



Leigh-Hunt N, Bagguley D, Bash K, Turner V, Turnbull S, Valtorta NK, Caan W.

An overview of systematic reviews on the public health consequences of social isolation and loneliness.

Public Health 2017, 152, 157-171.

_						
Co	ทง	/rı	σ	n	t	٠
-	ν,		ה	••	٠	•

© 2017. This manuscript version is made available under the CC-BY-NC-ND 4.0 license

DOI link to article:

https://doi.org/10.1016/j.puhe.2017.07.035

Date deposited:

11/01/2018

**Embargo release date:** 

12 September 2018



This work is licensed under a

<u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International licence</u>

#### Manuscript Draft

Manuscript Number: PUHE-D-17-00338R1

Title: An overview of systematic reviews on the public health

consequences of social isolation and loneliness

Article Type: Review Article

Keywords: social isolation; loneliness; consequences; public health;

systematic overview

Corresponding Author: Dr. nicholas leigh-hunt, MA MBBS MMedSci MPH

Corresponding Author's Institution: Doncaster Council

First Author: nicholas leigh-hunt, MA MBBS MMedSci MPH

Order of Authors: nicholas leigh-hunt, MA MBBS MMedSci MPH; David Bagguley, MBChB MPH LLM; Kristin Bash; Victoria Turner; Stephen Turnbull;

Nicole Valtorta ; Woody Caan

#### Abstract: Objectives

Social isolation and loneliness have been associated with ill health and are common in the developed world. A clear understanding of their implications for morbidity and mortality is needed to gauge the extent of the associated public health challenge and the potential benefit of intervention.

#### Study design

A systematic review of systematic reviews (systematic overview) was undertaken to determine the wider consequences of social isolation and loneliness, identify any differences between the two, determine differences from findings of non-systematic reviews, and to clarify the direction of causality.

#### Methods

Eight databases were searched from 1950 to 2016 for English language reviews covering social isolation and loneliness but not solely social support. Suitability for inclusion was determined by two or more reviewers, the methodological quality of included systematic reviews assessed using the AMSTAR checklist, and the quality of evidence within these reviews using the GRADE approach. Non-systematic reviews were sought for a comparison of findings but not included in the primary narrative synthesis.

#### Results

Forty systematic reviews of mainly observational studies were identified, largely from the developed world. Meta-analyses have identified a significant association between social isolation and loneliness with increased all-cause mortality, and social isolation with cardiovascular disease. Narrative systematic reviews suggest associations with poorer mental health outcomes, with less strong evidence for behavioural and

other physical health outcomes. No reviews were identified for wider socio-economic or developmental outcomes.

#### Conclusions

This overview highlights that social isolation and loneliness have a considerable impact on morbidity and mortality through cardiovascular and mental health. The role of social isolation and loneliness in other conditions and their socio-economic consequences is less clear. More research is needed on associations with cancer, health behaviours, the impact across the life course and wider socio-economic consequences. Policy makers and health and local government commissioners should consider social isolation and loneliness as important upstream factors impacting on morbidity and mortality due to their effects on cardiovascular and mental health. Prevention strategies should therefore be developed across the public and voluntary sectors, using an assetbased approach.

Leeds Institute of Health Sciences, Charles Thackrah Building, University of Leeds, Leeds LS2 9LJ

n.leigh-hunt@leeds.ac.uk

5<sup>th</sup> April 2017

Phil Mackie and Fiona Sim Editors – Public Health c/o Public Health Editorial Office, Royal Society for Public Health, John Snow House, 59 Mansell Street, London, E1 8AN

Dear Phil and Fiona,

On behalf of my colleagues, I would like to submit to Public Health this manuscript of original research entitled "An overview of systematic reviews on the public health consequences of social isolation and loneliness".

This paper was commissioned by your journal, and the work undertaken by a group of public health registrars in the Yorkshire and Humber deanery following a discussion with Andrew Lee, with expert advice in the drafting and analysis from those working in the field.

Our research has systematically brought together key literature, and highlighted the strength of the evidence for social isolation and loneliness having an impact on cardiovascular and mental health. It has also identified important gaps in the evidence base on their role in other conditions and their wider socio-economic consequences.

The review has a word count of 3296, which is just under 10 percent more than officially allowed, and contains 106 references. We feel this is necessary to maintain the integrity of the paper, but are prepared to reduce this further if you feel it would be desirable.

We welcome your review of this manuscript and the constructive feedback we hope to receive. We confirm that this paper has not been published elsewhere.

Yours sincerely, Nicholas Leigh-Hunt Honorary lecturer and Specialty Registrar in Public Health

#### **Response to Reviewers' Comments**

#### Reviewer #1:

This paper provides an overview of systematic reviews on the public health consequences of social isolation and loneliness. The authors summarize previous reviews. The claim that social isolation and loneliness have a considerable impact on morbidity and mortality through cardiovascular and mental health is perhaps overstated and only indirectly inferred from the summary of previous reviews, not direct mediation tests.

The first line in the conclusions in the abstract has been rephrased as: "This systematic overview highlights that there is consistent evidence linking social isolation and loneliness to worse cardiovascular and mental health outcomes." The first sentence in the highlights has also been changed to reflect this.

The introduction talks about how social isolation and loneliness are related to poorer health behaviours through psychological relief mechanisms, however, these associations are made from information derived from social networks.

The first sentence discussing psychological relief mechanisms contains two references, one of which discusses loneliness and health behaviours (Lauder et al), the other discusses social isolation and health behaviours (Cacioppo and Hawkley 2003), with a validated measurement scale being used in both. The following sentence regarding networks supporting unhealthy behaviours has a reference that uses information derived from social networks (Christakis & Fowler 2013). When writing this paper we included social networks and relationships based on our understanding of constructs (e.g. Cornwell & Waite, 2009, Social Disconnectedness, Perceived Isolation, and Health among Older Adults, Journal of Health and Social Behaviour, 50, 31–48).

The discussion could be stronger, as it is currently primarily a restatement of the abstract and results.

The discussion contains material not included in either the abstract or results, in particular a summary of findings from the non-systematic reviews we identified in the search process but did not include in the primary syntheses in the results, and is only briefly alluded to in the abstract; one of the stated aims of this paper was to bring together findings from systematic reviews in a systematic process and highlight differences (if any) with the body of non-systematic reviews for the benefit of policy makers, etc. Section headings have also now been added to make the content that does not appear in the results more apparent, e.g limitations, implications for policy and research.

#### Reviewer #2:

This paper is a review of systematic reviews, and arguably feels more like a list of results rather than any kind of integration or synthesis of results. While it is useful to have them all in one place, little more is offered other than what is already known. I don't feel like I came away from reading this knowing anything new or understanding the data in a new way. The reviews and meta-analyses contained in this synthesize it in a way that, for example, provide the magnitude of the size of the effect across studies, identify moderating factors, etc. Other than a summary table, further explanation is needed of what this adds to the current literature.

In writing this paper our aim was to provide a clear summary of the evidence on the wider consequences of social isolation and loneliness based on systematic principles for those who are not experts in the field, e.g policy makers and commissioners. The included systematic reviews cover specific topic areas, whereas our paper provides a summary across topics for non-experts. As there is now a growing body of literature, we also sought to highlight differences (if any) with the body of non-systematic reviews for those unfamiliar with the subject area, and this paper clarifies these. We have not attempted to undertake further statistical analysis due to the diverse nature of the reviews identified, and we feel we have provided a narrative synthesis that covers physical and mental health, health behaviours and mortality. We had hoped to find evidence of wider impacts, including non-health ones, e.g. effect on employment, which would be of interest to a wider audience, but did not identify any despite a wide search process.

I also would have liked to have seen a more thoughtful discussion of the state of the literature and where there are gaps that need to be addressed.

Sub-headings have now been added to the discussion with gaps that need to be addressed covered in the implications for research. A longer discussion of the state of the literature would be interesting but given the word limits to the paper we have covered this succinctly: a summary of potential causal mechanisms is in the introduction to explain how social isolation and loneliness might lead to outcomes for the benefit of a non-expert audience. Non-systematic reviews in the subject area are covered in the discussion; as this is an overview paper we did not feel it appropriate to discuss single studies at length.

The GRADE approach is meant to guide recommendations, however, no recommendations are made.

The GRADE approach was used in accordance with Cochrane guidance for systematic overviews to assess the quality of the evidence within the included reviews (Cochrane handbook 5.1, Part 3, 22.3.4 Text of a Cochrane Overview, Quality of evidence in included reviews); this was done in addition to an assessment of the methodology of the reviews using the AMSTAR tool.

Please cite Perissinotto 2012. This paper, that includes data from the Health and Retirement Study, estimates the prevalence of loneliness as 43%, thus the statement at the top of page 3 should be updated to reflect this.

Paper by Perissinotto 2012 referenced and statement updated.

The 2010 Holt-Lunstad meta-analyses included 148 prospective (longitudinal) studies, please correct this.

Second sentence in Mortality and General Health section amended

It appears that Suicide might be included both in the Mortality section and the Mental Health section. Perhaps clarify that successful attempt were included in the mortality section and unsuccessful attempts in the mental-health section—assuming that is correct.

The four reviews in the Mortality section considered all-cause mortality; two of them (Holt-Lunstad 2010, 2015) excluded suicide and the sentences discussing the findings from them have been updated to explicitly state this. The reviews discussed in the second paragraph of the Mental Health section consider suicide, completed and attempted and first sentence of the paragraph has been update to explicitly state this; the sentences discussing the findings from these reviews explicitly state whether ideation, behaviour, attempted or completed is being referred to.

On p 12 please clarify what is meant by developmental and educational outcomes.

The sentence has been reworded to "Even though evidence was identified across the life course, this overview did not find any systematic reviews considering an association between social isolation and loneliness with physical and psychological developmental outcomes or educational achievement in children."

P 12 it is confusing why childhood abuse is being discussed when that was not a variable that was specifically searched or evaluated here

Childhood abuse is mentioned here as associations between social isolation and loneliness with child abuse <u>as a perpetrator</u> were found (third paragraph section 2 of results); no association with abuse in childhood <u>as a victim</u> was identified in the systematic reviews but mixed evidence was discussed in a number of non-systematic reviews identified during the search process. This is an example of differences between non-systematic reviews and systematic reviews our paper sought to highlight for non-experts. It is also mentioned here as it follows on from the previous sentence regarding other childhood associations.

P 13 said that no age analyses were included in the reviews. Yet, the 2010 Holt-Lunstad meta-analysis reports no age effect, and the 2015 Holt-Lunstad meta-analysis reports the effect was significantly stronger for those under 65 compared to those older than 65.

This sentence has been revised "The effect of age was not analysed in the majority of the included reviews, with the exception of two meta-analyses. One of these (Holt Lunstad 2010) reported no age effect while the other (Holt Lunstad 2016) found a stronger effect for individuals aged less than 65 years; therefore this overview cannot provide firm conclusions with regards to impact of age on any associations."

In the conclusion, please clarify what is meant by an "asset-approach." Also provide a citation for this recommendation.

The last sentence has been altered to "Taking an asset-based approach, the existing resources in communities and the skills of individuals within them to maintain and sustain health should be utilised to develop prevention strategies and promote resilience across the public and voluntary sectors" and referenced accordingly.

#### Tables and Figures

It is unclear what criteria were used to create the strength of evidence by topic displayed in Table 4. No key is provided to indicate, or define, what each + stands for.

This table has been revised with a key to indicate what + and ++ stands for, with the reviews for each topic listed so comparison with the AMSTAR and GRADE scores can be made. The paragraph in section 5 has been amended to make this more explicit. We had considered merging Tables 3 and 4 to make it more explicit but this would be less easy to read.

Please reconfigure figure 1, the text contained in figure 1 is cut off in places.

Text boxes have now been amended in figure 1

Figure 1 appears to be misleading—or at least very confusing. This indicates a search of individual studies, but this paper is reviewing reviews and meta-analyses. It would be more informative to display what was included and excluded from this review—as no meta-analysis was conducted here.

Wording has been changed to reviews and articles to avoid any confusion as there was no search for individual studies. The current diagram is based on PRISMA guidance and we think provides a concise means of what was included and excluded as a full list would be very long. The non-systematic reviews identified in the search are referenced in the discussion.

The second bullet point in the highlights should specify what "this" refers to.

The first two bullet points have been merged into one "There is consistent evidence linking social isolation and loneliness to worse cardiovascular and mental health outcomes"

## Title Page

## **Title**

An overview of systematic reviews on the public health consequences of social isolation and loneliness

## **Author Names and Affiliations**

Nicholas Leigh-Hunt<sup>1,2</sup> (NLH), Public Health Specialty Registrar & Honorary Lecturer, n.leigh-hunt@leeds.ac.uk

David Bagguley<sup>2</sup> (DB), Public Health Specialty Registrar, d.bagguley@nhs.net Kristin Bash<sup>2</sup> (KB), Public Health Specialty Registrar, kristin.bash@nhs.net Victoria Turner<sup>2</sup> (VT), Public Health Specialty Registrar, victoria.turner15@nhs.net Stephen Turnbull<sup>2</sup> (ST), Public Health Specialty Registrar, stephenturnbull1@nhs.net Nicole Valtorta<sup>3</sup> (NV), Research Assistant, nicole.valtorta@ncl.ac.uk Woody Caan<sup>4</sup> (WC), Professorial Fellow, Royal Society for Public Health, wcaan@rsph.org.uk

- 1. Centre for Primary Care and Public Health, Leeds Institute for Health Sciences, Leeds University, 101 Clarendon Road, Leeds, LS2 9JT, United Kingdom.
- 2. Health Education England Yorkshire and Humber, Willow Terrace Road, University of Leeds, Leeds, LS2 9JT, United Kingdom.
- 3. Institute of Health Society/Newcastle University Institute for Ageing, Biomedical Research Building, Campus for Ageing and Vitality, Newcastle University, Newcastle upon Tyne, NE4 5PL, United Kingdom.
- 4. 47 Hurdles Way, Duxford, Cambridgeshire, CB22 4PA, United Kingdom.

## **Corresponding Author**

Nicholas Leigh-Hunt

#### <u>Abstract</u>

## **Objectives**

Social isolation and loneliness have been associated with ill health and are common in the developed world. A clear understanding of their implications for morbidity and mortality is needed to gauge the extent of the associated public health challenge and the potential benefit of intervention.

## Study design

A systematic review of systematic reviews (systematic overview) was undertaken to determine the wider consequences of social isolation and loneliness, identify any differences between the two, determine differences from findings of non-systematic reviews, and to clarify the direction of causality.

#### **Methods**

Eight databases were searched from 1950 to 2016 for English language reviews covering social isolation and loneliness but not solely social support. Suitability for inclusion was determined by two or more reviewers, the methodological quality of included systematic reviews assessed using the AMSTAR checklist, and the quality of evidence within these reviews using the GRADE approach. Non-systematic reviews were sought for a comparison of findings but not included in the primary narrative synthesis.

## Results

Forty systematic reviews of mainly observational studies were identified, largely from the developed world. Meta-analyses have identified a significant association between social isolation and loneliness with increased all-cause mortality, and social isolation with cardiovascular disease. Narrative systematic reviews suggest associations with poorer mental health outcomes, with less strong evidence for behavioural and other physical health outcomes. No reviews were identified for wider socio-economic or developmental outcomes.

#### **Conclusions**

This systematic overview highlights that there is consistent evidence linking social isolation and loneliness to worse cardiovascular and mental health outcomes. The role of social isolation and loneliness in other conditions and their socio-economic consequences is less clear. More research is needed on associations with cancer, health behaviours, and the impact across the life course and wider socio-economic consequences. Policy makers and health and local government commissioners

should consider social isolation and loneliness as important upstream factors impacting on morbidity and mortality due to their effects on cardiovascular and mental health. Prevention strategies should therefore be developed across the public and voluntary sectors, using an asset-based approach.

# **Keywords**

Social isolation

Loneliness

Consequences

Public health

Systematic overview

#### Introduction

Alone and feeling sick: do isolation and loneliness carry specific risks to health? In populations throughout the world, social isolation (defined as an objective lack of interactions with others or the wider community) and loneliness (defined as the subjective feeling of the absence of a social network or a companion) are common. Surveys in Europe and the USA estimate the prevalence of loneliness ranges from 5% to 43% in the elderly <sup>1-4</sup>, with similar figures for China <sup>5</sup>. While loneliness may be more common in the elderly, it also affects younger age groups <sup>6</sup>. Precise estimates for the prevalence of loneliness and social isolation are difficult to obtain due to: variation across the life course; cultural and gender differences with respect to how prepared individuals are to talk about them from a personal perspective; and the use of many different measurement scales, some of which are based on self-report questionnaires while others involve more objective assessment of social contact or networks (or a combination of both).

Loneliness and social isolation have both been associated with ill health, but determining causality is difficult as much of the research in this area involves observational studies. Researchers have primarily focused on the association with mortality, mental and cardiovascular health. Biological pathways have been suggested as an explanation for the effect of loneliness and social isolation on health including reduced levels of protective hormones leading to adverse effects on heart rate, blood pressure and the repair of blood vessel walls; downregulation of the immune system; and neuro-endocrine dysregulation from a paucity or poor quality of sleep 7-10. Lonely individuals may be more likely to initiate harmful health behaviours such as smoking, excess alcohol consumption, overeating or transient sexual encounters as a psychological relief mechanism. They may then go on to maintain these harmful behaviours if they are less exposed to healthy behavioural norms or have less access to health advice as a result of fewer social contacts 7, 11. While social networks of friends and family can support healthy behaviours, they may also allow unhealthy behaviours to become normative <sup>12</sup>. Stress responses as a result of perceived social isolation can adversely precondition the neuroendocrine system, with genetic differences determining the degree to which this might occur <sup>13</sup>. Socially isolated individuals may suffer more stress than others due to their lack of social networks and support, and when they do they might be more likely to withdraw into themselves <sup>7</sup>.

Although the exact causal pathways remain unclear, given the prevalence of social isolation and loneliness it is important to have a clear understanding of their consequences to the individual and society. The evidence base on the impact of social isolation and loneliness

has expanded over recent decades and now includes many reviews with different health foci. To provide decision-makers with the evidence they need to assess and tackle the public health challenge associated with weaker social relationships, we conducted a review of reviews on the health implications of loneliness and social isolation. Our aims were to: provide a clear summary of the evidence on the wider consequences of social isolation and loneliness based on systematic principles; identify any differences from findings of the many non-systematic reviews that have been published; clarify the direction of causality; and determine whether there are clear differences in consequences observed for the perceived state of loneliness versus the objective state of social isolation.

#### Methods

Methodology for this overview followed recognised guidance for conducting systematic overviews <sup>14, 15</sup>. The following databases were searched from 1950 to March 2016: Web of Knowledge; SCOPUS; EMBASE; ASSIA; Medline; PsycINFO; Campbell Collaboration; Database of Abstracts of Reviews of Effects, using the following terms: social environment; social isolation; social vulnerability; social engagement; loneliness; psychosocial support.

Systematic reviews (including narrative reviews and meta-analyses) written in English were included. Well researched (as judged by two reviewers) non-systematic reviews were also included for a comparison of findings but not as part of the primary synthesis. Reviews of interest were those that contained studies of individuals from any population of any age or gender, where any health or socio-economic outcome as a result of social isolation or loneliness was studied. For the purpose of this overview the term social isolation was defined as the objective state of lack of social contact with others while loneliness was defined as the subjective feeling of being unhappy with one's relationships. Reviews focusing on social support were excluded, although those that did not set out to study loneliness or social isolation explicitly but did in fact consider the concepts as defined above were included. References in included reviews were inspected to identify any other potential reviews.

Reviews were selected from the search process according to whether they met the criteria as described above. The process was confirmed by a second reviewer to ensure validity of inclusion. Differences of opinion were discussed and consensus reached over inclusion or exclusion of the study. The methodological quality of the reviews selected for inclusion was also assessed by two reviewers for each review, using the AMSTAR checklist <sup>16</sup> and the quality of the evidence in these reviews was assessed using the GRADE approach <sup>17</sup>.

Data were extracted from the selected reviews using a pre-designed data extraction sheet to standardise reporting of results across the included reviews. Extracted data were: review characteristics, including both the design of the review and design of included studies, geographical location of included studies, duration of longitudinal studies; participant characteristics including age range, gender, co-morbidities; measurement scales used for social isolation and loneliness; health and social outcomes and their associated measures; and summary findings.

#### Results

The search process of eight databases identified 90 papers (40 systematic reviews, 47 non-systematic reviews and 3 metasyntheses) that considered social isolation, loneliness, social relationships or networks (Figure 1). Of the forty systematic reviews included in this overview, ten involved a meta-analysis. Eight reviews were undertaken in two or more countries, while the rest were carried out by teams from single countries, all from the developed world except one. All were published between 2000 and 2015, with eighteen of them declaring their sources of funding, which included government funding, charitable funding, universities and other private institutions. Age range was not identified in twelve of the systematic reviews, seven of them considered only individuals over 65 years of age, five exclusively studied adolescents while sixteen considered individuals of any age. Two systematic reviews looked exclusively at one gender; sixteen looked at both genders while twenty-two did not identify gender proportions. Most reviews contained studies that contained between ten and 100,000 participants. In half of the reviews loneliness or social isolation were identified as a factor associated with the variable of interest but a validated scale was not used (Table 1).

Sixty-two different self-report questionnaires were used to measure loneliness, social isolation and related concepts (Table 2). For forty-nine measures, information could be sourced which allowed mapping using a two-dimensional framework <sup>18</sup> (Figure 2). This diagram illustrates the diversity of tools both in terms of their content and how their items are phrased. A majority of instruments were concerned more with the function of relationships (e.g. whether people might have access to a confident or help if they need it) than with their structural characteristics (e.g. the frequency with which people interact).

When assessed using the AMSTAR checklist, seventeen of the systematic reviews were of moderate quality (score 5-7) and thirteen of low quality (score 0-4). Those reviews which scored poorly using AMSTAR also tended to have low GRADE scores. Seven of the meta-analyses were of moderate or high quality (score 8-10); the majority were also assessed as containing evidence of moderate GRADE quality (Table 3). Generally, the meta-analyses were of superior methodological quality to the systematic reviews. Nevertheless, whilst these scores suggest the findings of these reviews can be accepted with some degree of confidence, significant clinical heterogeneity existed between both the reviews and the primary studies they contained.

Insert Figure 1 Here

Insert Table 1 Here

Insert Table 2 Here

Insert Figure 2 Here

Insert Table 3 Here

#### Synthesis of evidence

# 1. Mortality & General Health

Two meta-analyses of cohort studies identified a significant association between social isolation, loneliness and social network size with all-cause mortality, identifying odds ratios of increased likelihood of mortality for social isolation (excluding suicide) of 1.29 (95 % CI 1.06, 1.56), for loneliness 1.26 (95 % CI 1.04, 1.53) and living alone 1.32 (95 % CI 1.14, 1.53) <sup>19</sup>; and hazard ratios for all-cause mortality for greater social participation of 0.87 (95 % CI 0.82, 0.91) and for better social networks of 0.91 (95 % CI 0.86, 0.97) <sup>20</sup>. This is comparable to findings from a prospective study which identified an odds ratio of increased likelihood of survival of 1.50 (95% CI 1.42 to 1.59) for stronger social relationships (excluding suicide) <sup>21</sup>, and a hazard ratio for mortality of 1.13 (95% CI 1.09, 1.17) for lower social contact frequency from a meta-analysis of mixed studies <sup>22</sup>. The similar odds ratios for loneliness and social isolation <sup>19</sup> suggest no difference between subjective or objective measures of social isolation. The impact of gender on the association was unclear as there were mixed findings from subgroup analyses in the above reviews.

An association between loneliness and fewer social relationships with poor health and wellbeing was suggested in three systematic reviews of worldwide studies using different methodologies and assessment measures in individuals aged over 50-55 years. The relative importance of the quality versus the quantity of such social relationships with respect to this association may vary depending on whether they are between family or friends <sup>23-25</sup>. In older adults attending emergency departments, social isolation and living alone were found to be associated with hospital admission in a systematic review of 14 studies <sup>26</sup>.

#### 2. Health Behaviours

Loneliness and social isolation were found to be associated with increased tobacco use in three systematic reviews; in one of these reviews a positive association between loneliness and tobacco use was reported in half of the included studies, whereas the other half reported no association or a negative association <sup>27</sup>. A review of observational studies of tobacco use in Brazilian adolescents reported one study demonstrating an association between loneliness and increased tobacco use in adolescents <sup>28</sup>. Consistent evidence that more socially isolated adolescents were more likely to use tobacco was found in a review of ten studies, though causality could not be proven and other variables may have confounded the relationship <sup>29</sup>.

A systematic review of observational studies reported mixed findings regarding an association between behaviour change and social isolation in the context of cardiovascular disease<sup>30</sup>. Only two systematic reviews were identified that looked at social isolation and physical activity; these reported an association between social isolation and low levels of physical activity in two well-defined patient groups (individuals with bipolar disorder and schizophrenia) but noted that only a minority of the included studies assessed this relationship <sup>31, 32</sup>. Only one systematic review of observational studies was identified which looked at diet; this found strong evidence of no association between social isolation and loneliness and malnutrition in older people living in community dwellings <sup>33</sup>.

Two systematic reviews relating to sexual health behaviours were identified, one of which found that social isolation was associated with HIV infection as a contextual risk factor in transsexuals, possibly mediated through feelings of discomfort or being unsafe in public <sup>34</sup>. Loneliness of parents and social isolation of adolescent sex offenders have been associated with child abuse in another systematic review and a meta-analysis <sup>35, 36</sup>

Two systematic reviews made comments on the relationship between adherence to treatments and social isolation; one suggested that social isolation may lead to reduced interaction and increased use of online sources of advice, potentially leading to sub-optimal adherence to treatments <sup>37</sup>; another found increased social isolation was associated with non-adherence to treatment in adult renal transplant patients <sup>38</sup>.

#### 3. Physical Health

The evidence base was strongest for the relationship between social isolation, loneliness and cardiovascular disease, with reviews that considered hypertension, cardiovascular risk, and post-myocardial infarction mortality (PMIM). One meta-analysis of prospective cohort studies identified an increased cardiovascular relative risk of 1.5 (95 % CI 1.2, 1.9) in adults with high levels of social isolation <sup>39</sup>. This is supported by findings of a systematic overview which found strong and consistent evidence for an independent causal association between levels of social isolation and the risk of CVD <sup>40</sup>. Two other systematic reviews suggested that adults with social isolation have an increased likelihood of PMIM, with individuals with stronger social relationships having a 50% increased likelihood of survival, with no variation between gender <sup>41</sup> and those with the highest levels of social isolation having two to three

times the risk of PMIM <sup>42</sup>. The evidence for an association between social isolation with hypertension is more mixed <sup>43</sup>.

The evidence base for an association with other physical health conditions was less strong with reviews identified for cancer, low back pain and chronic obstructive pulmonary disease (COPD). One systematic review focusing on the risk of mortality in cancer patients found that those with the largest network size had a reduced relative risk of mortality of 0.80 (95% CI, 0.72-0.89)<sup>44</sup>. Another systematic review of cohort studies looking at the duration of sick leave for individuals with low back pain found social isolation to be associated with longer sick leave <sup>45</sup>, while two studies in another systematic review found a positive association between social network size and COPD <sup>46</sup>.

## 4. Mental Health

For mental health there was a moderately strong evidence base, with reviews identified for well-being, depression, suicide and dementia. One meta-analysis found an association between subjective mental wellbeing and social relationships, with the quality of relationships more important than the quantity of them <sup>25</sup>. Two other systematic reviews suggested an association between social networks and depression, with large and diverse social networks with high quality relationships protecting against depression <sup>47, 48</sup>. These findings were also true in relation to post-stroke depression, with diverse social networks of friends and family associated with a reduction in reported depression <sup>49</sup>. In keeping with this, a systematic review of immigrant women in the perinatal period in Japan identified an association between social isolation and negative mental health outcomes after childbirth such as anxiety, stress and regret <sup>50</sup>. A meta-analysis identified an association between social anxiety disorder, though causality was unclear <sup>51</sup>.

Five systematic reviews covering suicide (ideation, behaviour, attempted and completed) were identified. One review found that a low sense of belonging was associated with a higher risk of suicidal ideation and suicide attempts, and another that found levels of social integration affected non-fatal suicidal behaviour amongst the elderly population <sup>52, 53</sup>. In specific population groups, social isolation was associated with suicidal ideation amongst individuals with multiple sclerosis <sup>54</sup> and nursing and care home residents <sup>55</sup>, while mixed outcomes were seen amongst those with learning disabilities <sup>56</sup>.

Two systematic reviews identified that loneliness and low social participation were associated with an increased risk of dementia, with two included longitudinal studies

showing an association between loneliness and the incidence of Alzheimer's disease and dementia  $^{57,\,58}$ .

# 5. Summary of evidence

Combining these findings alongside the hierarchy of evidence, taking into account the number, quality of the reviews (from the AMSTAR scores) and the evidence contained within them (from the GRADE scores) shows that there is strong evidence that both social isolation and loneliness are associated with increased all-cause mortality, and social isolation with cardiovascular disease and depression (Table 4).

Insert Table 4 Here

#### **Discussion**

## Main findings

This overview has identified that there is strong evidence that both social isolation and loneliness are associated with increased all-cause mortality. While proof of causality cannot be confirmed, this may be mediated through the cardiovascular system and mental health. Only limited evidence was identified for an association with other physical health conditions, including cancer, and evidence for the effects of social isolation and loneliness being mediated through behaviours is less strong. The pattern of health risk appears similar for both the subjective state of loneliness and the objective state of social isolation, but the most consistent significant effects were reported in relation to measures of isolation.

Even though evidence was identified across the life course, this overview did not find any systematic reviews considering an association between social isolation and loneliness with physical and psychological developmental outcomes or educational achievement in children. Whilst abuse in both childhood and adulthood is associated with some of the outcomes identified, such as depression and suicide, this review could not demonstrate the role of social isolation in a causal pathway between them, such as, for example, previous abuse causing withdrawal from social networks and subsequent depression.

#### What is already known

Non-systematic reviews have identified similar findings with respect to increased risk of mortality <sup>59-64</sup>, cardiovascular disease and outcomes <sup>62, 65-72</sup>, mental health <sup>61, 62, 64, 73-90</sup>, with less evidence for other physical health conditions and behaviours <sup>72, 76, 80, 91-93</sup>. There is no clear evidence from non-systematic reviews as to whether parental social isolation or loneliness is associated with child abuse or adverse parenting behaviours <sup>94-98</sup>, though social isolation and loneliness of children may be associated with abuse or poorer developmental and educational outcomes <sup>65, 87, 97, 99-101</sup>.

While no systematic reviews were identified in this overview that looked at causal physiological mechanisms by which social isolation and loneliness may influence health, a number of non-systematic reviews have identified associations with changes to brain structure and processes, sympathetic neural tone, vascular stress responses, altered sleep and reduced sleep quality, cortisol secretion patterns, impaired cellular and humoral immunity, and reduced inflammatory responses <sup>61, 80, 96, 102-106</sup>.

#### Limitations

Most of the research in this overview came from developed countries and only English language publications were considered, so this may limit applicability of findings elsewhere. No reviews considered health economic considerations, so this review is not able to give insight into wider socio-economic consequences of social isolation and loneliness. The effect of age was not analysed in the majority of the included reviews, with the exception of two meta-analyses; one of which <sup>21</sup> reported no age effect while the other <sup>19</sup> found a stronger effect for individuals aged less than 65 years. Therefore this overview cannot provide firm conclusions with regards to the impact of age on any associations.

Similarly this review cannot infer any associations with ethnicity, as it was infrequently recorded in the included reviews. Most of the systematic reviews were of moderate quality but none were of high quality, which most likely is a reflection of them containing predominantly observational studies; very few of the reviews contained longitudinal studies so causality cannot be inferred from the associations identified. As all of the tools used in the reviews were self-report measures which depend on the degree of subjectivity from respondents, findings should also be considered with caution.

#### Implications for research

As this overview identified only limited evidence for an association with physical health conditions other than cardiovascular disease; more research is needed on the association with other conditions, using longitudinal studies or designs that could provide more information on causality. Further research is also needed on the association with health behaviours, the impact across the life course and wider socio-economic consequences. It may also be helpful to undertake systematic reviews on the impact of parental or child social isolation and loneliness on child abuse and developmental outcomes.

# Implications for practice

In the meantime policy makers and health and local government commissioners should consider social isolation and loneliness as important upstream factors impacting on morbidity and mortality due to their effects on cardiovascular and mental health; their possible influence on behavioural change should also be taken note of. Taking an asset-based approach<sup>107</sup>, resources and skills in communities and individuals that maintain and sustain health should be utilised to promote resilience and develop prevention strategies across the public and voluntary sectors.

## **Additional Information**

NLH, DB, KB, ST, and VT undertook the overview, NV provided input into the analysis of measures using the framework, WC provided guidance on the overall analysis. All authors contributed to the drafting, reviewing of the article, and have approved the final paper.

## <u>Acknowledgements</u>

Acknowledgements are due to Judy Wright and Natalie King who provided support on the search process.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Competing interests: All authors state that they have no competing interests

Ethical approval: Ethical approval was not required for this secondary research

#### References

- 1. Office of National Statistics. Measuring national well being, older people and loneliness. 2013.
- 2. Dykstra P. Older adult loneliness: myths and realities. Eur J Ageing. 2009; 6:91-100.
- 3. Sörensen S, Pinquart M. Vulnerability and Access to Resources as Predictors of Preparation for Future Care Needs in the Elderly. Journal of Aging and Health. 2000; 12:275-300.
- 4. Perissinotto CM, Stijacic Cenzer I, Covinsky KE. Loneliness in older persons: A predictor of functional decline and death. Archives of Internal Medicine. 2012; 172:1078-84.
- 5. Yang K, Victor CR. The prevalence of and risk factors for loneliness among older people in China. Ageing & Society. 2008; 28:305-27.
- 6. Griffin J. The Lonely Society. 2010.
- 7. Cacioppo JT, Hawkley LC. Social Isolation and Health, with an Emphasis on Underlying Mechanisms. Perspectives in Biology and Medicine,. 2003; 46:S39-52.
- 8. Uchino BN, Cacioppo JT, Kiecolt-Glaser JK. The relationship between social support and physiological processes: A review with emphasis on underlying mechanisms and implications for health. Psychological Bulletin. 1996; 119:488-531.
- 9. Heffner KL, Waring ME, Roberts MB, Eaton CB, Gramling R. Social isolation, C-reactive protein, and coronary heart disease mortality among community-dwelling adults. Social Science & Medicine. 2011; 72:1482-8.
- 10. Cacioppo JT, Hawkley LC, Berntson GG, Ernst JM, Gibbs AC, Stickgold R, et al. Do Lonely Days Invade the Nights? Potential Social Modulation of Sleep Efficiency. Psychological Science. 2002; 13:384-7.
- 11. Lauder W, Mummery K, Jones M, Caperchione C. A comparison of health behaviours in lonely and non-lonely populations. Psychology, Health & Medicine. 2006; 11:233-45.
- 12. Christakis NA, Fowler JH. Social contagion theory: examining dynamic social networks and human behavior. Statistics in Medicine. 2013; 32:556-77.
- 13. Immordino-Yang MH, McColl A, Damasio H, Damasio A. Neural correlates of admiration and compassion. Proceedings of the National Academy of Sciences. 2009; 106:8021-6.
- 14. Becker LA, Oxman AD. Cochrane Handbook for Systematic Reviews of Interventions. Chapter 22: Overviews of reviews. 2011.
- 15. Smith V, Devane D, Begley CM, Clarke M. Methodology in conducting a systematic review of systematic reviews of healthcare interventions. BMC Medical Research Methodology. 2011; 11:15.

- 16. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology. 2007; 7:10.
- 17. GRADE working group. GRADE guidelines best practices using the GRADE framework. 2011.
- 18. 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.
- 19. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and Social Isolation as Risk Factors for Mortality: A Meta-Analytic Review. Perspectives on Psychological Science. 2015; 10:227-37.
- 20. Nyqvist F, Pape B, Pellfolk T, Forsman AK, Wahlbeck K. Structural and Cognitive Aspects of Social Capital and All-Cause Mortality: A Meta-Analysis of Cohort Studies. Social Indicators Research. 2014; 116:545-66.
- 21. Holt-Lunstad J, Smith TB, Layton JB. Social Relationships and Mortality Risk: A Meta-analytic Review PLoS Medicine. 2010; 7:e1000316.
- 22. Shor E, Roelfs DJ. Social contact frequency and all-cause mortality: a meta-analysis and meta-regression. Social science & medicine. 2015; 128:76-86.
- 23. Annear M, Keeling S, Wilkinson T, Cushman G, Gidlow B, Hopkins H. Environmental influences on healthy and active ageing: A systematic review. Ageing & Society. 2014:590-622.
- 24. Chen Y, Hicks A, While AE. Loneliness and social support of older people in China: a systematic literature review. Health & Social Care in the Community. 2014; 22:113-23.
- 25. Pinquart M, Sörensen S. Influences of socioeconomic status, social network, and competence on subjective well-being in later life: A meta-analysis. Psychology and Aging. 2000; 15:187-224.
- 26. Aminzadeh F, Dalziel WB. Older adults in the emergency department: a systematic review of patterns of use, adverse outcomes, and effectiveness of interventions. Annals of emergency medicine. 2002; 39:238-47.
- 27. Dyal SR, Valente TW. A Systematic Review of Loneliness and Smoking: Small Effects, Big Implications. Substance Use & Misuse. 2015; 50:1697.
- 28. Barbosa Filho VC, de Campos W, Lopes AdS. Prevalence of alcohol and tobacco use among Brazilian adolescents: a systematic review. Revista De Saude Publica. 2012; 46:901-17.
- 29. Seo D-C, Huang Y. Systematic Review of Social Network Analysis in Adolescent Cigarette Smoking Behavior. Journal of School Health. 2012; 82:21-7.

- 30. Murray J, Craigs CL, Hill KM, Honey S, House A. A systematic review of patient reported factors associated with uptake and completion of cardiovascular lifestyle behaviour change. BMC Cardiovascular Disorders. 2012; 12:120-32.
- 31. Vancampfort D, Knapen J, Probst M, Scheewe T, Remans S, De Hert M. A systematic review of correlates of physical activity in patients with schizophrenia. Acta Psychiatrica Scandinavica. 2012; 125:352-62.
- 32. Vancampfort D, Correll CU, Probst M, Sienaert P, Wyckaert S, De Herdt A, et al. A review of physical activity correlates in patients with bipolar disorder. Journal of Affective Disorders. 2013; 145:285-91.
- 33. van der Pols-Vijlbrief R, Wijnhoven HAH, Schaap LA, Terwee CB, Visser M. Determinants of protein-energy malnutrition in community-dwelling older adults: a systematic review of observational studies. Ageing research reviews. 2014; 18:112-31.
- 34. Herbst JH, Jacobs ED, Finlayson TJ, McKleroy VS, Neumann MS, Crepaz N. Estimating HIV prevalence and risk behaviors of transgender persons in the united states: A systematic review. Aids and Behavior. 2008; 12:1-17.
- 35. Black DA, Heyman RE, Slep AMS. Risk factors for child physical abuse. Aggression and Violent Behavior. 2001; 6:121-88.
- 36. Seto MC, Lalumiere ML. What Is So Special About Male Adolescent Sexual Offending? A Review and Test of Explanations Through Meta-Analysis. Psychological Bulletin. 2010; 136:526-75.
- 37. De Freitas J, Falls BA, Haque OS, Bursztajn HJ. Vulnerabilities to misinformation in online pharmaceutical marketing. Journal of the Royal Society of Medicine. 2013; 106:184-9.
- 38. Denhaerynck K, Dobbels F, Cleemput I, Desmyttere A, Schafer-Keller P, Schaub S, et al. Prevalence, consequences, and determinants of nonadherence in adult renal transplant patients: a literature review. Transplant International. 2005; 18:1121-33.
- 39. Steptoe A, Kivimaeki M. Stress and Cardiovascular Disease: An Update on Current Knowledge. Annual Review of Public Health. 2013; 34:337-54.
- 40. Bunker SJ, Colquhoun DM, Esler MD, Hickie IB, Hunt D, Jelinek VM, et al. "Stress" and coronary heart disease: psychosocial risk factors National Heart Foundation of Australia position statement update. Medical Journal of Australia. 2003; 178:272-6.
- 41. Glozier N, Tofler GH, Colquhoun DM, Bunker SJ, Clarke DM, Hare DL, et al. Psychosocial risk factors for coronary heart disease. Medical Journal of Australia. 2013; 199:179-80.
- 42. Mookadam F, Arthur HM. Social support and its relationship to morbidity and mortality after acute myocardial infarction Systematic overview. Archives of Internal Medicine. 2004; 164:1514-8.

- 43. Cuffee Y, Ogedegbe C, Williams NJ, Ogedegbe G, Schoenthaler A. Psychosocial Risk Factors for Hypertension: an Update of the Literature. Current Hypertension Reports. 2014; 16.
- 44. Pinquart M, Duberstein PR. Associations of social networks with cancer mortality: A meta-analysis. Critical Reviews in Oncology/Hematology. 2010; 75:122-37.
- 45. Steenstra IA, Verbeek JH, Heymans MW, Bongers PM. Prognostic factors for duration of sick leave in patients sick listed with acute low back pain: a systematic review of the literature. Occupational and Environmental Medicine. 2005; 62:851-60.
- 46. Barton C, Effing TW, Cafarella P. Social Support and Social Networks in COPD: A Scoping Review. COPD. 2015; 12:690-702.
- 47. Santini ZI, Koyanagi A, Tyrovolas S, Mason C, Haro JM. The association between social relationships and depression: A systematic review. Journal of Affective Disorders. 2015; 175:53-65.
- 48. Schwarzbach M, Luppa M, Forstmeier S, Konig H-H, Riedel-Heller SG. Social relations and depression in late life-A systematic review. International Journal of Geriatric Psychiatry. 2014; 29:1-21.
- 49. Ouimet MA, Primeau F, Cole MG. Psychosocial risk factors in poststroke depression: A systematic review. Canadian Journal of Psychiatry. 2001; 46:819-28.
- 50. Kita S, Minatani M, Hikita N, Matsuzaki M, Shiraishi M, Haruna M. A Systematic Review of the Physical, Mental, Social, and Economic Problems of Immigrant Women in the Perinatal Period in Japan. Journal of Immigrant and Minority Health. 2015; 17:1863-81.
- 51. Teo AR, Lerrigo R, Rogers MAM. The role of social isolation in social anxiety disorder: A systematic review and meta-analysis. Journal of Anxiety Disorders. 2013; 27:353-64.
- 52. Hatcher S, Stubbersfield O. Sense of Belonging and Suicide: A Systematic Review. Canadian Journal of Psychiatry-Revue Canadienne De Psychiatrie. 2013; 58:432-6.
- 53. Fässberg MM, van Orden KA, Duberstein P, Erlangsen A, Lapierre S, Bodner E, et al. A Systematic Review of Social Factors and Suicidal Behavior in Older Adulthood. International Journal of Environmental Research and Public Health. 2012; 9:722-45.
- 54. Pompili M, Forte A, Palermo M, Stefani H, Lamis DA, Serafini G, et al. Suicide risk in multiple sclerosis: A systematic review of current literature. Journal of Psychosomatic Research. 2012; 73:411-7.
- 55. Mezuk B, Rock A, Lohman MC, Choi M. Suicide risk in long-term care facilities: a systematic review. International Journal of Geriatric Psychiatry. 2014; 29:1198-211.
- 56. Mollison E, Chaplin E, Underwood L, McCarthy J. A review of risk factors associated with suicide in adults with intellectual disability. Advances in Mental Health and Intellectual Disabilities. 2014; 8:302-8.

- 57. Boss L, Kang D-H, Branson S. Loneliness and cognitive function in the older adult: A systematic review. International Psychogeriatrics. 2015; 27:541-53.
- 58. Kuiper JS, Zuidersma M, Voshaar RCO, Zuidema SU, van den Heuvel ER, Stolk RP, et al. Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. Ageing Research Reviews. 2015; 22:39-57.
- 59. Berkman LF. Social networks, support and health taking the next step forward. American Journal of Epidemiology. 1986; 123:559-62.
- 60. Callaghan P, Morrissey J. Social support and health: a review. Journal of Advanced Nursing. 1993; 18:203-10.
- 61. Hawkley LC, Cacioppo JT. Loneliness Matters: A Theoretical and Empirical Review of Consequences and Mechanisms. Annals of Behavioral Medicine. 2010; 40:218-27.
- 62. Ong AD, Uchino BN, Wethington E. Loneliness and Health in Older Adults: A Mini-Review and Synthesis. Gerontology. 2015.
- 63. Ottmann G, Dickson J, Wright P. Social connectedness and health: A literature review. DigitalCommons@ILR: <a href="http://digitalcommonsilrcornelledu/gladnetcollect/471">http://digitalcommonsilrcornelledu/gladnetcollect/471</a>. 2006.
- 64. Seeman TE. Social ties and health: The benefits of social integration. Annals of Epidemiology. 1996; 6:442-51.
- 65. Public Health England. Reducing social isolation across the lifecourse. 2015.
- 66. Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. Circulation. 1999; 99:2192-217.
- 67. Arthur HM. Depression, isolation, social support, and cardiovascular disease in older adults. Journal of Cardiovascular Nursing. 2006; 21:S2-S7.
- 68. Ruwanpathirana T, Owen A, Reid CM. Review on Cardiovascular Risk Prediction. Cardiovascular Therapeutics. 2015; 33:62-70.
- 69. Stuart-Shor EM, Buselli EF, Carroll DL, Forman DE. Are Psychosocial Factors Associated With the Pathogenesis and Consequences of Cardiovascular Disease in the Elderly? Journal of Cardiovascular Nursing. 2003; 18:169-83.
- 70. Stuller KA, Jarrett B, DeVries AC. Stress and social isolation increase vulnerability to stroke. Experimental Neurology. 2012; 233:33-9.
- 71. Wielgosz AT, Nolan RP. Biobehavioral factors in the context of ischemic cardiovascular diseases. Journal of Psychosomatic Research. 2000; 48:339-45.
- 72. Tay L, Tan K, Diener E, Gonzalez E. Social relations, health behaviors, and health outcomes: a survey and synthesis. Applied psychology Health and well-being. 2013; 5:28-78.
- 73. Davidson S, Rossall P. Age UK Evidence review: loneliness in later life. 2013.

- 74. Luanaigh CO, Lawlor BA. Loneliness and the health of older people. International Journal of Geriatric Psychiatry. 2008; 23:1213-21.
- 75. O'Rourke HM, Duggleby W, Fraser KD, Jerke L. Factors that affect quality of life from the perspective of people with dementia: A metasynthesis. Journal of the American Geriatrics Society. 2015; 63:24-38.
- 76. Heinrich LA, Gullone E. The clinical significance of loneliness: A literature review. Clinical Psychology Review. 2006; 26:695-718.
- 77. Blai B, Jr. Health consequences of loneliness: a review of the literature. Journal of American college health. 1989; 37:162-7.
- 78. Andersson L. Loneliness research and interventions: A review of the literature. Aging & Mental Health. 1998; 2:264-74.
- 79. Cacioppo JT, Hawkey LC. Perceived social isolation and cognition. Trends in Cognitive Sciences. 2009; 13:447-54.
- 80. Hawkley LC, Cacioppo JT. Loneliness and pathways to disease. Brain Behavior and Immunity. 2003; 17:S98-S105.
- 81. Soundy A, Stubbs B, Roskell C, Williams SE, Fox A, Vancampfort D. Identifying the facilitators and processes which influence recovery in individuals with schizophrenia: a systematic review and thematic synthesis. Journal of mental health (Abingdon, England). 2015; 24:103-10.
- 82. Levine MP. Loneliness and Eating Disorders. Journal of Psychology. 2012; 146:243-57.
- 83. Simoni-Wastila L, Yang HK. Psychoactive drug abuse in older adults. The American journal of geriatric pharmacotherapy. 2006; 4:380-94.
- 84. Joiner TE, Brown JS, Wingate LR. The psychology and neurobiology of suicidal behavior. Annual Review of Psychology. 2005; 56:287-314.
- 85. King CA, Merchant CR. Social and Interpersonal Factors Relating to Adolescent Suicidality: A Review of the Literature. Archives of Suicide Research. 2008; 12:181-96.
- 86. Meltzer HY. Suicidality in schizophrenia: a review of the evidence for risk factors and treatment options. Current psychiatry reports. 2002; 4:279-83.
- 87. Merrick J, Merrick E, Lunsky Y, Kandel I. A review of suicidality in persons with intellectual disability. Israel Journal of Psychiatry and Related Sciences. 2006; 43:258-64.
- 88. Montross LP, Zisook S, Kasckow J. Suicide among patients with schizophrenia: a consideration of risk and protective factors. Annals of clinical psychiatry: official journal of the American Academy of Clinical Psychiatrists. 2005; 17:173-82.
- 89. O'Connell H, Chin AV, Cunningham C, Lawlor BA. Recent developments: Suicide in older people. British Medical Journal. 2004; 329:895-9.

- 90. Darke S, Ross J. Suicide among heroin users: rates, risk factors and methods. Addiction. 2002; 97:1383-94.
- 91. Vesnaver E, Keller HH. Social Influences and Eating Behavior in Later Life: A Review. Journal of Nutrition in Gerontology and Geriatrics. 2011; 30:2-23.
- 92. Albert M, Becker T, McCrone P, Thornicroft G. Social networks and mental health service utilisation a literature review. International Journal of Social Psychiatry. 1998; 44:248-66.
- 93. Akerlind I, Hornquist JO. Loneliness and alcohol abuse: a review of evidences of an interplay. Social Science and Medicine. 1992; 34:405-14.
- 94. Attree P. Parenting support in the context of poverty: a meta-synthesis of the qualitative evidence. Health & Social Care in the Community. 2005; 13:330-7.
- 95. Seagull EAW. Social support and child maltreatment: a review of the evidence. Child Abuse and Neglect. 1987; 11:41-52.
- 96. West DA, Kellner R, Moorewest M. The effects of loneliness a review of the literature. Comprehensive Psychiatry. 1986; 27:351-63.
- 97. Anooshian LJ. Violence and aggression in the lives of homeless children: A review. Aggression and Violent Behavior. 2005; 10:129-52.
- 98. DePanfilis D. Social isolation of neglectful families: a review of social support assessment and intervention models. Child Maltreatment. 1996; 1:37-52.
- 99. Vizard E, Monck E, Misch P. Child and adolescent sex abuse perpetrators a review of the research literature. Journal of Child Psychology and Psychiatry and Allied Disciplines. 1995; 36:731-56.
- 100. Whittle H, Hamilton-Giachritsis C, Beech A, Collings G. A review of young people's vulnerabilities to online grooming. Aggression and Violent Behavior. 2013; 18:135-46.
- 101. Normand CL, Sallafranque-St-Louis F. Cybervictimization of Young People With an Intellectual or Developmental Disability: Risks Specific to Sexual Solicitation. Journal of Applied Research in Intellectual Disabilities. 2016; 29:99-110.
- 102. Cacioppo S, Capitanio JP, Cacioppo JT. Toward a Neurology of Loneliness. Psychological Bulletin. 2014; 140:1464-504.
- 103. Cacioppo JT, Hawkley LC, Norman GJ, Berntson GG. Social isolation. In: McEwen BS, Akil H, Barchas JD, Kreek MJ, editors. Social Neuroscience: Gene, Environment, Brain, Body2011. p. 17-22.
- 104. Hawkley LC, Cole SW, Capitanio JP, Norman GJ, Cacioppo JT. Effects of social isolation on glucocorticoid regulation in social mammals. Hormones and Behavior. 2012; 62:314-23.
- 105. Cacioppo JT, Hawkley LC. Social isolation and health, with an emphasis on underlying mechanisms. Perspectives in Biology and Medicine. 2003; 46:S39-S52.

106. Knutson KL. Sociodemographic and cultural determinants of sleep deficiency: Implications for cardiometabolic disease risk. Social Science & Medicine. 2013; 79:7-15.

107. Local Government Association and Improvement and Development Agency. A glass half-full: how an asset approach can improve community health and well-being, 2010.

Table 1: Characteristics of included systematic reviews

Paper	Topic	Included studies	Population characteristics	Loneliness and/or social isolation measure(s)	Outcome
Aminzadeh & Dalziel 2002, Canada	Use of accident & emergency services by the elderly	11 studies - 6 retrospective and 5 prospective	Age: ≥65 years Gender: mixed M/F Size: 455 to 2,126,578	Not identified in review	Percentages of ≥ 65 years admitted and re-admitted via accident & emergency
Annear et al 2014, New Zealand	Environmental influences on ageing	83 studies - 72 quantitative studies and 11 qualitative or mixed methods studies	Age: ≥50 years Gender: 10 F, 73 mixed M/F Size: Not identified	Not identified in review	Mortality and longevity, mental health outcomes, morbidity and functional ability, activity participation
Barbosa et al 2012, Brazil	Alcohol and tobacco use among Brazilian adolescents	59 observational studies	Age: 10-19 years Gender: mixed M/F Size: 281 to 60,973	Not identified in review	Prevalence of tobacco and alcohol use, prevalence of frequent tobacco and alcohol use
Barton et al 2015, Australia	Chronic obstructive pulmonary disease	31 studies - mainly cross sectional but 3 prospective, 2 before and after, and 3 randomised trials	Age: not identified Gender: not identified Size: 30 to 1,475	5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17	Depression, anxiety, stress, self-efficacy and self-care behaviour, functional status
Black et al 2000, USA	Risk factors for child abuse	46 case control studies	Age: not identified Gender: not identified Size: 16 to 148	4	Child abuse, parent to child aggression measured by: Conflict Tactics Scale, Parent and Child Conflict Tactics Scale, and Diagnostic Interview Schedule
Boss et al 2015, USA	Loneliness and cognitive function in the elderly	10 studies - 5 cross sectional, 5 longitudinal	Age: mean age ≥60 years Gender: mixed M/F Size: 466 to 13,176	18, 19, Likert scales	Cognitive function

Bunker et al 2003, Australia	Psychosocial risk factors for coronary heart disease	15 systematic reviews	Age: not identified Gender: not identified Size: not identified	Not identified in review	Coronary heart disease
Chen et al 2014 UK	Loneliness in the elderly	26 studies – 25 cross sectional, 1 longitudinal	Age: >60 years Gender: mixed M/F Size: 91 to 20,083	18	Health status
Cuffee et al 2015, USA	Psychosocial risk factors for hypertension	3 prospective cohort studies covering social isolation	Age: ≥18 years Gender: not identified Size: 229 to 4,724 participants	Not identified in review	Diagnosis of hypertension.
De Freitas et al 2013, USA	Vulnerabilities to misinformation in online pharmaceutical marketing	All study types	Age: not identified Gender: not identified Size: not identified	Not identified in review	Factors of vulnerability to online pharmaceutical misinformation
Denhaerynck et al 2009, Belgium & Switzerland	Adherence to renal transplant medication	4 prospective cohort studies covering determinants of nonadherence	Age: >18 years Gender: not identified Size: 60 to 196	Not identified in review	Measures of non-adherence to immunosuppressive drug therapy
Dyal & Valente 2015, USA	Loneliness and smoking	25 studies, design not specified	Age: 11 studies ≤18 years, 14 studies >18 years Gender: mixed M/F Size: 103 to 89,348	18, 33, 34	Various measures of smoking
Fassberg et al 2012, Sweden, Israel, Canada, USA, Australia,	Social risk factors for suicide in the elderly	14 observational studies in 16 papers	Age: >65 years Gender: mixed M/F Size: <100 to ≥1000	28, 29, 30, 31, 32	Death wishes, suicide, ideation, deliberate self-harm, non-fatal suicidal behaviour
Glozier et al 2013, Australia	Psychosocial risk factors for coronary heart disease	Systematic reviews	Age: not identified Gender: not identified Size: not identified	Not identified in review	Coronary heart disease

Hatcher et al 2013, Canada & New Zealand	Suicide	16 cross-sectional studies	Age: not identified Gender: not identified Size: not identified	22, 23, 24, 25, 26, 27	Suicidal ideation, suicide attempts
Herbst et al 2008, USA	HIV risk behaviours in transgendered individuals	29 studies, design not specified	Age: teens to 60s Gender: transgender Size: 19 to 515	Not identified in review	HIV seropositivity or risk factors
Holt Lunstad et al 2010, USA	Mortality risk	148 studies - design not specified, although 60% involved community cohorts.	Age: 6 to 92 years Gender: 49% F, 51% M Size: 37 to 22,236	18, 36, 37, 38, 39, 19, 40, 3, 41, 35	Mortality
Holt Lunstad et al 2015, USA	Mortality risk	70 prospective cohort studies	Age: mean 66 years Gender: mixed M/F (mean 52.6% F) Size: mean 48,673	3, 18, 35, 19	Mortality
Kita et al 2015, Japan	Physical, mental, social, and economic problems of perinatal immigrant women	36 studies - 12 quantitative, 15 qualitative, 3 mixed methods, 5 expert opinions, 1 brief report	Age: not identified Gender: all female Size: 1 to 706	Not identified in review	Psychological outcomes
Kuiper et al 2015, Netherlands	Dementia risk	19 prospective cohort studies	Age: 55 to ≥ 90 years Gender: most mixed M/F, 1 M, 1 F Size: 732 to 5447	Not identified in review	Dementia incidence
Mezuk et al 2014, USA	Suicide in long term care facilities	37 studies - 21 cross- sectional, 8 cohort, 3 qualitative, and 5 interventional	Age: mean 76 to 87 years Gender: 2 F, 2 M, 3 not identified, rest mixed M/F Size: 57 to 294592	Not identified in review	Completed and attempted suicide, suicidal ideation
Mollinson et al 2014, UK	Suicide and learning disability	11 studies – 2 cohort, 3 reviews, 4 qualitative, rest not reported	Age: 8 to 63 years Gender: not identified Size: 2 to 2369	Not identified in review	Completed and attempted suicide, suicidal ideation

Mookadam et al 2004, USA	Morbidity and mortality after myocardial infarction	5 prospective cohort studies	Age: not identified Gender: not identified Size: 194 to1234	1, 2, 3	Mortality and morbidity associated after acute myocardial infarction
Murray et al 2012b, UK	Behaviour change for cardiovascular risk	31 observational studies, 1 RCT	Age: not identified Gender: mixed M/F Size: not identified	Not identified in review	Barriers and facilitators to behavioural change
Nyqvist et al 2013, Finland & Sweden	All cause mortality	20 observational cohort studies	Age: 18 to 102 years Gender: 2 M, rest mixed M/F Size: 1060 to 17433	Not identified in review	All-cause mortality
Ouimet et al 2001, Canada	Depression after stroke	9 prospective cohort studies	Age: 25 to 100 years Gender: not identified Size: 90 to 486	20, 21	Major or minor depressive episode following stroke
Pinquart & Rubenstein 2010, USA & Germany	Cancer mortality	94 prospective community-based studies (87 in meta- analysis)	Age: mean 65.9 years Gender: 57% female Size: 40 to 10,789,239	10, 3	Mortality in cancer patients
Pinquart & Sorensen 2000, USA & Germany	Subjective well-being in the elderly	286 studies, design not specified	Age: 18 to 109 years Gender: not identified Size: 20 to 4,350	Not identified in review	Subjective well-being and ability to live independently
Pompili 2012, Italy	Suicide risk in multiple sclerosis	12 studies - 4 cohort, 5 retrospective, 2 observational	Age: not identified Gender: not identified Size: 11 to 10,174	Not identified in review	Completed and attempted suicide, suicidal ideation
Santini et al 2015, UK & Spain	Depression and social relationships	51 studies - 28 cross- sectional, 23 prospective	Age: ≥18 years Gender: not identified Size: 971 to 40659	Social network and engagement measures	Depression as measured by 15-20 validated scales

Schwarzbach et al 2014, Germany & Switzerland	Depression in the elderly	37 studies - 25 cross sectional, 12 longitudinal	Age: ≥60 years Gender: mixed M/F Size: 207 to 4391	Standardised questionnaires and self-report questions	Depression as measured by 4 validated scales
Seo et al 2012, USA	Tobacco adolescent smoking	10 studies - 8 quantitative, 2 mixed	Age: mean ≥13 <18 years Gender: mixed M/F Size: 44 to 6695	Not identified in review	Smoking behaviour
Seto & Lalumiere 2010, Canada	Sexual offending in male adolescents	59 studies, design not specified	Age: 11 to 20 years Gender: male only Size: not identified	42, 43, 44, 45, 46, 47, 48	Differences between adolescent sexual offenders and adolescent non-sexual offenders
Shor & Roelfs 2015, Canada	All cause mortality	91 studies, design not specified	Age: not identified Gender: not identified Size: 119 to 30070	Not identified in review	All-cause mortality
Steenstra et al 2005, Netherlands	Musculoskeletal low back pain	14 studies – 8 retrospective, 6 prospective	Age: working-age adults Gender: mixed M/F Size: 120 to 8628	Not identified in review	Duration of sick leave or time to return to work
Steptoe et al 2013, UK	Cardiovascular Disease	27 prospective cohort studies	Age: not identified Gender: not identified Size: not identified	Not identified in review	Relative risk of incident coronary heart disease
Teo et al 2013, USA	Social isolation and social anxiety disorder	34 studies - 3 cross sectional,11 population based, 14 case control,3 uncontrolled trial, 1 randomised trials,1 prospective cohort,1 case series	Age: ≥13 years Gender: mixed M/F Size: 27 to 33368	3, 9, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 46, 60, 61, 62	Social anxiety disorder as measured by a validated scale
Vancampfort et al 2012a, Belgium	Physical activity and bipolar disorder	11 cross sectional studies	Age: ≥15 years Gender: not identified Size: 18 to 9522	Not identified in review	Self-reported physical activity

Vancampfort et al 2012b, Belgium	Physical activity & schizophrenia	25 cross sectional studies	Age: 28 to 54.9 years Gender: mainly M Size: 8 to 1704	Not identified in review	Self-reported physical activity, objective measure of physical activity levels
Van der Pols- Vijlbrief et al 2014, Netherlands	Protein energy malnutrition in elderly	28 studies - 10 longitudinal, 18 cross sectional	Age: ≥ mean 65 years Gender: not identified Size: 45 to 12883	Not identified in review	Low body mass index, weight loss, low appetite, low intake, low mid-upper arm circumference

# Table 2: Key to measurement scales used in Table 1

1.	Mannheim Interview on Social Support	32.	Recent Life Change Questionnaire
2.	Multidimensional Scale of Perceived Social Support (MSPSS)	33.	University of California, Los Angeles (UCLA) Three-Item Loneliness Scale
3.	Berkman-Syme Social Network Index (SNI)	34.	Direct single item question about loneliness with Likert scale answer
4.	Child Abuse Potential Inventory Loneliness Scale	35.	Social Isolation Scale
5.	McKay 13-item Social Support Index	36.	Inventory of Socially Supportive Behaviour (ISSB)
6.	Social Support Questionnaire	37.	University of California, Los Angeles (UCLA) Social Support Inventory (SSI)
7.	Rheumatoid Arthritis Social Support Scale	38.	Established Populations for Epidemiologic Studies of the Elderly (EPESE)
8.	Perceived Social Support from Friends and Family Scale		Support Questions
9.	Duke Social Support Index (DSSI)	39.	Malmo Support Scale
10.	Medical Outcome Study (MOS) Social Support Questionnaire	40.	Malmo Influence, Contact & Anchorage Measure
11.	Family Assessment Device – General Family Functioning Subscale	41.	RAND Social Health Battery
12.	Positive and Negative Social Exchanges Scale	42.	California Personality Inventory Revised (CPI-R) – Sociability Scale
13.	Personal Resource Questionnaire (PRQ2000)	43.	California Personality Inventory Revised (CPI-R) – Internality Scale
14.	Utrecht Coping List	44.	Fundamental Interpersonal Relations Orientation (FIRO-B) Expressed Inclusion
15.	Social Support List – Interactions Subscale		Scale
16.	Older Americans Resources and Services (OARS) Social Resources Scale	45.	Millon Adolescent personality Inventory (MAPI) Introversive Scale
17.	Enhancing Recovery in Coronary Heart Disease (ENRICHD) Social Support	46.	Minnesota Multiphasic Personality Inventory (MMPI) Social Introversion Scale
	Inventory (ESSI)	47.	Piers-Harris Self-Concept (PIERS) – Popularity Scale
18.	University of California, Los Angeles (UCLA) Loneliness Scale	48.	Inventory of Peer and Parent Attachment (IPPA) Peer Attachment Scale
19.	De Jong Gierveld Loneliness Scale	49.	Asher Loneliness Scale
20.	Social Activities Index	50.	Liebowitz Social Anxiety Scale – Avoidance Subscale
21.	Interview Schedule for Social Interaction	51.	Liebowitz Social Anxiety Scale
22.	Interpersonal Needs Questionnaire	52.	Eysenck Personality Inventory – Extraversion Score
23.	Sense of Belonging Instrument	53.	Sheehan Disability Scale – Social Life Item
24.	Provision of Social Relations Scale	54.	Anxiety Disorder Interview
25.	Wellness Circles Survey	55.	Disability Profile – Social Phobia Subscale
26.	Interpersonal Support Evaluation List	56.	Empowerment Scale
27.	Interpersonal Relationships Inventory – Social Support Subscale	57.	Fear Questionnaire
28.	Social Network Questionnaire	58.	Illness Intrusiveness Rating Scale
29.	Social Contact Schedule	59.	Inventory of Interpersonal Problems
30.	Lubben Social Network Scale	60.	Retrospective Self-report of Inhibition
31.	Neighbourhood Quality Index	61.	Short-form (SF) 36 – Social Functioning Subscale
0	Togethous duality mack	62.	Social Adjustment Self-rating Scale

Table 3: AMSTAR scores for included systematic reviews

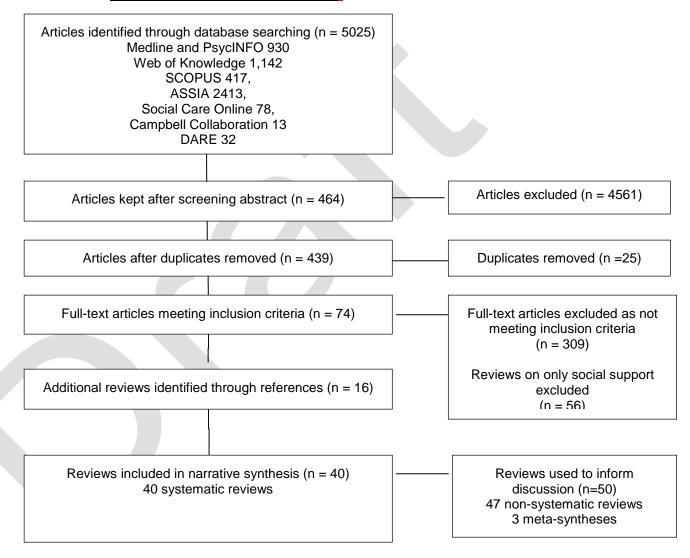
Systematic reviews	Author & date	AMSTAR	GRADE
		Score	score
	Aminzadeh & Dalziel 2002	7	Moderate
	Annear et al 2014	6	Moderate
	Barbosa et al 2012	7	Moderate
	Barton et al 2015	7	Moderate
	Black et al 2000	4	Moderate
	Boss et al 2015	5	Moderate
	Bunker et al 2003	6	Moderate
	Chen et al 2014	7	Moderate
	Cuffee et al 2015	5	Low
	De Freitas et al 2013	4	Low
	Denhaerynck et al 2009	2	Low
	Dyal & Valente 2015	5	Low
	Fassberg et al 2012	4	Low
	Glozier et al 2013	6	High
	Hatcher et al 2013	2	Low
	Herbst et al 2008	3	Very low
	Kita et al 2015	4	Low
	Mezuk et al 2014	3	Low
	Mollinson et al 2014	1	Low
	Mookadam et al 2004	1	Moderate
	Murray et al 2012	7	Moderate
	Ouimet et al 2001	5	Moderate
	Pompili 2012	6	Moderate
	Santini et al 2015	5	Moderate
	Schwarzbach et al 2014	3	Low
	Seo et al 2012	5	Low
	Steenstra et al 2005	5	Low
	Vancampfort et al 2012a	4	Low
	Vancampfort et al 2012b	4	Low
	Van der Pols-Vijlbrief et al 2014	5	Low
Meta-Analysis	Holt Lunstad et al 2010	8	Moderate
	Holt Lunstad et al 2015	6	Moderate
	Kuiper et al 2015	6	Moderate
	Nyqvist et al 2013	7	Moderate
	Pinquart & Sorensen 2000	3	Moderate
	Pinquart & Duberstein 2010	4	Moderate
	Seto & Lalumiere 2010	6	Moderate
	Shor & Roelfs 2015	9	Moderate
	Steptoe et al 2013	2	Low
	Teo et al 2013	8	Low

Table 4: Strength of Evidence by Topic

Topic	Social Isolation	Loneliness	Social networks & relationships
All-cause mortality (Holt Lunstad et al 2010*, Holt Lunstad et al 2015*, Nyqvist et al 2013*, Shor & Roelfs 2015)	++	++	++
General health & wellbeing (Aminzadeh & Dalziel 2002, Annear et al 2014, Chen et al 2014, Pinquart & Sorensen 2000)	+	+	
Tobacco use (Barbosa et al 2012, Dyal & Valente 2015, Seo et al 2012)	+	+	
Behaviour change (Murray et al 2012)			+
Physical activity (Vancampfort et al 2012a, Vancampfort et al 2012b)	+		
<b>Diet</b> (Van der Pols-Vijlbrief et al 2014)		+	
Sexual health behaviours (Black et al 2000, Herbst et al 2008, Seto & Lalumiere 2010*)	+	+	
Adherence to treatment (De Freitas et al 2013, Denhaerynck et al 2009)	+		
Cardiovascular disease (Bunker et al 2003, Cuffee et al 2015, Glozier et al 2013, Mookadam et al 2004, Steptoe et al 2013)	++		
Cancer (Pinquart & Duberstein 2010*)			+
Other physical health (Barton et al 2015, Steenstra et al 2005)	+		+
Depression and anxiety (Ouimet et al 2001, Kita et al 2015, Santini et al 2015, Schwarzbach et al 2014, Teo et al 2013)	++		+
Suicide (Fassberg et al 2012, Hatcher et al 2013, Mezuk et al 2014, Mollinson et al 2014, Pompili 2012)	+	+	+
<b>Dementia</b> (Boss et al 2015, Kuiper et al 2015*)		+	
+ association in one review, or multip	olo lower aug	ity roviowe	

+ association in one review, or multiple lower quality reviews
++ association in one or more higher quality reviews
\* Meta-analysis

Figure 1: PRISMA Flow Diagram 1

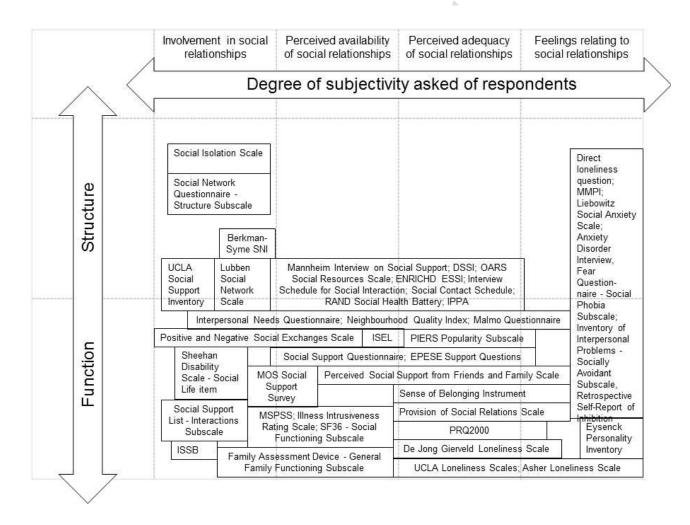


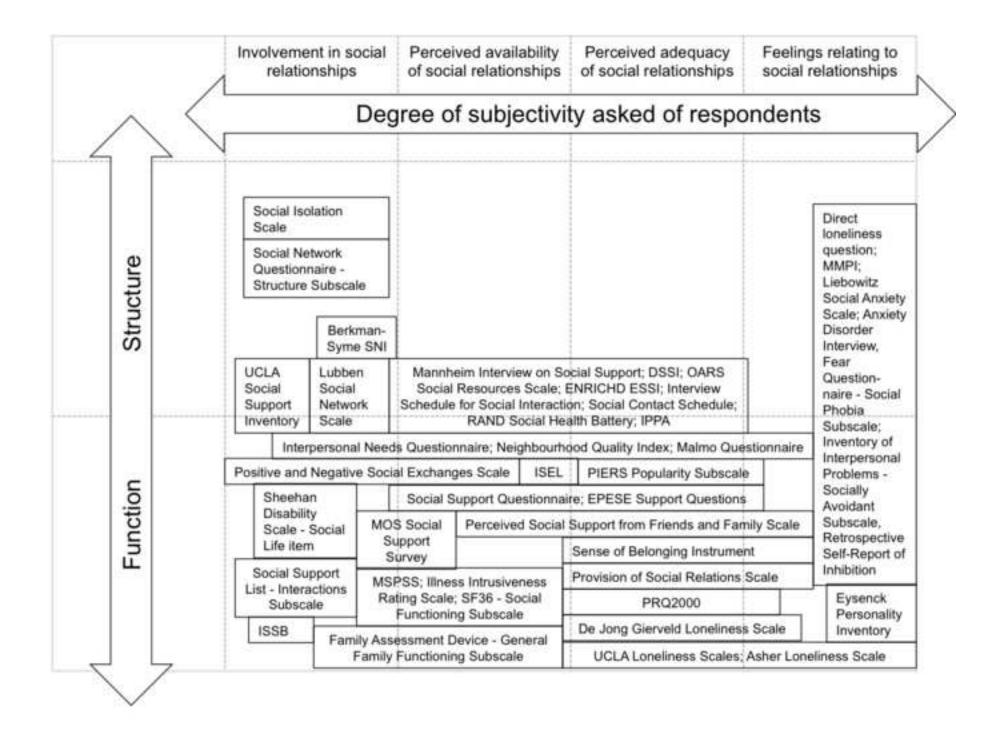
1. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Medicine. 2009; 6:e1000097.



Figure 2: Mapping of social relationships measures identified in the review,

based on the framework developed by Valtorta et al., 2016





\*Highlights (for review)

# <u>Highlights</u>

- There is consistent evidence linking social isolation and loneliness to worse cardiovascular and mental health outcomes
- Less is known on the role of other conditions and wider socio-economic consequences
- Policy makers and commissioners should consider asset-based prevention strategies