rev Implement Rep.* 2019;17(7).
234. Laurenzi CA, du Toit S, Ameyan W, Melendez-Torres GJ, Kara T, Brand A, et al. Psychosocial interventions for improving engagement in care and health and behavioural outcomes for adolescents and young people living with HIV: a systematic review and meta-analysis. *J Int AIDS Soc.* 2021;24(8):e25741.
235. Walters R, Leslie SJ, Polson R, Cusack T, Gorely T. Establishing the efficacy of interventions to improve health literacy and health behaviours: a systematic review. *BMC Pub Health.* 2020;20(1):1040.
236. Bighelli I, Rodolico A, García-Mieres H, Pitschel-Walz G, Hansen W-P, Schneider-Thoma J, et al. Psychosocial and psychological interventions for relapse prevention in schizophrenia: a systematic review and network meta-analysis. *Lancet Psychiat.* 2021;8(11):969-80.

237. Alhadidi MMB, Lim Abdullah K, Yoong TL, Al Hadid L, Danaee M. A systematic review of randomized controlled trials of psychoeducation interventions for patients diagnosed with schizophrenia. *Int J Soc Psych.* 2020;66(6):542-52.
238. Barbui C, Purgato M, Abdulmalik J, Acarturk C, Eaton J, Gastaldon C, et al. Efficacy of psychosocial interventions for mental health outcomes in low-income and middle-income countries: an umbrella review. *Lancet Psychiat.* 2020;7(2):162-72.
239. Asher L, Patel V, De Silva MJ. Community-based psychosocial interventions for people with schizophrenia in low and middle-income countries: systematic review and meta-analysis. *BMC Psychiat.* 2017;17(1):355.
240. Hui EK, Tischler V, Wong GHY, Lau WYT, Spector A. Systematic review of the current psychosocial interventions for people with moderate to severe dementia. *Int J Geriatr Psych.* 2021;36(9):1313-29.
241. Whitty E, Mansour H, Aguirre E, Palomo M, Charlesworth G, Ramjee S, et al. Efficacy of lifestyle and psychosocial interventions in reducing cognitive decline in older people: Systematic review. *Ageing Res Rev.* 2020;62:101113.
242. Chow G, Gan JKE, Chan JKY, Wu XV, Klainin-Yobas P. Effectiveness of psychosocial interventions among older adults with mild cognitive impairment: a systematic review and meta-analysis. *Aging Ment Health.* 2021;25(11):1986-97.
243. Duan Y, Lu L, Chen J, Wu C, Liang J, Zheng Y, et al. Psychosocial interventions for Alzheimer's disease cognitive symptoms: a Bayesian network meta-analysis. *BMC Geriatr.* 2018;18(1):175.
244. McDermott O, Charlesworth G, Hogervorst E, Stoner C, Moniz-Cook E, Spector A, et al. Psychosocial interventions for people with dementia: a synthesis of systematic reviews. *Aging Ment Health.* 2019;23(4):393-403.
245. Chernoff RA, Messineo G, Kim S, Pizano D, Korouri S, Danovitch I, IsHak WW. Psychosocial interventions for patients with heart failure and their impact on depression, anxiety, quality of life, morbidity, and mortality: a systematic review and meta-analysis. *Psychosom Med.* 2022;84(5):560-80.

246. Fu WW, Popovic M, Agarwal A, Milakovic M, Fu TS, McDonald R, et al. The impact of psychosocial intervention on survival in cancer: a meta-analysis. *Ann Palliat Med*. 2016;5(2):93-106.

CHAPTER TWO: Theoretical framework and research overview

2.1. Thesis rational

The current literature review identified several gaps in the study of loneliness, particularly in its associations with individual and social determinants and health outcomes. Building upon these findings, the current research attempts to fill these gaps and offer comprehensive insights into the intricate interplay between loneliness, its determinants, and its implications for health outcomes. The majority of studies that examined the relationship between loneliness and health relied on cross-sectional analyses (1, 2), hence lack of temporality limits the understanding of the bidirectionality nature of loneliness and cannot support causality. Although the strength, consistency and biological gradient of the association between loneliness and health have been well demonstrated across longitudinal studies, most studies have used one point of exposure (2, 3). Consequently, researchers were unable to account for the variations in the relationship between loneliness and health over time (1). This might have introduced a biased perspective on the effect of loneliness, which may not accurately reflect its diverse effects across time (1). To address this gap, the current thesis has utilised longitudinal data collected from population-based studies spanning over 18 years and encompassing up to 12 exposure assessments at different time points.

Loneliness and health outcomes have a bidirectional relationship that is likely to be moderated and/or confounded by various sociodemographic factors (4, 5). Therefore, accurately quantifying the independent effect of loneliness that has not resulted from an underlying risk factor, may be challenging, even in a longitudinal design (2, 6). The possibility of exposure-affected time-varying confounding adds another layer of complexity (7). Exposure-affected time-varying confounding is present when a time-varying confounder that influences the relationship between an exposure and an outcome is itself affected by previous exposures (8). One established approach for tackling exposure-affected time-varying confounding is causal inference models such as marginal structural models estimated with the counterfactual frameworks and informed by directed acyclic graphs. Causal inference models allow researchers to estimate causal effects in the presence of such complex confounding, providing several structural assumptions are met (7). This methodological framework is employed in observational settings to identify the underlying causal mechanisms (9), thus providing models that can predict an outcome based on two equal comparison groups and ensure that the exposure occurred before the outcome (7). Causal inference methods were developed originally for infectious disease research to address bias in Human

immunodeficiency virus (HIV) research. In addition, these models were previously used to investigate the effect of several epidemiological phenomena such as addiction, smoking and physical activity on health outcomes (10-12). Only a few studies have used causal inference models to examine loneliness determinants and outcomes, with previous studies examining the effect of loneliness on depression (13) schizophrenia (14) and unemployment (15) and another study examining the effect of major life events on loneliness (16). In the present thesis, robust analytical methods are employed, including causal inference approaches, which control for complex confounding variables and facilitate accurate estimation of the independent effect of different determinants on loneliness and conversely, the independent effect of loneliness on health outcomes.

Further advanced analytical methods such as latent class analysis and meta-analysis were applied. Latent class analysis was utilised to examine patterns of loneliness across adulthood and their relationship with health-related quality of life (HRQoL). Given that loneliness is a dynamic concept influenced by individual, social, and environmental factors, this approach is particularly useful for identifying specific at-risk groups, that is, those experiencing moderate or high levels of loneliness throughout adulthood. This contributes to a deeper understanding of how loneliness impacts health outcomes, particularly among middle-aged and older women (as further explained below). A meta-analysis of randomised controlled trials (RCTs) was also conducted to assess the cumulative evidence on the impact of social interventions. This method represents the highest level of evidence, offering critical insights into the burden of disease and its implications for the healthcare system.

Current research on loneliness trends shows that loneliness does not necessarily increase among all populations (17). Previous research has demonstrated an inverse relationship between age and loneliness, with evidence suggesting that younger adults are at higher risk of experiencing loneliness compared to older adults (18). However, loneliness in middle-aged and older adults can result in serious health and social consequences, as this population is more susceptible to chronic and life-threatening conditions. Furthermore, these life stages often involve significant transitions, such as retirement, caregiving for a spouse or aging parents, and adjusting to an empty nest, all of which can exacerbate feelings of loneliness and could independently affect physical, mental and social health and could have great implications on loneliness (19). More specifically, retirement as one of the major determinants of loneliness among older adults, has been associated with modified health and social outcomes due to changes in daily routines, lifestyles and social networks (19). As

retirement is often shaped by modifiable macro-level factors such as national policies and financial support, loneliness may be mitigated by increasing resources for retirees and improving post-retirement support systems. Therefore, this study specifically focuses on loneliness among older adults, with particular attention to retirement as a key contributor, aiming to raise awareness and present the most up-to-date evidence on the issue within this population across countries.

This thesis predominantly focuses on women as a high-risk group for various poor physical and mental health outcomes, as well as social disadvantages (20). Although both men and women experience loneliness, and current evidence does not suggest that one gender is at greater risk than the other, women are more vulnerable to mental health issues such as depression and anxiety (21). They are also more likely to take on caregiving roles and experience widowhood, all of which are risk factors for loneliness (22). Although women tend to have a longer lifespan, many older women experience a reduced quality of life due to physical, mental, and social health challenges. Therefore, this thesis aims to contribute to the growing body of knowledge by examining women's quality of life and mortality risk concerning loneliness.

Another gap in the existing literature is the predominance of evidence on individual-level determinants of loneliness, with relatively less research focusing on socio-environmental determinants (23, 24). Therefore, this thesis adopts a wider lens to consider the role of factors at the community and society levels using population-based data. It explores the effect of life changes, culture and geographical regions on loneliness as well as the effect of social interventions at the community level on healthcare use and social well-being among different population groups. This recognises the potential importance of cultural norms on social determinants of loneliness and considers the moderating effects these factors may have. These findings aim to inform public health as well as health professionals about the importance of improving the social well-being of individuals, mainly those with at-risk features. Additionally, the current thesis focuses on the potential economic and health service benefits of reducing loneliness. This approach not only highlights the direct advantages of addressing loneliness, such as improved health and well-being but also underscores the indirect benefits like decreased demand for health services. Such insights carry significant implications for understanding the burden of disease and its implications on the healthcare system. By providing evidence on the effect of psychosocial interventions on social well-being and healthcare utilisation among different population groups, this research contributes

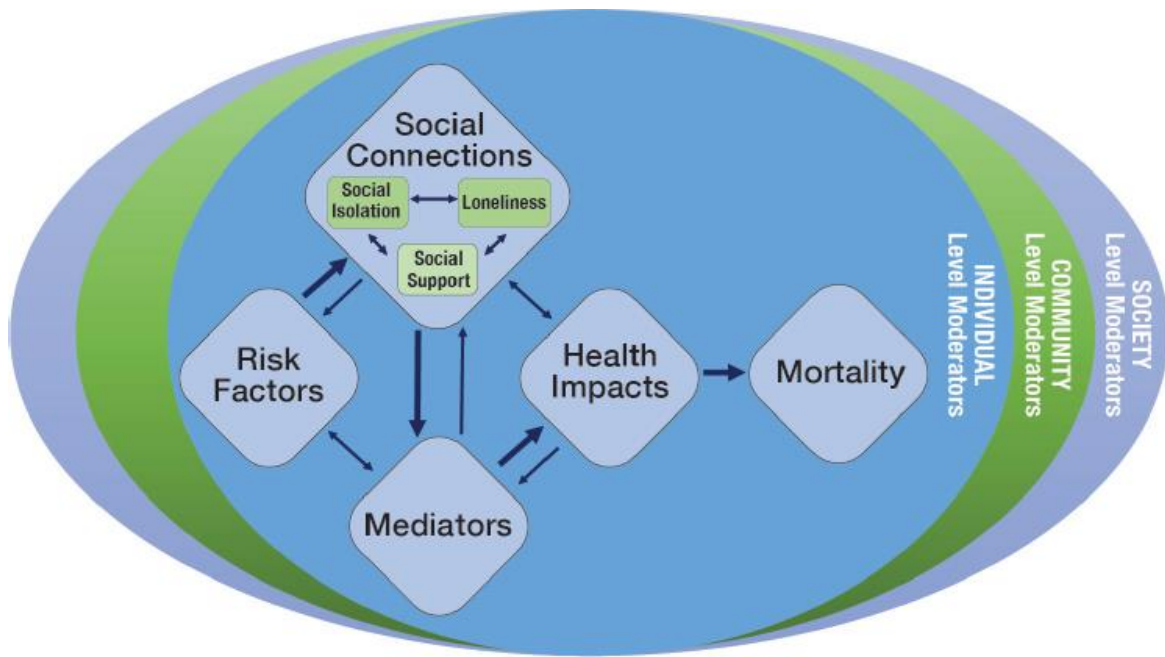
to shaping more effective healthcare strategies and interventions. These strategies may be used as valuable tools for enhancing individuals' well-being. By doing so, these interventions hold the potential to prevent or at least stabilise existing mental and physical chronic illnesses.

2.2. Theoretical framework

As described in **Chapter 1**, the association between loneliness and health outcomes is complex and includes multidirectional associations at the individual, community, and societal levels. Loneliness can be both the exposure and the outcome of health conditions and health behaviours. To better understand the associations between loneliness and health and the mediators and moderators affecting this association, this research has used a guiding framework of loneliness, social connections, and associated health outcomes, developed by the Committee on the Health and Medical Dimensions of Social Isolation and Loneliness in Older Adults (25). This conceptual framework is aimed at focusing on loneliness from social determinants of health perspective.

Figure 4 depicts the conceptual framework illustrating how loneliness is influenced by various determinants (risk factors) and in turn impacts them, while also being moderated by factors across individual, community, and societal levels. The arrows indicate the associations between risk factors (including sociodemographic characteristics, genetics or biological predispositions), social connections (including social isolation, loneliness and social support as independent concepts and the interactions between them), mediators (including physical, behavioural and psychosocial pathways), health outcomes and mortality. All the variables in the model can be considered as moderators. For example, the association between loneliness and health outcomes may vary by gender, age group, socioeconomic status, or a pre-existing health condition. The bold arrows indicate a causal one-directional association, and the thinner arrows indicate bi-directional associations. For example, loneliness may have an effect on health, however, it is also affected by the health status or condition of an individual.

Figure 1. Theoretical framework of loneliness, social isolation, and associated health outcomes. A guiding framework developed by the National Academies of Sciences, Engineering, and Medicine (NASEM) on the Health and Medical Dimensions of Social Isolation and Loneliness in Older Adults 2020 (25).



Note.

Mediator: a risk factor that lies on the causal pathway between exposure and outcome.

Moderator: a risk factor that affects the relationship between exposure and outcome (e.g., changes the magnitude or direction of the effect) but is not a part of the causal pathway.

The relationships presented in the model represent a social-ecological perspective (25). This model suggests that the factors influencing social well-being at an *individual level*, i.e., personal characteristics, attitudes and interpersonal relationships with family, friends, and the community, are potentially influenced by broader contextual elements at the levels of the community and society. The *community level* includes elements that exist in a specific community such as access to transportation, parks, health care, crime, neighbourhood safety, social capital, gentrification and more. The *societal level* includes social norms and trends such as racism, ageism, family structures, technology use, laws, and policies at the local, state or federal levels that may affect loneliness (25, 26). The current thesis examines loneliness from a socio-ecological perspective to clarify the associations between loneliness and health outcomes. The independent effect of loneliness on health is often obscured by multiple moderators and mediators, and it is challenging to isolate the effect of loneliness from other related aspects of health and sociodemographic confounders.

2.3. Purpose and outline of the current thesis

The purpose of this thesis is to investigate the independent long-term effect of loneliness on health and mortality, alongside exploring community and societal determinants that influence loneliness. This thesis also examines how intervention and prevention can mitigate loneliness

and reduce the economic burden of poor social health. The specific objectives of this thesis are as follows:

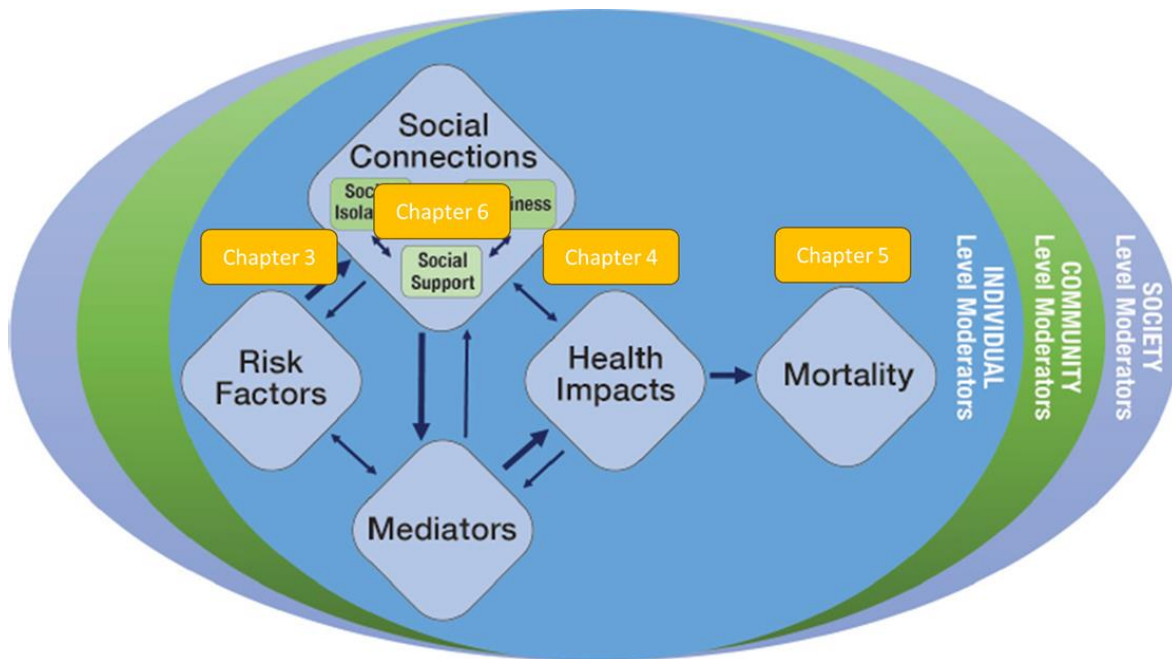
- 1) To compare the effect of retirement on loneliness across diverse cultures and social contexts and the moderating effect of social engagement (**Chapter 3**).
- 2) To examine the effect of different longitudinal patterns of loneliness ('Low', 'Medium', 'High' and 'Increasing' trajectories) on the physical and mental health-related quality of life (HRQoL) across adulthood (**Chapter 4**).
- 3) To examine the causal effect of persistent and chronic loneliness on mortality among middle-aged and older women using a causal inference approach (**Chapter 5**).
- 4) To systematically examine and meta-analyse RCTs on the effect of psychosocial interventions on health care utilisation and social wellbeing (**Chapter 6**).

2.3.1. Thesis outline

Figure 5 provides an overview of the chapters and thesis flow according to the theoretical framework. **Chapter 1** sets out the foundations and context for the thesis, including definitions and measurements, determinants, health and economic outcomes, and evidence concerning interventions aimed at mitigating loneliness. **Chapter 2** provides a theoretical framework and explains the purpose and objectives of the studies conducted in the scope of the thesis. **Chapter 3** explores social-ecological factors affecting the prevalence of loneliness. This chapter features a longitudinal comparative analysis across three countries, examining the implications of retirement on long-term loneliness and assessing the moderating influence of social engagement. The effect of retirement was compared between Australia, China and the US, using population-base longitudinal data from the Household, Income and Labor Dynamics in Australia (HILDA) Survey, the China Health and Retirement Longitudinal Study (CHARLS) and the Health and Retirement Study (HRS). In **Chapter 4**, findings from the Australian Longitudinal Study of Women's Health (ALSWH) are presented, focusing on the effect of longitudinal patterns of loneliness ('Increasing' loneliness, 'Stable-low', 'Stable-middle' and 'Stable-high') on the physical and mental HRQoL. **Chapter 5** presents the findings of a longitudinal causal inference analysis of the effect of loneliness on mortality using the ALSWH data. The findings provide a better understanding of the relative risk and the excess risk of persistent and chronic loneliness. The findings from **Chapters 3-5** highlight the necessity to enhance social connection as a preventive measure against the decline in physical and mental health. Therefore, **Chapter 6** explores the effects of psychosocial

interventions on healthcare utilisation and social well-being using the findings of a systematic review and meta-analysis of psychosocial interventions delivered in a wide variety of populations. The effectiveness of these interventions on the use of different health care services and social wellbeing is presented and implications for health policy and practice are discussed.

Figure 2. The thesis outline according to the theoretical framework of loneliness, social isolation, and associated health outcomes (25)



2.4. References

1. Smith KJ, Gavey S, Riddell NE, Kontari P, Victor C. The association between loneliness, social isolation and inflammation: A systematic review and meta-analysis. *Neurosci Biobehav R*. 2020;112:519-41.
2. Park C, Majeed A, Gill H, Tamura J, Ho RC, Mansur RB, et al. The Effect of Loneliness on Distinct Health Outcomes: A Comprehensive Review and Meta-Analysis. *Psy Res*. 2020;294:113514.
3. Holt-Lunstad J, Smith TB. Loneliness and social isolation as risk factors for CVD: implications for evidence-based patient care and scientific inquiry. *BMJ*. 2016;102(13):987-9.
4. Phillips DM, Finkel D, Petkus AJ, Muñoz E, Pahlen S, Johnson W, et al. Longitudinal analyses indicate bidirectional associations between loneliness and health. *Aging Ment Health*. 2023;27(6):1217-25.
5. Hawkey LC. Loneliness and health. *Nat Rev Dis Primers*. 2022;8(1):22.
6. Suarez D, Borràs R, Basagaña X. Differences Between Marginal Structural Models and Conventional Models in Their Exposure Effect Estimates: A Systematic Review. *Epidemiol*. 2011;22(4).
7. Clare PJ, Dobbins TA, Mattick RP. Causal models adjusting for time-varying confounding—a systematic review of the literature. *Int J Epidemiol*. 2019;48(1):254-65.
8. Daniel RM, Cousens SN, De Stavola BL, Kenward MG, Sterne JA. Methods for dealing with time-dependent confounding. *Stat Med*. 2013;32(9):1584-618.
9. Cole SR, Hudgens MG, Tien PC, Anastos K, Kingsley L, Chmiel JS, Jacobson LP. Marginal structural models for case-cohort study designs to estimate the association of antiretroviral therapy initiation with incident AIDS or death. *Am J Epidemiol*. 2012;175(5):381-90.
10. Clare PJ, Dobbins T, Bruno R, Peacock A, Boland V, Yuen WS, et al. The overall effect of parental supply of alcohol across adolescence on alcohol-related harms in early adulthood—a prospective cohort study. *Addiction*. 2020;115(10):1833-43.

11. Taylor G, Girling A, McNeill A, Aveyard P. Does smoking cessation result in improved mental health? A comparison of regression modelling and propensity score matching. *BMJ Open*. 2015;5(10):e008774.
12. García-Esquinas E, Ortolá R, Martínez-Gómez D, Damián J, Prina M, Rodríguez-Artalejo F, Pastor-Barriuso R. Causal effects of physical activity and sedentary behaviour on health deficits accumulation in older adults. *Int J Epidemiol*. 2021;50(3):852-65.
13. Sbarra DA, Ramadan FA, Choi KW, Treur JL, Levey DF, Wootton RE, et al. Loneliness and depression: bidirectional mendelian randomization analyses using data from three large genome-wide association studies. *Mol Psychiatr*. 2023:1-8.
14. Andreu-Bernabeu A, Díaz-Caneja CM, Costas J, De Hoyos L, Stella C, Gurriarán X, et al. Unraveling the relationship of loneliness and isolation in schizophrenia: Polygenic dissection and causal inference. *medRxiv*. 2020:2020-11.
15. Morrish N, Mujica-Mota R, Medina-Lara A. Understanding the effect of loneliness on unemployment: propensity score matching. *BMC Pub Health*. 2022;22(1):740.
16. Buecker S, Denissen JJA, Luhmann M. A propensity-score matched study of changes in loneliness surrounding major life events. *J Pers Soc Psychol*. 2021;121(3):669-90.
17. Surkalim DL, Clare PJ, Eres R, Gebel K, Bauman A, Ding D. Have Middle-Aged and Older Americans Become Lonelier? 20-Year Trends From the Health and Retirement Study. *J Gerontol B Psychol Sci Soc Sci*. 2023;78(7):1215-23.
18. Barreto M, Victor C, Hammond C, Eccles A, Richins MT, Qualter P. Loneliness around the world: Age, gender, and cultural differences in loneliness. *Pers Individ Dif*. 2021;169:110066.
19. Segel-Karpas D, Ayalon L, Lachman ME. Loneliness and depressive symptoms: the moderating role of the transition into retirement. *Aging Ment Health*. 2018;22(1):135-40.
20. Gordon EH, Hubbard RE. Do sex differences in chronic disease underpin the sex-frailty paradox? *Mech Ageing Dev*. 2019;179:44-50.
21. Rokach A. Loneliness of the marginalized. *Open J Depress*. 2014;3:147-53.

22. Dahlberg L, McKee KJ. Correlates of social and emotional loneliness in older people: evidence from an English community study. *Aging Ment Health*. 2014;18(4):504-14.
23. Meehan DE, Grunseit A, Condie J, HaGani N, Merom D. Social-ecological factors influencing loneliness and social isolation in older people: a scoping review. *BMC Geriatr*. 2023;23(1):726.
24. Gerst-Emerson K, Jayawardhana J. Loneliness as a public health issue: the impact of loneliness on health care utilization among older adults. *Am J Public Health*. 2015;105(5):1013-9.
25. National Academies of Sciences Engineering & Medicine, Division of Behavioral Social Sciences Education Health & Medicine, Division Board on Behavioral Cognitive Sensory Sciences, Board on Health Sciences Policy, Committee on the Health Medical, Dimensions of Social Isolation Loneliness in Older Adults. *Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System*. Washington (DC): National Academies Press (US); 2020.
26. Holt-Lunstad J. Why social relationships are important for physical health: A systems approach to understanding and modifying risk and protection. *Ann Rev Psychol*. 2018;69:437-58.

CHAPTER THREE: The effect of retirement on loneliness: A longitudinal comparative analysis across Australia, China, and the United States

3.1. Preface to the chapter

The current chapter presents findings from a peer-reviewed published paper that compared the causal effect of retirement on loneliness among adults ages 50 and older in Australia, China, and the US. The study emphasises the role of macro-level moderators, including geographical regions and cultural differences, in shaping the connections between loneliness and its determinants. Longitudinal population-based data from the Household, Income and Labor Dynamics in Australia Survey, the China Health and Retirement Longitudinal Study and the Health and Retirement Study, are employed. The findings highlight the differences and similarities in the effect of retirement on loneliness between Western and non-Western countries, as well as between urban and rural areas by using a causal inference approach. In addition, the study examines the moderating effect of social engagement on the retirement-loneliness association in all three countries. All results are presented with lagged models, examining the exposure and confounders before the outcome. For the main analysis, fully lagged models are also presented, with confounders measured at time t , exposure at $t+1$ and outcome at $t+2$. This chapter addresses specific aim #1 of this thesis as described in **Chapter 2**. Dissemination of this research and the author's contributions to this paper are described below.

3.2. Research dissemination

The research presented in this chapter has been disseminated as follows:

Published peer-review paper

Hagani N, Clare PJ, Luo M, Merom D, Smith BJ, Ding D. Effect of retirement on loneliness: a longitudinal comparative analysis across Australia, China and the USA. *J Epidemiol Community Health*. 2024. Epub ahead of print: [4 June 2024]. doi: 10.1136/jech-2023-221606

Impact factor: 6.3

Conference presentations

1. Emerging Health Policy & Economics Research Conference. February 2024. Menzies Centre for Health Policy & Economics, Faculty of Medicine and Health. The University of Sydney. Sydney, Australia (Oral presentation).
2. Ending Loneliness Together Research Conference. November 2023. The Charles Perkins Centre. The University of Sydney. Sydney, Australia (Long oral presentation).
3. The HILDA survey research conference. September 2023. The Melbourne Institute: Applied Economic & Social Research, Melbourne, Australia (Long oral presentation including radio broadcasting).
4. The Charles Perkins EMCR Symposium. September 2023. The University of Sydney. Sydney, Australia (Oral presentation).
5. Faculty of Medicine and Health HDR Conference. July 2023. The University of Sydney. Sydney, Australia (Oral presentation).

3.3. Author attribution statement

I, Neta HaGani, was responsible for designing the study, obtaining the data, conducting the analysis and interpretation of the results, writing the drafts of the manuscript, submitting the manuscript, responding to reviewers' comments, and coordinating the submission and publication of the manuscript. My co-authors, P. Clare, M. Luo, D. Merom, B. Smith & D. Ding helped conceptualise and design the study and developed the study protocol; P. Clare supervised the data analysis and M. Luo assisted. All authors have reviewed, edited, and approved the final version of the manuscript.

3.4. Paper in published format



OPEN ACCESS

Effect of retirement on loneliness: a longitudinal comparative analysis across Australia, China and the USA

Neta Hagani ^{1,2} Philip J Clare ^{1,2,3} Mengyun Luo ^{1,2,4} Dafna Merom ⁵
Ben J Smith ^{1,2} Ding Ding ^{1,2}

► Additional supplemental material is published online only. To view, please visit the journal online (<https://doi.org/10.1136/jech-2023-221606>).

¹School of Public Health, and Charles Perkins Centre, University of Sydney, Sydney, New South Wales, Australia

²Prevention Research Collaboration, School of Public Health, University of Sydney, Sydney, New South Wales, Australia

³National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW, Australia

⁴School of Public Health, Shanghai Jiao Tong University, Shanghai, China

⁵Western Sydney University School of Health Sciences, Penrith, New South Wales, Australia

Correspondence to

Ms Neta Hagani, The University of Sydney Faculty of Medicine and Health, Sydney, NSW 2006, Australia; neta.hagani@sydney.edu.au

Received 26 October 2023

Accepted 20 May 2024

Published Online First

4 June 2024

ABSTRACT

Background There is evidence that the transition to retirement can bring social challenges and may increase loneliness. Few studies have examined the impact of retirement on loneliness; most have been conducted in Western countries. It is important to examine the differences in loneliness postretirement across countries to identify patterns and risk factors that might influence the health and well-being of older adults. We aimed to examine the effect of retirement on loneliness among older adults in Australia, China and the USA.

Methods Longitudinal analysis of data from population-based samples of Australian, Chinese and American adults over 50. Lagged and fully lagged adjusted models were applied. Social engagement was examined as an effect modifier and a sensitivity analysis was conducted among urban participants.

Results Retirees had a higher predicted prevalence of loneliness than non-retirees in Australia (19.4% (95% CI 18.0% to 20.9%) vs 17.0% (95% CI 15.7% to 18.4%)) and in the USA (19.3% (95% CI 17.5% to 21.1%) vs 15.7% (95% CI 14.3% to 17.3%)). These differences were significant only in the USA. In China, loneliness was significantly lower in those who had retired (10.0% (95% CI 7.9% to 12.5%) vs 17.1% (95% CI 15.7% to 18.5%)). In Australia and the USA, voluntary retirees had the lowest loneliness and involuntary retirees had the highest. Social engagement did not modify the association between retirement and loneliness.

Conclusions Our findings imply that the effect of retirement should be considered within a cultural context to inform suitable and effective strategies to alleviate loneliness.

INTRODUCTION

The increase in life expectancy has made retirement a significant phase in later life with long-term implications on health and well-being.¹ The transition to retirement can lead to a decline in physical and mental functioning and social connections and relationships.² As a result, people may experience a decrease in social engagement and higher levels of loneliness.^{2,3}

Social well-being and social health are umbrella terms for concepts such as social support, relationships and connections. These concepts refer to feelings towards the amount, frequency and quality of social relationships. Loneliness refers to the subjective feelings derived from a gap between the observed and expected level of social

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ A small number of studies have examined the relationship between retirement transition and the experience of loneliness and found that retirement is associated with increased loneliness in Western countries.

WHAT THIS STUDY ADDS

⇒ While retirement is a risk factor for loneliness in Australia and the USA, it may be viewed as a protective factor in China.
⇒ In Australia and the USA, voluntary retirees had the lowest loneliness and involuntary retirees had the highest.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Cultural differences in loneliness should be taken into consideration in interventions among older adults.
⇒ Policy-makers, healthcare professionals and community organisations can design and implement more effective interventions to support the well-being of older adults in diverse cultural contexts.
⇒ Future research could benefit from further examining the association between loneliness and retirement in non-western countries with traditional cultures.

connectedness⁴ and prolonged loneliness is associated with adverse health outcomes such as heart disease, stroke, dementia, depression, anxiety and premature death.^{5,6} Loneliness affects a sizeable proportion of populations globally but with varying prevalence across countries.⁷

There is evidence that loneliness is influenced by cultural norms and is therefore experienced differently by older adults across cultures.^{8–10} Cultures can be differentiated by the level of individualism versus collectivism inherent in their cultural norms. Collectivism tends to prevail in traditional Eastern cultures such as in Southeast Asia and focuses on the interdependency and responsibility of the group for the behaviours and outcomes of individuals.¹¹ For example, in China, family and community needs are of a higher priority than individual needs and intergenerational dependency is more commonplace.^{12,13} Cultures on the individualistic end of the spectrum, mostly



© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Hagani N, Clare PJ, Luo M, et al. *J Epidemiol Community Health* 2024;**78**:602–608.

prevailing in Northern Europe, the USA and Australia, encourage self-reliance and are characterised by single-residence households, competitiveness and looser and more remote social relationships.¹⁴ For example, in the USA, it was estimated that on average 27% of households are single-person and in some cities, it is over 40%.¹⁵ However, transitions such as decreasing birth rates, urbanisation and globalisation in collectivistic societies have led to changes in traditional social norms and lifestyles,^{11 16} with more older adults living in 'empty-nested' households that may have an impact on their physical, mental and social well-being.^{17 18} It remains unclear whether people from individualistic or collective cultures experience more loneliness as the evidence so far is mixed.^{9 19–21}

Retirement is considered a major life event that is often associated with changes in time availability, financial resources, social networks, roles and purposes. The effects of retirement on physical, mental and social health are multifaceted and are shaped by individual attributes such as age, gender, health, social support and life events^{22 23}; cultural aspects, including attitudes towards ageing and social roles postretirement^{24 25}; and environmental characteristics such as economic stability, community resources and technological access.²⁶ A small number of studies have examined the relationship between retirement transition and the experience of loneliness and found that retirement is associated with increased loneliness and that social support buffers the adverse effects of retirement on loneliness.^{2 22}

While there are no studies on the association between loneliness and retirement in non-western nations, one study of Chinese adults has found that decreased social participation after retirement is associated with depressive symptoms.²⁷ Because of differences in cultural norms, retirement policies, social relationships and living arrangements across countries, one may expect that retirement has varying effects on social health. However, to this date, nearly all evidence on retirement and loneliness comes from Western countries and no cross-country comparisons have been conducted. It is important to examine the differences in loneliness postretirement between countries to identify patterns and risk factors that might influence the health and well-being of older adults.

Based on longitudinal population data from China, Australia and the USA, the primary aim of this study was to examine and compare the association between retirement and loneliness. The secondary aim was to examine the moderating effect of social engagement on the association between retirement and loneliness across the three countries.

METHODS

We report the study using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. The STROBE statement is included in online supplemental table 1.1.

Study population

Data on adults aged 50 and above are from three publicly available, nationally representative longitudinal, household surveys from Australia, China and the USA.

Household, Income and Labour Dynamics in Australia (HILDA) includes 17 000 respondents each year, commencing in 2001. Data for the current study were derived from waves 2008 to 2019 (waves 8–19).²⁸

China Health and Retirement Longitudinal Study (CHARLS) includes 17 500 individuals from 28 provinces. The data have been collected every 2–3 years since 2011.²⁹ Data for the current study were derived from waves 2011 to 2015 (waves 1–3).

Health and Retirement Study (HRS) has been conducted in the USA every 2 years since 1992 among 22 000 respondents.³⁰ The data were derived from waves 2008 to 2018 (waves 9–14).^{31 32}

Data on loneliness and social engagement in the HRS were only available consistently since 2008, and therefore, we excluded previous waves. To keep consistency across the surveys, we excluded any waves before 2008 in the HILDA survey as well. We did not include waves after 2019 for any of the surveys due to the COVID-19 pandemic potential influence.

Measures

Variables were recoded to be consistent within and between the three surveys. For a full description of the data handling and recoding process, see online supplemental appendix 2 and online supplemental table 2.1.

Exposure variables

Retirement status was measured by an item regarding the reported status of retirement and included three categories: 0='not retired'/ 'partly retired', 1='retired', 2='never worked'. To further examine the nature of retirement in a sensitivity analysis, a 5-level retirement item was created: 1=not retired, 2=voluntary retirement, 3=involutionary retirement, 4=partly voluntary and partly involuntary retirement, 5=never worked. Nature of retirement was not asked in China.

Outcome variable

Loneliness was measured subjectively by a single binary variable (0=not lonely, 1=lonely) in all three surveys. In China and the USA, the item was taken from the Centre for Epidemiologic Studies Depression Scale (CES-D) regarding experiencing loneliness during the past week. We recoded levels 1–2 in the original CES-D scale as not 'lonely' and level 3–4 as 'lonely'.³² In Australia, the item 'I often feel very lonely' on a 7-point Likert scale (1=strongly disagree, 7=strongly agree), was derived from a loneliness and social isolation scale³³ and dichotomised into 0=levels 1–4, 1=levels 5–7 (indicating agreement with the statement), based on previous studies that used the same item.^{34 35}

Confounders

Reported health status was measured by one item from the Short Form Health Survey (SF-36) questionnaire³⁶ and reported mental health was measured by a scale regarding the frequency of experiencing different emotions, such as happy, depressed, sad, etc.^{36 37} Sociodemographic characteristics measures included age, gender (man/woman), education (below high school, high school, tertiary-not university, college/university), marital status (married/partnered, divorced/separated/never-married, widowed) and location of residence (urban, rural).

Effect modifier

Social engagement included the frequency of interactions with friends and/or family who do not reside with you (in the CHARLS questionnaire this included only interactions with friends) and was examined as a confounder and an effect modifier.

Data analysis

We report descriptive statistics of each sample using means and SD for continuous variables and numbers and percentages for categorical variables.

To examine the causal evidence on retirement and loneliness, which has been unexplored by previous studies, causal inference models can lend a unique contribution. We estimated the effect

of retirement on loneliness using marginal structural models (MSMs), applying inverse probability of treatment weights (IPTW).³⁸ IPTW-MSMs are a method for estimating causal effects in the counterfactual framework³⁹ and producing unbiased causal estimates under four structural assumptions (online supplemental appendix 3). To ensure that all participants will have the probability to be exposed (retire) during the study period, according to the positivity assumption, we excluded participants aged <50 ($n_{\text{(HILDA)}}=11\,430$, $n_{\text{(CHARLS)}}=6769$). For more details, see online supplemental figure 3.1.

We estimated propensity weights separately in each cohort using the set of confounders described above, allowing us to use covariates that could not be harmonised between the surveys. We estimated the propensity using multinomial logistic regression, using vector generalised linear models (online supplemental figure 3.12). Assuming there will be temporal delays or lags between the cause and its observed effect, we used lagged models to be certain that the exposure preceded the outcome. We modelled the effect of retirement at time 't' on loneliness in the subsequent wave (time t+1). The analysis data included up to 11 observations for each individual participant so we carried out analysis using random intercept mixed effects models. We conducted a secondary analysis testing the multiplicative effect modification by social engagement using the same procedure.

Sensitivity analysis

We also conducted the following sensitivity analyses: (1) A subanalysis among urban participants from all three countries to address differences in the definition of 'retirement' in the rural Chinese sample. Since rural agriculture workers in China differ from urban workers in work conditions and retirement benefits,⁴⁰ they tend to work in more labour-intensive jobs for as long as they can and then stop working according to their physical capability and financial resources,⁴¹ without a mandatory retirement age. Such different working and retirement conditions may have an impact on loneliness, social isolation and other health and well-being outcomes in older adults in China.^{17 18} In this case, the subsample of urban participants in China may be more comparable to the US and Australian samples; (2) To address exposure-affected time-varying confounding, where the confounder for an association between an exposure and an outcome is affected by previous exposures,⁴² we conducted fully lagged models analysis, to ensure that confounders preceded exposure by taking confounders from the wave prior to exposure (time t-1 not time t).

Missing data

The survey weights included adjustments for retention so that the current sample is representative, regardless of loss to follow-up. Since retention was accounted for by the sample weights, there was no need to impute or adjust for it in the sample itself.⁴³⁻⁴⁵ Therefore, we used complete case analysis for the 'exposure' wave (ie, the wave from which we took the 'retirement' variable, in each of our paired waves). When conditioning on variables in a model, complete case analysis is unbiased, provided that missingness is related to those variables.⁴⁶ To account for missingness in the 'lagged' outcome we used the inverse probability of censoring weights. Complete cases were weighted by the inverse of their probability of being a complete case.⁴⁷ More information on missing data and pooled samples can be found in online supplemental appendix 3 and online supplemental tables 3.1-S3.2.

Results are presented as the weighted marginal predicted prevalence of subsequent loneliness (time t+1), by retirement status (time t), as well as their 95% CIs. All analyses were performed using R software V.4.1.3⁴⁸ and Stata Statistical Software: Release V.17.⁴⁹

RESULTS

The final samples included 6018 participants in Australia, 13 107 participants in China and 19 968 participants in the USA.

The baseline characteristics of the study's participants are presented in table 1. In all three samples, the majority were women (Australia=53.6%, China=58.7%, USA=59.6%). China had the youngest sample (mean=62.0, SD=7.8) and the USA had the oldest (mean=67.9, SD=9.8). The proportion of participants with a college/university education was, 19.6% in Australia, 0.5% in China and 23.4% in the USA. In all three samples, the majority of participants were married/partnered (70.9% in Australia, 82.7% in China and 64.3% in the USA). Most participants in China were from rural areas (78.9%), compared with Australia (41.9% regional and rural) and the USA (51.7%). About half of the Australian (50.6%) and the USA (49.7%) samples were retired, compared with 14.8% in China. The prevalence of loneliness was 17.3% in Australia, 17.9% in China and 14.7% in the USA. Most participants in all three samples reported good-excellent health status (Australia=75.2%, China=73.7% and USA=75.2%).

Figure 1 and online supplemental table 4.1 show the adjusted marginal prevalence of loneliness by retirement status. According to the lagged model, those who retired experienced higher levels of loneliness in subsequent waves, compared with those who had not retired in Australia (19.4% (95% CI 18.0% to 20.9%) vs 17.0% (95% CI 15.7% to 18.4%)) and in the USA (19.3% (95% CI 17.5% to 21.1%) vs 15.7% (95% CI 14.3% to 17.3%)). However, these differences were significant only in the USA. In China, those who had retired were significantly less lonely compared with those who had not retired (10.0% (95% CI 7.9% to 12.5%) vs 17.1% (95% CI 15.7% to 18.5%)). Results of the fully lagged model show similar trends in retirement effects on loneliness to the lagged model, however, they were significant only in the US data. In the Chinese sample, however, loneliness was higher in the fully lagged model, and the adjusted prevalence precision in the retired group was lower, compared with the lagged model (online supplemental figure 4.1 and online supplemental table 4.2).

The models were run with the nature of retirement as the exposure variable in the Australian and US samples. The models compared loneliness among those who were (1) not retired/partly retired, (2) voluntarily retired, (3) involuntarily retired, (4) retired due to voluntary and involuntary reasons (retired-mixed) and (4) never worked.

Figure 2 and online supplemental table 4.3 show that in both samples, those who voluntarily retired had significantly lower loneliness (Australia: 9.6%, 95% CI 7.4% to 12.4%; USA: 10.5%, 95% CI 8.6% to 12.8%) compared with those who involuntarily retired (Australia: 16.9%, 95% CI 13.8% to 20.6%; USA: 18.1%, 95% CI 15.3% to 21.4%) and compared with non-retirees.

Figure 3 and online supplemental table 4.4 present the modifying effect of social engagement on the association between loneliness and retirement. In the USA and Australia, loneliness was significantly lower for those who were socially engaged compared with those who were not, regardless of retirement status (In Australian non-retirees: 15.0% (95% CI 13.7% to

Table 1 Baseline characteristics of participants in Australia (2008), China (2011) and the USA (2008–2010)

		Australia n=3412		China n=7347		US n=12 346	
		n	%	n	%	n	%
Gender (women)		1828	53.6	4314	58.7	7359	59.6
Age (mean, SD)		63.8	9.3	62.0	7.8	67.9	9.9
Education	Below high school	1439	42.2	6608	89.9	2041	16.5
	High school	286	8.4	451	6.1	4425	35.8
	Tertiary no university	1018	29.8	253	3.4	2992	24.2
	College/university	669	19.6	35	0.5	2888	23.4
Marital status	Married/partnered	2418	70.9	6076	82.7	7935	64.3
	Not married	601	17.6	407	5.5	2183	17.7
	Widowed	393	11.5	864	11.8	2228	18.0
Location of residence	Urban	1985	58.2	1548	21.1	5958	48.3
	Regional	1377	40.4	–	–	–	–
	Rural	50	1.5	5799	78.9	6388	51.7
Retirement (yes)		1726	50.6	1087	14.8	6130	49.7
Loneliness (yes)		589	17.3	1317	17.9	1810	14.7
Social engagement (active)		2923	85.7	2560	34.8	11 617	94.1
Health status	Very good-excellent	1202	35.2	1573	21.4	5279	42.7
	Good	1366	40.0	3843	52.3	4008	32.5
	Fair-poor	844	24.7	1931	26.3	3059	24.8
Mental health status mean (range), SD		10.8 (4–30)	4.1	17.2 (1–36)	5.9	–0.8	1.7 (–2–5)

16.4%) vs 29.8% (95% CI 25.8% to 34.2%) and retirees: 17.5% (95% CI 16.2% to 18.8%) vs 32.8% (95% CI 28.9% to 37.0%). In the US non-retirees: 15.2% (95% CI 13.7% to 16.7%) vs 20.4% (95% CI 17.3% to 26.4%) and retirees: 18.4% (95% CI 16.7% to 20.1%) vs 28.5% (95% CI 24.2% to 33.1%). In addition, in both Australia and the USA, the association between retirement and loneliness was not significant among those who were not socially engaged and was close to significant among those who were socially engaged. In China, there were no significant differences in loneliness between non-retirees who were socially engaged and those who were not (17.7% (95% CI 15.7% to 19.8%) vs 16.6% (95% CI 15.1% to 18.4%)), and this was the same for retirees (11.3%, 95% CI 7.8% to 16.0%) vs 9.2%, 95% CI (6.8% to 12.3%).

However, in contrast to Australia and the USA, the association between retirement and loneliness was significant among the not socially engaged whereas among the socially engaged this association was not significant.

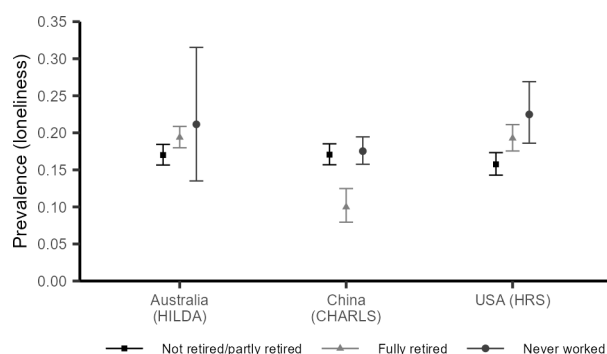


Figure 1 Adjusted marginal prevalence of loneliness according to retirement status in Australia, China and the USA. CHARLS, China Health and Retirement Longitudinal Study; HILDA, Household, Income and Labour Dynamics in Australia; HRS, Health and Retirement Study.

The model was run among urban participants from the three countries. In the Australian and the US samples, there were slight decreases in loneliness among the urban sample compared with the overall analysis that included both rural and urban participants. In the Chinese urban sample, loneliness was lower among the urban non-retirees (7.4% (95% CI 5.6% to 9.8%)), in contrast to the trend found in the overall Chinese sample so non-retirees had lower loneliness compared with retirees, similar to that in Australian and the US samples. However, this trend was not significant (figure 4 and online supplemental table 4.5).

DISCUSSION

The current study examined the effect of retirement on loneliness. Our findings from Australia and the USA confirmed the negative effect of retirement on loneliness previously reported.² However, in China, particularly in rural China, retirement seemed to have a protective effect on loneliness.

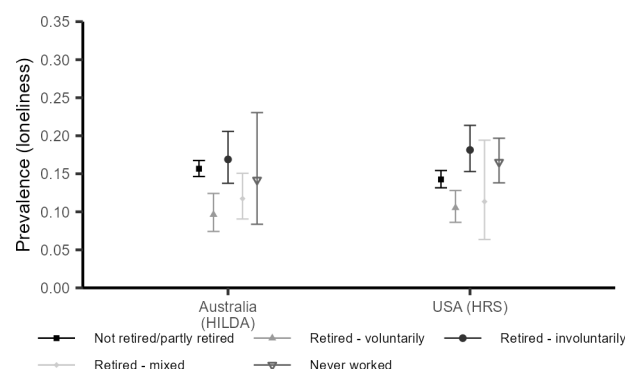


Figure 2 Adjusted marginal prevalence of loneliness according to the nature of retirement in Australia and the USA. HILDA, Household, Income and Labour Dynamics in Australia; HRS, Health and Retirement Study.

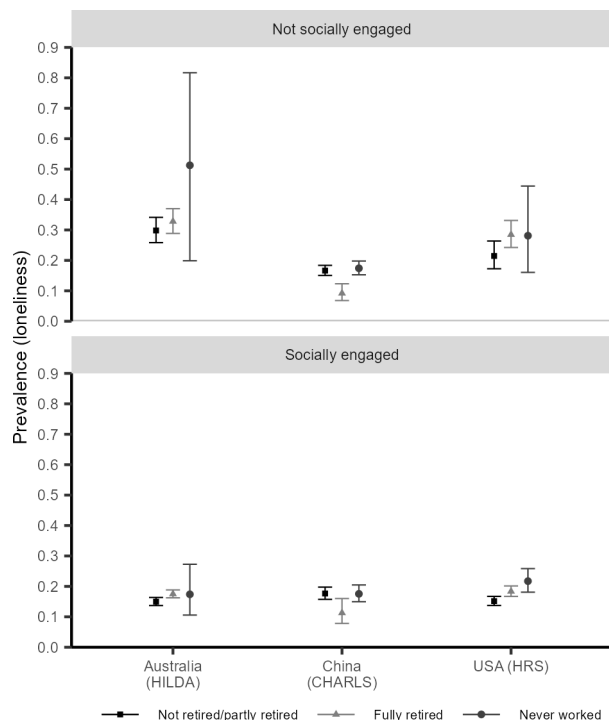


Figure 3 Associations between the adjusted marginal prevalence of loneliness and retirement according to social engagement status in Australia, China and the USA. CHARLS, China Health and Retirement Longitudinal Study; HILDA, Household, Income and Labour Dynamics in Australia; HRS, Health and Retirement Study.

The transition to retirement may be accompanied by a sense of loss of identity.^{50 51} The adjustment to new roles after retirement may lead to anxiety, depression and a decline in physical health.^{52 53} Previous studies supported this assertion by demonstrating a positive association between retirement and depressive symptoms among those who were lonely.² Our findings from Australia and the USA show the negative effect of retirement on loneliness. However, in China, an opposite trend was observed, where those who had retired had lower loneliness compared with those who were still in the workforce. One possible explanation is culture and social norms. Chinese traditional culture follows the 'filial piety' concept which prioritises the family unit and respects older adults.⁵⁴ Older adults rely on family for support and care^{55 56} and engage in reciprocal caregiving.⁵⁷

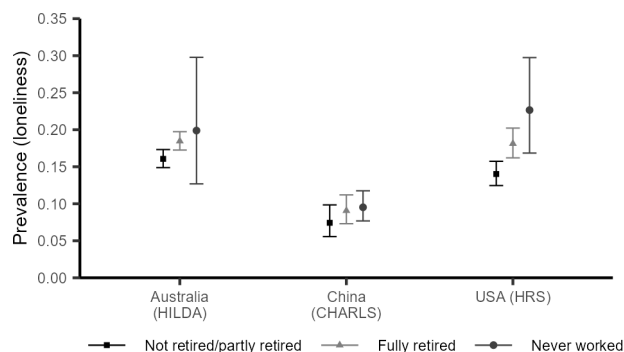


Figure 4 Adjusted marginal prevalence of loneliness among urban participants in Australia, China and the USA. CHARLS, China Health and Retirement Longitudinal Study; HILDA, Household, Income and Labour Dynamics in Australia; HRS, Health and Retirement Study.

These caregiving responsibilities have been identified as protective against identity loss and loneliness.^{57–59} In contrast, in Western cultures, being dependent on family for support is often associated with a sense of guilt and shame among Western older adults.⁶⁰ These cultural differences in the roles of older adults in society may explain the differences in the effect of retirement on loneliness observed in the current study.

Analysis of the urban-dwelling people showed no major differences in the association between retirement and loneliness in Australia and the USA. In addition, in the urban sample in China, retirement had a harmful effect on loneliness. Urban workers in China generally have job security, medical care, disability pay and pensions and have to retire on reaching a relatively young mandatory retirement age (50–60 years)⁶¹ while rural workers tend to work in labour-intensive jobs with less benefits⁴⁰ for as long as they can physically cope.⁴¹ Our findings may reflect the trend observed previously, where urban Chinese society is becoming more similar to Western society in values and in the importance of social roles outside of the family unit.¹⁸ In addition, our findings may reflect the disparities in stable employment and working conditions between rural and urban workers in China, with those in urban areas experiencing financial, mental and social benefits.⁶² The lack of social and financial stability was found to generate relatively higher stress and lower social and mental well-being among those living in rural areas,^{63 64} which may explain some of the differences in social outcomes among the urban non-retirees in China that were observed in the current study.

Our findings from the fully lagged model show that in China, loneliness was higher in all three groups compared with the lagged model. In addition, the estimate precision was lower, resulting in non-significant effects. This could be due to only including two waves of data which is likely to have impacted precision. However, this finding could also be a result of a weaker control for confounding as confounders were measured 2 years before the exposure.

In Australia and the USA, voluntary retirees had the lowest loneliness and involuntary retirees had the highest, which was consistent with previous studies.²² Voluntary retirement is usually planned and expected whereas involuntary retirement may be sudden, and retirees may not have sufficient time or resources to adjust to the changes that this entails.⁶⁵ Involuntary retirement is associated with lower life satisfaction,⁶⁶ unhealthy lifestyle, poorer physical and mental health,^{67 68} more family strain and negative social relationships, which contribute to higher loneliness.²² Involuntary retirees may experience a lower sense of control and self-esteem due to sudden and unexpected changes which are usually undesirable.⁶⁷

In both retirees and workers in the Australian and the US samples, loneliness was significantly lower for those who were socially engaged compared with those who were not. These findings emphasise the importance of social engagement after retirement and are consistent with previous literature on the positive effect of social engagement on loneliness, health and health behaviour indicators such as improvements in cognition, function, memory, chronic illness self-management and decreased suicidal ideation.^{69–71} In China, however, our findings show that loneliness decreased after retirement regardless of social engagement. This finding may be explained by the social engagement variable in the CHARLS survey which did not include familial relationships. Family is considered highly important in Chinese society. A previous study identified family, as the strongest predictor of loneliness, especially among rural older adults.⁷² There is also evidence that people from Asian cultures tend to

not want to reach out for help during difficult times. Therefore, the question on social engagement outside of family networks in the Chinese survey may not be very relevant when it comes to mitigation of loneliness.⁷³

Limitations

The current analysis used lagged and fully lagged models to infer causality of the effect of retirement on loneliness. The data are population based and longitudinal, and therefore, provide an accurate estimation of the effect of retirement on loneliness. However, the study had some limitations. First, the utilisation of a one-item direct measure for loneliness has faced criticism in the past, primarily due to reporting bias driven by stigma and potentially different interpretations of what loneliness means to respondents. However, the one-item loneliness measure has been previously validated and shown to be highly reliable within longitudinal research^{74 75} and was correlated with other more comprehensive, common loneliness measures such as the UCLA and the de Jong loneliness scales.^{76 77} Second, the exposure and outcome measurements had to be recoded in order to be consistent within and between the different countries, which may have caused loss of information or bias in the results. Third, the social engagement variable in China did not include engaging with family which may influence the association between retirement and loneliness in China. Last, data in HRS and CHARLS were available every 2 years and in HILDA data were for every year. Since we conducted lagged models, with exposure in one wave and outcome in the consecutive wave, we wanted to have similar gaps between outcomes and therefore we used the outcomes every 2 years in HILDA, similar to HRS. Therefore, some of the waves in HILDA were not included in the analysis. However, the consistency between the waves was more important to the comparability of the results and therefore justifies the loss of data from the excluded waves.

CONCLUSIONS

Our findings show that retirement's effect on loneliness and the moderating effect of social engagement differentiates between countries. While retirement is a risk factor for older adults in Australia and the USA, it may be seen as a protective factor in China, particularly in rural China where traditional culture and values are likely to be more prominent. Our findings also highlight the importance of cultural context when designing and implementing interventions among older adults. In Chinese rural communities, the focus should be on those still in the workforce since they may experience more loneliness, while in urban China and Western societies, the focus should be on those who have retired. As most research to this date is focused on Western countries, future research could benefit from further examining the association between loneliness and retirement and social engagement modifying effect in Eastern countries with traditional cultures such as China. It is also recommended to further examine the differences between rural and urban societies as our findings suggest social health may be affected differently.

Correction notice This article has been corrected since it first published. Additional author ORCID iDs have been added and figures have been changed to black and white.

X Philip J Clare @pjclare

Contributors NH is the guarantor. NH planned the study, performed the statistical analysis and wrote the manuscript. PJC planned the study, supervised the data analysis, performed the statistical analysis and revised the manuscript. ML performed the statistical analysis and revised the manuscript. DM and BJS planned the study

and revised the manuscript. DD planned the study and wrote and revised the manuscript.

Funding DD is funded by the National Health and Medical Research Council Emerging Leader Fellowship (award No. 2009254).

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Neta Hagani <http://orcid.org/0000-0002-5442-1025>

Philip J Clare <http://orcid.org/0000-0002-2009-7386>

Mengyun Luo <http://orcid.org/0000-0002-6482-7299>

Dafna Merom <http://orcid.org/0000-0001-6459-8628>

Ben J Smith <http://orcid.org/0000-0002-6227-5566>

Ding Ding <http://orcid.org/0000-0001-9850-9224>

REFERENCES

- Hansson I, Buratti S, Thorvaldsson V, *et al.* Changes in life satisfaction in the retirement transition: interaction effects of transition type and individual resources. *Work, Aging and Retirement* 2018;4:352–66.
- Segel-Karpas D, Ayalon L, Lachman ME. Loneliness and depressive symptoms: the moderating role of the transition into retirement. *Aging Ment Health* 2018;22:135–40.
- Crowe CL, Domingue BW, Graf GH, *et al.* Associations of loneliness and social isolation with health span and life span in the U.S health and retirement study. *J Gerontol A Biol Sci Med Sci* 2021;76:1997–2006.
- de Jong-Gierveld J. Developing and testing a model of loneliness. *J Pers Soc Psychol* 1987;53:119–28.
- Courtin E, Knapp M. Social isolation, loneliness and health in old age: a Scoping review. *Health Soc Care Community* 2017;25:799–812.
- National Academies of Sciences E. Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System. Washington (DC): National Academies Press (US), 2020.
- Surkalim DL, Luo M, Eres R, *et al.* The prevalence of loneliness across 113 countries: systematic review and meta-analysis. *BMJ* 2022;376:e067068.
- Beller J, Wagner A. Loneliness and health: the moderating effect of cross-cultural individualism/collectivism. *J Aging Health* 2020;32:1516–27.
- Fokkema T, De Jong Gierveld J, Dykstra PA. Cross-national differences in older adult loneliness. *J Psychol* 2012;146:201–28.
- Swader CS. Loneliness in Europe: personal and societal individualism-collectivism and their connection to social isolation. *Soc Forces* 2019;97:1307–36.
- North MS, Fiske ST. Modern attitudes toward older adults in the aging world: a cross-cultural meta-analysis. *Psychol Bull* 2015;141:993–1021.
- Kim D. The concept of filial piety in East Asian Confucian culture from the perspectives of Gadamer and Habermas. *KK* 2020;33/34:36–64.
- Haiyan HAO. Inheritance and innovation of Chinese filial piety culture. *PS* 2021;11:89–95.
- Rokach A. The effect of gender and culture on loneliness: a mini review. *ESJ* 2018;2:59–64.
- Snell KDM. The rise of living alone and loneliness in history. *Social History* 2017;42:2–28.
- Tu M. Chinese one-child families in the age of migration: middle-class transnational mobility, ageing parents, and the changing role of filial piety. *J Chin Sociol* 2016;3:15.
- Luo Y, Waite LJ. Loneliness and mortality among older adults in China. *J Gerontol B Psychol Sci Soc Sci* 2014;69:633–45.
- Liu J, Rozelle S, Xu Q, *et al.* Social engagement and elderly health in China: evidence from the China health and retirement longitudinal survey (CHARLS). *IJERPH* 2019;16:278.

- 19 Kostikidou S. Culture and grief: the concepts of social support and loneliness among bereaved individuals from collectivistic and individualistic cultures. 2020.
- 20 Heu LC, van Zomeren M, Hansen N. Lonely alone or lonely together? A cultural-psychological examination of individualism-collectivism and loneliness in five European countries. *Pers Soc Psychol Bull* 2019;45:780–93.
- 21 Barreto M, Victor C, Hammond C, et al. Loneliness around the world: age, gender, and cultural differences in loneliness. *Pers Individ Dif* 2021;169:110066.
- 22 Shin O, Park S, Amano T, et al. Nature of retirement and loneliness: the moderating roles of social support. *J Appl Gerontol* 2020;39:1292–302.
- 23 Chiao C, Kuo PH, Li DC, et al. The changes in feeling of loneliness after retirement among baby boomers and pre-boomers in Taiwan: do work-family conflict before retirement and social engagement after retirement matter *SSM Popul Health* 2022;20:101264.
- 24 Lytle MC, Foley PF, Cotter EW. Career and retirement theories: relevance for older workers across cultures. *J Career Dev* 2015;42:185–98.
- 25 Thorsen S, Rugulies R, Løngaard K, et al. The association between psychosocial work environment, attitudes towards older workers (Ageism) and planned retirement. *Int Arch Occup Environ Health* 2012;85:437–45.
- 26 de Breij S, Huisman M, Deeg DJH. Macro-level determinants of post-retirement health and health inequalities: a multilevel analysis of 18 European countries. *Soc Sci Med* 2020;245:112669.
- 27 Liu H, Fang B, Chan J, et al. Continued social participation protects against depressive symptoms across the retirement transition: longitudinal evidence from three waves of the China health and retirement longitudinal survey. *Geriatr Gerontol Int* 2019;19:972–6.
- 28 Wilkins R, Lass I, Butterworth P, et al. *The household, income and labour dynamics in Australia survey: selected findings from waves 1 to 12*. Melbourne: Institute of Applied Economic and Social Research, The University of Melbourne, 2015.
- 29 Phillips D, Green H, Petrosyan S, et al. *Gateway to global aging data. The Harmonised CHARLS dataset and codebook, Version D June 2021 (R01 AG030153, RC2 AG036619, R03 AG043052)*. The National Institute on Aging, 2021.
- 30 Servais M. *Overview of HRS public data files for cross-sectional and longitudinal analysis*. Ann Arbor, Michigan: Institute for Social Research, University of Michigan, 2010.
- 31 RAND HRS Longitudinal File. *Produced by the RAND center for the study of aging, with funding from the National Institute on Aging and the Social Security Administration*. Santa Monica, CA, 2022.
- 32 Health and Retirement Study. RAND HRS longitudinal file (V2) public use Dataset. produced and distributed by the University of Michigan with funding from the National Institute on aging (grant number NIA U01Ag009740). 2018.
- 33 Manera KE, Smith BJ, Owen KB, et al. Psychometric assessment of scales for measuring loneliness and social isolation: an analysis of the household, Income and Labour Dynamics in Australia (HILDA) survey. *Health Qual Life Outcomes* 2022;20:40.
- 34 Kung CSJ, Kunz JS, Shields MA. Economic aspects of loneliness in Australia. *Aust Econ Rev* 2021;54:147–63.
- 35 Astell-Burt T, Hartig T, Eckermann S, et al. More green, less lonely? A longitudinal cohort study. *Int J Epidemiol* 2022;51:99–110.
- 36 Ware JE, Sherbourne CD. The MOS 36-Item short-form health survey (SF-36). *Medical Care* 1992;30:473–83.
- 37 Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Assessment* 1977;1:385–401.
- 38 Robins JM, Hernán MA, Brumback B. Marginal structural models and causal inference in epidemiology. *Epidemiology* 2000;11:550–60.
- 39 Rubin D. Estimating causal effects of treatments in experimental and observational studies. *ETS Research Bulletin Series* 1972;1972:i–31.
- 40 Giles J, Lei X, Wang G, et al. One country, two systems: evidence on retirement patterns in China. *Journal of Pension Economics and Finance* 2023;22:188–210.
- 41 Feng Z. Chapter 17: filial piety and old-age support in China: tradition, continuity, and change. In: *Handbook on the family and marriage in China*. Edward Elgar Publishing, 2017: 266–85.
- 42 Daniel RM, Cousens SN, De Stavola BL, et al. Methods for dealing with time-dependent confounding. *Stat Med* 2013;32:1584–618.
- 43 Watson N. *HILDA project technical paper series No.2/12. Longitudinal and cross-sectional weighting methodology for the HILDA survey*. The Melbourne Institute, Faculty of Business and Economics, The University of Melbourne, 2012.
- 44 Lee S, Nishimura R, Burton P, et al. *2016 sampling weights*. Ann Arbor, MI: Survey Research Center, Institute for Social Research, University of Michigan, 2021.
- 45 Zhao Y, Hu Y, Smith JP, et al. Cohort profile: the China health and retirement longitudinal study (CHARLS). *Int J Epidemiol* 2014;43:61–8.
- 46 Hughes RA, Heron J, Sterne JAC, et al. Accounting for missing data in statistical analyses: multiple imputation is not always the answer. *Int J Epidemiol* 2019;48:1294–304.
- 47 Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. *Stat Methods Med Res* 2013;22:278–95.
- 48 R Core Team. *R: A Language and Environment for Statistical Computing [Program]. 4.1.3 Version*. Vienna: R Foundation for Statistical Computing: R Core Team, 2019.
- 49 StataCorp LLC. *Stata Statistical Software: Release 17 [Program]*. College Station, TX: StataCorp LLC, 2021.
- 50 Henning G, Lindwall M, Johansson B. Continuity in well-being in the transition to retirement. *GeroPsych* 2016;29:225–37.
- 51 Osborne JW. Psychological effects of the transition to retirement. *Can J Counsel Psych* 2011;46:45–58.
- 52 Carter MAT, Cook K. Adaptation to retirement: role changes and psychological resources. *The Career Development Quart* 1995;44:67–82.
- 53 Wang M, Henkens K, van Solinge H. Retirement adjustment: a review of theoretical and empirical advancements. *Am Psychol* 2011;66:204–13.
- 54 Chou RJ-A. "Filial piety by contract? The emergence, implementation, and implications of the "family support agreement" in China". *Gerontologist* 2011;51:3–16.
- 55 Leung JC. Family support and community services for older adults in China: integration and partnership. In: *Handbook of Asian aging*. Routledge, n.d.: 2018. 405–30.
- 56 Shen Y, Yeatts DE. Social support and life satisfaction among older adults in China: family-based support versus community-based support. *Int J Aging Hum Dev* 2013;77:189–209.
- 57 Li LW, Zhang J, Liang J. Health among the oldest-old in China: which living arrangements make a difference? *Soc Sci Med* 2009;68:220–7.
- 58 Lou VWQ. Life satisfaction of older adults in Hong Kong: the role of social support from grandchildren. *Soc Indic Res* 2010;95:377–91.
- 59 Zhang J, Fokkema T, Arpino B. Loneliness among Chinese older adults: the role of Grandparenthood and Grandparental Childcare by gender. *Journal of Family Issues* 2022;43:3078–99.
- 60 Cahill E, Lewis LM, Barg FK, et al. "You don't want to burden them": older adults' views on family involvement in care. *J Fam Nurs* 2009;15:295–317.
- 61 Qi L. China is facing a moment of truth about its low retirement age. *The Wall Street Journal* 2023. Available: <https://www.wsj.com/articles/china-is-facing-a-moment-of-truth-about-its-low-retirement-age-5ed9b57f>
- 62 Shen Z, Fang X, Zheng X. The impact of women's off-farm employment on depressive symptoms: evidence from rural China. *Soc Sci Med* 2022;311:115309.
- 63 Li C, Wu Q, Liang Z. Effect of poverty on mental health of children in rural China: the mediating role of social capital. *Applied Research Quality Life* 2019;14:131–53.
- 64 Liu LJ, Guo Q. Loneliness and health-related quality of life for the empty nest elderly in the rural area of a mountainous county in China. *Qual Life Res* 2007;16:1275–80.
- 65 Shin O, Park S, Lee H, et al. Gender differences in the mechanism of involuntary retirement affecting loneliness through vulnerability and coping resources. *Ageing and Society* 2024;44:1–22.
- 66 van der Heide I, van Rijn RM, Broekse SJ, et al. Is retirement good for your health? A systematic review of longitudinal studies. *BMC Public Health* 2013;13:1180.
- 67 Rhee MK, Mor Barak ME, Gallo WT. Mechanisms of the effect of involuntary retirement on older adults' self-rated health and mental health. *J Gerontol Soc Work* 2016;59:35–55.
- 68 Ding D, Grunseit AC, Chau JY, et al. Retirement-a transition to a healthier lifestyle?: evidence from a large Australian study. *Am J Prev Med* 2016;51:170–8.
- 69 Gyasi RM, Phillips DR, Asante F, et al. Physical activity and predictors of loneliness in community-dwelling older adults: the role of social connectedness. *Geriatr Nurs* 2021;42:592–8.
- 70 Park NS, Lee BS, Chiriboga DA, et al. Loneliness as a mediator in the relationship between social engagement and depressive symptoms: age differences among community-dwelling Korean adults. *Health Soc Care Community* 2019;27:706–16.
- 71 Kelly ME, Duff H, Kelly S, et al. The impact of social activities, social networks, social support and social relationships on the cognitive functioning of healthy older adults: a systematic review. *Syst Rev* 2017;6:259.
- 72 Wang G, Zhang X, Wang K, et al. Loneliness among the rural older people in Anhui, China: prevalence and associated factors. *Int J Geriatr Psychiatry* 2011;26:1162–8.
- 73 Taylor SE, Sherman DK, Kim HS, et al. Culture and social support: who seeks it and why *J Pers Soc Psychol* 2004;87:354–62.
- 74 Butterworth P, Crosier T. The validity of the SF-36 in an Australian national household survey: demonstrating the applicability of the household income and labour Dynamics in Australia (HILDA) survey to examination of health inequalities. *BMC Public Health* 2004;4:44.
- 75 Powers J, Russell A. *ALSWH data dictionary supplement. Section 2 core survey dataset 2.7 psychosocial variables. Center for Epidemiologic Studies Depression Scale - shortened version: Australian longitudinal study on women's health*. Australian Longitudinal Study on Women's Health, 2002.
- 76 Nicolaissen M, Thorsen K. Who are lonely? Loneliness in different age groups (18-81 years old), using two measures of loneliness. *Int J Aging Hum Dev* 2014;78:229–57.
- 77 Peplau L, Perlman D, Russell D. The measurement of loneliness. In: Peplau L, Perlman D, eds. *Loneliness: a sourcebook of current theory, research and theory*. John Wiley & Sons, 1982: 81–104.

3.5. Appendices

The effect of retirement on loneliness: A longitudinal comparative analysis across Australia, China, and the United States - Supplementary files

Appendix 1 - STROBE Statement—Checklist of items that should be included in reports of cohort studies

Table S1.1. STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	10, Tables

			S4.1-S4.2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8, Appendix 2
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-10, Appendix 3
		(b) Describe any methods used to examine subgroups and interactions	9
		(c) Explain how missing data were addressed	9-10, Appendix 4
		(d) If applicable, explain how loss to follow-up was addressed	9-10, Appendix 4
		(e) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10, Tables S4.1-S4.2
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	Figure S4.1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	Table S4.1
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12
		(b) Report category boundaries when continuous variables were categorized	11-12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12

Discussion

Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Appendix 2 – recoding process and original variables

Retirement

Australia: Retirement was measured by the item “retired completely from the workforce” (‘yes’, ‘no’, ‘never in workforce’) which was asked only among those who were not working and above the age of 45. Those who were not asked this question were recoded as having a working status. This question was available in all waves except from wave 11 which had a similar question: “Do you consider yourself to be completely retired from the paid workforce, partly retired or not retired at all?” with four optional answers: ‘completely retired’, ‘partly retired’, ‘not retired at all’, ‘not relevant - have never been in paid work’. Both items were recoded as 0 = ‘not retired’/ ‘partly retired’, 1 = ‘retired’, 2 = ‘never worked’, in the final analysis.

China: Measured by ‘work status’ with possible answers including: ‘Work in agriculture’, ‘work in non-agriculture’, ‘retired’, ‘unemployed’, ‘never worked’. The item was recoded to the following: 0 = ‘work in agriculture’/ ‘work in non-agriculture’, 1 = ‘retired’, 2 = ‘unemployed’/ ‘never worked’.

US: Participants were asked about their retirement: “do you consider yourself to be completely retired, partly retired, or not retired at all?” Answers were recoded to the following: 0 = ‘not retired’/ ‘partly retired’, 1 = ‘completely retired’, 2 = ‘not relevant’ (never worked).

Nature of retirement

Was available only in HRS and HILDA.

HILDA: Twenty-three items regarding different reason for retirement (e.g., “could not find another job”, “own ill health”, “reached compulsory retirement age”). These items were available only in waves 2011 and 2015. Data on nature of retirement was available in 2019 as well. However, since we used a lagged model analysis, the loneliness outcome for that wave should have been taken from the subsequent wave. Since we excluded waves after 2019 due to potential COVID-19 impact, we could not include the 2019 nature of retirement data). A new item was computed in which 1 = those who only indicated voluntary reasons for retirement, 2 = those who only indicated involuntary reasons for retirement, 3 = those who indicated both voluntary and involuntary reasons for retirement. Health problems, caring responsibilities and employment issues (e.g., made redundant/ dismisses/ had no choice) reflected involuntary reasons, while age and lifestyle considerations (e.g., to spend more time with spouse/ partner) reflected voluntary reasons [1, 2].

HRS: examined by an item which asked whether retirement was wanted or forced with possible answers (1 = Wanted, 2 = Forced, 3 = Part wanted, part forced).

Loneliness

HILDA: Loneliness was measured by a single item (“I often feel very lonely”) derived from a loneliness and social isolation scale constructed for the HILDA survey purposes [3]. The item was on a 7-point Likert scale (1 = Strongly disagree, 7 = Strongly agree). To be consistent with the two other surveys, loneliness was dichotomised to: 0 = levels 1-4, 1 = levels 5-7 (indicating agreement with the statement), based on previous studies that used the same item [4, 5].

CHARLS: Loneliness was measured by a single item from the Center for Epidemiologic Studies Depression Scale (CES-D) regarding experiencing loneliness during the past week [6]. The item was on a 4-point Likert scale: 1. ‘Rarely or none of the time (less than 1 day)’, 2. ‘Some or a little of the time (1-2 days)’, 3. ‘Occasionally or a moderate amount of time (3-4 days)’, 4. ‘Most or all of the time (5-7 days)’. To be consistent with the HRS loneliness item, the item was recoded to 0 = levels 1-2 in the original scale, 1 = level 3-4 in the original scale.

HRS: Similar to CHARLS, loneliness was measured by a single item from the Center for Epidemiologic Studies Depression Scale (CES-D) regarding experiencing loneliness during the past week [6]. The original scale had Four levels: 1. ‘Rarely or none of the time (less than 1 day)’, 2. ‘Some or a little of the time (1-2 days)’, 3. ‘Occasionally or a moderate amount of time (3-4 days)’, 4. ‘Most or all of the time (5-7 days)’. The item was recoded by HRS as 0 = levels 1-2 in the original scale, 1 = level 3-4 in the original scale [7].

Social Engagement:

Australia: Measured by one item from the HILDA self-completion questionnaire: “In general, how often do you get together socially with friends or relatives not living with you?” The item was measured on a 7-point Likert scale (1 = ‘every day’, 7 = ‘less often than once every 3 months’). To be consistent with the other two surveys, the item was recoded as follows: 0 = levels 6-7 (not socially active), 1 = levels 1-5 (socially active).

China: Social Engagement was assessed by the item: “Have you interacted with friends in the past month?” (‘no’/‘yes’). This item was part of a list of activities for which participants were asked whether they participated in these activities. Since most of the activities were not necessarily indicative of social engagements, and since the social engagement items that were

available in the two other surveys referred to friends or family engagements, we decided to use this item alone.

US: An overall score was built from a series of questions assessing the number of social interactions and frequency of engagements. Four questions ask respondents if they have spouses/partners, children, family, and friends ('no'/'yes'), followed by four questions to assess the extent to which respondents are in contact with each of their social networks excluding spouses: meet up, speak on the phone, write or email and using social media (from 2014 onwards). The Four items were rated on a 6-point Likert scale (1 = Three or more times a week, 6 = Less than once a year or never) [8]. For the current study, we used the questions evaluating relationships with family and friends, similar to the CHARLS and HILDA items. Communication by social media was excluded as it was not available for all of the waves [9]. The Three items included were dichotomised to 0 = 'three or more times a week' – 'once or twice a month', 1 = 'every few months' – 'less than once a year or never'. A count variable was built from the Six items (Three for each contact) which was then dichotomised to 0 = 'no social engagements', 1 = 'at least one social engagements'.

Mental health:

Australia: Mental health was measured by 5 items from the emotional wellbeing section of the 36-Item Short Form Health Survey (SF-36) [10]. Participants were asked about the frequency of experiencing different emotions. Items were on a 6-point Likert scale (1 = 1 all of the time, 6 = none of the time). Negative items were recoded to reflect worse mental health with a higher score. Total items were summarised and ranged between 5-30.

China: Mental health was measured by the 10-items CES-D-R10 scale regarding how participants felt and behaved during the past week [6]. Items were on a 4-point Likert scale (0 = Rarely or none of the time, 3 = Most or all of the time). We excluded the item: "I felt lonely" since it was already used as a measure of loneliness. Positive items were recorded, and the total items were summarised. Scores ranged from 0-30 with a higher score indicating worse mental health [11].

US: The mental health scale included Eight items from the CES-D scale regarding how participants felt and behaved during the past week [6]. The original scale was 4-point Likert scale (as described above). Answers were recoded by HRS as 0 = levels 1-3 in the original CES-D scale, 1 = level 4 in the original CES-D scale. A count score of negative items (i.e., "I had trouble keeping my mind on what I was doing") minus the positive items (i.e., "I was happy") was created [7]. We excluded the item: "I felt lonely" since it was already used as a

measure of loneliness. Scores ranged between -2 and 5 with a higher score indicating worse mental health.

Health status

In all three surveys, reported health status was measured by one item from the SF-36 questionnaire [10] on a 5-point Likert scale (1 = Excellent, 5 = poor).

A summary of the recoding process is in **Table S2.1**.

References

1. Ding D, Grunseit AC, Chau JY, Vo K, Byles J, Bauman AE. Retirement-A Transition to a Healthier Lifestyle?: Evidence From a Large Australian Study. *Am J Prev Med*. 2016;51(2):170-8.
2. Vo K, Forder PM, Tavenor M, Rodgers B, Banks E, Bauman A, Byles JE. Retirement, age, gender and mental health: findings from the 45 and Up Study. *Aging Ment Health*. 2015;19(7):647-57.
3. Manera KE, Smith BJ, Owen KB, Phongsavan P, Lim MH. Psychometric assessment of scales for measuring loneliness and social isolation: an analysis of the household, income and labour dynamics in Australia (HILDA) survey. *Health Qual Life Out*. 2022;20(1):40.
4. Kung CSJ, Kunz JS, Shields MA. Economic Aspects of Loneliness in Australia. *Aust Econ Rev*. 2021;54(1):147-63.
5. Astell-Burt T, Hartig T, Eckermann S, Nieuwenhuijsen M, McMunn A, Frumkin H, Feng X. More green, less lonely? A longitudinal cohort study. *Int J Epidemiol*. 2022;51(1):99-110.
6. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Appl Psychol Measur*. 1977;1:385-401.
7. Health and Retirement Study. RAND HRS Longitudinal File (V2) public use dataset. . Produced and distributed by the University of Michigan with funding from the National Institute on Aging (grant number NIA U01AG009740). 2018
8. Smith J, Ryan G, Fisher GG, Sonnega A, Weir W. HRS Psychosocial and Lifestyle Questionnaire 2006-2016. Documentation Report Core Section LB. Ann Arbor, Michigan: Survey Research Center Institute for Social Research University of Michigan; 2017.

9. Smith J, Ryan L, Fisher G, Sonnega A, Weir D. HRS Psychosocial and Lifestyle Questionnaire 2006-2016. Ann Arbor, Michigan: Survey Research Center, Institute for Social Research, University of Michigan; 2017.
10. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30(6):473-83.
11. Phillips D, Green H, Petrosyan S, Shao K, Wilkens J, Lee J. Gateway to Global Aging Data. The Harmonised CHARLS dataset and Codebook, Version D June 2021 (R01 AG030153, RC2 AG036619, R03 AG043052). The National Institute on Aging 2021. <https://charls.pku.edu.cn/en/team/Codebook.pdf>

Table S2.1. Surveys original questions, responses options and recoding

		Australia [1]	China [2]	US [3]	Final item recoding
Retirement	Question	Retired completely from the workforce:	Work status	Do you consider yourself to be completely retired, partly retired, or not retired at all?	0 = not retired 1 = retired 2 = never worked
	Responses	1. Yes 2. No 3. Never in the workforce	1. Work in agriculture 2. Work in non-agriculture 3. Retired 4. Unemployed 5. Never worked	1. Completely retired 2. Partly retired 3. Not retired at all 4. Not relevant (never worked)	
	Recode	0 = level 2 1 = level 1 2 = level 3	0 = levels 1-2 1 = level 3 2 = levels 4-5	0 = levels 2-3 1 = level 1 2 = level 4	
Nature of retirement	Question	Twenty-three items regarding different possible reason for retirement (e.g., “could not find another job”, “own ill health”, “reached compulsory retirement age”).	No variable available	Thinking back to the time you [partly/completely] retired, was that something you wanted to do or something you felt you were forced into?	0 = not retired 1 = retired voluntary 2 = retired involuntary 3 = retired partly voluntary partly involuntary 4 = never worked
	Responses	0 = no 1 = yes		1. Wanted to 2. Forced to 3. Partly wanted partly forced	
	Recode	1 = those who only indicated voluntary reasons for retirement 2 = those who only indicated involuntary reasons for retirement 3 = those who indicated both voluntary and involuntary reasons for retirement		1 = level 1 2 = level 2 3 = level 3	
Loneliness	Question	The following statements have been used by many people to describe how much support	I felt lonely during the past week (CES-D)	I felt lonely during the past week (CES-D)	0 = not lonely 1 = lonely

		Australia [1]	China [2]	US [3]	Final item recoding
		they get from other people. How much do you agree or disagree with each? The more you agree, the higher the number of the box you should cross. The more you disagree, the lower the number of the box you should cross. I often feel very lonely (HILDA questionnaire [4]). 7-point Likert scale			
	Responses	1. Strongly disagree 7. Strongly agree	1. Rarely or none of the time (less than 1 day) 2. Some or a little of the time (1-2 days) 3. Occasionally or a moderate amount of time (3-4 days) 4. Most or all of the time (5-7 days)	1. Rarely or none of the time (less than 1 day) 2. Some or a little of the time (1-2 days) 3. Occasionally or a moderate amount of time (3-4 days) 4. Most or all of the time (5-7 days)	
	Recode	0 = levels 1-4 1 = levels 5-7	0 = levels 1-2 1 = levels 3-4	0 = levels 1-2 1 = levels 3-4	
Social engagement	Question	In general, how often do you get together socially with friends or relatives not living with you?	Have you interacted with friends in the past month?	1. Do you have any other immediate family, for example, any brothers or sisters, parents, cousins or grandchildren 2. Do you have any friends? 3. How often do you a) meet up, b) speak on the phone, c) write or email?	0 = not socially engaged 1 = socially engaged

		Australia [1]	China [2]	US [3]	Final item recoding
	Responses	1. Every day 2. Several times a week 3. About once a week 4. 2 or 3 times a month 5. About once a month 6. Once or twice every 3 months 7. Less often than once every 3 months	1. no 2. yes	1-2. yes/no 3(a-c). 6-point Likert scale (1 = Three or more times a week, 6 = Less than once a year or never)	
	Recode	0 = levels 6-7 (not socially active) 1 = levels 1-5 (socially active)	0 = level 1 1 = level 2	6 items recoded: 0 = 'three or more times a week' – 'once or twice a month' 1 = 'every few months' – 'less than once a year or never' A count variable was built from the Six items (Three for each contact) which was then dichotomised to 0 = 'no social engagements' 1 = 'at least one social engagements'.	
Mental health	Question	SF-36 [5]: emotional wellbeing scale	Eight items from the CES-D scale [6] (excluding 'loneliness')		Summary score from each survey was used
	Responses	1. All of the time 2. Most of the time 3. A good bit of the time 4. Some of the time 5. A little of the time 6. None of the time	1. Rarely or none of the time (less than 1 day) 2. Some or a little of the time (1-2 days) 3. Occasionally or a moderate amount of time (3-4 days) 4. Most or all of the time (5-7 days)	1. no = 'none' – 'occasionally' in the original scale 2. yes = 'most or all of the time' in the original scale.	

		Australia [1]	China [2]	US [3]	Final item recoding
	Recode	Five items summary score	Summary score of 8 items	A count score of negative items minus the positive items.	
Health status		Self-assessed health- SF-36 [5] 1. Excellent 2. Very good 3. Good 4. Fair 5. Poor			
Age		Numerical values			
Gender		1. Male 2. Female			
Education	Responses	1. Postgrad - masters or doctorate 2. Grad diploma, grad certificate 3. Bachelor or honours 4. Adv diploma, diploma 5. Cert III or IV 6. Year 12 7. Year 11 and below	1. Did not finish primary school but capable of reading and/or writing 2. Elementary school 3. Middle school 4. No formal education (illiterate) 5. Sishu/home school 6. High school 7. Two-/Three-Year College/Associate degree 8. Vocational school 9. Doctoral degree/Ph.D. 10. Four-Year College/Bachelor's degree 11. Master's degree	1. Lt High-school 2. GED 3. High-school graduate 4. Some college 5. College and above	1. Below high school 2. High school 3. Tertiary-not university 4. College/university
	Recode	1 = level 7 2 = level 6 3 = levels 2, 4-5	1 = levels 1-5 2 = level 6 3 = 7-8	1 = level 1 2 = levels 2-3 3 = level 4	

		Australia [1]	China [2]	US [3]	Final item recoding
		4 = levels 1, 3	4 = 9-11	4 = level 5	
Marital status	Responses	1. Legally married 2. De facto 3. Separated 4. Divorced 5. Widowed 6. Never married and not de facto	1. Cohabitated 2. Married with spouse present 3. Married but not living with spouse temporarily for reasons such as work 4. Divorced 5. Never married 6. Separated 7. Widowed	1. Married 2. Married, spouse absent 3. Partnered 4. Separated 5. Divorced 6. Separated/ divorced 7. Widowed 8. Never married	1. Married/partnered 2. Not married 3. Widowed
	Recode	1 = levels 1-2 2 = levels 3-4, 6 3 = 5	1 = levels 1-2 2 = levels 3-6 3 = 7	1 = levels 1, 3 2 = levels 2, 4-6, 8 3 = levels 7	
Location of residence	Responses	1. Major City 2. Inner Regional Australia 3. Outer Regional Australia 4. Remote Australia 5. Very Remote Australia	1. Urban community 2. Rural village	1. Urban (Beale Rural-Urban Continuum code 1) 2. Suburban (Beale Rural-Urban Continuum code 2) 3. Ex-urban (Beale Rural-Urban Continuum codes 3,4,5,6,7,8,9) 9. No match for Rural-Urban code	1. Urban 2. Rural
	Recode	0 = level 1 1 = levels 2-3 2 = levels 4-5		1 = level 1 2 = level 2 3 = level 3	

Abbreviations: CES-D: Center for Epidemiologic Studies Depression Scale; SF-36: The Short Form survey 36 items

References

1. Summerfield M, Garrard, B, Jin, Y, Kamath, R, Macalalad, N, Watson, N, Wilkins, R, Wooden, M. HILDA User Manual – Release 20. Melbourne Institute: Applied Economic and Social Research. University of Melbourne; 2021.
2. Phillips D, Green H, Petrosyan S, Shao K, Wilkens J, Lee J. Gateway to Global Aging Data. The Harmonised CHARLS dataset and Codebook, Version D June 2021 (R01 AG030153, RC2 AG036619, R03 AG043052). The National Institute on Aging 2021.
<https://charls.pku.edu.cn/en/team/Codebook.pdf>
3. Health and Retirement Study. RAND HRS Longitudinal File (V2) public use dataset. . Produced and distributed by the University of Michigan with funding from the National Institute on Aging (grant number NIA U01AG009740). 2018
4. Manera KE, Smith BJ, Owen KB, Phongsavan P, Lim MH. Psychometric assessment of scales for measuring loneliness and social isolation: an analysis of the household, income and labour dynamics in Australia (HILDA) survey. *Health Qual Life Out.* 2022;20(1):40.
5. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473-83.
6. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Appl Psych Meas.* 1977;1:385-401.

Appendix 3 – Statistical analysis

We estimated the effect of retirement on loneliness using marginal structural models estimated using inverse probability of treatment weights (IPTW) [1].

IPTW marginal structural models are a method of estimating unbiased causal effects, even in the presence of complex confounding [2]. In order to produce valid inference, MSMs requires four assumptions be met: 1) no interference; 2) consistency; 3) positivity; and 4) conditional exchangeability.

1. The no interference assumption states that the effect of the exposure on the outcome is independent of the exposure of other participants [3]. In this case, because the samples are large population samples, it is unlikely that there would be interference between participants of the study.
2. The consistency assumption assumes that the potential (possibly counterfactual) outcome associated with a given exposure, is the same as the actual outcome observed if that exposure occurs [4]. This assumption can be violated if, for example, the exposure is defined ambiguously, but is unlikely in this study.
3. Positivity [5] (or near-positivity), assumes that there are no participants for whom the probability of exposure is zero (or very close to zero). In this case, given the age of the samples included and the fact that most people retire at ages covered by the study, makes positivity violations highly unlikely.
4. Last, conditional exchangeability, also commonly called *no unmeasured confounding* [6], assumes that all common causes of the exposure and outcomes can be eliminated via modelling. While it is impossible to be certain that no residual confounding exists, there are no major sources of confounding identified in the literature beyond those controlled for in the study, making it unlikely there are major sources of unmeasured confounding.

To estimate the IPTW-MSM, we first estimated the propensity score, the probability of being exposed, in each of the three cohorts, using the set of confounders described in Appendix B1. Because the exposure variable is categorical, we estimated the propensity using multinomial logistic regression, fit using vector generalised linear models (VGLMs) via the ‘VGAM’ package in R [7]. To allow for possible non-linear effects of continuous variables (eg age and mental health), we fit continuous variables using natural splines, varying the degrees of

freedom between 1 and 5 [8], and selecting the version with the best model fit based on Bayesian information criteria (BIC) [9]. We then used the propensity score to estimate a stabilised inverse probability weight, using the raw probability of exposure as the numerator:

$$W_A = \frac{P(A = a)}{P(A = a|L = l)}$$

where A is the exposure variable and L is the set of confounding variables.

We then assessed the balance in the covariates between groups. Plots showing the between group balance are included in **Figures S3.2-S3.12**.

We then estimated the probability of being lost to follow-up using a similar procedure, but using logistic regression:

$$W_C = \frac{P(C)}{P(C|L)}$$

Both the propensity and loss to follow-up models incorporated the survey weights for the survey, to account for the fact the samples are not simple random samples.

We then created a final analysis weight, as the product of the three weights (propensity, loss, and sampling):

$$W_{final} = W_A \times W_C \times W_{sampling}$$

We then created a new data set including the outcome variable (loneliness), exposure variable (retirement), the final analysis weight, the social support variable, and a categorical indicator variable labelling each dataset. We then estimated the effect of exposure on the outcome (loneliness) using a robust log-Poisson model to estimate relative risks. We then used these models to calculate marginal predicted probabilities (prevalence), with standard errors estimated using the delta method [8]. To be certain that the exposure preceded the outcome, the outcome variable was drawn from the wave subsequent to exposure.

Missing data

Since the surveys were used for prevalence estimates, they were reweighted each wave, so that the current sample is representative, regardless of who is lost to follow-up. Since retention was accounted for by the sample weights, there was no need to impute or adjust for retention in the sample itself [10-12].

Second, we used complete case analysis instead of imputing the ‘exposure’ wave (i.e., the wave in which we took the ‘retirement’ variable from, in each of our paired waves). When conditioning on variables in a model, complete case analysis is unbiased, provided that missingness is related to those variables. That means that imputing baseline variables does not reduce bias, it only increases power [13]. However, the current sample sizes were large enough not to warrant that.

Third, bias can occur when there is missingness in the outcome. Therefore, wherever the ‘lagged’ outcome was not available, a censoring weight was created to adjust for the missing outcome [14].

The pooled samples and missing data can be found in **Tables S3.1-S3.2. Participants flow chart is in Figure S3.1.**

References

1. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. *Epidemiol.* 2000;550-60.
2. Clare PJ, Dobbins T, Mattick RP. Causal models adjusting for time-varying confounding – a systematic review of the literature. *Int J Epidemiol.* 2018;48(1):254-65.
3. VanderWeele TJ, Tchetgen Tchetgen EJ, Halloran ME. Interference and sensitivity analysis. *Stat Sci.* 2014;29(4):687-706.
4. Rehkopf DH, Glymour MM, Osypuk TL. The consistency assumption for causal inference in social epidemiology: when a rose is not a rose. *Curr Epidemiol Rep.* 2016;3(1):63-71.
5. Petersen ML, Porter KE, Gruber S, Wang Y, van der Laan MJ. Diagnosing and responding to violations in the positivity assumption. *Stat Method Med Res.* 2012;21(1):31-54.
6. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiol.* 1999;10(1):37-48.
7. Yee TW. Vector generalized linear and additive models: with an implementation in R: Springer; 2015.

8. Yelland LN, Salter AB, Ryan P. Performance of the modified Poisson regression approach for estimating relative risks from clustered prospective data. *Am J Epidemiol.* 2011;174(8):984-92.
9. Neath AA, Cavanaugh JE. The Bayesian information criterion: background, derivation, and applications. *Wiley Interdisciplinary Reviews: Computation Stat.* 2012;4(2):199-203.
10. Watson N. HILDA Project Technical Paper Series No. 2/12. Longitudinal and Cross-sectional Weighting Methodology for the HILDA Survey. The Melbourne Institute, Faculty of Business and Economics, The University of Melbourne, December 2012.
11. Lee S, Nishimura R, Burton P, et al. HRS 2016 Sampling Weights. Ann Arbor, MI: Survey Research Center, Institute for Social Research, University of Michigan, 2021.
12. Zhao Y, Hu Y, Smith JP, et al. Cohort Profile: The China Health and Retirement Longitudinal Study (CHARLS). *Int J Epi* 2014;43(1):61-68. doi: 10.1093/ije/dys203.
13. Hughes RA, Heron J, Sterne JAC, et al. Accounting for missing data in statistical analyses: multiple imputation is not always the answer. *Int J Epi* 2019;48(4):1294-304. doi: 10.1093/ije/dyz032
14. Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. *Stat Methods Med Res* 2013;22(3):278-95. doi: 10.1177/0962280210395740 [published Online First: 2011/01/12]

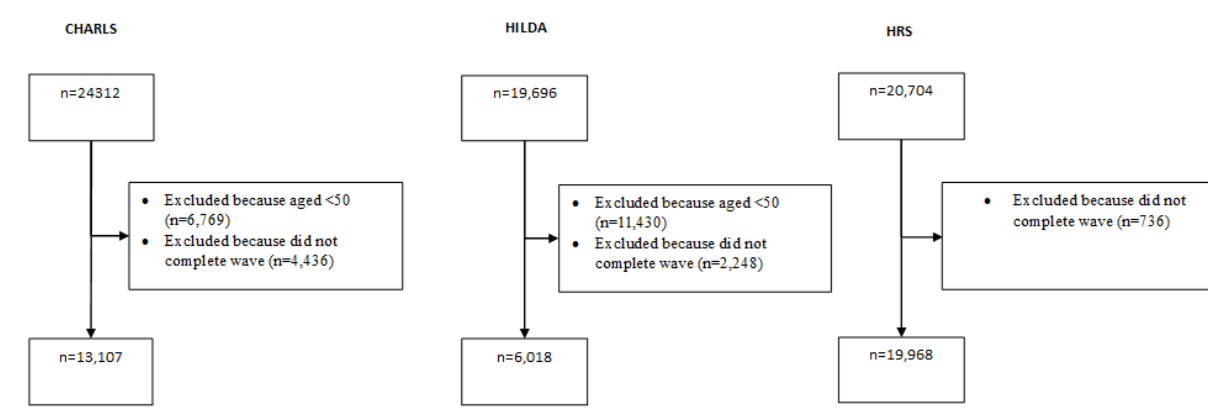
Table S3.1. Summary of pooled samples and missing data according to wave

Year	Australia (n = 6,018)		Unites States (n = 19,968)		China (n = 13,107)	
	Included in year	Missing lagged outcome	Included in year	Missing lagged outcome	Included in year	Missing lagged outcome
2008	3531 (58.7%)	119 (3.4%)	6280 (31.5%)	851 (13.6%)		
2009	3596 (59.8%)	137 (3.8%)				
2010	3817 (63.4%)	160 (4.2%)	7526 (37.7%)	609 (8.1%)		
2011	3831 (63.7%)	146 (3.8%)			8385 (64.0%)	1038 (12.4%)
2012	3915 (65.1%)	138 (3.5%)	6693 (33.5%)	712 (10.6%)		
2013	4018 (66.8%)	149 (3.7%)			6143 (46.9%)	855 (13.9%)
2014	4119 (68.4%)	129 (3.1%)	6714 (33.6%)	841 (12.5%)		
2015	4160 (69.1%)	153 (3.7%)				
2016	4244 (70.5%)	135 (3.2%)	5916 (29.6%)	900 (15.2%)		
2017	4234 (70.4%)	127 (3.0%)				

Table S3.2. Summary of pooled samples according to retirement status and wave

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Unites States											
Not retired	2037		3336		2772		2603		2362		13110
Fully retired	2820		3310		3023		3143		2552		14848
Never worked	572		271		186		127		102		1258
Total	5429		6917		5981		5873		5016		29216
Australia											
Not retired	1653	1732	1834	1878	1894	1953	2048	2039	2059	2039	19129
Fully retired	1726	1703	1799	1761	1861	1891	1925	1936	2016	1950	18568
Never worked	33	24	24	46	22	25	17	32	34	30	287
Total	3412	3459	3657	3685	3777	3869	3990	4007	4109	4019	37984
China											
Not retired				4427		3444					7871
Fully retired				1087		300					1387
Never worked				1833		1544					3377
Total				7347		5288					12635

Figure S3.1. Participants flow chart



Note.

Number of incomplete cases in HRS is low due to higher number of missing/zero weights that were dropped.

Figure S3.2. Household, Income and Labour Dynamics in Australia (HILDA) primary analysis balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹

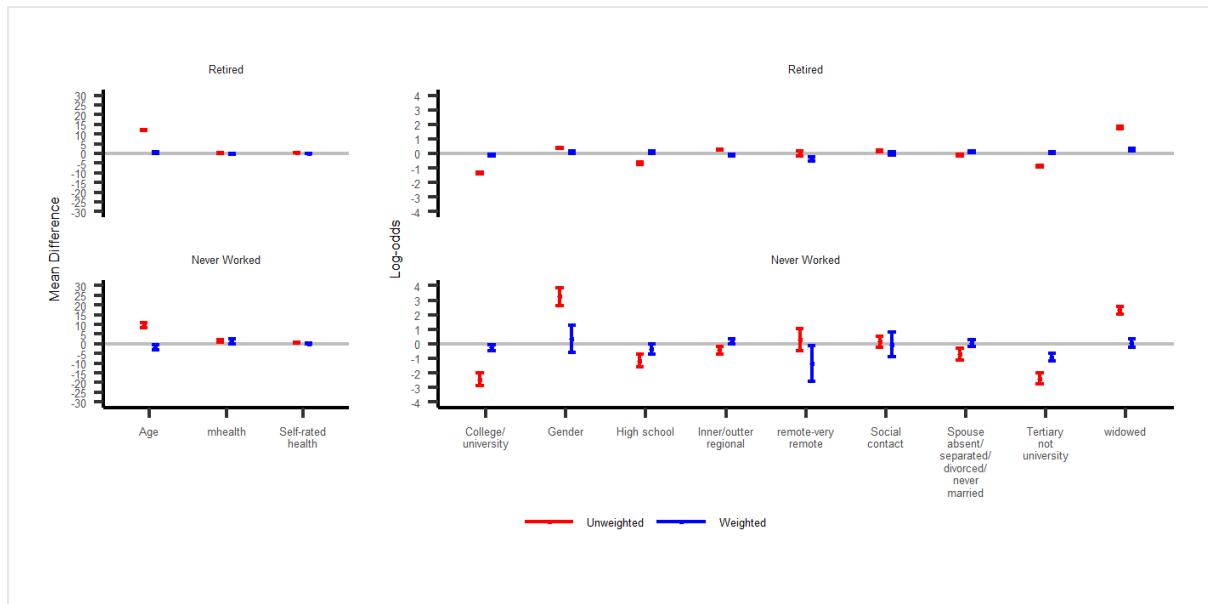
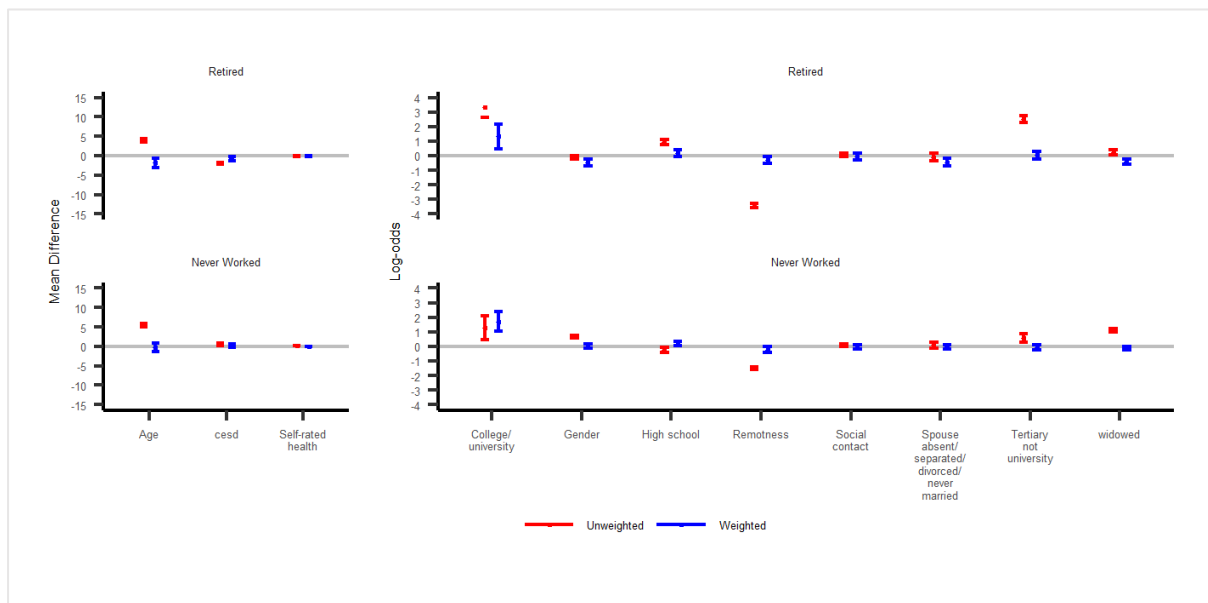


Figure S3.3. China Health and Retirement Study (CHARLS) primary analysis balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹



¹ Note: point estimates are the difference between exposed and unexposed groups. If the propensity model performs well the weighted differences should be smaller than the unweighted differences, and ideally close to zero.

Figure S3.4. United-States Health and Retirement Study (HRS) primary analysis
balanced weights: mean differences of weighted outcomes compared to the unweighted
outcomes (reference group = not retired) ¹

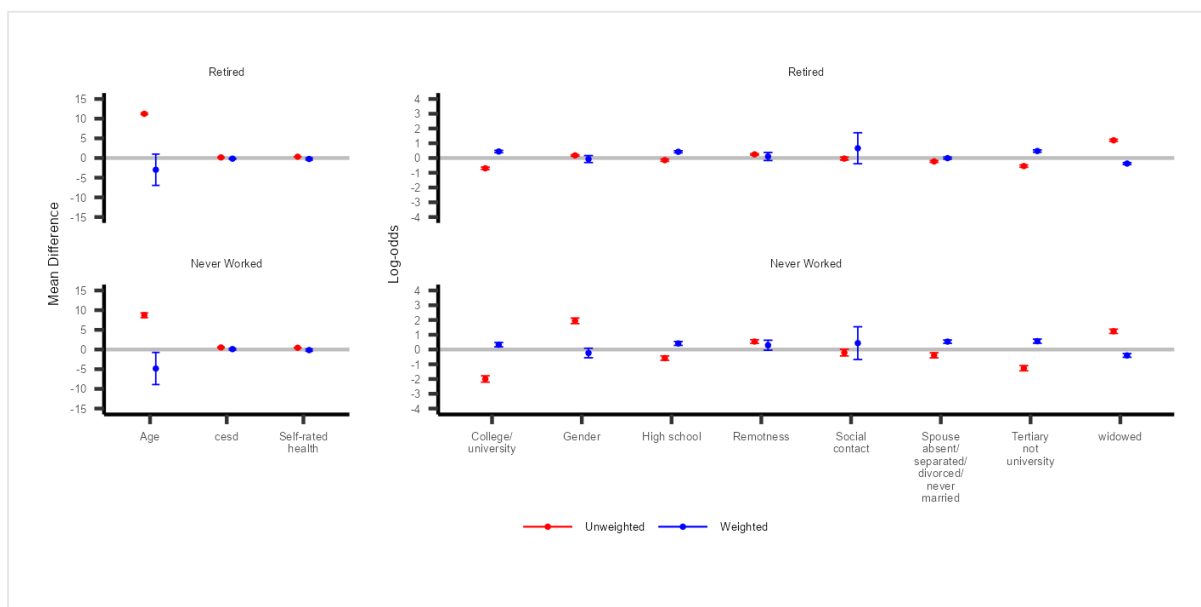


Figure S3.5. Household, Income and Labour Dynamics in Australia (HILDA) nature of
retirement balanced weights: mean differences of weighted outcomes compared to the
unweighted outcomes (reference group = not retired) ¹

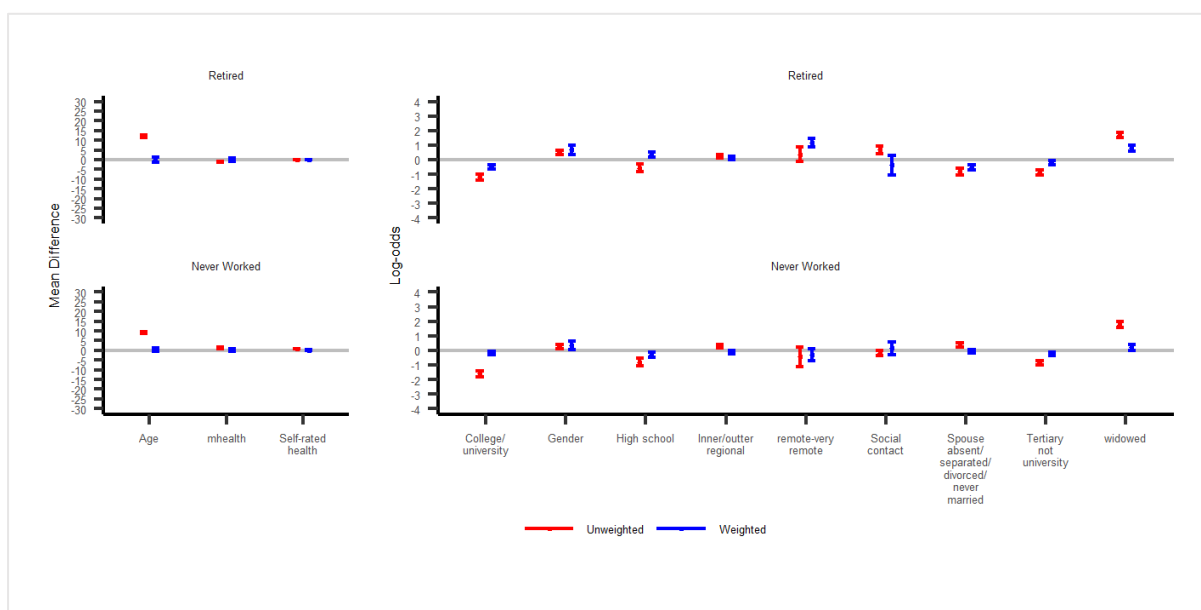


Figure S3.6. United-States Health and Retirement Study (HRS) nature of retirement balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹

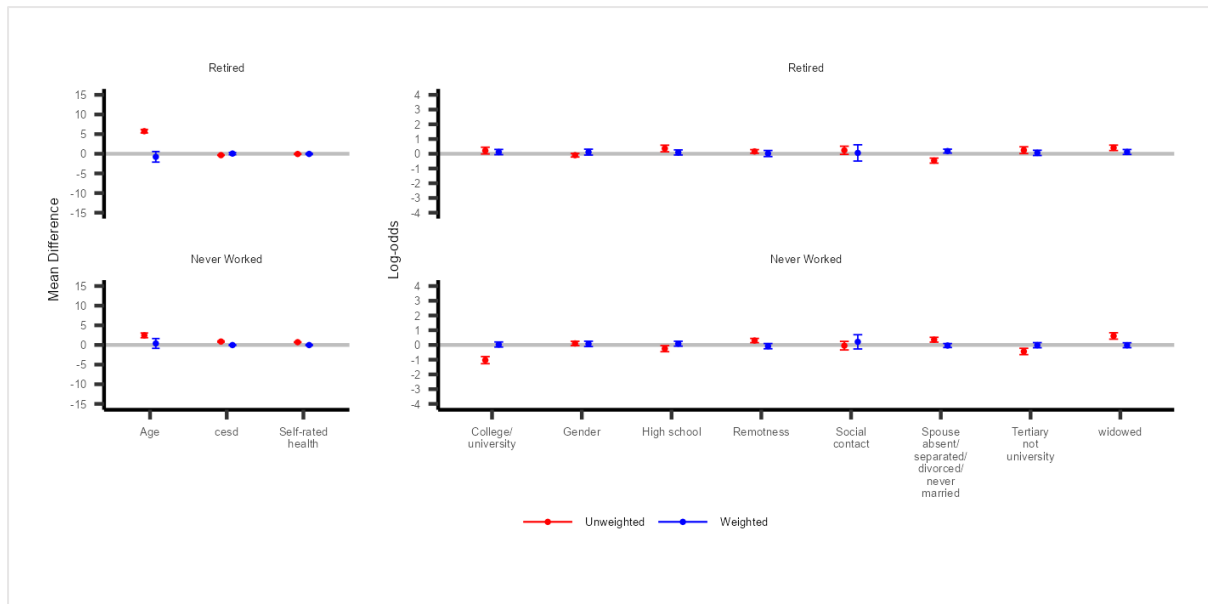


Figure S3.7. Household, Income and Labour Dynamics in Australia (HILDA) urban sample balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹

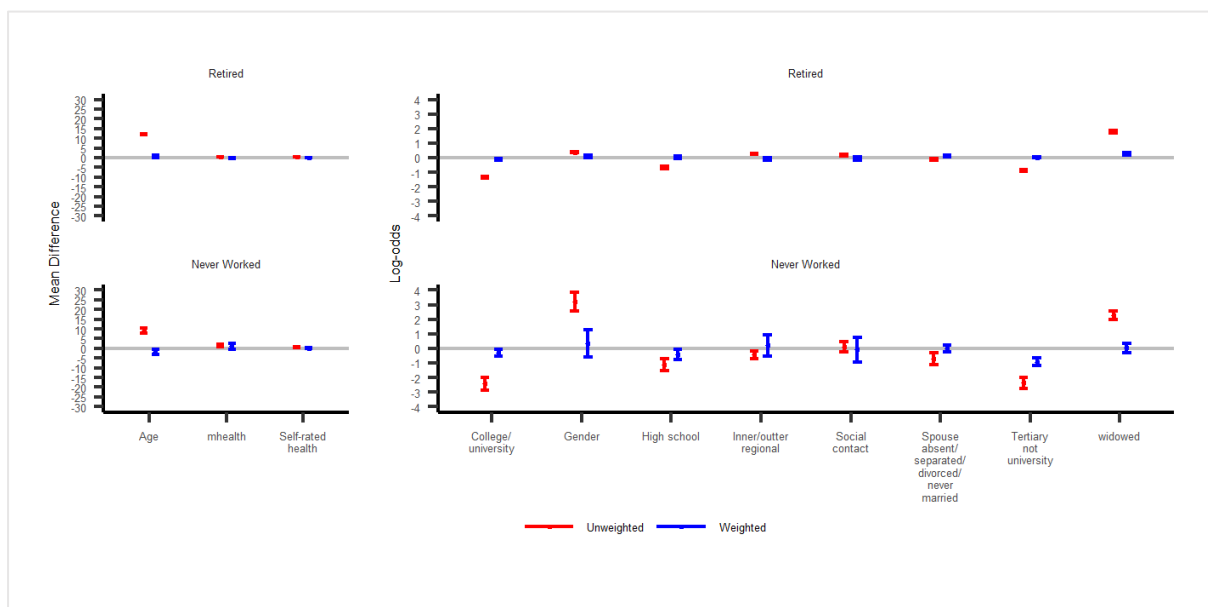


Figure S3.8. China Health and Retirement Study (CHARLS) urban sample balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹

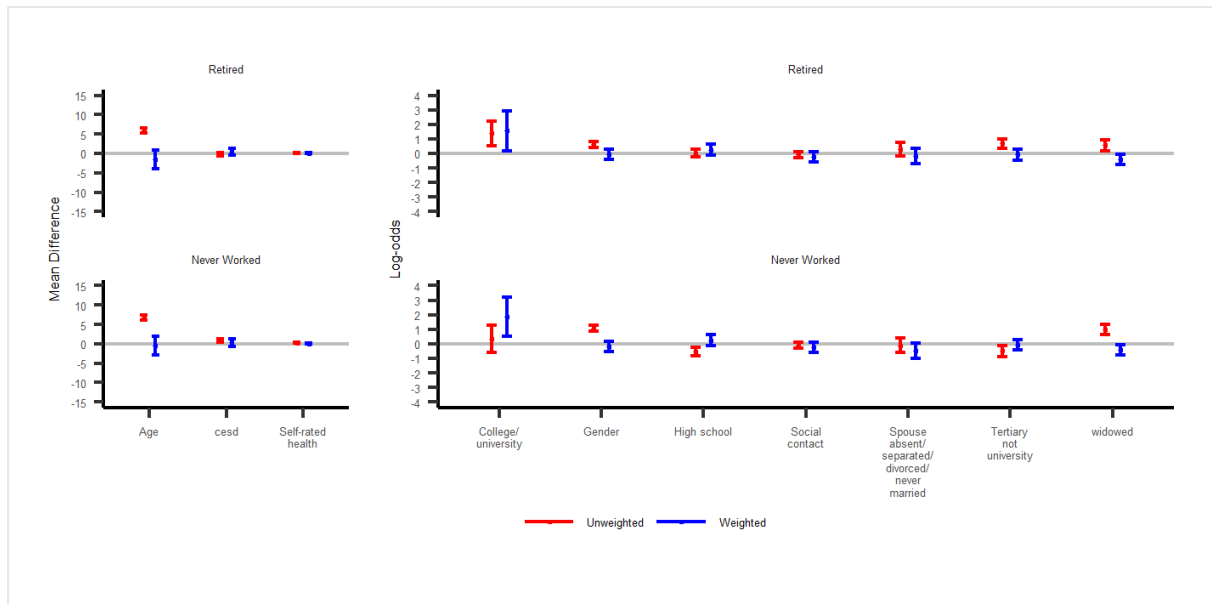


Figure S3.9. United-States Health and Retirement Study (HRS) urban sample balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹

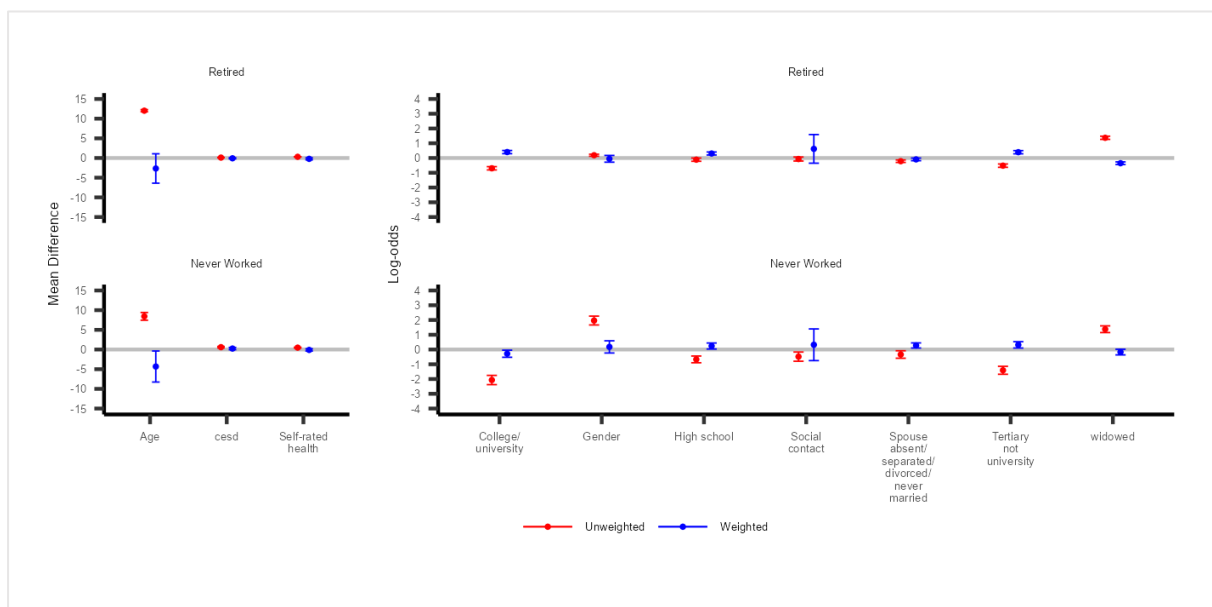


Figure S3.10. Household, Income and Labour Dynamics in Australia (HILDA) fully lagged model balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹

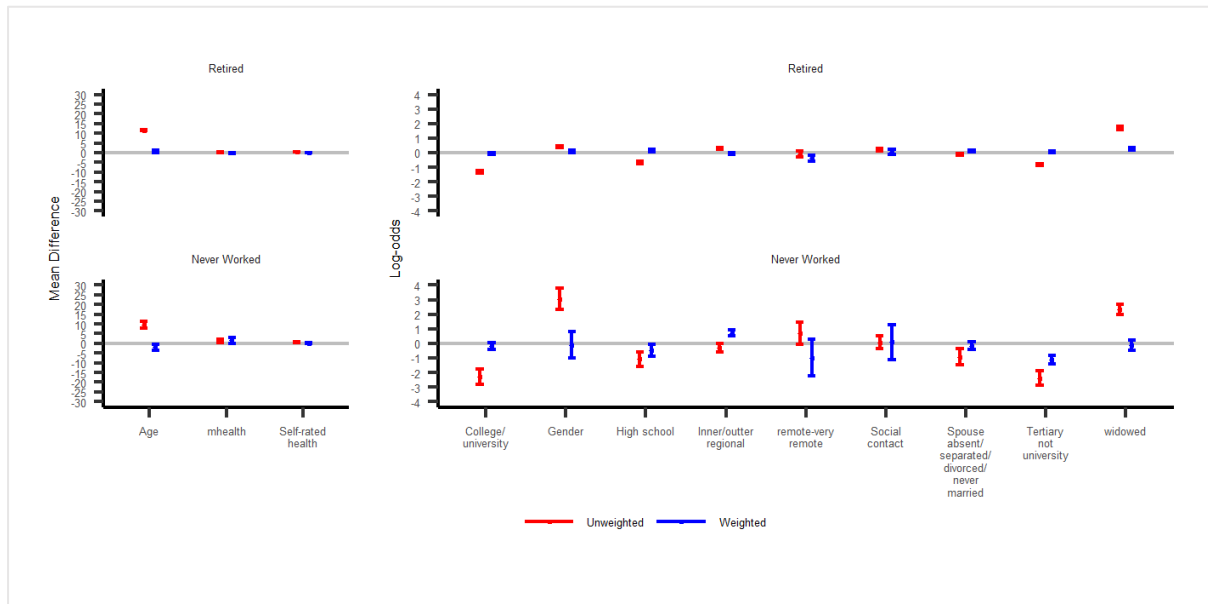
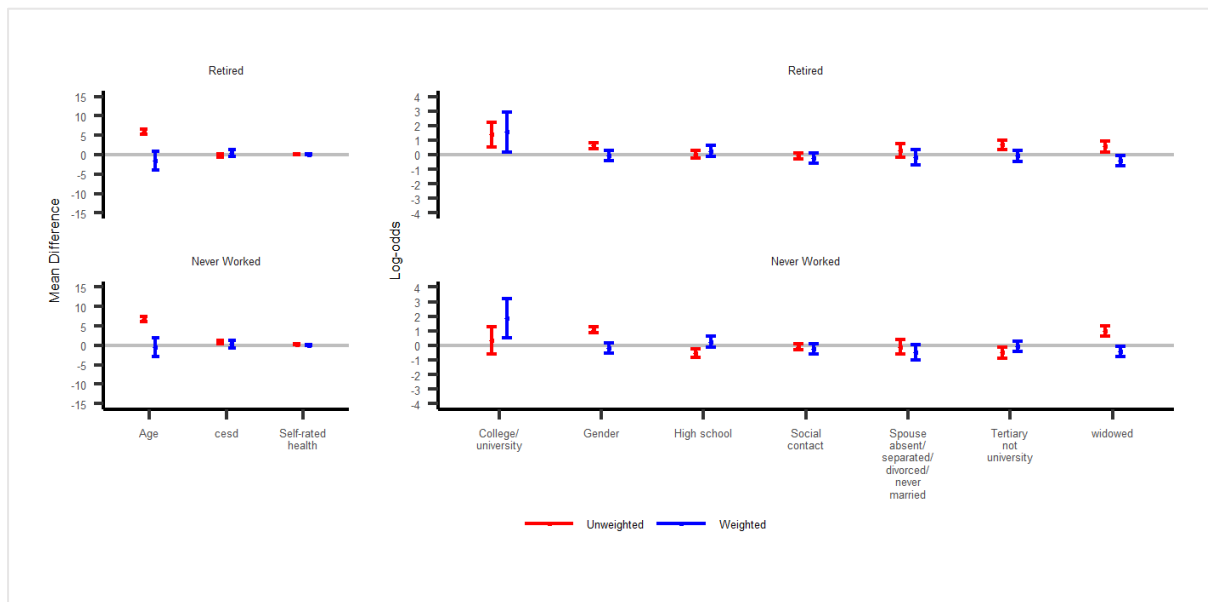
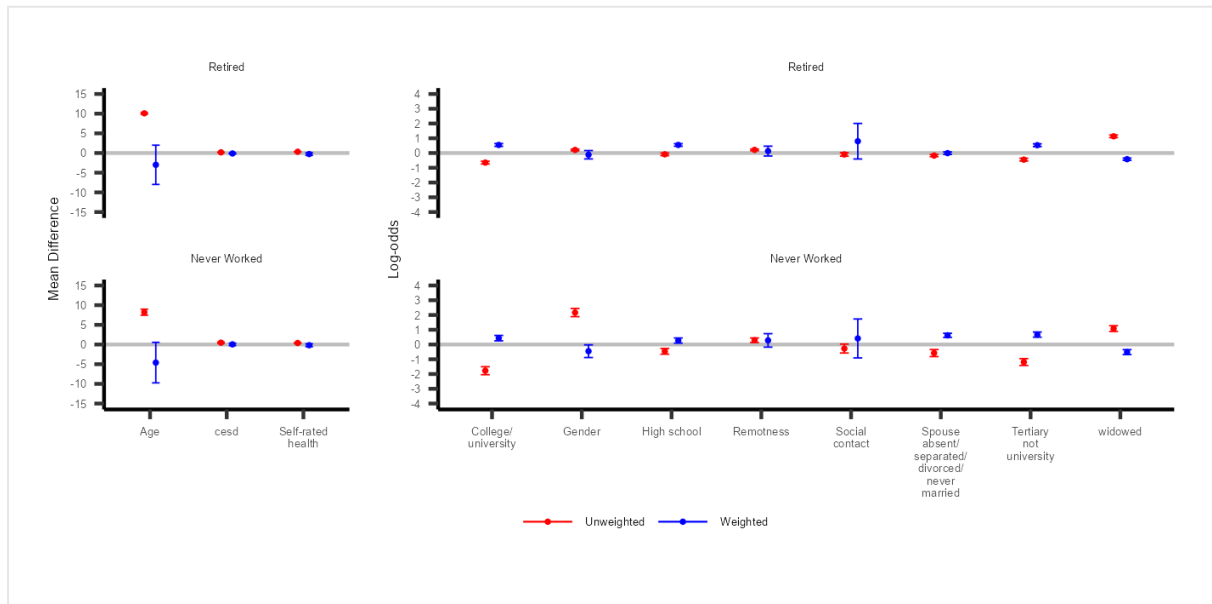


Figure S3.11. China Health and Retirement Study (CHARLS) fully lagged model balanced weights: mean differences of weighted outcomes compared to the unweighted outcomes (reference group = not retired) ¹



**Figure S3.12. United-States Health and Retirement Study (HRS) fully lagged model
balanced weights: mean differences of weighted outcomes compared to the unweighted
outcomes (reference group = not retired) ¹**



Appendix 4 – Additional results

Table S4.1. Lagged model of loneliness prevalence according to retirement status in Australia, China and US

Retirement status	Sample	Prevalence estimate	95%CI Lower	95%CI Upper
Not retired	Australia	0.17	0.16	0.18
Not retired	China	0.17	0.16	0.19
Not retired	US	0.16	0.14	0.17
Retired	Australia	0.19	0.18	0.21
Retired	China	0.10	0.08	0.12
Retired	US	0.19	0.18	0.21
Never worked	Australia	0.21	0.14	0.32
Never worked	China	0.18	0.16	0.19
Never worked	US	0.22	0.19	0.27

Abbreviations: 95%CI: confidence interval.

Table S4.2. Fully lagged model of loneliness estimated adjusted prevalence according to retirement status in Australia, China and US

Retirement status	Sample	Prevalence estimate	95%CI Lower	95%CI Upper
Not retired	Australia	0.16	0.15	0.18
Not retired	China	0.22	0.20	0.24
Not retired	US	0.15	0.14	0.17
Retired	Australia	0.19	0.17	0.20
Retired	China	0.14	0.09	0.21
Retired	US	0.19	0.17	0.20
Never worked	Australia	0.16	0.10	0.25
Never worked	China	0.20	0.18	0.22
Never worked	US	0.20	0.17	0.24

Abbreviations: CI: confidence interval.

Table S4.3. loneliness estimated adjusted prevalence according to nature of retirement among Australia and the US

Retirement status	Sample	Prevalence estimate	95%CI Lower	95%CI Upper
Not retired	Australia	0.16	0.15	0.17
Not retired	US	0.14	0.13	0.15
Voluntary retired	Australia	0.10	0.07	0.12
Voluntary retired	US	0.11	0.09	0.13
Involuntary retired	Australia	0.17	0.14	0.21
Involuntary retired	US	0.18	0.15	0.21
Mixed reasons	Australia	0.12	0.09	0.15
Mixed reasons	US	0.11	0.06	0.19
Never worked	Australia	0.14	0.08	0.23
Never worked	US	0.17	0.14	0.20

Abbreviations: CI: confidence interval.

Table S4.4. The modifying effect of social engagement on the association between the estimated adjusted prevalence of loneliness and retirement according to social engagement status among the three surveys: Australia, China and the US

Retirement status	Sample	Social engagement	Prevalence estimate	95%CI Lower	95%CI Upper
Not retired	Australia	Not social	0.30	0.26	0.34
Not retired	Australia	Social	0.15	0.14	0.16
Not retired	China	Not social	0.17	0.15	0.18
Not retired	China	Social	0.18	0.16	0.20
Not retired	US	Not social	0.21	0.17	0.26
Not retired	US	Social	0.15	0.14	0.17
Retired	Australia	Not social	0.33	0.29	0.37
Retired	Australia	Social	0.18	0.16	0.19
Retired	China	Not social	0.09	0.07	0.12
Retired	China	Social	0.11	0.08	0.16
Retired	US	Not social	0.28	0.24	0.33
Retired	US	Social	0.18	0.17	0.20
Never worked	Australia	Not social	0.51	0.20	0.82
Never worked	Australia	Social	0.17	0.11	0.27
Never worked	China	Not social	0.17	0.15	0.20
Never worked	China	Social	0.18	0.15	0.20
Never worked	US	Not social	0.28	0.16	0.44
Never worked	US	Social	0.22	0.18	0.26

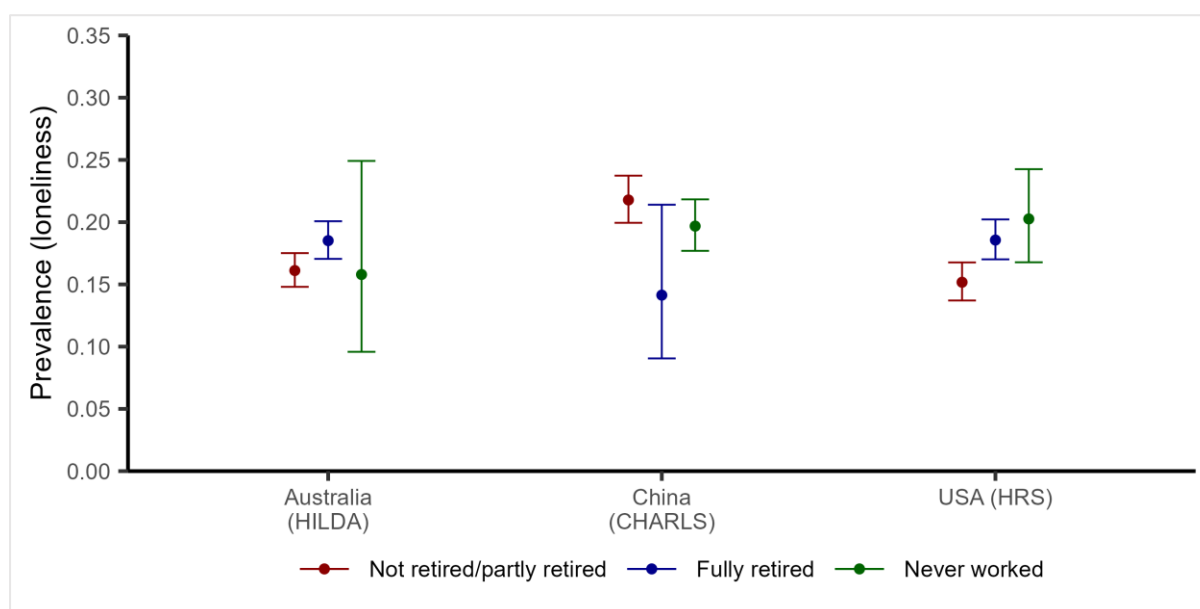
Abbreviations: CI: confidence interval.

Table S4.5. Adjusted estimated adjusted prevalence of loneliness according to retirement status among urban participants in Australia, China and the US

Retirement status	sample	Prevalence estimate	95%CI Lower	95%CI Upper
Not retired	Australia	0.16	0.15	0.17
Not retired	China	0.07	0.06	0.10
Not retired	US	0.14	0.12	0.16
Retired	Australia	0.18	0.17	0.20
Retired	China	0.09	0.07	0.11
Retired	US	0.18	0.16	0.20
Never worked	Australia	0.20	0.13	0.30
Never worked	China	0.10	0.08	0.12
Never worked	US	0.23	0.17	0.30

Abbreviations: CI: confidence interval.

Figure S4.1. Adjusted estimated prevalence of loneliness according to retirement status among the three countries: Australia, China and the US (fully lagged model)



3.6. Concluding summary for this chapter and knowledge gained from this study

This study is the first to our knowledge to examine macro-level moderators of the association between loneliness and its determinants. It is also the first to examine the causal effect of loneliness determinants. The findings indicate that the effect of retirement on loneliness differs between countries. While in Australia and the USA, retirement is associated with an increased risk of loneliness among older adults, retirement seems to have a protective effect against loneliness in China. The study also found that compared to voluntary retirement, involuntary retirement was associated with worse loneliness outcomes in Australia and the US. Furthermore, socially engaged participants experienced less loneliness before and after retirement in Australia and the US, while in China levels of social engagement did not appear to influence loneliness outcomes. Another interesting finding from the sensitivity analysis was that the protective effect of retirement on loneliness disappeared in the subsample of urban participants in China. In fact, the association trended in the opposite direction, similar to the findings in Australia and the United States.

These findings highlight the importance of considering cultural context in understanding how certain determinants, such as retirement, affect the experience of loneliness. Our findings show variations not only between countries but also within different geographical regions in China. This may suggest a cultural shift in urban areas towards values typically associated with Western individualistic societies. Alternatively, these differences might reflect socio-economic disparities between rural and urban workers in China. Our findings point to the complex interplay of cultural, economic, and social factors influencing the experiences of loneliness among retirees. Given that most studies on the determinants of loneliness are conducted in Western countries, there is a pressing need for more research on loneliness and its determinants in non-Western contexts. This broader perspective could help develop more culturally sensitive approaches to addressing loneliness globally.

CHAPTER FOUR: Loneliness and long-term health-related quality of life: A latent class analysis among middle-aged and older Australian women

4.1. Preface to the chapter

This chapter presents findings from a submitted paper (currently under review) that examined the association between long-term loneliness trajectories and health-related quality of life (HRQoL) among middle-aged and older women from the Australian Longitudinal Study of Women's Health. Existing research on the association between loneliness and HRQoL has predominantly been cross-sectional and often failed to account for the dynamic nature of loneliness throughout adulthood. This chapter addresses this gap by employing 18 years of longitudinal data to identify the main trajectories of loneliness throughout adulthood and their associations with physical and mental HRQoL scales. Latent class analysis is employed to determine the primary loneliness trajectories, followed by logistic regressions to identify the baseline predictors for each loneliness class. Last, linear regressions are used to analyse associations with the physical and mental subscales of HRQoL. This chapter addresses the individual determinants as well as health outcomes of long-term loneliness trends. It discusses loneliness as a critical social determinant of health and explores the implications for health prevention strategies. This study addresses specific aim #2 of this thesis as described in **Chapter 2**. Dissemination of this research and the author's contributions to this paper are described below.

4.2. Research dissemination

The research presented in this chapter has been disseminated as follows:

Paper resubmitted to Journal after review

Journal: Communication Psychology

4.3. Author attribution statement

I, Neta HaGani, was responsible for designing the study, obtaining the data, conducting the analysis and interpretation of the results, writing the drafts of the manuscript and submitting the manuscript to the journal. My co-authors, P. Clare, D. Merom, B. Smith & D. Ding helped conceptualise and design the study and developed the study protocol; K. Owen & P. Clare

supervised and assisted in conducting the data analysis. All authors have reviewed, edited, and approved the final version of the manuscript.

4.4. Manuscript

ABSTRACT

Background: Loneliness has been long associated with poor health outcomes including health-related quality of life (HRQoL). However, few studies used longitudinal data and none to our knowledge considered the dynamic nature of loneliness over time.

Objective: To identify longitudinal patterns of loneliness over 18 years and its association with physical and mental HRQoL of middle-aged and older women.

Methods: Data were from the Australian Longitudinal Study of Women's Health. Latent Class Analysis was conducted to identify long-term loneliness patterns. Multinomial logistic regression was used to examine the prospective associations between baseline predictors of loneliness and loneliness trajectories. Linear regression was used to examine the association between loneliness trajectories and HRQoL.

Results: Baseline predictors such as current smoking, depression, anxiety, stress and low social support were associated with higher odds of 'Increasing', 'Stable-medium' and 'Stable-high' loneliness. Compared to 'Stable-low' loneliness, 'Increasing' [$B = -3.73$ (95%CI = -5.42, -2.04)], 'Medium' [$B = -3.12$ (95%CI = -5.08, -1.15)] and 'High' loneliness [$B = -5.67$ (95%CI = -6.84, -4.49)] were associated with lower mental HRQoL. The 'Increasing' loneliness class was also associated with lower physical HRQoL [$B = -1.06$ (95%CI = -2.11, -0.02)]. Out of all HRQoL sub-scales, emotional role, social functioning and physical role were the most strongly associated with loneliness.

Conclusions: Long-term loneliness patterns are consistently associated with prospective physical and mental HRQoL. This finding highlights the importance of addressing loneliness among women to promote their health and well-being.

Keywords: Loneliness, health-related quality of life, mental health, latent class analysis

Key points

- The most common loneliness trajectories across mid-old age are 'Increasing', 'Stable-low', 'Stable-medium' and 'Stable-high' trends.
- Elevated levels of loneliness, whether 'Increasing', 'Stable-medium' or 'High', were linked to a lower physical and mental HRQoL.

- The 'Stable-high' loneliness class was associated with the most adverse HRQoL outcomes.
- HRQoL sub-scales: emotional role, social functioning, and physical role had the strongest link to loneliness across classes.
- Smoking, depression, anxiety, stress and lack of social support were linked to the 'Increasing', 'Medium' and 'High' loneliness classes.

INTRODUCTION

Loneliness stems from a perceived deficit in social relationships often described as a gap between the desired and actual levels of social connections (1). While episodic loneliness is a common human experience and considered an important survival mechanism linked to pain and hunger (2), chronic loneliness has been associated with various physical and mental illnesses such as diabetes, heart disease, cancer, low social functioning and premature death (3-8). Loneliness has also been associated with risky health behaviours such as smoking (9, 10) and with a higher likelihood of risky drinking (11). There is also evidence of a strong inverse association between loneliness and health-related quality of life (HRQoL) (12, 13). HRQoL is a multidimensional concept that goes beyond the presence or absence of disease. It encompasses diverse aspects of physical, mental and social health and functioning (14). HRQoL is a common measure in medicine and public health for assessing and predicting population health outcomes and mortality (15-17).

The association between loneliness and HRQoL has been demonstrated across different populations, such as older adults and patients with multimorbidity (18-20). While loneliness can contribute to worsening health outcomes (21), poor health can also lead to increased loneliness due to challenges in fulfilling different social roles (22, 23). To date, most studies that examined the association between loneliness and HRQoL were cross-sectional (3), and the small number of longitudinal studies only assessed loneliness at one point in time, which was unable to capture the long-term patterns of loneliness across the lifespan (13, 24-26).

Loneliness is a dynamic experience that evolves throughout life. During middle-to-older age significant life transitions, such as retirement, empty nesting and the loss of loved ones (27, 28), as well as an unhealthy lifestyle (29) can disrupt established routines and social networks, thus triggering a sense of loneliness and decreased HRQoL (30, 31). Moreover, the

middle-to-older stage of life often coincides with a higher likelihood of developing chronic illnesses and disabilities, further contributing to loneliness and HRQoL (32). As a result, addressing the dynamic nature of loneliness is critical to understanding and enhancing HRQoL for individuals in mid-to-older age.

To better understand the long-term experience of loneliness among middle-aged and older adults and inform interventions to improve HRQoL across the lifespan, it is essential to provide an accurate depiction of the association between long-term trajectories of loneliness and the various dimensions of HRQoL. Therefore, the aims of the current study are threefold: 1) to identify the patterns of loneliness spanning from middle to older age; 2) to identify the demographic characteristics and health behaviours associated with different loneliness patterns and 3) to examine the association between loneliness trajectories and physical and mental dimensions of HRQoL.

METHODS

The current study followed the strengthening of the reporting of observational studies in epidemiology (STROBE) guidelines (**Appendix 1**).

Study Population

Data were derived from nine waves of the Australian Longitudinal Study of Women's Health (ALSWH) 1946-51 population representative cohort. Participants were between the ages of 43 and 51 at baseline in the year 1996 and were originally selected from the Medicare database to represent Australian citizens and permanent residents. Sampling from the population followed a random selection process, with the exception that women residing in rural and remote areas were sampled at a rate doubling that of women in urban areas. The cohort included 13,714 women at baseline. Collected at three-year intervals starting from 1996 (baseline), the data included self-reported information on health status, health behaviours, physical function, and social and mental well-being. The response rate was between 53% and 56% (33). Ethical approval for this study was obtained from the Human Research Ethics Committees (HRECs) of the Universities of Newcastle and Queensland (approval numbers H-076-0795 and 2004000224). All participants provided their informed consent prior to their participation (34) and more information about the study can be found elsewhere (35).

Measures

Main exposure: Loneliness

Loneliness was assessed in waves 3 (year 2001, participants aged 48-55 years) to wave 8 (year 2016, aged 64- 71 years) using a single item from the Centre for Epidemiologic Studies Depression Scale (CES-D) (36). This item measured the extent of loneliness experienced in the past week on a 4-point Likert scale: 1 = Rarely or none of the time (less than 1 day); 2 = Some or a little of the time (1-2 days); 3 = Occasionally or a moderate amount of time (3-4 days); and 4 = Most or all of the time (5-7 days)'. These responses were recategorised into a binary variable: 0 for levels 1-2 in the original scale and 1 for levels 3-4 in the original scale. One-item loneliness measures were previously validated and shown to have a reliability measure of correlation > 0.70 (37). Direct one-item loneliness measures were found to be correlated with other more comprehensive, common loneliness measures such as the UCLA and the de Jong loneliness scales, as well as with the indirect one-item loneliness measures (37-39).

Main outcome: Health-related quality of life (HRQoL)

The HRQoL of participants was assessed using the SF-36, a self-reported questionnaire that encompasses eight dimensions of health and well-being in the past 4 weeks or on a typical day, namely (40): 1) vitality, the amount of energy or fatigue; 2) physical functioning, the ability to perform different types of vigorous or moderate activities on a typical day; 3) bodily pain, which is the severity of pain experienced in general and at work; 4) general health ratings overall and in comparison to others; 5) role limitations due to physical health, including difficulties performing activities or accomplishing work due to physical limitations; 6) role limitations of the same types due to emotional problems; 7) social role functioning, the extent to which physical health or emotional problems interfered with normal social activities with family, friends, neighbours, or groups; and, 8) mental health/emotional well-being, including feeling nervous, peaceful, happy etc. Each dimension is quantified on a scale from 0 to 100, where higher values reflect a more positive perception of health. The individual subscales were subsequently aggregated to create two overarching summary measures: 1) Physical Component Summary (PCS), which includes the subscales for general health, physical functioning, role physical, and bodily pain, and 2) Mental Component Summary (MCS), that combines the subscales for vitality, social functioning, role emotional, and mental health. The SF-36 is a validated and reliable measure that was examined among a variety of populations, including middle-aged and older adults (41, 42). In a population-

representative Australian household survey (Australian National Household Survey), the internal consistency ranged between 0.82-0.93 across the HRQoL dimension (41). Similar reliability was observed in other studies among diverse populations (43-45).

Baseline predictors of loneliness

Information regarding the re-categorisation of the baseline predictors is provided in **Appendix 2**. To ensure that the baseline predictors occurred before the outcome (loneliness), they were derived from waves 1-2 and included: age; marital status (partnered, not partnered, widowed); current employment status (no, yes); living arrangement (live alone/ live with others); highest level of education completed (high school or less, tertiary not university, college/university); language spoken at home (English, non-English European, Asian, other); country of birth (Australia, other); area-level socioeconomic status using the Index of Relative Socio-Economic Disadvantage (IRSD) (46); location of residence based on the postcode-level Accessibility-Remoteness Index of Australia Plus (ARIA+; major city, regional, remote) (47); self-reported body mass index (BMI; underweight, healthy, overweight, obese); smoking status (never smoked, ex-smoker, currently smoking); self-reported previous diagnosis or symptoms of anxiety and depression; current depression based on the Centre for Epidemiological Studies-Depression (CES-D) scale (36); risky alcohol consumption (consuming more than 10 standard drinks in a week or more than four standard drinks per day) and binge drinking (consuming five or more drinks on a single occasion) based on the 2020 National Health Medical Research Council guidelines (48); social support using the Medical Outcomes Study (MOS) measure of the frequency of receiving support from others on a scale of 1-5 (higher score reflects better support); stress measured using the Perceived Stress Questionnaire (mean score of 10 items ranging from 0-4) (49).

Data analysis

Initially, we constructed a range of latent class models encompassing one to five loneliness classes. Goodness-of-fit through metrics such as Akaike's Information Criterion (AIC), Bayesian Information Criterion (BIC), and Sample-Size Adjusted BIC (SSABIC), were used to identify the most suitable number of classes. Because the sample was not random, the latent class analysis was estimated using sample weights. Next, multivariable multinomial logistic regression models were employed to examine the relationship between demographic characteristics and loneliness patterns, using multinomial odds ratios (mOR) as effect sizes.

Next, linear regression models were employed to investigate the association between loneliness class membership from Waves 3 to 8 and HRQoL at Wave 9 as a continuous outcome. The assumptions of linear regression models were tested. The data appear to show slight non-normality, especially in the tails, which is typical with very large datasets (50) (**Figure S3.1**). The results of the linear regressions are presented as unstandardised coefficients. Since individuals cannot be definitively assigned to latent classes, the three-step Bolck–Croon–Hagenaars estimation method (BCH) was employed to accommodate the uncertainty in classification (51). All models were weighted using the BCH weight, and distal outcome models adjusted for variables including age, education, marital status, country of birth, language spoken at home, living arrangement, area remoteness, area-level socioeconomic status, employment, smoking, alcohol consumption, anxiety, depression, stress, BMI, social support and baseline HRQoL. These analyses were conducted using Stata Version 17.0 (52).

To assess the robustness of the results and to examine the confounding effect of baseline predictors on the association between loneliness and HRQoL, the linear regression models were run 1) without adjustments for any baseline predictors and 2) adjusting for sociodemographic baseline predictors only (i.e., without the mental health, social support and health behaviour variables).

Missing data

There were 9154 (66.75%) incomplete cases which contributed to a total of 20.7% missing data in the dataset. **Figures S3.2-S3.3** present the missing data for each variable used in the model. Little's test indicated that data were not missing completely at random and therefore it was assumed to be missing at random. Multiple imputations were used to handle missing data, with twenty imputations using the Mice package in R version 4.3.1 (53), with random forests to accommodate potential non-linear relationships and interactions during the data imputation process (54). Analyses were conducted on all twenty datasets (imputations), and the resulting estimates were aggregated using Rubin's rules (55).

Sensitivity analysis

Further assessments were conducted to test the robustness of the models. We conducted the latent class models using a Probit link function, which assumes that the error terms follow a standard normal distribution compared to the logit model which assumes the error terms

follow a logistic distribution. We also conducted a sensitivity analysis using a different cut-point of the outcome variable loneliness (1. Rarely or none of the time vs. levels 2-4). The reversed cut point (the lowest loneliness levels 1-3 vs. the highest level 4) was not tested as the highest loneliness category (Most or all of the time) constituted less than 5% of the sample.

RESULTS

Demographic characteristics

Table 1 shows the sociodemographic characteristics of the sample at baseline ($n = 13,714$). The flow diagram of participants included in the study can be found in **Table S3.1**. The median age was 49.5 years (interquartile range = 2.5), and the majority of participants were married or partnered (83.9%), had a high school education (67.1%) and were employed (79.5%). Most participants were Australian-born (76.3%) and spoke English at home (94.0%), and 9.1% reported experiencing loneliness 3-7 days a week. The MOS social support score was 3.9 (SD = 1.0, Range = 1-5).

Loneliness latent classes

Goodness of fit as assessed by AIC, BIC and SSABIC suggested the best fit was a four-class model, which indicated optimal model fit (**Table S3.2**). The average classification probabilities are 0.67 for class 1, 0.91 for class 2, 0.67 for class 3 and 0.77 for class 4. The average classification probabilities refer to the average likelihood that a given observation belongs to each of the respective classes. For example, for Class 1, the average classification probability is 0.67, indicating that on average, the model assigns 67% likelihood to observations being classified as Class 1 (**Figure 1**).

Class 1 was labelled as ‘Increasing’ loneliness ($n = 10,121$, 73.8%) due to the increasing trend of loneliness throughout time. The mean loneliness across waves 3-8 among individuals in class 1 was 33.5%. Class 2 was labelled as ‘Stable-low’ loneliness ($n = 727$, 5.3%) which was characterised by consistently low loneliness across all waves (Mean_(waves 3-8) = 2.8%). Class 3 was labelled as ‘Stable-medium’ loneliness ($n = 2345$, 17.1%) and was characterised by a stable trend of medium-level loneliness throughout time (Mean_(waves 3-8) = 38.1%), and class 4 was labelled as ‘Stable-high’ loneliness ($n = 507$, 3.8%) and was characterised by a stable high level of loneliness throughout time (Mean_(waves 3-8) = 77.2%).

Predictors of loneliness latent class

Table 2 presents the predictors of the latent class membership with ‘Stable-low’ loneliness as the comparison class. Widows had higher odds of being in the ‘Stable-high’ loneliness class [mOR = 2.08 (95%CI = 1.15, 3.78)]. Those who were current smokers had higher odds of being in the ‘Increasing’ loneliness [mOR = 1.24 (95%CI = 1.01, 1.54)] or ‘Stable-medium’ [mOR = 1.28 (95%CI = 1.01, 1.61)] classes than non-smokers. A higher CES-D score was associated with higher odds of being in the ‘Increasing loneliness’ [mOR = 1.06 (95%CI = 1.02, 1.09)], ‘Stable-medium’ [mOR = 1.07 (95%CI = 1.04, 1.11)] or ‘Stable-high’ [mOR = 1.11 (95%CI = 1.07, 1.15)] loneliness classes. A higher stress score was associated with higher odds of being in the ‘Increasing’ loneliness [mOR = 1.37 (95%CI = 1.12, 1.68)], ‘Stable-medium’ [mOR = 1.36 (95%CI = 1.09, 1.70)] or ‘Stable-high’ [mOR = 1.72 (95%CI = 1.34, 2.20)] classes. Reporting a past depression diagnosis was associated with higher odds of being in the ‘Stable-medium’ loneliness class [mOR = 1.47 (95%CI = 1.11, 1.93)]. Lower social support was associated with higher odds of being in the ‘Increasing’ loneliness [mOR = 0.75 (95%CI = 0.62, 0.90)], ‘Stable-medium’ [mOR = 0.70 (95%CI = 0.59, 0.84)] or ‘Stable-high’ [mOR = 0.55 (95%CI = 0.48, 0.62)] classes.

Health-related Quality of life predicted by loneliness class

Multivariate linear regression was conducted to examine the unadjusted, sociodemographic adjusted (without health, mental health and risky health behaviours) and fully adjusted associations (the main model), between loneliness classes and HRQoL components, with ‘Stable-low’ loneliness as the comparison group. The results are presented as unstandardised coefficients (**Table 3 and Table S3.3**).

In the fully adjusted models, increasing loneliness compared to ‘Stable-low’ loneliness, was associated with a significantly lower quality of life at wave 9 on all the physical and mental scales and sub-scales. ‘Increasing’ loneliness was inversely associated with the overall physical component [B = -1.06 (95%CI = -2.11, -0.02)]. The strongest associations with physical components were in the sub-scales of physical role limitations [B = -3.19 (95%CI = -6.27, -0.11)], pain [B = -4.36 (95%CI = -7.05, -1.67)] and general health [B = -4.36 (95%CI = -7.05, -1.67)]. ‘Increasing’ loneliness had a strong association with the overall mental component [B = -3.73 (95%CI = -5.42, -2.04)]. The strongest associations with mental functioning sub-scales were found in emotional role limitations [B = -9.57 (95%CI = -14.30, -4.84)], social functioning [B = -7.53 (95%CI = -10.67, -4.39)] and mental health [B = -6.50 (95%CI = -9.58, -3.42)].

Compared to ‘Stable-low’ loneliness, the ‘Stable-medium’ loneliness class was associated with significantly lower scores on HRQoL components and subscales except for the overall physical component summary and the physical functioning sub-scale. However, an inverse association with HRQoL was observed for physical role limitations [B = -7.18 (95%CI = -12.60, -1.76)], pain [B = -4.36 (95%CI = -7.05, -1.67)] and general health [B = -4.36 (95%CI = -7.05, -1.67)]. In addition, strong inverse associations were found with the mental component summary scale [B = -3.12 (95%CI = -5.08, -1.15)] and its sub-scales, with the strongest association occurring with emotional role limitations [B = -8.12 (95%CI = -13.44, -2.80)] and social functioning [B = -6.38 (95%CI = -10.07, -2.69)].

Compared to ‘Stable-low’ loneliness, the ‘Stable-high’ loneliness class was strongly associated with all of the HRQoL components except for the overall physical component summary. The strongest associations with physical sub-scales were physical role limitations [B = -9.69 (95%CI = -13.72, -5.66)] and general health perceptions [B = -4.78 (95%CI = -7.00, -2.55)]. ‘Stable-high’ loneliness was also strongly associated with all of the mental health components including the overall mental component summary [B = -5.67 (95%CI = -6.84, -4.49)] and its subscales. The strongest associations were found with emotional role limitations [B = -15.25 (95%CI = -13.48, -7.88)], social functioning [B = -10.68 (95%CI = -6.84, -4.49)] and emotional wellbeing [B = -9.30 (95%CI = -11.36, -7.25)]. The unadjusted and sociodemographic-adjusted models followed similar patterns to the main model but were of a larger magnitude.

Sensitivity analysis

Results from the probit model were consistent with the main analyses (**Tables S4.1-S4.2**). When using the different loneliness cut-point, we found that the four-class model was still the optimal fit (**Table S4.3**) and similar associations were found between the predictors of the latent class membership and the four classes. However, as expected when defining the loneliness group as those who responded as being lonely “some or a little of the time”, the associations became weaker and less precise than those in the main analysis, except in the cases of depression and social support (**Table S4.4**). Attenuations were also in the associations between loneliness classes and HRQoL components in the unadjusted, sociodemographic-adjusted and fully adjusted models. There were no significant associations in the ‘Increasing’ loneliness class compared to the ‘Stable low’. However, in the ‘Stable medium’ and ‘Stable high’ classes, loneliness was significantly associated with almost all of

the HRQoL components (**Table S4.5**). Overall, these sensitivity analyses have demonstrated the robustness of our findings.

DISCUSSION

The current study reveals that over the course of 18 years, elevated levels of loneliness, whether 'Increasing' or stable at a 'Medium' or 'High' level, were linked to a lower overall mental HRQoL. Additionally, the 'Increasing' loneliness class was the only class correlated with lower overall physical HRQoL. Out of the HRQoL sub-scales, emotional role, social functioning, and physical role had the strongest association with loneliness across classes. The current findings strengthen the previous evidence by using a longitudinal design to examine the associations between loneliness patterns and HRQoL over the longest period of time to our knowledge (18 years).

To our knowledge, no studies have yet examined the association between different trajectories of loneliness and HRQoL. Our research sheds light on the dynamic nature of loneliness, revealing variations in its associations with HRQoL over time. The 'Stable-high' class was associated with the most adverse outcomes, with a significantly lower HRQoL in all scales and sub-scales, except for the overall physical health measure. 'Stable-high' loneliness was also associated with several risk factors such as obesity, depression, stress and less social support. Previous studies showed that prolonged (chronic) loneliness is a more serious health concern compared to transient loneliness (56). Our findings from the 'Stable-high' class echo this finding, suggesting that high chronic loneliness remains a major risk to overall health (56, 57). Our findings also reveal that 'Stable-high' loneliness was more likely to occur in widows, which aligns with previous studies showing associations between widowhood and loneliness (58, 59). Therefore, despite the relatively small size of the 'Stable-high' class (4% of the total sample), it represents a high-risk category and therefore should be prioritised for health promotion interventions.

While the 'Stable-medium' loneliness had a weaker association with HRQoL compared to the 'Stable-high' and 'Increasing' loneliness classes, it was still inversely associated with physical and emotional role functions. These findings suggest that even a moderate amount of loneliness, over time, may be associated with a major risk for health. Given that this class constituted 17% of the sample, it is important to be vigilant to the potential deteriorating HRQoL of this group. Incorporating loneliness assessments into primary healthcare for population screening targeting moderate loneliness, and facilitating

referrals to community programs and interventions, may be important for alleviating the experience of loneliness and improving HRQoL (60-62).

The predominant loneliness class (78.3%) identified in this study was those who experienced a progressive increase in loneliness over time. This class initiates with a moderate level of loneliness prevalence, similar to the 'Stable-medium' loneliness, and increases gradually up to an average of 50% loneliness prevalence within this class. This pattern reflects the increase of loneliness from middle to older age which has been found previously among women (63). 'Increasing' loneliness was the only class that was significantly associated with the overall physical health component, in addition to the mental health component and the sub-scales. A trajectory of 'Increasing' loneliness could be attributed to different life events such as illness, disability, retirement, caregiving responsibilities, and the loss of loved ones, which all contribute to a deterioration in physical health (58, 63, 64).

Our findings suggest that 'Increasing' loneliness, as well as 'Stable-medium', and 'Stable-high' loneliness classes were all associated with current smoking, depression, anxiety, and stress. The association between loneliness and other risky health behaviours, such as smoking, highlight the broader health implications of loneliness. Loneliness has been an important and neglected population health determinant (65). Individuals experiencing loneliness may turn to high-risk behaviours, such as smoking, as a coping mechanism or as a part of a broader pattern of unhealthy behaviours (66). Similarly, the associations with depression, anxiety, and stress confirm that loneliness is intertwined with mental health (8, 67, 68). There is evidence that loneliness may trigger a maladaptive biological stress response that can create further social withdrawal, which reinforces feelings of loneliness (69). This cycle of loneliness and stress may contribute to the adoption of other maladaptive health behaviours, such as an unhealthy lifestyle, ultimately leading to adverse health outcomes (70).

Limitations

Several limitations should be acknowledged. First, despite adjusting the analyses for demographics and health-related covariates, there may still be potential residual confounding arising from unmeasured or insufficiently measured confounders. In addition, there may be reverse causation bias due to underlying illnesses. However, by adjusting the models for baseline HRQoL, we minimised the risk for this potential bias. Second, the three-year

intervals at which data were collected raises the possibility that the reported loneliness levels during survey years may not precisely reflect the experience of loneliness in the interim periods. However, given the multi-wave nature of our study, it is reasonable to infer that the reported levels of loneliness during survey years offer a reasonably representative snapshot of the overall loneliness patterns. Third, self-reported data may not be accurate and are prone to biases. The one-item loneliness scale may be susceptible to underreporting, due to societal stigma surrounding loneliness. In addition, there is no standardised cutoff point for the one-item loneliness measure. This ambiguity may have contributed to a variability in loneliness prevalence and its associated outcomes. However, the sensitivity analysis yielded consistent results across various cut points, further strengthening the robustness of our findings. In addition, the measures used in this study were found to have high validity and reliability in previous studies among Australian populations and longitudinal studies (71, 72). Despite these limitations, our findings still provide valuable insights into the association between loneliness trajectories and dimensions of HRQoL.

Conclusions

Overall, our findings highlight the importance of social well-being for middle-aged and older women's physical and mental health. Our research reveals a strong longitudinal connection between elevated levels of loneliness over the course of 18 years and a range of subsequent health outcomes among middle-aged women. These findings emphasise the importance of fostering social well-being as a universal public health approach in health care. There is a need to address loneliness, not only as a social concern but also as a determinant of both mental and physical well-being. Developing strategies to enhance social connections and alleviate loneliness may prove crucial in promoting overall health and improving HRQoL throughout the course of life. Recognising the complex interplay between loneliness and HRQoL underscores the need for holistic strategies that address the association between social, psychological, and physiological dimensions.

Competing interests: We have no known conflict of interest to disclose.

Funding: Ding Ding is funded by the National Health and Medical Research Council Emerging Leader Fellowship (award No. 2009254).

Data availability: Data are publicly available and can be obtained upon application approval.

Code availability: the code is available at: <https://github.com/Netahag/Loneliness-and-long-term-health-related-quality-of-life.git>

4.5. References

1. Gierveld JdJ. A review of loneliness: concept and definitions, determinants and consequences. *Rev Clin Gerontol*. 1998;8(1):73-80.
2. Hawkley LC, Cacioppo JT. Loneliness Matters: A Theoretical and Empirical Review of Consequences and Mechanisms. *Ann Behav Med*. 2010;40(2):218-27.
3. Park C, Majeed A, Gill H, Tamura J, Ho RC, Mansur RB, et al. The Effect of Loneliness on Distinct Health Outcomes: A Comprehensive Review and Meta-Analysis. *Psy Res*. 2020;294:113514.
4. Rico-Urbe LA, Caballero FF, Martín-María N, Cabello M, Ayuso-Mateos JL, Miret M. Association of loneliness with all-cause mortality: A meta-analysis. *PloS One*. 2018;13(1):e0190033.
5. Valtorta NK, Kanaan M, Gilbody S, Ronzi S, Hanratty BJH. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. 2016;102(13):1009-16.
6. Kraav S-L, Lehto SM, Kauhanen J, Hantunen S, Tolmunen T. Loneliness and social isolation increase cancer incidence in a cohort of Finnish middle-aged men. A longitudinal study. *Psy Res*. 2021;299:113868.
7. Erzen E, Çikrikci Ö. The effect of loneliness on depression: A meta-analysis. *Int J Soc Psych*. 2018;64(5):427-35.
8. Domènech-Abella J, Mundó J, Haro JM, Rubio-Valera M. Anxiety, depression, loneliness and social network in the elderly: Longitudinal associations from The Irish Longitudinal Study on Ageing (TILDA). *Journal of Affective Disorders*. 2019;246:82-8.
9. Dyal SR, Valente TW. A Systematic Review of Loneliness and Smoking: Small Effects, Big Implications. *Substance Use & Misuse*. 2015;50(13):1697-716.

10. Wootton RE, Greenstone HSR, Abdellaoui A, Denys D, Verweij KJH, Munafò MR, Treur JL. Bidirectional effects between loneliness, smoking and alcohol use: evidence from a Mendelian randomization study. *Addiction*. 2021;116(2):400-6.
11. Wakabayashi M, Sugiyama Y, Takada M, Kinjo A, Iso H, Tabuchi T. Loneliness and increased hazardous alcohol use: data from a nationwide internet survey with 1-year follow-up. *Int J Environ Res Public Health*. 2022;19(19):12086.
12. Freak-Poli R, Ryan J, Neumann JT, Tonkin A, Reid CM, Woods RL, et al. Social isolation, social support and loneliness as predictors of cardiovascular disease incidence and mortality. *BMC Geriatr*. 2021;21(1):711.
13. Lee S. Loneliness, Volunteering, and Quality of Life in European Older Adults. *Activ Adapt Aging*. 2023;47(2):250-61.
14. Kaplan RM, Hays RD. Health-Related Quality of Life Measurement in Public Health. *Annu Rev Pub Health*. 2022;43(1):355-73.
15. Grazulyte D, Norkiene I, Kazlauskas E, Truskauskaite-Kuneviciene I, Kolevinskaite S, Ringaitiene D, Sipylaite J. Predictors of long-term HRQOL following cardiac surgery: a 5-year follow-up study. *Health Qual Life Out*. 2021;19(1):197.
16. Vélez-Toral M, Godoy-Izquierdo D, de Guevara NML, de Teresa Galván C, Ballesteros AS, García JFG. Improvements in health-related quality of life, cardio-metabolic health, and fitness in postmenopausal women after an exercise plus health promotion intervention: A randomized controlled trial. *J Phys Act Health*. 2017;14(5):336-43.
17. Phyo AZZ, Freak-Poli R, Craig H, Gasevic D, Stocks NP, Gonzalez-Chica DA, Ryan J. Quality of life and mortality in the general population: a systematic review and meta-analysis. *BMC Pub Health*. 2020;20(1):1596.
18. Vespa A, Spatuzzi R, Fabbietti P, Di Rosa M, Bonfigli AR, Corsonello A, et al. Association between Sense of Loneliness and Quality of Life in Older Adults with Multimorbidity. *Int J Environ Res Public Health*. 2023;20(3):2615.

19. Musich S, Wang SS, Hawkins K, Yeh CS. The Impact of Loneliness on Quality of Life and Patient Satisfaction Among Older, Sicker Adults. *Gerontol Geriatr Med*. 2015;1:2333721415582119.
20. Arslantaş H, Adana F, Abacigil Ergin F, Kayar D, Acar G. Loneliness in Elderly People, Associated Factors and Its Correlation with Quality of Life: A Field Study from Western Turkey. *Iran J Public Health*. 2015;44(1):43-50.
21. Christiansen J, Lund R, Qualter P, Andersen CM, Pedersen SS, Lasgaard M. Loneliness, social isolation, and chronic disease outcomes. *J Annals Behavioral Medicine*. 2021;55(3):203-15.
22. Westergaard ML, Lau CJ, Allesøe K, Andreassen AH, Jensen RH. Poor social support and loneliness in chronic headache: Prevalence and effect modifiers. *Cephalalgia*. 2021;41(13):1318-31.
23. Ansari S, Muhammad T, Dhar M. How Does Multi-Morbidity Relate to Feeling of Loneliness among Older Adults? Evidence from a Population-Based Survey in India. *J Pop Ageing*. 2023;16(1):45-66.
24. Victor CR, Bowling A. A longitudinal analysis of loneliness among older people in Great Britain. *J Psychol*. 2012;146(3):313-31.
25. Beridze G, Ayala A, Ribeiro O, Fernández-Mayoralas G, Rodríguez-Blázquez C, Rodríguez-Rodríguez V, et al. Are Loneliness and Social Isolation Associated with Quality of Life in Older Adults? Insights from Northern and Southern Europe. *Int J Environ Res Public Health*. 2020;17(22).
26. Tseng H-Y, Lee C-Y, Wu C-S, Wu IC, Chang H-Y, Hsu C-C, Hsiung CA. Examining the role of living alone and loneliness in predicting health-related quality of life: results from the Healthy Aging Longitudinal Study in Taiwan (HALST). *Qual Life Res*. 2024.
27. Sheftel MG, Margolis R, Verdery AM. Life Events and Loneliness Transitions Among Middle-Aged and Older Adults Around the World. *J Gerontol B Psychol Sci Soc Sci*. 2024;79(1):gbad149.

28. Cheng P, Jin Y, Sun H, Tang Z, Zhang C, Chen Y, et al. Disparities in prevalence and risk indicators of loneliness between rural empty nest and non-empty nest older adults in Chizhou, China. *Geriatr Gerontol Int*. 2015;15(3):356-64.
29. Bu F, Steptoe A, Fancourt D. Relationship between loneliness, social isolation and modifiable risk factors for cardiovascular disease: a latent class analysis. *J Epidemiol Community Health*. 2021;75(8):749-54.
30. Shin O, Park S, Amano T, Kwon E, Kim B. Nature of Retirement and Loneliness: The Moderating Roles of Social Support. *J Appl Gerontol*. 2020;39(12):1292-302.
31. Liu L-J, Guo Q. Loneliness and health-related quality of life for the empty nest elderly in the rural area of a mountainous county in China. *Qual Life Res*. 2007;16(8):1275-80.
32. Karvonen-Gutierrez CA. The importance of disability as a health issue for mid-life women. *Women Midlife Health*. 2015;1(1):10.
33. Brown WJ, Bryson L, Byles JE, Dobson AJ, Lee C, Mishra G, Schofield M. Women's Health Australia: Recruitment for a National Longitudinal Cohort Study. *Women Health*. 1999;28(1):23-40.
34. Dobson AJ, Hockey R, Brown WJ, Byles JE, Loxton DJ, McLaughlin D, et al. Cohort Profile Update: Australian Longitudinal Study on Women's Health. *International Journal of Epidemiology*. 2015;44(5):1547-f.
35. The Australian Longitudinal Study on Women's Health. Technical Report #45. 2022.
36. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement*. 1977;1(3):385-401.
37. Mund M, Maes M, Drewke PM, Gutzeit A, Jaki I, Qualter P. Would the Real Loneliness Please Stand Up? The Validity of Loneliness Scores and the Reliability of Single-Item Scores. *Assessment*. 2023;30(4):1226-48.
38. Nicolaisen M, Thorsen K. Who are lonely? Loneliness in different age groups (18-81 years old), using two measures of loneliness. *Int J Aging Hum Dev*. 2014;78(3):229-57.

39. Peplau L, Perlman, D, Russell, Daniel. The measurement of loneliness. In: Peplau L, Perlman, D, editor. *Loneliness: A Sourcebook of Current Theory, Research and Theory*: John Wiley & Sons; 1982. p. 81-104.
40. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual Framework and Item Selection. *Med Care*. 1992;30(6):473-83.
41. Butterworth P, Crosier T. The validity of the SF-36 in an Australian National Household Survey: demonstrating the applicability of the Household Income and Labour Dynamics in Australia (HILDA) Survey to examination of health inequalities. *BMC Pub Health*. 2004;4(1):44.
42. Barile JP, Horner-Johnson W, Krahn G, Zack M, Miranda D, DeMichele K, et al. Measurement characteristics for two health-related quality of life measures in older adults: The SF-36 and the CDC Healthy Days items. *Disabil Health J*. 2016;9(4):567-74.
43. Wu Q, Chen Y, Zhou Y, Zhang X, Huang Y, Liu R. Reliability, validity, and sensitivity of short-form 36 health survey (SF-36) in patients with sick sinus syndrome. *Medicine (Baltimore)*. 2023;102(24):e33979.
44. Alzahrani H, Alshehri YS, Barcaccia B, Alshehri MA, Alzhrani M, Bjorner JB. Health-related quality of life in Welsh adults: psychometric properties of the SF-36v2 and normative data. *Pub Health*. 2023;214:153-62.
45. Kathe N, Hayes CJ, Bhandari NR, Payakachat N. Assessment of Reliability and Validity of SF-12v2 among a Diabetic Population. *Value in Health*. 2018;21(4):432-40.
46. Australian Bureau of Statistics. Technical Paper: Socio-Economic Indexes for Areas (SEIFA). 2016.
47. Australian Bureau of Statistics. The Australian statistical geography standard (ASGS) remoteness structure. 2018.
48. Australian Government National Health and Medical Research Council. Australian guidelines to reduce health risks from drinking alcohol 2020.

49. Bell S, Lee C. Development of the Perceived Stress Questionnaire for Young Women. *Psychol Health Med*. 2002;7(2):189-201.
50. University of Wisconsin-Medison. Chapter 4: Normality. <https://sscc.wisc.edu/sscc/pubs/RegDiag-Stata/normality.html> [cited 2024 18/10/2024]. Available from: <https://sscc.wisc.edu/sscc/pubs/RegDiag-Stata/normality.html>.
51. Vermunt JK. Latent Class Modeling with Covariates: Two Improved Three-Step Approaches. *Polit Anal*. 2017;18(4):450-69.
52. StataCorp. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC; 2021.
53. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *J Stat Softw*. 2011;45(3):1-67.
54. Van Buuren S, & Oudshoorn, K. Flexible Multivariate Imputation by MICE. TNO Prevention and Health. Leiden, The Netherlands (Technical Report); 1999.
55. Rubin DB. Multiple Imputation for Nonresponse in Surveys.: John Wiley & Sons.; 1987.
56. Shiovitz-Ezra S, Ayalon L. Situational versus chronic loneliness as risk factors for all-cause mortality. *Int Psychogeriatr*. 2010;22(3):455-62.
57. Martín-María N, Caballero FF, Miret M, Tyrovolas S, Haro JM, Ayuso-Mateos JL, Chatterji S. Differential impact of transient and chronic loneliness on health status. A longitudinal study. *Psychol Health*. 2020;35(2):177-95.
58. Pagan R. Gender and Age Differences in Loneliness: Evidence for People without and with Disabilities. *Int J Environ Res Public Health*. 2020;17(24).
59. Liu H, Jiang Q, Feldman MW. Widowhood and mortality risk of older people in rural China: do gender and living arrangement make a difference? *Aging Soc*. 2020;40(9):1939-55.
60. Crowe CL, Liu L, Bagnarol N, Fried LP. Loneliness prevention and the role of the Public Health system. *Perspect Public Heal*. 2022:17579139221106579.

61. Howarth C, Bryant P, Corner A, Fankhauser S, Gouldson A, Whitmarsh L, Willis R. Building a social mandate for climate action: Lessons from COVID-19. *Environment Resource Econ.* 2020;76:1107-15.
62. National Academies of Sciences E, Medicine, Division of B, Social S, Education, Health, et al. Washington (DC): National Academies Press (US); 2020.
63. von Soest T, Luhmann M, Hansen T, Gerstorf D. Development of loneliness in midlife and old age: Its nature and correlates. *J Pers Soc Psychol.* 2020;118(2):388-406.
64. Shin O, Park S, Amano T, Kwon E, Kim B. Nature of Retirement and Loneliness: The Moderating Roles of Social Support. *J Appl Gerontol.* 2019;39(12):1292-302.
65. Lim MH, Qualter P, Ding D, Holt-Lunstad J, Mikton C, Smith BJ. Advancing loneliness and social isolation as global health challenges: taking three priority actions. *Pub Health Res Pract.* 2023;33(3):3332320-.
66. Philip KEJ, Bu F, Polkey MI, Brown J, Steptoe A, Hopkinson NS, Fancourt D. Relationship of smoking with current and future social isolation and loneliness: 12-year follow-up of older adults in England. *Lancet Reg Health Eur.* 2022;14.
67. Richardson T, Elliott P, Roberts R. Relationship between loneliness and mental health in students. *J Pub Mental Health.* 2017;16(2):48-54.
68. Meltzer H, Bebbington P, Dennis MS, Jenkins R, McManus S, Brugha TS. Feelings of loneliness among adults with mental disorder. *Soc Psychiatry Psychiatr Epidemiol.* 2013;48:5-13.
69. Campagne DM. Stress and perceived social isolation (loneliness). *Arch Gerontol Geriat.* 2019;82:192-9.
70. Abdellaoui A, Sanchez-Roige S, Sealock J, Treur JL, Dennis J, Fontanillas P, et al. Phenome-wide investigation of health outcomes associated with genetic predisposition to loneliness. *Human Molecular Genetics.* 2019;28(22):3853-65.

71. Crosier T, Butterworth P. The Validity of the SF-36 in an Australian National Household Survey: Demonstrating the Applicability of the Household Income and Labour Dynamics in Australia (HILDA) Survey to Examination of Health Inequalities. 2004.
72. Powers J YA, Russell A. ALSWH Data Dictionary Supplement. Section 2 Core Survey Dataset 2.7 Psychosocial Variables. Center for Epidemiologic Studies Depression Scale - Shortened Version. Australian Longitudinal Study on Women's Health; 2002.

1 Tables

2 **Table 1. Baseline characteristics of participants- The Australian Longitudinal Study of**
3 **Women's Health (ALSWH) 1946-51 cohort (waves 1-2; n = 13, 714)**

		Median (IQR)	SD
Age (years)		49.5 (2.5)	1.5
		n	%
Education	High school or less	9200	67.1
	Vocational	2613	19.1
	College/ university	1901	13.9
Marital status	Partnered	11,509	83.9
	Single/divorced/separated	1928	14.1
	Widowed	277	2.0
Location of residence	Major city	4604	33.6
	Regional	8441	61.6
	Remote	669	4.9
Currently employed	Yes	10,906	79.5
Language spoken at home	English	12,885	94.0
Born in Australia	Yes	10,461	76.3
Living arrangement	Live alone	759	5.5
Smoking status	Never smoked	8060	58.8
	Ex-smoker	3483	25.4
	Currently smoking	2171	15.8
Body Mass Index	Underweight (<18.5)	175	1.3
	Healthy (18.5≤ BMI≤24.9)	6705	48.9
	Overweight (25.0≤ BMI ≤29.9)	4183	30.5
	Obese (≥30.0)	2651	19.3
Depression ¹	Yes	4130	30.1
Anxiety ²	Yes	4279	31.2
Risky alcohol consumption (>10 drinks p/week) ³	Yes	1681	12.3
Loneliness (feeling lonely 3+ days in a week)	Yes	1243	9.1
		Mean (range)	SD

MOS Social support score ⁴	3.9 (1-5)	1.0
Stress score ⁵	0.6 (0-4)	0.5

Note.

Abbreviations: MOS: Medical Outcomes Study, IRQ: Interquartile range

¹ Depression: ever being told by a doctor about having depression or having symptoms of depression.

² Anxiety: ever being told by a doctor about having anxiety or having symptoms of anxiety.

³ Risky alcohol consumption: consuming more than 10 standard drinks in a week or more than four standard drinks per day.

⁴ Higher scores represent better outcomes

⁵ Higher scores represent worse outcomes

25 **Table 2. Multivariate multinomial logistic regression predicting latent class membership**
 26 **using baseline predictors**

	Increasing ^a mOR (95%CI)	Stable-medium ^a mOR (95%CI)	Stable-high ^a mOR (95%CI)
Age	1.00 (0.95, 1.06)	1.01 (0.95, 1.07)	1.01 (0.93, 1.09)
Education			
Highschool or less	Reference	Reference	Reference
Tertiary not university	0.90 (0.73, 1.11)	0.90 (0.71, 1.15)	0.82 (0.57, 1.19)
College/ university	0.96 (0.74, 1.26)	0.95 (0.72, 1.27)	0.76 (0.48, 1.19)
Living arrangement			
Live alone	Reference	Reference	Reference
Live with others	1.23 (0.79, 1.91)	1.10 (0.63, 1.92)	0.98 (0.61, 1.58)
Marital status			
Partnered	Reference	Reference	Reference
Non-partnered	1.21 (0.94, 1.54)	1.28 (0.97, 1.69)	1.28 (0.92, 1.78)
Widowed	1.56 (0.87, 2.80)	1.70 (0.98, 2.94)	2.08 (1.15, 3.78) *
Currently employed			
No	Reference	Reference	Reference
Yes	0.95 (0.77, 1.18)	0.99 (0.79, 1.24)	0.85 (0.64, 1.12)
IRSD	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Location of residence			
Major city	Reference	Reference	Reference
Regional	1.04 (0.82, 1.32)	1.10 (0.84, 1.46)	0.95 (0.71, 1.26)
Remote	1.01 (0.65, 1.58)	0.97 (0.57, 1.64)	1.37 (0.77, 2.42)
Born in Australia			
Yes	Reference	Reference	Reference
No	1.01 (0.77, 1.31)	0.94 (0.71, 1.25)	0.86 (0.62, 1.20)
Language spoken at home			
English	Reference	Reference	Reference
European	1.07 (0.65, 1.75)	1.20 (0.68, 2.12)	1.14 (0.60, 2.15)
Asian	0.89 (0.32, 2.48)	0.96 (0.31, 2.92)	1.08 (0.30, 3.81)

	Increasing ^a mOR (95%CI)	Stable-medium ^a mOR (95%CI)	Stable-high ^a mOR (95%CI)
Other	1.06 (0.38, 2.98)	1.34 (0.46, 3.87)	1.73 (0.51, 5.90)
Risky alcohol consumption (>10 drinks p/week) ¹			
No	Reference	Reference	Reference
Yes	1.08 (0.74, 1.57)	1.24 (0.87, 1.79)	0.98 (0.64, 1.50)
Binge drinking (>1 episode p/week)			
No	Reference	Reference	Reference
Yes	1.10 (0.85, 1.43)	1.00 (0.76, 1.33)	0.98 (0.72, 1.35)
Smoking status			
Non-smoker	Reference	Reference	Reference
Ex-smoker	1.09 (0.86, 1.36)	1.06 (0.82, 1.37)	1.05 (0.75, 1.45)
Current smoker	1.24 (1.01, 1.54) *	1.28 (1.01, 1.61) *	1.13 (0.80, 1.61)
Body mass index			
Healthy (18.5≤ BMI≤24.9)	Reference	Reference	Reference
Underweight (<18.5)	0.86 (0.41, 1.80)	0.86 (0.40, 1.85)	1.41 (0.60, 3.32)
Overweight (25.0≤ BMI ≤29.9)	1.12 (0.91, 1.37)	1.05 (0.83, 1.33)	1.28 (0.94, 1.73)
Obese (≥30.0)	1.18 (0.93, 1.49)	1.08 (0.81, 1.45)	1.55 (1.12, 2.15) *
Depression (CES-D score)	1.06 (1.02, 1.09) ***	1.07 (1.04, 1.11) ***	1.11 (1.07, 1.15) ***
Stress score	1.37 (1.12, 1.68) ***	1.36 (1.09, 1.70) *	1.72 (1.34, 2.20) ***
Depression ²			
No	Reference	Reference	Reference
Yes	1.34 (0.98, 1.83)	1.47 (1.11, 1.93) *	1.34 (0.97, 1.85)
Anxiety ³			
No	Reference	Reference	Reference
Yes	1.06 (-0.16, 0.27)	1.00 (0.78, 1.28)	0.83 (0.60, 1.15)
Social support score	0.75 (0.62, 0.90) ***	0.70 (0.59, 0.84) ***	0.55 (0.48, 0.62) ***

27 * p < 0.05 ** p < 0.01 *** p < 0.001

28 Note.

^a Reference class: ‘Stable-low’. mORs refer to the odds of having the attribute in a certain class compared to the stable-low class.

Abbreviations: mOR: Multinomial odds ratio, CES-D: Center for Epidemiological Studies- Depression, IRSD: Index of Relative Socio-Economic Disadvantage

¹ Risky alcohol consumption: consuming more than 10 standard drinks in a week or more than four standard drinks per day.

² Depression: ever being told by a doctor about having depression or having symptoms of depression.

³ Anxiety: ever being told by a doctor about having anxiety or having symptoms of anxiety.

Table 3. Multivariate multinomial linear regression predicting latent class membership using baseline predictors (Beta coefficients, 95%CI): Data fully adjusted, adjusted only for sociodemographic characteristics and unadjusted

		Increasing ^a	Stable-medium ^a	Stable-high ^a	M (SD)
		B (95%CI)	B (95%CI)	B (95%CI)	
PCS	Fully adjusted	-1.06 (-2.11, -0.02) *	-0.83 (-2.01, 0.35)	-0.78 (-1.87, 0.31)	44.95 (10.48)
	Sociodemographic adjusted	-3.65 (-5.10, -2.19) ***	-3.70 (-4.98, -2.41) ***	-4.85 (-6.22, -3.49) ***	
	Unadjusted	-4.02 (-5.55, -2.49) ***	-4.18 (-5.45, -2.90) ***	-5.58 (-6.99, -4.18) ***	
MCS	Fully adjusted	-3.73 (-5.42, -2.04) **	-3.12 (-5.08, -1.15) **	-5.67 (-6.84, -4.49) ***	52.53 (9.56)
	Sociodemographic adjusted	-6.96 (-8.69, -5.23) ***	-6.99 (-8.67, -5.31) ***	-10.53 (-12.11, -8.95) ***	
	Unadjusted	-7.19 (-8.98, -5.41) ***	-7.26 (-8.97, -5.55) ***	-10.93 (-12.53, -9.33) ***	
Physical functioning	Fully adjusted	-3.19 (-6.27, -0.11) *	-2.59 (-5.79, 0.61)	-4.32 (-7.04, -1.60) **	74.66 (23.15)
	Sociodemographic adjusted	-9.38 (-13.32, -5.45) ***	-9.50 (-12.74, -6.27) ***	-14.00 (-17.18, -10.82) ***	
	Unadjusted	-10.36 (-14.44, -6.27) ***	-10.73 (-13.88, -7.57) ***	-15.88 (-19.16, -12.60) ***	
Role physical	Fully adjusted	-8.09 (-12.59, -3.58) **	-7.18 (-12.60, -1.76) *	-9.69 (-13.72, -5.66)	71.04 (40.9)
	Sociodemographic adjusted	-18.80 (-25.03, -12.58) ***	-19.51 (-24.71, -14.31) ***	-26.31 (-31.38, -21.24) ***	
	Unadjusted	-20.06 (-26.52, -13.59) ***	-21.11 (-26.29, -15.93) ***	-28.65 (-33.85, -23.45) ***	

Pain index	Fully adjusted	-4.36 (-7.05, -1.67) **	-3.45 (-6.51, -0.38) *	-4.67 (-6.96, -2.38)	66.29 (23.83)
	Sociodemographic adjusted	-11.05 (-14.20, -7.90) ***	-11.05 (-14.01, -8.08) ***	-14.97 (-18.04, -11.90) ***	
	Unadjusted	-11.77 (-15.01, -8.53) ***	-11.94 (-14.89, -8.99) ***	-16.33 (-19.51, -13.14) ***	
General health	Fully adjusted	-3.99 (-6.15, -1.84) ***	-3.29 (-5.75, -0.83) *	-4.78 (-7.00, -2.55) ***	70.38 (19.99)
	Sociodemographic adjusted	-10.39 (-13.06, -7.71) ***	-10.68 (-13.03, -8.32) ***	-14.71 (-17.61, -11.81) ***	
	Unadjusted	-11.07 (-13.94, -8.20) ***	-11.52 (-13.94, -9.10) ***	-15.98 (-18.95, -13.01) ***	
Vitality	Fully adjusted	-5.12 (-8.52, -1.72) *	-4.00 (-7.40, -0.60) *	-7.20 (-9.28, -5.12) ***	63.97 (20.46)
	Sociodemographic adjusted	-12.58 (-16.06, -9.10) ***	-12.75 (-15.77, -9.73) ***	-18.67 (-21.48, -15.86) ***	
	Unadjusted	-13.23 (-16.83, -9.62) ***	-13.55 (-16.60, -10.49) ***	-19.86 (-22.72, -17.00) ***	
Social functioning	Fully adjusted	-7.53 (-10.67, -4.39) ***	-6.38 (-10.07, -2.69) **	-10.68 (-13.48, -7.88) ***	84.02 (23.53)
	Sociodemographic adjusted	-14.64 (-18.64, -10.63) ***	-14.67 (-18.10, -11.25) ***	-21.58 (-24.98, -18.18) ***	
	Unadjusted	-15.36 (-19.53, -11.20) ***	-15.58 (-19.00, -12.15) ***	-22.90 (-26.35, -19.45) ***	
Role emotional	Fully adjusted	-9.57 (-14.30, -4.84) ***	-8.12 (-13.44, -2.80) **	-15.25 (-19.86, -10.62) ***	84.79 (32.56)
	Sociodemographic adjusted	-17.66 (-23.28, -12.04) ***	-17.58 (-22.83, -12.34) ***	-27.47 (-32.97, -21.98) ***	
	Unadjusted	-18.53 (-24.40, -12.66) ***	-18.66 (-23.93, -13.39) ***	-29.03 (-34.68, -23.39) ***	
Mental health index	Fully adjusted	-6.50 (-9.58, -3.42) ***	-5.29 (-8.82, -1.76) *	-9.30 (-11.36, -7.25) ***	78.93 (16.14)

Sociodemographic adjusted	-12.28 (-15.54, -9.03) ***	-12.22 (-15.26, -9.18) ***	-18.00 (-20.78, -15.23) ***
Unadjusted	-12.70 (-16.05, -9.35) ***	-12.71 (-15.78, -9.63) ***	-18.74 (-21.52, -15.95) ***

* p < 0.05 ** p < 0.01 *** p < 0.001

Note.

Reference group = 'Stable-low' loneliness

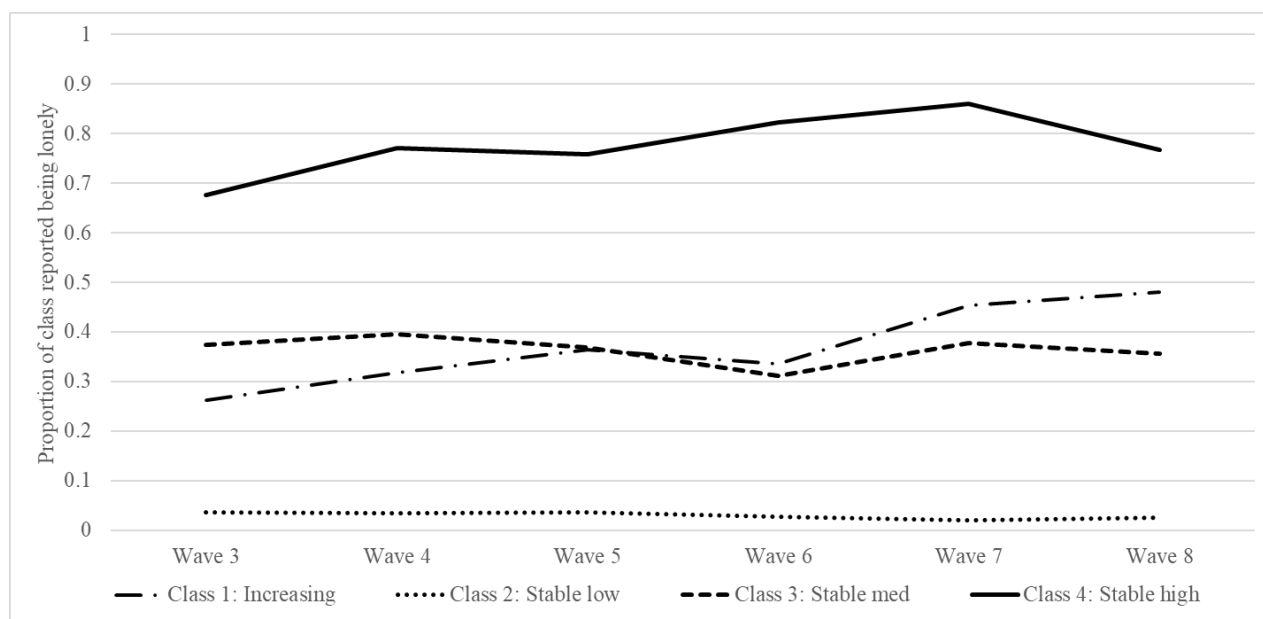
Abbreviations: PCS: Physical Component Summary; MCS: Mental Component Summary; B: unstandardised Beta coefficients; M: Mean; SD: Standard deviation

Sociodemographic models were adjusted for age, gender, education, marital status, living arrangement, employment, area remoteness, country of birth and language spoken at home.

Fully adjusted models were adjusted for age, gender, education, marital status, living arrangement, employment, area remoteness, country of birth, language spoken at home, BMI, smoking, alcohol consumption, depression, anxiety, social support and stress.

Figures

Figure 1. Probabilities of loneliness for each loneliness class over time



Note.

Class 1 = 'Increasing' loneliness; Class 2 = 'Stable-low' loneliness; Class 3 = 'Stable-medium' loneliness; Class 4 = 'Stable-high' loneliness

4.6. Appendices

Can loneliness affect the long-term health-related quality of life? A latent class analysis among middle-aged Australian women - Supplementary Appendices

Appendix 1. STROBE reporting

Table S1.1. Statement- Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7-9
Study size	10	Explain how the study size was arrived at	9, Table S3.1

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-7, Appendix 2,
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7-9
		(b) Describe any methods used to examine subgroups and interactions	9
		(c) Explain how missing data were addressed	9, Figures S3.2-S3.3
		(d) If applicable, explain how loss to follow-up was addressed	9, Figures S3.2-S3.3
		(e) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5, 9, Table S3.1
		(b) Give reasons for non-participation at each stage	9, Table S3.1
		(c) Consider use of a flow diagram	Table S3.1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-10, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Figures S3.2-S3.3
		(c) Summarise follow-up time (eg, average and total amount)	Table S3.1
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-12, Tables 2-3, Table S3.3
		(b) Report category boundaries when continuous variables were categorized	10-12, Tables 2-3, Table S3.3
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13, Table 3, Tables S4.1-S4.5

Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Appendix 2. Baseline predictors

Marital status

Marital status was measured by asking participants about their current marital status. Answers included: 1. married, de Facto/opposite sex, de Facto/same sex, 2. separated, divorced, widowed, and 3. single. We recoded the answers into the following categories: 1. partnered, 2. not partnered, 3. widowed.

Index of Relative Socio-Economic Disadvantage (IRSD)

The residential areas of participants were analysed by the Index of Relative Socio-Economic Disadvantage (IRSD) from the Socio-Economic Indexes for Areas (SEIFA) (1). This is a population-based metric, evaluating the relative disadvantage of geographic regions by considering multiple socioeconomic factors including household income, educational attainment, occupational status, housing costs (rent and mortgage payments), dwelling size, occupancy, and disability rates. The data used for this index is obtained from the Australian Census, providing a comprehensive snapshot of the socio-economic conditions prevalent in each area (2).

Area remoteness

The Accessibility-Remoteness Index of Australia Plus (ARIA+) (3) was used to examine the geographical remoteness of participants. This index is a classification system based on the Australian Statistical Geography Standard (ASGS) from the Australian Census (4). Utilizing participants' residential postcodes, they were categorized into one of three groups: major city, regional, or remote.

Employment status

In all waves except the second one, participants were asked about their primary current occupation. The response options included roles such as manager, professional, paraprofessional, trade, admin. assist, sales/service, machine operator, manual worker, never engaged in paid work, and other. The responses to this question were classified, with a designation of 0 indicating "not employed" and 1 denoting "employed."

In the second wave, participants were presented with two distinct inquiries regarding their primary and secondary occupational statuses. The questions prompted them to specify the nature of their main and secondary occupations, with response options such as no secondary occupation, full-time, part-time/casual, work without pay, home duties, studying,

unemployed-looking, unpaid voluntary, retired, and unable to work. All unpaid occupations, including home duties, studying, retirement, etc., were collectively treated as unpaid work and recategorized as 0, indicating unemployed. both full-time and part-time positions were classified as paid work and recoded as 1, representing employed status.

Living alone

Participants indicated whether they lived alone with response options coded as 0 = no, 1 = yes. However, in the second wave, participants were asked to specify the number of people living with them, including categories such as partner/spouse, children under 16 years, children 16-18 years, children over 18 years, parents, other adult relatives, and other non-family members. The responses to this question were subsequently recoded, with a value of 0 denoting "not live alone" and 1 signifying "live alone."

Country of birth

Participants were inquired about their country of birth, with response options including Australian born, other English-Speaking Background, Europe, Asia, and Other. These responses were subsequently categorized into a binary variable, distinguishing between individuals who were Australian born and those who were not Australian born.

Language spoken at home

Participants were surveyed about the language spoken at home. Potential responses included English, Aust, English, Other, European, Asian, and Other. Subsequently, a variable was derived from this information, categorizing participants into four distinct levels based on the language spoken at home: English, European, Asian, and Other.

Level of education

Education levels were assessed based on the highest qualification completed by participants, with potential responses ranging from 'no formal qualification' to 'higher university degree'. For the purpose of analysis, these responses were recategorized into a three-level variable: 1 = high school or less, 2 = tertiary not university, 3 = college/university.

Alcohol consumption

The assessment of alcohol consumption adhered to the revised Australian guidelines introduced in 2020. These guidelines suggest that adults should limit their alcohol intake to no more than 10 standard drinks per week and no more than four standard drinks on any single day (5). Participants were asked to specify the frequency of their alcohol consumption,

ranging from 'never' to 'every day.' Additionally, participants indicated the typical number of drinks they usually have in a day, with response options ranging from one to more than nine drinks, and the frequency with which they engage in heavy episodic drinking, defined as consuming five or more drinks on a single occasion, using a scale from 'never drink' to 'more than once a week.' Participants reported the consumption of more than 10 standard drinks in a week or more than four standard drinks on any one day or if they consumed more than five drinks at a time, they were defined as being at 'levels that increase the risk of alcohol-related disease or injury'.

Smoking

Participants' smoking status was assessed using the Australian Institute of Health and Welfare measure, which includes response options such as never smoker, ex-smoker, irregular smoker, weekly smoker, and daily smoker (6). The responses were subsequently recategorized into three broader categories: 0 for "never smoked," 1 for "ex-smoker," and 2 for "currently smoking."

Body Mass Index

Participants provided self-reported data on their height and weight, from which their Body Mass Index (BMI) was calculated. The BMI values were then classified into four levels according to the World Health Organization guidelines:

- 1) Underweight ($BMI < 18.5$)
- 2) Healthy weight ($18.5 \leq BMI < 25$)
- 3) Overweight ($25 \leq BMI < 30$)
- 4) Obese ($30 \leq BMI$)

Anxiety and depression diagnoses

Participants were asked about whether they had received a diagnosis or treatment for various physical and mental conditions within the past three years. For the purposes of the current study, the focus was specifically on the items related to diagnoses of anxiety and depression. The response options for each of the two variables were 0. never, 1. last two years, 2. >two years ago, 3. Both. The responses were recoded as 0 for "never" and 1 for "ever". Participants were also asked about having symptoms of anxiety and depression on a scale of never-often. Responses for each of the two variables were recoded as 0 = never/rarely, 2 = sometimes/often. New variables were constructed for anxiety and depression with those ever

having a diagnosis or experiencing symptoms sometimes/often categorised as having the condition.

Depression

The Centre for Epidemiologic Studies Depression (CES-D) Scale was used to examine depression. Participants were asked about the ways they felt or behave during the past week using 10 items on a 4-point Likert scale (0 = Rarely or none of the time, 3 = Most or all of the time) (7).

Stress

Stress levels were assessed using the Perceived Stress Questionnaire (8). This measure is derived from the average of 10 items, each rated on a scale ranging from 0 (not at all stressed) to 4 (extremely stressed). The items encompass various sources of stress, including but not limited to health, work, money, and relationships. The cumulative score provides an overall indication of participants' perceived stress levels across multiple dimensions.

Social support

From Survey 2 onwards, social support was obtained using the 6-item Medical Outcomes Study (MOS) scale, which is an abbreviated version of the larger 19-item MOS support index (9, 10). This scale assesses various domains of social support, including tangible support, affectionate support, positive social interaction, and emotional/informational support. Participants provided responses on a scale ranging from 1 (none of the time) to 5 (all of the time), where a higher score indicates a higher level of perceived support.

References

1. Australian Bureau of Statistics. Technical Paper: Socio-Economic Indexes for Areas (SEIFA). 2016.
2. Pink B. Information paper: An introduction to Socio-Economic Indexes for Areas (SEIFA) 2006. Information paper: An introduction to Socio-Economic Indexes for Areas (SEIFA) 2006. Canberra: Australian Bureau of Statistics, Commonwealth of Australia; 2008. Contract No.: ABS Catalogue No. 2039.0.
3. Glover JD, Tennant SK. Remote areas statistical geography in Australia: notes on the Accessibility/Remoteness Index for Australia (ARIA+ version): Public Health Information Development Unit, The University of Adelaide; 2003.

4. Australian Bureau of Statistics. The Australian statistical geography standard (ASGS) remoteness structure. Australian Bureau of Statistics Canberra; 2018.
5. Australian Government National Health and Medical Research Council. Australian guidelines to reduce health risks from drinking alcohol. 2020 [Available from: <https://www.nhmrc.gov.au/file/15923/download?token=t0Hrxdvq>].
6. AIHW. (2021). Australian Burden of Disease Study 2018: Key findings. Canberra: Australian Institute of Health and Welfare. Retrieved from <https://www.aihw.gov.au/reports/burden-of-disease/burden-of-disease-study2018-key-findings/contents/about>
7. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Assessment*. 1977;1:385-401.
8. Bell S, Lee C. Development of the Perceived Stress Questionnaire for Young Women. *Psychology, Health Med*. 2002;7(2):189-201.
9. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). Conceptual framework and item selection. *Med Care*. 1992;30(6):473–483.
10. Holden, L., Lee, C., Hockey, R., Ware, R. S., & Dobson, A. J. (2014). Validation of the MOS Social Support Survey 6-item (MOS-SSS-6) measure with two large population-based samples of Australian women. *Qual Life Res*, 23(10), 2849- 2853. doi:10.1007/s11136-014-0741-5.

Appendix 3. Additional results

Table S3.1. Number of participants according to wave and the total number of participants included in the analysis

Wave	n
Wave 1	13,714
Wave 2	12,338
Wave 3	11,226
Wave 4	10,905
Wave 5	10,638
Wave 6	10,011
Wave 7	9151
Wave 8	8622
Wave 9	7956
Sample size included in the analysis	13,714

Table S3.2. Criteria for selecting the number of trajectories (waves 3-8)

Model	AIC	BIC	SSABIC	Model group membership proportion				
				(1)	(2)	(3)	(4)	(5)
Overall loneliness								
1 class	38454.3	38498.4	38479.3	100.0%				
2 class	34955.5	35051.1	35009.8	84.9%	15.1%			
3 class	34836.4	34983.6	34920.0	71.6%	4.4%	24.0%		
4 class	34796.1	34994.7	34908.9	73.8%	5.3%	17.1%	3.7%	
5 class	34785.2	35035.3	34927.3	68.2%	3.7%	1.7%	20.9%	5.5%

Abbreviations: AIC = Akaike information criterion; BIC = Bayesian information criterion; SSABIC = sample size adjusted BIC.

Table S3.3. Multivariate linear regression of the predictors of the physical component summary (PCS) and mental component summary (MCS)

	PCS B (95%CI)	MCS B (95%CI)
Loneliness classes		
Stable-low	Reference	Reference
Increasing	-1.06 (-2.11, -0.02)	-3.73 (-5.42, -2.04)
Stable-medium	-0.83 (-2.01, 0.35)	-3.12 (-5.08, -1.15)
Stable-high	-0.78 (-1.87, 0.31)	-5.67 (-6.84, -4.49)
Risky alcohol consumption ¹		
No	Reference	Reference
Yes	0.22 (-0.37, 0.80)	-0.09 (-0.60, 0.41)
Binge drinking		
No	Reference	Reference
Yes	0.20 (-0.27, 0.67)	0.19 (-0.20, 0.57)
Smoking		
Non-smoker	Reference	Reference
Ex smoker	0.06 (-0.43, 0.55)	-0.31 (-0.73, 0.11)
Current smoker	-1.43 (-2.09, -0.78)	-0.35 (-0.90, 0.19)
Baseline PCS	0.37 (0.34, 0.40)	0.11 (0.08, 0.13)
Baseline MCS	0.10 (0.07, 0.13)	0.19 (0.16, 0.22)
BMI		
Normal weight	Reference	Reference
Underweight	-0.14 (-2.11, 1.82)	0.53 (-1.30, 2.35)
Overweight	-2.15 (-2.61, -1.70)	-0.20 (-0.67, 0.27)
Obese	-4.90 (-5.51, -4.29)	-0.49 (-0.97, -0.003)
CES-D (Depression)	-0.05 (-0.11, 0.02)	-0.11 (-0.17, -0.05)
Stress	-0.76 (-1.31, -0.20)	-1.04 (-1.57, -0.51)
Ever had depression ²		
No	Reference	Reference
Yes	-0.29 (-0.87, 0.29)	-1.24 (-1.78, -0.70)
Ever had anxiety ³		
No	Reference	Reference
Yes	-0.04 (-0.61, 0.53)	-0.51 (-1.03, 0.02)
Language		
English	Reference	Reference
European	-0.61 (-1.75, 0.53)	-0.66 (-1.71, 0.38)
Asian	-0.99 (-2.72, 0.74)	0.18 (-1.63, 1.99)
other	-0.26 (-2.40, 1.89)	0.78 (-1.16, 2.73)
Age	-0.19 (-0.32, -0.06)	0.004 (-0.11, 0.12)
Area-level socioeconomic status	0.004 (0.001, 0.01)	0.001 (-0.002, 0.005)
Marital status		
Married	Reference	Reference
Not married	-0.18 (-0.84, 0.48)	0.32 (-0.31, 0.95)
Widower	-0.18 (-1.52, 1.16)	0.45 (-0.88, 1.79)
Area remoteness		

	PCS B (95%CI)	MCS B (95%CI)
Major city	Reference	Reference
Regional	-0.17 (-0.63, 0.29)	-0.01 (-0.42, 0.41)
Remote	-0.57 (-1.58, 0.45)	-0.01 (-0.83, 0.80)
Employment		
Not employed	Reference	Reference
Employed	0.40 (-0.10, 0.89)	0.49 (0.005, 0.97)
Country of birth		
Australia	Reference	Reference
Other	0.22 (-0.24, 0.68)	-0.22 (-0.68, 0.25)
Education		
High school and below	Reference	Reference
Trade/apprentice/certificate/diploma	-0.001 (-0.47, 0.47)	0.37 (-0.07, 0.81)
University	0.59 (0.06, 1.12)	0.19 (-0.32, 0.70)
Living arrangement		
Live alone	Reference	Reference
Live with someone	0.81 (-0.40, 2.02)	-0.50 (-1.56, 0.56)
MOS social support	0.21 (-0.02, 0.44)	0.42 (0.21, 0.63)

¹ Risky alcohol consumption: consuming more than 10 standard drinks in a week or more than four standard drinks per day.

² Depression: ever being told by a doctor about having depression or having symptoms of depression.

³ Anxiety: ever being told by a doctor about having anxiety or having symptoms of anxiety.

Figure S3.1. Q-Q plot for assessing normality of standardised residuals

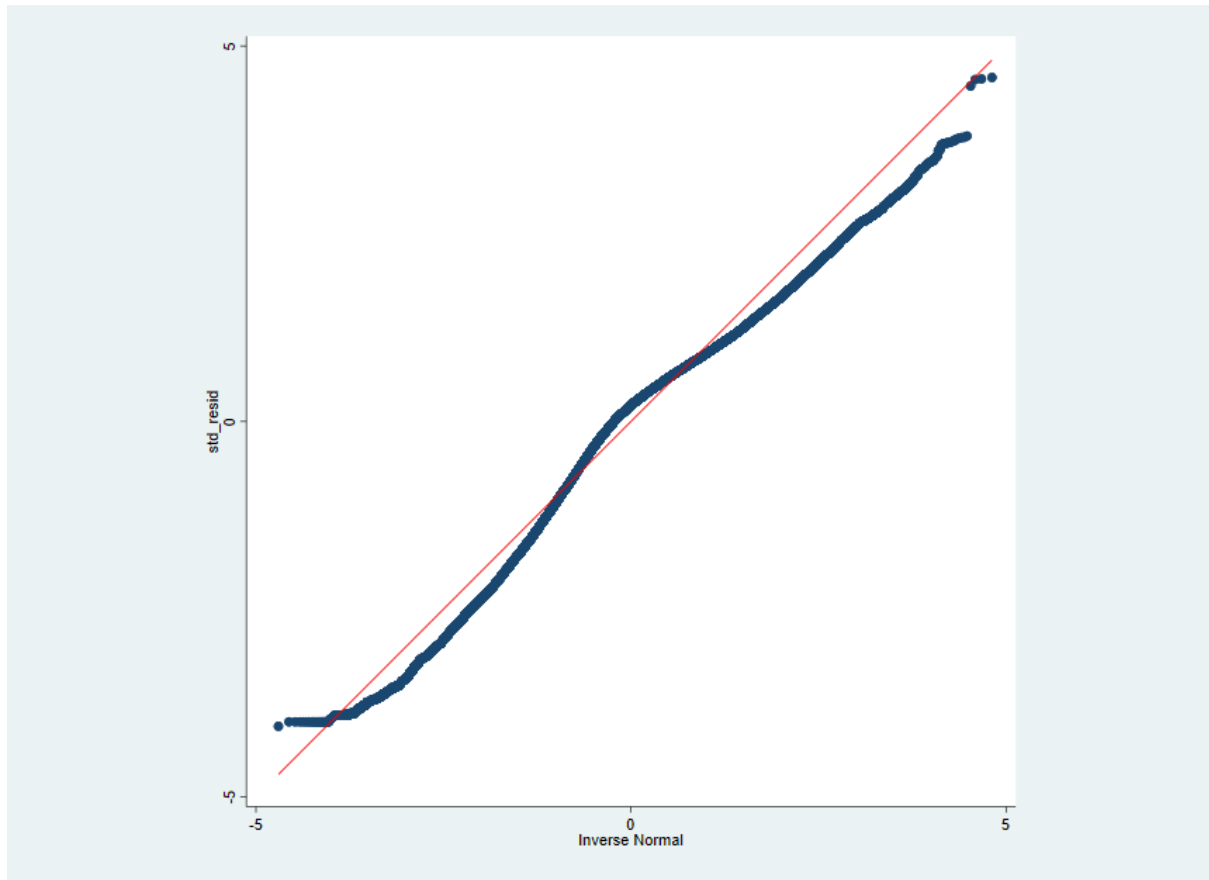


Figure S3.2. Summary of missing data in each analysis variable

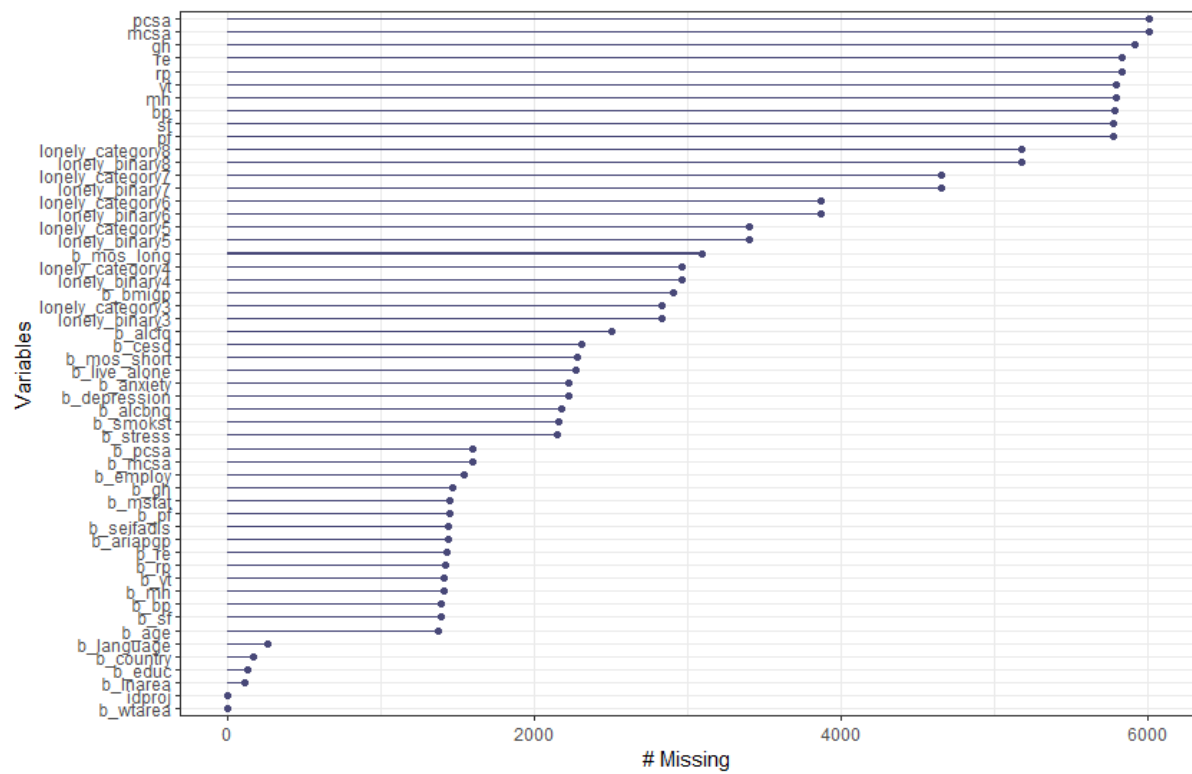
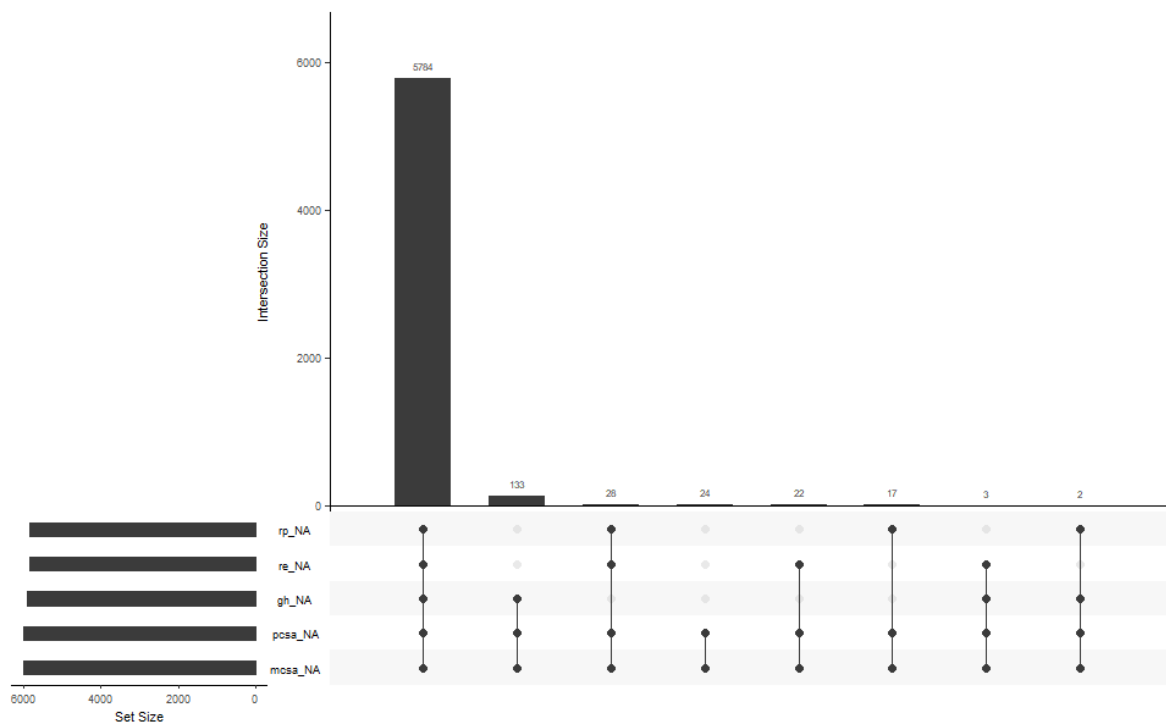


Figure S3.3. Common patterns of missing data



Appendix 4. Sensitivity analyses

Table S4.1. Sensitivity analysis: Multivariate multinomial logistic regression predicting latent class membership using baseline predictors- Probit model results

	Increasing ^a mOR (95%CI)	Stable-medium ^a mOR (95%CI)	Stable-high ^a mOR (95%CI)
Age	1.00 (0.95, 1.07)	1.01 (0.95, 1.07)	1.01 (0.93, 1.09)
Education			
Highschool or less	Reference	Reference	Reference
Tertiary not university	0.91 (0.72, 1.16)	0.89 (0.72, 1.10)	0.82 (0.57, 1.19)
College/ university	0.97 (0.73, 1.29)	0.95 (0.72, 1.24)	0.76 (0.48, 1.19)
Living arrangement			
Live alone	Reference	Reference	Reference
Live with others	1.04 (0.65, 1.66)	1.30 (0.82, 2.04)	0.98 (0.61, 1.58)
Marital status			
Partnered	Reference	Reference	Reference
Non-partnered	1.26 (0.96, 1.66)	1.23 (0.95, 1.60)	1.28 (0.92, 1.78)
Widowed	1.74 (1.00, 3.03)	1.53 (0.87, 2.66)	2.08 (1.15, 3.78)*
Currently employed			
No	Reference	Reference	Reference
Yes	0.98 (0.78, 1.25)	0.96 (0.78, 1.18)	0.85 (0.64, 1.12)
IRSD	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Location of residence			
Major city	Reference	Reference	Reference
Regional	1.12 (0.86, 1.44)	1.03 (0.81, 1.31)	0.95 (0.71, 1.26)
Remote	0.95 (0.55, 1.64)	1.03 (0.69, 1.55)	1.37 (0.77, 2.42)
Born in Australia			
Yes	Reference	Reference	Reference
No	0.94 (0.69, 1.27)	1.01 (0.80, 1.28)	0.86 (0.62, 1.20)
Language spoken at home			
English	Reference	Reference	Reference
European	1.18 (0.64, 2.17)	1.09 (0.69, 1.73)	1.14 (0.60, 2.15)
Asian	0.96 (0.30, 3.10)	0.89 (0.34, 2.32)	1.08 (0.30, 3.81)
Other	1.42 (0.54, 3.75)	1.00 (0.35, 2.83)	1.73 (0.51, 5.90)

	Increasing ^a mOR (95%CI)	Stable-medium ^a mOR (95%CI)	Stable-high ^a mOR (95%CI)
Risky alcohol consumption (>10 drinks p/week) ¹			0.98 (0.64, 1.50)
No	Reference	Reference	Reference
Yes	1.26 (0.86, 1.87)	1.06 (0.78, 1.45)	0.98 (0.64, 1.50)
Binge drinking (>1 episode p/week)			
No	Reference	Reference	Reference
Yes	0.98 (0.74, 1.30)	1.12 (0.91, 1.39)	0.98 (0.72, 1.34)
Smoking status			
Non-smoker	Reference	Reference	Reference
Ex-smoker	1.03 (0.80, 1.34)	1.11 (0.91, 1.35)	1.05 (0.75, 1.45)
Current smoker	1.28 (1.00, 1.62)*	1.25 (1.00, 1.54)*	1.13 (0.80, 1.61)
Body mass index			
Healthy (18.5 ≤ BMI ≤ 24.9)	Reference	Reference	Reference
Underweight (<18.5)	0.83 (0.40, 1.73)	0.89 (0.41, 1.91)	1.41 (0.60, 3.32)
Overweight (25.0 ≤ BMI ≤ 29.9)	1.05 (0.83, 1.33)	1.12 (0.92, 1.37)	1.28 (0.94, 1.73)
Obese (≥30.0)	1.07 (0.82, 1.41)	1.19 (0.92, 1.52)	1.55 (1.12, 2.15)**
Depression (CES-D score)	1.07 (1.04, 1.11)***	1.06 (1.03, 1.09)***	1.11 (1.07, 1.15)***
Stress score	1.33 (1.10, 1.62)	1.40 (1.13, 1.74)**	1.72 (1.34, 2.20)***
Depression ²			
No	Reference	Reference	Reference
Yes	1.50 (1.11, 2.01)**	1.31 (1.02, 1.70)*	1.34 (0.97, 1.85)
Anxiety ³			
No	Reference	Reference	Reference
Yes	0.99 (0.77, 1.28)	1.06 (0.86, 1.31)	0.83 (0.60, 1.15)
Social support score	0.70 (0.59, 0.83)***	0.76 (0.64, 0.90)**	0.55 (0.48, 0.62)***

* p < 0.05 ** p < 0.01 *** p < 0.001

Note.

^a Reference class: 'stable low'. mORs refer to the odds of having the attribute in a certain class compared to the stable-low class.

Abbreviations: mOR: Multinomial odds ratio, CES-D: Center for Epidemiological Studies- Depression, IRSD: Index of Relative Socio-Economic Disadvantage

¹ Risky alcohol consumption: consuming more than 10 standard drinks in a week or more than four standard drinks per day.

² Depression: ever being told by a doctor about having depression or having symptoms of depression.

³ Anxiety: ever being told by a doctor about having anxiety or having symptoms of anxiety.

Table S4.2. Sensitivity analysis: Multivariate multinomial linear regression predicting latent class membership using baseline predictors (Beta coefficients, 95%CI): Data fully adjusted, adjusted only for sociodemographic characteristics and unadjusted- Probit model results

		Increasing ^a	Stable-medium ^a	Stable-high ^a
		B (95%CI)	B (95%CI)	B (95%CI)
PCS	Fully adjusted	-0.80 (-1.92, 0.31)	-1.09 (-2.17, -0.11)*	-0.78 (-1.87, 0.31)
	Sociodemographic adjusted	-3.62 (-4.97, -2.26)***	-3.73 (-5.10, -2.35)***	-4.85 (-6.22, -3.49)***
	Unadjusted	-4.10 (-5.51, -2.68)***	-4.11 (-5.53, -2.68)***	-5.58 (-6.99, -4.18)***
MCS	Fully adjusted	-2.87 (-4.51, -1.24)**	-3.97 (-5.40, -2.55)***	-9.56 (-6.84, -4.49)****
	Sociodemographic adjusted	-6.78 (-8.23, -5.33)***	-7.17 (-8.23, -5.33)***	-10.53 (-12.11, -8.95)***
	Unadjusted	-7.05 (-8.54, -5.56)***	-7.41 (-9.30, -5.50)***	-10.93 (-12.53, -9.33)***
Physical functioning	Fully adjusted	-2.26 (-5.06, 0.55)	-3.52 (-6.50, -0.54)*	-4.32 (-7.04, -1.60)**
	Sociodemographic adjusted	-9.08 (-12.45, -5.71)***	-9.81 (-13.46, -6.15)***	-14.00 (-17.18, -10.82)***
	Unadjusted	-10.29 (-13.79, -6.80)***	-10.79 (-14.55, -7.02)***	-15.88 (-19.16, -12.60)***
Role physical	Fully adjusted	-6.69 (-10.98, -2.41)**	-8.57 (-13.57, -3.57)**	-9.69 (-13.72, -5.66)***
	Sociodemographic adjusted	-18.93 (-24.15, -13.72)***	-19.38 (-25.64, -13.11)***	-26.31 (-31.38, -21.24)***
	Unadjusted	-20.53 (-26.00, -15.07)***	-20.63 (-27.06, -14.20)***	-28.65 (-33.85, -23.45)***
Pain index	Fully adjusted	-3.23 (-6.05, -0.42)*	-4.57 (-7.11, -2.03)**	-4.67 (-6.96, -2.38)***
	Sociodemographic adjusted	-10.76 (-13.70, -7.82)***	-11.34 (-14.39, -8.29)***	-14.97 (-18.04, -11.90)***
	Unadjusted	-11.65 (-14.67, -8.64)***	-12.06 (-15.19, -8.93)***	-16.33 (-19.51, -13.14)***
General health	Fully adjusted	-3.11 (-5.19, -1.03)**	-4.18 (-7.00, -2.55)***	-4.78 (-7.00, -2.55)***
	Sociodemographic adjusted	-10.47 (-12.73, -8.21)***	-10.59 (-13.38, -7.81)***	-14.71 (-17.61, -11.81)***

Vitality	Unadjusted	-11.31 (-13.73, -8.89)***	-7.76 (-14.23, -8.33)***	-15.98 (-18.95, -13.01)***
	Fully adjusted	-3.65 (-7.01, -0.29)*	-5.47 (-8.11, -2.83)***	-7.20 (-9.28, -5.12)***
	Sociodemographic adjusted	-12.42 (-15.50, -9.34)***	-12.91 (-16.26, -9.56)***	-18.67 (-21.48, -15.86)***
Social functioning	Unadjusted	-13.21 (-16.39, -10.03)***	-13.56 (-17.04, -10.08)***	-19.86 (-22.72, -17.00)***
	Fully adjusted	-6.11 (-9.47, -2.76)**	-7.79 (-10.73, -4.86)***	-10.68 (-13.47, -7.88)***
	Sociodemographic adjusted	-14.39 (-17.93, -10.85)***	-14.92 (-18.74, -11.10)***	-21.58 (-24.98, -18.18)***
Role emotional	Unadjusted	-15.30 (-18.94, -11.65)***	-15.64 (-19.59, -11.70)***	-22.90 (-26.35, -19.45)***
	Fully adjusted	-7.60 (-12.66, -2.54)**	-10.09 (-14.00, -6.18)***	-15.24 (-19.86, -10.62)***
	Sociodemographic adjusted	-17.09 (-22.21, -11.97)***	-18.15 (-23.65, -12.65)***	-27.47 (-32.97, -21.98)***
Mental health index	Unadjusted	-18.15 (-23.38, -12.92)***	-19.04 (-24.79, -13.29)***	-29.03 (-34.67, -23.39)***
	Fully adjusted	-4.82 (-7.51, -2.13)**	-6.97 (-9.62, -4.33)***	-9.30 (-11.35, -7.25)***
	Sociodemographic adjusted	-11.80 (-14.21, -9.40)***	-12.70 (-16.19, -9.22)***	-18.00 (-20.78, -15.23)***
	Unadjusted	-12.28 (-14.77, -9.80)***	-13.12 (-16.71, -9.53)***	-18.74 (-21.52, -15.95)***

* p < 0.05 ** p < 0.01 *** p < 0.001

Note.

Reference group = 'Stable low' loneliness

Abbreviations: PCS: Physical Component Summary; MCS: Mental Component Summary; B: unstandardised Beta coefficients; M: Mean; SD: Standard deviation

Sociodemographic models were adjusted for age, gender, education, marital status, living arrangement, employment, area remoteness, country of birth and language spoken at home.

Fully adjusted models were adjusted for age, gender, education, marital status, living arrangement, employment, area remoteness, country of birth, language spoken at home, BMI, smoking, alcohol consumption, depression, anxiety, social support and stress.

Table S4.3. Sensitivity analysis: criteria for selecting the number of trajectories (waves 3-8) using a new cut-point for loneliness (1. Rarely or none of the time vs. levels 2-4)

Model	AIC	BIC	SSABIC	Modal group membership proportion					
				(1)	(2)	(3)	(4)	(5)	(6)
Overall loneliness									
1 class	80636.62	80688.45	80666.20	100%					
2 class	69762.83	69873.89	69826.22	66.90%	33.10%				
3 class	68978.24	69148.53	69075.43	50.68%	35.91%	13.41%			
4 class	68731.29	68960.82	68862.30	51.98%	13.07%	16.62%	18.32%		
5 class	68708.33	68997.09	68873.15	37.53%	17.46%	15.95%	16.11%	12.94%	
6 class	68694.43	69035.01	68888.83	34.56%	15.13%	12.61%	11.43%	18.00%	8.27%

Abbreviations: AIC = Akaike information criterion; BIC = Bayesian information criterion; SSABIC = sample size adjusted BIC.

Table S4.4. Sensitivity analysis: Multivariate multinomial logistic regression predicting latent class membership using baseline predictors using a new cut-point for loneliness (1. Rarely or none of the time vs. levels 2-4)

	Increasing ^a mOR (95%CI)	Stable-medium ^a mOR (95%CI)	Stable-high ^a mOR (95%CI)
Age	0.99 (0.93, 1.06)	0.98 (0.91, 1.06)	0.97 (0.91, 1.03)
Education			
Highschool or less	Reference	Reference	Reference
Tertiary not university	1.05 (0.88, 1.25)	0.95 (0.77, 1.18)	0.93 (0.76, 1.13)
College/ university	1.01 (0.81, 1.26)	0.95 (0.73, 1.24)	0.87 (0.68, 1.11)
Living arrangement			
Live alone	Reference	Reference	Reference
Live with others	1.01 (0.73, 1.39)	1.05 (0.73, 1.50)	0.96 (0.70, 1.32)
Marital status			
Partnered	Reference	Reference	Reference
Non-partnered	1.01 (0.64, 1.59)	1.28 (0.72, 2.29)	1.38 (0.95, 2.01)
Widowed	1.01 (0.40, 2.48)	1.10 (0.75, 1.62)	2.00 (0.94, 4.27)
Currently employed			
No	Reference	Reference	Reference
Yes	1.03 (0.86, 1.24)	1.02 (0.86, 1.21)	0.91 (0.76, 1.08)
IRSD	0.99 (0.99, 1.00)	1.00 (0.99, 1.00)	1.00 (1.00, 1.00)
Location of residence			
Major city	Reference	Reference	Reference
Regional	1.02 (0.80, 1.31)	1.10 (0.86, 1.41)	1.04 (0.83, 1.30)
Remote	1.01 (0.67, 1.51)	1.11 (0.75, 1.62)	1.33 (0.93, 1.92)
Born in Australia			
Yes	Reference	Reference	Reference
No	1.05 (0.86, 1.30)	1.08 (0.92, 1.26)	0.98 (0.80, 1.20)
Language spoken at home			
English	Reference	Reference	Reference
European	0.92 (0.62, 1.38)	0.95 (0.66, 1.37)	0.98 (0.67, 1.44)
Asian	0.68 (0.24, 1.94)	0.90 (0.48, 1.67)	1.16 (0.57, 2.33)

	Increasing ^a mOR (95%CI)	Stable-medium ^a mOR (95%CI)	Stable-high ^a mOR (95%CI)
Other	0.58 (0.17, 1.93)	1.09 (0.33, 3.61)	1.69 (0.82, 3.47)
Risky alcohol consumption (>10 drinks p/week) ¹			
No	Reference	Reference	Reference
Yes	1.06 (0.80, 1.40)	1.13 (0.86, 1.48)	1.01 (0.77, 1.31)
Binge drinking (>1 episode p/week)			
No	Reference	Reference	Reference
Yes	1.06 (0.91, 1.24)	0.98 (0.82, 1.17)	1.01 (0.84, 1.20)
Smoking status			
Non-smoker	Reference	Reference	Reference
Ex-smoker	1.03 (0.86, 1.25)	1.04 (0.89, 1.21)	1.08 (0.90, 1.31)
Current smoker	1.06 (0.80, 1.42)	1.11 (0.87, 1.40)	1.07 (0.84, 1.37)
Body mass index			
Healthy (18.5≤ BMI≤24.9)	Reference	Reference	Reference
Underweight (<18.5)	0.64 (0.25, 1.63)	0.89 (0.49, 1.60)	0.90 (0.51, 1.60)
Overweight (25.0≤ BMI ≤29.9)	1.04 (0.90, 1.22)	0.89 (0.49, 1.60)	1.13 (0.95, 1.35)
Obese (≥30.0)	1.06 (0.87, 1.30)	1.03 (0.86, 1.23)	1.31 (1.07, 1.59)**
Depression (CES-D score)	1.03 (0.92, 1.15)	1.05 (0.98, 1.13)	1.10 (1.03, 1.17)**
Stress score	1.22 (0.62, 2.41)	1.34 (0.88, 2.05)	1.63 (1.11, 2.38)*
Depression ²			
No	Reference	Reference	Reference
Yes	1.00 (0.82, 1.24)	1.22 (0.84, 1.75)	1.51 (1.08, 2.10)*
Anxiety ³			
No	Reference	Reference	Reference
Yes	1.00 (0.82, 1.24)	1.08 (0.83, 1.40)	0.96 (0.78, 1.19)
Social support score	0.83 (0.46, 1.48)	0.78 (0.58, 1.05)	0.58 (0.43, 0.79)**

* p < 0.05 ** p < 0.01 *** p < 0.001

Note.

^a Reference class: 'Stable-low'. mORs refer to the odds of having the attribute in a certain class compared to the stable-low class.

Abbreviations: mOR: Multinomial odds ratio, CES-D: Center for Epidemiological Studies-Depression, IRSD: Index of Relative Socio-Economic Disadvantage

¹ Risky alcohol consumption: consuming more than 10 standard drinks in a week or more than four standard drinks per day.

² Depression: ever being told by a doctor about having depression or having symptoms of depression.

³ Anxiety: ever being told by a doctor about having anxiety or having symptoms of anxiety.

Table S4.5. Sensitivity analysis: multivariate multinomial linear regression predicting latent class membership using baseline predictors (Beta coefficients, 95%CI) using a new cut-point for loneliness (1. Rarely or none of the time vs. levels 2-4): Data fully adjusted, adjusted only for sociodemographic characteristics and unadjusted

		Increasing ^a	Stable-medium ^a	Stable-high ^a
		B (95%CI)	B (95%CI)	B (95%CI)
PCS	Fully adjusted	-0.59 (-2.04, 0.86)	-0.63 (-1.32, 0.07)	-1.07 (-2.08, -0.05)*
	Sociodemographic adjusted	-1.77 (-6.44, 2.89)	-2.12, (-4.05, -0.18)*	-4.56 (-6.94, -2.17)**
	Unadjusted	-1.87 (-6.90, 3.16)	-2.29 (-4.44, -0.15)*	-5.10, -7.68, -2.52)***
MCS	Fully adjusted	-2.56 (-6.85, 1.74)	-1.53 (-2.51, -0.55)**	-5.15 (-6.45, -3.83)***
	Sociodemographic adjusted	-4.00 (-12.65, 4.65)	-3.46 (-5.05, -1.88)***	-9.46 (-12.70, -6.22)***
	Unadjusted	-4.04 (-12.87, 4.78)	-3.55 (-5.23, -1.86)***	-9.70 (-13.03, -6.38)***
Physical functioning	Fully adjusted	-1.57 (-5.58, 2.45)	-1.67 (-3.49, 0.16)	-4.31 (-6.95, -1.67)**
	Sociodemographic adjusted	-4.36 (-16.13, 7.4)	-5.21 (-10.20, -0.22)*	-12.59 (-18.51, -6.62)***
	Unadjusted	-4.58 (-17.25, 8.10)	-5.64 (-11.18, -0.10)*	-13.96 (-20.38, -7.55)***
Role physical	Fully adjusted	-5.68 (-16.35, 4.99)	-4.46 (-7.04, -1.86)**	-10.23 (-15.14, -5.32) ***
	Sociodemographic adjusted	-10.45 (-34.96, 14.05)	-10.69 (-17.93, -3.45)**	-24.54 (-35.29, -13.78)***
	Unadjusted	-10.74 (-36.42, 14.93)	-11.24 (-19.13, -3.36)**	-26.20 (-37.61, -14.79)***
Pain index	Fully adjusted	-2.60 (-7.94, 2.73)	-2.09 (-3.45, -0.74)**	-4.92 (-7.34, -2.50)***
	Sociodemographic adjusted	-5.64 (-19.61, 8.34)	-6.01 (-10.52, -1.50)*	-13.87 (-20.13, -7.62)***
	Unadjusted	-5.81 (-20.44, 8.83)	-6.31 (-11.16, 1.45)*	-14.83 (-21.41, -8.24) ***

General health	Fully adjusted	-2.56 (-7.23, 2.12)	-1.66 (-2.99, -0.32)*	-4.84 (-6.88, -2.81)***
	Sociodemographic adjusted	-5.48 (-18.55, 7.59)	-5.45 (-9.12, 1.78)**	-13.56 (-19.33, -7.79)***
	Unadjusted	-5.62 (-19.29, 8.05)	-5.73 (-9.75, -1.71)**	-14.47 (-20.56, -8.38)***
Vitality	Fully adjusted	-3.66 (-10.48, 3.15)	-2.40 (-3.82, -0.99)**	-6.54 (-9.09, -4.02)***
	Sociodemographic adjusted	-7.09 (-23.92, 9.74)	-6.87 (-11.45, -2.29)**	-16.72 (-23.80, 9.65)***
	Unadjusted	-7.24 (-24.65, 10.18)	-7.14 (-12.04, -2.24)**	-17.55 (-24.94, -10.16)***
Social functioning	Fully adjusted	-5.03 (-13.13, 3.06)	-2.93 (-5.38, -0.48)*	-9.88 (-13.02, -6.74)***
	Sociodemographic adjusted	-8.21 (-25.65, 9.24)	-7.12 (-10.17, -4.06)***	-19.37 (-26.55, -12.18)***
	Unadjusted	-8.37 (-26.53, 9.80)	-7.44 (-10.88, -4.00)***	-20.31 (-27.84, -12.77)***
Role emotional	Fully adjusted	-6.11 (-16.04, 3.82)	-3.72 (-6.93, -0.52)*	-13.29 (-17.25, -9.33)***
	Sociodemographic adjusted	-9.69 (-30.02, 10.65)	-8.48 (-12.55, -4.40)***	-24.00 (-31.82, -16.19)***
	Unadjusted	-9.88 (-30.94, 11.19)	-8.84 (-13.28, -4.40)***	-25.06 (-33.31, -16.80)***
Mental health index	Fully adjusted	-4.26 (-12.04, 3.52)	-2.86 (-3.98, -1.74)***	-9.00 (-11.74, -6.27)***
	Sociodemographic adjusted	-6.81 (-22.41, 8.78)	-6.30 (-9.87, -2.73)**	-16.65 (-23.00, -10.35)***
	Unadjusted	-6.89 (-22.77, 9.00)	-6.43 (-10.15, -2.71)**	-17.08 (-23.52, -10.64)***

* p < 0.05 ** p < 0.01 *** p < 0.001

Note.

Reference group = 'Stable-low' loneliness

Abbreviations: PCS: Physical Component Summary; MCS: Mental Component Summary; B: unstandardised Beta coefficients; M: Mean; SD: Standard deviation

Sociodemographic models were adjusted for age, gender, education, marital status, living arrangement, employment, area remoteness, country of birth and language spoken at home.

Fully adjusted models were adjusted for age, gender, education, marital status, living arrangement, employment, area remoteness, country of birth, language spoken at home, BMI, smoking, alcohol consumption, depression, anxiety, social support and stress

4.7. Concluding summary for this chapter and knowledge gained from this study

This chapter introduced the first study to examine the association between longitudinal patterns of loneliness and HRQoL. The findings demonstrate increased odds of elevated loneliness trends ('Increasing' loneliness, 'Stable-medium' and 'Stable-high') among individuals with baseline predictors such as smoking, stress, depression and low social support. In addition, widows had twice the odds of having a 'Stable-high' loneliness trajectory compared to 'Stable-low' loneliness. Higher levels of loneliness were associated with lower levels of both mental and physical HRQoL, with the most significant association observed in the emotional role, social functioning, and physical role domains. The results also showed that 'Stable-high' loneliness had the worst HRQoL outcomes. The current study underscores the importance of considering the dynamic nature of loneliness over time when examining its association with HRQoL. Our findings highlight the importance of social well-being for middle-aged and older women's physical and mental health and indicate that loneliness poses a threat to poor HRQoL not only for those who experience 'Stable-high' loneliness but also for 'Stable medium' and 'Increasing' trends of loneliness. Furthermore, the majority of the sample reported 'Increasing' loneliness. This suggests that loneliness tends to rise throughout adulthood for most individuals, which has significant implications for health-related outcomes in this population. These findings highlight the need for targeted interventions aimed at addressing loneliness and its adverse effects on various dimensions of HRQoL, particularly in mental health.

CHAPTER FIVE: Loneliness and all-cause mortality in middle-aged Australian women: A causal inference analysis of longitudinal data

5.1. Preface to the chapter

This thesis has outlined the health consequences of loneliness, highlighting its association with numerous adverse health outcomes. Similarly, mortality has also been linked to loneliness. While observational research suggests a link between loneliness and mortality, addressing biases such as time-varying confounding is essential to understanding the true nature of this relationship. To address this gap, the current chapter presents findings from a submitted paper under review that aims to examine the causal effect of loneliness on mortality among older Australian women. Data were utilised from the Australian Longitudinal Study on Women's Health (ALSWH), which covers over 18 years. To estimate the causal effect of loneliness, marginal structural models employing propensity scores were used and an analysis using a counterfactual framework was performed. The adjusted risk of death associated with 1) the total number of loneliness waves (loneliness persistency) and 2) the consecutive number of loneliness waves (loneliness chronicity) is presented using relative risks and risk differences. This chapter addresses the independent effect of loneliness on health. By investigating both the persistency and chronicity of loneliness over an extended period, this study provides a nuanced understanding of how loneliness affects mortality risk among Australian women. This study addresses aim #3 of this thesis as described in **Chapter 2**. Dissemination of this research and the authors' contributions to this paper are described below.

5.2. Research dissemination

The research presented in this chapter has been disseminated as follows:

Paper submitted to a journal

Journal: BMJ Medicine

5.3. Author attribution statement

I, Neta HaGani, was responsible for designing the study, obtaining the data, conducting the analysis and interpretation of the results, writing the drafts of the manuscript and submitting the manuscript. My co-authors, P. Clare, D. Merom, B. Smith & D. Ding helped

conceptualise and design the study and developed the study protocol; P. Clare supervised and assisted in conducting the data analysis. All authors have reviewed, edited, and approved the final version of the manuscript.

5.4. Manuscript

Loneliness and all-cause mortality in middle-aged Australian women: A causal inference analysis of longitudinal data

ABSTRACT

Objective: Loneliness has been linked to a broad range of adverse health outcomes, including early mortality. However, the causal effect of loneliness on mortality or other health outcomes remains unexplored. This study aimed to examine the causal effects of loneliness on mortality among middle-aged Australian women.

Design: We employed targeted maximum likelihood estimations, a causal inference method, to analyse the causal relationship between loneliness and all-cause mortality over 18 years.

Participants: a population-based sample of Australian women aged 45 and older.

Main outcome measures: The adjusted risk of death associated with 1) the total number of loneliness waves (loneliness persistency) and 2) the consecutive number of loneliness waves (loneliness chronicity) was presented using relative risks (RRs) and risk differences (RDs) with 99.5% confidence intervals (CIs).

Results: The association between the number of waves of reported loneliness and mortality risk showed a dose-dependent pattern. Compared with those who did not report loneliness in any wave, those who reported loneliness at two, four and six waves had an incrementally higher risk of dying during the follow-up period [RR (99.5%CI) = 1.49 (1.26, 1.75), 2.18 (1.79, 2.66), 3.15 (2.35, 4.23)], respectively. The RDs showed a similar trend to the RRs with higher excess mortality among those who reported experiencing loneliness for six waves compared to those who did not report loneliness at all [10.86% (99.5%CI: 10.58%, 11.15%)]. Similar trends were found when loneliness was experienced across consecutive waves.

Conclusions: Loneliness is causally linked to mortality risk with a dose-dependent relationship. Acknowledging loneliness as an independent health risk underscores the importance of screening for loneliness and incorporating public health interventions into healthcare practices.

Protocol registration: <https://doi.org/10.17605/OSF.IO/H9RZN>

Keywords: loneliness, mortality, older adults, women's health, longitudinal analysis, causal inference

What is already known on this topic

- Loneliness has been recognised as a public health concern worldwide due to the elevated risk for multiple health outcomes.
- Findings are mixed as to whether loneliness is independently associated with mortality risk after adjusting for various potential confounders.
- Most studies to date did not account for time-varying confounding and no study attempted to examine the causal relationship between loneliness and mortality.

What this study adds

- Loneliness is causally linked to the risk of mortality regardless of physical and mental health status.
- There appears to be a dose-dependent relationship between the persistency of loneliness and the risk of mortality.
- Experiencing loneliness over an extended period poses a risk for mortality, whether or not the experience has been reported in consecutive survey measures.

BACKGROUND

Loneliness is often defined as the unpleasant emotions resulting from the gap between the desired levels of social connectedness and one's actual experiences (1). The prevalence of loneliness varies greatly by country and across the lifespan, with young adults and elderly people often identified as being at risk (2). Loneliness can manifest episodically, which is a common human experience that can be understood as a prompt to connect socially, or chronically (persisting over an extended period), which is more problematic (3). According to a recent Australian study conducted over five years, 21% of adults experienced episodic loneliness while 13% experienced chronic loneliness, defined as being lonely for two or more consecutive years (4).

Loneliness has been recognised as a public health priority worldwide (5) due to its association with numerous adverse physical and mental health outcomes such as heart disease, stroke, dementia, depression, anxiety, and suicide ideation (5, 6). In addition, several meta-analyses have linked loneliness to all-cause mortality with an estimated increased risk ranging from 14% to 26% (7, 8). However, such associations obtained from observational studies are often subject to biases (7), particularly confounding bias, as people who are lonely

tend to be more likely to experience other risk factors, such as socioeconomic disadvantage, lifestyle risk factors and poor health (9, 10).

Indeed, across studies, findings are mixed as to whether loneliness is independently associated with mortality risk after adjusting for initial health status, health behaviours, depression, and social isolation (11), with a significant attenuation of effects in models that fully adjust for these potential confounders (8, 12). According to a recent meta-analysis among older adults, loneliness was not significantly associated with mortality in the adjusted models in 18 of the 28 studies included (13). Such mixed findings suggest that biases, such as confounding or selection bias, are affecting the risk estimates. A bias of particular relevance is time-varying confounding, where the confounder for an association between an exposure and an outcome is affected by previous exposures (e.g., current health behaviours and status, which affect future mortality risk, may be a result of previous loneliness) (14). Such bias needs to be addressed beyond conventional statistical adjustment of confounders (15).

An established method to address time-varying confounding is the inverse probability of the treatment-weighted marginal structural model (16). The application of these causal inference methods can potentially provide novel insights into the causal effects of loneliness on health and mortality, but this has not yet been explored. Considering that the experience of loneliness could be situational and may fluctuate across time, measuring loneliness repeatedly over an extended period can more accurately capture the persistency and chronicity of this exposure. However, few studies have examined long-term patterns of loneliness and health-related outcomes (17, 18). It should be added that most studies concerning loneliness and mortality have been conducted in Europe and North America (7, 8), with limited evidence from other contexts.

Therefore, this study aims to address the aforementioned gaps in evidence by examining the causal effect of loneliness on mortality among older Australian women. Specifically, we hypothesised that the risk of mortality increases as the number of occasions of loneliness increases, and that the association is stronger when we consider consecutive occasions of loneliness (i.e., chronic loneliness). We focused on middle-aged and older women because some evidence suggests that women are at a higher risk of experiencing loneliness compared to men (19-21). Additionally, women may be more likely to experience risk factors and circumstances that predispose them to experience loneliness, such as

depression, caregiving responsibilities, and longer life spans (hence more likely to outlive their partners (22-24).

METHODS

The reporting of this study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines (**Appendix 1**).

Patient and Public Involvement

Patients and the public were not included in the design and execution phases of the current study. Nevertheless, we plan to actively involve the public in the dissemination of the results through media outreach, social media campaigns, newsletters, and public lectures and presentations.

Study Population

We used data from the Australian Longitudinal Study of Women's Health (ALSWH) 1946-51 cohort. Data were collected every three years, commencing in 1996 (baseline). Participants were originally selected from the national public health insurance database (Medicare) to represent Australian citizens and permanent residents. Sampling from the population was random within each age group, except that women from rural and remote areas were sampled at twice the rate compared with women in urban areas. The response rates at recruitment ranged from 53% to 56%. Ethical approval was received from the Human Research Ethics Committees (HRECs) at the Universities of Newcastle and Queensland (Approval No. H-076-0795 and 2004000224). Prior to their participation, all participants provided written informed consent (25, 26). For the current study, we excluded participants with a history of life-threatening diseases such as heart disease (n = 292), stroke (n = 113), or cancer (n = 597) to avoid reverse causation. The final analytical sample included 11,412 women aged 45 years and above at baseline (participants flow chart is in **Table S4.2**).

Measures

Exposure variable

Loneliness was assessed over 15 years from wave 3 (the year 2001 when participants were aged 48 to 55 years) to wave 8 (the year 2016 when participants were aged 64 to 71 years) and was measured by a single item "I felt lonely" adapted from the Centre for Epidemiologic Studies Depression Scale (CES-D) (27). The response options for this item were on a 4-point

scale: 1. 'Rarely or none of the time (less than 1 day)', 2. 'Some or a little of the time (1-2 days)', 3. 'Occasionally or a moderate amount of time (3-4 days)', 4. 'Most or all of the time (5-7 days)'. These responses were further categorised into a binary variable, with 0 = levels 1-2 on the original scale (i.e., not lonely), and 1 = levels 3-4 on the original scale (i.e., lonely). The loneliness one-item has been found to have concurrent validity with established scales such as the UCLA Loneliness Scale and the de Jong Gierveld Loneliness Scale (28, 29).

Outcome variable

Time of death over the 18-year duration of the study. All-cause mortality was obtained from the linked National Death Index. The outcome was defined as a binary variable of whether death occurred in the period since the completion of the previous wave and up to the end of the study period (31st December 2021). For example, a participant who completed the survey at wave 4 but subsequently died was coded as having died at wave 5 and was censored thereafter. The outcome was obtained from wave 3 (January 2001 – July 2002) and up to the end of the study period (31st December 2021).

Confounders

Time-varying confounders were drawn from waves 2-7 (to ensure that confounders occurred before exposure) and included age; marital status (partnered, not partnered, widowed); area-level socioeconomic status using the Index of Relative Socio-Economic Disadvantage (IRSD) (30); geographical remoteness based on the postcode-level Accessibility-Remoteness Index of Australia Plus (ARIA+; major city, regional, remote) (31); employment status (not employed, employed); living alone (no, yes); health related quality of life using the eight dimensions and two main components (physical and mental) of the SF-36 health-related quality of life questionnaire on a scale of 0-100 (higher score indicates a higher reported quality of life); risky alcohol consumption (having more than 10 standard drinks per week or more than four standard drinks a day as per Australian guidelines) (32); smoking (never smoked, ex-smoker, currently smoking); body mass index [BMI: underweight ($<18.5 \text{ kg/m}^2$), healthy ($18.5 < \text{BMI} < 24.9 \text{ kg/m}^2$), overweight ($25.0 \leq \text{BMI} \leq 29.9 \text{ kg/m}^2$), obesity ($\geq 30.0 \text{ kg/m}^2$)]; history of ever being diagnosed with anxiety or depression; stress measured by the Perceived Stress Questionnaire (mean score of 10 items ranging from 0-4) (33); and the Medical Outcomes Study (MOS) Social Support Survey measuring the frequency of receiving support from others on a scale of 1-5 (higher score reflecting more support).

Baseline time-constant variables were drawn from waves 1-2 of the study and included country of birth (Australia, other); language spoken at home (English, European, Asian, other); and the highest level of education completed (high school or less, tertiary not university, college/university). More details on the confounding variables and categorisation process are in **Appendix 2**.

Data analysis

To estimate the effect of loneliness on mortality, we used marginal structural models. These models use propensity scores to construct weighted exposure or outcome models which serve as a consistent estimator of causal effects. To estimate the causal effect of loneliness in waves 3-8 on mortality, a counterfactual framework analysis was conducted. That is, each participant had several ‘potential outcomes’, related to the different exposure scenarios, however, only one of those outcomes is observed (related to their actual exposure), while the remainder are counterfactual. In the counterfactual framework, all available information is used to estimate the expected mean outcome if all participants follow the same pattern of exposure. These expected outcomes can then be compared, in the same way as the between-group comparisons in a randomised controlled trial. The analyses were conducted using targeted maximum likelihood estimation (TMLE) [19]. This method aims to mitigate the impact of time-varying confounding in the association between loneliness and mortality and to manage the influence of past exposure on confounding variables. The initial step involved estimating models for the likelihood of exposure (propensity) and the anticipated outcome. Subsequently, these initial estimates were employed to refine the outcome model. This refined model was then assessed across various counterfactual exposure values, yielding an estimate of the expected outcome under those counterfactual exposure patterns. The directed acyclic graphs (DAGs) of the causal relationships over time are in **Figures S3.1-S3.2**.

In addition, assuming conditional exchangeability, positivity, consistency, and no interference, the estimates derived from TMLE were constructed as causal effects. The initial models within TMLE were computed using an ensemble machine learning algorithm (Super Learner) that incorporates adaptive and flexible algorithms. These algorithms are capable of capturing intricate, non-linear relationships, including interactions and polynomial effects, without explicitly defining those effects. The final refined outcome model was executed using General Linear Models (GLMs; For additional details see **Appendix 3**).

We tested the association between loneliness and mortality using 1) the total number of waves experiencing loneliness, regardless of ordering, as a proxy for the persistency of the loneliness experience over the 15 years of exposure and 2) the consecutive waves where participants experienced loneliness (number of consecutive waves that participants reported being lonely) as a proxy for the chronicity of loneliness. The results were significant if they met the threshold of $p < 0.005$ to avoid type I errors (34). Results are presented as incidence rates, relative risks and risk differences and are reported with 99.5% confidence intervals. We conducted all analyses using longitudinal TMLE (LTMLE), via the 'ltmle' program in R 4.2.1 (35). The analysis code is available at <https://www.philipclare.com/code/alswh/>. More details on the model's estimands are in **Appendix 3**.

Sensitivity analysis

We conducted an E-value analysis to assess the potential impact of unmeasured confounding. In addition, due to a lack of evidence for the cutoff point of the loneliness measure, we conducted sensitivity analyses, using alternative cut-points as follows:

- 1) The lowest loneliness level cut point: 'Rarely or none of the time (less than 1 day)', versus the three upper loneliness levels: 'Some or a little of the time (1-2 days)', 'Occasionally or a moderate amount of time (3-4 days)', or 'Most or all of the time (5-7 days)'.
- 2) The highest loneliness level cut point: 'Most or all of the time (5-7 days)' versus the three lower loneliness levels: 'Rarely or none of the time (less than 1 day)', 'Some or a little of the time (1-2 days)', or 'Occasionally or a moderate amount of time (3-4 days)'.

Missing data

Because ignoring missing information on both the outcome and exposure variables can introduce bias (36), we handled missing data using multiple imputations and inverse probability of censoring weights. There was 25% missing information across study waves. We imputed the data using chained equations with the data in long form, using the R package 'mice' (37). To handle possible complexity in the data, we imputed all variables using random forests, from the package 'ranger'. Based on the proportion of missing information in the data, we used $M = 30$ imputations (38). Further information on missing data is in **Appendix 4**.

RESULTS

The baseline characteristics (waves 1-2) of the study participants are presented in **Table 1**. The average age was 49.5 years (SD = 1.5), and the majority of participants were married or partnered (83.0%), employed (78.9%), and had a high school education (65.8%). Most participants were Australian-born (76.8%) and spoke English at home (94.6%); 10.7% reported experiencing loneliness 3-7 days a week. The mean MOS social support score was 3.8 (SD = 1.0, Range = 1-5), which can be interpreted as having support ‘most of the time’. The mean SF-36 Physical Component of quality-of-life score was 49.1 (SD = 9.2, Range = 5.5-72.3) and the mean Mental Component score was 47.9 (SD = 12.3, Range = 0-74.6). These scores were found to be similar to another Australian population-based cohort study (39). The demographic characteristics of respondents have been compared with those of women of the same age in the Australian population, using data from the Australian Census. ALSWH participants were more likely to be Australian-born, married, have tertiary education, be employed and work longer hours compared to the general population. However, some of these differences stemmed from variations in the survey questions and the sampling criteria (40).

Figures 1-2 present the incidence risk of mortality according to the overall number of waves of being lonely and the consecutive number of waves of being lonely. The incidence risks and 99.5% CIs are presented in **Table S5.1**.

As shown in **Figure 1**, there was a positive association between the number of waves of reported loneliness and mortality risk that demonstrated a dose-dependent pattern. For example, compared with those who did not report loneliness in any wave, those who reported loneliness in two, four and six waves had an incrementally higher risk of dying during the follow-up period [RR (99.5%CI) = 1.49 (1.26, 1.75), 2.18 (1.79, 2.66), 3.15 (2.35, 4.23), respectively; **Table S5.2**]. The results on the absolute scale (risk difference) were consistent with the RRs in terms of the dose-dependent pattern. For example, compared with those who did not report loneliness at any wave, the risk differences for those who reported loneliness at two, four and six waves were RD (99.5%CI) = 2.46% (2.43%, 2.49%), 5.98% (5.87%, 6.08%), and 10.86% (10.58%, 11.15%) respectively (**Table S5.2**).

We also examined the effect of consecutive waves of loneliness on mortality (**Figure 2 and Table S5.2**). The association was similar to that between the total number of waves and mortality. Participants who reported consecutive loneliness across two, four and six

waves had incrementally higher risks of dying during the follow-up period [RR (99.5%CI) = 1.38 (1.19, 1.60), 1.89 (1.59, 2.26), 2.56 (1.98, 3.32), respectively; **Table S5.2**]. Consistent trends were found for the absolute risk of mortality. Compared with those who did not report loneliness at any wave, the risk difference for those who reported loneliness at two, four and six consecutive waves were RD (99.5%CI) = 2.13% (2.10%, 2.15%), 4.97% (4.88%, 5.06%), and 8.71% (8.49%, 8.94%) respectively (**Table S5.2**).

Sensitivity analysis

The sensitivity analysis examined the findings using variations in the thresholds for defining loneliness, as at least ‘some or a little of the time’ (1-2 days per week) and ‘most or all of the time’ (5 or more days per week). The results of the total number of waves show that using the lower loneliness cut point (1-2 days per week) attenuated the effect slightly but it was still consistent [e.g., RR = 2.72 (99.5%CI = 2.00, 3.70) when comparing a total of 6 vs 0 waves of reported loneliness]. Using a higher cut-point (5 or more days per week) strengthened the effect [e.g., RR = 4.14 (99.5%CI = 1.84, 9.31 for the same comparison of total 6 vs 0 waves of reported loneliness], but at the cost of more error, as demonstrated by wider CIs. Similar trends were found in the sensitivity analysis of consecutive waves of loneliness. Using the loneliness lower cut-point attenuated the effect [RR_(6 vs 0 waves) = 1.72 (99.5%1.46, 2.02)] and using a higher cut-point strengthened the effect [RR_(6 vs 0 waves) = 4.09 (99.5%1.26, 13.26)] (**Tables S5.3-S5.4 and Figures S5.1-S5.4**).

E-values were calculated to evaluate how robust the observed association between loneliness and mortality is to potential unmeasured confounding (**Table S5.5**). The results indicate that to alter the conclusions regarding the estimated effect of the effect of 1- or 2-waves of loneliness, an unmeasured confounder would need to have a moderate effect on loneliness and mortality (RR = 1.74 for 1 wave and RR = 2.34 for 2 waves), although only a relatively weak effect (RR = 1.45) would be required if the true effect of 1-wave of loneliness lies at the lower bound of the confidence interval. For 3 to 6 waves of loneliness, the confounder would need to have a strong effect on loneliness and mortality (greater than 3) to fully explain the observed association even if the true effect lies at the edge of the confidence interval.

Discussion

Based on 18 years of longitudinal data from a population-representative cohort of Australian women, we found a strong dose-dependent association between loneliness and all-cause mortality. Using causal inference modelling, this is the first study to our knowledge to provide causal evidence for the association between loneliness and any health-related outcomes. Our findings are consistent with previous studies and meta-analyses that linked loneliness with all-cause mortality (7, 41). The current study suggests that loneliness functions as a significant social determinant of health and can become life-threatening if experienced over an extended period. Although there is a vast literature regarding the association between loneliness and mortality (7), there are currently no studies that examine the incremental increase in mortality risk according to the number of years of experiencing loneliness. Our findings identified a dose-dependent association suggesting that the more persistent or chronic one's experience of loneliness is, the higher the risk for mortality.

In the current study, we distinguished between persistent and chronic loneliness and found their associations with mortality to be comparable and strong (albeit slightly larger magnitude for persistent loneliness). Only one previous study to our knowledge examined the association between chronic loneliness and mortality (42). This study defined chronic loneliness as experiencing loneliness over four consecutive years. Findings from this study are similar to ours regarding the magnitude of association. While there is a consensus in the field about chronic loneliness being the most detrimental to health, our results highlight that in addition to chronic loneliness, the persistency of loneliness, whether or not experienced continuously (measured by consecutive survey waves as a proxy) can also be harmful.

Loneliness has been linked to higher levels of stress and alterations in immune function, particularly with inflammation (43). These changes are linked with autoimmune disorders, cardiovascular diseases, and certain types of cancer (44, 45), although not usually with the magnitude of the effect seen here. Although participants with pre-existing life-threatening illnesses such as cancer and cardiovascular diseases were excluded from the study to avoid reverse causation, the study spanned over 18 years. During this time, participants could have developed these illnesses, potentially with loneliness as a contributing factor.

In addition, loneliness has been associated with unhealthy behaviours such as smoking, unhealthy diet, and physical inactivity, which are known risk factors for premature mortality (46, 47). Finally, those experiencing loneliness may lack the necessary support system that prevents a health condition from deteriorating, thereby contributing to impaired

health and early mortality (48, 49). Such a relationship between loneliness and health may be considered a vicious cycle as individuals with chronic illnesses might subsequently experience more loneliness due to physical limitations that impede their ability to engage in social activities (50). In the current study, applying TMLE allows us to assess the causal relationship between loneliness and mortality while accounting for previous physical and mental health status, and sociodemographic and behavioural risk factors. Therefore, our findings may imply that loneliness has an underlying physiological effect (51). There is evidence that loneliness may trigger a maladaptive biological stress response that can create further social withdrawal, which in turn, leads to more loneliness, stress and poor health (52). This underlying risk may not only lead to a higher incidence of disease, potentially resulting in increased mortality but it can also be associated with poorer prognosis among individuals who get ill which may also explain the higher risk of mortality among lonely individuals (53). Our findings may be explained by these mechanisms and lend support for considering loneliness as an important risk factor for adverse health outcomes.

Strengths and weaknesses of the study

Our study has a few limitations. First, using a one-item direct measure of loneliness has been previously criticised as it may be subject to reporting bias due to stigma and different interpretations of what loneliness means to the respondent. The loneliness measure used in this study was previously found to have strong validity and reliability among Australian samples (54, 55) and was strongly correlated with other common scale-based loneliness measures (29). Second, since the data were collected every three years, it is possible that the loneliness experience reported in the survey may not reflect the overall exposure during the years between surveys. However, our analysis uses information from each wave to estimate the effect of long-term loneliness, and while it is likely this long-term loneliness is at least somewhat intermittent, being lonely at all exposure waves still suggests a pattern of recurring, persistent loneliness. Third, although we adjusted for a variety of sociodemographic, health and mental health confounders that were selected apriori based on the DAG and the literature, there is still a risk of residual confounding due to unmeasured and/or insufficiently measured confounders. The E-value analysis suggests that only very strong unmeasured confounding would substantively change the conclusions of the paper (**Table S5.5**), highlighting the robustness of the findings. Finally, the linkage data to the National Death Index did not include the causes of death. Despite these limitations, our

findings provide valuable insights into the causal relationship between loneliness and mortality using longitudinal data from 15 years.

Strengths and limitations in relation to other studies

There is evidence that some of the previous literature may have been subjected to bias due to insufficient adjustments for health and illnesses (8) and relying on the assessment of loneliness at one point in time (13), likely contributing to mixed findings regarding the effect of loneliness on mortality (11, 12). In the present study, we controlled for time-varying confounding and the effect of previous exposures, which revealed a more accurate effect of loneliness on mortality irrespective of confounders related to physical and health status. Our sensitivity analysis using alternative cut points for loneliness showed that the association with the risk of mortality remained robust.

Meaning of the study

Our findings show that loneliness is a significant risk factor and has a dose-dependent relationship with all-cause mortality among middle- and older-aged Australian women, regardless of their physical and mental health status. Our findings suggest that experiencing loneliness over an extended period poses a risk for mortality, whether or not the experience has been reported in consecutive survey waves. The causal association between loneliness and increased risk of mortality is a complex issue with significant implications for public health and healthcare delivery. Recognising loneliness as a critical social determinant of health is essential for developing targeted interventions and support systems to improve the well-being and longevity of women. Effective interventions are needed among the general population, particularly for at-risk populations such as people with chronic illnesses. Previous systematic reviews found that social interventions can be effective in increasing social support and reducing loneliness (56, 57). Actions should be taken to address loneliness as a public health priority at individual, institutional, social and environmental levels to reduce the preventable disease burden and early deaths (58).

Future research

Given that most of the existing literature on the health outcomes of loneliness relies on either cross-sectional data or longitudinal data that measured loneliness at one-time point, there is a need for more longitudinal studies with repeated measures of loneliness over time. Additionally, future loneliness research should employ causal inference approaches that

control for complex confounding and selection biases. Finally, future studies should consider examining cause-specific mortality as well as more immediate health outcomes that could potentially underpin the mechanisms for the observed link between loneliness and mortality.

Ethics statements

Ethical approval: Not required

Data availability statement: No additional data is available.

Footnotes

Contributors: NH, PC, DM, BS and DD contributed to the conception and design of the study. NH and PC developed the study protocol. NH and DD drafted the manuscript. All authors provided critical input during the writing and revision of the paper. NH and DD acquired the data. NH and PC conducted the analysis. PC supervised the analysis. DD supervised the study. NH and DD are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Copyright: The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive license (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ editions and any other BMJ PGL products and sublicences such use and exploit all subsidiary rights, as set out in our license.

Transparency declaration: The lead authors (DD and NH) affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Conflict of interest: All authors have completed the [Unified Competing Interest form](#) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

Funding: Ding Ding is funded by the National Health and Medical Research Council Emerging Leader Fellowship (award No. 2009254).

5.5. References

1. de Jong-Gierveld J. Developing and testing a model of loneliness. *J Pers Soc Psychol.* 1987;53(1):119-28.
2. Surkalim DL, Luo M, Eres R, Gebel K, van Buskirk J, Bauman A, Ding D. The prevalence of loneliness across 113 countries: systematic review and meta-analysis. *BMJ.* 2022;376:e067068.
3. de Jong Gierveld J, Raadschelders J. Types of loneliness. In: Peplau LA, Perlman D, editors. *Loneliness: A Sourcebook of Current Theory, Research and Therapy* New York: Wiley-Interscience; 1982. p. 105-19.
4. Lim MH, Manera KE, Owen KB, Phongsavan P, Smith BJ. The prevalence of chronic and episodic loneliness and social isolation from a longitudinal survey. *Sci Rep.* 2023;13(1):12453.
5. National Academies of Sciences Engineering & Medicine, Division of Behavioral Social Sciences Education Health & Medicine, Division Board on Behavioral Cognitive Sensory Sciences, Board on Health Sciences Policy, Committee on the Health Medical, Dimensions of Social Isolation Loneliness in Older Adults. *Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System.* Washington (DC): National Academies Press (US); 2020.
6. Courtin E, Knapp M. Social isolation, loneliness and health in old age: a scoping review. *Health Soc Care Community.* 2017;25(3):799-812.
7. Rico-Urbe LA, Caballero FF, Martín-María N, Cabello M, Ayuso-Mateos JL, Miret M. Association of loneliness with all-cause mortality: A meta-analysis. *PloS One.* 2018;13(1):e0190033.
8. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect Psychol Sci.* 2015;10(2):227-37.
9. Kung CSJ, Kunz JS, Shields MA. Economic Aspects of Loneliness in Australia. *Aust Econ Rev.* 2021;54(1):147-63.

10. Hawkley LC. Loneliness and health. *Nat Rev Dis Primers*. 2022;8(1):22.
11. Ong AD, Uchino BN, Wethington E. Loneliness and Health in Older Adults: A Mini-Review and Synthesis. *Gerontol*. 2016;62(4):443-9.
12. Hakulinen C, Pulkki-Råback L, Virtanen M, Jokela M, Kivimäki M, Elovainio M. Social isolation and loneliness as risk factors for myocardial infarction, stroke and mortality: UK Biobank cohort study of 479 054 men and women. *Heart*. 2018;104(18):1536-42.
13. Schutter N, Holwerda TJ, Comijs HC, Stek ML, Peen J, Dekker JJM. Loneliness, social network size and mortality in older adults: a meta-analysis. *Eur J Ageing*. 2022;19(4):1057-76.
14. Daniel RM, Cousens SN, De Stavola BL, Kenward MG, Sterne JA. Methods for dealing with time-dependent confounding. *Stat Med*. 2013;32(9):1584-618.
15. Suarez D, Borràs R, Basagaña X. Differences Between Marginal Structural Models and Conventional Models in Their Exposure Effect Estimates: A Systematic Review. *Epidemiol*. 2011;22(4).
16. Clare PJ, Dobbins TA, Mattick RP. Causal models adjusting for time-varying confounding—a systematic review of the literature. *Int J Epidemiol*. 2019;48(1):254-65.
17. Stessman J, Rottenberg Y, Shimshilashvili I, Ein-Mor E, Jacobs JM. Loneliness, Health, and Longevity. *J Gerontol A-Biol*. 2014;69(6):744-50.
18. Ward M, May P, Normand C, Kenny RA, Nolan A. Mortality risk associated with combinations of loneliness and social isolation. Findings from The Irish Longitudinal Study on Ageing (TILDA). *Age Aging*. 2021;50(4):1329-35.
19. Dong X, Chen R. Gender differences in the experience of loneliness in U.S. Chinese older adults. *Journal of women & aging*. 2017;29(2):115-25.
20. Pagan R. Gender and Age Differences in Loneliness: Evidence for People without and with Disabilities. *Int J Environ Res Public Health*. 2020;17(24).

21. Nicolaisen M, Thorsen K, Tjønnhøj A, Development H. Gender Differences in Loneliness Over Time: A 15-Year Longitudinal Study of Men and Women in the Second Part of Life. 2023.
22. McQuaid RJ, Cox SM, Ogunlana A, Jaworska NJ. The burden of loneliness: Implications of the social determinants of health during COVID-19. 2021;296:113648.
23. Dahlberg L, Andersson L, McKee KJ, Lennartsson C. Predictors of loneliness among older women and men in Sweden: A national longitudinal study. *Aging Ment Health*. 2015;19(5):409-17.
24. World Health Organization. Mental health of older adults- fact sheets 2017 [updated 20 October 2023. Available from: <https://www.who.int/news-room/fact-sheets/detail/mental-health-of-older-adults#:~:text=Mental%20health%20and%20well-being%20are%20as%20important%20in,60%20and%20over%20suffer%20from%20a%20mental%20disorder.>
25. Brown WJ, Bryson L, Byles JE, Dobson AJ, Lee C, Mishra G, Schofield M. Women's Health Australia: Recruitment for a National Longitudinal Cohort Study. *Women Health*. 1999;28(1):23-40.
26. Dobson AJ, Hockey R, Brown WJ, Byles JE, Loxton DJ, McLaughlin D, et al. Cohort Profile Update: Australian Longitudinal Study on Women's Health. *Int J Epidemiol*. 2015;44(5):1547-f.
27. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Appl Psych Meas*. 1977;1:385-401.
28. Peplau L, Perlman, D, Russell, Daniel. The measurement of loneliness. In: Peplau L, Perlman, D, editor. *Loneliness: A Sourcebook of Current Theory, Research and Theory*: John Wiley & Sons; 1982. p. 81-104.
29. Nicolaisen M, Thorsen K. Who are lonely? Loneliness in different age groups (18-81 years old), using two measures of loneliness. *Int J Aging Hum Dev*. 2014;78(3):229-57.
30. Australian Bureau of Statistics. Technical Paper: Socio-Economic Indexes for Areas (SEIFA). 2016.

31. Australian Bureau of Statistics. The Australian statistical geography standard (ASGS) remoteness structure. 2018.
32. Australian Government National Health and Medical Research Council. Australian guidelines to reduce health risks from drinking alcohol 2020.
33. Bell S, Lee C. Development of the Perceived Stress Questionnaire for Young Women. *Psychol Health Med*. 2002;7(2):189-201.
34. Benjamin DJ, Berger JO, Johannesson M, Nosek BA, Wagenmakers EJ, Berk R, et al. Redefine statistical significance. *Nat Hum Behav*. 2018;2(1):6-10.
35. Lendle SD, Schwab J, Petersen ML, van der Laan MJ. ltmle: An R Package Implementing Targeted Minimum Loss-Based Estimation for Longitudinal Data. *J Stat Softw*. 2017;81(1):1-21.
36. Hughes RA, Heron J, Sterne JAC, Tilling K. Accounting for missing data in statistical analyses: multiple imputation is not always the answer. *Int J Epidemiol*. 2019;48(4):1294-304.
37. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *J Stat Softw*. 2011;45(3):1-67.
38. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. *Prevention Science*. 2007;8(3):206-13.
39. Lins L, Carvalho FM. SF-36 total score as a single measure of health-related quality of life: Scoping review. *SAGE Open Med*. 2016;4:2050312116671725.
40. Australian Longitudinal Study on Women's Health. Comparison of the ALSWH cohorts with women of the same ages in the 2011 Census. In: Technical Report No. 36. 107-135.; 2013.
41. Beller J. Loneliness and mortality: The moderating effect of positive affect. *Appl Psychol Health Well Being*. 2023;15(1):49-65.

42. Shiovitz-Ezra S, Ayalon L. Situational versus chronic loneliness as risk factors for all-cause mortality. *Int Psychogeriatr*. 2010;22(3):455-62.
43. Smith KJ, Gavey S, Riddell NE, Kontari P, Victor C. The association between loneliness, social isolation and inflammation: A systematic review and meta-analysis. *Neurosci Biobehav R*. 2020;112:519-41.
44. Kraav S-L, Lehto SM, Kauhanen J, Hantunen S, Tolmunen T. Loneliness and social isolation increase cancer incidence in a cohort of Finnish middle-aged men. A longitudinal study. *Psy Res*. 2021;299:113868.
45. Pourriyahi H, Yazdanpanah N, Saghazadeh A, Rezaei N. Loneliness: An Immunometabolic Syndrome. *Int J Environ Res Public Health*. 2021;18(22):12162.
46. Philip KEJ, Bu F, Polkey MI, Brown J, Steptoe A, Hopkinson NS, Fancourt D. Relationship of smoking with current and future social isolation and loneliness: 12-year follow-up of older adults in England. *Lancet Reg Health Eur*. 2022;14.
47. Hanna K, Cross J, Nicholls A, Gallegos D. The association between loneliness or social isolation and food and eating behaviours: A scoping review. *Appetite*. 2023;191:107051.
48. McFarlane WR. Family Interventions for Schizophrenia and the Psychoses: A Review. *Fam Process*. 2016;55(3):460-82.
49. Spiers G, Matthews FE, Moffatt S, Barker RO, Jarvis H, Stow D, et al. Impact of social care supply on healthcare utilisation by older adults: a systematic review and meta-analysis. *Age Aging*. 2019;48(1):57-66.
50. Macdonald SJ, Deacon L, Nixon J, Akintola A, Gillingham A, Kent J, et al. 'The invisible enemy': disability, loneliness and isolation. *Dis Soc*. 2018;33(7):1138-59.
51. Roddick CM, Chen FS. Effects of Chronic and State Loneliness on Heart Rate Variability in Women. *Ann Behav Med*. 2021;55(5):460-75.
52. Campagne DM. Stress and perceived social isolation (loneliness). *Arch Gerontol Geriatr*. 2019;82:192-9.

53. Christensen AV, Juel K, Ekholm O, Thrysøe L, Thorup CB, Borregaard B, et al. Significantly increased risk of all-cause mortality among cardiac patients feeling lonely. *Heart*. 2020;106(2):140-6.
54. Crosier T, Butterworth P. The Validity of the SF-36 in an Australian National Household Survey: Demonstrating the Applicability of the Household Income and Labour Dynamics in Australia (HILDA) Survey to Examination of Health Inequalities. 2004.
55. Powers J YA, Russell A. ALSWH Data Dictionary Supplement. Section 2 Core Survey Dataset 2.7 Psychosocial Variables. Center for Epidemiologic Studies Depression Scale - Shortened Version. Australian Longitudinal Study on Women's Health; 2002.
56. Veronese N, Galvano D, D'Antiga F, Vecchiato C, Furegon E, Allocco R, et al. Interventions for reducing loneliness: An umbrella review of intervention studies. *Health Soc Care Community*. 2021;29(5):e89-e96.
57. HaGani N, Surkalim DL, Clare PJ, Merom D, Smith BJ, Ding DJJNO. Health care utilization following interventions to improve social well-being: A systematic review and meta-analysis. *JAMA Netw Open*. 2023;6(6):e2321019-e.
58. Ding D, Eres R, Surkalim DL. A lonely planet: time to tackle loneliness as a public health issue. *Bmj*. 2022;377:o1464.

Tables

Table 1. Baseline characteristics of participants: The Australian Longitudinal Study of Women's Health (ALSWH) 1946-51 cohort (waves 1-2; n = 11,412)

Age (Mean, range), SD		49.5 (44.6-53.1)	1.5
		n	%
Education	High school or less	7441	65.8
	Vocational	2213	19.6
	College/ university	1655	14.6
Marital status	Partnered	9414	83.0
	Single/divorced/separated	1667	14.7
	Widowed	256	2.3
Location of residence	Major city	3794	33.4
	Regional	6987	61.6
	Remote	570	5.0
Currently employed	Yes	8880	78.9
Language spoken at home	English	10606	94.6
Born in Australia	Yes	8666	76.8
Living arrangement	Live alone	633	6.0
Smoking status	Never smoked	6102	57.0
	Ex-smoker	2838	26.5
	Currently smoking	1770	16.5
Body Mass Index (BMI)	Underweight (<18.5)	147	1.5
	Healthy (18.5 ≤ BMI ≤ 24.9)	4705	46.9
	Overweight (25.0 ≤ BMI ≤ 29.9)	3152	31.4
	Obesity (≥30.0)	2019	20.1
Depression (past 3 years) ¹	Yes	1936	17.0
Anxiety (past 3 years) ²	Yes	1536	13.5
Risky alcohol consumption (>10 drinks p/week) ³	Yes	1482	13.0
Loneliness	Yes	1142	10.7
		Mean (range)	SD
MOS Social support score ⁴		3.8 (1-5)	1.0
Stress score ⁵		0.6 (0-4)	0.5
Quality of life scales (SF-36) ⁴			
	Physical health	49.1 (5.5-72.3)	9.2
	Mental health	47.9 (0-74.6)	12.3

Note.

Abbreviations: MOS: Medical Outcomes Study, SD: Standard deviation

¹ Depression: In the past three years, have you been diagnosed or treated for depression

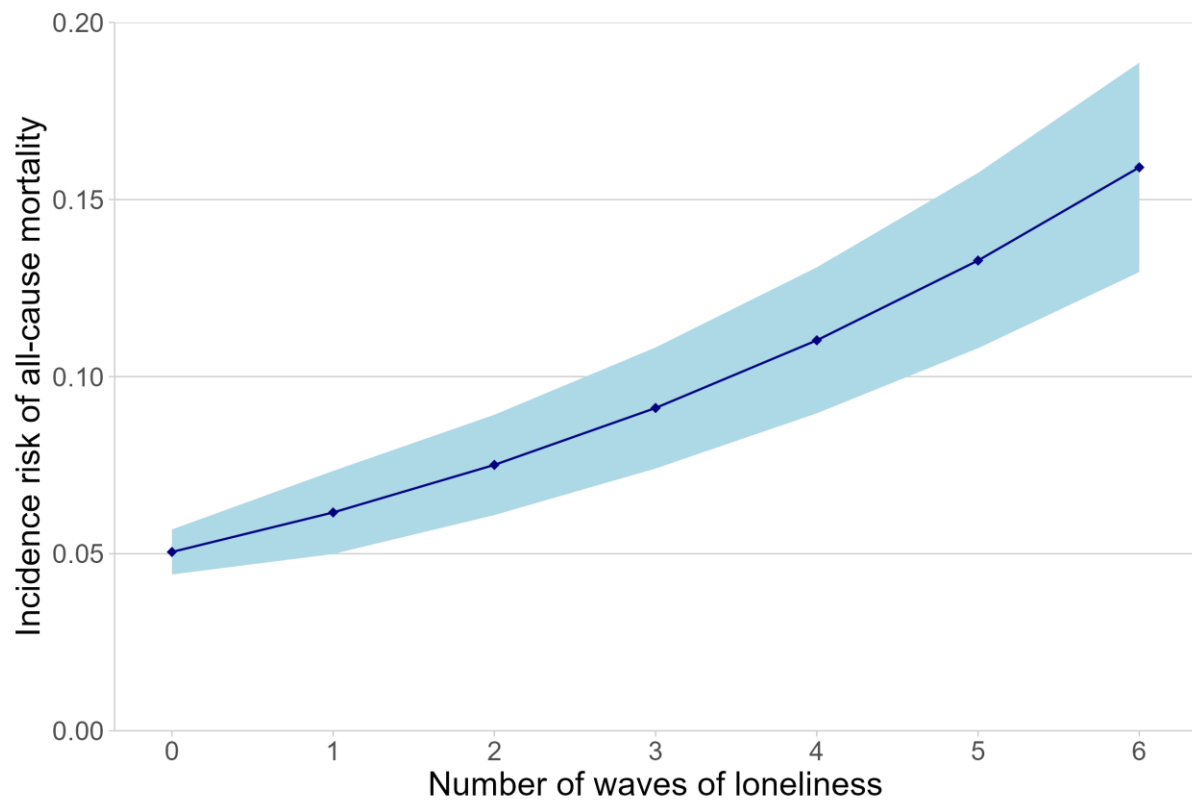
² Anxiety: In the past three years, have you been diagnosed or treated for anxiety

³ Risky drinking: consuming more than 10 standard drinks in a week or more than four standard drinks per day.

⁴ Higher scores represent better outcomes

⁵ Higher scores represent worse outcomes

Figure 1. Risk of all-cause mortality (1 Jan 2001 to 31 Dec 2021) according to the total number of waves of experiencing loneliness

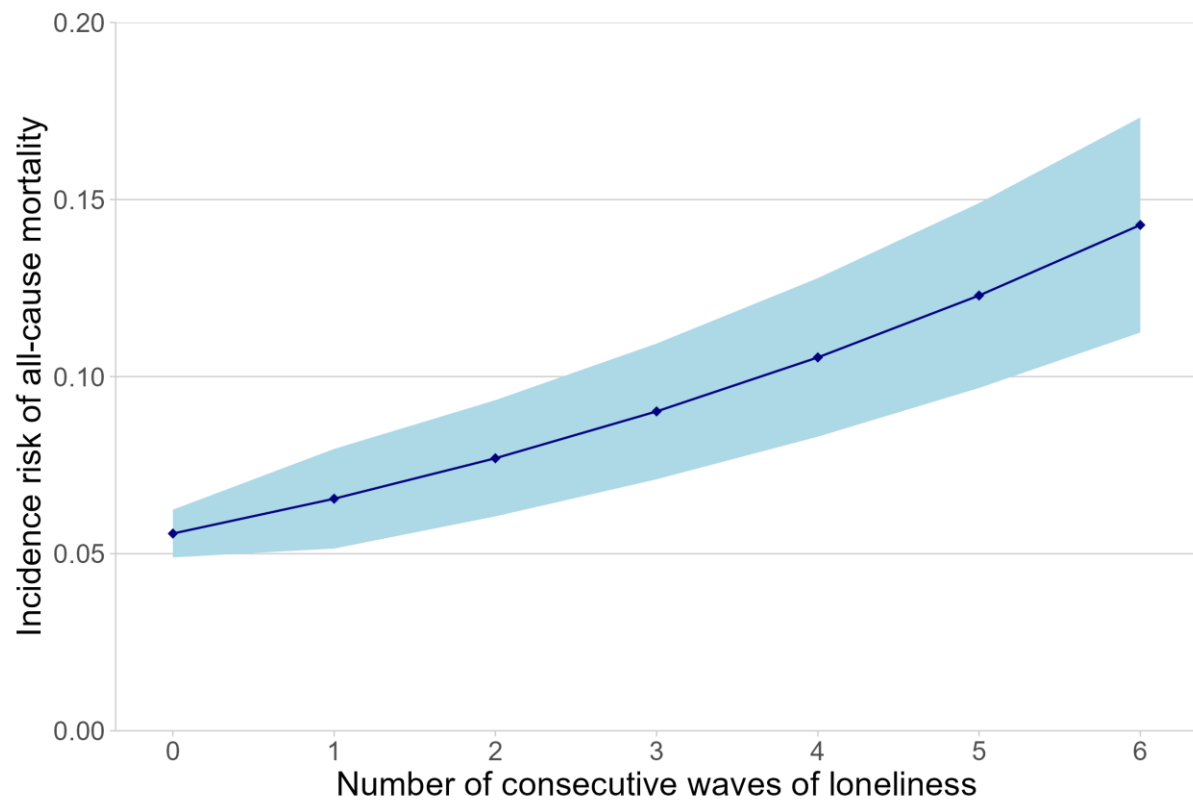


Note.

Gaps between waves were ~3 years apart

The shaded blue area refers to 99.5% Confidence Interval

Figure 2. All-cause mortality according to the number of consecutive waves of experiencing loneliness



Note.

Gaps between waves were ~3 years apart

The shaded blue area refers to 99.5% Confidence Interval

5.6. Appendices

Loneliness and all-cause mortality in middle-aged Australian women: A causal inference analysis of longitudinal data - Supplementary Appendices

Appendix 1. STROBE reporting

Table S1.1. Statement- Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7, Appendix 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	10, Table S4.2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10, Appendix 2, Figures S3.1-S3.2
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-10, Appendix 3
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10,

			Appendix 4
(d) If applicable, explain how loss to follow-up was addressed			10
(e) Describe any sensitivity analyses			10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6, Table S4.2
(b) Give reasons for non-participation at each stage			6
(c) Consider use of a flow diagram			Table S4.2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11, Table 1
(b) Indicate number of participants with missing data for each variable of interest			Appendix 4, Tables S4.1-S4.2, Figure S4.1
(c) Summarise follow-up time (eg, average and total amount)			Table S5.1
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-12, Figures 1-2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12, Appendix 5, Tables S5.1-S5.2
(b) Report category boundaries when continuous variables were categorized			11-12, Appendix 5
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			11-12, Tables S5.2-S5.4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12, Figures S5.1-S5.4, Tables S5.2-S5.4
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16, Table S5.5
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Appendix 2. Confounders

Time-varying confounders

Marital status

Participants were asked about their present marital status, with answers including married, de Facto/opposite sex, de Facto/same sex, separated, divorced, widowed, and single. These answers were recategorised into three categories: 1. partnered, 2. not partnered, 3. widowed.

Area-level socioeconomic status (SEIFA)

Participants' residential areas was examined using the Index of Relative Socio-Economic Disadvantage (IRSD) from the Socio-Economic Indexes for Areas (SEIFA) [1]. This index is a population-based measure that assesses the relative disadvantage of geographic regions, drawing on various socioeconomic factors such as household income, educational attainment, occupational status, housing costs (rent and mortgage payments), dwelling size, occupancy, and disability rates. The data is derived from the Australian Census and captures a comprehensive overview of the socio-economic conditions within each area [2].

Area remoteness

The geographical remoteness of participants was examined using the Accessibility-Remoteness Index of Australia Plus (ARIA+) [3], a classification system based on the Australian Statistical Geography Standard (ASGS) from the Australian Census [4]. Participants were categorised into one of three groups: major city, regional, or remote, based on their residential postcode.

Employment status

In all the waves except wave 2, participants were asked about their current main occupation, with possible responses include manager, professional, paraprofessional, trade, admin. assist, sales/service, machine operator, manual worker, never paid work, other. This question was recategorized to 0 = not employed, 1 = employed.

In wave 2 participants were asked two separate questions about their main and secondary occupations: “which of the following best describes your main and secondary occupation status (e.g. if you work part-time and do home duties, the one which takes the most time would be main and the other would be secondary), with potential responses include: no secondary occupation, full time, part time/casual, work without pay, home duties, studying,

unemployed-looking, unpaid voluntary, retired, unable to work. All unpaid occupations, i.e., home duties, studying, retirement etc., were considered as unpaid work and were recoded as 0 = unemployed. Full or part time were considered as paid work and were recoded as 1 = employed.

Living alone

In all the waves except wave 2, participants were asked to indicate whether they lived alone with potential answers 0 = no, 1 = yes. In wave 2 participants were asked how many people are living with them from the following: partner/spouse, children under 16 years, children 16-18 years, children over 18 years, parents, other adult relatives, other non-family members, with potential answers including: None, one, two, three or more. These answers were recoded to 0 = not live alone, 1 = live alone.

Health-related Quality of life

The health-related quality of life (HRQoL) of participants was measured by the SF-36 which includes Eight dimensions of health status that are measured using the self-reported SF-36 health-related quality of life questionnaire [5]. The dimensions are vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health. Each dimension is reported on a 0-100 scale with higher values indicating higher perceived health. These subscales were then combined to form two summary measures. 1. Physical Component Summary (PCS) including general health, physical functioning, role physical, and bodily pain subscales. and 2. the Mental Component Summary (MCS) including vitality, social functioning, role emotional, and mental health subscales.

Alcohol consumption

Consumption of alcohol was measured based on the revised Australian guidelines for alcohol consumption, released in 2020, which recommend that adults should drink no more than 10 standard drinks a week and no more than four standard drinks on any one day (and that pregnant women and those who are breastfeeding should not drink alcohol) [6]. Participants were asked to report how often they usually drink alcohol (on a scale of 'never' to 'every day'), how many drinks they usually have (on a scale of one to more than 9 per day) and how often they have five or more drinks of alcohol on one occasion (on a scale of 'never drink' to 'more than once a week'). These items formed the measures of risky drinking. If participants

reported the consumption of more than 10 standard drinks in a week or more than four standard drinks on any one day or if they consumed more than five drinks at a time, they were defined as being at ‘levels that increase the risk of alcohol-related disease or injury’.

Smoking

Participants were asked about their smoking status using the Australian Institute of Health and Welfare measure [7] with possible responses including never smoker, ex-smoker, irregular smoker, weekly smoker, and daily smoker. This question was recategorized to include Three categories: 0 = never smoked, 1 = ex-smoker, 2 = currently smoking.

BMI

The height and weight of participants were self-reported. Participants’ BMI was calculated and classified to Four levels according to the World Health Organization guidelines: 1 = underweight, $BMI < 18.5$, 2 = healthy weight $18.5 \leq BMI < 25$, 3 = Overweight, $25 \leq BMI < 30$, 4 = Obese, $30 \leq BMI$.

History of anxiety and depression diagnoses

Participants were asked about having been diagnosed or treated for a variety of physical and mental conditions in the past three years with possible responses 0 = no, 1 = yes. For the current study, we used the items asking about anxiety and depression diagnoses.

Stress

Stress was measured by the Perceived Stress Questionnaire, a scale for the assessment of stress that was developed specifically for the younger cohort of the ALSWH [8]. This measure is the average of 10 items on a scale from 0 = not at all stressed to 4 = extremely stressed, referring to different sources of stress such as health, work, money, relationships etc.

Social support

Social support from Survey 2 onwards using the 6-item Medical Outcomes Study (MOS) scale abbreviated form of the (19 items) MOS support index [5]. This scale measures domains of tangible support, affectionate support and positive social interaction, and emotional/informational support [9] on a scale between 1 = none of the time and 5 = all of the time (higher score reflects better support).

Baseline-time-constant variables

Country of birth

Participants were asked at baseline on their country of birth with possible responses include Australian born, other English-Speaking Background, Europe, Asia, Other. These responses were categorised to a binary variable (Australian born, not Australian-born).

Language spoken at home

Participants were asked at baseline on the language spoken at home with possible responses include English, Aust, English, Other, European, Asian, Other. From this, we created a variable with Four levels: English, European, Asian and other.

Level of education

Education was measured at baseline using the highest qualification completed by participants. Possible responses ranged between 'no formal qualification' through to 'higher university degree'. These were recategorised to a Three level variable: 1 = high school or less, 2 = tertiary not university, 3 = college/university.

References

- Australian Bureau of Statistics. Technical Paper: Socio-Economic Indexes for Areas (SEIFA). 2016.
- Pink B. Information paper: An introduction to Socio-Economic Indexes for Areas (SEIFA) 2006. Information paper: An introduction to Socio-Economic Indexes for Areas (SEIFA) 2006. Canberra: Australian Bureau of Statistics, Commonwealth of Australia; 2008. Contract No.: ABS Catalogue No. 2039.0.
- Glover JD, Tennant SK. Remote areas statistical geography in Australia: notes on the Accessibility/Remoteness Index for Australia (ARIA+ version): Public Health Information Development Unit, The University of Adelaide; 2003.
- Australian Bureau of Statistics. The Australian statistical geography standard (ASGS) remoteness structure. Australian Bureau of Statistics Canberra; 2018.
- Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). Conceptual framework and item selection. *Med Care*. 1992;30(6):473–483.
- Australian Government National Health and Medical Research Council. Australian guidelines to reduce health risks from drinking alcohol. 2020 [Available from: <https://www.nhmrc.gov.au/file/15923/download?token=t0Hrxdvq>].

- AIHW. (2021). Australian Burden of Disease Study 2018: Key findings. Canberra: Australian Institute of Health and Welfare. Retrieved from <https://www.aihw.gov.au/reports/burden-of-disease/burden-of-disease-study2018-key-findings/contents/about>
- Bell S, Lee C. Development of the Perceived Stress Questionnaire for Young Women. *Psychology, Health Med.* 2002;7(2):189-201.
- Holden, L., Lee, C., Hockey, R., Ware, R. S., & Dobson, A. J. (2014). Validation of the MOS Social Support Survey 6-item (MOS-SSS-6) measure with two large population-based samples of Australian women. *Qual Life Res*, 23(10), 2849- 2853. doi:10.1007/s11136-014-0741-5.

Appendix 3. model estimands

Counterfactuals

The main estimands focus on determining the expected outcomes for each counterfactual exposure scenario according to different treatment regimens (denoted as d), while considering observed confounding variables. Specifically, for each treatment regime (t), we aim to estimate the mean outcome $E_0(Y_d)$. By comparing intervention-specific means across different regimes (d and d'), we calculated additive effects that correspond to average treatment effects:

$$ATE = E_0(Y_d) - E_0(Y_{d'}) . \quad (C-1)$$

Initially, we assessed a fixed counterfactual exposure pattern, specifically examining the impact of being lonely consistently across all six waves of the exposure period compared to not being lonely in any of the six waves. Following this, we analysed dynamic treatment effects by considering age thresholds in the wave preceding each exposure:

$$d(A_t = 1) = age_{t-1} > \theta , \quad (C-2)$$

where θ serves as the age threshold.

We then assessed the counterfactual effect of experiencing loneliness upon reaching a particular age, but not before that age. Different age thresholds were examined, including 50, 55, 60, and 65 years. Considering the cohort's age range during the study, we incorporated the initial static exposure pattern into this framework by treating age thresholds at the minimum age in wave 2 (44.6 years) and the maximum age in wave 7 (68.4 years).

Targeted maximum likelihood estimation

Targeted Maximum Likelihood Estimation (TMLE) is an approach to estimate causal effects [1] that exhibits 'double robustness.' This stems from its utilisation of two-component models, while only necessitating the correct specification of one of the two.

In the TMLE process, the initial step involves estimating the expectation of the outcome $Q_n^0(A, L)$ using maximum likelihood [2, 3], Simultaneously, a conditional expectation of the exposure probability is estimated $g_n^0(A|L)$, which is comparable to the propensity score model employed in Inverse Probability Weighting (IPW) (formula C-4).

$$Q_n^0(A, L) = E(Y|A, L), \quad (C-3)$$

$$g_n^0(A|L) = \text{logit} \left(\frac{P(A|L)}{1-P(A|L)} \right), \quad (C-4)$$

The propensity model is utilized to construct a 'clever' covariate denoted as h :

$$h(A, L) = \frac{I(A=1)}{g_n^0(1|L)} - \frac{I(A=0)}{g_n^0(0|L)}. \quad (C-5)$$

The preliminary estimate of the outcome expectation $E(Y|A, L)$ is then updated by incorporating a function of both the initial estimate and the clever covariate:

$$Q_n^*(A, L) = Q_n^0(A, L) + \epsilon_n h(A, L), \quad (C-6)$$

In this context, ϵ_n represents the coefficient associated with $h(A, L)$, with the constraint that the coefficient of $Q_n^0(A, L)$ is set to one. The estimation of TMLE involves assessing the final model at various treatment values:

$$\theta_n^{TMLE} = \frac{1}{n} \sum_{i=1}^n [Q_n^*(1, L) - Q_n^*(0, L)]. \quad (C-7)$$

This estimator aligns with the G-computation estimator, with the distinction being the replacement of the initial estimate $Q_n^*(A, L)$ with the updated $Q_n^0(A, L)$. TMLE shares similarities with the doubly robust approach, utilizing an IPTW outcome model to standardize the mean outcome through G-computation. This approach enables targeted estimation of the target parameter (the exposure effect) while accepting potential bias in other model parameters, treated as nuisance parameters and therefore not reported.

As TMLE operates as a substitution estimator, employing initial models for information in the final model but not directly incorporating them, it allows for estimation through machine learning methods. The Super Learner ensemble machine learning algorithm is commonly employed to estimate TMLE [4]. In this analysis, Q and g were estimated using a variety of prediction algorithms, including means, generalized linear models, generalized additive models [5], and random forests [6].

Assumptions for Causal Inference

Marginal structural models, whether estimated through TMLE or other methods, offer valid causal inference contingent upon a set of structural assumptions. These include:

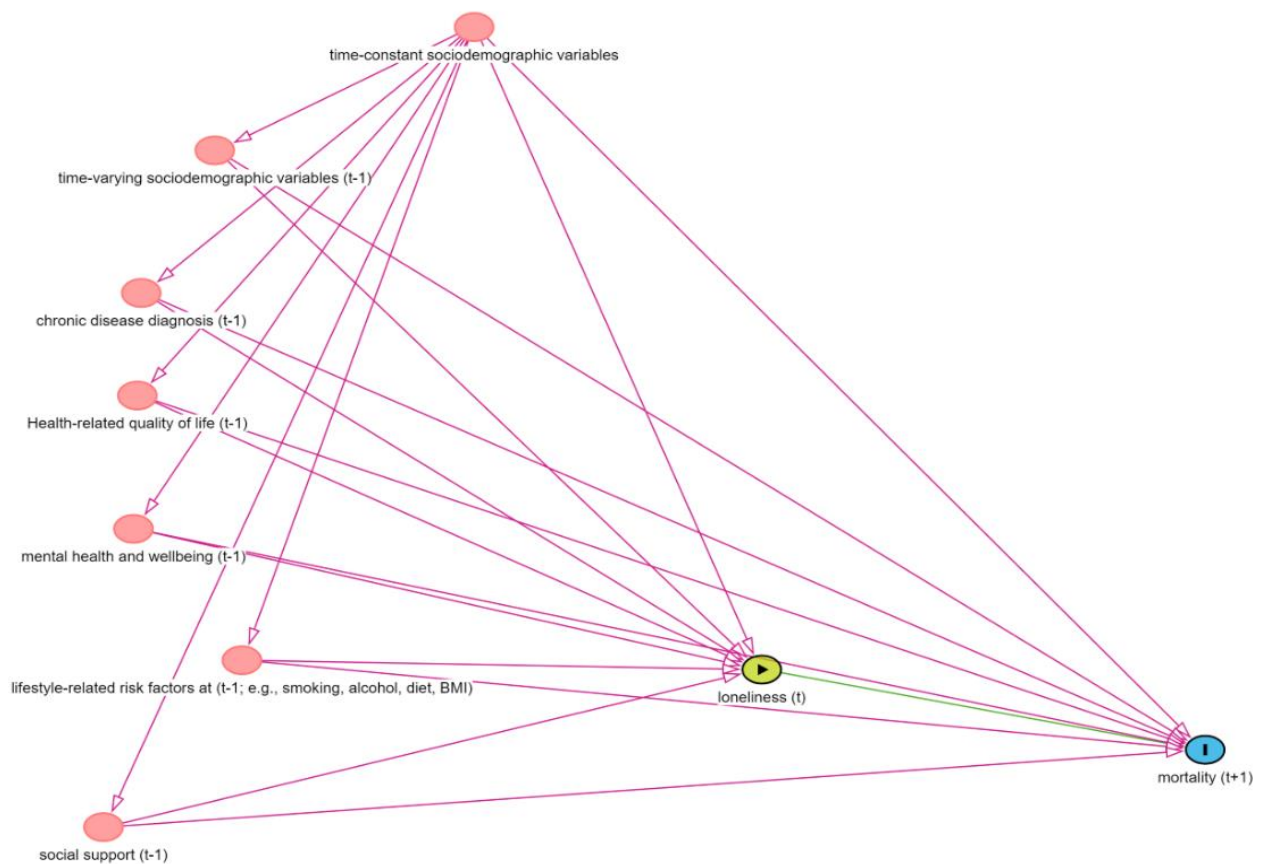
Conditional Exchangeability: Often referred to as 'no unmeasured confounding,' this assumption necessitates that exposure assignment is conditional solely on measured confounders [7].

Positivity: This assumption requires that all participants had at least some possibility of being exposed [8]. Targeted Maximum Likelihood Estimation has demonstrated greater robustness to near violations of positivity [9].

Consistency: This assumption posits that there is no scenario where the observed outcome differs from the potential outcome under the observed exposure, typically only arising when the exposure is ambiguously defined [10] .

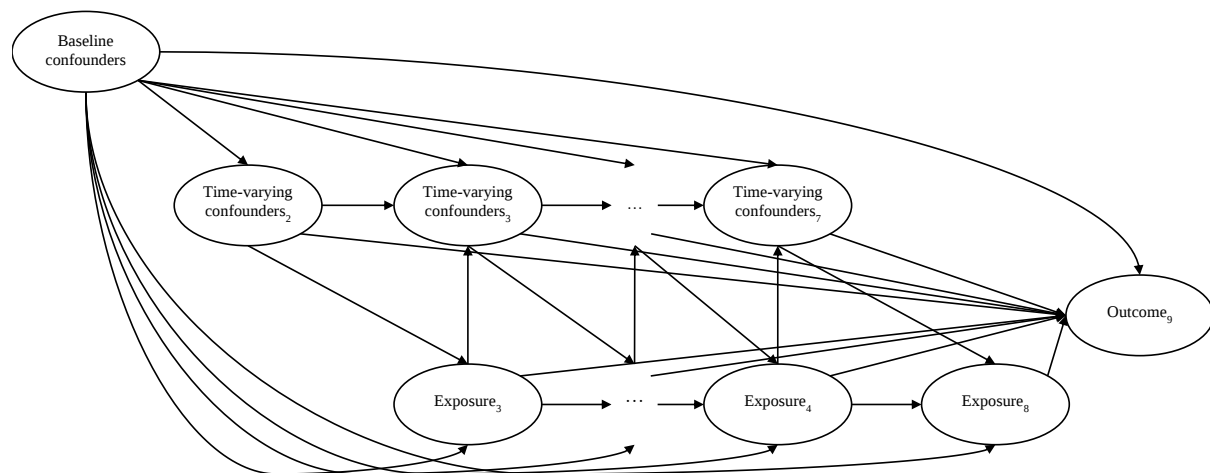
No interference: This assumption asserts that the exposure of each participant is independent of the outcome of other participants [11].

Figure S3.1. Directed acyclic graph of the causal relationships over time: selection of covariates



* No causal connections were drawn between the t-1 confounders, because they were measured contemporaneously, and thus do not meet ‘temporality’ requirements of cause-effect relationships.

Figure S3.2 Directed acyclic graph of the causal relationships over time: selection of waves



References

1. van der Laan MJ, Rubin DB. Targeted maximum likelihood learning. *The International Journal of Biostatistics*. 2006;2(1).
2. Bembom O, Petersen ML, Rhee SY, Fessel WJ, Sinisi SE, Shafer RW, et al. Biomarker discovery using targeted maximum-likelihood estimation: application to the treatment of antiretroviral-resistant HIV infection. *Statistics in Medicine*. 2009;28(1):152-72.
3. Arnold B, Arana B, Mausezahl D, Hubbard A, Colford JM. Evaluation of a pre-existing, 3-year household water treatment and handwashing intervention in rural Guatemala. *International Journal of Epidemiology*. 2009;38(6):1651-61.
4. van der Laan MJ, Polley EC, Hubbard AE. Super learner. *Stat Appl Genet Mol Biol*. 2007;6:Article25.
5. Hastie TJ, Tibshirani RJ. *Generalized Additive Models*: Chapman and Hall/CRC; 1990.
6. Breiman L. Random Forests. *Machine Learning*. 2001;45(1):5-32.
7. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology*. 1999;10(1):37-48.

8. Petersen ML, Porter KE, Gruber S, Wang Y, van der Laan MJ. Diagnosing and responding to violations in the positivity assumption. *Statistical Methods in Medical Research*. 2012;21(1):31-54.
9. Porter KE. The Relative Performance of Targeted Maximum Likelihood Estimators Under Violations of the Positivity Assumption: UC Berkeley; 2011.
10. Cole SR, Frangakis CE. Commentary: the consistency statement in causal inference: a definition or an assumption? *Epidemiology*. 2009;20(1):3-5.
11. Liu L, Hudgens MG, Becker-Dreps S. On inverse probability-weighted estimators in the presence of interference. *Biometrika*. 2016;103(4):829-42.

Appendix 4. missing data

There are a number of different ways in which data was missing data in the ALSWH cohort:

- Loss to follow-up;
- Questions that were not asked in all waves; and
- Intermittent missingness such as refusal to answer

The amount of missing data in each variable included in the analysis is shown in **Table D1**, with the most common patterns of missing data shown in **Figure D1**. We used Little's test to confirm data was not missing completely at random. As such, we have assumed the missing data was missing at random. Because ignoring missing information on both the outcome and exposure variables can introduce bias [1], we handled missing data using multiple imputation and inverse probability of censoring weights.

Based on past recommendations [2], we first to use the 'just another variable' approach for imputation, treating each repeated measurement as a separate variable. However, this approach failed to converge.

As such, we imputed the data using chained equations with the data in long form, using the R package 'mice' [3]. To handle possible complexity in the data, we imputed all variables using random forests, from the package 'ranger' [4]. Based on the proportion of missing information in the data, we used M=30 imputations [5].

We then conducted analyses on each imputed dataset and combined the results using Rubin's rules with the R package 'Amelia' [6].

References

1. Hughes RA, Heron J, Sterne JAC, Tilling K. Accounting for missing data in statistical analyses: multiple imputation is not always the answer. *International Journal of Epidemiology*. 2019;48(4):1294-304.
2. Huque MH, Carlin JB, Simpson JA, Lee KJ. A comparison of multiple imputation methods for missing data in longitudinal studies. *BMC Medical Research Methodology*. 2018;18(1):168.
3. van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. *Journal of Statistical Software*. 2011;45(3).

4. Wright MN, Wager S, Probst P. Ranger: A fast implementation of random forests. R package version 012. 2020;1.
5. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. *Prevention Science*. 2007;8(3):206-13.
6. Honaker J, King G, Blackwell M. Amelia II: a program for missing data. *Journal of Statistical Software*. 2011;45(7):47.

Table S4.1. Summary of missing data in each analysis variable

Variable		Missing data in variable (% of wave)						
		Wave 1/2	Wave 3	Wave 4	Wave 5	Wave 6	Wave 7	Wave 8
Exposure	Loneliness	-	1659 (15%)	1846 (16%)	2233 (20%)	2613 (23%)	3295 (29%)	3725 (33%)
Time-varying confounders	Alcohol - frequency ^a	1014 (9%)	11412 (100%)	2051 (18%)	2264 (20%)	2757 (24%)	3542 (31%)	
	Alcohol - binge drinking ^a	716 (6%)	11412 (100%)	1863 (16%)	2035 (18%)	2522 (22%)	3323 (29%)	
	BMI	1389 (12%)	2024 (18%)	2279 (20%)	2206 (19%)	2686 (24%)	3508 (31%)	
	Employment status	155 (1%)	1628 (14%)	1988 (17%)	2179 (19%)	2692 (24%)	3345 (29%)	
	MOS	814 (7%)	1525 (13%)	1781 (16%)	2033 (18%)	2540 (22%)	3309 (29%)	
	SEIFA	65 (1%)	1432 (13%)	1819 (16%)	2055 (18%)	2546 (22%)	3245 (28%)	
	Marital status	75 (1%)	1412 (12%)	1835 (16%)	2029 (18%)	2530 (22%)	3286 (29%)	
	Smoking status	702 (6%)	1423 (12%)	1733 (15%)	1996 (17%)	2495 (22%)	3277 (29%)	
	Mean stress	703 (6%)	1412 (12%)	1763 (15%)	1990 (17%)	2503 (22%)	3255 (29%)	
	ARIA	61 (1%)	1429 (13%)	1710 (15%)	1977 (17%)	2481 (22%)	3230 (28%)	
	Age	0 (0%)	1366 (12%)	1701 (15%)	1953 (17%)	2465 (22%)	3206 (28%)	
	3-year diagnosis/treatment for depression		1473 (13%)	1959 (17%)	2072 (18%)	2561 (22%)	3247 (28%)	
	3-year diagnosis/treatment for		1473	1959	2072	2561	3247	

	anxiety		(13%)	(17%)	(18%)	(22%)	(28%)	
	SF-36 Physical component score	207 (2%)	1797 (16%)	2105 (18%)	2286 (20%)	2609 (23%)	3472 (30%)	
	SF-36 Mental component score	207 (2%)	1797 (16%)	2105 (18%)	2286 (20%)	2609 (23%)	3472 (30%)	
	SF-36 Physical functioning	75 (1%)	1458 (13%)	1806 (16%)	2024 (18%)	2535 (22%)	3224 (28%)	
	SF-36 Role physical	41 (0%)	1436 (13%)	1756 (15%)	1995 (17%)	2515 (22%)	3249 (28%)	
	SF-36 Bodily pain	20 (0%)	1388 (12%)	1711 (15%)	1960 (17%)	2477 (22%)	3215 (28%)	
	SF-36 Vitality	39 (0%)	1435 (13%)	1742 (15%)	1987 (17%)	2486 (22%)	3232 (28%)	
	SF-36 General health	88 (1%)	1664 (15%)	1936 (17%)	2161 (19%)	2484 (22%)	3396 (30%)	
	SF-36 Role emotional	54 (0%)	1435 (13%)	1778 (16%)	2010 (18%)	2521 (22%)	3249 (28%)	
	SF-36 Social functioning	20 (0%)	-	-	-	-	-	-
	SF-36 Mental health	36 (0%)	-	-	-	-	-	-
Baseline confounders	Baseline - ever diagnosis/treatment for depression	0 (0%)	-	-	-	-	-	-
	Baseline - ever diagnosis/treatment for anxiety	0 (0%)	-	-	-	-	-	-
	Baseline - language spoken at home	205 (2%)	-	-	-	-	-	-
	Baseline - country of birth	128 (1%)	-	-	-	-	-	-
	Baseline - education	103 (1%)	-	-	-	-	-	-

Note: Exposure was drawn from Waves 3-8; time-varying confounders were drawn from Waves 2-7; baseline/time-constant confounders were drawn from waves 1 and 2.

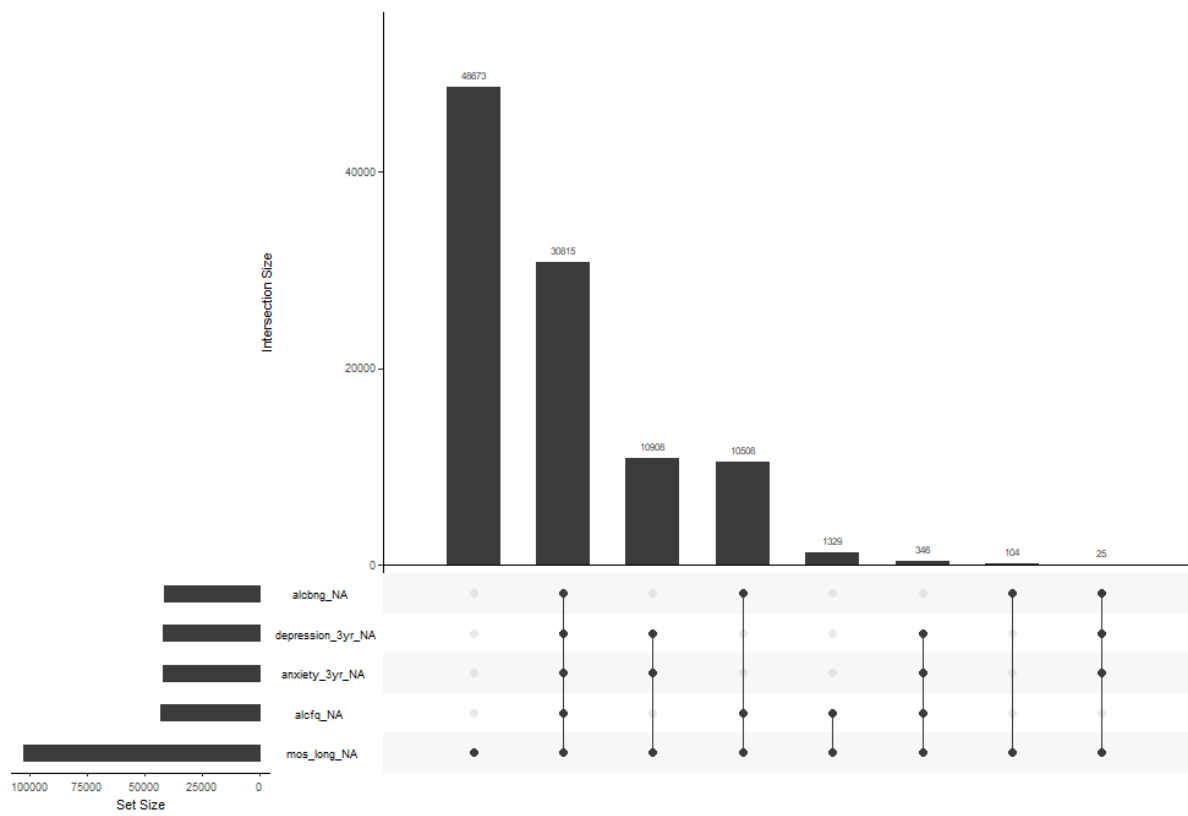
^a This was not asked in Wave 3.

Table S4.2. Number of participants according to wave and the total number of participants included in the analysis

Wave	n
Wave 1	13,714
Wave 2	12,338
Wave 3	11,226
Wave 4	10,905
Wave 5	10,638
Wave 6	10,011
Wave 7	9151
Wave 8	8622
Wave 9	7956
Total observations	12,338
Participants with a history of life-threatening illnesses removed	heart disease = 292 stroke = 113 cancer = 597 total* = 926
Sample size included in the analysis	11,412

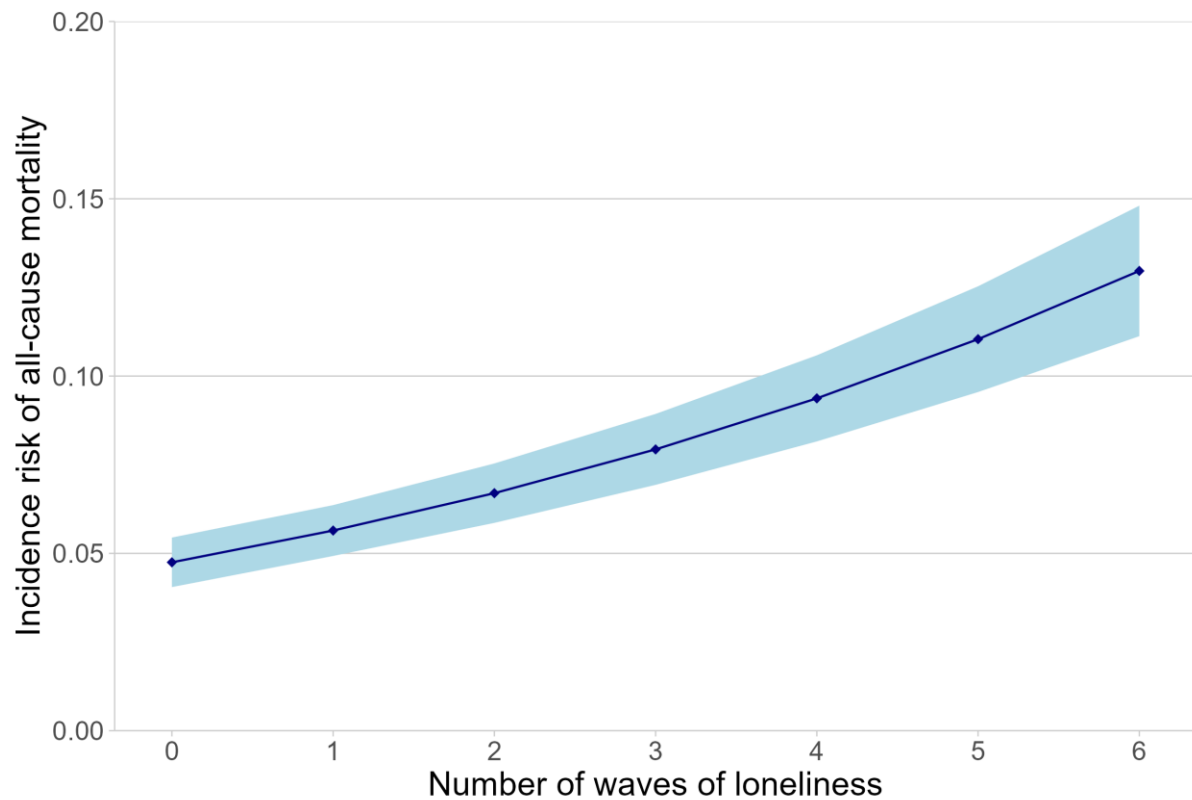
* The total exclusions are lower than the added numbers of all three conditions due to some participants having more than one medical condition.

Figure S4.1. Most common patterns of missing data.



Appendix 5. Additional results

Figure S5.1. Risk of all-cause mortality (1 Jan 2001 to 31 Dec 2021) according to the total number of waves of experiencing loneliness (lowest loneliness category vs. the three higher categories)

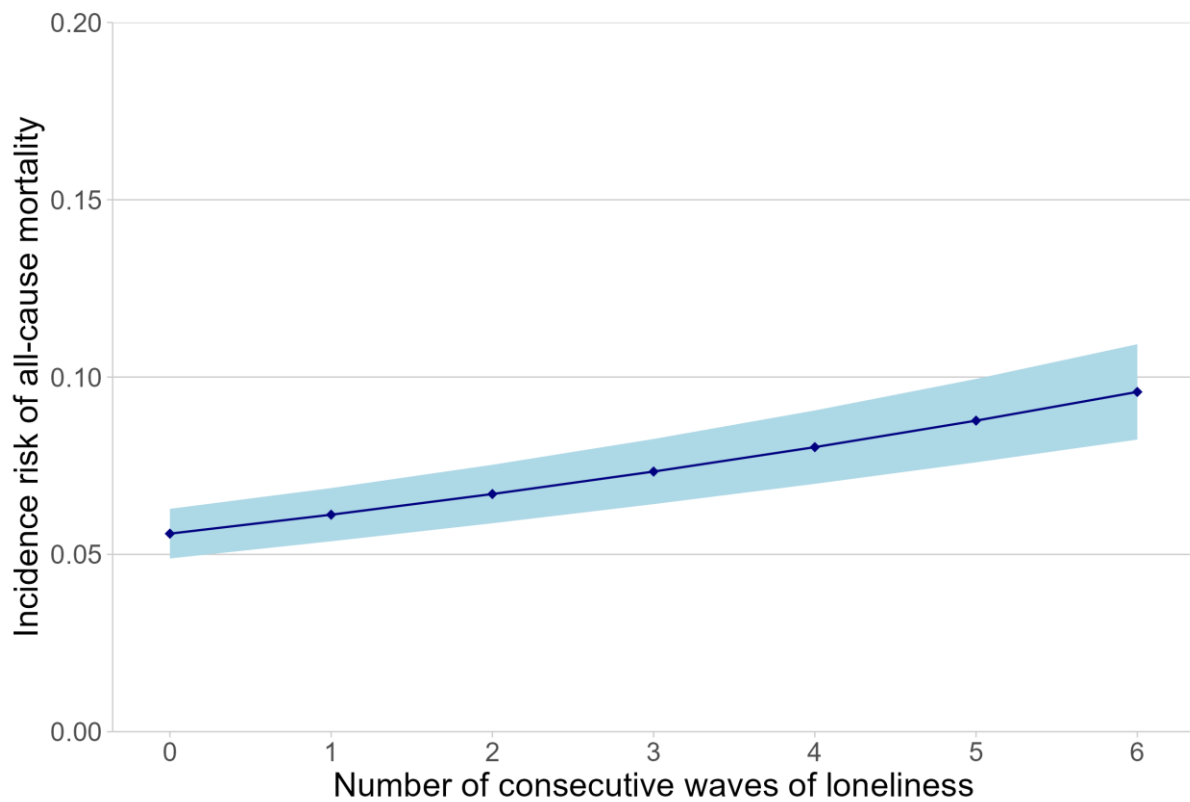


Note.

Gaps between waves were ~3 years apart

The shaded blue area refers to 99.5% Confidence Interval

Figure S5.2. Risk of all-cause mortality (1 Jan 2001 to 31 Dec 2021) according to the number of consecutive waves of experiencing loneliness (lowest loneliness category vs. the three higher categories)

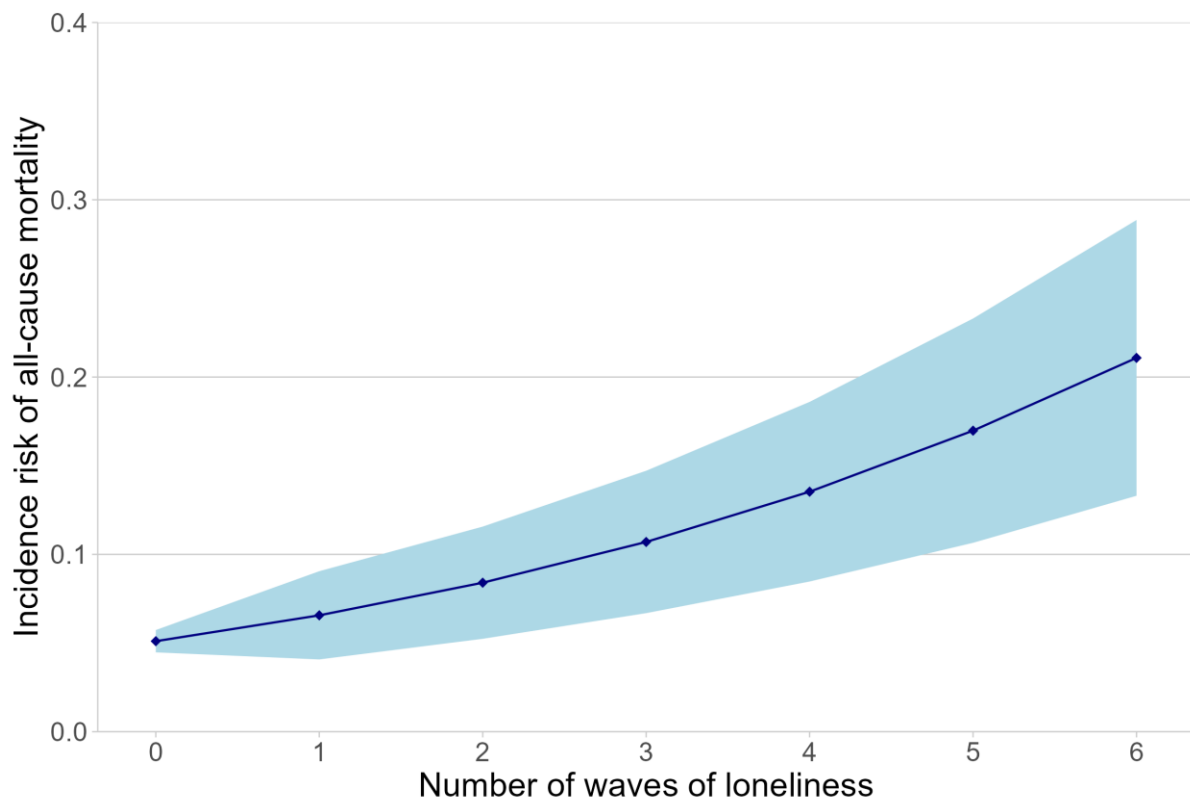


Note.

Gaps between waves were ~3 years apart

The shaded blue area refers to 99.5% Confidence Interval

Figure S5.3. Risk of all-cause mortality (1 Jan 2001 to 31 Dec 2021) according to the total number of waves of experiencing loneliness (highest loneliness category vs. the three lower categories)

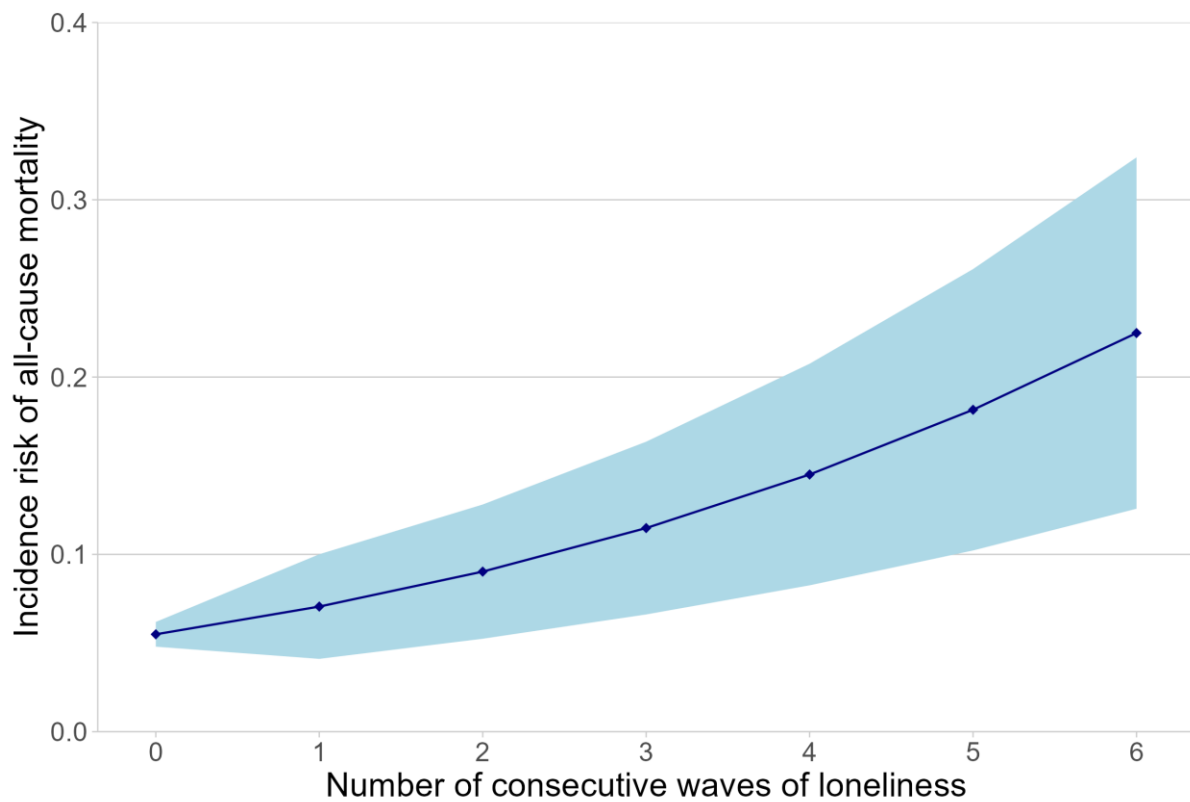


Note.

Gaps between waves were ~3 years apart

The shaded blue area refers to 99.5% Confidence Interval

Figure S5.4. Risk of all-cause mortality (1 Jan 2001 to 31 Dec 2021) according to the number of consecutive waves of experiencing loneliness (highest loneliness category vs. the three lower categories)



Note.

Gaps between waves were ~3 years apart

The shaded blue area refers to 99.5% Confidence Interval

Table S5.1. Mortality incidence risks according to the total number of waves of being lonely and according to number of consecutive waves of being lonely

	Incidence Risk and 99.5% Confidence Interval	
	Number of waves of being lonely	Number of consecutive waves of being lonely
0 waves of loneliness	0.05 (0.04, 0.06)	0.06 (0.05, 0.06)
1 wave of loneliness	0.06 (0.05, 0.07)	0.07 (0.05, 0.08)
2 waves of loneliness	0.08 (0.06, 0.09)	0.08 (0.06, 0.09)
3 waves of loneliness	0.09 (0.07, 0.11)	0.09 (0.07, 0.11)
4 waves of loneliness	0.11 (0.09, 0.13)	0.11 (0.08, 0.13)
5 waves of loneliness	0.13 (0.11, 0.16)	0.12 (0.10, 0.15)
6 waves of loneliness	0.16 (0.13, 0.19)	0.14 (0.11, 0.17)

Table S5.2. Risk ratios and risk differences between key levels of exposure – results from the primary analysis

	Relative Risk and 99.5% Confidence Interval		Risk Difference and 99.5% Confidence Interval (percentages)	
	Number of waves	Number of consecutive waves	Number of waves	Number of consecutive waves
1 wave of loneliness versus 0 waves of loneliness	1.22 (1.04, 1.43)	1.18 (1.02, 1.36)	1.12% (1.10%, 1.13%)	0.98% (0.97%, 0.99%)
2 waves of loneliness versus 0 waves of loneliness	1.49 (1.26, 1.75)	1.38 (1.19, 1.60)	2.46% (2.43%, 2.49%)	2.13% (2.10%, 2.15%)
3 waves of loneliness versus 0 waves of loneliness	1.81 (1.52, 2.15)	1.62 (1.38, 1.89)	4.07% (4.01%, 4.13%)	3.45% (3.40%, 3.50%)
4 waves of loneliness versus 0 waves of loneliness	2.18 (1.79, 2.66)	1.89 (1.59, 2.26)	5.98% (5.87%, 6.08%)	4.97% (4.88%, 5.06)
5 waves of loneliness versus 0 waves of loneliness	2.63 (2.08, 3.33)	2.21 (1.79, 2.73)	8.23% (8.05%, 8.41%)	6.72% (6.58%, 6.87%)
6 waves of loneliness versus 0 waves of loneliness	3.15 (2.35, 4.23)	2.56 (1.98, 3.32)	10.86% (10.58%, 11.15%)	8.71% (8.49%, 8.94%)

Table S5.3. Risk ratios and risk differences between key levels of exposure – results from sensitivity analysis using lower cut-point for loneliness

	Relative Risk and 99.5% Confidence Interval		Risk Difference and 99.5% Confidence Interval (percentages)	
	Number of waves	Number of consecutive waves	Number of waves	Number of consecutive waves
1 wave of loneliness versus 0 waves of loneliness	1.19 (1.11, 1.27)	1.10 (1.04, 1.16)	0.89% (0.89%, 0.90%)	0.53% (0.53%, 0.54%)
2 waves of loneliness versus 0 waves of loneliness	1.41 (1.30, 1.53)	1.20 (1.12, 1.28)	1.94% (1.94%, 1.95%)	1.12% (1.11%, 1.12%)
3 waves of loneliness versus 0 waves of loneliness	1.67 (1.49, 1.87)	1.31 (1.21, 1.42)	3.17% (3.16%, 3.19%)	1.75% (1.74%, 1.76%)
4 waves of loneliness versus 0 waves of loneliness	1.97 (1.67, 2.32)	1.44 (1.30, 1.59)	4.61% (4.57%, 4.64%)	2.44% (2.42%, 2.46%)
5 waves of loneliness versus 0 waves of loneliness	2.32 (1.85, 2.91)	1.57 (1.38, 1.79)	6.37% (6.20%, 6.34%)	3.19% (3.16%, 3.21%)
6 waves of loneliness versus 0 waves of loneliness	2.72 (2.00, 3.70)	1.72 (1.46, 2.02)	8.18% (8.06%, 8.30%)	4.00% (3.96%, 4.04%)

Table S5.4. Risk ratios and risk differences between key levels of exposure – results from sensitivity analysis using higher cut-point for loneliness

	Relative Risk and 99.5% Confidence Interval		Risk Difference and 99.5% Confidence Interval	
	Number of waves	Number of consecutive waves	Number of waves	Number of consecutive waves
1 wave of loneliness versus 0 waves of loneliness	1.29 (0.94, 1.75)	1.29 (0.91, 1.82)	1.46% (1.43%, 1.49%)	1.56% (1.53%, 1.61%)
2 waves of loneliness versus 0 waves of loneliness	1.65 (1.19, 2.27)	1.64 (1.13, 2.40)	3.30% (3.22%, 3.39%)	3.54% (3.42%, 3.66%)
3 waves of loneliness versus 0 waves of loneliness	2.10 (1.46, 3.03)	2.09 (1.31, 3.33)	5.60% (5.41%, 5.80%)	5.99% (5.73%, 6.27%)
4 waves of loneliness versus 0 waves of loneliness	2.65 (1.68, 4.20)	2.64 (1.41, 4.93)	8.44% (8.07%, 8.83%)	9.01% (8.50%, 9.56%)
5 waves of loneliness versus 0 waves of loneliness	3.33 (1.82, 6.11)	3.31 (1.39, 7.84)	11.89% (11.23%, 12.59%)	12.66% (11.74%, 13.66%)
6 waves of loneliness versus 0 waves of loneliness	4.14 (1.84, 9.31)	4.09 (1.26, 13.26)	16.01% (14.91%, 17.18%)	16.99% (15.44%, 18.70%)

Table S5.5. E-Value analysis for the strength of unmeasured confounding required to alter primary results

	E-Values			
	Number of waves		Number of consecutive waves	
	At estimate	At CI bound	At estimate	At CI bound
1 wave of loneliness versus 0 waves of loneliness	1.74	1.45	1.63	1.36
2 waves of loneliness versus 0 waves of loneliness	2.34	2.09	2.11	1.88
3 waves of loneliness versus 0 waves of loneliness	3.01	2.76	2.62	2.39
4 waves of loneliness versus 0 waves of loneliness	3.79	3.51	3.19	2.94
5 waves of loneliness versus 0 waves of loneliness	4.70	4.37	3.84	3.54
6 waves of loneliness versus 0 waves of loneliness	5.76	5.34	4.57	4.20

5.7. Concluding summary for this chapter and knowledge gained from this study

The current study presents the findings on the causal effect of loneliness on mortality. We employed rigorous controls for time-varying confounding variables and accounted for the effect of baseline exposures. These methodological refinements enabled a potentially less biased estimation of the independent effect of loneliness on mortality, unaffected by confounders associated with health. The findings provide strong evidence for a dose-response association between loneliness and mortality, indicating that the consistency and chronicity of loneliness significantly affect mortality. Specifically, individuals experiencing loneliness at two, four and six waves had an incrementally higher risk of mortality compared to those who reported no loneliness. The incremental increase in mortality risk with each additional wave of loneliness underscores the importance of addressing loneliness as a public health concern. Furthermore, the results suggest that interventions aimed at alleviating loneliness could potentially prevent up to 11% of all-cause mortality among lonely individuals. This highlights the potential effect of targeted loneliness interventions in improving overall health outcomes among middle-aged women.

CHAPTER SIX: Health care utilization following interventions to improve social well-being: A systematic review and meta-analysis

6.1. Preface to the chapter

As discussed in previous chapters, loneliness has significant implications for health outcomes and imposes an economic burden, particularly among middle-aged and older adults. Enhancing social well-being and providing social support have been shown to mitigate loneliness, thereby reducing the strain on health systems. Given the strong association between social health and both disease and economic burden, it is crucial to explore strategies to improve social well-being. There has been previous evidence on psychosocial interventions' effect on health care use, however, this evidence has never been systematically synthesised nor meta-analysed. This gap in research is significant as it hinders the optimisation of intervention strategies and the development of informed healthcare policies. Therefore, this chapter presents findings published in a peer-reviewed paper that synthesised and meta-analysed evidence from 41 RCTs on the effect of psychosocial interventions on healthcare use, social well-being and loneliness. A three-level meta-analysis was used to generate the random effect of the intervention compared to the control group with odds ratios and mean differences. The effect of the interventions is examined across different health services including general practice, outpatient, inpatient, emergency care and the overall use of health care services. Sub-group analysis is conducted according to socio-demographic characteristics: gender, age, country and population group, as well as intervention characteristics: length of intervention, number of components and intervention deliverers. This chapter addresses specific aim #4 of this thesis as described in **Chapter 2**. Dissemination of this research and the author's contributions to this paper are described below.

6.2. Research dissemination

The research presented in this chapter has been disseminated as follows:

Published peer-review paper

HaGani N, Surkalim DL, Clare PJ, Merom D, Smith BJ, Ding D. Health care utilization following interventions to improve social well-being: A systematic review and meta-analysis. JAMA Network Open. 2023;6(6):e2321019. doi:10.1001/jamanetworkopen.2023.21019.

Impact factor: 13.35

Citations (based on Google Scholar): 4 (21 October 2024)

Conference presentations

1. The Charles Perkins EMCR committee- The breakfast seminar. December 2023. The University of Sydney. Sydney, Australia (Long oral presentation).
2. The Preventive Health Conference. May 2023, Public Health Association Australia. Adelaide, Australia (Oral presentation).
3. The Charles Perkins EMCR Symposium. September 2022. The University of Sydney. Sydney, Australia (Oral presentation).
4. Faculty of Medicine and Health HDR Conference. July 2022. The University of Sydney. Sydney, Australia (Oral presentation).

6.3. Author attribution statement

I, Neta HaGani, was responsible for designing the study, conducting the data review, extraction, and analysis, interpreting the results, writing the drafts of the manuscript, submitting the manuscript, responding to reviewers' comments, and coordinating the submission and publication of the manuscript. My co-authors, D. Merom, B. Smith & D. Ding helped conceptualise and design the study and developed the review protocol; D. Surkalim, D. Merom, B. Smith & D. Ding participated in the review process, data extraction and quality assessment. P. Clare and D. Ding assisted with the data analysis. All authors have reviewed, edited, and approved the final version of the manuscript.

6.4. Paper in published format



Original Investigation | Public Health

Health Care Utilization Following Interventions to Improve Social Well-Being A Systematic Review and Meta-analysis

Neta HaGani, MSW; Daniel L. Surkalim, MPH; Philip J. Clare, PhD; Dafna Merom, PhD; Ben J. Smith, PhD; Ding Ding, PhD

Abstract

IMPORTANCE It has been suggested that interventions that aim to improve social well-being may contribute to decreased health care use; however, such evidence has not been fully systematically synthesized.

OBJECTIVE To systematically review and meta-analyze available evidence on the associations between psychosocial interventions and health care utilization.

DATA SOURCES Medline, Embase, PsycInfo, Cumulated Index to Nursing and Allied Health Literature, Cochrane, Scopus, Google Scholar, and reference lists of systematic reviews were searched from inception until November 31, 2022.

STUDY SELECTION Included studies were randomized clinical trials reporting on both health care utilization and social well-being outcomes.

DATA EXTRACTION AND SYNTHESIS The reporting of the systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline. Full-text and quality assessments were conducted by 2 reviewers independently. Multilevel random-effects meta-analyses were used to synthesize the data. Subgroup analyses were conducted to examine the characteristics associated with decreased health care use.

MAIN OUTCOMES AND MEASURES The outcome of interest was health care utilization, including primary, emergency, inpatient, and outpatient care services. Social well-being was measured as social support, social participation, social relationships, community support, social integration, or loneliness.

RESULTS A total of 41 studies were retrieved from 18 969 citations; 37 studies were eligible for meta-analysis. Data were analyzed for 7842 participants, including 2745 older adults, 1579 young women considered to be at risk of social and mental health disadvantages, 1118 people with chronic illnesses, 1597 people with mental illnesses, and 803 caregivers. The odds ratio (OR) random-effects model showed an overall reduction in health care use (OR, 0.75; 95% CI, 0.59 to 0.97), but the standardized mean difference (SMD) random effect model showed no association. An improvement in health care utilization was observed in association with social support interventions (SMD, 0.25; 95% CI, 0.04 to 0.45) but not in loneliness interventions. Subgroup analysis indicated a reduced length of inpatient visits (SMD, -0.35; 95% CI, -0.61 to -0.09) and number of emergency care visits (OR, 0.64; 95% CI, 0.43 to 0.96) following the intervention. However, an increase in outpatient care associated with psychosocial interventions was observed (SMD, 0.34; 95% CI, 0.05 to 0.62). The largest reductions in health care use were associated with interventions among caregivers (OR, 0.23; 95% CI, 0.07 to 0.71) and individuals with mental illnesses (OR, 0.31; 95% CI, 0.13 to 0.74).

(continued)

Key Points

Question Is there an association between psychosocial interventions and health care service use, and does the association differ by sociodemographic or intervention characteristic?

Findings This systematic review and meta-analysis including 41 studies and 7842 participants found that psychosocial interventions were associated with decreased health care use in most health services and increased use of outpatient care. The greatest health care decrease was among caregivers and individuals with mental illnesses and in interventions delivered 1-on-1 by health professionals.

Meaning These findings suggest that psychosocial interventions were associated with reduced health care use.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Open Access. This is an open access article distributed under the terms of the CC-BY License.

Abstract (continued)

CONCLUSIONS These findings suggest that psychosocial interventions were associated with most measures of health care utilization. As the association differed by participant and intervention delivery characteristics, these characteristics should be considered in the design of future interventions.

JAMA Network Open. 2023;6(6):e2321019. doi:10.1001/jamanetworkopen.2023.21019

Introduction

Social well-being is an umbrella term that refers to the actual or perceived availability of social resources, such as social networks.¹ A lack of social well-being can manifest in problems, such as loneliness and social isolation, that are important public health concerns²⁻⁴ and can lead to chronic diseases and premature mortality.⁵⁻⁷

Another public health challenge faced by many countries is escalating health care costs associated with population aging and increasing prevalence of chronic disease. As this trend is expected to continue,⁸ decision-makers need to find solutions to reduce health care spending by designing and implementing efficient and equitable health services and minimizing unnecessary health care use. Promising evidence from observational studies has suggested that better social well-being is associated with lower health care utilization,⁹⁻¹² indicating that psychosocial interventions to address social well-being may reduce health care demand.^{13,14}

To date, psychosocial interventions have been conducted among a variety of populations^{15,16} using myriad approaches, such as individual or group therapy, group-based activities, peer support, and outreach and befriending strategies.^{17,18} Besides positive associations with loneliness, social interaction, and perceptions of support,^{19,20} some psychosocial interventions have been found to be associated with decreases in unnecessary health service use and costs in some populations, such as older adults, survivors of breast cancer, and people with mental illnesses.^{17,18,21} For example, peer support interventions and multicomponent psychosocial interventions were associated with decreased use of general practitioners and emergency care among variety of populations.^{18,22} However, for outpatient care, such as visits to specialists, most studies showed no significant changes.²²⁻²⁴

Despite the associations found between psychosocial interventions and health care utilization, evidence on this topic has not been systematically synthesized or quantitatively summarized, to our knowledge.¹³ Furthermore, we do not yet know what intervention characteristics are associated with lower health care use. To address these gaps, we aimed to synthesize the associations among psychosocial interventions, health care utilization, and social well-being and identify characteristics associated with the variability in effect sizes of these outcomes.

Methods

The reporting of the systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline. The protocol is registered in the PROSPERO database under record No. [CRD42021273388](https://doi.org/10.1111/CRD4.2021273388).

Eligibility Criteria

Psychosocial interventions that used a randomized clinical trial design to improve social well-being were included. To be eligible, studies needed to report on at least 1 health care utilization-related outcome and at least 1 social well-being-related outcome. *Health care utilization* refers to using primary care (visits to the general practitioner or nurse), emergency care (visits to the emergency department), inpatient care (eg, number of hospitalizations and readmissions, length of stay), and

outpatient care (visits to a specialist, such as a cardiologist, obstetrician, or psychiatrist) services. Social well-being covers multiple domains, including social support, social participation, social relationships, community support, and loneliness. The population, intervention, control, and outcomes data are presented in eTable 1 in [Supplement 1](#).

Study Selection and Data Extraction

A comprehensive search was conducted from inception until May 31, 2021, and an update search until November 31, 2022, in the following databases: Medline, Embase, PsycInfo, Cumulated Index to Nursing and Allied Health Literature, Cochrane, and Scopus. Search terms on the concepts of health care utilization, social well-being, and psychosocial interventions were combined with AND (specific search terms and search results are presented in eTables 2-8 in [Supplement 1](#)). Google Scholar, reference lists of the included studies, and relevant systematic reviews^{10,13,14,25} were manually searched for additional potential studies. All records were imported to Covidence reference management software (Veritas Health Innovation). After duplicates were removed, titles and abstracts were assessed according to the eligibility criteria. The full-text review was conducted by 2 reviewers (N.H. and D.S.) independently. Disagreements were resolved by a third reviewer (D.D., D.M., or B.J.S.). Data were extracted by 1 reviewer (N.H.) and a sample of the extracted data (approximately 30%) was reviewed by a second reviewer (D.D.). Where means and SDs were missing, they were estimated from other measures of effect²⁶ or imputed from other studies,^{22,26,27} as suggested by Cochrane.²⁸

For the main outcome of health care utilization, 2 types of data were extracted for the intervention and control groups: raw means and SDs to calculate standardized mean differences (SMDs) and numbers and percentages of health care users to calculate odds ratios (ORs). Some studies included multiple follow-ups after their intervention. Data were extracted and analyzed from each study for the first follow-up immediately after the intervention and for the last follow-up after the intervention, regardless of specific durations of the follow-ups.

Risk of Bias

All studies were assessed for risk of bias (ROB) using the *Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0*.²⁹ Assessment was done using Covidence and RevMan version 5.4 (Cochrane) tools. Studies were assessed by 2 independent reviewers (N.H. and D.L.S.). Conflicts were resolved by consultations with a third reviewer (D.M., B.J.S., or D.D.). Each study was assessed on 7 different domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Each domain received a judgement of low, high, or unclear ROB.

Publication Bias

Publication bias was examined using funnel plots and an extension of Egger regression test was used to quantify the funnel plot asymmetry.³⁰ This included using a measure of effect size precision as a predictor in a meta-regression.³¹ $P < .05$ indicated a substantial asymmetry in the funnel plot that could have been caused by publication bias.

Assessing the Certainty of the Evidence

Certainty of evidence was assessed for each of the overall outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.^{32,33} The assessment was performed using the GRADEpro GDT software (McMaster University and Evidence Prime). GRADE domains were assessed according to the level of uncertainty (ie, not serious, serious, or very serious). The overall certainty was categorized as very low, low, moderate, or high. Certainty was downgraded 1 level per limitation, starting from high certainty.³³

Statistical Analysis

Results were combined and analyzed using random-effects models. Separate meta-analytic estimates were calculated for studies that reported on SMDs and ORs. To account for multiple dependent effect sizes,³⁴ we performed a 3-level meta-analysis. The effect sizes of the overall and different types of health care utilization were calculated for the immediate and sustained outcomes after interventions. Subgroup analyses were used to identify differences according to participant characteristics, such as age, gender, and population groups, and intervention characteristics, including type (individual vs group), duration (number of months), and delivery personnel (health professionals, peers, and activity coordinators). All analyses were performed using the meta and metafor libraries of R software version 4.1.3 (R Project for Statistical Computing). Bayes factors (BFs) were calculated to examine the strength of evidence using an online calculator.³⁵ BFs with a value between 3 and 10 indicate moderate relative evidence for the alternative hypothesis; BFs between 0.3 and 3, inconclusive evidence; and BFs less than 0.3, moderate evidence for the null hypothesis.³⁶ Expected effect sizes were estimated based on previous meta-analyses on related topics.^{14,37} For the SMD random-effects model, the expected SMD was set to -0.3 . Similarly, the expected OR was set to 0.70 (30% reduction). For the alternative hypothesis of the social support measure and outpatient care use, we used an SMD of 0.3 and an OR of 1.5, since they were associated positively with intervention effect size.

P values were 2-sided, and statistical significance was set at $P < .05$. The last analysis update was conducted between January 12 and 19, 2023.

Results

Systematic Review

Of 18 968 records identified, 268 full texts articles were assessed for eligibility, 41 studies met the inclusion criteria for the systematic review.^{18,21-24,26,27,38-71} Of these, 21 studies^{22-24, 27, 40, 41, 44-46, 49, 50, 53, 54, 58, 59, 63, 65-69} were included in the OR health care utilization meta-analysis, 18 studies^{18, 23, 24, 26, 38-43, 48, 51, 55, 58, 60, 64, 67, 70} were included in the SMD health care utilization meta-analysis, 27 studies^{18, 22-24, 26, 27, 38-40, 42-44, 46, 51, 52, 54, 55, 58-64, 67, 68, 71} were included in the social support SMD meta-analysis, and 3 studies^{26,40,70} were included in the loneliness SMD meta-analysis (**Figure 1**). Data were analyzed for 7842 participants, including 2745 older adults, 1579 young women considered at risk of social and mental health disadvantages (1 study among women in a shelter for family violence survivors, 1 study among women at risk for postpartum depression and 1 study among women from disadvantage living areas), 1118 people with chronic illnesses, 1597 people with mental illnesses, and 803 caregivers.

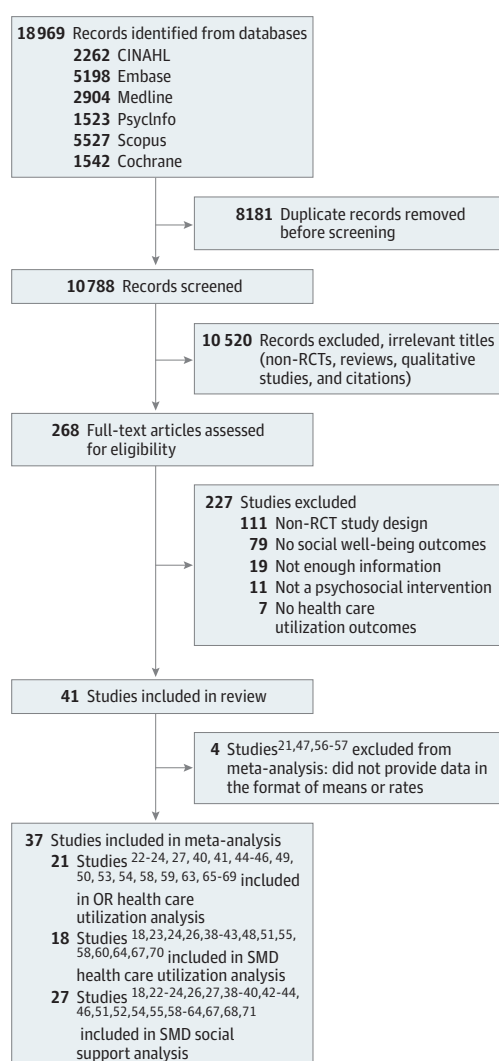
eTable 9 in [Supplement 1](#) presents the characteristics of the included studies. The included studies were published between 1995 and 2022. Most were conducted in the UK (10 studies^{21,23,38,39,41,51,61,67,69,71}) or other European countries (8 studies^{18,26,42,48,49,65,66,70}); 6 studies^{43,44,54,55,59,60} were undertaken in China, 7 studies^{22,24,27,46,47,52,64} were undertaken in Canada, 6 studies^{38,40,45,50,58,68} were undertaken in the US, and 1 study each was conducted in Singapore,⁶² Columbia,⁶³ Australia,⁵³ and Zambia.⁵⁷ Fourteen studies^{24,38-49,72} had sample sizes of fewer than 100 participants, 18 studies^{18,22,27,50-64} had samples of 100 to 200 participants, 7 studies^{23,26,65-69} included 200 to 1000 participants, and 2 studies^{70,71} had sample sizes of more than 1000 participants. Studied populations included 7 studies^{43,47,49,50,53-55} of caregivers, 9 studies of people with physical illnesses (6 on heart disease,^{22,41,44,48,51,62} 1 on HIV,⁶⁶ 1 on stroke,⁵⁷ and 1 on multimorbidity⁴²), 11 studies^{21,27,45,56,58-61,63,68,69} of people with mental illnesses, 7 studies^{18,26,39,46,52,65,70} of older adults, 6 studies^{23,24,40,64,67,71} of postnatal young women, and 1 study³⁸ of women at a domestic violence shelter. Interventions were delivered by health professionals (28 studies^{18,23,26,38,40,42-44,46-50,52-54,56-60,62-66,70,71}), peer volunteers (8 studies^{21,22,24,27,45,55,68,69} with individuals with lived experience of health challenges or services), or a coordinator on behalf of the intervention team (5 studies^{39,41,51,61,67}). Sixteen interventions^{18, 26,}

27, 38, 39, 41, 42, 49, 51, 55, 60, 63-65, 68, 71 were group-based, 18 interventions^{18, 21-24, 40, 43, 44, 46, 47, 52-54, 56, 61, 62, 66, 67, 69} were delivered to individuals 1-on-1, and 7 interventions^{45, 48, 50, 57-59, 70} included both individual and group components. Most of the control groups received standard care (31 studies^{18, 21-24, 27, 40, 41, 43-49, 52-56, 58-63, 65-67, 69, 70}). Two studies^{26, 42} used a waitlist control, whereas 8 studies^{38, 39, 50, 51, 57, 64, 68, 71} had a minimal intervention as a control condition. Seventeen interventions^{18, 40, 41, 43, 44, 46, 47, 49, 51, 52, 55, 60, 65-68, 70} were 6 to 12 months long, and the remainder^{18, 21-24, 26, 27, 38, 39, 42, 45, 48, 50, 53, 54, 56-59, 61-64, 69, 71} were 4 months or shorter.

Risk of Bias

Sixteen studies^{18, 21, 40, 42, 46, 50, 52, 54-56, 60, 62, 64, 66, 67, 69} were classified as low risk of bias; 6 studies,^{23, 26, 44, 47, 49, 57} medium risk; and 19 studies^{22, 24, 27, 38, 39, 41, 43, 45, 48, 51, 53, 58, 59, 61, 63, 65, 68, 70, 71} high risk. Most interventions were classified as low risk for randomization (31 interventions^{18, 21-23, 26, 27, 38-41, 44, 46, 48-50, 52-57, 60-62, 64, 65, 67, 69, 71} [76%]), allocation concealment (27 interventions^{21-24, 26, 38, 40-44, 46, 47, 49, 50, 52, 54-57, 60, 62, 64-67, 69} [66%]) and attrition bias (30 interventions^{18, 21, 22, 24, 27, 40-44, 46-50, 52-56, 58, 60, 62-65, 67-70} [73%]). There were 23 interventions^{18, 21, 23, 24, 26, 39, 40, 42, 46, 48, 53-57, 60, 62-64, 66, 67, 69, 70} (56%) considered low risk for reporting bias. Only 2 studies^{18, 21, 23, 24, 26, 39, 40, 42, 46, 48, 53-57, 60, 62-64, 66, 67, 69, 70} (5%) had low risk in the blinding of participants and personnel domain,

Figure 1. Flowchart of Identification of Studies Via Databases and Registers



CINAHL indicates Cumulated Index to Nursing and Allied Health Literature; OR, odds ratio; RCT, randomized clinical trial; SMD, standardized mean difference.

and 19 studies^{18, 21, 23, 24, 27, 44, 46, 50, 52, 54, 55, 58, 60, 62-64, 66, 68, 69} (46%) had low risk in the blinding of outcome data domain (eFigure 1 in [Supplement 1](#)).

GRADE Certainty of Evidence Results

The evidence for the immediate postintervention health care utilization and social support outcomes using ORs was evaluated with a moderate level of certainty. The evidence for the sustained health care utilization and loneliness outcomes was assessed with low levels of certainty. Evidence for both immediate and sustained health care utilization outcomes using SMDs was assessed with a very low level of certainty (eTable 10 in [Supplement 1](#)).

Meta-Analyses of Immediate Postintervention Health Care Utilization Outcomes

According to the random-effects model of studies reporting ORs, the intervention group had significant lower odds of using health care compared with the control group (OR, 0.75; 95% CI, 0.59 to 0.97). However, the SMD random-effects model was not significant. When looking at different services, the OR model showed sizeable and significant reductions in the odds of emergency care use (OR, 0.64; 95% CI, 0.43-0.96) among the intervention groups. The SMD model showed significant increase in outpatient care (SMD, 0.34; 95% CI, 0.05-0.62), a decrease in length of inpatient care (SMD, -0.35; 95% CI, -0.61 to -0.09) by the intervention group. Heterogeneity was significant for both the OR and SMD random-effects models, suggesting that the amount of between-study variability was greater than would be expected by chance (**Figure 2** and **Figure 3**).

Bayes Factors

The strength of evidence was moderate for the overall OR random-effects model (BF = 5.63) and was inconclusive for the overall SMD random-effects model (BF = 0.84). Strong relative evidence for the alternative hypothesis was found in the SMD model for inpatient length (BF > 10) and moderate evidence was found for inpatient and outpatient services utilization (BF, 3-10). In the OR models, we found moderate evidence for the alternative hypothesis for primary care, inpatient, and emergency care. We also found moderate evidence for the alternative hypothesis for social support in the SMD model (BF = 7.21) (eTable 11 in [Supplement 1](#)).

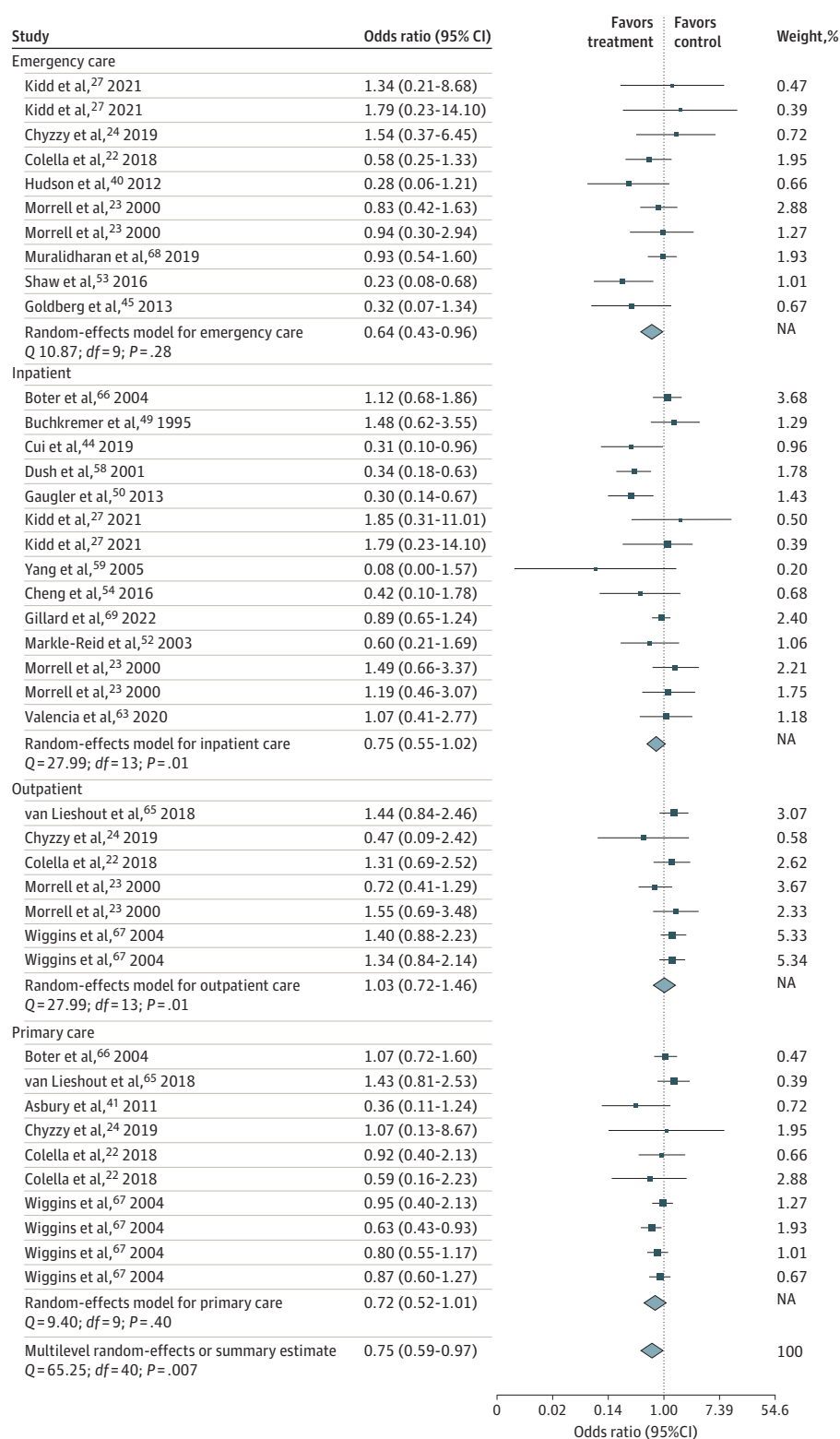
Subgroup Analysis

In both the OR and SMD models, we observed significant decreases in health care use after interventions in studies conducted in China compared with other countries.^{43-55,59,60} In the OR model only, we observed significant decreases in health care use after interventions in studies conducted in the US and Australia.^{40,45,50,53,58,68} In the OR model, we also observed a decrease in health care use in studies that included participants aged 30 to 60 years.^{27,44,45,50,53,54,59,68,69} Reductions in health care use were observed in studies among caregivers^{49,50,53,54} and individuals with mental illnesses^{27,45,58,59,63,68,69} compared with other population groups, but only in the OR model. Single-component interventions that were based on the individual level, shorter (1-4 months), and delivered by health professionals were associated with significant decreases in health care use as well. However, in the SMD model, longer interventions were significantly associated with lower health care use after the interventions (eTable 12 in [Supplement 1](#)).

Meta-Analyses of Sustained Postintervention Health Care Utilization Outcomes

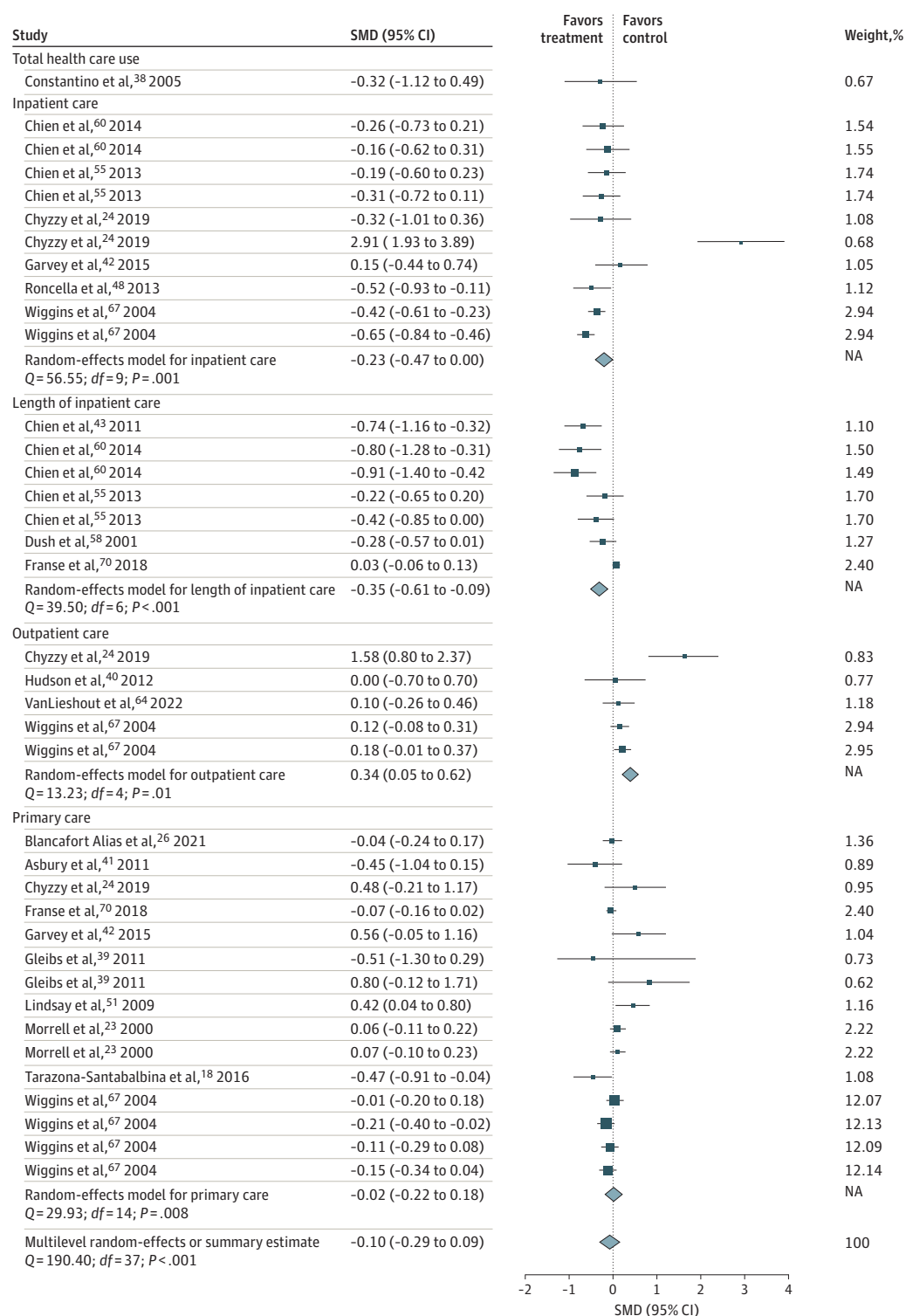
Measures of effect were calculated for the last follow-up measure in a subset of 5 studies^{22,23,54,59,67} that included ORs and 5 studies^{23,61,66,70,73} that included 13 SMDs that included more than 1 follow-up (eFigure 3 and eFigure 4 in [Supplement 1](#)). The OR random-effects model showed a significant decrease only in inpatient care (OR, 0.52; 95% CI, 0.28 to 0.98) and the SMD model showed a lower length of inpatient care (SMD, -1.21; 95% CI, -1.67 to -0.75).

Figure 2. Pooled 95% CI Odds Ratio of the Association of Psychosocial Interventions With Health Care Utilization



Since multilevel meta-analyses included several effect estimates from each study, studies may be listed more than once for each analysis. Dots indicate estimates; whiskers, 95% CIs; diamond, summary estimate.

Figure 3. Pooled 95% CI Standardized Mean Difference of the Association of Psychosocial Interventions With Health Care Utilization



Since multilevel meta-analyses included several effect estimates from each study, studies may be listed more than once for each analysis. Dots indicate estimates; whiskers, 95% CIs; diamond, summary estimate; SMD, standardized mean difference.

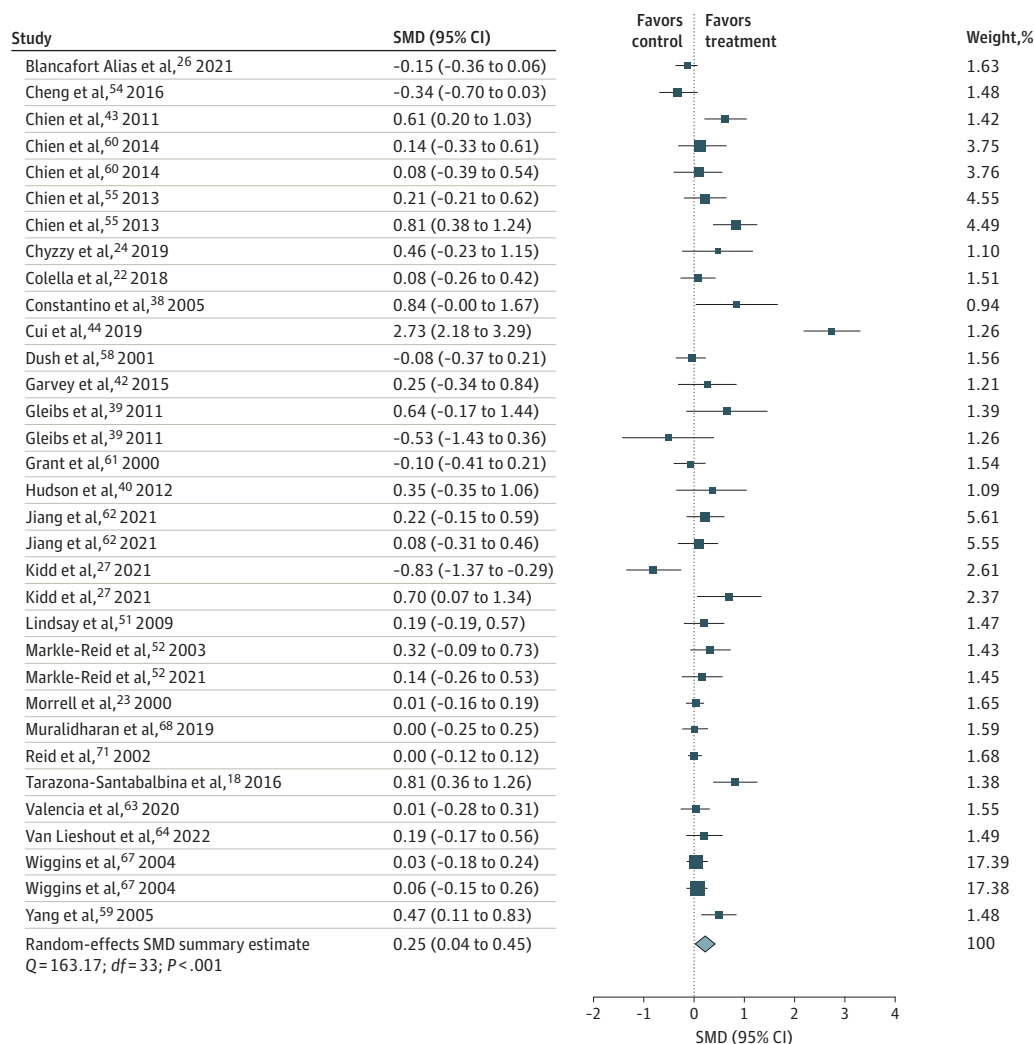
Meta-Analyses of Social Support and Loneliness Outcomes

Social support and loneliness were the primary domains of social well-being reported, and these were examined as secondary outcomes only in an SMD meta-analysis (**Figure 4** and **Figure 5**). There was a statistically significant postintervention increase in social support but not in loneliness. Subgroup analyses of participants' characteristics revealed a significant increase in social support following interventions conducted in China,^{43,44,54,55,59,60} among participants aged 30 to 60 years,^{27,38,43,44,54,55,59,61,64,68} men,^{22,27,44,51,55,60,62,63,68} and people with chronic illnesses.^{22,42,44,51,62} Analyses by intervention characteristics found improvements in social support following longer interventions, 1-on-1 interventions, and interventions delivered by health professionals.

Assessment of Publication Bias

All the OR and SMD random-effects models were tested for publication bias, except for the model for loneliness due to the small number of studies (eFigure 2 in [Supplement 1](#)). No publication bias was found for the meta-analyses of ORs in either the immediate or sustained effect models. For the meta-analysis of SMD, the regression test for asymmetry reached statistical significance in both the

Figure 4. Pooled 95% CI Standardized Mean Difference of the Association of Psychosocial Interventions With Social Support



Since multilevel meta-analyses included several effect estimates from each study, studies may be listed more than once for each analysis. Dots indicate estimates; whiskers, 95% CIs; diamond, summary estimate; SMD, standardized mean difference.

immediate and sustained effect models, indicating significant publication bias. There was no bias found in the funnel plot of the SMD social support model (eFigure 2 in Supplement 1).

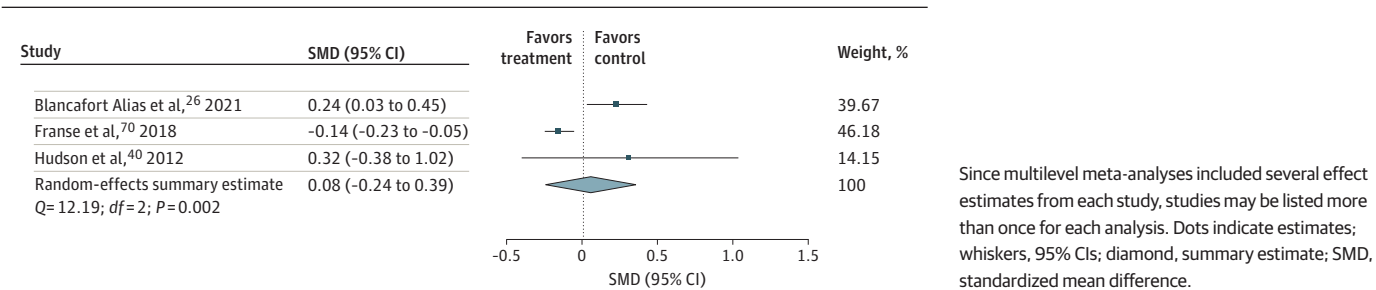
Discussion

This systematic review and meta-analysis found that psychosocial interventions were associated with improved health care utilization. Models showed strong to moderate strength of evidence by BFs for number of inpatient visits and length of inpatients visits associated with social support. Emergency and primary care utilization also showed moderate strength of evidence for the OR model. Additionally, these interventions were associated with improvements in social support but not loneliness. Considering the need to reduce unnecessary health care spending in many countries, our findings have highlighted the potential for psychosocial interventions to reduce health care utilization. The largest reduction in health care use occurred in inpatient visit numbers and length of stay, emergency admissions, and primary care services. The reduction in inpatient and emergency care utilization could be due to an instrumental support system that may have prevented a health condition from deteriorating⁷³ by direct care or by encouraging patients to seek treatment earlier.¹⁴ In addition, the support provided could also prevent or lower stress and anxiety associated with different health conditions,⁷⁴ which may have contributed to reduction in unnecessary visits to the hospital.^{75,76} The decrease in health care use could also be a result of an improvement in overall health.^{77,78} These findings suggest that the emotional, informational, and instrumental support provided by psychosocial interventions may decrease the need to seek medical care excessively and may contribute to reduced health care expenses and improved service efficiency.^{52,79-81} Such outcomes may last over longer periods, although the current evidence on sustained outcomes is limited by the small number of studies with sustained follow-up.

Outpatient care was the only outcome that showed an increase. This supports previous findings of a positive association between social well-being and outpatient visits.^{10,82} Outpatient care often supports tertiary-level prevention, which can sustain recovery and reduce the need for urgent care.⁸³ Therefore, our findings suggest that psychosocial interventions may lead to improved preventive care in the outpatient context, which in turn, may lead to less emergency and inpatient care utilization.^{84,85}

Our subgroup analysis found a significant decrease in health care use among caregivers, suggesting the importance of including caregivers in psychosocial interventions. A significant decrease in health care use was also found among people with mental illness. As people with mental illnesses can experience poor social well-being due to isolation and perceived stigma,⁸⁶⁻⁸⁸ psychosocial interventions may provide much-needed social support for this group. Our subgroup analysis also found that interventions conducted in China and the US showed significant decreases in postintervention health care use, possibly due to differences in measurements or sample sizes.⁸⁹ However, some of these differences may reflect country-specific variations in standards of care, service availability, health professional capacity, and cultural differences in health-seeking

Figure 5. Pooled 95% CI Standardized Mean Difference of the Association of Psychosocial Interventions With Loneliness



practices.⁹⁰⁻⁹² We found that in interventions delivered by health professionals, there was a significant decrease in postintervention health care use. Health care professionals are often perceived as trusted sources of information and support, which may have contributed to more favorable outcomes. This finding echoes previous observations regarding implementing social care within health care settings^{93,94} and including health professionals in the delivery of psychosocial interventions.⁸⁵ Finally, the decrease in health care use was more pronounced in individual-based interventions that included 1-on-1 activities. This finding highlights the importance of tailoring psychosocial interventions according to patients' needs, as applied in case and disease management models.^{85,95}

Our analysis also found a significant increase in postintervention social support. Previous studies found that loneliness and low social support were associated with more health care utilization,^{10,96,97} although a rapid review did not find a consistent association between psychosocial interventions and improvement in loneliness.¹³ Likewise, our study found no association of psychosocial interventions with loneliness, which is most likely due to the inconsistency in the results and the lack of power. These findings highlight the complex and measure-specific nature of the association between social well-being and health care utilization.¹⁰

Limitations

This systematic review and meta-analysis has several limitations. First, the number of studies included in the analysis and the small sample sizes limited the certainty about the effect sizes and our ability to conduct multivariate analyses. Second, the use of ORs and SMDs is prone to measurement bias and therefore may have contributed to bias in the pooled effect size. Furthermore, most studies included in the SMD analysis reported means and SDs despite the underlying distributions being nonparametric. However, assuming that the SMD distribution shape remained the same, the SMD should provide a consistent estimate of the mean difference. In addition, synthesizing both ORs and SMDs should provide stronger and more complete evidence than relying on 1 measure of effect only. Third, the high level of heterogeneity among the studies may have contributed to the variability in the outcomes. We addressed this by conducting subgroup analyses. Fourth, the regression test for asymmetry indicated significant publication bias in the SMD meta-analysis, but since this analysis showed no association, the inclusion of unpublished data is unlikely to change our results. Fifth, relying on English abstracts may have led to the exclusion of eligible studies published in other languages.

Conclusions

The findings of this systematic review and meta-analysis suggest that psychosocial interventions were associated with improvements in patients' social support and health care use, possibly through increasing outpatient care while reducing the use of emergency and inpatient care. Our results also suggest that interventions should be tailored to the needs of patients and include health professionals as the deliverers. In addition, our findings about individual- and intervention-level characteristics may inform the design and implementation of future psychosocial interventions by providing information on the variables associated with intervention success. More randomized clinical trials with longer-term follow-ups are needed to better understand the sustained postintervention outcomes of health care use associated with psychosocial interventions.

ARTICLE INFORMATION

Accepted for Publication: May 16, 2023.

Published: June 29, 2023. doi:[10.1001/jamanetworkopen.2023.21019](https://doi.org/10.1001/jamanetworkopen.2023.21019)

Open Access: This is an open access article distributed under the terms of the [CC-BY License](#). © 2023 HaGani N et al. *JAMA Network Open*.

Corresponding Author: Neta HaGani, MSW, Prevention Research Collaboration, School of Public Health, The Hub Charles Perkins Centre (D17), The University of Sydney, Level 6, Sydney, NSW 2006, Australia (neta.hagani@sydney.edu.au).

Author Affiliations: Prevention Research Collaboration, Sydney School of Public Health, The University of Sydney, Sydney, Australia (HaGani, Surkalim, Clare, Smith, Ding); National Drug and Alcohol Research Centre, UNSW Sydney, Sydney, Australia (Clare); School of Health Science, Western Sydney University, Sydney, Australia (Merom); Charles Perkins Centre, the University of Sydney, Sydney, Australia (HaGani, Surkalim, Clare, Smith, Ding).

Author Contributions: Ms HaGani had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Senior authorship shared: Drs Merom, Smith, and Ding.

Concept and design: HaGani, Merom, Smith, Ding.

Acquisition, analysis, or interpretation of data: HaGani, Surkalim, Clare, Merom, Ding.

Drafting of the manuscript: HaGani, Smith.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: HaGani, Clare.

Obtained funding: HaGani.

Administrative, technical, or material support: HaGani, Smith, Ding.

Supervision: Clare, Merom, Smith, Ding.

Conflict of Interest Disclosures: None reported.

Funding/Support: Prof Ding is funded by the National Health and Medical Research Council Emerging Leader fellowship (award No. 2009254).

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See [Supplement 2](#).

REFERENCES

1. National Academies of Sciences, Engineering, and Medicine. *Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System*. National Academies Press; 2020. doi:[10.17226/25663](#)
2. Centers for Disease Control and Prevention. Loneliness and social isolation linked to serious health conditions. Accessed August 30, 2022. <https://www.cdc.gov/aging/publications/features/lonely-older-adults.html>
3. Killgore WDS, Cloonan SA, Taylor EC, Dailey NS. Loneliness: a signature mental health concern in the era of COVID-19. *Psychiatry Res*. 2020;290:113117. doi:[10.1016/j.psychres.2020.113117](#)
4. Surkalim DL, Luo M, Eres R, et al. The prevalence of loneliness across 113 countries: systematic review and meta-analysis. *BMJ*. 2022;376:e067068. doi:[10.1136/bmj-2021-067068](#)
5. Lin FH, Yih DN, Shih FM, Chu CM. Effect of social support and health education on depression scale scores of chronic stroke patients. *Medicine (Baltimore)*. 2019;98(44):e17667. doi:[10.1097/MD.00000000000017667](#)
6. Courtin E, Knapp M. Social isolation, loneliness and health in old age: a scoping review. *Health Soc Care Community*. 2017;25(3):799-812. doi:[10.1111/hsc.12311](#)
7. Bell CM, Ridley JA, Overholser JC, et al. The role of perceived burden and social support in suicide and depression. *Suicide Life Threat Behav*. 2018;48(1):87-94. doi:[10.1111/sltb.12327](#)
8. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204-1222. doi:[10.1016/S0140-6736\(20\)30925-9](#)
9. Prang KH, Berecki-Gisolf J, Newnam S. The influence of social support on healthcare service use following transport-related musculoskeletal injury. *BMC Health Serv Res*. 2016;16:310. doi:[10.1186/s12913-016-1582-4](#)
10. Valtorta NK, Moore DC, Barron L, Stow D, Hanratty B. Older adults' social relationships and health care utilization: a systematic review. *Am J Public Health*. 2018;108(4):e1-e10. doi:[10.2105/AJPH.2017.304256](#)
11. Lim KK, Chan A. Association of loneliness and healthcare utilization among older adults in Singapore. *Geriatr Gerontol Int*. 2017;17(11):1789-1798. doi:[10.1111/ggi.12962](#)

12. Shaw JG, Farid M, Noel-Miller C, et al. Social isolation and Medicare spending: among older adults, objective social isolation increases expenditures while loneliness does not. *J Aging Health*. 2017;29(7):1119-1143. doi:10.1177/0898264317703559
13. Veazie S, Gilbert J, Winchell K, Paynter R, Guise JM. *Addressing Social Isolation to Improve the Health of Older Adults: A Rapid Review*. Agency for Healthcare Research and Quality; 2019. doi:10.23970/AHRQEPIC-RAPIDISOLATION
14. Spiers G, Matthews FE, Moffatt S, et al. Impact of social care supply on healthcare utilisation by older adults: a systematic review and meta-analysis. *Age Ageing*. 2019;48(1):57-66. doi:10.1093/ageing/afy147
15. Forsman AK, Nordmyr J, Wahlbeck K. Psychosocial interventions for the promotion of mental health and the prevention of depression among older adults. *Health Promot Int*. 2011;26(suppl 1):i85-i107. doi:10.1093/heapro/dar074
16. Barbui C, Purgato M, Abdulmalik J, et al. Efficacy of psychosocial interventions for mental health outcomes in low-income and middle-income countries: an umbrella review. *Lancet Psychiatry*. 2020;7(2):162-172. doi:10.1016/S2215-0366(19)30511-5
17. Pitkala KH, Routasalo P, Kautiainen H, Tilvis RS. Effects of psychosocial group rehabilitation on health, use of health care services, and mortality of older persons suffering from loneliness: a randomized, controlled trial. *J Gerontol A Biol Sci Med Sci*. 2009;64(7):792-800. doi:10.1093/gerona/glp011
18. Tarazona-Santabalbina FJ, Gómez-Cabrera MC, Pérez-Ros P, et al. A multicomponent exercise intervention that reverses frailty and improves cognition, emotion, and social networking in the community-dwelling frail elderly: a randomized clinical trial. *J Am Med Dir Assoc*. 2016;17(5):426-433. doi:10.1016/j.jamda.2016.01.019
19. Alaviani M, Khosravan S, Alami A, Moshki M. The effect of a multi-strategy program on developing social behaviors based on Pender's Health Promotion model to prevent loneliness of old women referred to Gonabad urban health centers. *Int J Community Based Nurs Midwifery*. 2015;3(2):132-140.
20. Hemingway A, Jack E. Reducing social isolation and promoting well being in older people. *J Quality in Ageing Older Adults*. 2013;14(1):25-35. doi:10.1108/14717791311311085
21. Simpson JS, Carlson LE, Trew ME. Effect of group therapy for breast cancer on healthcare utilization. *Cancer Pract*. 2001;9(1):19-26. doi:10.1046/j.1523-5394.2001.91005.x
22. Colella TJ, King-Shier K. The effect of a peer support intervention on early recovery outcomes in men recovering from coronary bypass surgery: a randomized controlled trial. *Eur J Cardiovasc Nurs*. 2018;17(5):408-417. doi:10.1177/1474515117725521
23. Morrell CJ, Spiby H, Stewart P, Walters S, Morgan A. Costs and benefits of community postnatal support workers: a randomised controlled trial. *Health Technol Assess*. 2000;4(6):1-100. doi:10.3310/hta4060
24. Chyzzy B. *Mobile Phone-Based Peer Support in the Prevention of Postpartum Depression Among Adolescent Mothers: A Pilot Randomized Controlled Trial*. Dissertation. University of Toronto; 2019. Accessed May 26, 2023. <https://tspace.library.utoronto.ca/handle/1807/95775>
25. Aminzadeh F, Dalziel WB. Older adults in the emergency department: a systematic review of patterns of use, adverse outcomes, and effectiveness of interventions. *Ann Emerg Med*. 2002;39(3):238-247. doi:10.1067/mem.2002.121523
26. Blancafort Alias S, Monteserín Nadal R, Moral I, Roqué Fígols M, Rojano I Luque X, Coll-Planas L. Promoting social capital, self-management and health literacy in older adults through a group-based intervention delivered in low-income urban areas: results of the randomized trial AEQUALIS. *BMC Public Health*. 2021;21(1):84. doi:10.1186/s12889-020-10094-9
27. Kidd SA, Mutschler C, Lichtenstein S, et al. Randomized trial of a brief peer support intervention for individuals with schizophrenia transitioning from hospital to community. *Schizophr Res*. 2021;231:214-220. doi:10.1016/j.schres.2021.03.019
28. Higgins JPT, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 6.3. Cochrane; 2022.
29. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0. The Cochrane Collaboration; 2011.
30. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315(7109):629-634. doi:10.1136/bmj.315.7109.629
31. Rodgers MA, Pustejovsky JE. Evaluating meta-analytic methods to detect selective reporting in the presence of dependent effect sizes. *Psychol Methods*. 2020;26(2):141-160. doi:10.1037/met0000300

32. Guyatt GH, Oxman AD, Vist GE, et al; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924-926. doi:10.1136/bmj.39489.470347.AD
33. Atkins D, Best D, Briss PA, et al; GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ*. 2004;328(7454):1490. doi:10.1136/bmj.328.7454.1490
34. Harrer M, Cuijpers P, Furukawa TA, Ebert DD. *Doing Meta-Analysis With R: A Hands-On Guide*. Chapman & Hall/CRC Press; 2021. doi:10.1201/9781003107347
35. Dienes Z. Making the most of your data with Bayes. Accessed May 26, 2023. http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm
36. Scott RB, Samaha J, Chrisley R, Dienes Z. Prevailing theories of consciousness are challenged by novel cross-modal associations acquired between subliminal stimuli. *Cognition*. 2018;175:169-185. doi:10.1016/j.cognition.2018.02.008
37. Chronister J, Chou CC, Frain M, Cardoso EdS: the relationship between social support and rehabilitation related outcomes: a meta-analysis. *J Rehabil*. 2008;74(2):16-32.
38. Constantino R, Kim Y, Crane PA. Effects of a social support intervention on health outcomes in residents of a domestic violence shelter: a pilot study. *Issues Ment Health Nurs*. 2005;26(6):575-590. doi:10.1080/01612840590959416
39. Gleibs IH, Haslam C, Haslam SA, Jones JM. Water clubs in residential care: is it the water or the club that enhances health and well-being? *Psychol Health*. 2011;26(10):1361-1377. doi:10.1080/08870446.2010.529140
40. Hudson DB, Campbell-Grossman C, Hertzog M. Effects of an internet intervention on mothers' psychological, parenting, and health care utilization outcomes. *Issues Compr Pediatr Nurs*. 2012;35(3-4):176-193. doi:10.3109/01460862.2012.734211
41. Asbury EA, Webb CM, Collins P. Group support to improve psychosocial well-being and primary-care demands among women with cardiac syndrome X. *Climacteric*. 2011;14(1):100-104. doi:10.3109/13697137.2010.499181
42. Garvey J, Connolly D, Boland F, Smith SM. OPTIMAL, an occupational therapy led self-management support programme for people with multimorbidity in primary care: a randomized controlled trial. *BMC Fam Pract*. 2015;16:59. doi:10.1186/s12875-015-0267-0
43. Chien WT, Lee IY. Randomized controlled trial of a dementia care programme for families of home-resided older people with dementia. *J Adv Nurs*. 2011;67(4):774-787. doi:10.1111/j.1365-2648.2010.05537.x
44. Cui X, Zhou X, Ma LL, et al. A nurse-led structured education program improves self-management skills and reduces hospital readmissions in patients with chronic heart failure: a randomized and controlled trial in China. *Rural Remote Health*. 2019;19(2):5270. doi:10.22605/RRH5270
45. Goldberg RW, Dickerson F, Lucksted A, et al. Living well: an intervention to improve self-management of medical illness for individuals with serious mental illness. *Psychiatr Serv*. 2013;64(1):51-57. doi:10.1176/appi.ps.201200034
46. Markle-Reid M, McAiney C, Fisher K, et al. Effectiveness of a nurse-led hospital-to-home transitional care intervention for older adults with multimorbidity and depressive symptoms: a pragmatic randomized controlled trial. *PLoS One*. 2021;16(7):e0254573. doi:10.1371/journal.pone.0254573
47. Roberts J, Browne G, Milne C, et al. Problem-solving counseling for caregivers of the cognitively impaired: effective for whom? *Nurs Res*. 1999;48(3):162-172. doi:10.1097/00006199-199905000-00006
48. Roncella A, Pristipino C, Cianfrocca C, et al. One-year results of the randomized, controlled, short-term psychotherapy in acute myocardial infarction (STEP-IN-AMI) trial. *Int J Cardiol*. 2013;170(2):132-139. doi:10.1016/j.ijcard.2013.08.094
49. Buchkremer G, Mönking HS, Holle R, Hornung W. The impact of therapeutic relatives' groups on the course of illness of schizophrenic patients. *Eur Psychiatry*. 1995;10(1):17-27. doi:10.1016/0767-399X(96)80071-X
50. Gaugler JE, Reese M, Mittelman MS. Effects of the NYU caregiver intervention-adult child on residential care placement. *Gerontologist*. 2013;53(6):985-997. doi:10.1093/geront/gns193
51. Lindsay S, Smith S, Bellaby P, Baker R. The health impact of an online heart disease support group: a comparison of moderated versus unmoderated support. *Health Educ Res*. 2009;24(4):646-654. doi:10.1093/her/cyp001
52. Markle-Reid M, Weir R, Browne G, Henderson S, Roberts CJ, Gafni A. *Frail Elderly Homecare Clients: The Costs and Effects of Adding Nursing Health Promotion and Preventive Care to Personal Support Services*. Dissertation. McMaster University; 2003.

53. Shaw JM, Young JM, Butow PN, et al. Improving psychosocial outcomes for caregivers of people with poor prognosis gastrointestinal cancers: a randomized controlled trial (Family Connect). *Support Care Cancer*. 2016;24(2):585-595. doi:10.1007/s00520-015-2817-3
54. Cheng HY. *The Effect of a Psychoeducational Intervention on Stroke Family Caregivers' Outcomes and Stroke Survivors' Utilisation of Health and Social Services*. Dissertation. The Chinese University of Hong Kong; 2014.
55. Chien WT, Chan SW. The effectiveness of mutual support group intervention for Chinese families of people with schizophrenia: a randomised controlled trial with 24-month follow-up. *Int J Nurs Stud*. 2013;50(10):1326-1340. doi:10.1016/j.ijnurstu.2013.01.004
56. Hengartner MP, Passalacqua S, Andreae A, Rössler W, von Wyl A. The role of perceived social support after psychiatric hospitalisation: post hoc analysis of a randomised controlled trial testing the effectiveness of a transitional intervention. *Int J Soc Psychiatry*. 2017;63(4):297-306. doi:10.1177/0020764017700664
57. Jones DL, Zulu I, Vamos S, Cook R, Chitalu N, Weiss SM. Determinants of engagement in HIV treatment and care among Zambians new to antiretroviral therapy. *J Assoc Nurses AIDS Care*. 2013;24(5):e1-e12. doi:10.1016/j.jana.2012.06.009
58. Dush DM, Ayres SY, Curtis C, Worthington GJ, Gabriel RM, Chinnery T. Reducing psychiatric hospital use of the rural poor through intensive transitional acute care. *Psychiatr Rehabil J*. 2001;25(1):28-34. doi:10.1037/h0095053
59. Yang FSZY, Guo ZH. Effect of psychosocial intervention on quality of life and other factors in patients with recurrent depression. Article in Chinese. *Chin J Clin Rehab*. 2005;9(4):16-18.
60. Chien WT, Thompson DR. Effects of a mindfulness-based psychoeducation programme for Chinese patients with schizophrenia: 2-year follow-up. *Br J Psychiatry*. 2014;205(1):52-59. doi:10.1192/bjp.bp.113.134635
61. Grant C, Goodenough T, Harvey I, Hine C. A randomised controlled trial and economic evaluation of a referrals facilitator between primary care and the voluntary sector. *BMJ*. 2000;320(7232):419-423. doi:10.1136/bmj.320.7232.419
62. Jiang Y, Koh KWL, Ramachandran HJ, et al. The effectiveness of a nurse-led home-based heart failure self-management programme (the HOM-HEMP) for patients with chronic heart failure: A three-arm stratified randomized controlled trial. *Int J Nurs Stud*. 2021;122:104026. doi:10.1016/j.ijnurstu.2021.104026
63. Valencia JG. Brief group psychoeducation for schizophrenia. Accessed May 26, 2023. <https://clinicaltrials.gov/ct2/show/NCT02911519>
64. Van Lieshout RJ, Layton H, Savoy CD, et al. Public health nurse-delivered group cognitive behavioural therapy for postpartum depression: a randomized controlled trial. *Can J Psychiatry*. 2022;67(6):432-440. doi:10.1177/07067437221074426
65. van Lieshout MRJ, Bleijenberg N, Schuurmans MJ, de Wit NJ. The effectiveness of a proactive multicomponent intervention program on disability in independently living older people: a randomized controlled trial. *J Nutr Health Aging*. 2018;22(9):1051-1059. doi:10.1007/s12603-018-1101-x
66. Boter H; HESTIA Study Group. Multicenter randomized controlled trial of an outreach nursing support program for recently discharged stroke patients. *Stroke*. 2004;35(12):2867-2872. doi:10.1161/01.STR.0000147717.57531.e5
67. Wiggins M, Oakley A, Roberts I, et al. The Social Support and Family Health Study: a randomised controlled trial and economic evaluation of two alternative forms of postnatal support for mothers living in disadvantaged inner-city areas. *Health Technol Assess*. 2004;8(32):iii, ix-x, 1-120. doi:10.3310/hta8320
68. Muralidharan A, Brown CH, E Peer J, et al. Living Well: an intervention to improve medical illness self-management among individuals with serious mental illness. *Psychiatr Serv*. 2019;70(1):19-25. doi:10.1176/appi.ps.201800162
69. Gillard S, Bremner S, Patel A, et al; ENRICH trial study group. Peer support for discharge from inpatient mental health care versus care as usual in England (ENRICH): a parallel, two-group, individually randomised controlled trial. *Lancet Psychiatry*. 2022;9(2):125-136. doi:10.1016/S2215-0366(21)00398-9
70. Franse CB, van Grieken A, Alhambra-Borrás T, et al. The effectiveness of a coordinated preventive care approach for healthy ageing (UHCE) among older persons in five European cities: a pre-post controlled trial. *Int J Nurs Stud*. 2018;88:153-162. doi:10.1016/j.ijnurstu.2018.09.006
71. Reid M, Glazener C, Murray GD, Taylor GS. A two-centred pragmatic randomised controlled trial of two interventions of postnatal support. *BJOG*. 2002;109(10):1164-1170. doi:10.1111/j.1471-0528.2002.01306.x
72. Simpson A, Flood C, Rowe J, et al. Results of a pilot randomised controlled trial to measure the clinical and cost effectiveness of peer support in increasing hope and quality of life in mental health patients discharged from hospital in the UK. *BMC Psychiatry*. 2014;14:30. doi:10.1186/1471-244X-14-30

73. McFarlane WR. Family interventions for schizophrenia and the psychoses: a review. *Fam Process*. 2016;55(3):460-482. doi:[10.1111/famp.12235](https://doi.org/10.1111/famp.12235)
74. Cohen S, McKay G. Social support, stress and the buffering hypothesis: a theoretical analysis. In: Taylor SE, Singer JE, Baum A, eds. *Handbook of Psychology and Health, Volume IV*. Routledge; 1984:253-267. doi:[10.4324/9781003044307](https://doi.org/10.4324/9781003044307)
75. Bernstein MT, Walker JR, Chhibba T, et al. Health care services in IBD: factors associated with service utilization and preferences for service options for routine and urgent care. *Inflamm Bowel Dis*. 2017;23(9):1461-1469. doi:[10.1097/MIB.0000000000001215](https://doi.org/10.1097/MIB.0000000000001215)
76. Morris R, Patel S, Malins S, et al. Clinical and economic outcomes of remotely delivered cognitive behaviour therapy versus treatment as usual for repeat unscheduled care users with severe health anxiety: a multicentre randomised controlled trial. *BMC Med*. 2019;17(1):16. doi:[10.1186/s12916-019-1253-5](https://doi.org/10.1186/s12916-019-1253-5)
77. Hunter RF, de la Haye K, Murray JM, et al. Social network interventions for health behaviours and outcomes: a systematic review and meta-analysis. *PLoS Med*. 2019;16(9):e1002890. doi:[10.1371/journal.pmed.1002890](https://doi.org/10.1371/journal.pmed.1002890)
78. Steffens NK, LaRue CJ, Haslam C, et al. Social identification-building interventions to improve health: a systematic review and meta-analysis. *Health Psychol Rev*. 2021;15(1):85-112. doi:[10.1080/17437199.2019.1669481](https://doi.org/10.1080/17437199.2019.1669481)
79. Lawn S, Smith A, Hunter K. Mental health peer support for hospital avoidance and early discharge: an Australian example of consumer driven and operated service. *J Ment Health*. 2008;17(5):498-508. doi:[10.1080/09638230701530242](https://doi.org/10.1080/09638230701530242)
80. Dieng M, Cust AE, Kasparian NA, Mann GJ, Morton RL. Economic evaluations of psychosocial interventions in cancer: a systematic review. *Psychooncology*. 2016;25(12):1380-1392. doi:[10.1002/pon.4075](https://doi.org/10.1002/pon.4075)
81. Jhanjee S. Evidence based psychosocial interventions in substance use. *Indian J Psychol Med*. 2014;36(2):112-118. doi:[10.4103/0253-7176.130960](https://doi.org/10.4103/0253-7176.130960)
82. Bremer D, Inhestern L, von dem Knesebeck O. Social relationships and physician utilization among older adults—a systematic review. *PLoS One*. 2017;12(9):e0185672. doi:[10.1371/journal.pone.0185672](https://doi.org/10.1371/journal.pone.0185672)
83. Tian WH, Chen CS, Liu TC. The demand for preventive care services and its relationship with inpatient services. *Health Policy*. 2010;94(2):164-174. doi:[10.1016/j.healthpol.2009.09.012](https://doi.org/10.1016/j.healthpol.2009.09.012)
84. Holt-Lunstad J, Smith TB. Loneliness and social isolation as risk factors for CVD: implications for evidence-based patient care and scientific inquiry. *Heart*. 2016;102(13):987-989. doi:[10.1136/heartjnl-2015-309242](https://doi.org/10.1136/heartjnl-2015-309242)
85. Doshmangir L, Khabiri R, Jabbari H, Arab-Zozani M, Kakemam E, Gordeev VS. Strategies for utilisation management of hospital services: a systematic review of interventions. *Global Health*. 2022;18(1):53. doi:[10.1186/s12992-022-00835-3](https://doi.org/10.1186/s12992-022-00835-3)
86. Chronister J, Chou CC, Liao HY. The role of stigma coping and social support in mediating the effect of societal stigma on internalized stigma, mental health recovery, and quality of life among people with serious mental illness. *J Community Psychol*. 2013;41(5):582-600. doi:[10.1002/jcop.21558](https://doi.org/10.1002/jcop.21558)
87. Ma R, Mann F, Wang J, et al. The effectiveness of interventions for reducing subjective and objective social isolation among people with mental health problems: a systematic review. *Soc Psychiatry Psychiatr Epidemiol*. 2020;55(7):839-876. doi:[10.1007/s00127-019-01800-z](https://doi.org/10.1007/s00127-019-01800-z)
88. Mojtabai R, Stuart EA, Hwang I, Eaton WW, Sampson N, Kessler RC. Long-term effects of mental disorders on marital outcomes in the National Comorbidity Survey ten-year follow-up. *Soc Psychiatry Psychiatr Epidemiol*. 2017;52(10):1217-1226. doi:[10.1007/s00127-017-1373-1](https://doi.org/10.1007/s00127-017-1373-1)
89. Yusuf S, Wittes J. Interpreting geographic variations in results of randomized, controlled trials. *N Engl J Med*. 2016;375(23):2263-2271. doi:[10.1056/NEJMr1510065](https://doi.org/10.1056/NEJMr1510065)
90. Garcés IC, Scarinci IC, Harrison L. An examination of sociocultural factors associated with health and health care seeking among Latina immigrants. *J Immigr Minor Health*. 2006;8(4):377-385. doi:[10.1007/s10903-006-9008-8](https://doi.org/10.1007/s10903-006-9008-8)
91. Srivastava A, Avan BI, Rajbangshi P, Bhattacharyya S. Determinants of women's satisfaction with maternal health care: a review of literature from developing countries. *BMC Pregnancy Childbirth*. 2015;15:97. doi:[10.1186/s12884-015-0525-0](https://doi.org/10.1186/s12884-015-0525-0)
92. Pocock S, Calvo G, Marrugat J, et al. International differences in treatment effect: do they really exist and why? *Eur Heart J*. 2013;34(24):1846-1852. doi:[10.1093/eurheartj/ehd071](https://doi.org/10.1093/eurheartj/ehd071)
93. Dineen-Griffin S, Garcia-Cardenas V, Williams K, Benrimoj SI. Helping patients help themselves: a systematic review of self-management support strategies in primary health care practice. *PLoS One*. 2019;14(8):e0220116. doi:[10.1371/journal.pone.0220116](https://doi.org/10.1371/journal.pone.0220116)

94. Betrán AP, Temmerman M, Kingdon C, et al. Interventions to reduce unnecessary caesarean sections in healthy women and babies. *Lancet*. 2018;392(10155):1358-1368. doi:10.1016/S0140-6736(18)31927-5
95. Grover CA, Close RJ, Villarreal K, Goldman LM. Emergency department frequent user: pilot study of intensive case management to reduce visits and computed tomography. *West J Emerg Med*. 2010;11(4):336-343.
96. Newall N, McArthur J, Menec VH. A longitudinal examination of social participation, loneliness, and use of physician and hospital services. *J Aging Health*. 2015;27(3):500-518. doi:10.1177/0898264314552420
97. Molloy GJ, McGee HM, O'Neill D, Conroy RM. Loneliness and emergency and planned hospitalizations in a community sample of older adults. *J Am Geriatr Soc*. 2010;58(8):1538-1541. doi:10.1111/j.1532-5415.2010.02960.x

SUPPLEMENT 1.

eTable 1. Population, Intervention, Comparison, and Outcome (PICO) Table of Study Eligibility Criteria

eTable 2. Study Search Strategy

eTable 3. CINAHL Search Results

eTable 4. Cochrane Search Results

eTable 5. Embase Search Results

eTable 6. Medline Search Results

eTable 7. PsycInfo Search Results

eTable 8. Scopus Search Results

eTable 9. Summary Description of Randomized Clinical Trials Included in the Systematic Review (N = 41)

eTable 10. Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence Profile

eTable 11. Strength of Evidence (Bayes Factors) in the OR and SMD According to Health Care Service

eTable 12. Subgroup Analyses of Postintervention Health Care Utilization According to Participant- and

Intervention-Level Factors

eFigure 1. Cochrane Risk-of-Bias Summary and Author Judgments of Low, High and Unclear Risk of Bias Across All Included Studies (N = 41)

eFigure 2. Publication Bias Funnel Plots for Standardized Mean Difference (SMD) and Log Odds Ratio (OR) Random Effect Models of Health Care Utilization Outcomes and Social Support

eFigure 3. Pooled 95% CI Odds Ratio of the Sustained Association of Psychosocial Interventions With Health Care Utilization

eFigure 4. Pooled 95% CI Standardized Mean Difference of the Sustained Association of Psychosocial Interventions With Health Care Utilization

SUPPLEMENT 2.

Data Sharing Statement

6.5. Appendices

Supplemental Online Content

HaGani N, Surkalim DL, Clare PJ, Merom D, Smith BJ, Ding D. Health Care Utilization Following Interventions to Improve Social Well-being: a systematic review and meta-analysis. *JAMA Netw Open*. 2023;6(6):e2321019. doi:10.1001/jamanetworkopen.2023.21019

eTable 1. Population, Intervention, Comparison, and Outcome (PICO) Table of Study Eligibility Criteria

eTable 2. Study Search Strategy

eTable 3. CINAHL Search Results

eTable 4. Cochrane Search Results

eTable 5. Embase Search Results

eTable 6. Medline Search Results

eTable 7. PsycInfo Search Results

eTable 8. Scopus Search Results

eTable 9. Summary Description of Randomized Clinical Trials Included in the Systematic Review (N = 41)

eTable 10. Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence Profile

eTable 11. Strength of Evidence (Bayes Factors) in the OR and SMD According to Health Care Service

eTable 12. Subgroup Analyses of Postintervention Health Care Utilization According to Participant- and Intervention-Level Factors

eFigure 1. Cochrane Risk-of-Bias Summary and Author Judgments of Low, High and Unclear Risk of Bias Across All Included Studies (N = 41)

eFigure 2. Publication Bias Funnel Plots for Standardized Mean Difference (SDM) and Log Odds Ratio (OR) Random Effect Models of Health Care Utilization Outcomes and Social Support

eFigure 3. Pooled 95% CI Odds Ratio of the Sustained Association of Psychosocial Interventions With Health Care Utilization

eFigure 4. Pooled 95% CI Standardized Mean Difference of the Sustained Association of Psychosocial Interventions With Health Care Utilization

This supplemental material has been provided by the authors to give readers additional

eTable 1. Population, Intervention, Comparison, and Outcome (PICO) Table of Study Eligibility Criteria

P	Patient, population, problem Participants from all population groups including healthy as well as clinical populations of all ages and genders.
I	Intervention, prognostic factor or exposure Studies that investigated the effect of psychosocial interventions on participants' health care utilisation patterns and on levels of social wellbeing using a Randomised Control Trial (RCT) design. Psychosocial interventions were defined as those who aim to improve social, using a range of techniques such as therapeutic individual/ group support, group activities, peer support, community integration and physical activity.
C	Comparison Interventions were compared to either standard care, an alternate intervention (e.g., individual activities, group activity without the main therapeutic component, providing information and manuals, medications) or wait-listed control.
O	Outcome The primary outcomes were utilisation of health care services such as primary care, emergency care, inpatient care/readmissions, and outpatient care. The secondary outcomes were social wellbeing measures such as social support, social participation, social relationships, community support, social integration and loneliness.

eTable 2. Study Search Strategy

Health care utilisation	Social wellbeing	Psychosocial interventions
Healthcare OR "health care" OR "re-admission*" OR admission* OR "emergency department*" OR "emergency room" OR hospitalization* OR hospitalisation OR "health service*" OR "general practi*" OR "ambulatory care" OR "urgent care" OR "physician* visit*" OR "primary care"	lonel* OR "social* isolat*" OR "social* disconnect*" OR "social support" OR "social interaction*" OR "peer support" OR "family support" OR "social network*" OR "social relationship*" OR "emotional support" OR "social problem*" OR "social capital" OR psychosocial.	"support intervention*" OR "brief intervention*" OR "group intervention*" OR "group-based program*" OR "Care Program*" OR "support program*" OR "psychosocial intervention*" OR "Multicomponent intervention*" OR "Self-Help Group*" OR "Transitional Care" OR "transitional intervention*" OR "education* intervention*" OR "follow-up care" OR "peer delivered intervention*" OR "support group*" OR "liaison service*".

eTable 3. CINAHL Search Results

Thursday, May 13, 2021 10:39:38 AM

#	Query	Limiters/Expanders	Last Run Via	Results
S48	S45 AND S46 AND S47	Limiters - Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	1,896
S47	S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	45,436
S46	S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	175,402
S45	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	573,412
S44	AB "liaison service*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	326
S43	(MH "Support Groups") OR AB "support group*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	14,008
S42	AB "peer delivered intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	15

S41	AB "follow up care"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,460
S40	AB "education* intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	8,544
S39	AB "transitional intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	19
S38	(MH "Transitional Care") OR AB "Transitional Care"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,795
S37	AB "Self Help Group*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	742
S36	AB "Multicomponent intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	671
S35	(MH "Psychosocial Intervention") OR AB "psychosocial intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	3,011
S34	AB "support program*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,461
S33	AB "Care Program*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	5,650
S32	AB "group based program*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	106

S31	AB "group intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,635
S30	AB "brief intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,562
S29	AB "support intervention*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	1,520
S28	(MH "Support, Psychosocial+") OR AB "psychosocial"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	129,174
S27	AB "social capital"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,587
S26	AB "social problem*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	2,993
S25	AB "emotional support"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	4,978
S24	AB "social relationship*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	3,224
S23	AB "social network*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	10,678
S22	AB "family support"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	3,903
S21	AB "peer	Expanders - Apply	Interface - EBSCOhost Research	3,664

	support"	equivalent subjects Search modes - Boolean/Phrase	Databases Search Screen - Advanced Search Database - CINAHL Complete	
S20	AB "social interaction*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	6,396
S19	AB "social support"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	25,924
S18	AB "social* disconnect*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	88
S17	(MH "Loneliness") OR AB "lonel*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	7,248
S16	(MH "Social Isolation+") OR AB "social* isolat*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	15,951
S15	(MH "Primary Health Care") OR AB "primary care"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	99,946
S14	AB "physician* visit*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	1,527
S13	AB "urgent care"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	1,437
S12	AB "ambulatory care"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	3,218
S11	AB "general practi*"	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases	26,807

		Search modes - Boolean/Phrase	Search Screen - Advanced Search Database - CINAHL Complete	
S10	(MH "Health Services")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	14,086
S9	AB "health service*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	60,164
S8	AB "hospitalisation*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	6,106
S7	AB "hospitalization*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	50,252
S6	AB "emergency room"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	5,548
S5	AB "emergency department*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	47,815
S4	AB "admission*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	77,407
S3	AB "re- admission*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	899
S2	AB "healthcare"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	135,531
S1	AB "health care"	Expanders - Apply equivalent subjects Search modes -	Interface - EBSCOhost Research Databases Search Screen - Advanced Search	176,976

		Boolean/Phrase	Database - CINAHL Complete	
--	--	----------------	----------------------------	--

Bottom of Form

eTable 4. Cochrane Search Results

Search Name: 13-5-21 search

Date Run: 13/05/2021 15:54:17

ID	Search Hits
#1	(healthcare):ti,ab,kw in Cochrane Reviews, Trials 21555
#2	("health care"):ti,ab,kw in Cochrane Reviews, Trials60101
#3	("re-admission*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 771
#4	(admission*):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 31651
#5	("emergency department*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 10945
#6	("emergency room*"):ti,ab,kw in Cochrane Reviews, Trials 2109
#7	(hospitalization*):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 40791
#8	("health service*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 20082
#9	("general practice"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 6323
#10	("general practitioner"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 7274
#11	("ambulatory care"):ti,ab,kw in Cochrane Reviews, Trials 4809
#12	("urgent care"):ti,ab,kw in Cochrane Reviews, Trials 346
#13	("physician* visit*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials 531
#14	MeSH descriptor: [Health Services] this term only 452
#15	("primary care"):ti,ab,kw in Cochrane Reviews, Trials 18852
#16	MeSH descriptor: [Physicians] explode all trees 2093
#17	MeSH descriptor: [Primary Health Care] explode all trees 7508

#18	MeSH descriptor: [Social Isolation] explode all trees	301
#19	(social isolation):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	1568
#20	(lonel*):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	780
#21	MeSH descriptor: [Social Isolation] explode all trees	301
#22	("social support"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	8345
#23	("social interaction*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	3576
#24	("peer support"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	1277
#25	("family support"):ti,ab,kw in Cochrane Reviews, Trials	586
#26	("social network*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	1665
#27	("social relationship*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	499
#28	("emotional support"):ti,ab,kw in Cochrane Reviews, Trials	624
#29	("social problems*"):ti,ab,kw in Cochrane Reviews, Trials	350
#30	(psychosocial):ti,ab,kw in Cochrane Reviews, Trials	16174
#31	("social capital"):ti,ab,kw in Cochrane Reviews, Trials	122
#32	("support intervention*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	1617
#33	("brief intervention*"):ti,ab,kw in Cochrane Reviews, Trials	2077
#34	("group intervention*"):ti,ab,kw in Cochrane Reviews, Trials	5057
#35	("group based program*"):ti,ab,kw in Cochrane Reviews, Trials	79
#36	("Care Program*"):ti,ab,kw in Cochrane Reviews, Trials	1863
#37	("support program*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	1241
#38	("psychosocial intervention*"):ti,ab,kw in Cochrane Reviews, Trials	1193

#39	MeSH descriptor: [Psychosocial Intervention] explode all trees	23
#40	("Multicomponent intervention*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	877
#41	("Self-Help Group*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	908
#42	("transitional intervention*"):ti,ab,kw in Cochrane Reviews, Trials	12
#43	("education intervention*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	6480
#44	("follow-up care"):ti,ab,kw in Cochrane Reviews, Trials	706
#45	("peer delivered intervention*"):ti,ab,kw in Cochrane Reviews, Trials	15
#46	("support group*"):ti,ab,kw (Word variations have been searched) in Cochrane Reviews, Trials	2111
#47	("liaison service*"):ti,ab,kw in Cochrane Reviews, Trials	49
#48	#1 #2 or #3 or #4 or #5 or #6 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17	94297
#49	#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31	30568
#50	#32 or #33 or #35 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47	162590
#51	#48 and #49 and #50	1321
#52	("Psychosocial Group*"):ti,ab,kw in Cochrane Reviews, Trials	96
#53	#50 or #52	162659
#54	#48 and #49 and #53	1328

Search Name: Cochrane update

Last Saved: 01/12/2022 11:04:40

Comment:

ID	Search
#1	(healthcare):ti,ab,kw
#2	("health care"):ti,ab,kw
#3	("re-admission*"):ti,ab,kw (Word variations have been searched)
#4	(admission*):ti,ab,kw (Word variations have been searched)
#5	("emergency department*"):ti,ab,kw (Word variations have been searched)
#6	("emergency room*"):ti,ab,kw
#7	(hospitalization*):ti,ab,kw (Word variations have been searched)
#8	("health service*"):ti,ab,kw (Word variations have been searched)
#9	("general practice"):ti,ab,kw (Word variations have been searched)
#10	("general practitioner"):ti,ab,kw (Word variations have been searched)
#11	("ambulatory care"):ti,ab,kw
#12	("urgent care"):ti,ab,kw
#13	("physician* visit*"):ti,ab,kw (Word variations have been searched)
#14	MeSH descriptor: [Health Services] this term only
#15	("primary care"):ti,ab,kw
#16	MeSH descriptor: [Physicians] explode all trees
#17	MeSH descriptor: [Primary Health Care] explode all trees
#18	MeSH descriptor: [Social Isolation] explode all trees
#19	(social isolation):ti,ab,kw (Word variations have been searched)
#20	(lonel*):ti,ab,kw (Word variations have been searched)
#21	("social support"):ti,ab,kw (Word variations have been searched)
#22	("social interaction*"):ti,ab,kw (Word variations have been searched)
#23	("peer support"):ti,ab,kw (Word variations have been searched)
#24	("family support"):ti,ab,kw
#25	("social network*"):ti,ab,kw (Word variations have been searched)
#26	("social relationship*"):ti,ab,kw (Word variations have been searched)
#27	("emotional support"):ti,ab,kw
#28	("social problems*"):ti,ab,kw
#29	(psychosocial):ti,ab,kw
#30	("social capital"):ti,ab,kw
#31	("support intervention*"):ti,ab,kw (Word variations have been searched)
#32	("brief intervention*"):ti,ab,kw
#33	("group intervention*"):ti,ab,kw
#34	("group based program*"):ti,ab,kw
#35	("Care Program*"):ti,ab,kw
#36	("support program*"):ti,ab,kw (Word variations have been searched)
#37	("psychosocial intervention*"):ti,ab,kw
#38	MeSH descriptor: [Psychosocial Intervention] explode all trees
#39	("Multicomponent intervention*"):ti,ab,kw (Word variations have been searched)

#40	("Self-Help Group*"):ti,ab,kw (Word variations have been searched)
#41	("transitional intervention*"):ti,ab,kw
#42	("education intervention*"):ti,ab,kw (Word variations have been searched)
#43	("follow-up care"):ti,ab,kw
#44	("peer delivered intervention*"):ti,ab,kw
#45	("support group*"):ti,ab,kw
#46	("liaison service*"):ti,ab,kw
#47	("Psychosocial Group*"):ti,ab,kw
#48	#1 #2 or #3 or #4 or #5 or #6 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17
#49	#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#50	#31 or #32 or #33 or # 35 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47
#51	#48 and #49 and #50 with Cochrane Library publication date Between May 2021 and Dec 2022, in Cochrane Reviews, Trials

eTable 5. Embase Search Results

Database: Embase Classic <1947 to 1973>, Embase <1974 to 2021 May 12>

Search Strategy:

1	healthcare.ti,ab. (387663)
2	"health care".ti,ab. (465341)
3	"re-admission*".ti,ab. (5862)
4	admission*.ti,ab. (422158)
5	"emergency department*".ti,ab. (155466)
6	"emergency room".ti,ab. (34498)
7	hospitali#ation*.ti,ab. (300864)
8	"health service*".ti,ab. (143650)
9	"general practi*".ti,ab. (109279)
10	"ambulatory care".ti,ab. (12607)
11	"urgent care".ti,ab. (3984)
12	"physician* visit*".ti,ab. or Health Services/ (167143)
13	Social Isolation/ or Loneliness/ or lonel*.ti,ab. (37906)
14	"social* isolat*".ti,ab. (12534)
15	"social* disconnect*".ti,ab. (198)
16	"social support".ti,ab. or Social Support/ (109555)
17	"social interaction*".ti,ab. (27181)
18	"peer support".ti,ab. (6943)
19	"family support".ti,ab. (8024)
20	"social network*".ti,ab. (22566)
21	"social relationship*".ti,ab. (8832)
22	"emotional support".ti,ab. (9032)
23	"social problem*".ti,ab. (11632)
24	"support intervention*".ti,ab. (3323)
25	"brief intervention*".ti,ab. (5691)
26	"group intervention*".ti,ab. (6208)
27	"social capital".ti,ab. (4155)
28	"group based program*".ti,ab. (218)
29	"Care Program*".ti,ab. (16651)
30	(support adj2 program*).ti,ab. (10650)
31	"primary care physician".ti,ab. or Physicians, Primary Care/ (114259)
32	psychosocial.ti,ab. (138715)
33	"psychosocial intervention".ti,ab. or Psychosocial Intervention/ (2936)
34	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 27 or 32 (341682)

35	(Multicomponent adj2 intervention*).ti,ab. (1648)
36	"Self-Help Group*".ti,ab. (2364)
37	Transitional Care/ or "transitional intervention*".ti,ab. (3688)
38	"education intervention*".ti,ab. (4518)
39	24 or 25 or 26 or 28 or 29 or 30 or 33 or 35 or 36 or 37 or 38 (56471)
40	"follow-up care".ti,ab. (7727)
41	39 or 40 (63969)
42	"peer delivered intervention*".ti,ab. (39)
43	41 or 42 (64001)
44	Support Groups/ or "support group*".ti,ab. (12173)
45	43 or 44 (74959)
46	"liaison service*".ti,ab. (1832)
47	45 or 46 (76747)
48	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 31 (1867401)
49	34 and 47 and 48 (4359)
50	limit 49 to humans (4108)

Embase Classic <1947 to 1973>

Embase <1974 to 2022 November 30>

1	healthcare.ti,ab.	470347
2	"health care".ti,ab.	509070
3	"re-admission*".ti,ab.	6798
4	admission*.ti,ab.	481845
5	"emergency department*".ti,ab.	180175
6	"emergency room".ti,ab.	39117
7	hospitali#ation*.ti,ab.	351309
8	"health service*".ti,ab.	158935
9	"general practi*".ti,ab.	114689
10	"ambulatory care".ti,ab.	13614
11	"urgent care".ti,ab.	4857
12	"physician* visit*".ti,ab. or Health Services/	174748
13	Social Isolation/ or Loneliness/ or lonel*.ti,ab.	45202
14	"social* isolat*".ti,ab.	15912
15	"social* disconnect*".ti,ab.	288
16	"social support".ti,ab. or Social Support/	122087
17	"social interaction*".ti,ab.	31122
18	"peer support".ti,ab.	8627
19	"family support".ti,ab.	9219
20	"social network*".ti,ab.	26260
21	"social relationship*".ti,ab.	10052
22	"emotional support".ti,ab.	10458
23	"social problem*".ti,ab.	12378
24	"support intervention*".ti,ab.	3977
25	"brief intervention*".ti,ab.	6271
26	"group intervention*".ti,ab.	6901

27	"social capital".ti,ab.	4827
28	"group based program*".ti,ab.	252
29	"Care Program*".ti,ab.	18163
30	(support adj2 program*).ti,ab.	12456
31	"primary care physician".ti,ab. or Physicians, Primary Care/	122056
32	psychosocial.ti,ab.	153351
33	"psychosocial intervention".ti,ab. or Psychosocial Intervention/	4141
34	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 27 or 32	385235
35	(Multicomponent adj2 intervention*).ti,ab.	2051
36	"Self-Help Group*".ti,ab.	2439
37	Transitional Care/ or "transitional intervention*".ti,ab.	4881
38	"education intervention*".ti,ab.	5238
39	24 or 25 or 26 or 28 or 29 or 30 or 33 or 35 or 36 or 37 or 38	65042
40	"follow-up care".ti,ab.	8793
41	39 or 40	73573
42	"peer delivered intervention*".ti,ab.	47
43	41 or 42	73612
44	Support Groups/ or "support group*".ti,ab.	13507
45	43 or 44	85775
46	"liaison service*".ti,ab.	2113
47	45 or 46	87832
48	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 31	2105865
49	34 and 47 and 48	5258
50	limit 49 to (human and yr="2021 -Current")	1090

eTable 6. Medline Search Results

Database: Ovid MEDLINE(R) ALL <1946 to May 12, 2021>

Search Strategy:

1	healthcare.ti,ab. (241421)
2	"health care".ti,ab. (363393)
3	"re-admission*".ti,ab. (2298)
4	admission*.ti,ab. (236552)
5	"emergency department*".ti,ab. (101017)
6	"emergency room".ti,ab. (19077)
7	hospitali#ation*.ti,ab. (173689)
8	"health service*".ti,ab. (115631)
9	"general practi*".ti,ab. (83153)
10	"ambulatory care".ti,ab. (9393)
11	"urgent care".ti,ab. (2429)
12	"physician* visit*".ti,ab. or Health Services/ (28654)
13	Social Isolation/ or Loneliness/ or lonel*.ti,ab. (22920)
14	"social* isolat*".ti,ab. (9243)
15	"social* disconnect*".ti,ab. (162)
16	"social support".ti,ab. or Social Support/ (93356)
17	"social interaction*".ti,ab. (21694)
18	"peer support".ti,ab. (4838)
19	"family support".ti,ab. (5776)
20	"social network*".ti,ab. (18841)
21	"social relationship*".ti,ab. (6783)
22	"emotional support".ti,ab. (6566)
23	"social problem*".ti,ab. (8366)
24	"support intervention*".ti,ab. (2545)
25	"brief intervention*".ti,ab. (4232)
26	"group intervention*".ti,ab. (3594)
27	"social capital".ti,ab. (3879)
28	"group based program*".ti,ab. (156)
29	"Care Program*".ti,ab. (12258)
30	(support adj2 program*).ti,ab. (7672)
31	"primary care physician".ti,ab. or Physicians, Primary Care/ (9596)
32	psychosocial.ti,ab. (100299)
33	"psychosocial intervention".ti,ab. or Psychosocial Intervention/ (2008)
34	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 27 or 32 (258905)
35	(Multicomponent adj2 intervention*).ti,ab. (1488)

36	"Self-Help Group*".ti,ab. (1705)
37	Transitional Care/ or "transitional intervention*".ti,ab. (927)
38	"education intervention*".ti,ab. (3347)
39	24 or 25 or 26 or 28 or 29 or 30 or 33 or 35 or 36 or 37 or 38 (39025)
40	"follow-up care".ti,ab. (4980)
41	39 or 40 (43882)
42	"peer delivered intervention*".ti,ab. (37)
43	41 or 42 (43915)
44	Support Groups/ or "support group*".ti,ab. (14930)
45	43 or 44 (56883)
46	"liaison service*".ti,ab. (963)
47	45 or 46 (57823)
48	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 31 (1169975)
49	34 and 47 and 48 (2850)
50	limit 49 to humans (2392)

Ovid MEDLINE(R) ALL <1946 to November 29, 2022>

1	healthcare.ti,ab.	303752
2	"health care".ti,ab.	402595
3	"re-admission*".ti,ab.	2665
4	admission*.ti,ab.	271514
5	"emergency department*".ti,ab.	117922
6	"emergency room".ti,ab.	21412
7	hospitali#ation*.ti,ab.	205033
8	"health service*".ti,ab.	129155
9	"general practi*".ti,ab.	88399
10	"ambulatory care".ti,ab.	10125
11	"urgent care".ti,ab.	2945
12	"physician* visit*".ti,ab. or Health Services/	30664
13	Social Isolation/ or Loneliness/ or lonel*.ti,ab.	27179
14	"social* isolat*".ti,ab.	11993
15	"social* disconnect*".ti,ab.	249
16	"social support".ti,ab. or Social Support/	102293
17	"social interaction*".ti,ab.	25531
18	"peer support".ti,ab.	6175
19	"family support".ti,ab.	6790
20	"social network*".ti,ab.	22721
21	"social relationship*".ti,ab.	8031
22	"emotional support".ti,ab.	7783
23	"social problem*".ti,ab.	9125
24	"support intervention*".ti,ab.	3124
25	"brief intervention*".ti,ab.	4722
26	"group intervention*".ti,ab.	4148
27	"social capital".ti,ab.	4717
28	"group based program*".ti,ab.	189

29	"Care Program*".ti,ab.	13476
30	(support adj2 program*).ti,ab.	9147
31	"primary care physician".ti,ab. or Physicians, Primary Care/	10476
32	psychosocial.ti,ab.	112801
33	"psychosocial intervention".ti,ab. or Psychosocial Intervention/	2817
34	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 27 or 32	294963
35	(Multicomponent adj2 intervention*).ti,ab.	1869
36	"Self-Help Group*".ti,ab.	1810
37	Transitional Care/ or "transitional intervention*".ti,ab.	1221
38	"education intervention*".ti,ab.	3949
39	24 or 25 or 26 or 28 or 29 or 30 or 33 or 35 or 36 or 37 or 38	45340
40	"follow-up care".ti,ab.	5708
41	39 or 40	50907
42	"peer delivered intervention*".ti,ab.	44
43	41 or 42	50945
44	Support Groups/ or "support group*".ti,ab.	15873
45	43 or 44	64731
46	"liaison service*".ti,ab.	1090
47	45 or 46	65794
48	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 31	1342007
49	34 and 47 and 48	3416
50	limit 49 to (human and yr="2021 -Current")	512

eTable 7. PsycInfo Search Results

Database: APA PsycInfo <1806 to May Week 1 2021>

Search Strategy:

1	healthcare.ti,ab. (47592)
2	"health care".ti,ab. (98809)
3	"re-admission*".ti,ab. (235)
4	admission*.ti,ab. (38649)
5	"emergency department*".ti,ab. (9255)
6	"emergency room".ti,ab. (3392)
7	hospitali#ation*.ti,ab. (27965)
8	"health service*".ti,ab. (48648)
9	"general practi*".ti,ab. (13209)
10	"ambulatory care".ti,ab. (1109)
11	"urgent care".ti,ab. (319)
12	"physician* visit*".ti,ab. or Health Services/ (790)
13	Social Isolation/ or Loneliness/ or lonel*.ti,ab. (18839)
14	"social* isolat*".ti,ab. (8435)
15	"social* disconnect*".ti,ab. (207)
16	"social support".ti,ab. or Social Support/ (62943)
17	"social interaction*".ti,ab. (31787)
18	"peer support".ti,ab. (4480)
19	"family support".ti,ab. (6519)
20	"social network*".ti,ab. (26040)
21	"social relationship*".ti,ab. (11856)
22	"emotional support".ti,ab. (7089)
23	"social problem*".ti,ab. (10998)
24	"support intervention*".ti,ab. (1474)
25	"brief intervention*".ti,ab. (3619)
26	"group intervention*".ti,ab. (4536)
27	"social capital".ti,ab. (8090)
28	"group based program*".ti,ab. (106)
29	"Care Program*".ti,ab. (4112)
30	(support adj2 program*).ti,ab. (6000)
31	"primary care physician".ti,ab. or Physicians, Primary Care/ (1234)
32	psychosocial.ti,ab. (83959)
33	"psychosocial intervention".ti,ab. or Psychosocial Intervention/ (1815)
34	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 27 or 32 (244612)
35	(Multicomponent adj2 intervention*).ti,ab. (741)

36	"Self-Help Group*".ti,ab. (1895)
37	Transitional Care/ or "transitional intervention*".ti,ab. (22)
38	"education intervention*".ti,ab. (1806)
39	24 or 25 or 26 or 28 or 29 or 30 or 33 or 35 or 36 or 37 or 38 (25542)
40	"follow-up care".ti,ab. (1109)
41	39 or 40 (26608)
42	"peer delivered intervention*".ti,ab. (29)
43	41 or 42 (26635)
44	Support Groups/ or "support group*".ti,ab. (9597)
45	43 or 44 (34866)
46	"liaison service*".ti,ab. (556)
47	45 or 46 (35411)
48	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 31 (248274)
49	34 and 47 and 48 (1433)
50	limit 49 to human (1374)

APA PsycInfo <1806 to November Week 3 2022>

1	healthcare.ti,ab.	57679
2	"health care".ti,ab.	107254
3	"re-admission*".ti,ab.	257
4	admission*.ti,ab.	41072
5	"emergency department*".ti,ab.	10507
6	"emergency room".ti,ab.	3616
7	hospitali#ation*.ti,ab.	30165
8	"health service*".ti,ab.	53487
9	"general practi*".ti,ab.	13822
10	"ambulatory care".ti,ab.	1176
11	"urgent care".ti,ab.	369
12	"physician* visit*".ti,ab. or Health Services/	830
13	Social Isolation/ or Loneliness/ or lonel*.ti,ab.	21631
14	"social* isolat*".ti,ab.	9886
15	"social* disconnect*".ti,ab.	277
16	"social support".ti,ab. or Social Support/	68983
17	"social interaction*".ti,ab.	34790
18	"peer support".ti,ab.	5270
19	"family support".ti,ab.	7134
20	"social network*".ti,ab.	28809
21	"social relationship*".ti,ab.	12912
22	"emotional support".ti,ab.	7898
23	"social problem*".ti,ab.	11579
24	"support intervention*".ti,ab.	1711
25	"brief intervention*".ti,ab.	3967
26	"group intervention*".ti,ab.	4950
27	"social capital".ti,ab.	8867

28	"group based program*".ti,ab.	129
29	"Care Program*".ti,ab.	4382
30	(support adj2 program*).ti,ab.	6725
31	"primary care physician".ti,ab. or Physicians, Primary Care/	1282
32	psychosocial.ti,ab.	90510
33	"psychosocial intervention".ti,ab. or Psychosocial Intervention/	1971
34	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 27 or 32	267169
35	(Multicomponent adj2 intervention*).ti,ab.	869
36	"Self-Help Group*".ti,ab.	1960
37	Transitional Care/ or "transitional intervention*".ti,ab.	23
38	"education intervention*".ti,ab.	1992
39	24 or 25 or 26 or 28 or 29 or 30 or 33 or 35 or 36 or 37 or 38	28030
40	"follow-up care".ti,ab.	1236
41	39 or 40	29219
42	"peer delivered intervention*".ti,ab.	34
43	41 or 42	29251
44	Support Groups/ or "support group*".ti,ab.	10106
45	43 or 44	37937
46	"liaison service*".ti,ab.	585
47	45 or 46	38510
48	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 31	273435
49	34 and 47 and 48	1643
50	limit 49 to (human and yr="2021 -Current")	149

eTable 8. Scopus Search Results

ID	Name	Query	Documents	Date last run
result#7	title search	(TITLE (healthcare OR "health care" OR "re-admission*" OR admission* OR "emergency department*" OR "emergency room" OR hospitalization* OR hospitalisation OR "health service*" OR "general practi*" OR "ambulatory care" OR "urgent care" OR "physician* visit*" OR "primary care") AND TITLE (lonel* OR "social* isolat*" OR "social* disconnect*" OR "social support" OR "social interaction*" OR "peer support" OR "family support" OR "social network*" OR "social relationship*" OR "emotional support" OR "social problem*" OR "social capital" OR psychosocial) AND TITLE ("support intervention*" OR "brief intervention*" OR "group intervention*" OR "group-based program*" OR "Care Program*" OR "support program*" OR "psychosocial intervention*" OR "Multicomponent intervention*" OR "Self-Help Group*" OR "Transitional Care" OR "transitional intervention*" OR "education* intervention*" OR "follow-up care" OR "peer delivered intervention*" OR "support group*" OR "liaison service*")) View Less_ _Edit query	71	17 May 2021_
result#6	AB search any year-2013	(ABS (healthcare OR "health care" OR "re-admission*" OR admission* OR "emergency department*" OR "emergency room" OR hospitalization* OR hospitalisation OR "health service*" OR "general practi*" OR "ambulatory care" OR "urgent care" OR "physician* visit*" OR "primary care") AND ABS (lonel* OR "social* isolat*" OR "social* disconnect*" OR "social support" OR "social interaction*" OR "peer support" OR "family support" OR "social network*" OR "social relationship*" OR "emotional support" OR "social problem*" OR "social capital" OR psychosocial) AND ABS ("support intervention*" OR "brief intervention*" OR "group intervention*" OR "group-based program*" OR "Care Program*" OR "support program*" OR "psychosocial intervention*" OR "Multicomponent intervention*" OR "Self-Help Group*" OR "Transitional Care" OR "transitional intervention*" OR "education* intervention*" OR "follow-up care" OR "peer delivered intervention*" OR "support group*" OR "liaison service*")) AND PUBYEAR < 2014 View Less_ _Edit query	1,695	17 May 2021_
result#3	AB search	(ABS (healthcare OR "health care" OR "re-admission*" OR admission* OR "emergency	1,758	17 May 2021_

ID	Name	Query	Documents	Date last run
	2014-today	department*" OR "emergency room" OR hospitalization* OR hospitalisation OR "health service*" OR "general practi*" OR "ambulatory care" OR "urgent care" OR "physician* visit*" OR "primary care") AND ABS (lonel* OR "social* isolat*" OR "social* disconnect*" OR "social support" OR "social interaction*" OR "peer support" OR "family support" OR "social network*" OR "social relationship*" OR "emotional support" OR "social problem*" OR "social capital" OR psychosocial) AND ABS ("support intervention*" OR "brief intervention*" OR "group intervention*" OR "group-based program*" OR "Care Program*" OR "support program*" OR "psychosocial intervention*" OR "Multicomponent intervention*" OR "Self-Help Group*" OR "Transitional Care" OR "transitional intervention*" OR "education* intervention*" OR "follow-up care" OR "peer delivered intervention*" OR "support group*" OR "liaison service*")) AND PUBYEAR > 2013 AND PUBYEAR < 2022 View Less_ Edit query		
result#2	search ti-ab- kw	(TITLE-ABS-KEY (healthcare OR "health care" OR "re-admission*" OR admission* OR "emergency department*" OR "emergency room" OR hospitalization* OR hospitalisation OR "health service*" OR "general practi*" OR "ambulatory care" OR "urgent care" OR "physician* visit*" OR "primary care") AND TITLE-ABS-KEY (lonel* OR "social* isolat*" OR "social* disconnect*" OR "social support" OR "social interaction*" OR "peer support" OR "family support" OR "social network*" OR "social relationship*" OR "emotional support" OR "social problem*" OR "social capital" OR psychosocial) AND TITLE-ABS-KEY ("support intervention*" OR "brief intervention*" OR "group intervention*" OR "group-based program*" OR "Care Program*" OR "support program*" OR "psychosocial intervention*" OR "Multicomponent intervention*" OR "Self-Help Group*" OR "Transitional Care" OR "transitional intervention*" OR "education* intervention*" OR "follow-up care" OR "peer delivered intervention*" OR "support group*" OR "liaison service*")) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "NURS") OR LIMIT-TO (SUBJAREA , "PSYC") OR LIMIT-TO (SUBJAREA , "SOCI")) ... View More_	10,022	17 May 2021_

Combine queries...e.g. #1 AND NOT #3

ID	Name	Query	Documents	Date last run
result#1	scopus update	(TITLE-ABS-KEY (healthcare OR "health care" OR "re-admission*" OR admission* OR "emergency department*" OR "emergency room" OR hospitalization* OR hospitalisation OR "health service*" OR "general practi*" OR "ambulatory care" OR "urgent care" OR "physician* visit*" OR "primary care") AND TITLE-ABS-KEY (lonel* OR "social* isolat*" OR "social* disconnect*" OR "social support" OR "social interaction*" OR "peer support" OR "family support" OR "social network*" OR "social relationship*" OR "emotional support" OR "social problem*" OR "social capital" OR psychosocial) AND TITLE-ABS-KEY ("support intervention*" OR "brief intervention*" OR "group intervention*" OR "group-based program*" OR "Care Program*" OR "support program*" OR "psychosocial intervention*" OR "Multicomponent intervention*" OR "Self-Help Group*" OR "Transitional Care" OR "transitional intervention*" OR "education* intervention*" OR "follow-up care" OR "peer delivered intervention*" OR "support group*" OR "liaison service*")) AND PUBYEAR > 2020 View Less Edit query	2,003	01 Dec 2022_

eTable 9. Summary Description of Randomized Clinical Trials Included in the Systematic Review (N = 41)

Author, year	Participants	n	Intervention	Dosage	Outcomes	Social well-being instrument	Follow-up (months)
Alias, 2021	Community-dwelling older adults	I = 194 C = 164	I: Physical and social group activities C: Offered intervention at the end of the study	3m (1 per 1w/ 2h)	Nurse, GP, ER, inpatient visits (health records)	Social support (Social Resources Inventory)	3, 12
Asbury, 2011	Women with cardiac syndrome x	I = 24 C = 25	I: Support groups C: Standard care	12m (1 per 1m/ 90 min)	Self-reported GP visits	ENRICH Social Support	6, 12
Boter, 2004	Stroke survivors	I = 263 C = 273	I: Individual support program C: Standard care	6m (3 phone calls, 1 home visit)	Self-reported GP visits and readmissions	Social Support List–Discrepancies [SSL-D]	6
Buchkremer, 1995	Caregivers of individuals with schizophrenia	I = 60 C = 31	I: Therapeutic self-help groups C: Standard care + offered intervention at the end of the study	12m (1 per 2w)	Patients' re-hospitalisations (health records)	Number of social contacts	12
Cheng, 2016	Caregivers of stroke survivors	I = 64 C = 64	I: Individual psychoeducational program C: Routine care - information leaflets on stroke and pre-discharge advice	3m (2 face-to-face meetings, 6 bi-weekly phone calls)	Stroke-related hospitalisations	Social support questionnaire (SSQ-6)	3
Chien, 2010	Caregivers of individuals with dementia	I = 46 C = 46	I: Multicomponent psychoeducational, case-management program C: Routine family support services	6m (1 per 2w (total = 10)/ 2h)	Duration of residential placement	SSQ6	1w, 6, 12, 18
Chien, 2013	Caregivers of individuals with schizophrenia	I1 = 45 I2 = 45 C = 45	I1: Family-led mutual support group I2: Psycho-education group C: Standard psychiatric care	9m (14 group sessions / 2h)	Patients' re-hospitalisations (health records)	SSQ-6	1w, 12, 24
Chien, 2014	Individuals with mental illnesses	I1 = 36 I2 = 36 C = 35	I1: Mindfulness-based psychoeducation group I2: Conventional psychoeducation group C: Standard psychiatric care	3m (1 per 2w/ 2h)	Frequency and duration of readmissions to psychiatric hospital (health records)	SSQ-6	1w, 12, 24
Chyzy, 2019	Pregnant adolescent women	I = 21 C = 19	I: Mobile phone-based individual peer support intervention C: Standard community support services	3m (minimum of 10 contacts)	Self-reported visits to nurses, midwives, GP, ER & specialists	SSQ-6	3
Colella, 2018	Post-coronary surgery men	I = 61 C = 124	I: Telephone calls with peer supporters C: Usual care: discharge teaching and booklet, routine check-ups	6w (1 per 1w)	Self-reported visits to GP, nurse, cardiologist, surgeon & ER	Funch's Shortened Social Support Scale (SSSS)	1.5, 3
Constantino, 2005	Family violence shelter residences	I = 13 C = 11	I: Support groups C: Free-flowing group chat sessions	2m (1 per 1w/ 90 min)	The Health Screening Questionnaire	The Interpersonal Self Evaluation List (ISEL)	2
Cui, 2019	Individuals with heart failure	I = 48 C = 48	I: Educational self-management intervention C: One group education session and information pamphlet	12m (1 per 4w/ 15-30 min)	Readmissions (health records)	The self-management ability - social support domain	12

Author, year	Participants	n	Intervention	Dosage	Outcomes	Social well-being instrument	Follow-up (months)
Dush, 2001	Individuals with mental illnesses	I = 90 C = 92	I: Cognitive-behavioural group and home care C: Routine care: psychiatric follow-ups and referrals to community mental health services	2w of prevention program and ongoing support	Number and duration of hospitalisations	The Shaw-Denmark Social Support Inventory	2w
Franse, 2018	Community-dwelling older adults	I = 986 C = 858	I: The Urban Health Centers Europe (UHCE) approach- multicomponent intervention C: Usual care: access to existing care services	12m	Self-reported doctor visits & hospitalisation length	De Jong Gierveld loneliness scale	12
Garvey, 2015	Individuals with multimorbidity	I = 26 C = 24	I: Multicomponent group intervention C: Offered intervention at the end of the study	6we (1 per 1w /3h)	GP, nurse and hospital VISIS (health records)	The Health Education Impact Questionnaire (HeiQ): Social integration and support scale	2
Gaugler, 2015	Caregivers of individuals with dementia	I = 54 C = 53	I: Individual and family counselling, support group C: Biannual newsletter and quarterly “check-in” calls	4m (two individual sessions, 3 family sessions, support groups and counselling)	Residential care placements	The Stokes Social Network scale	4, 8, 12, 18, 24 ²
Gillard, 2022	Individuals with mental disorder	I = 287 C = 291	I: Individual peer support C: Standard care	4m (1 per 1w/ 1-1.5h)	Readmissions (health records)	The Social Contacts Assessment	4, 12
Gleibs, 2011	Older adults residing in care	I1 = 13 I2 = 11 C1 = 12 C2 = 9	I1: Group water clubs I2: Individual activity focused on the benefits of water C1: Group discussions daily life C2: One-on-one sessions on daily life	2m (1 per 1w / 30 min)	Number of GP calls (health records)	Perceived social support	2
Goldberg, 2013	Individuals with mental disorder	I = 32 C = 31	I: Self-management peer-support C: Standard care	3m (1 per 1w / 60-75 min)	Use of emergency department services	18-item Self-Management-access to social support scale	3, 5
Grant, 2000	Individuals with psychosocial problems	I = 90 C = 71	I: Referral facilitation to voluntary organisations C: Standard care	1 assessment, 2-3 follow-ups	Number and cost of contacts with primary healthcare	The Duke-UNC functional social support questionnaire	1, 4
Hengartner, 2017	Individuals with mental disorder	I = 76 C = 75	I: Individual transitional intervention C: usual care: assistance from a social worker during inpatient	3m (tailored to patients)	Frequency of readmissions, duration of inpatient stays according to medical records	F-SozU K-14 perceived social support	3, 12
Hudson, 2012	Pregnant adolescent women	I = 21 C = 21	I: New Mothers Network program: online psychological and informational resources C: Usual care: parenting instructions	6m (resources available at all times)	Infants’ clinic visits, and ER visits (self-reported)	Revenson’s and Schiaffino’s Social Support	1w, 6w, 3, 6

² Quarterly follow-up assessments during the first 12 months of participation and every 6 months thereafter for a minimum of 2 years or until the study ended, loss to follow up or death.

Author, year	Participants	n	Intervention	Dosage	Outcomes	Social well-being instrument	Follow-up (months)
Jiang, 2021	Patients with chronic heart failure	I = 49 I2 = 57 C = 56	I: Self-management programme C: Standard care I2: Self-management programme + smartphone app	6w (1 per 2w)	Unplanned hospital admissions and medical consultations (health records)	SSQ-6	6w, 3, 6
Jones, 2013	Individuals with HIV	I = 83 I2 = 77	I: Monthly individual visits and group sessions I2: One-on-one sessions	3m (1 per 1m / 90min)	Self-reported increased/decreased clinic visits	SSQ-8	3, 6
Kidd, 2021	Individuals with schizophrenia	I = 22 I2 = 41 C = 44	I: Peer support-delivered transitional intervention C: usual care: referrals to outpatient case management and services I2: I1 + 4 weekly visits (2h) after discharge	1w (1–2 meetings before discharge / 30–60 min and 1 visit (3h) after discharge)	Rehospitalisations and lengths of stay through the hospital electronic database	19-item Social Support Survey	1, 6
Lindsay, 2009	Individuals with coronary heart disease	I = 54 C = 54	I: New home computer and 1-year broadband subscription. Online group support, weekly drop-in sessions and phone support C: New home computer and 1-year broadband subscription. Weekly drop-in sessions and phone support	9m	Visits to a GP, nurse, specialist and other healthcare providers in the past month	Social support questionnaire	6, 9
Markle-Reid, 2003	Older home care clients	I = 62 C = 64	I: Proactive nursing health promotion C: Usual care: Home care services	6m (minimum of 1 per 1m/ 60 min)	Self-reported use of all types of health services	Personal Resource Questionnaire (PRQ-2000)	6
Markle-Reid, 2021	Community-dwelling older adults with multimorbidity and depressive symptoms	I = 47 C = 52	I: hospital-to-home transitional care intervention C: Standard care	6m (1 per month)	Self-reported costs of use of primary care, emergency department and specialists, hospital days, other health	PRQ-2000	
Morrell, 2000	Post-natal women	I = 311 C = 312	I: Practical and emotional support C: Routine visits by the community midwife	1m (up to 10 sessions/ 3h)	GP contacts, hospital services, NHS costs	Duke social support questionnaire	6w, 3, 6
Muralidharan, 2019	Individuals with mental disorder	I = 124 C = 118	I: Self-Management co-led peer support C: Medical Illness Education and non-peer support group	3m (1 per week/ 75 minutes)	ER use (health records)	18-item Self-Management-access to social support scale	3, 6
Reid, 2002	Primiparous women	I = 503 C = 501	I: Support groups C: Self-help manual (PACK)	3m (1 per 1w/ 2h)	Self-reported contact with health professionals	SSQ-6	3, 6
Roberts, 1999	Caregivers of individuals with cognitive impairment	I = 29 C = 29	I: Problem-Solving Counselling C: Standard care	6m (up to 10 sessions)	Costs of primary care, emergency room and specialists, hospital	The Duke Social Support questionnaire	6, 12

Author, year	Participants	n	Intervention	Dosage	Outcomes	Social well-being instrument	Follow-up (months)
					days and other health professionals		
Roncella, 2013	Individuals with acute myocardial infarction	I = 49 C = 45	I: Short-term psychotherapy C: Cardiac rehabilitation	Individual therapy: 3m (3-11 sessions/1h) Group therapy: 3m (5 sessions/ 2h)	Rehospitalisations (health records)	Social Support Questionnaire	6, 12
Shaw, 2016	Caregivers of gastrointestinal cancer patients	I = 64 C = 64	I: Family Connect telephone intervention: emotional and practical support for caregivers C: Usual care	2.5m (4 sessions)	Reported ER & readmissions	Caregiver Reaction Assessment	3, 6
Simpson, 2014	Individuals with mental disorder	I = 23 C = 23	I: Individual peer-support C: Care as usual from community mental health services	4w	Client Service Receipt Inventory	The UCLA loneliness scale	1, 3
Tarazona-Santabalbina, 2016	Community-Dwelling Frail older adults	I = 51 C = 49	I: Supervised-facility multicomponent exercise program C: Regular primary care program	6m (5 per 1week/ 65min)	ER and primary care visits	The Duke Social Support questionnaire	6
Valencia, 2020	Individuals with schizophrenia	I = 90 C = 86	I: Brief psychoeducation group for patients and families C: Standard care	1m (1 per week/ 2h)	Hospitalisations	WHOQOL-BREF- social domain	12
Van Lieshout, 2018	Community-dwelling pre-frail older adults	I = 139 C = 142	I: SPRY program interdisciplinary multicomponent intervention C: Health and welfare services as usual; Invitation for the program after the study ended	6 months (11 meetings/ 1-2.5h)	Self-reported hospital/ nursing home admissions & primary care visits	De Jong Gierveld loneliness scale	3, 12
VanLieshout, 2022	Individuals with post-partum depression (PPD)	I = C =	I: Group cognitive behavioural therapy C: Standard care including PPD services such as psychotherapy	9w (1 per week/ 2h)	Self-reported mental healthcare visits	The Social Provisions Scale	2, 6
Wiggins, 2004	Post-natal at-risk women	I = 183 I2 = 184 C = 184	I: Supportive listening visits I2: Community Group Support C: 1 NHS health visiting and clinic support	12m (1 visit per 1m)	Self-reported GP, nurse, ER visits & hospitalisations	The Duke Social Support questionnaire	12, 18
Yang, 2005	Individuals with recurrent depression	I = 60 C = 61	I: Hospital-based psychosocial intervention-group and individual activities C: Antidepressants	3m (daily)	Readmissions	WHO QOL-100- social relationships component	6, 12, 24

Abbreviations: I: Intervention group, C: Control group, GP: General practitioner, ER: emergency room, min: minutes, h: hours, w: weeks, m: months

eTable 10. Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence Profile

Outcome	Nº of studies	Study design	Risk of bias ¹	Inconsistency ²	Indirectness ³	Imprecision ⁴	Other considerations ⁵	Overall certainty
HCU- OR	41	RCT	not serious	serious ^a	not serious	not serious	none	⊕⊕⊕○ Moderate
HCU- OR (long-term effect)	18	RCT	not serious	serious ^b	not serious	serious ^c	none	⊕⊕○○ Low
HCU-SMD	38	RCT	not serious	serious ^a	not serious	serious ^c	publication bias strongly suspected ^d	⊕○○○ ○ Very low
HCU-SMD (long-term effect)	13	RCT	not serious	serious ^b	not serious	very serious ^c	publication bias strongly suspected ^d	⊕○○○ ○ Very low
Social support-SMD	33	RCT	not serious	serious ^a	not serious	not serious	none	⊕⊕⊕○ Moderate
Loneliness-SMD	3	RCT	serious ^e	not serious ^a	not serious	serious ^c	none	⊕⊕○○ Low

Abbreviations: HCU: health care utilisation; **OR:** odds ratio; **SMD:** standardised mean difference; **RCT:** randomised control trial

Explanations

^a $I^2 > 50\%$ $p < 0.05$

^b $I^2 > 50\%$ $p > 0.05$

^c Confidence intervals include outcomes with different clinical meanings

^d Egger regression test $p < 0.05$

^e Equal or greater than 50% of studies' weights are 'high risk'

¹ Risk-of-bias: certainty was downgraded if more than 50% of the weights of individual trials in each outcome assessed came from high-risk studies.

² Inconsistency: based on the variability and heterogeneity across individual trials. Certainty was downgraded if $I^2 > 50\%$ and/or if the p-value of the heterogeneity test was < 0.05 .

³ Indirectness: assessed qualitatively by the extent to which the population, interventions, and outcome measures directly reflect the aims of the systematic review.

⁴ Imprecision: based on inspection of the pooled estimate and the 95% confidence interval (95% CIs). Certainty was downgraded when 95% CIs included values that would have different clinical implications.

⁵ Publication bias: assessed by a funnel plot and an extension to Egger's regression test. Certainty downgraded when $p < 0.05$.

eTable 11. Strength of Evidence (Bayes Factors) in the OR and SMD According to Health Care Service

		Random effect (95% CI)	Bayes	Evidence of effect for H_1 *
OR	Primary care	0.72 (0.52, 0.1.01)	3.62	Moderate
	Inpatient	0.74 (0.54, 1.02)	3.22	Moderate
	Outpatient	1.03 (0.72, 1.46)	0.40	Inconclusive
	ER	0.64 (0.43, 0.96)	5.56	Moderate
	Total health care	0.75 (0.59, 0.97)	5.63	Moderate
SMD	Primary care	-0.02 (-0.22, 0.18)	0.38	Inconclusive
	Inpatient length	-0.35 (-0.61, -0.09)	12.03	Strong
	Inpatient	-0.23 (-0.47, 0.00)	3.35	Moderate
	Outpatient	0.34 (0.05, 0.62)	6.99	Moderate
	Total health care	-0.10 (-0.29, 0.09)	0.84	Inconclusive
	Social support	0.25 (0.04, 0.45)	7.21	Moderate

* Bayes factors determine how well the data are predicted by H_1 (the assumption that there is intervention effect) relative to H_0 (no intervention effect). $10 < \text{BFs} < 30$ indicates strong evidence for an effect; $10 > \text{BFs} > 3$ indicates moderate relative evidence for an effect; $3 < \text{BFs} < 0.3$ inconclusive evidence; and $\text{BF} < 0.3$ moderate evidence for no effect.

Abbreviations: OR: odds ratio; SMD: standardised mean difference; CI: confidence interval

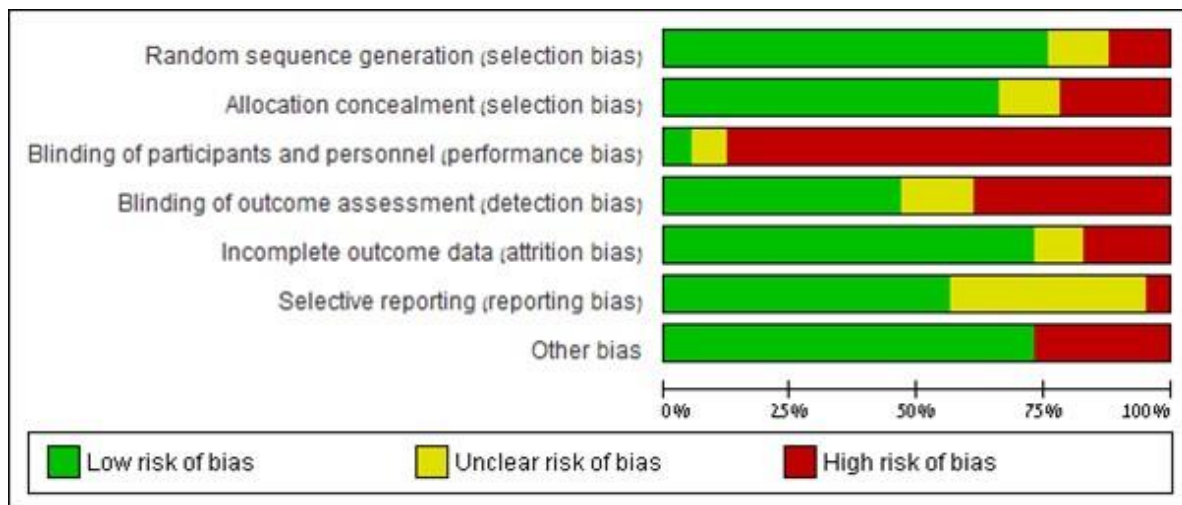
eTable 12. Subgroup Analyses of Postintervention Health Care Utilization According to Participant- and Intervention-Level Factors

		SMD (95%CI)	OR (95%CI)
Participant characteristics			
Age	<30	0.02 (-0.32, 0.35)	0.93 (0.66, 1.32)
	30-60	-0.34 (-0.72, 0.04)	0.61 (0.43, 0.86)
	>60	0.00 (-0.30, 0.31)	0.99 (0.70, 1.39)
Population group	Caregivers	-0.45 (-0.95, 0.05)	0.23 (0.07, 0.71)
	Chronic illness	-0.01 (-0.42, 0.40)	0.94 (0.66, 1.34)
	Mental health	-0.42 (-0.91, 0.07)	0.31 (0.13, 0.74)
	Older adults	-0.10 (-0.48, 0.28)	1.07 (0.39, 2.94)
	Post-natal women	0.15 (-0.16, 0.47)	1.03 (0.88, 1.20)
	Violence survivors	-0.32 (-1.12, 0.49)	-
	Men majority	-0.26 (-0.63, 0.10)	0.84 (0.44, 1.63)
	Women majority	-0.02 (-0.24, 0.20)	0.98 (0.44, 2.17)
Gender	Men majority	-0.26 (-0.63, 0.10)	0.84 (0.44, 1.63)
	Women majority	-0.02 (-0.24, 0.20)	0.98 (0.44, 2.17)
	Men majority	-0.02 (-0.24, 0.20)	0.98 (0.44, 2.17)
Country	Australia	-	0.23 (0.07, 0.71)
	Canada	0.58 (0.19, 0.97)	0.94 (0.66, 1.34)
	China	-0.44 (-0.68, -0.20)	0.31 (0.13, 0.74)
	Columbia	-	1.07(0.39, 2.94)
	Europe (including the UK)	-0.07 (-0.22, 0.08)	1.03 (0.88, 1.20)
	USA	-0.22 (-0.65, 0.21)	0.47 (0.32, 0.69)
	USA	-0.22 (-0.65, 0.21)	0.47 (0.32, 0.69)
Intervention characteristics			
Intervention type	Group	-0.13 (-0.33, 0.07)	0.77 (0.56, 1.06)
	Individual	0.00 (-0.28, 0.28)	0.74 (0.55, 0.98)
Components	Single	-0.08 (-0.31, 0.16)	0.73 (0.53, 1.01)
	Multi	-0.14 (-0.48, 0.20)	0.77 (0.51, 1.16)
Intervention delivery	Coordinators	-0.04 (-0.44, 0.37)	0.74 (0.34, 1.64)
	Health professionals	-0.19 (-0.70, 0.32)	0.65 (0.46, 0.93)
	Peers	0.23 (-0.26, 0.72)	0.91 (0.56, 1.47)
	Peers	0.23 (-0.26, 0.72)	0.91 (0.56, 1.47)
Intervention length	Short (1-4 months)	0.15 (-0.09, 0.39)	0.69 (0.51, 0.94)
	Long	-0.26 (-0.47, -0.06)	0.87 (0.60, 1.26)

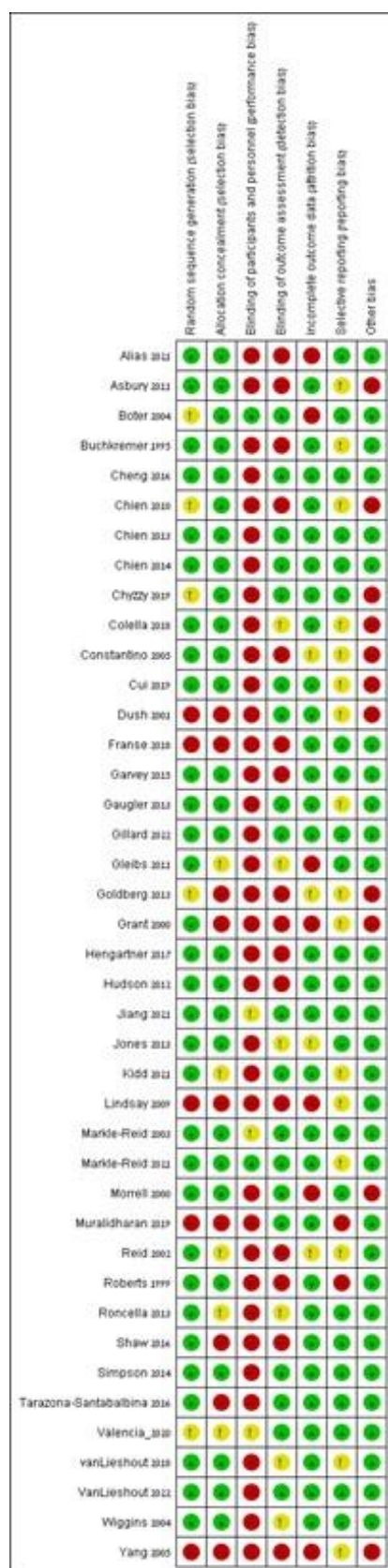
	SMD (95%CI)	OR (95%CI)
(6-12 months)		

Abbreviations: **SMD:** standardised mean difference, **OR:** odds ratio, **CI:** confidence interval

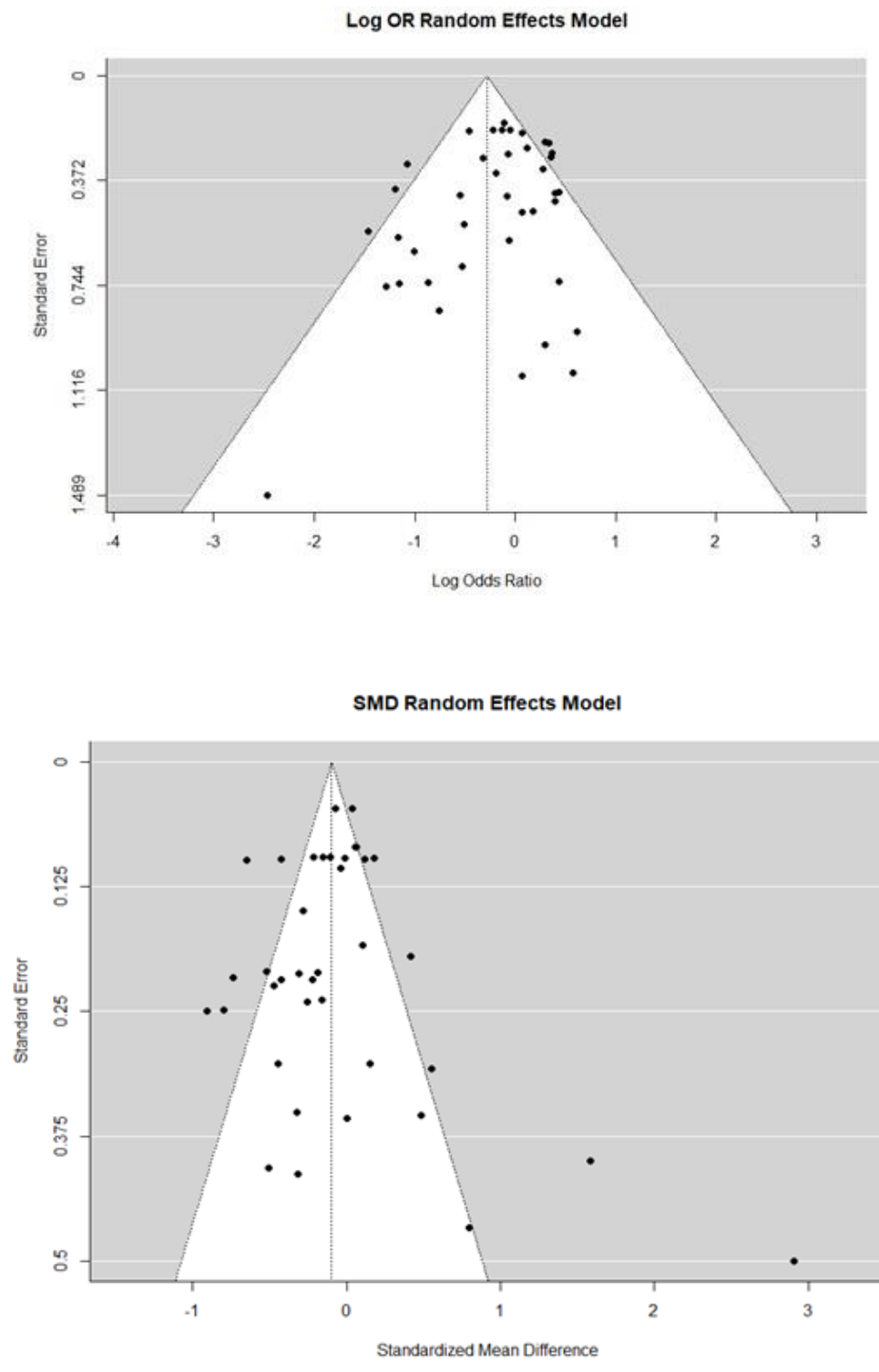
eFigure 1. Cochrane Risk-of-Bias Summary of Low, High and Unclear Risk of Bias Across All Included Studies (N = 41)



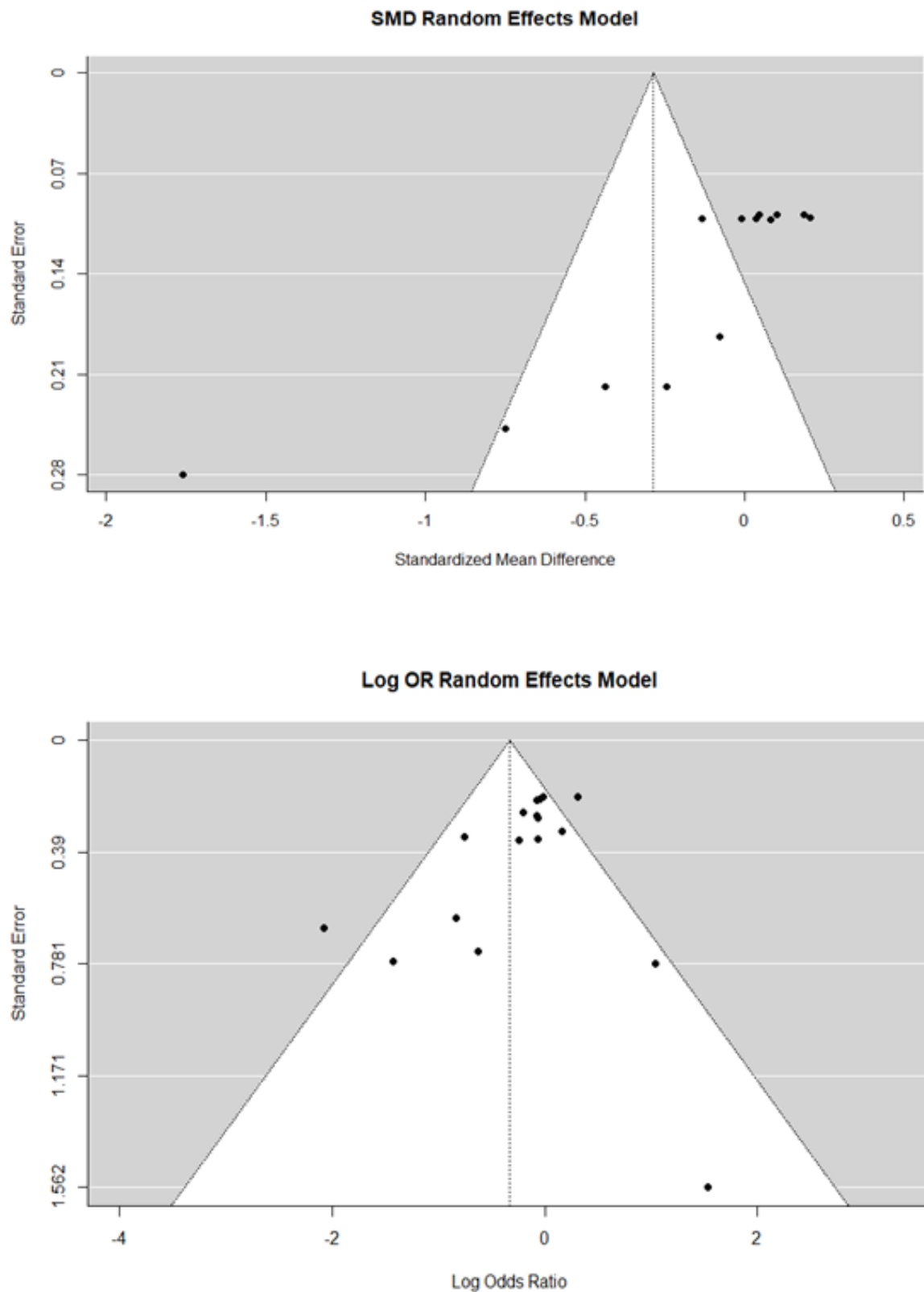
eFigure 1b. Cochrane risk-of-bias summary: review authors' judgments about each risk of bias item for each included study (n = 41)



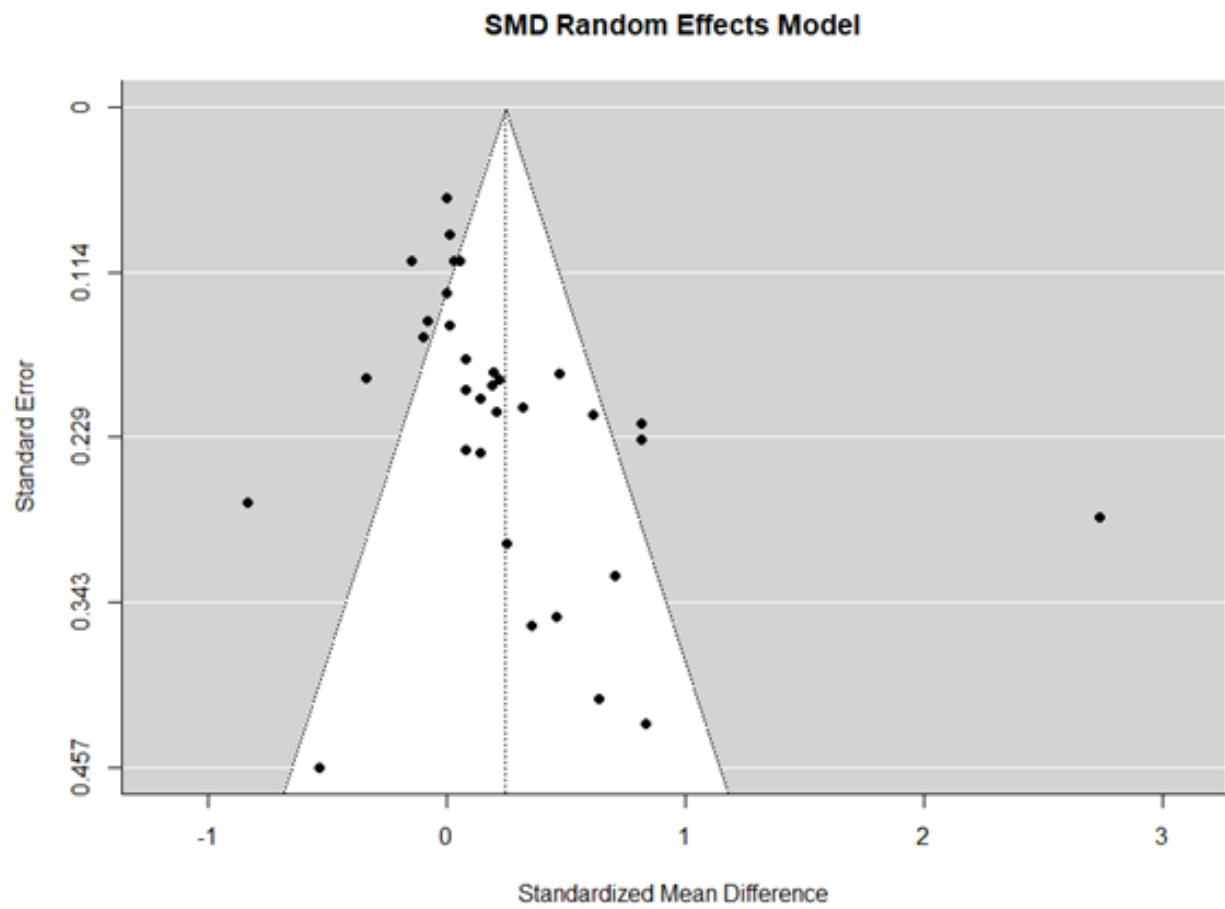
eFigure 2. Publication Bias Funnel Plots for Standardized Mean Difference (SDM) and Log Odds Ratio (OR) Random Effect Models of Health Care Utilization Outcomes and Social Support



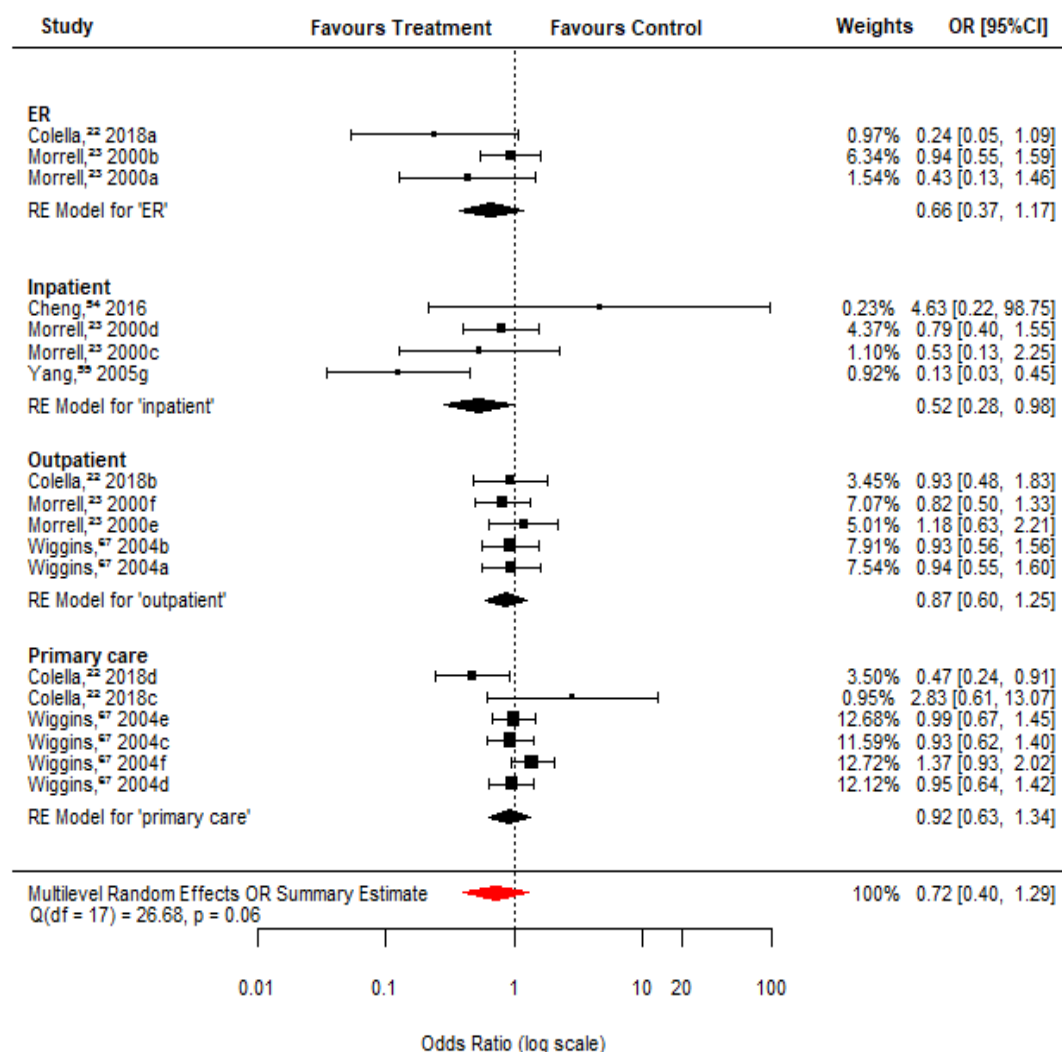
eFigure 2b. Publication bias funnel plots for standardised mean difference (SDM) and log odds ratio (OR) random effect models of sustained health care utilisation outcomes



eFigure 2c. Publication bias funnel plot for standardised mean difference (SDM) random effect model of social support

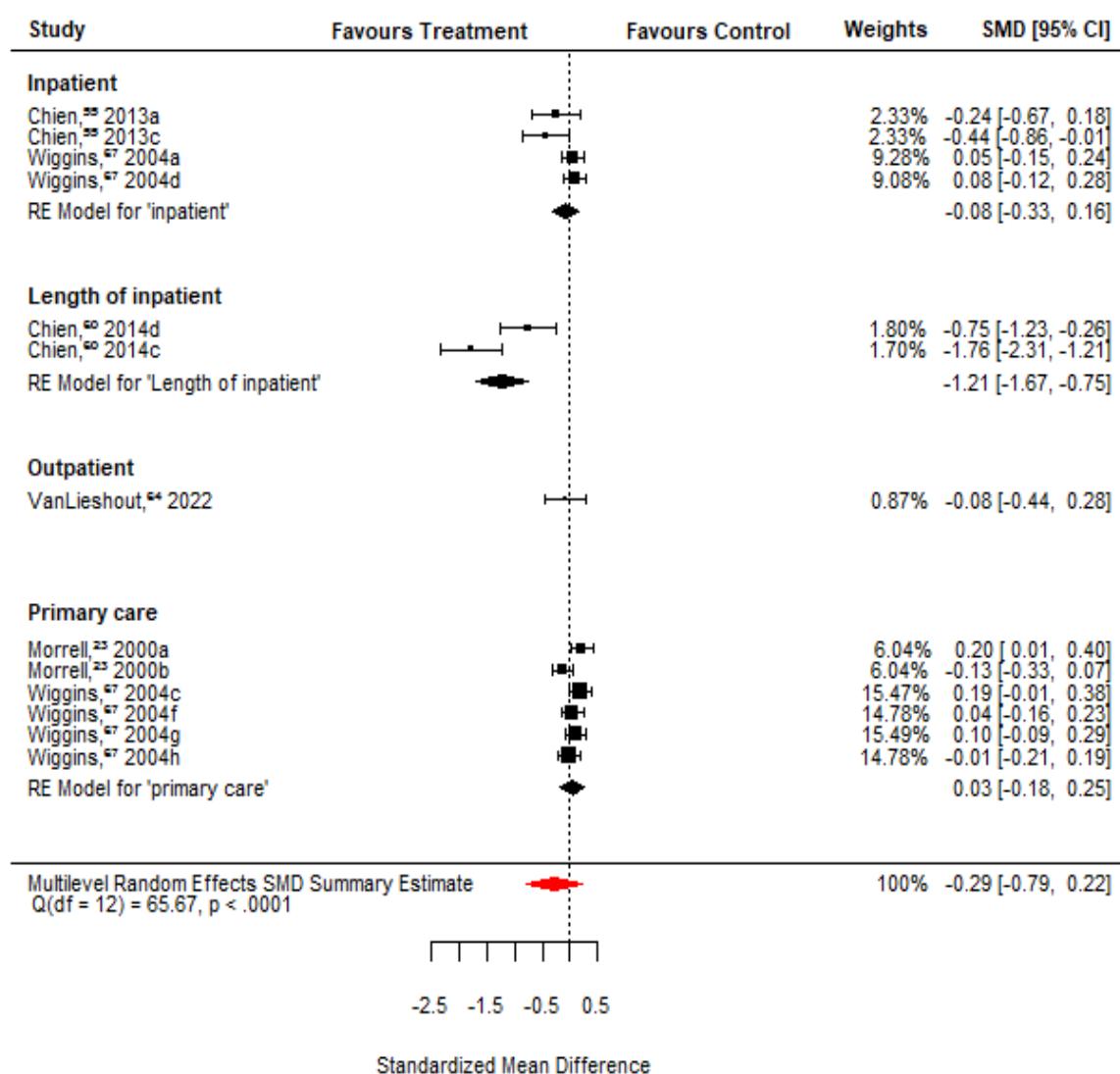


eFigure 3. Pooled 95% CI Odds Ratio of the Sustained Association of Psychosocial Interventions With Health Care Utilization



Abbreviations: ER: emergency room

eFigure 4. Pooled 95% CI Standardized Mean Difference of the Sustained Association of Psychosocial Interventions With Health Care Utilization



6.6. Concluding summary for this chapter and knowledge gained from this study

This systematic review and meta-analysis emphasise the critical interaction between social and healthcare systems, demonstrating how social interventions for reducing loneliness and improving social well-being, can potentially reduce the strain on healthcare services. The findings indicate significant reductions in the use of critical care, including inpatient and emergency services, as well as a decrease in the length of stay. Additionally, there were notable increases in outpatient care and social well-being. No significant changes were observed in loneliness. However, that may have been due to only three studies that were included in the loneliness meta-analysis. There were variations in interventions' effect according to country and age. In addition, reductions in healthcare use were observed in studies among caregivers and individuals with mental illnesses compared to other population groups. Interventions run by health professionals also yielded significant results. Our findings imply that integrating social interventions into healthcare systems represents a promising approach to optimise resource allocation, improving patient health outcomes, and alleviating pressure on healthcare services. These findings have important implications for loneliness as a component of social well-being, given its association with poor health and increased healthcare utilisation. Providing social support through targeted interventions can help reduce both the health and economic burden of loneliness.

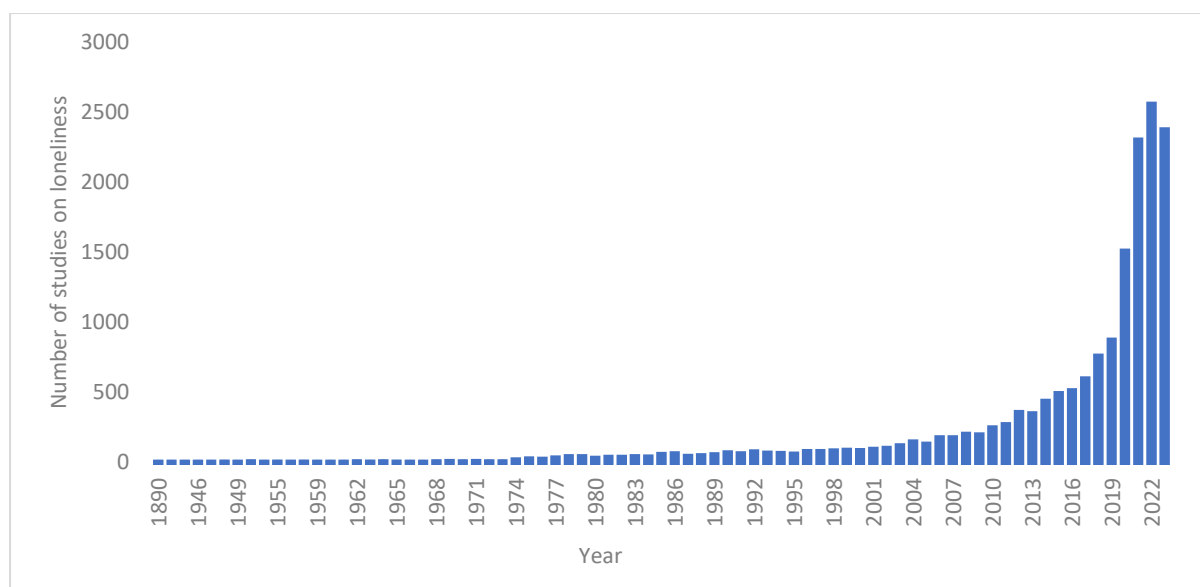
CHAPTER 7: Discussion

7.1. Overview

The present thesis explored the health outcomes and determinants of loneliness in a longitudinal analysis while discussing potential solutions to address loneliness and mitigate its adverse effects. As urbanisation, technological advancements, and other environmental shifts have unfolded over the years, loneliness has emerged as a major risk factor for poor health and mortality (1, 2). Loneliness has also been identified as a source of excess healthcare use and spending (3). Given this economic burden and the added pressure on an already strained healthcare system, loneliness is now addressed at national and global levels (4-6). To effectively tackle the issue of loneliness and guide an adequate response, it is important to understand the possible obstacles and enablers of social well-being.

The research on loneliness spans several decades. However, it wasn't until the COVID-19 pandemic in the 2020s that a surge of research emerged (**Figure 1**), fuelled by an increasing awareness of loneliness and its implications. Although the number of studies in many research fields is increasing yearly, the surge in loneliness research following the onset of the COVID-19 pandemic (1.73-fold increase between 2019 - 2020) (7) appears to be higher compared to other fields, such as physical activity (1.14-fold increase) (8) and depression (1.18-fold increase) (9) during the same period. The rise in public discourse and awareness of loneliness has sparked a wave of research exploring different aspects of loneliness, its determinants and outcomes as well as prevention and intervention strategies (7, 10, 11). This could be viewed as a positive outcome of the COVID-19 pandemic, as it has brought attention to a hidden public health concern, prompting researchers, practitioners, and policymakers to address the issue of loneliness more prominently. Revisiting data collected before the COVID-19 pandemic shows that loneliness had already been identified as an issue affecting health and well-being (12, 13). The current thesis has contributed to this growing body of literature by adding insights about the effect of loneliness and its socio-demographic moderators and identifying strategies to improve social well-being and reduce unnecessary health service usage among different population groups.

Figure 1. Number of studies on loneliness across time (7)



7.1. Thesis key findings and significance

The current thesis aims to explore the long-term independent effect of loneliness and identify determinants and potential solutions. The theoretical framework of loneliness and associated health outcomes was used in this thesis to provide a setting for the complexity of associations that can occur at individual, community and societal levels. However, our focus primarily centred on the community and societal levels, as these domains have received comparatively less research attention. Moreover, there are indications that community and social determinants play a significant role in both the onset of loneliness and in the measures aimed at mitigating its health and economic burdens (14).

The current thesis addresses several significant gaps in the literature concerning social-ecological determinants of long-term patterns of loneliness, the role of life transition (i.e., retirement) plays in loneliness, long-term health outcomes of loneliness, as well as the effect of psychosocial interventions, which address loneliness, on healthcare utilisation. To help obtain an overall view of the significance of the findings in this thesis, **Table 1** summarises the main findings according to the thesis's theoretical framework alongside the individual importance of each study. The primary significance of the current thesis lies in establishing and demonstrating loneliness as a social determinant of health. Moreover, our results uniquely identify retirement as a determinant for loneliness in older adults and establish a link between long-term patterns of loneliness and health risks. To our knowledge, our findings are the first to demonstrate the associations between long-term loneliness and Health-Related Quality of Life (HRQoL) and the effect on mortality.

Despite decades of investigation into loneliness, the current evidence has limitations. Although it is acknowledged that loneliness and health share a bidirectional relationship, the independent effect of loneliness on health has not been thoroughly explored due to limited access to longitudinal data and robust statistical modelling techniques. Using novel causal inference methods and other robust methods such as meta-analysis, our findings provide a clear understanding of the independent effect of loneliness on health, mortality and healthcare utilisation. Additionally, considering the changes in loneliness and its association with health outcomes over 18 years at multiple time points of measurement, facilitated a potentially less biased estimate. Moreover, using the above approaches, our findings are the first to show longitudinal patterns of loneliness, recognising that loneliness is dynamic and can fluctuate throughout the lifespan and in response to life changes (**Chapters 3-5**).

The current thesis also attempts to understand the role of life transitions, namely retirement, on loneliness within the context of other determinants, and explore this question within an international comparative context. Our findings demonstrate how the same determinants can have varying effects on loneliness depending on country and area remoteness (**Chapter 3**). This understanding emphasises the significance of macro-level elements that can influence the perception and expression of loneliness, suggesting that measures to alleviate it should also address social-ecological determinants.

Additionally, the present thesis also bears implications for the effect of loneliness on the healthcare system. Our findings reveal that by providing social support to individuals through psychosocial interventions, the use of urgent care is decreased and the use of outpatient, preventive care is increased. These findings carry important implications for the regulations of the health care system services and costs. They offer potential solutions to challenges such as the overburdened healthcare systems and excess expenditures, by providing insights into the populations most vulnerable to loneliness and the interventions most effective in reducing inappropriate healthcare utilisation (**Chapter 6**).

Table 1. Summary of the key findings from the thesis chapters according to the theoretical framework of loneliness and associated health outcomes

Thesis chapter	Manuscript title (status)	Methodological approach	Main findings	Findings significance
----------------	---------------------------	-------------------------	---------------	-----------------------

Thesis chapter	Manuscript title (status)	Methodological approach	Main findings	Findings significance
Chapter 3	The effect of retirement on loneliness: A longitudinal comparative analysis across Australia, China, and the United States (Published; Journal of Epidemiology and Community Health)	Causal inference (marginal structural models)	Retirees had a higher predicted prevalence of loneliness than non-retirees in Australia and the US. In China, retirees had a lower predicted prevalence of loneliness than non-retirees. In Australia and the US, voluntary retirees had the lowest loneliness and involuntary retirees had the highest. Only in Australia and the US, loneliness was significantly lower for those who were socially engaged compared to those who were not, regardless of retirement status.	This is the first study to conduct a cross-country analysis to examine the causal effect of retirement on loneliness in three different countries. This is also the first study on the effect of retirement on loneliness in a non-Western country. The findings imply that loneliness determinants may be culturally dependent and may differentiate according to area remoteness. Our findings have implications for countries with diverse cultural and socioeconomic attributes, particularly in terms of the effect of work and retirement status on loneliness.
Chapter 4	Loneliness and long-term health-related quality of life: A latent class analysis among middle-aged and older Australian women (under review)	Latent class analysis	Compared to ‘Stable-low’ loneliness, ‘Increasing’, Medium’ and ‘High’ loneliness were associated with HRQoL mental component. The ‘Increasing’ loneliness class was also associated with lower physical HRQoL. Baseline predictors such as current smoking, depression, anxiety, stress and low social engagement were associated with higher odds of ‘Increasing’, ‘Stable-medium’ and ‘Stable-high’ loneliness.	This is the first study to examine the association between longitudinal patterns of loneliness and HRQoL. Our findings highlight the importance of social well-being for middle-aged and older women’s physical and mental health. The findings indicate that loneliness poses a threat to poor HRQoL not only for those who experience ‘Stable-high’ loneliness but also for ‘Stable-medium’ and ‘Increasing’ trends of loneliness.

Thesis chapter	Manuscript title (status)	Methodological approach	Main findings	Findings significance
Chapter 5	Loneliness and all-cause mortality in middle-aged Australian women: A causal inference analysis of longitudinal data (under review)	Causal inference (targeted maximum likelihood estimation)	The association between the number of waves of loneliness (total and consecutive) and mortality showed a dose-dependent pattern. Compared with those who did not report loneliness in any wave, those who reported loneliness at two, four and six waves had an incrementally higher risk of dying during the follow-up period. Both persistent and chronic loneliness demonstrated a significant risk for mortality.	This is the first study to examine the causal effect of loneliness on mortality, quantifying the independent risk of loneliness. The findings provide evidence of the persistence and chronicity of loneliness and show that loneliness may yield adverse effects whether experienced continuously or not.
Chapter 6	Health care utilization following interventions to improve social well-being: A systematic review and meta-analysis (Published; JAMA Network open) (15)	Systematic review and meta-analysis	There were reductions in overall healthcare use, length of inpatient stays and the number of emergency care visits post-intervention, as well as a borderline reduction in inpatient and primary care. In addition, an increase in outpatient care was observed. There was a significant improvement in social well-being measures post-intervention.	This is the only study that has aggregated and quantified all available RCTs on the effect of psychosocial interventions on social well-being and healthcare use. The findings have the potential to guide the design and execution of psychosocial interventions by furnishing the essential components for successful intervention strategies. These findings carry implications for the healthcare costs associated with loneliness. Implementing psychosocial interventions can potentially decrease healthcare utilisation and subsequently

Thesis chapter	Manuscript title (status)	Methodological approach	Main findings	Findings significance
				reduce associated costs.

Note.

Abbreviations: HRQoL: Health-related quality of life

7.2. Determinants and outcomes of loneliness from a social-ecological perspective

Loneliness, along with its determinants and outcomes, is approached within the theoretical framework of this thesis from a social-ecological perspective. This perspective integrates individual, community, and socio-environmental factors, acknowledging their interplay in shaping the experience of loneliness. The majority of the previous literature has focused on individual determinants and outcomes of loneliness. However, there is an indication that community and social factors pose significant contributors to loneliness and in addition, can moderate the associations between loneliness and individual-level determinants.

7.2.1. Individual-level determinants and outcomes of loneliness

Loneliness determinants

There is extensive research regarding individual determinants for loneliness spanning genetics, personality and sociodemographic factors to health conditions and behaviours (16-20). The findings of the current thesis coincide with the previous ones, showing increased odds of loneliness over time among individuals with baseline predictors such as smoking, stress, depression and low social engagement (**Chapter 4**). These findings indicate that loneliness is a part of a detrimental cycle where poor health behaviours, mental health and social disengagement may contribute to increased loneliness which amplifies poor lifestyle and contributes to the development of serious health conditions.

Our findings regarding loneliness determinants among middle-aged and older Australian women did not reveal associations with most of the sociodemographic characteristics such as age, education level, employment, living arrangement, country of birth and location of residence. These characteristics were not associated with any of the loneliness trends in our study ('Stable-low', 'Increasing', 'Stable-medium' and 'Stable-high'), even though there is previous evidence that these factors are associated with loneliness (17, 21-23).

There was only one sociodemographic feature that was significantly associated with elevated loneliness trends. Widows had twice the odds of having a ‘Stable-high’ loneliness trajectory compared to ‘Stable-low’ loneliness. Relationship status is one of the more consistent determinants of loneliness, with those who are in a relationship having a significantly lower risk of being affected by loneliness compared to those who are not, as evidenced by a recent review from 2023 (24). Previous longitudinal research (2015) has shown that widowhood is a predictor of loneliness (25). The increased risk is attributed to the change in relationship status that traditionally happens later in life and requires great adjustments to a new social situation (26, 27). Our research findings align with these previous studies and underscore the importance of recognising and addressing the needs of this high-risk group in terms of social support, coping mechanisms, and the rebuilding of social networks.

Since the loneliness determinants were examined in a sample of women, we could not examine the association with gender, and our analysis of determinants and health outcomes of loneliness hold particular implications for this demographic subgroup. Women were identified in the literature as having numerous risk factors that could potentially increase their vulnerability to loneliness. For example, women are more vulnerable to numerous health and mental health risks (28, 29) and in some studies, they have been found to be at a higher risk of loneliness as well (30-32). In addition, women often assume multiple roles throughout their lives, including those of caregiver, spouse, parent, and worker (33-35). Importantly, women are more frequently exposed to lower socioeconomic status and are more likely to experience long-term widowhood (36, 37). All of these added stressors may increase the risk for depression and anxiety and may limit the amount of time women have for social interactions (25, 38). Consequentially, this could amplify prolonged loneliness and poor health (25, 39). Our findings affirm that women are at risk for negative health outcomes including death, attributable to loneliness. As a vulnerable and often marginalised social group, it is essential to consider these gender-related risk factors when addressing loneliness in this population.

Health outcomes

The current thesis contributes evidence regarding the effect of loneliness on major health outcomes such as HRQoL and mortality, building on prior studies about the link between loneliness and poor health outcomes (40). Our findings regarding the relationship between loneliness and HRQoL offer a novel perspective on the dynamic nature of loneliness. By using longitudinal data spanning 18 years, this study sheds light on the evolving relationship

between loneliness and HRQoL over time. Four main loneliness trends were identified and compared to the 'Stable-low' trend of loneliness. All of the elevated loneliness trajectories (i.e., 'Increasing', 'Stable-medium', and 'Stable high') were associated with lower HRQoL. Although this is the first study to examine long-term loneliness trajectories, previous studies have examined patterns of prolonged (chronic) loneliness compared to transient loneliness (41, 42). Chronic loneliness was defined previously as experiencing loneliness for at least two consecutive waves of measurement (43). Previous studies showed that prolonged loneliness is a major health concern compared to transient loneliness (44, 45). While some degree of loneliness can be beneficial and serve as a vital survival mechanism for health and well-being (46), social, environmental, and technological shifts may contribute to heightened and prolonged experiences of loneliness among individuals (47). Our findings reveal that all elevated patterns of loneliness, even a 'Stable-medium' pattern, can be detrimental to HRQoL outcomes.

Our findings indicated associations between loneliness trajectories and all of the HRQoL scales and subscales except for the overall physical HRQoL, which was only associated with the 'Increasing' loneliness trend. These findings may be explained by the fact that an 'Increasing' trend of loneliness coincides with diminished health or could be a reaction to life transitions such as relationship or work status changes (25, 48). Conversely, the 'Stable' loneliness trajectories may be affected by personality traits or sociodemographic characteristics such as socioeconomic status (SES) that persist throughout adult life (21, 49). Since the 'Increasing' trend of loneliness is the most prevalent, these findings imply that for the most part, loneliness is a dynamic experience that evolves over the course of adulthood. A significant proportion of individuals may experience heightened feelings of loneliness as they age, which can have profound implications for both declining physical and mental HRQoL. Our results imply that loneliness is influenced by life transitions and changing situations. Therefore, it may be amendable to change through preventive measures and intervention strategies.

Notably, the strongest associations were observed between loneliness trajectories and the mental HRQoL scales and subscales. Prior research widely acknowledges the robust association between loneliness and mental health (50), suggesting that this association is stronger than that with physical health (20, 51). One explanation for the stronger associations between loneliness and mental HRQoL may be the pervasive stigma surrounding mental illnesses (52). Mental illnesses are often 'invisible' and may be perceived as 'not real' (53).

While physical illnesses can be traced through objective measures such as biomarkers and clinical assessments, the spectrum of mental illnesses is less straightforward to define and diagnose (54). This lack of clarity may leave individuals with no validation of their condition and may lead to decreased self-worth (53) and elevated feelings of loneliness (55). In addition, an individual's ability to interact socially may be impaired due to symptoms such as depression or paranoia, leading to loneliness and social isolation (56).

Another major health outcome that was explored in the current thesis is mortality. Our study was the first to examine this health outcome with a causal inference approach. Since most of the evidence is based on observational data and only a few studies have examined long-term patterns of loneliness and health-related outcomes (57, 58), the current evidence using traditional epidemiological approaches may be subject to biases, such as residual and time-varying confounding bias. Loneliness and health have a bi-directional association, where loneliness can lead to poor health through different mechanisms but also be the outcome of health conditions and behaviours as a result of lower social functioning (59). Our results revealed for the first time that regardless of baseline health, loneliness has a dose-dependent effect on mortality, with those experiencing persistent or chronic loneliness at a higher risk. These findings further emphasise the effect of long-term loneliness on health and mortality. In addition, while previous studies have predominantly concentrated on the chronic nature of loneliness, perceiving it as a continuous experience over time (43, 44), our results suggest that even intermittent loneliness, when persisting over time, can pose a substantial risk.

7.2.2. Social and community level determinants of loneliness

Moderators of the association between loneliness and its determinants

Chapter 3 of this thesis focused on examining moderators to the effect of retirement on loneliness, focusing on macro-level determinants such as cultural norms, geographical environment and area deprivation. Our findings revealed significant differences across Western and non-Western countries, as well as between urban and rural residents. We attributed our findings to the cultural norms that are prevalent in different countries and regions. In rural China, collectivistic values may be more prevalent which may alleviate some of the difficulties of adjustment to retirement (60). However, the findings may also be attributed to economic deprivation making working life more difficult in rural China compared to urban workers who receive social and health benefits (61).

Although the moderators of the effect of retirement on loneliness have not been examined before, some macro-level moderators of other loneliness determinants and health outcomes were previously discussed (62, 63). For example, in a study that compared nine countries from the Former Soviet Union in 2013, authors found cross-country differences in the association between loneliness and risky health behaviours. In some countries, there was no association while in others the association was significant. The authors interpreted these differences as resulting from the potential moderating effect of economic deprivation and religion (62). Another study found differences between countries (Finland, Poland and Spain) in the strength of the association between loneliness and self-rated health. The differences were attributed to financial and socioeconomic factors, as well as the different characteristics of the health and welfare systems (64). Our findings are in line with previous ones, indicating that the rural-urban differences in China observed in this study may be attributed to economic differences between those residing in these regions which may contribute to loneliness before and after retirement (65). Previous literature has shown that it is not necessarily the remoteness of a geographical area, but rather the level of deprivation that affects loneliness (66). Our findings are consistent with this notion, given that rural areas in China typically accommodate residents with lower SES (67, 68). This underscores the importance of economic development and equity as significant macro-factors in improving the social well-being of individuals.

Our findings can also be interpreted through the lens of cultural individualism/collectivism implying that the social roles older adults assume after retirement could significantly affect their experience of loneliness. In traditional collectivistic societies, older adults are typically viewed as wise and respected figures, often having a significant caregiving role. It is common for them to live with grown children or other family members (69, 70). This extended family and community support may be the reason why older adults in China are less lonely after retirement compared to older adults in Western countries such as Australia and the US (60, 71, 72). Conversely, in Western countries family ties can be less strong. Being dependent on family for support is often associated with a sense of guilt and shame among Western older adults (73). Furthermore, our sensitivity analysis revealed that in urban areas in China, trends in loneliness before and after retirement are becoming closer to those in Western countries. This shift may be attributed to changes in traditional norms in urban areas in China that are becoming more individualistic compared to previous times (74).

Previous studies found variations in loneliness across countries with differing cultural norms (75, 76). However, these previous findings are inconsistent, with some studies showing collectivistic cultures have higher levels of loneliness due to higher expectations from family for support, and other studies showing that individualistic cultures have higher loneliness due to independent and separated lifestyles as well as higher single-person households (76-79). The variation between the studies could be attributed to the different countries that were included in each study and to the use of different loneliness measures (one-item vs. multiple items).

Social engagement was also examined as a potential moderator of the retirement-loneliness association across countries. Findings showed significant attenuation of loneliness before and after retirement among those who were socially engaged. However, this effect was observed only in Australia and the US, and not in China. These findings can be interpreted by the fact that the measure of social engagement included only social and not familial interactions. In China, the most meaningful engagements often occur within the family unit (80), which could explain why, in this study, social engagement did not exhibit a significant effect on loneliness within the Chinese population. These results underscore the significance of macro-level moderators and advocate for a culturally attuned approach to understanding loneliness, its contributing factors, and devising effective solutions to address it.

Psychosocial interventions and the implications on the health care system

Macro-level outcomes of loneliness have not been thoroughly examined, and there are gaps in the literature regarding the effect of loneliness on communities and society as a whole (81). However, there are indications that loneliness imposes an economic burden, stemming from work-related challenges such as absenteeism, turnover, and burnout (82). Additionally, it has been reported that loneliness is associated with increased healthcare utilisation and costs (83), as well as expenses related to prevention and intervention efforts (84). Social support and connectedness have been recognised as potential avenues for enhancing social well-being and health, as well as for mitigating healthcare costs (85). Consequently, interventions have explored the effectiveness of these approaches in reducing healthcare utilisation and associated expenses (86-88). The findings of **Chapter 6** of this thesis showed that psychosocial interventions, those interventions that include cognitive behavioural therapy, psychoeducation, peer support, support groups and case management, are effective in reducing the burden of care on the healthcare system. More specifically our findings show a decrease in urgent and inpatient care which are considered to be the costliest healthcare

services (89). In addition, outpatient visits were found to increase following psychosocial interventions alongside social well-being measures.

These findings imply that psychosocial interventions are effective in reducing healthcare use by improving social well-being. Our findings also suggest that psychosocial interventions may improve the use of preventive care in the outpatient context, which in turn, may lead to less emergency and inpatient use (90, 91). These findings may also align with previous research on the cost-effectiveness of psychosocial interventions (81), showing these interventions can potentially save costs by reducing healthcare use, while also improving the well-being of individuals. However, in the current study, we were unable to aggregate and analyse the costs of healthcare use due to the low number of studies and high heterogeneity in interventions, currencies and healthcare services. While certain studies have suggested potential economic benefits associated with psychosocial interventions, the evidence regarding their cost-effectiveness remains inconclusive (14, 92, 93) and there is a need for an economic evaluation of these interventions.

Our review of psychosocial interventions also revealed how they affect different population groups. According to the results, some populations derived greater benefits from these interventions, for example, individuals with mental illnesses and caregivers. Social and mental health share a similar stigma which can be attributed to the invisibility of these concepts (15, 94). Individuals dealing with mental health issues or with loneliness may encounter challenges in receiving recognition for their struggles, both from their social circles and even from themselves. This lack of emotional validation may exacerbate symptoms and contribute to increased loneliness (95, 96). Our findings highlight the importance of attending to the social health of individuals with mental illnesses, as a way of improving their health and preventing deterioration of the health condition. This also echoes our finding on the relationship between loneliness and the mental health sub-scale of HRQoL (**Chapter 4**). Caregivers represent another vulnerable group, often experiencing heightened loneliness due to the demanding nature of their responsibilities and the potential lack of social support (33, 38). Most of the caregivers included in this review were caregivers of individuals with mental or cognitive illnesses, which puts them at an even higher risk due to the mental health stigma (97, 98). It is plausible that both caregivers and individuals with mental illnesses are among the most in need of support, thus exhibiting the most significant improvements through interventions. The heightened vulnerability of these groups underscores the importance of tailored support and intervention strategies to address their specific needs.

The current thesis also provides information regarding intervention characteristics that contribute to effectiveness in reducing healthcare use. For example, it was found that one-on-one interventions and interventions delivered by health professionals had significant effects. Health professionals play a pivotal role in interventions by leveraging their expertise in medicine, promoting healthy behaviours, and offering stress management techniques (90, 99). Moreover, their credibility in the eyes of patients may enhance their motivation to adhere to the interventions that are offered. However, it is important to acknowledge that health professionals, particularly those in primary care and hospital settings, often face heavy workloads, limiting their ability to deliver psychosocial interventions (100, 101). Therefore, when designing interventions involving health professionals, it is essential to allocate adequate human resources to facilitate the intervention effectively. To establish a more consistent approach to identifying and offering psychosocial support, the healthcare system would require additional resources to alleviate the strain on an already burdened system (101).

Our findings also suggest that when implementing an intervention, a one-on-one approach led to significant reductions in healthcare use. This personalised method may have been particularly effective in addressing the specific needs and circumstances of individuals, thereby enhancing the intervention's effect on improving social well-being and healthcare use. That said, we found that while group interventions did show some effects, they did not reach a level of statistical significance. Previous studies have found both group and one-on-one formats to be efficacious (102, 103). However, whether it is one-on-one or group interventions that are delivered, customising interventions based on individual needs may be essential.

Despite the sustained intervention effect observed in our findings, lasting up to 24 months post-intervention, it is notable that the majority of psychosocial interventions were short-term and only offered temporary effects. Most of the psychosocial interventions were initiatives by health and community organisations that are time and funding-limited (104-106). Limited-duration interventions may create significant improvements in social well-being and decrease the need for health care. However, there remains a gap in understanding the long-term effects beyond the last follow-up period. Furthermore, intervening on the more 'upstream' determinants through systematic and policy changes may be more likely to lead to sustained improvements.

7.3. Implications for health professionals and policymakers

The findings from the thesis have several important policy implications. First, demonstrating that loneliness is a significant health risk, with implications for HRQoL and mortality (**Chapters 4-5**), is important for priority setting among policymakers. Considering social health on par with physical and mental well-being, and implementing screening and preventive measures, accordingly, could potentially prevent numerous chronic and even life-threatening illnesses. To improve social well-being as well as save costs and lower the burden on the healthcare system, there is a need for more permanent and consistent interventions that are based on changes in policy and adjustments in healthcare systems. Similar to other significant determinants of health such as smoking, obesity, and physical inactivity, which are targeted through multi-level strategies including advocacy and policies, community-based prevention strategies and interventions, loneliness should be recognised as a major health risk and appropriate steps should be taken within the public health system to address it. Certain countries, such as the UK and Japan have already initiated the incorporation of such strategies into primary health care. GPs and nurses receive training to identify patients susceptible to loneliness and social isolation. They offer social prescriptions by linking patients with non-governmental organisations and community entities for social, emotional, and practical support (4, 5). In Australia, there was previous discussion about implementing loneliness as a social health policy by appointing an official governmental entity dedicated to addressing loneliness (107). However, such attempts have been so far unsuccessful. The findings of the current thesis contribute to the ongoing efforts to recognise loneliness as a major determinant of health and create an appropriate response on a policy level.

The literature on loneliness interventions shows that a selection of strategies has proven successful in decreasing loneliness and strengthening social networks and support systems, including support groups, individual therapy, peer support, and technology-based solutions (108, 109). These interventions also have shown effectiveness in enhancing physical, mental, and cognitive health outcomes (110-112). These findings carry important policy implications, underscoring the substantial impact that improving social well-being can have on both health outcomes and healthcare utilisation. Incorporating social care into the public health system to reduce loneliness, will contribute not only to the health and well-being of individuals, but may have significant economic benefits for the healthcare system. Our findings regarding the efficacy of psychosocial interventions in reducing healthcare utilisation while simultaneously enhancing perceived social support validate this assertion.

Our findings imply that providing social support to at-risk individuals results in the reduction of the most costly healthcare services- urgent and inpatient care and an increase in the most cost-effective health services- preventive care (89). Therefore, psychosocial interventions can be used to reduce healthcare utilisation and to relieve the workload as well as the economic burden on the healthcare system. To achieve this, it is pivotal to raise awareness about social health among health professionals and implement standardised tools to screen for loneliness during health checkups and hospital visits. Similar to other mental health conditions such as self-harm, suicidal ideation and addictions, the healthcare system is an opportunity to identify people in need and conduct interventions to change the course of lives (113). By creating a systematic approach to social health, many re-hospitalisations and other health care visits may be prevented.

Although our results from the meta-analysis support the use of systemic psychosocial interventions, the results of our cross-country comparisons indicate that loneliness determinants and outcomes may differ across populations. This culturally sensitive approach has significant implications for designing and implementing interventions for loneliness. Our findings underscore the importance of tailored interventions designed to meet the specific needs of different populations. Given the substantial knowledge gaps regarding loneliness in low- to middle-income countries, the present thesis emphasises the necessity of a global response to gather information on the risk of loneliness in these regions and its effect on both health and economic outcomes (6).

7.4. Methodological strengths and limitations

The current thesis had a few limitations. First, due to COVID-19 lockdowns at the start of the thesis, my research plans had to be drastically modified, switching from primary data collection to secondary data analysis. Therefore, my thesis research had to depend on existing data, which have limitations beyond the control of our research team. For example, most of these studies applied a single-item direct measure for loneliness has previously encountered criticism, largely stemming from potential issues related to differing interpretations of loneliness among respondents and the influence of reporting bias driven by stigma (114, 115). Nevertheless, the one-item loneliness measure has been previously validated and demonstrated to be highly reliable within longitudinal research (116, 117). Furthermore, it was found to correlate with other more comprehensive and commonly used loneliness measures, such as the UCLA and the de Jong loneliness scales (118, 119). Regarding the ambiguity surrounding the cut-point of one-item measures (120, 121), I addressed this issue

by conducting sensitivity analysis in these studies. The results demonstrated that while varying cut-points led to differences in the strength of results (lower cut-point attenuated the effect and higher cut-point strengthened it but at the cost of more error), the dose-dependent association persisted consistently (**Chapter 5**). Additionally, our analysis of the relationship between loneliness, HRQoL and mortality used the Australian Longitudinal Study of Women's Health (**Chapters 4-5**) and therefore cannot be generalised to Australian men and to women in non-Western societies.

Second, in **Chapter 3**, we had to exclude several waves of data from the Household, Income and Labour Dynamic in Australia survey to harmonise it with the other two countries of comparison, which may have contributed to data loss. Third, in most surveys (**Chapters 3-5**), data were collected in gaps of 2-3 years which means that there is a risk that the loneliness that was reported in the years of the surveys was not reflective of the time between measurement points. However, considering most surveys included multiple waves, it is reasonable to infer that the reported levels of loneliness during survey years provide a reasonably representative snapshot of the overall loneliness patterns. Finally, the results of the meta-analysis (**Chapter 6**) are prone to potential bias due to the small number of studies, small sample sizes and high heterogeneity. Moreover, the exclusion of unpublished data or non-English studies could potentially introduce bias into the results. The models were tested for publication bias and only one model, which showed non-significant effects, was at risk for publication bias. Hence, we assume that the inclusion of unpublished data is unlikely to alter the results, as such data typically do not yield statistically significant findings.

Despite the limitations presented in the current thesis, we maintain confidence in its robustness and validity, suggesting that our results can be generalised to the broader population. The current study employed strong modelling techniques for causal inferences. These models are the closest to resembling an RCT design within the context of observational data, specifically tailored to address situations involving complex confounding, such as those encountered in the study of loneliness, its determinants and outcomes. The use of lagged models, where the exposure is measured before the outcome, along with adjustments to baseline exposures are all techniques to ensure temporality, thus strengthening the causality of associations. The adjustments to a variety of sociodemographic, health and health behaviours variables that were pre-determined as well as an E-value analysis (**Chapter 5**), ensured that the risk of residual confounding would be minimised.

The use of population-based longitudinal data is a major strength of the current thesis. Most of the research on loneliness is based on cross-sectional or single-timepoint designs, which are prone to bias and cannot capture the dynamic nature of loneliness. Further, the inclusion of data from various countries constitutes a significant strength of this thesis. This approach enhances the generalisability of the findings beyond Western countries and also sheds light on countries and regions that have been underrepresented in loneliness research. In addition to using robust modelling for observational data, the current thesis aggregated and quantified the evidence on psychosocial interventions' effectiveness in a meta-analytic design. The inclusion of only RCTs in the meta-analysis ensured that bias would be minimised. In addition, we used multi-level random effect models in these meta-analyses to allow us to include all effect estimates that are available in each study. All of these methods ensured that the data that was used in the current thesis were of the highest quality and that the methods of analysis would produce the most accurate and representable measures of effect.

7.5. Directions for future research

This body of work collectively provides a significant contribution to the literature on loneliness determinants, health outcomes and prevention strategies. However, through this investigation, many gaps in the literature have been unveiled that require clarification by future research. First, since this study is one of the few to examine causal mechanisms in the association between loneliness and different determinants and health outcomes, future research should focus on examining the causal effects of individual, social and environment level determinants such as genetics, SES, life transitions, cultural norm and the built environment. In addition, causal inference models should be applied to examine the effect of loneliness on different health outcomes such as chronic and life-threatening illnesses, mortality and the biological mechanisms associated with illnesses and death such as inflammation measures. Furthermore, longitudinal analysis across multiple measurement points is needed to capture the dynamic effect of loneliness across time and to control time-varying confounding in the associations between loneliness, its determinants and outcomes. It is also recommended to use other measurement tools rather than the one-item loneliness measure across databases. Consistent findings across different countries and measurement tools will strengthen the validity regarding causality.

Loneliness has been examined among a variety of population groups. However, some populations have been neglected compared to others. Future studies should focus on

examining loneliness in non-Western countries and among a variety of ethnicities and cultures. Loneliness determinants may vary between countries, and results from Western countries may not generalise well across countries. In addition, as the research on loneliness has focused on older adults, there is a need for more research on loneliness among middle-aged and prime-aged adults. Additionally, there is a need to examine the economic implications of loneliness among the younger population (81). Current research has solely assessed the economic burden of loneliness among older adults. Nonetheless, there is reason to believe that loneliness among younger populations imposes a notable economic impact, particularly considering evidence indicating that loneliness is most prevalent among this demographic (122).

The current thesis also found that psychosocial interventions can reduce healthcare use and improve social well-being. However, there is very little information on the effect of psychosocial interventions on the costs of health care. Although some studies examined the costs before and after the intervention (93, 123), it is challenging to aggregate the data and quantify the evidence in a meta-analytic design, due to the heterogeneity of health services, currencies and health systems (81). Therefore, further research is necessary to address these challenges and to determine whether these interventions can lead to a reduction in healthcare costs through a meta-analytic design. Likewise, there is a notable scarcity of studies on the cost-benefit of psychosocial interventions. Therefore, future research that offers an economic evaluation of existing loneliness interventions is imperative to provide insights into the most cost-effective interventions.

The challenge in assessing the effectiveness of psychosocial interventions partly lies in the varying definitions of what constitutes such interventions. Psychosocial interventions encompass a range of approaches, including those focused on social well-being and involve social activities to alleviate loneliness and social isolation (104, 124). However, psychosocial interventions extend beyond addressing social well-being and can be applied to alleviating different conditions, symptoms and behaviours, such as surgery recovery, addiction and obesity. These interventions can therefore encompass a diverse array of therapies and activities tailored to address different facets of the targeted condition or behaviour, including, rehabilitation, diet regime, pain management and even medications (125-127). Yet, there remains a lack of clarity regarding the definition of a psychosocial intervention and the specific characteristics or activities it should entail to effectively address social well-being.

Future studies should delve into refining the definition of a psychosocial intervention, aiming to enhance clarity and precision in assessing its efficacy.

7.6. Conclusions

The current thesis examined the dynamic effect of loneliness on health, mortality, and the potential burden on healthcare, and pinpointed key determinants and potential solutions. Our research indicates that the factors contributing to loneliness can change in response to significant life events and may differ depending on cultural norms and geographical regions. Long trajectories of loneliness across 18 years exposed that elevated trajectories of loneliness are associated with poor HRQoL and that persistent or chronic loneliness had a dose-dependent effect on mortality. These findings imply that loneliness is a significant social determinant of health that has serious health and economic implications. Therefore, addressing social health should be a priority from a public health standpoint, on par with the prevention of physical and mental health issues. Our findings regarding the efficacy of psychosocial interventions suggest that systematically addressing loneliness through prevention and intervention, can effectively mitigate its negative effect on health. Taking such measures can enhance the health and well-being of individuals across various risk groups, including those with chronic illnesses and disabilities, caregivers, and socially deprived individuals. Moreover, implementing systematic interventions through policy and integrating social interventions into healthcare may alleviate the substantial financial burden of loneliness on the healthcare system.

7.7. References

1. Ciolfi ML. Historical Perspectives on the Research of Social Isolation, Loneliness, and Social Support. In: Kaye LW, Singer CM, editors. New York: Springer Publishing Company; 2018. p. 17-34.
2. Burnett C. The Historical Roots of Loneliness. Vulcan Historical Review [Internet]. 2023 [cited 2024 2 June]; 27:[14 p.]. Available from: <https://digitalcommons.library.uab.edu/cgi/viewcontent.cgi?article=1135&context=vulcan>.
3. Duncan A, Kiely D, Mavisakalyan A, Peters A, Seymour R, Twomey C, L V. Stronger Together: Loneliness and social connectedness in Australia. Bankwest Curtin Economics Centre; 2021.
4. Wahlquist C. Loneliness minister' proposed to tackle Australian social isolation. The Gurdian. 2018.
5. Social recovery beyond COVID-19: A National Strategy to Address Loneliness and Social Isolation. Ending Loneliness Together In partnership with R U OK? and the Australian Psychological Society; 2021-2022.
6. World Health Organization. WHO launches commission to foster social connection 2023 [updated 15 November 2023; cited 2024 5 February]. Available from: <https://www.who.int/news/item/15-11-2023-who-launches-commission-to-foster-social-connection>.
7. PubMed timeline results: loneliness by year [Internet]. 2024 [cited 3 June 2024]. Available from: <https://pubmed.ncbi.nlm.nih.gov/?term=loneliness&timeline=expanded>.
8. PubMed timeline results: physical activity by year [Internet]. PubMed. 2024 [cited 8 June 2024]. Available from: <https://pubmed.ncbi.nlm.nih.gov/?term=physical%20activity&timeline=expanded>.
9. PubMed timeline results: depression by year [Internet]. PubMed. 2024 [cited 8 June 2024]. Available from: <https://pubmed.ncbi.nlm.nih.gov/?term=depression>.

10. Ernst M, Niederer D, Werner AM, Czaja SJ, Mikton C, Ong AD, et al. Loneliness before and during the COVID-19 pandemic: A systematic review with meta-analysis. *Am Psychol.* 2022;77(5):660-77.
11. Luchetti M, Lee JH, Aschwanden D, Sesker A, Strickhouser JE, Terracciano A, Sutin AR. The trajectory of loneliness in response to COVID-19. *Am Psychol.* 2020;75(7):897-908.
12. Malhotra R, Tareque MI, Saito Y, Ma S, Chiu C-T, Chan A. Loneliness and health expectancy among older adults: A longitudinal population-based study. *J Am Geriatr Soc.* 2021;69(11):3092-102.
13. Phillips DM, Finkel D, Petkus AJ, Muñoz E, Pahlen S, Johnson W, et al. Longitudinal analyses indicate bidirectional associations between loneliness and health. *Aging Ment Health.* 2023;27(6):1217-25.
14. Markle-Reid M, McAiney C, Fisher K, Ganann R, Gauthier AP, Heald-Taylor G, et al. Effectiveness of a nurse-led hospital-to-home transitional care intervention for older adults with multimorbidity and depressive symptoms: A pragmatic randomized controlled trial. *PloS One.* 2021;16(7):e0254573.
15. HaGani N, Surkalim DL, Clare PJ, Merom D, Smith BJ, Ding DJJNO. Health care utilization following interventions to improve social well-being: A systematic review and meta-analysis. *JAMA Netw Open.* 2023;6(6):e2321019-e.
16. Cacioppo S, Capitanio JP, Cacioppo JT. Toward a neurology of loneliness. *Psychol Bull.* 2014;140(6):1464.
17. Luhmann M, Buecker S, Rüsberg M. Loneliness across time and space. *Nat Rev Psychol.* 2023;2(1):9-23.
18. Zuo S, Lin L, Chen S, Wang Z, Tian L, Li H, Xu Y. Influencing factors of loneliness among older adults in China: a systematic review and meta-analysis. *Psychogeriatrics.* 2023;23(1):164-76.
19. Wang F, Gao Y, Han Z, Yu Y, Long Z, Jiang X, et al. A systematic review and meta-analysis of 90 cohort studies of social isolation, loneliness and mortality. *Nat Hum Behav.* 2023;7(8):1307-19.

20. Park C, Majeed A, Gill H, Tamura J, Ho RC, Mansur RB, et al. The Effect of Loneliness on Distinct Health Outcomes: A Comprehensive Review and Meta-Analysis. *Psy Res*. 2020;294:113514.
21. Bosma H, Jansen M, Schefman S, Hajema KJ, Feron F. Lonely at the bottom: a cross-sectional study on being ill, poor, and lonely. *Pub Health*. 2015;129(2):185-7.
22. Wei K, Liu Y, Yang J, Gu N, Cao X, Zhao X, et al. Living arrangement modifies the associations of loneliness with adverse health outcomes in older adults: evidence from the CLHLS. *BMC Geriatr*. 2022;22(1):59.
23. Fierloos IN, Tan SS, Williams G, Alhambra-Borrás T, Koppelaar E, Bilajac L, et al. Socio-demographic characteristics associated with emotional and social loneliness among older adults. *BMC Geriatr*. 2021;21(1):114.
24. Barjaková M, Garneró A, d'Hombres B. Risk factors for loneliness: A literature review. *Soc Sci Med*. 2023;334:116163.
25. Dahlberg L, Andersson L, McKee KJ, Lennartsson C. Predictors of loneliness among older women and men in Sweden: A national longitudinal study. *Aging Ment Health*. 2015;19(5):409-17.
26. Davies N, Crowe M, Whitehead L. Establishing routines to cope with the loneliness associated with widowhood: a narrative analysis. *J Psychiatr Ment healt*. 2016;23(8):532-9.
27. Yang F, Gu D. Widowhood, widowhood duration, and loneliness among older adults in China. *Soc Sci Med*. 2021;283:114179.
28. Gordon EH, Hubbard RE. Do sex differences in chronic disease underpin the sex-frailty paradox? *Mech Ageing Dev*. 2019;179:44-50.
29. McQuaid RJ, Cox SML, Ogunlana A, Jaworska N. The burden of loneliness: Implications of the social determinants of health during COVID-19. *Psy Res*. 2021;296:113648.
30. Dong X, Chen R. Gender differences in the experience of loneliness in U.S. Chinese older adults. *J Women Aging*. 2017;29(2):115-25.

31. Pagan R. Gender and Age Differences in Loneliness: Evidence for People without and with Disabilities. *Int J Environ Res Public Health*. 2020;17(24).
32. Nicolaisen M, Thorsen KJ. Gender Differences in Loneliness Over Time: A 15-Year Longitudinal Study of Men and Women in the Second Part of Life. *Int J Aging Hum Dev*. 2023;98(1):103-32.
33. Schulz R, Beach SR, Czaja SJ, Martire LM, Monin JK. Family Caregiving for Older Adults. *Ann Rev Psychol*. 2020;71(1):635-59.
34. Revenson TA, Griva K, Luszczynska A, Morrison V, Panagopoulou E, Vilchinsky N, Hagedoorn M. Gender and Caregiving: The Costs of Caregiving for Women. In: Revenson TA, Griva K, Luszczynska A, Morrison V, Panagopoulou E, Vilchinsky N, Hagedoorn M, editors. *Caregiving in the Illness Context*. London: Palgrave Macmillan UK; 2016. p. 48-63.
35. Lin KY, Burgard SA. Working, parenting and work-home spillover: Gender differences in the work-home interface across the life course. *Adv Life Course Res*. 2018;35:24-36.
36. Dahlberg L, McKee KJ. Correlates of social and emotional loneliness in older people: evidence from an English community study. *Aging Ment Health*. 2014;18(4):504-14.
37. Brown TH, Richardson LJ, Hargrove TW, Thomas CS. Using Multiple-hierarchy Stratification and Life Course Approaches to Understand Health Inequalities: The Intersecting Consequences of Race, Gender, SES, and Age. *J Health Soc Behav*. 2016;57(2):200-22.
38. Kovaleva M, Spangler S, Clevenger C, Hepburn K. Chronic Stress, Social Isolation, and Perceived Loneliness in Dementia Caregivers. *J Psychosocial Nurs Ment Health Service*. 2018;56(10):36-43.
39. Golaszewski NM, LaCroix AZ, Godino JG, Allison MA, Manson JE, King JJ, et al. Evaluation of Social Isolation, Loneliness, and Cardiovascular Disease Among Older Women in the US. *JAMA Netw Open*. 2022;5(2):e2146461.

40. Valtorta NK, Kanaan M, Gilbody S, Ronzi S, Hanratty BJ. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. *Heart*. 2016;102(13):1009-16.
41. Hosozawa M, Cable N, Yamasaki S, Ando S, Endo K, Usami S, et al. Predictors of chronic loneliness during adolescence: a population-based cohort study. *Child Adol Psych Men*. 2022;16(1):107.
42. Martín - María N, Caballero FF, Lara E, Domènech - Abella J, Haro JM, Olaya B, et al. Effects of transient and chronic loneliness on major depression in older adults: A longitudinal study. *Int J Geriatr Psych*. 2021;36(1):76-85.
43. Lim MH, Manera KE, Owen KB, Phongsavan P, Smith BJ. The prevalence of chronic and episodic loneliness and social isolation from a longitudinal survey. *Sci Rep*. 2023;13(1):12453.
44. Shiovitz-Ezra S, Ayalon L. Situational versus chronic loneliness as risk factors for all-cause mortality. *Int Psychogeriatr*. 2010;22(3):455-62.
45. Martín-María N, Caballero FF, Miret M, Tyrovolas S, Haro JM, Ayuso-Mateos JL, Chatterji S. Differential impact of transient and chronic loneliness on health status. A longitudinal study. *Psychol Health*. 2020;35(2):177-95.
46. Hawkley LC, Cacioppo JT. Loneliness Matters: A Theoretical and Empirical Review of Consequences and Mechanisms. *Ann Behav Med*. 2010;40(2):218-27.
47. Buecker S, Mund M, Chwastek S, Sostmann M, Luhmann M. Is loneliness in emerging adults increasing over time? A preregistered cross-temporal meta-analysis and systematic review. *Psychol Bull*. 2021;147(8):787-805.
48. Shin O, Park S, Amano T, Kwon E, Kim B. Nature of Retirement and Loneliness: The Moderating Roles of Social Support. *J Appl Gerontol*. 2020;39(12):1292-302.
49. Mund M, Freuding MM, Möbius K, Horn N, Neyer FJ. The Stability and Change of Loneliness Across the Life Span: A Meta-Analysis of Longitudinal Studies. *Pers Soc Psychol Rev*. 2019;24(1):24-52.

50. Richardson T, Elliott P, Roberts R. Relationship between loneliness and mental health in students. *J Pub Mental Health*. 2017;16(2):48-54.
51. Richard A, Rohrmann S, Vandeleur CL, Schmid M, Barth J, Eichholzer M. Loneliness is adversely associated with physical and mental health and lifestyle factors: Results from a Swiss national survey. *PloS One*. 2017;12(7):e0181442.
52. Prizeman K, Weinstein N, McCabe C. Effects of mental health stigma on loneliness, social isolation, and relationships in young people with depression symptoms. *BMC Psychiat*. 2023;23(1):527.
53. Shpigelman CN, HaGani N. The impact of disability type and visibility on self - concept and body image: Implications for mental health nursing. *J Psychiatr Ment healt*. 2019;26(3-4):77-86.
54. Boschloo L, van Borkulo CD, Rhemtulla M, Keyes KM, Borsboom D, Schoevers RA. The network structure of symptoms of the diagnostic and statistical manual of mental disorders. *PloS One*. 2015;10(9):e0137621.
55. Ali LAE, Sabra AI, Ahmed FM. Effect of Internalized Stigma on Self-Esteem and Loneliness among Mentally Ill Patients. *Menoufia Nurs J*. 2019;4(1):25-33.
56. Rüsch N, Corrigan PW, Powell K, Rajah A, Olschewski M, Wilkniss S, Batia K. A stress-coping model of mental illness stigma: II. Emotional stress responses, coping behavior and outcome. *Schizophrenia Res*. 2009;110(1-3):65-71.
57. Stessman J, Rottenberg Y, Shimshilashvili I, Ein-Mor E, Jacobs JM. Loneliness, Health, and Longevity. *J Gerontol A-Biol*. 2014;69(6):744-50.
58. Ward M, May P, Normand C, Kenny RA, Nolan A. Mortality risk associated with combinations of loneliness and social isolation. Findings from The Irish Longitudinal Study on Ageing (TILDA). *Age Aging*. 2021;50(4):1329-35.
59. National Academies of Sciences Engineering & Medicine, Division of Behavioral Social Sciences Education Health & Medicine, Division Board on Behavioral Cognitive Sensory Sciences, Board on Health Sciences Policy, Committee on the Health Medical, Dimensions of Social Isolation Loneliness in Older Adults. *Social Isolation and Loneliness in*

Older Adults: Opportunities for the Health Care System. Washington (DC): National Academies Press (US); 2020.

60. Zhang J, Fokkema T, Arpino B. Loneliness among Chinese older adults: The role of grandparenthood and grandparental childcare by gender. *J Fam Issues*. 2022;43(11):3078-99.
61. Qi L. China Is Facing a Moment of Truth About Its Low Retirement Age. *The Wall Street Journal*. 11/4/2023.
62. Stickley A, Koyanagi A, Roberts B, Richardson E, Abbott P, Tumanov S, McKee M. Loneliness: its correlates and association with health behaviours and outcomes in nine countries of the former Soviet Union. *PloS One*. 2013;8(7):e67978.
63. Beller J, Wagner A. Loneliness and Health: The Moderating Effect of Cross-Cultural Individualism/Collectivism. *J Aging Health*. 2020;32(10):1516-27.
64. Rico-Uribe LA, Caballero FF, Olaya B, Tobiasz-Adamczyk B, Koskinen S, Leonardi M, et al. Loneliness, social networks, and health: a cross-sectional study in three countries. *PloS One*. 2016;11(1):e0145264.
65. Shen Z, Fang X, Zheng X. The impact of women's off-farm employment on depressive symptoms: Evidence from rural China. *Soc Sci Med*. 2022;311:115309.
66. Victor CR, Pikhartova J. Lonely places or lonely people? Investigating the relationship between loneliness and place of residence. *BMC Pub Health*. 2020;20(1):778.
67. Booth A. Invisible China: How the Urban - Rural Divide Threatens China's Rise - by Scott Rozelle and Natalie Hell. *Asian-Pac Econ Lit*. 2021;35(1):161-2.
68. Chen L, Shen W. Spatiotemporal differentiation of urban-rural income disparity and its driving force in the Yangtze River Economic Belt during 2000-2017. *PloS One*. 2021;16(2):e0245961.
69. Leung JC. Family support and community services for older adults in China: Integration and partnership. *Handbook of Asian aging: Routledge*; 2018. p. 405-30.

70. Shen Y, Yeatts DE. Social support and life satisfaction among older adults in China: family-based support versus community-based support. *Int J Aging Hum Dev*. 2013;77(3):189-209.
71. Lou VWQ. Life Satisfaction of Older Adults in Hong Kong: The Role of Social Support from Grandchildren. *Soc Indic Res*. 2010;95(3):377-91.
72. Li LW, Zhang J, Liang J. Health among the oldest-old in China: which living arrangements make a difference? *Soc Sci Med*. 2009;68(2):220-7.
73. Cahill E, Lewis LM, Barg FK, Bogner HR. "You don't want to burden them": older adults' views on family involvement in care. *J Fam Nurs*. 2009;15(3):295-317.
74. Liu J, Rozelle S, Xu Q, Yu N, Zhou T. Social Engagement and Elderly Health in China: Evidence from the China Health and Retirement Longitudinal Survey (CHARLS). *Int J Environ Res Public Health*. 2019;16(2).
75. Newmyer L, Verdery AM, Margolis R, Pessin L. Measuring Older Adult Loneliness Across Countries. *J Gerontol B Psychol Sci Soc Sci*. 2021;76(7):1408-14.
76. Barreto M, Victor C, Hammond C, Eccles A, Richins MT, Qualter P. Loneliness around the world: Age, gender, and cultural differences in loneliness. *Pers Individ Dif*. 2021;169:110066.
77. Swader CS. Loneliness in Europe: Personal and societal individualism-collectivism and their connection to social isolation. *Soc Forces*. 2019;97(3):1307-36.
78. Fokkema T, De Jong Gierveld J, Dykstra PA. Cross-national differences in older adult loneliness. *J Psychol*. 2012;146(1-2):201-28.
79. Heu LC, van Zomeren M, Hansen N. Lonely Alone or Lonely Together? A Cultural-Psychological Examination of Individualism-Collectivism and Loneliness in Five European Countries. *Pers Soc Psychol Bull*. 2019;45(5):780-93.
80. Wang G, Zhang X, Wang K, Li Y, Shen Q, Ge X, Hang W. Loneliness among the rural older people in Anhui, China: prevalence and associated factors. *Int J Geriatr Psychiatry*. 2011;26(11):1162-8.

81. Mihalopoulos C, Le LK-D, Chatterton ML, Bucholc J, Holt-Lunstad J, Lim MH, Engel L. The economic costs of loneliness: a review of cost-of-illness and economic evaluation studies. *Soc Psychiatry Psychiatr Epidemiol*. 2020;55(7):823-36.
82. Bryan BT, Andrews G, Thompson KN, Qualter P, Matthews T, Arseneault L. Loneliness in the workplace: a mixed-method systematic review and meta-analysis. *Occup Med (Lond)*. 2023;73(9):557-67.
83. Valtorta NK, Moore DC, Barron L, Stow D, Hanratty B. Older adults' social relationships and health care utilization: a systematic review. *Am J Public Health*. 2018;108(4):e1-e10.
84. Kung CSJ, Kunz JS, Shields MA. Economic Aspects of Loneliness in Australia. *Aus Econ Rev*. 2021;54(1):147-63.
85. Chatterjee HJ, Camic PM, Lockyer B, Thomson LJM. Non-clinical community interventions: a systematised review of social prescribing schemes. *Arts Health*. 2018;10(2):97-123.
86. Mosher CE, Winger JG, Given BA, Shahda S, Helft PR. A systematic review of psychosocial interventions for colorectal cancer patients. *Support Care Cancer*. 2017;25(7):2349-62.
87. Veazie S, Gilbert J, Winchell K, Paynter R, Guise J-M. Addressing social isolation to improve the health of older adults: a rapid review. Agency for Healthcare Research and Quality (US); 2019.
88. Dieng M, Cust AE, Kasparian NA, Mann GJ, Morton RL. Economic evaluations of psychosocial interventions in cancer: a systematic review. *Psycho-Oncol*. 2016;25(12):1380-92.
89. Richter DL, Diduch DR. Cost Comparison of Outpatient Versus Inpatient Unicompartmental Knee Arthroplasty. *Orthop J Sports Med*. 2017;5(3):2325967117694352.
90. Doshmangir L, Khabiri R, Jabbari H, Arab-Zozani M, Kakemam E, Gordeev VS. Strategies for utilisation management of hospital services: a systematic review of interventions. *Globalization Health*. 2022;18(1):53.

91. Holt-Lunstad J, Smith TB. Loneliness and social isolation as risk factors for CVD: implications for evidence-based patient care and scientific inquiry. *Heart*. 2016;102(13):987-9.
92. Markle-Reid M. Frail elderly home care clients: The effects and expense of adding nursing health promotion and preventive care to personal support services: Canadian Health Services Research Foundation; 2002.
93. Simpson A, Flood C, Rowe J, Quigley J, Henry S, Hall C, et al. Results of a pilot randomised controlled trial to measure the clinical and cost effectiveness of peer support in increasing hope and quality of life in mental health patients discharged from hospital in the UK. *BMC Psychiat*. 2014;14:30.
94. Suri S, Garg S, Tholia G. Attachment style, perceived social support and loneliness among college students. *Int J Innov Stud Sociol Human*. 2019;4(5):135-42.
95. Nicola M, Correia H, Ditchburn G, Drummond PD. Defining pain-validation: The importance of validation in reducing the stresses of chronic pain. *Front Pain Res (Lausanne)*. 2022;3:884335.
96. Mahtani S, Hasking P, Melvin GA. Shame and Non-suicidal Self-injury: Conceptualization and Preliminary Test of a Novel Developmental Model among Emerging Adults. *J Youth Adolescence*. 2019;48(4):753-70.
97. Mehra A, Kumar A, Grover S, Chakrabarti S, Avasthi A. Relationship of Stigma with Burden and Coping Among Caregivers of Patients with Severe Mental Disorders. *Indian J Soc Psychiatry*. 2020;36(1).
98. Tabatabaee M, Yousefi Nooraie R, Mohammad Aghaei A, Rostam-Abadi Y, Ansari M, Sharifi S, Sharifi V. Loneliness in the presence of others: A mixed-method study of social networks of caregivers of patients with severe mental disorders. *Int J Soc Psych*. 2022;69(1):190-9.
99. Swan S, Keen N, Reynolds N, Onwumere J. Psychological interventions for post-traumatic stress symptoms in psychosis: a systematic review of outcomes. *Front Psychol*. 2017;8:341.

100. Pérez-Francisco DH, Duarte-Clíments G, Del Rosario-Melián JM, Gómez-Salgado J, Romero-Martín M, Sánchez-Gómez MB. Influence of Workload on Primary Care Nurses' Health and Burnout, Patients' Safety, and Quality of Care: Integrative Review. *Healthcare (Basel)*. 2020;8(1).
101. Bird VJ, Davis S, Jawed A, Qureshi O, Ramachandran P, Shahab A, Venkatraman L. Implementing psychosocial interventions within low and middle-income countries to improve community-based care for people with psychosis-A situation analysis. *Front Psychiatry*. 2022;13:807259.
102. Hogan BE, Linden W, Najarian B. Social support interventions: Do they work? *Clin Psychol Rev*. 2002;22(3):381-440.
103. Poscia A, Stojanovic J, La Milia DI, Duplaga M, Grysztar M, Moscato U, et al. Interventions targeting loneliness and social isolation among the older people: An update systematic review. *Expl Gerontol*. 2018;102:133-44.
104. Lorente-Martínez R, Brotons-Rodes P, Sitges-Maciá E. Benefits of a psychosocial intervention programme using volunteers for the prevention of loneliness among older women living alone in Spain. *Health Soc Care Community*. 2022;30(5):2000-12.
105. Blancafort Alias S, Monteserín Nadal R, Moral I, Roqué Fígols M, Rojano i Luque X, Coll-Planas L. Promoting social capital, self-management and health literacy in older adults through a group-based intervention delivered in low-income urban areas: results of the randomized trial AEQUALIS. *BMC Pub Health*. 2021;21:1-12.
106. Colella TJ, King-Shier K. The effect of a peer support intervention on early recovery outcomes in men recovering from coronary bypass surgery: A randomized controlled trial. *Eur J Cardiovasc Nur*. 2018;17(5):408-17.
107. Purcell C. Why we need a minister for loneliness. *The Sydney Morning Herald*. 2021 25 February.
108. Morrish N, Choudhury S, Medina-Lara A. What works in interventions targeting loneliness: a systematic review of intervention characteristics. *BMC Pub Health*. 2023;23(1):2214.

109. Masi CM, Chen H-Y, Hawkey LC, Cacioppo JT. A meta-analysis of interventions to reduce loneliness. *Pers Soc Psychol Rev.* 2011;15(3):219-66.
110. Hui EK, Tischler V, Wong GHY, Lau WYT, Spector A. Systematic review of the current psychosocial interventions for people with moderate to severe dementia. *Int J Geriatr Psych.* 2021;36(9):1313-29.
111. Pascoe MC, Thompson DR, Castle DJ, Jenkins ZM, Ski CF. Psychosocial Interventions and Wellbeing in Individuals with Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Front Psychol.* 2017;8.
112. Santos EJF, Duarte C, Marques A, Cardoso D, Apóstolo J, da Silva JAP, Barbieri-Figueiredo M. Effectiveness of non-pharmacological and non-surgical interventions for rheumatoid arthritis: an umbrella review. *JBIM Database System Rev Implement Rep.* 2019;17(7).
113. Graham HL, Copello A, Griffith E, Clarke L, Walsh K, Baker AL, Birchwood M. Mental Health Hospital Admissions: a Teachable Moment and Window of Opportunity To Promote Change in Drug and Alcohol Misuse. *Intl J Ment Health Ad.* 2019;17(1):22-40.
114. Badcock J, Lim M. A Guide to Measuring Loneliness for Community Organizations2021 [cited 2024 2 June]. Available from: <https://endingloneliness.com.au/wp-content/uploads/2021/08/A-Guide-to-Measuring-Loneliness-for-Community-Organisations-Ending-Loneliness-Together.pdf>.
115. Mund M, Maes M, Drewke PM, Gutzeit A, Jaki I, Qualter P. Would the Real Loneliness Please Stand Up? The Validity of Loneliness Scores and the Reliability of Single-Item Scores. *Assessment.* 2022;30(4):1226-48.
116. Powers J YA, Russell A. ALSWH Data Dictionary Supplement. Section 2 Core Survey Dataset 2.7 Psychosocial Variables. Center for Epidemiologic Studies Depression Scale - Shortened Version. Australian Longitudinal Study on Women's Health; 2002.
117. Crosier T, Butterworth P. The Validity of the SF-36 in an Australian National Household Survey: Demonstrating the Applicability of the Household Income and Labour Dynamics in Australia (HILDA) Survey to Examination of Health Inequalities. *BMC Pub Health.* 2004;7(4):44.

118. Nicolaisen M, Thorsen K. Who are lonely? Loneliness in different age groups (18-81 years old), using two measures of loneliness. *Int J Aging Hum Dev.* 2014;78(3):229-57.
119. Peplau L, Perlman, D, Russell, Daniel. The measurement of loneliness. In: Peplau L, Perlman, D, editor. *Loneliness: A Sourcebook of Current Theory, Research and Theory*: John Wiley & Sons; 1982. p. 81-104.
120. Eccles AM, Qualter P, Madsen KR, Holstein BE. Loneliness in the lives of Danish adolescents: Associations with health and sleep. *Scand J Public Health.* 2020;48(8):877-87.
121. Shiovitz-Ezra S, Ayalon L. Use of direct versus indirect approaches to measure loneliness in later life. *Res Aging.* 2012;34(5):572-91.
122. Hawkey LC, Buecker S, Kaiser T, Luhmann M. Loneliness from young adulthood to old age: Explaining age differences in loneliness. *Int J Behav Dev.* 2020;46(1):39-49.
123. Grant C, Goodenough T, Harvey I, Hine C. A randomised controlled trial and economic evaluation of a referrals facilitator between primary care and the voluntary sector. *Bmj.* 2000;320(7232):419-23.
124. Fuhr DC, Salisbury TT, De Silva MJ, Atif N, van Ginneken N, Rahman A, Patel V. Effectiveness of peer-delivered interventions for severe mental illness and depression on clinical and psychosocial outcomes: a systematic review and meta-analysis. *Soc Psychiatry Psychiatr Epidemiol.* 2014;49(11):1691-702.
125. Francey SM, O'Donoghue B, Nelson B, Graham J, Baldwin L, Yuen HP, et al. Psychosocial intervention with or without antipsychotic medication for first-episode psychosis: a randomized noninferiority clinical trial. *Schizophrenia Bull Open.* 2020;1(1):sgaa015.
126. Mallorquí-Bagué N, Lozano-Madrid M, Vintrolá-Alcaraz C, Forcano L, Díaz-López A, Galera A, et al. Effects of a psychosocial intervention at one-year follow-up in a PREDIMED-plus sample with obesity and metabolic syndrome. *Sci Rep.* 2021;11(1):9144.
127. Li Y, Bressington D, Chien WT. Systematic review of psychosocial interventions for people with spinal cord injury during inpatient rehabilitation: Implications for evidence - based practice. *Worldv Evid - Based Nu.* 2017;14(6):499-506.

APPENDICES

Appendix 1. Additional publications

Below are additional peer-reviewed publications, beyond the scope of my thesis, in which I collaborated as a lead or co-author during my PhD candidacy.

Green MS, Peer V, Magid A, **HaGani N**, Anis E, Nitzan D. Gender Differences in Adverse Events Following the Pfizer-BioNTech COVID-19 Vaccine. *Vaccines*. 2022;10(2):233.

HaGani N, Eilon Y, Zeevi S, Vaknin L, Baruch H. The psychosocial impact of quarantine due to exposure to COVID-19 among healthcare workers in Israel. *Health Promot Int*. 2022;1-22.

HaGani N, Englard Hershler M, Ben Shlush E. The relationship between burnout, commuting crashes and drowsy driving among hospital health care workers. *Int Arch Occ Env Hea*. 2022;95(6):1357-67.

HaGani N, Sznitman S, Dor M, Bar-Sela G, Oren D, Margolis-Dorfman L, Goor-Aryeh I, Green MS. Attitudes Toward the Use of Medical Cannabis and the Perceived Efficacy, Side-effects and Risks: A Survey of Patients, Nurses and Physicians. *J Psych Drug*. 2021;12.

HaGani N, Yagil D, Cohen M. Burnout among Oncologists and Oncology Nurses: A Systematic Review and Meta-Analysis. *Health Psychol*. 2022;41(1):53.

HaGani N, Zeevi S, Smik L. Changes and Challenges in Hospital Social Workers' work during the COVID Outbreak (The First "Wave"). *Meida'Os*. 2021;96:18-27. [In Hebrew]

Manera K, **HaGani N**, Owens K, Phongsavan H, Surkalim D, Ding D, Lim M, Smith B. Systematic review of interventions to address loneliness and social isolation in people with chronic physical diseases. (In progress).

Meehan DE, Grunseit A, Condie J, **HaGani N**, Merom D. Social-ecological factors influencing loneliness and social isolation in older people: a scoping review. *BMC Geriatrics*. 2023;23(1):726.