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# BMJ Open

## **A potential impact of social distancing on physical and mental health. A rapid narrative umbrella review of meta-analyses on the link between social isolation and health**

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8 **A potential impact of social distancing on physical and mental health. A rapid**  
9 **narrative umbrella review of meta-analyses on the link between social isolation**  
10 **and health**  
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## Abstract

**Background:** The imperative for social distancing during the coronavirus disease 2019 (COVID-19) pandemic may deteriorate physical and mental health. We aimed at summarizing the strength of evidence in the published literature on the association of social isolation and loneliness with physical and mental health.

**Methods:** We conducted a systematic search in April 2020 to identify meta-analyses using the Medline, PsycINFO, and Web of Science databases. The search strategy included terms of social isolation, loneliness, living alone, and meta-analysis. Eligible meta-analyses needed to report any sort of association between an indicator of social isolation and any physical or mental health outcome. The findings were summarized in a narrative synthesis.

**Results:** Twenty-five meta-analyses met our criteria, of which 10 focused on physical health and 15 on mental health outcomes. A total of more than 3 million individuals had participated in the 692 primary studies. The results suggest that social isolation is associated with chronic physical symptoms, frailty, coronary heart disease, malnutrition, hospital readmission, reduced vaccine uptake, early mortality, depression, social anxiety, psychosis, cognitive impairment in later life, and suicidal ideation.

**Conclusions:** The existing evidence clearly indicates that social isolation is associated with a range of poor physical and mental health outcomes. A potential negative impact on these outcomes needs to be considered in future decisions on social distancing measures.

**Keywords:** Social isolation, loneliness, physical health, mental health, disease.

**Strengths and limitations of this study:**

- This rapid umbrella review focuses on a timely and societally relevant issue.
- The systematic literature search was conducted in three major databases from inception up to April 2020 warranting an extensive and up-to-date overview on relevant meta-analyses in the field.
- Quality of included meta-analyses was rated with a standardized measure.
- Different indicators of social isolation were included.
- The utilized method did not allow for a quantitative comparison of associations with health outcomes.

## Background

The coronavirus 2019 (COVID-19) pandemic poses a global public health threat. In order to slow the spread of the virus by reducing contact rates, governments around the world have taken unprecedented political decisions that have transformed societies. The exact form and extent of these measures have varied, but they always include some type of social distancing making it impossible for people to maintain their normal social life.

In many countries, the restrictions have already been in place for several weeks or months. Depending on the further course of the pandemic with potential new waves, restrictions might continue for longer periods of time or be re-imposed after periods of loosening or abandoning them. When deciding about imposing, continuing or relaxing measures of social distancing, governments have to consider and balance different risks. Whilst social distancing is likely to reduce the risk of spreading the virus, it might generate other risks. These include potential damages to the economy and also possible negative consequences for the health of the population. For a balanced decision on further social distancing measures, evidence is required on whether the measures are likely to impact on a range of health outcomes.

For many people, social distancing can translate into social isolation, when they are prevented from travelling, physical meetings with friends and social activities, in some cases even from leaving their home other than for essential activities. Social isolation is a wide term without a consistent definition in the literature. Three indicators of social isolation are commonly used in research: low number of social contacts, loneliness and living alone.<sup>1</sup> The number of social contacts is a behavioral measure that can – at least in theory – be objectively quantified. Loneliness is an individual's subjective assessment of the quality and quantity of their

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3 social relationships, reflecting a belief that they have too few or too poor  
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5 relationships, or both. Living alone describes a basic characteristic of an individual's  
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7 social situation which can be associated with reduced social relationships, but is not  
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9 necessarily so. Although these three indicators capture distinct aspects of social  
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11 isolation, they commonly overlap and are associated with each other.  
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15 The extent to which individuals are socially isolated can have a profound  
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17 impact on both physical and psychological well-being.<sup>2</sup> Social isolation is thought to  
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19 influence health through behavioral and biological pathways.<sup>3</sup> Several studies  
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21 demonstrate that social isolation is associated with health-relevant behaviors, such as  
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23 lack of physical activity, poorer sleep, obsessive behavior, as well as neuroendocrine  
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25 dysregulation,<sup>3</sup> chronic allostatic load,<sup>4</sup> high blood pressure and poor immune  
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27 functioning.<sup>2,5,6</sup> Furthermore, the magnitude of the effect of social isolation on  
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29 mortality may be equivalent to or exceed the impacts of deleterious behaviors such as  
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31 excessive drinking or obesity.<sup>7</sup>  
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35 Social distancing with its inevitable increase of social isolation may therefore  
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37 have a negative impact on physical and mental health. For weighing up this potential  
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39 impact in policy decisions, the existing evidence needs to be considered. Against this  
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41 background, we conducted a systematic umbrella review to synthesize the evidence  
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43 on the association between social isolation and physical and mental health outcomes.  
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45 As recommended by the World Health Organization (WHO), we explored relevant  
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47 meta-analyses by means of a rapid review of evidence.<sup>8</sup>  
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## 52 53 **Methods**

54  
55 The aims and methods of this umbrella review were registered with the PROSPERO  
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57 database (<http://www.crd.york.ac.uk/prospero>). To select relevant meta-analyses on  
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3 the association between social isolation and physical or mental health outcomes we  
4 conducted a systematic search on 6<sup>th</sup> April 2020 using the databases Medline,  
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8 PsycINFO, and Web of Science. We conducted multi-field searches (in titles,  
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12 abstracts, and key concepts) using the following terms: social isolation, loneliness,  
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15 living alone, and meta-analy\*, which we combined using the Boolean operators “or”  
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17 plus “and”. Relevant outcomes included any sort of physical or mental health  
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20 outcome. We applied no restrictions on age of participants, applied research designs  
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22 (i.e., cross-sectional, longitudinal), or publication language. We first inspected the  
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24 title and abstract of all hits and then read full texts of the hits that seemed to meet the  
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the aforementioned inclusion criteria. The Preferred Reporting Items for Systematic Reviews and Meta-analyses reporting standards were followed to document the process of systematic review selection.<sup>9</sup>

### **Coding of trial characteristics**

Systematic reviews with a quantitative synthesis of trial results (meta-analysis) were retained. Two reviewers (NM & THH) coded and extracted from each meta-analysis several objectively verifiable characteristics: Authors and year of publication, inclusion criteria, number of included primary studies, number of participants and their composition by age and health conditions, study design, type of social connection (number of social contacts/living alone/loneliness) evaluated, clinical outcome, length of follow-up, number of databases searched, and search areas. Furthermore, we extracted the main findings on the association between number of social contacts/living alone/loneliness and health outcomes (correlation values, odds ratios, or hazard ratios, and the corresponding 95% confidence intervals). With respect to the 95% confidence intervals, both values greater than one (or both values

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3 less than one) represent a significant increase (or decrease) as a function of social  
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5 isolation.  
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### 7 **Quality Assessment**

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10 The quality of included systematic meta-analyses was independently assessed by two  
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12 reviewers (AK & TM) using A Measurement Tool to Assess Systematic Reviews – 2  
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14 (AMSTAR-2).<sup>10</sup> Following the tool's guidelines, the raters assigned one of four  
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16 global quality ratings (i.e., high, moderate, low, or critically low) after consideration  
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18 of 16 potential critical and non-critical weaknesses. Items addressing the following  
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20 criteria were considered as critical: Clear research question including definitions of  
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22 population, intervention, control group, and outcomes (PICO), adequacy of the  
23  
24 literature search, and adequate assessment and/or consideration of risk of bias in the  
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26 primary studies. Typically, high and moderate ratings reflect the presence of one or  
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28 more non-critical weakness, while low and critically low ratings indicate one or more  
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30 critical weaknesses. Any discrepancies among the independent raters were discussed  
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32 until consensus was reached.  
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## 41 **Results**

### 42 **Selection and characteristics of included studies**

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45 Figure 1 displays a PRISMA<sup>9</sup> flow diagram of the publication selection process. After  
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47 reading 530 abstracts, 89 full text publications were reviewed. The final review  
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49 resulted in 25 meta-analyses. Relevant characteristics of these meta-analyses are  
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51 summarized in Table 1.  
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**Table 1: Overview of the included meta-analyses**

Publication	Social connections	Clinical outcome	Study design	Age: <i>M (SD)</i> , range, or cut-off	Search: timespan	Range of follow-up	<i>N</i> data-bases searched	Quality score
<b>Results:</b>								
<i>Studies on physical health:</i>								
Besora-Moreno et al., 2020	Living alone	Malnutrition/ malnutrition risk	Cross-sectional	60+	01.2000 - 12.2018	n.a.	2	L
Results:	Living alone	Combined effect			<b>OR=1.92</b> (95% CI: 1.73–2.14); <i>k</i> =10; <i>N</i> =9,042			
Heidari Gorji et al., 2019	Living alone, low number of social contacts, loneliness	Hospital readmission in heart failure patients	Longitudinal	70.87 (8.62)	up to 11.2018	13 months	6	H
Results:	Any type of poor social connection	Combined effect			<b>OR=1.55</b> (95% CI: 1.39–1.73); <i>k</i> =13; <i>N</i> =6,468			
	Living alone or low number of social contacts	Combined effect			<b>OR=1.52</b> (95% CI: 1.24–1.86); <i>k</i> =6; <i>N</i> =3,812			
	Loneliness	Combined effect			<b>OR=1.63</b> (95% CI: 1.31–2.01); <i>k</i> =7; <i>N</i> =2,656			
Holt-Lunstad et al., 2015	Living alone, low number of social contacts, loneliness	Early mortality	Longitudinal	66.00 (n.r.)	01.1980 - 02.2014	7.1 years	5	L
Results:	Living alone	Unadjusted studies			<b>OR=1.51</b> (95% CI: 1.32–1.74); <i>k</i> =20; <i>N</i> =n.r.			
	Living alone	Studies with multiple covariates			<b>OR=1.32</b> (95% CI: 1.14–1.53); <i>k</i> =25; <i>N</i> =n.r.			
	Low number of social contacts	Unadjusted studies			<b>OR=1.83</b> (95% CI: 1.27–2.63); <i>k</i> =3; <i>N</i> =n.r.			
	Low number of social contacts	Studies with multiple covariates			<b>OR=1.29</b> (95% CI: 1.06–1.56); <i>k</i> =14; <i>N</i> =n.r.			
	Loneliness	Unadjusted studies			<b>OR=1.49</b> (95% CI: 1.22–1.84); <i>k</i> =8; <i>N</i> =n.r.			
	Loneliness	Studies with multiple covariates			<b>OR=1.26</b> (95% CI: 1.04–1.53); <i>k</i> =13; <i>N</i> =n.r.			
Jain et al., 2017	Living alone	Reduced vaccine uptake in older adults	Cross-sectional <sup>a</sup>	60+	up to 02.2016	n.r.	2	M
Results:	Living alone	Seasonal influenza vaccine			<b>OR=1.39</b> (95% CI: 1.16–1.68); <i>k</i> =9; <i>N</i> =40,551			
	Living alone	Pneumococcal vaccine			<b>OR=1.71</b> (95% CI: 1.20–2.46); <i>k</i> =1; <i>N</i> =1,702			

Kojima et al., 2020	Living alone	Frailty in older adults	Cross-sectional & longitudinal	60+	2000 - 02.2019	n.r.	1	L
Results:	Living alone		Cross-sectional studies					<b>OR=1.28</b> (95% CI: 1.13–1.45); <i>k</i> =44; <i>N</i> =113,374
			Sub-analysis: only men					<b>OR=1.71</b> (95% CI: 1.49–1.96); <i>k</i> =20; <i>N</i> =n.r.
			Sub-analysis: only women					OR=1.00 (95% CI: 0.83–1.20); <i>k</i> =22; <i>N</i> =n.r.
			Sub-analysis: >=60, <70 years old					<b>OR=1.67</b> (95% CI: 1.51–1.86); <i>k</i> =4; <i>N</i> =n.r.
			Sub-analysis: >=80 years old					OR=0.96 (95% CI: 0.69–1.31); <i>k</i> =6; <i>N</i> =n.r.
	Living alone		Longitudinal studies					OR=0.88 (95% CI: 0.76–1.03); <i>k</i> =6; <i>N</i> =38,549
Maes et al., 2017	Loneliness	Chronic physical conditions in children/adolescents	Cross-sectional <sup>a</sup>	children < 12 and adolescents < 21	1987 – 06.2016	n.r.	4	L
Results:	Loneliness		Combined effect (excl. 3 outliers)					<b>g=0.17</b> (95% CI: 0.03–0.30); <i>k</i> =40; <i>N</i> =3,981
			Sub-analysis: control group studies					<b>g=0.13</b> (95% CI: 0.01–0.26); <i>k</i> =23; <i>N</i> =2,995
			Sub-analysis: hearing/visual problems					<b>g=0.43</b> (n.r.); <i>k</i> =8; <i>N</i> =770
Rico-Uribe et al., 2018	Loneliness	Early mortality	Longitudinal	Mainly 50+	up to 06.2016	n.r.	4	H
Results:	Loneliness		Combined effect					<b>HR=1.22</b> (95% CI: 1.10–1.35); <i>k</i> =31; <i>N</i> =77,220
			Sub-analysis: only men					<b>HR=1.44</b> (95% CI: 1.19–1.76); <i>k</i> =7; <i>N</i> =5,815
			Sub-analysis: only women					<b>HR=1.26</b> (95% CI: 1.07–1.48); <i>k</i> =7; <i>N</i> =10,248
Smith et al, 2020	Low number of social contacts, loneliness	Inflammation markers	Cross-sectional <sup>a</sup>	16+	up to 07.2019	n.r.	5	H
Results:	Low number of social contacts		C-reactive protein: unadjusted studies					<b>r=-.186</b> (95% CI: .063–.303); <i>k</i> =7; <i>N</i> =41,126
			C-reactive protein: adjusted studies					<i>r</i> =.021 (95% CI: .051–.092); <i>k</i> =11; <i>N</i> =41,911
			Fibrinogen: unadjusted studies					<b>r=.103</b> (95% CI: .043–.163); <i>k</i> =6; <i>N</i> =15,421
			Fibrinogen: adjusted studies					<b>r=.039</b> (95% CI: .011–.067); <i>k</i> =6; <i>N</i> =22,161
			Interleukin-6: unadjusted studies					<i>r</i> =.267 (95% CI: -.341–.718); <i>k</i> =4; <i>N</i> =12,291
			Interleukin-6: adjusted studies					<i>r</i> =-.003 (95% CI: -.148–.141); <i>k</i> =6; <i>N</i> =14,243
	Loneliness		C-reactive protein: unadjusted studies					<i>r</i> =.047 (95% CI: -.003–.098); <i>k</i> =8; <i>N</i> =17,835
			C-reactive protein: adjusted studies					<i>r</i> =.023 (95% CI: -.018–.065); <i>k</i> =6; <i>N</i> =19,292
			Fibrinogen: unadjusted studies					<i>r</i> =.006 (95% CI: -.057–.070); <i>k</i> =3; <i>N</i> =1,806

									Fibrinogen: adjusted studies Interleukin-6: unadjusted studies Interleukin-6: adjusted studies	$r=.037$ (95% CI: -.015–.089); $k=4$ ; $N=7,672$ $r=.082$ (95% CI: -.001–.163); $k=4$ ; $N=4,219$ $r=.070$ (95% CI: .015–.124); $k=2$ ; $N=1,451$
Steptoe & Kivimäki, 2013	Social isolation, loneliness	Cardiovascular disease	Longitudinal	n.r.	up to 2011	n.r.	n.r.	CL		
Results:	Low number of social contacts or loneliness		Combined effect			<b>RR=1.51</b> (95% CI: 1.21–1.88); $k=7$ ; $N=n.r.$				
Valtorta et al., 2016	Social isolation, loneliness	Coronary heart disease and stroke	Longitudinal	18+	up to 05.2015	3 to 21 years	16	H		
Results:	Low number of social contacts or loneliness Low number of social contacts		Coronary heart disease Stroke incidence			<b>RR=1.29</b> (95% CI: 1.04–1.59); $k=11$ ; $N=n.r.$ <b>RR=1.32</b> (95% CI: 1.04–1.68); $k=9$ ; $N=n.r.$				
<b>Studies on mental health:</b>										
Chang et al., 2017	Living alone, loneliness	Late-life suicidal ideation	Cross-sectional <sup>a</sup>	50+	01.2000 - 11.2016	n.r.	7	L		
Results:	Living alone Loneliness		Combined effect Combined effect			<b>OR=1.38</b> (95% CI: 1.19–1.61); $k=8$ ; $N=102,401$ <b>OR=2.24</b> (95% CI: 1.73–2.90); $k=3$ ; $N=58,482$				
Chatterjee et al., 2018	Low number of social contacts, loneliness	Depression in civilians after 9/11	Longitudinal	43.78 (n.r.)	09.2001 - 07.2016	n.r.	3	L		
Results:	Low number of social contacts or loneliness		Combined effect			<b>OR=1.68</b> (99.5% CI: 1.13–2.49); $k=4$ ; $N=27,395$				
Chau et al., 2019	Loneliness	Psychosis	Cross-sectional <sup>a</sup>	Adults (mainly)	up 10.2018	n.r.	5	M		
Results:	Loneliness		Positive symptoms			<b><math>r=.302</math></b> (95% CI: .243–.359); $k=30$ ; $N=17,832$				
			Sub-analysis: clinical populations			<b><math>r=.149</math></b> (95% CI: .057–.238); $k=14$ ; $N=n.r.$				
			Sub-analysis: non-clinical populations			<b><math>r=.389</math></b> (95% CI: .232–.526); $k=5$ ; $N=n.r.$				
			Sub-analysis: mixed populations			<b><math>r=.366</math></b> (95% CI: .308–.422); $k=12$ ; $N=n.r.$				
			Sub-analysis: Paranoia			<b><math>r=.448</math></b> (95% CI: .371–.519); $k=7$ ; $N=n.r.$				
			Sub-analysis: Hallucinations			<b><math>r=.201</math></b> (95% CI: .101–.297); $k=10$ ; $N=n.r.$				
	Loneliness		Negative psychotic symptoms			<b><math>r=.347</math></b> (95% CI: .239–.446); $k=15$ ; $N=5,567$				
			Sub-analysis: clinical populations			<b><math>r=.127</math></b> (95% CI: .029–.223); $k=9$ ; $N=n.r.$				
			Sub-analysis: non-clinical populations			<b><math>r=.479</math></b> (95% CI: .351–.589); $k=4$ ; $N=n.r.$				
			Sub-analysis: mixed populations			<b><math>r=.547</math></b> (95% CI: .464–.620); $k=2$ ; $N=n.r.$				

Choi & Smith, 2013	Low number of social contacts	Adolescents' smoking behaviors	Cross-sectional	< 19	n.r.	n.a.	3	CL
Results:	Low number of social contacts		Network position: isolate vs. member		<b>OR=1.55</b> (95% CI: 1.32–1.81); <i>k</i> =8; <i>N</i> =5,067			
			Network position: isolated vs. liaison		<b>OR=1.49</b> (95% CI: 1.07–2.07); <i>k</i> =8; <i>N</i> =5,067			
Erzen & Çikrikci, 2018	Loneliness	Depression	Cross-sectional <sup>a</sup>	Adults	up to 01.2018	n.r.	2	CL
Results:	Loneliness		Combined effect		<i>r</i> =.50 (95% CI: .44–.55); <i>k</i> =88; <i>N</i> =40,068			
			Sub-analysis: clinical populations		<i>r</i> =.54 (95% CI: .38–.67); <i>k</i> =10; <i>N</i> =n.r.			
			Sub-analysis: other populations		<i>r</i> =.44 (95% CI: .16–.66); <i>k</i> =12; <i>N</i> =n.r.			
Evans et al., 2018	Low number of social contacts	Cognitive functioning	Longitudinal	50+	up to 01.2018	2-24 years	4	M
Results:	Low number of social contacts		Combined effect		<i>r</i> =.054 (95% CI: .043–.065); <i>k</i> =51; <i>N</i> =102,035			
			Sub-analysis: global measures		<i>r</i> =.061 (95% CI: .044–.079); <i>k</i> =43; <i>N</i> =74,933			
			Sub-analysis: memory		<i>r</i> =.050 (95% CI: .028–.072); <i>k</i> =13; <i>N</i> =35,230			
			Sub-analysis: executive functioning		<i>r</i> =.031 (95% CI: .015–.047); <i>k</i> =7; <i>N</i> =30,528			
Kuiper et al., 2015	Low number of social contacts, loneliness	Risk of dementia	Longitudinal	60+	up to 07.2012	2 to 15 years	3	M
Results:	Low number of social contacts		Low social network size		RR=1.17 (95% CI: 0.92–1.48); <i>k</i> =5; <i>N</i> =7,749			
	Low number of social contacts		Low level of participation		<b>RR=1.41</b> (95% CI: 1.13–1.75); <i>k</i> =6; <i>N</i> =7,687			
	Low number of social contacts		Low frequency of contacts		<b>RR=1.57</b> (95% CI: 1.32–1.85); <i>k</i> =8; <i>N</i> =15,762			
	Loneliness		Feeling lonely		<b>RR=1.58</b> (95% CI: 1.19–2.09); <i>k</i> =3; <i>N</i> =3,252			
	Loneliness		Low satisfaction with social network		RR=1.25 (95% CI: 0.96–1.62); <i>k</i> =4; <i>N</i> =6,207			
Lara et al., 2019	Loneliness	Dementia & mild cognitive impairment	Longitudinal	50+	up to 11.2018	n.r.	6	H
Results:	Loneliness		Combined effect		<b>RR=1.26</b> (95% CI: 1.14–1.40); <i>k</i> =8; <i>N</i> =33,555			
Maes et al., 2019	Loneliness	Social anxiety in children/adolescents	Cross-sectional & longitudinal	15.59 (4.27)	1981 – 06.2016	1.25 to 72 months	4	CL
Results:	Loneliness		Cross-sectional effects		<i>r</i> =.46 (95% CI: .43–.48); <i>k</i> =98; <i>N</i> =41,776			
	Loneliness		Longitudinal/cross-lagged effects		<i>r</i> =.12 (95% CI: .04–.21); <i>k</i> =10; <i>N</i> =3,995			
Mahon et al., 2006	Loneliness	Depression & social anxiety in adolescence	Cross-sectional <sup>a</sup>	Adolescents (11 to 23)	1980 – 2004	n.r.	4	CL

Results: Loneliness		Depression				<i>r</i> =.61 (n.r.); <i>k</i> =30; <i>N</i> =17,691		
Loneliness		Sub-analysis: outliers removed				<i>r</i> =.55 (n.r.); <i>k</i> =18; <i>N</i> =6,058		
Loneliness		Anxiety				<i>r</i> =.41 (n.r.); <i>k</i> =12; <i>N</i> =3,853		
Loneliness		Sub-analysis: outliers removed				<i>r</i> =.35 (n.r.); <i>k</i> =10; <i>N</i> =2,705		
Michalska da Rocha et al., 2018	Loneliness	Psychosis	Cross-sectional <sup>a</sup>	Adults	up to 02.2016	n.r.	4	H
Results: Loneliness		Combined effect				<b><i>r</i>=.32</b> (95% CI: 0.20–0.44); <i>k</i> =13; <i>N</i> =15,647		
Penninkilampi et al., 2018	Living alone, Low number of social contacts, loneliness	Risk of dementia	Longitudinal & case-control	60+	01.2012 – 05.2017	5.9 years	8	L
Results: Any type of poor social connection		Combined effect				<b>RR=1.41</b> (95% CI: 1.21–1.65); <i>k</i> =15; <i>N</i> =2,330,163		
Low number of social contacts		Combined effect				<b>RR=1.59</b> (95% CI: 1.31–1.93); <i>k</i> =6; <i>N</i> =25,373		
Living alone		Combined effect				<b>RR=1.41</b> (95% CI: 1.07–1.84); <i>k</i> =4; <i>N</i> =5,401		
Loneliness		Combined effect				RR=1.38 (95% CI: 0.98–1.94); <i>k</i> =4; <i>N</i> =4,698		
Teo et al., 2013	Living alone	Social anxiety disorder	Cross-sectional <sup>a</sup>	Adults (mainly)	01.1980 - 02.2011	n.r.	4	M
Results: Living alone		Combined effect				<b>OR=1.73</b> (95% CI: 1.34–2.24); <i>k</i> =4; <i>N</i> =12,831		
		Sub-analysis: large survey studies				<b>OR=1.70</b> (95% CI: 1.38–2.10); <i>k</i> =3; <i>N</i> =12,773		
Xiu-Ying et al., 2012	Living alone	Late life depression	Cross-sectional & longitudinal	55+	1966 - 08.2007	n.r.	3	CL
Results: Living alone		Cross-sectional effects				<b>OR=1.44</b> (95% CI: 1.04–1.99); <i>k</i> =16; <i>N</i> =34,090		
Living alone		Sub-analysis: vs. living with family				<b>OR=2.59</b> (95% CI: 1.60–4.20); <i>k</i> =5; <i>N</i> =12,537		
Living alone		Longitudinal/cross-lagged effects				RR=1.27 (95% CI: 0.89–1.80); <i>k</i> =4; <i>N</i> =1,345		
Yuan et al., 2019	Living alone	Post-acute coronary syndrome depression	Longitudinal & case-control	19+	01.1996 - 03.2018	n.r.	4	L
Results: Living alone		Combined effect				<b>OR=1.17</b> (95% CI: 1.12–1.22); <i>k</i> =11; <i>N</i> =n.r.		

Note: For each result, we specify the type of social connection, the focus of the (sub-)analysis, followed by the reported effect size (in brackets: confidence intervals), as well as included numbers of independent studies and participants. Effect sizes printed in boldface are statistically significant at alpha = 0.05. Abbreviations: n.a.: not applicable; n.r.: not reported; H: High; M: Moderate; L: Low; CL: Critically low.

<sup>a</sup> These studies included different study designs and extracted cross-sectional data or aggregated longitudinal and cross-sectional data.

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2  
3 All publications were journal articles in English. Ten meta-analyses reported  
4  
5 associations of number of social contacts, living alone, and loneliness with physical  
6  
7 health outcomes, and 15 with mental health outcomes. Different indicators of social  
8  
9 isolation were measured in the included studies. We considered as indicators a *low*  
10  
11 *number of social contacts* defined as an objectively quantifiable variable of one's  
12  
13 social contacts irrespective of its perceived quality; *loneliness* representing the  
14  
15 subjective emotional appraisal of the extent and quality of social relationships; and  
16  
17 *living alone* as an objective characteristic of the living situation. The meta-analyses  
18  
19 differed with respect to whether they kept these three measures of social isolation  
20  
21 separate of whether they combined them (see Tab. 1).  
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25

#### 26 Figure 1 & Table 1

27  
28 A total of 276 primary studies were included in the 10 meta-analyses on  
29  
30 physical health. The reported results in Table 1 were based on sample sizes ranging  
31  
32 from 1,451<sup>11</sup> to 113,374<sup>12</sup> participants, with three meta-analyses not reporting on the  
33  
34 sample size. Four meta-analyses were based on longitudinal studies only, one on  
35  
36 cross-sectional studies only, and the remaining five on a combination of both cross-  
37  
38 sectional and longitudinal studies. Only one of these studies was conducted with  
39  
40 children and adolescents.<sup>13</sup> The meta-analyses revealed that there is a significant  
41  
42 association between social isolation and the following health problems: chronic  
43  
44 physical complaints in children and adolescents,<sup>13</sup> cardiovascular disease,<sup>14</sup> coronary  
45  
46 heart disease and stroke,<sup>15</sup> and frailty in older male (but not female) adults.<sup>12</sup>  
47  
48  
49 Additionally, social isolation was associated with early mortality,<sup>7,16</sup> malnutrition,<sup>17</sup>  
50  
51 hospital readmission in heart failure patients,<sup>18</sup> and vaccine uptake amongst older  
52  
53 adults.<sup>19</sup> One meta-analysis<sup>11</sup> reported mostly non-significant results on a positive  
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2  
3 association between social isolation and inflammation (acute-phase C-reactive protein  
4 and fibrinogen).  
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6

7  
8 The 15 meta-analyses on mental health were based on a total of 416 primary  
9  
10 studies. The reported results are based on sample sizes ranging from 1,345<sup>20</sup> to  
11  
12 2,330,163<sup>21</sup> participants, with one meta-analysis failing to report on the sample size.  
13  
14 Four of the 15 meta-analyses provided longitudinal data only, one provided cross-  
15  
16 sectional data only, and the remaining ten meta-analyses reported on both cross-  
17  
18 sectional and longitudinal studies. Three meta-analyses focused on studies with  
19  
20 children and adolescents.<sup>22-24</sup> The included meta-analyses reported a positive  
21  
22 association between social isolation and late-life suicidal ideation,<sup>25</sup> depression in  
23  
24 adults,<sup>26,27</sup> late life depression,<sup>20</sup> psychosis,<sup>22,28,29</sup> smoking behavior in adolescents,<sup>23</sup>  
25  
26 dementia and cognitive impairment in later life,<sup>30-32,21</sup> depression and social anxiety in  
27  
28 childhood and adolescence,<sup>22,24</sup> social anxiety disorder in adults,<sup>33</sup> and post-acute  
29  
30 coronary syndrome depression.<sup>34</sup> See Table 1 for detailed information.  
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### 35 Study quality

36  
37 The Intraclass Correlation Coefficient (ICC) of the global quality ratings among the  
38  
39 two raters was .83, 95% CI = .62 – .93, indicating good inter-rater reliability. Study  
40  
41 quality was very heterogeneous among meta-analyses both on physical and mental  
42  
43 health (see Tab. 1). With respect to the meta-analyses on physical health, the global  
44  
45 rating was high in 40%, medium in 10%, low in 40%, critically low in 10% of the  
46  
47 meta-analyses. In the 15 meta-analyses on mental health, study quality was rated as  
48  
49 high in 13%, medium in 27%, low in 27%, and critically low in 33% of the meta-  
50  
51 analyses. Among the AMSTAR-2 criteria, inadequate assessment of risk of bias  
52  
53 and/or lack of consideration of risk of bias represented the most frequent critical  
54  
55 weaknesses of included meta-analyses.  
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## Discussion

The review clearly demonstrates that social isolation is associated with poorer health. This applies to a range of physical and mental health outcomes and has been found in different populations and contexts. The evidence is substantial for physical health outcome and even more extensive for mental health outcomes. More specifically, social isolation is linked with chronic physical symptoms, frailty, coronary heart disease, stroke, early mortality, malnutrition, hospital readmission in heart failure patients, and vaccine uptake. With respect to mental health, social isolation is linked with depression in young and adult populations, social anxiety, psychosis, dementia and cognitive impairment in later life, and late-life suicidal ideation.

## Strengths and limitations

This is, to our knowledge, the first review to synthesize the existing evidence that has been reported in meta-analyses on the link between social isolation and physical and mental health outcomes. The findings reflect a reasonable number of meta-analyses which in total included 692 studies. Thus, the overall conclusions of this umbrella review are based on an extensive body of empirical evidence.

However, the review also has several limitations. Firstly, we considered different indicators of social isolation, and our method did not allow us to identify whether one indicator is more relevant than another. Secondly, half of the included meta-analyses for both physical and mental health outcomes had an overall quality rated on AMSTAR-2 as low or critically low, with inadequate consideration of risk of bias being the most frequent critical flaw. Thirdly, the quality of the primary research studies that went into the included meta-analyses also varied and their different

1  
2  
3 methodological shortcomings cannot be adequately considered in this review. Finally,  
4  
5 the review included a wide range of health outcomes and did not quantify the strength  
6  
7 of the associations for different outcomes.  
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9

## 12 Implications

15 The review leaves little doubt that social isolation is linked with poorer physical and  
16  
17 mental health. However, the findings are all based on observational studies and do not  
18  
19 provide evidence on the causal direction of the association. Poor physical and mental  
20  
21 health can lead to social isolation, and social isolation can lead to poorer health. For  
22  
23 establishing a causal relationship experimental studies are required, which were not  
24  
25 the subject of this review. Some evidence from randomized controlled trials, however,  
26  
27 suggests that expanding the social connections of individuals, e.g., through  
28  
29 befriending programs, may indeed improve different health outcomes.<sup>35</sup> For most of  
30  
31 the considered outcomes, a causal effect of social isolation is plausible and likely to  
32  
33 explain at least part of the identified associations. The casual direction is definite in  
34  
35 case of the greater risk of isolated people to die early.<sup>7</sup> For an explanation of the  
36  
37 damaging effect of social isolation on health outcomes, one may refer to different  
38  
39 theoretical models. Theorists from different perspectives have postulated that the  
40  
41 impact of social isolation on health is mediated by impairments in social capital,<sup>36</sup>  
42  
43 social control,<sup>37</sup> social identification,<sup>38</sup> and social support.<sup>39</sup>  
44  
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49 All the included studies assessed social isolation as it occurs in a normal  
50  
51 societal context. Social distancing as part of measures to limit the spread of COVID-  
52  
53 19 is different from the situations considered in the research synthesized in this  
54  
55 review. Firstly, for the vast majority of the population, the required social distancing  
56  
57 leads to a much more pronounced social isolation than what they have experienced  
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3 before. Secondly, social distancing is externally imposed and not due to individual  
4  
5 life style decisions, lack of material means, poor social skills or other barriers to  
6  
7 socialize. And thirdly, social distancing is requested from people in an overall context  
8  
9 of uncertainty that comes with further stressors, health risks, and often a reduced  
10  
11 accessibility of health care.  
12  
13

14  
15 It is important to note that social distancing is a broad umbrella term that  
16  
17 incorporates a wide range of potential measures, with highly divergent implications  
18  
19 for social routines. It can include a full lock down and curfew, specific guidelines for  
20  
21 meetings and gatherings of people, physical distancing in public, and a recommended  
22  
23 or mandatory wearing of face masks. The type, degree, and duration of social  
24  
25 distancing measures have been variable across countries and will affect how isolated  
26  
27 different groups in the population become.  
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30  
31 One can only speculate as to whether and, if so, to what extent the increased  
32  
33 social isolation resulting from social distancing measures in the current situation will  
34  
35 have an even greater impact on health outcomes than has been suggested in this  
36  
37 review. Arguably, an even greater impact can be expected for certain risk groups,  
38  
39 such as older people who are more threatened by COVID-19 and socially  
40  
41 disadvantaged groups who often face even more economic adversity than before the  
42  
43 pandemic. Further research is required to identify which populations are at particular  
44  
45 risk to suffer health problems as a result of social distancing and to explore whether  
46  
47 the resulting social isolation may – at least to some extent and in some people – be  
48  
49 compensated through positive effects of the pandemic, such as strengthened local  
50  
51 communities and increased options for online social activities.<sup>40</sup>  
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## Conclusions

In governmental decisions about future social distancing measures, a potential negative impact of the resulting social isolation on the health of the population needs to be considered. This review suggests that this can affect both physical and mental health outcomes and include an excess mortality. To what extent the presumed impact of social distancing on health outcomes can be balanced with its benefits in curbing the impact of COVID-19 is ultimately a governmental decision based on values as much as on evidence.

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2  
3 **Figure Captions:** Fig.1. Flow diagram of study selection process.  
4  
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6 ---

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8  
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12  
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14  
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16 responsibility for the integrity of the data and the accuracy of the data analysis.  
17 NM designed the search strategy with input from AK and TM. NM and AK carried  
18 out the literature searches and screening. NM, THH, and TM carried out the data  
19 extraction. AK and TM assessed the quality of the included meta-analyses. NM and  
20 SP wrote the first draft of the manuscript and all authors contributed to and have  
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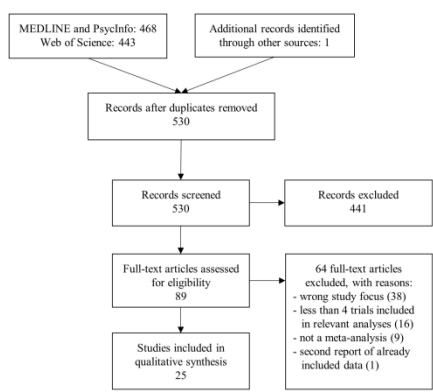


Fig. 1. Flow diagram of study selection process

338x190mm (300 x 300 DPI)

## MOOSE (Meta-analyses Of Observational Studies in Epidemiology) Checklist

A reporting checklist for Authors, Editors, and Reviewers of Meta-analyses of Observational Studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Reporting Criteria	Reported (Yes/No)	Reported on Page No.
<b>Reporting of Background</b>		
Problem definition		
Hypothesis statement		
Description of Study Outcome(s)		
Type of exposure or intervention used		
Type of study design used		
Study population		
<b>Reporting of Search Strategy</b>		
Qualifications of searchers (eg, librarians and investigators)		
Search strategy, including time period included in the synthesis and keywords		
Effort to include all available studies, including contact with authors		
Databases and registries searched		
Search software used, name and version, including special features used (eg, explosion)		
Use of hand searching (eg, reference lists of obtained articles)		
List of citations located and those excluded, including justification		
Method for addressing articles published in languages other than English		
Method of handling abstracts and unpublished studies		
Description of any contact with authors		
<b>Reporting of Methods</b>		
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested		
Rationale for the selection and coding of data (eg, sound clinical principles or convenience)		
Documentation of how data were classified and coded (eg, multiple raters, blinding, and interrater reliability)		
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)		

Reporting Criteria	Reported (Yes/No)	Reported on Page No.
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results		
Assessment of heterogeneity		
Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated		
Provision of appropriate tables and graphics		
<b>Reporting of Results</b>		
Table giving descriptive information for each study included		
Results of sensitivity testing (eg, subgroup analysis)		
Indication of statistical uncertainty of findings		
<b>Reporting of Discussion</b>		
Quantitative assessment of bias (eg, publication bias)		
Justification for exclusion (eg, exclusion of non-English-language citations)		
Assessment of quality of included studies		
<b>Reporting of Conclusions</b>		
Consideration of alternative explanations for observed results		
Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)		
Guidelines for future research		
Disclosure of funding source		

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# BMJ Open

## A potential impact of physical distancing on physical and mental health. A rapid narrative umbrella review of meta-analyses on the link between social isolation and health

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Keywords:	PUBLIC HEALTH, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, MENTAL HEALTH, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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## Abstract

**Background:** The imperative for physical distancing during the coronavirus disease 2019 (COVID-19) pandemic may deteriorate physical and mental health. We aimed at summarizing the strength of evidence in the published literature on the association of social isolation and loneliness with physical and mental health.

**Methods:** We conducted a systematic search in April 2020 to identify meta-analyses using the Medline, PsycINFO, and Web of Science databases. The search strategy included terms of social isolation, loneliness, living alone, and meta-analysis. Eligible meta-analyses needed to report any sort of association between an indicator of social isolation and any physical or mental health outcome. The findings were summarized in a narrative synthesis.

**Results:** Twenty-five meta-analyses met our criteria, of which 10 focused on physical health and 15 on mental health outcomes. A total of more than 3 million individuals had participated in the 692 primary studies. The results suggest that social isolation is associated with chronic physical symptoms, frailty, coronary heart disease, malnutrition, hospital readmission, reduced vaccine uptake, early mortality, depression, social anxiety, psychosis, cognitive impairment in later life, and suicidal ideation.

**Conclusions:** The existing evidence clearly indicates that social isolation is associated with a range of poor physical and mental health outcomes. A potential negative impact on these outcomes needs to be considered in future decisions on physical distancing measures.

**Keywords:** Social isolation, loneliness, physical health, mental health, disease.

**Strengths and limitations of this study:**

- This rapid umbrella review focuses on a timely and societally relevant issue.
- The systematic literature search was conducted in three major databases from inception up to April 2020 warranting an extensive and up-to-date overview on relevant meta-analyses in the field.
- Quality of included meta-analyses was rated with a standardized measure.
- Different indicators of social isolation were included.
- The utilized method did not allow for a quantitative comparison of associations with health outcomes.

## Background

The coronavirus 2019 (COVID-19) pandemic poses a global public health threat. In order to slow the spread of the virus by reducing contact rates, governments around the world have taken unprecedented political decisions that have transformed societies. The exact form and extent of these measures have varied, but they always include some type of physical distancing (mostly referred to as social distancing) making it impossible for people to maintain their normal social life.

In many countries, the restrictions have already been in place for several months. Depending on the further course of the pandemic with potential new waves, restrictions might continue for longer periods of time or be re-imposed after periods of loosening or abandoning them. When deciding about imposing, continuing or relaxing measures of physical distancing, governments have to consider and balance different risks. Whilst physical distancing is likely to reduce the risk of spreading the virus, it might generate other risks. These include potential damages to the economy and also possible negative consequences for the health of the population. For a balanced decision on further physical distancing measures, evidence is required on whether the measures are likely to impact on a range of health outcomes.

A recent general population survey revealed that physical distancing can increase social isolation and loneliness.<sup>1</sup> This may happen when people are prevented from travelling, physical meetings with significant others, and in some cases even from leaving their home other than for essential activities. Of note, some individuals can be physically isolated and not feel lonely and others can feel lonely even if they are not isolated. Furthermore, many individuals are able to remain socially connected by means of remote communication while physically isolated. Accordingly, we should not assume that physical distancing inevitably leads to social isolation and

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3 loneliness. However, physical distancing is likely to have a disproportionate effect on  
4 those most vulnerable, in particular older adults, individuals in need of intensive  
5 physical or mental health care, and individuals with limited access to technology who  
6 lack the means of engaging in creative forms of contact with loved ones. Older  
7 patients, for example, may lose access to important parts of their usual routine (e.g.,  
8 day care programs or informal gatherings with significant others). Similarly,  
9 caregivers residing with patients need also to physically isolate themselves due to the  
10 ramifications of quarantines.  
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21 Social isolation is a broad term without a consistent definition in the literature.  
22 Three indicators of social isolation (also referred to as social connections) are  
23 commonly used in research: few social network ties, living alone, and loneliness.<sup>2-4</sup>  
24 Social network ties is a behavioral measure that can – at least in theory – be  
25 objectively quantified. Living alone describes a basic characteristic of an individual's  
26 social situation which can be associated with reduced social relationships, but is not  
27 necessarily so.<sup>5</sup> Loneliness, on the other hand, is an individual's subjective  
28 assessment of the quality and quantity of their social relationships, reflecting a belief  
29 that they have too few or too poor relationships, or both. Accordingly, social network  
30 ties and living alone represent structural indicators, whereas loneliness represents a  
31 quality measure of social connections.<sup>4,5</sup>  
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47 Although these three indicators capture distinct aspects of social isolation,  
48 they commonly overlap and are associated with each other. Literature suggests that  
49 many individuals are socially isolated or lonely or both and that social isolation and  
50 loneliness may occur unequally across age groups. For example, Hawkley and  
51 colleagues<sup>6</sup> reported that loneliness decreased with age through the early 70s and then  
52 increased again. Several studies indicate that at least a fifth of adults report frequent  
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3 loneliness,<sup>7,8</sup> and that more than 40 percent of adults aged 60 and older report feeling  
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5 lonely.<sup>9</sup>  
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8 The extent to which individuals are socially isolated can have a profound  
9  
10 impact on both physical and psychological well-being.<sup>5</sup> Social isolation is thought to  
11  
12 influence health through behavioral and biological pathways.<sup>10</sup> Several studies  
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14 demonstrate that social isolation is associated with health-relevant behaviors, such as  
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16 lack of physical activity, poorer sleep, obsessive behavior, as well as neuroendocrine  
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18 dysregulation,<sup>10</sup> chronic allostatic load,<sup>11</sup> high blood pressure and poor immune  
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20 functioning.<sup>5,12,13</sup> Furthermore, the magnitude of the effect of social isolation on  
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22 mortality may be equivalent to or exceed the impacts of deleterious behaviors such as  
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24 excessive drinking or obesity.<sup>3</sup>  
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29 Physical distancing may increase social isolation therefore have a negative  
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31 impact on physical and mental health. For weighing up this potential impact in policy  
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33 decisions, the existing evidence needs to be considered. Against this background, we  
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35 conducted a systematic umbrella review to synthesize the evidence on the association  
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37 between social isolation and physical and mental health outcomes. As recommended  
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39 by the World Health Organization (WHO), we explored relevant meta-analyses by  
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41 means of a rapid review of evidence.<sup>14</sup>  
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## 47 **Methods**

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49 The aims and methods of this umbrella review were registered with the PROSPERO  
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51 database (<http://www.crd.york.ac.uk/prospero>). To select relevant meta-analyses on  
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53 the association between social isolation and physical or mental health outcomes we  
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55 conducted a systematic search on 6<sup>th</sup> April 2020 using the databases Medline,  
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57 PsycINFO, and Web of Science. We conducted multi-field searches (in titles,  
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3 abstracts, and key concepts) using the following terms: social isolation, loneliness,  
4 living alone, and meta-analy\*, which we combined using the Boolean operators “or”  
5 plus “and”. The full search string for Medline and PsycINFO was "( ( TI Loneliness  
6 OR AB loneliness OR SU Loneliness ) OR ( TI social isolation OR AB social  
7 isolation OR SU social isolation ) OR ( TI living alone OR AB living alone OR SU  
8 living alone ) ) AND ( TI meta-analy\* OR AB meta-analy\* OR SU meta-analy\* )".  
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17 Relevant outcomes included any sort of physical or mental health outcome. We  
18 applied no restrictions on age of participants, applied research designs (i.e., cross-  
19 sectional, longitudinal), or publication language. Furthermore, we did not apply any  
20 limits. We first inspected the title and abstract of all hits and then read full texts of the  
21 hits that seemed to meet the aforementioned inclusion criteria. The Preferred  
22 Reporting Items for Systematic Reviews and Meta-analyses reporting standards were  
23 followed to document the process of systematic review selection.<sup>15</sup>

### 33 **Coding of trial characteristics**

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35 Systematic reviews with a quantitative synthesis of trial results (meta-analysis) were  
36 retained. Two reviewers (NM & THH) coded and extracted from each meta-analysis  
37 several objectively verifiable characteristics: Authors and year of publication,  
38 inclusion criteria, number of included primary studies, number of participants and  
39 their composition by age and health conditions, study design, type of social  
40 connection (social network ties/living alone/loneliness) evaluated, clinical outcome,  
41 length of follow-up, number of databases searched, and search areas. Furthermore, we  
42 extracted the main findings on the association between social network ties/living  
43 alone/loneliness and health outcomes (correlation values, odds ratios, or hazard ratios,  
44 and the corresponding 95% confidence intervals). With respect to the 95% confidence  
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3 intervals, both values greater than one (or both values less than one) represent a  
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5 significant increase (or decrease) as a function of social isolation.  
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### 8 **Quality Assessment**

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10 The quality of included systematic meta-analyses was independently assessed by two  
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12 reviewers (AK & TM) using A Measurement Tool to Assess Systematic Reviews – 2  
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14 (AMSTAR-2).<sup>16</sup> Following the tool's guidelines, the raters assigned one of four  
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16 global quality ratings (i.e., high, moderate, low, or critically low) after consideration  
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18 of 16 potential critical and non-critical weaknesses. Items addressing the following  
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20 criteria were considered as critical: Clear research question including definitions of  
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22 population, intervention, control group, and outcomes (PICO), adequacy of the  
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24 literature search, and adequate assessment and/or consideration of risk of bias in the  
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26 primary studies. Typically, high and moderate ratings reflect the presence of one or  
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28 more non-critical weakness, while low and critically low ratings indicate one or more  
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30 critical weaknesses. Any discrepancies among the independent raters were discussed  
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32 until consensus was reached.  
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## 41 **Results**

### 42 **Selection and characteristics of included studies**

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44 Figure 1 displays a PRISMA<sup>15</sup> flow diagram of the publication selection process.  
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46 After reading 530 abstracts, 89 full text publications were reviewed. The final review  
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48 resulted in 25 meta-analyses. Relevant characteristics of these meta-analyses are  
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50 summarized in Table 1.  
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**Table 1:** Overview of the included meta-analyses

Publication	Social connections	Clinical outcome	Study design	Age: <i>M (SD)</i> , range, or cut-off	Literature search: timespan	Range of follow-up	<i>N</i> data-bases searched	Quality score
<b>Results:</b>								
<b><i>Studies on physical health:</i></b>								
Besora-Moreno et al., 2020	Living alone	Malnutrition/ malnutrition risk	Cross-sectional	60+	01.2000 - 12.2018	n.a.	2	L
Results:	Living alone		Combined effect					<b>OR=1.92</b> (95% CI: 1.73–2.14); <i>k</i> =10; <i>N</i> =9,042
Heidari Gorji et al., 2019	Living alone, few social network ties, loneliness	Hospital readmission in heart failure patients	Longitudinal	70.87 (8.62)	up to 11.2018	13 months	6	H
Results:	Any type of poor social connection		Combined effect					<b>OR=1.55</b> (95% CI: 1.39–1.73); <i>k</i> =13; <i>N</i> =6,468
	Living alone or few social network ties		Combined effect					<b>OR=1.52</b> (95% CI: 1.24–1.86); <i>k</i> =6; <i>N</i> =3,812
	Loneliness		Combined effect					<b>OR=1.63</b> (95% CI: 1.31–2.01); <i>k</i> =7; <i>N</i> =2,656
Holt-Lunstad et al., 2015	Living alone, few social network ties, loneliness	Early mortality	Longitudinal	66.00 (n.r.)	01.1980 - 02.2014	7.1 years	5	L
Results:	Living alone		Unadjusted studies					<b>OR=1.51</b> (95% CI: 1.32–1.74); <i>k</i> =20; <i>N</i> =n.r.
	Living alone		Studies with multiple covariates					<b>OR=1.32</b> (95% CI: 1.14–1.53); <i>k</i> =25; <i>N</i> =n.r.
	Few social network ties		Unadjusted studies					<b>OR=1.83</b> (95% CI: 1.27–2.63); <i>k</i> =3; <i>N</i> =n.r.
	Few social network ties		Studies with multiple covariates					<b>OR=1.29</b> (95% CI: 1.06–1.56); <i>k</i> =14; <i>N</i> =n.r.
	Loneliness		Unadjusted studies					<b>OR=1.49</b> (95% CI: 1.22–1.84); <i>k</i> =8; <i>N</i> =n.r.
	Loneliness		Studies with multiple covariates					<b>OR=1.26</b> (95% CI: 1.04–1.53); <i>k</i> =13; <i>N</i> =n.r.
Jain et al., 2017	Living alone	Reduced vaccine uptake in older adults	Cross-sectional <sup>a,b</sup>	60+	up to 02.2016	n.r.	2	M
Results:	Living alone		Seasonal influenza vaccine					<b>OR=1.39</b> (95% CI: 1.16–1.68); <i>k</i> =9; <i>N</i> =40,551
	Living alone		Pneumococcal vaccine					<b>OR=1.71</b> (95% CI: 1.20–2.46); <i>k</i> =1; <i>N</i> =1,702



Kojima et al., 2020	Living alone	Frailty in older adults	Cross-sectional <sup>b</sup> & longitudinal <sup>b</sup>	60+	2000 - 02.2019	n.r.	1	L
Results: Living alone			Cross-sectional studies				<b>OR=1.28</b> (95% CI: 1.13–1.45); <i>k</i> =44; <i>N</i> =113,374	
			Sub-analysis: only men				<b>OR=1.71</b> (95% CI: 1.49–1.96); <i>k</i> =20; <i>N</i> =n.r.	
			Sub-analysis: only women				OR=1.00 (95% CI: 0.83–1.20); <i>k</i> =22; <i>N</i> =n.r.	
			Sub-analysis: >=60, <70 years old				<b>OR=1.67</b> (95% CI: 1.51–1.86); <i>k</i> =4; <i>N</i> =n.r.	
			Sub-analysis: >=80 years old				OR=0.96 (95% CI: 0.69–1.31); <i>k</i> =6; <i>N</i> =n.r.	
Living alone			Longitudinal studies				OR=0.88 (95% CI: 0.76–1.03); <i>k</i> =6; <i>N</i> =38,549	
Maes et al., 2017	Loneliness	Chronic physical conditions in children/adolescents	Cross-sectional <sup>a</sup>	children < 12 and adolescents < 21	1987 – 06.2016	n.r.	4	L
Results: Loneliness			Combined effect (excl. 3 outliers)				<b>g=0.17</b> (95% CI: 0.03–0.30); <i>k</i> =40; <i>N</i> =3,981	
			Sub-analysis: control group studies				<b>g=0.13</b> (95% CI: 0.01–0.26); <i>k</i> =23; <i>N</i> =2,995	
			Sub-analysis: hearing/visual problems				<b>g=0.43</b> (n.r.); <i>k</i> =8; <i>N</i> =770	
Rico-Uribe et al., 2018	Loneliness	Early mortality	Longitudinal <sup>b</sup>	Mainly 50+	up to 06.2016	n.r.	4	H
Results: Loneliness			Combined effect				<b>HR=1.22</b> (95% CI: 1.10–1.35); <i>k</i> =31; <i>N</i> =77,220	
			Sub-analysis: only men				<b>HR=1.44</b> (95% CI: 1.19–1.76); <i>k</i> =7; <i>N</i> =5,815	
			Sub-analysis: only women				<b>HR=1.26</b> (95% CI: 1.07–1.48); <i>k</i> =7; <i>N</i> =10,248	
Smith et al, 2020	Few social network ties, loneliness	Inflammation markers	Cross-sectional <sup>a</sup>	16+	up to 07.2019	n.r.	5	H
Results: Few social network ties			C-reactive protein: unadjusted studies				<b>r=.186</b> (95% CI: .063–.303); <i>k</i> =7; <i>N</i> =41,126	
			C-reactive protein: adjusted studies				<b>r=.021</b> (95% CI: .051–.092); <i>k</i> =11; <i>N</i> =41,911	
			Fibrinogen: unadjusted studies				<b>r=.103</b> (95% CI: .043–.163); <i>k</i> =6; <i>N</i> =15,421	
			Fibrinogen: adjusted studies				<b>r=.039</b> (95% CI: .011–.067); <i>k</i> =6; <i>N</i> =22,161	
			Interleukin-6: unadjusted studies				<b>r=.267</b> (95% CI: -.341–.718); <i>k</i> =4; <i>N</i> =12,291	
			Interleukin-6: adjusted studies				<b>r=-.003</b> (95% CI: -.148–.141); <i>k</i> =6; <i>N</i> =14,243	
Loneliness			C-reactive protein: unadjusted studies				<b>r=.047</b> (95% CI: -.003–.098); <i>k</i> =8; <i>N</i> =17,835	
			C-reactive protein: adjusted studies				<b>r=.023</b> (95% CI: -.018–.065); <i>k</i> =6; <i>N</i> =19,292	
			Fibrinogen: unadjusted studies				<b>r=.006</b> (95% CI: -.057–.070); <i>k</i> =3; <i>N</i> =1,806	

									Fibrinogen: adjusted studies Interleukin-6: unadjusted studies Interleukin-6: adjusted studies	$r=.037$ (95% CI: -.015–.089); $k=4$ ; $N=7,672$ $r=.082$ (95% CI: -.001–.163); $k=4$ ; $N=4,219$ $r=.070$ (95% CI: .015–.124); $k=2$ ; $N=1,451$
6	7	8	9	10	11	12	13	14	15	16
Step toe & Kivimäki, 2013	Few social network ties, loneliness	Cardiovascular disease	Longitudinal <sup>b</sup>	n.r.	up to 2011	n.r.	n.r.	CL		
Results:	Few social network ties or loneliness		Combined effect			<b>RR=1.51</b> (95% CI: 1.21–1.88); $k=7$ ; $N=n.r.$				
Valtorta et al., 2016	Few social network ties, loneliness	Coronary heart disease and stroke	Longitudinal <sup>b</sup>	18+	up to 05.2015	3 to 21 years	16	H		
Results:	Few social network ties or loneliness		Coronary heart disease			<b>RR=1.29</b> (95% CI: 1.04–1.59); $k=11$ ; $N=n.r.$				
	Few social network ties		Stroke incidence			<b>RR=1.32</b> (95% CI: 1.04–1.68); $k=9$ ; $N=n.r.$				
<b>Studies on mental health:</b>										
18	19	20	21	22	23	24	25	26	27	28
Chang et al., 2017	Living alone, loneliness	Late-life suicidal ideation	Cross-sectional <sup>a,c</sup>	50+	01.2000 - 11.2016	n.r.	7	L		
Results:	Living alone Loneliness		Combined effect			<b>OR=1.38</b> (95% CI: 1.19–1.61); $k=8$ ; $N=102,401$				
			Combined effect			<b>OR=2.24</b> (95% CI: 1.73–2.90); $k=3$ ; $N=58,482$				
23	24	25	26	27	28	29	30	31	32	33
Chatterjee et al., 2018	Few social network ties, loneliness	Depression in civilians after 9/11	Longitudinal	43.78 (n.r.)	09.2001 - 07.2016	n.r.	3	L		
Results:	Few social network ties or loneliness		Combined effect			<b>OR=1.68</b> (99.5% CI:1.13–2.49); $k=4$ ; $N=27,395$				
34	35	36	37	38	39	40	41	42	43	44
Chau et al., 2019	Loneliness	Psychosis	Cross-sectional <sup>a,c</sup>	Adults (mainly)	up 10.2018	n.r.	5	M		
Results:	Loneliness		Positive symptoms			<b><math>r=.302</math></b> (95% CI: .243–.359); $k=30$ ; $N=17,832$				
			Sub-analysis: clinical populations			<b><math>r=.149</math></b> (95% CI: .057–.238); $k=14$ ; $N=n.r.$				
			Sub-analysis: non-clinical populations			<b><math>r=.389</math></b> (95% CI: .232–.526); $k=5$ ; $N=n.r.$				
			Sub-analysis: mixed populations			<b><math>r=.366</math></b> (95% CI: .308–.422); $k=12$ ; $N=n.r.$				
			Sub-analysis: Paranoia			<b><math>r=.448</math></b> (95% CI: .371–.519); $k=7$ ; $N=n.r.$				
			Sub-analysis: Hallucinations			<b><math>r=.201</math></b> (95% CI: .101–.297); $k=10$ ; $N=n.r.$				
	Loneliness		Negative psychotic symptoms			<b><math>r=.347</math></b> (95% CI: .239–.446); $k=15$ ; $N=5,567$				
			Sub-analysis: clinical populations			<b><math>r=.127</math></b> (95% CI: .029–.223); $k=9$ ; $N=n.r.$				
			Sub-analysis: non-clinical populations			<b><math>r=.479</math></b> (95% CI: .351–.589); $k=4$ ; $N=n.r.$				
			Sub-analysis: mixed populations			<b><math>r=.547</math></b> (95% CI: .464–.620); $k=2$ ; $N=n.r.$				

Choi & Smith, 2013	Few social network ties	Adolescents' smoking behaviors	Cross-sectional	< 19	n.r.	n.a.	3	CL
Results:	Few social network ties		Network position: isolate vs. member		<b>OR=1.55</b> (95% CI: 1.32–1.81); <i>k</i> =8; <i>N</i> =5,067			
			Network position: isolated vs. liaison		<b>OR=1.49</b> (95% CI: 1.07–2.07); <i>k</i> =8; <i>N</i> =5,067			
Erzen & Çikrikci, 2018	Loneliness	Depression	Cross-sectional <sup>a</sup>	Adults	up to 01.2018	n.r.	2	CL
Results:	Loneliness		Combined effect		<i>r</i> =.50 (95% CI: .44–.55); <i>k</i> =88; <i>N</i> =40,068			
			Sub-analysis: clinical populations		<i>r</i> =.54 (95% CI: .38–.67); <i>k</i> =10; <i>N</i> =n.r.			
			Sub-analysis: other populations		<i>r</i> =.44 (95% CI: .16–.66); <i>k</i> =12; <i>N</i> =n.r.			
Evans et al., 2018	Few social network ties	Cognitive functioning	Longitudinal	50+	up to 01.2018	2-24 years	4	M
Results:	Few social network ties		Combined effect		<i>r</i> =.054 (95% CI: .043–.065); <i>k</i> =51; <i>N</i> =102,035			
			Sub-analysis: global measures		<i>r</i> =.061 (95% CI: .044–.079); <i>k</i> =43; <i>N</i> =74,933			
			Sub-analysis: memory		<i>r</i> =.050 (95% CI: .028–.072); <i>k</i> =13; <i>N</i> =35,230			
			Sub-analysis: executive functioning		<i>r</i> =.031 (95% CI: .015–.047); <i>k</i> =7; <i>N</i> =30,528			
Kuiper et al., 2015	Few social network ties, loneliness	Risk of dementia	Longitudinal <sup>b</sup>	60+	up to 07.2012	2 to 15 years	3	M
Results:	Few social network ties		Low social network size		RR=1.17 (95% CI: 0.92–1.48); <i>k</i> =5; <i>N</i> =7,749			
	Few social network ties		Low level of participation		<b>RR=1.41</b> (95% CI: 1.13–1.75); <i>k</i> =6; <i>N</i> =7,687			
	Few social network ties		Low frequency of contacts		<b>RR=1.57</b> (95% CI: 1.32–1.85); <i>k</i> =8; <i>N</i> =15,762			
	Loneliness		Feeling lonely		<b>RR=1.58</b> (95% CI: 1.19–2.09); <i>k</i> =3; <i>N</i> =3,252			
	Loneliness		Low satisfaction with social network		RR=1.25 (95% CI: 0.96–1.62); <i>k</i> =4; <i>N</i> =6,207			
Lara et al., 2019	Loneliness	Dementia & mild cognitive impairment	Longitudinal <sup>b</sup>	50+	up to 11.2018	n.r.	6	H
Results:	Loneliness		Combined effect		<b>RR=1.26</b> (95% CI: 1.14–1.40); <i>k</i> =8; <i>N</i> =33,555			
Maes et al., 2019	Loneliness	Social anxiety in children/adolescents	Cross-sectional & longitudinal	15.59 (4.27)	1981 – 06.2016	1.25 to 72 months	4	CL
Results:	Loneliness		Cross-sectional effects		<i>r</i> =.46 (95% CI: .43–.48); <i>k</i> =98; <i>N</i> =41,776			
	Loneliness		Longitudinal/cross-lagged effects		<i>r</i> =.12 (95% CI: .04–.21); <i>k</i> =10; <i>N</i> =3,995			
Mahon et al., 2006	Loneliness	Depression & social anxiety in adolescence	Cross-sectional <sup>a</sup>	Adolescents (11 to 23)	1980 – 2004	n.r.	4	CL

Results: Loneliness		Depression				<i>r</i> =.61 (n.r.); <i>k</i> =30; <i>N</i> =17,691		
Loneliness		Sub-analysis: outliers removed				<i>r</i> =.55 (n.r.); <i>k</i> =18; <i>N</i> =6,058		
Loneliness		Anxiety				<i>r</i> =.41 (n.r.); <i>k</i> =12; <i>N</i> =3,853		
Loneliness		Sub-analysis: outliers removed				<i>r</i> =.35 (n.r.); <i>k</i> =10; <i>N</i> =2,705		
Michalska da Rocha et al., 2018	Loneliness	Psychosis	Cross-sectional <sup>a,c</sup>	Adults	up to 02.2016	n.r.	4	H
Results: Loneliness		Combined effect				<i>r</i> =.32 (95% CI: 0.20–0.44); <i>k</i> =13; <i>N</i> =15,647		
Penninkilampi et al., 2018	Living alone, few social network ties, loneliness	Risk of dementia	Longitudinal & case-control	60+	01.2012 – 05.2017	5.9 years	8	L
Results: Any type of poor social connection		Combined effect				<b>RR=1.41</b> (95% CI: 1.21–1.65); <i>k</i> =15; <i>N</i> =2,330,163		
Few social network ties		Combined effect				<b>RR=1.59</b> (95% CI: 1.31–1.93); <i>k</i> =6; <i>N</i> =25,373		
Living alone		Combined effect				<b>RR=1.41</b> (95% CI: 1.07–1.84); <i>k</i> =4; <i>N</i> =5,401		
Loneliness		Combined effect				RR=1.38 (95% CI: 0.98–1.94); <i>k</i> =4; <i>N</i> =4,698		
Teo et al., 2013	Living alone	Social anxiety disorder	Cross-sectional <sup>a</sup>	Adults (mainly)	01.1980 - 02.2011	n.r.	4	M
Results: Living alone		Combined effect				<b>OR=1.73</b> (95% CI: 1.34–2.24); <i>k</i> =4; <i>N</i> =12,831		
		Sub-analysis: large survey studies				<b>OR=1.70</b> (95% CI: 1.38–2.10); <i>k</i> =3; <i>N</i> =12,773		
Xiu-Ying et al., 2012	Living alone	Late life depression	Cross-sectional & longitudinal	55+	1966 - 08.2007	n.r.	3	CL
Results: Living alone		Cross-sectional effects				<b>OR=1.44</b> (95% CI: 1.04–1.99); <i>k</i> =16; <i>N</i> =34,090		
Living alone		Sub-analysis: vs. living with family				<b>OR=2.59</b> (95% CI: 1.60–4.20); <i>k</i> =5; <i>N</i> =12,537		
Living alone		Longitudinal/cross-lagged effects				RR=1.27 (95% CI: 0.89–1.80); <i>k</i> =4; <i>N</i> =1,345		
Yuan et al., 2019	Living alone	Post-acute coronary syndrome depression	Longitudinal & case-control	19+	01.1996 - 03.2018	n.r.	4	L
Results: Living alone		Combined effect				<b>OR=1.17</b> (95% CI: 1.12–1.22); <i>k</i> =11; <i>N</i> =n.r.		

Note: For each result, we specify the type of social connection, the focus of the (sub-)analysis, followed by the reported effect size (in brackets: confidence intervals), as well as included numbers of independent studies and participants. Most meta-analyses included studies both with adjusted and with unadjusted

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effect sizes (typically controlling for potential confounders like age, sex, education, socioeconomic status, chronic conditions, depression or anxiety). Unless specified in the table, the authors did not indicate a preference for adjusted or for unadjusted effect sizes. Note that adequate consideration of confounding is also in part reflected in the quality scores. Effect sizes printed in boldface are statistically significant at alpha = 0.05. Abbreviations: n.a.: not applicable; n.r.: not reported; H: High; M: Moderate; L: Low; CL: Critically low.

<sup>a</sup> These studies included different study designs and extracted cross-sectional data or aggregated longitudinal and cross-sectional data.

<sup>b</sup> Effect sizes with adjustment for confounders were preferred in this meta-analysis.

<sup>c</sup> Effect sizes with no or minimal adjustment were preferred in this meta-analysis.

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3 All publications were journal articles in English. Ten meta-analyses reported  
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5 associations of few social network ties, living alone, and loneliness with physical  
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7 health outcomes, and 15 with mental health outcomes. Different indicators of social  
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9 isolation were measured in the included studies. We considered as structural  
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11 indicators of social isolation *social network ties* defined as an objectively quantifiable  
12  
13 variable of one's social contacts irrespective of its perceived quality and *living alone*  
14  
15 as an objective characteristic of the living situation. Furthermore, we defined  
16  
17 *loneliness* as a quality indicator representing the subjective emotional appraisal of the  
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19 extent and quality of social relationships.<sup>5</sup> The meta-analyses differed with respect to  
20  
21 whether they kept these three measures of social isolation separate of whether they  
22  
23 combined them (see Tab. 1).  
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#### 28 Figure 1 & Table 1

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31 A total of 276 primary studies were included in the 10 meta-analyses on  
32  
33 physical health. The reported results in Table 1 were based on sample sizes ranging  
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35 from 1,451<sup>17</sup> to 113,374<sup>18</sup> participants, with three meta-analyses not reporting on the  
36  
37 sample size. Five meta-analyses were based on longitudinal studies only, one on  
38  
39 cross-sectional studies only, and the remaining four on a pooled combination of both  
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41 cross-sectional and longitudinal studies. Furthermore, social network ties and living  
42  
43 alone were examined in 5 meta-analyses on physical health, respectively. Loneliness,  
44  
45 on the other hand, was examined in 7 meta-analyses on mental health. Only one of  
46  
47 these studies was conducted with children and adolescents.<sup>19</sup> The meta-analyses based  
48  
49 on cross-sectional studies revealed a significant association between social isolation  
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51 and the following health problems: chronic physical complaints in children and  
52  
53 adolescents,<sup>19</sup> coronary heart disease and stroke,<sup>20</sup> and frailty in older male (but not  
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55 female) adults.<sup>18</sup> Additionally, social isolation was associated with malnutrition<sup>21</sup> and  
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3 vaccine uptake amongst older adults.<sup>22</sup> One meta-analysis<sup>17</sup> reported mostly non-  
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5 significant results on a positive association between social isolation and inflammation  
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7 (acute-phase C-reactive protein and fibrinogen). The meta-analyses conducted with  
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9 longitudinal studies indicate that social isolation is associated with increased risk of  
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11 cardiovascular disease,<sup>23</sup> early mortality,<sup>3,24</sup> and hospital readmission in heart failure  
12  
13 patients.<sup>25</sup>  
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17 The 15 meta-analyses on mental health were based on a total of 416 primary  
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19 studies. The reported results are based on sample sizes ranging from 1,345<sup>26</sup> to  
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21 2,330,163<sup>27</sup> participants, with one meta-analysis failing to report on the sample size.  
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23 Four of the 15 meta-analyses provided longitudinal data only, one provided cross-  
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25 sectional data only, and the remaining ten meta-analyses reported on both cross-  
26  
27 sectional and longitudinal studies. In addition, social network ties, living alone, and  
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29 loneliness were examined in 5, 5, and 10 meta-analyses on mental health,  
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31 respectively. Three meta-analyses focused on studies with children and adolescents.<sup>28-</sup>  
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30 The included meta-analyses based on cross-sectional designs reported a significant  
positive association between social isolation and late-life suicidal ideation,<sup>31</sup>  
depression in adults,<sup>32</sup> late life depression,<sup>26</sup> psychosis,<sup>28,33,34</sup> smoking behavior in  
adolescents,<sup>29</sup> depression and social anxiety in childhood and adolescence,<sup>28,30</sup> and  
social anxiety disorder in adults.<sup>35</sup> The meta-analyses based on longitudinal studies  
suggest that social isolation is associated with higher risk of depression in adults,<sup>36</sup>  
post-acute coronary syndrome depression,<sup>37</sup> and dementia and cognitive impairment  
in later life.<sup>27,38-40</sup> See Table 1 for detailed information.

### Study quality

The Intraclass Correlation Coefficient (ICC) of the global quality ratings among the two raters was .83, 95% CI = .62 – .93, indicating good inter-rater reliability. Study

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3 quality was very heterogeneous among meta-analyses both on physical and mental  
4 health (see Tab. 1). With respect to the meta-analyses on physical health, the global  
5 rating was high in 40%, medium in 10%, low in 40%, critically low in 10% of the  
6 meta-analyses. In the 15 meta-analyses on mental health, study quality was rated as  
7 high in 13%, medium in 27%, low in 27%, and critically low in 33% of the meta-  
8 analyses. Among the AMSTAR-2 criteria, inadequate assessment of risk of bias  
9 and/or lack of consideration of risk of bias represented the most frequent critical  
10 weaknesses of included meta-analyses.  
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## 24 **Discussion**

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26 The review clearly demonstrates that social isolation is associated with poorer health.  
27 This applies to a range of physical and mental health outcomes and has been found in  
28 different populations and contexts. The evidence based on both cross-sectional and  
29 longitudinal data is substantial for physical health outcome and even more extensive  
30 for mental health outcomes. More specifically, social isolation is linked with chronic  
31 physical symptoms, frailty, coronary heart disease, stroke, early mortality,  
32 malnutrition, hospital readmission in heart failure patients, and vaccine uptake. With  
33 respect to mental health, social isolation is linked with depression in young and adult  
34 populations, social anxiety, psychosis, dementia and cognitive impairment in later  
35 life, and late-life suicidal ideation.  
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## 51 **Strengths and limitations**

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53 This is, to our knowledge, the first review to synthesize the existing evidence that has  
54 been reported in meta-analyses on the link between social isolation and physical and  
55 mental health outcomes. The findings reflect a reasonable number of meta-analyses  
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3 which in total included 692 studies. Thus, the overall conclusions of this umbrella  
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5 review are based on an extensive body of empirical evidence.  
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8 However, the review also has several limitations. Firstly, we considered  
9  
10 different indicators of social isolation, and our method did not allow us to identify  
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12 whether one indicator is more relevant than another. Secondly, half of the included  
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14 meta-analyses for both physical and mental health outcomes had an overall quality  
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16 rated on AMSTAR-2 as low or critically low, with inadequate consideration of risk of  
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18 bias being the most frequent critical flaw. Thirdly, the quality of the primary research  
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20 studies that went into the included meta-analyses also varied and their different  
21  
22 methodological shortcomings cannot be adequately considered in this review.  
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24 Fourthly, the results on the association between living alone and health outcomes  
25  
26 need to be interpreted with caution. As reported above, living alone is not necessarily  
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28 indicative of feeling lonely.<sup>2</sup> Finally, the review included a wide range of health  
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30 outcomes and did not quantify the strength of the associations for different outcomes.  
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### 38 Implications

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40 The review leaves little doubt that social isolation is linked with poorer physical and  
41  
42 mental health. The findings are strengthened by the fact that several meta-analyses  
43  
44 were conducted with longitudinal studies. In particular, longitudinal data indicate that  
45  
46 social isolation is associated with increased risk of several physical and mental health  
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48 outcomes, cardiovascular disease, hospital readmission in heart failure patients, early  
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50 mortality, cognitive impairment, and depression.<sup>3,23-25,27,36-40</sup> However, the findings  
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52 are all based on observational studies and do not provide evidence on the causal  
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54 direction of the association. Poor physical and mental health can lead to social  
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56 isolation, and social isolation can lead to poorer health. For establishing a causal  
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3 relationship and examining the strength of the predictive relationship of social  
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5 isolation and loneliness with health outcomes experimental studies are required,  
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7 which were not the subject of this review.<sup>4,41</sup> Experimental research with animals,  
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9 however, suggests that social isolation increases mortality.<sup>42</sup> Furthermore,  
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11 experimental studies with humans indicate that randomly inducing loneliness or  
12  
13 exclusion leads to different health relevant physiological responses than being  
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15 randomly assigned to a support condition.<sup>42</sup> For most of the considered outcomes in  
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17 this review, a causal effect of social isolation is plausible and likely to explain at least  
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19 part of the identified associations. The casual direction is definite in case of the  
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21 greater risk of isolated people to die early.<sup>3</sup> For an explanation of the damaging effect  
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23 of social isolation on health outcomes, one may refer to different theoretical models.  
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25 Theorists from different perspectives have postulated that the impact of social  
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27 isolation on health is mediated by impairments in social capital,<sup>43</sup> social control,<sup>44</sup>  
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29 social identification,<sup>45</sup> and social support.<sup>46</sup>

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36 Furthermore, some evidence from randomized controlled trials, however,  
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38 suggests that expanding the social connections of individuals, e.g., through  
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40 befriending programs, may indeed improve different health outcomes.<sup>47</sup> Altogether,  
41  
42 the literature on interventions to reduce loneliness and social isolation indicates that a  
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44 policy focus on social connection is a cost-effective strategy for enhancing health at  
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46 the population level due to the potential pay-offs in health care costs that would  
47  
48 otherwise occur. Existing volunteer friendly visiting programs or psychosocial group  
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50 interventions<sup>48</sup> may need to be redesigned to the point that they can be readily  
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52 implemented in accordance with existing rules of physical distancing. Creative  
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54 programs and interventions to foster social connections, including technology-based  
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56 social networking programs, are needed.<sup>49</sup> Furthermore, existing policies should  
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3 ensure that populations at greater risk, such as the poor and the elderly, receive most  
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5 support.<sup>1</sup>  
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8 All the included studies assessed social isolation as it occurs in a normal  
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10 societal context. Physical distancing as part of measures to limit the spread of  
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12 COVID-19 is different from the situations considered in the research synthesized in  
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14 this review. Firstly, for the vast majority of the population, the required physical  
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16 distancing leads to a much more pronounced social isolation than what they have  
17  
18 experienced before. Secondly, physical distancing is externally imposed and not due  
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20 to individual life style decisions, lack of material means, poor social skills or other  
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22 barriers to socialize. And thirdly, physical distancing is requested from people in an  
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24 overall context of uncertainty that comes with further stressors, health risks, and often  
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26 a reduced accessibility of health care.  
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31 It is important to note that physical distancing is a broad umbrella term that  
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33 incorporates a wide range of potential measures, with highly divergent implications  
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35 for social routines. It can include a full lock down and curfew, specific guidelines for  
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37 meetings and gatherings of people, physical distancing in public, and a recommended  
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39 or mandatory wearing of face masks. The type, degree, and duration of physical  
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41 distancing measures have been variable across countries and will affect how isolated  
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43 different groups in the population become.  
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48 One can only speculate as to whether and, if so, to what extent the increased  
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50 social isolation resulting from physical distancing measures in the current situation  
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52 will have an even greater impact on health outcomes than has been suggested in this  
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54 review. Arguably, an even greater impact can be expected for certain risk groups,  
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56 such as older people who are more threatened by COVID-19 and socially  
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58 disadvantaged groups (e.g., individuals in need of mental or physical health care or  
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3 individuals with low income) who often face even more economic adversity than  
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5 before the pandemic. Further research is required to identify which populations are at  
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7 particular risk to suffer health problems as a result of physical distancing and to  
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9 explore whether the resulting social isolation may – at least to some extent and in  
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11 some people – be compensated through positive effects of the pandemic, such as  
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13 strengthened local communities and increased options for online social activities.<sup>47,50</sup>  
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## 20 Conclusions

21  
22 In governmental decisions about future physical distancing measures, a potential  
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24 negative impact of the resulting physical isolation on the health of the population  
25  
26 needs to be considered. The existing literature suggests that social isolation and  
27  
28 loneliness may affect both physical and mental health outcomes and include an excess  
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30 mortality. However, the potential impact of physical distancing on social isolation and  
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32 loneliness and ultimately on physical and mental health outcomes need to be  
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34 thoroughly examined. In addition, the existing knowledge on the association between  
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36 social connection and physical and mental health should be considered in clinical  
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38 practice. Finally, more experimental research is needed to increase our understanding  
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40 of the causal relationship between social connection and physical and psychological  
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42 well-being.  
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3 **Figure Captions:** Fig.1. Flow diagram of study selection process.  
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9

10 **Report about dual (co-)authorship:** No authors co-authored any of the systematic  
11 reviews and meta-analyses included in our overview.  
12  
13

14  
15 **Authors' Contributions:** NM had full access to all of the data in the study and takes  
16 responsibility for the integrity of the data and the accuracy of the data analysis.  
17 NM designed the search strategy with input from AK and TM. NM and AK carried  
18 out the literature searches and screening. NM, THH, and TM carried out the data  
19 extraction. AK and TM assessed the quality of the included meta-analyses. NM and  
20 SP wrote the first draft of the manuscript and all authors contributed to and have  
21 approved the final manuscript.  
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37 are included in this published article and supplementary material.  
38

39 Ethics approval and consent to participate: This study did not require ethical approval.  
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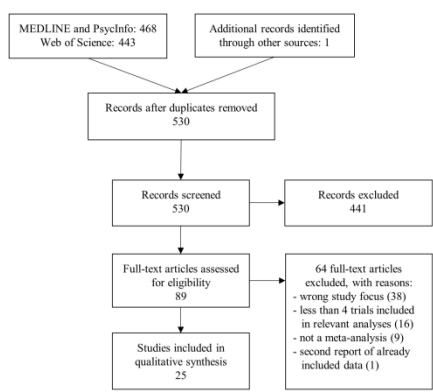


Fig. 1. Flow diagram of study selection process

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Problem definition		
Hypothesis statement		
Description of Study Outcome(s)		
Type of exposure or intervention used		
Type of study design used		
Study population		
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Qualifications of searchers (eg, librarians and investigators)		
Search strategy, including time period included in the synthesis and keywords		
Effort to include all available studies, including contact with authors		
Databases and registries searched		
Search software used, name and version, including special features used (eg, explosion)		
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Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results		
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# BMJ Open

## A potential impact of physical distancing on physical and mental health. A rapid narrative umbrella review of meta-analyses on the link between social connection and health

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## Abstract

**Background:** The imperative for physical distancing (mostly referred to as social distancing) during the coronavirus disease 2019 (COVID-19) pandemic may deteriorate physical and mental health. We aimed at summarizing the strength of evidence in the published literature on the association of physical and mental health with social connection via social isolation, living alone, and loneliness.

**Methods:** We conducted a systematic search in April 2020 to identify meta-analyses using the Medline, PsycINFO, and Web of Science databases. The search strategy included terms of social isolation, loneliness, living alone, and meta-analysis. Eligible meta-analyses needed to report any sort of association between an indicator of social connection and any physical or mental health outcome. The findings were summarized in a narrative synthesis.

**Results:** Twenty-five meta-analyses met our criteria, of which 10 focused on physical health and 15 on mental health outcomes. The results suggest that lack of social connection is associated with chronic physical symptoms, frailty, coronary heart disease, malnutrition, hospital readmission, reduced vaccine uptake, early mortality, depression, social anxiety, psychosis, cognitive impairment in later life, and suicidal ideation.

**Conclusions:** The existing evidence clearly indicates that social connection is associated with a range of poor physical and mental health outcomes. A potential negative impact on these outcomes needs to be considered in future decisions on physical distancing measures.

**Keywords:** Social isolation, living alone, loneliness, physical health, mental health, disease.

**Strengths and limitations of this study:**

- This rapid umbrella review focuses on a timely and societally relevant issue.
- The systematic literature search was conducted in three major databases from inception up to April 2020 warranting an extensive and up-to-date overview on relevant meta-analyses in the field.
- Quality of included meta-analyses was rated with a standardized measure.
- Different indicators of social connection were included.
- The utilized method did not allow for a quantitative comparison of associations with health outcomes.

## Background

The coronavirus 2019 (COVID-19) pandemic poses a global public health threat. In order to slow the spread of the virus by reducing contact rates, governments around the world have taken unprecedented political decisions that have transformed societies. The exact form and extent of these measures have varied, but they always include some type of physical distancing (mostly referred to as social distancing) making it impossible for people to maintain their normal social life.

In many countries, the restrictions have already been in place for several months. Depending on the further course of the pandemic with potential new waves, restrictions might continue for longer periods of time or be re-imposed after periods of loosening or abandoning them. When deciding about imposing, continuing or relaxing measures of physical distancing, governments have to consider and balance different risks. Whilst physical distancing is likely to reduce the risk of spreading the virus, it might generate other risks. These include potential damages to the economy and also possible negative consequences for the health of the population. For a balanced decision on further physical distancing measures, evidence is required on whether the measures are likely to impact on a range of health outcomes.

A recent general population survey revealed that physical distancing can increase the lack of social connection.<sup>1</sup> This may happen when people are prevented from travelling, physical meetings with significant others, and in some cases even from leaving their home other than for essential activities. Social connection has been suggested as an umbrella term representing the extent to which an individual connects to others.<sup>2</sup> Three indicators of social connection are commonly used in research: social isolation, living alone, and loneliness.<sup>3-5</sup> Social isolation is a behavioral measure of a person's social network that can – at least in theory – be objectively

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3 quantified. Living alone describes a basic characteristic of an individual's social  
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5 situation which can be associated with reduced social relationships, but is not  
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7 necessarily so.<sup>2</sup> Loneliness, on the other hand, is an individual's subjective  
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9 assessment of the quality and quantity of their social relationships, reflecting a belief  
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11 that they have too few or too poor relationships, or both. Accordingly, social isolation  
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13 and living alone represent structural indicators, whereas loneliness represents a  
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15 quality measure of social connections.<sup>5,2</sup>  
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20 Although these three indicators capture distinct aspects of social connection,  
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22 they commonly overlap and are associated with each other. Literature suggests that  
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24 many individuals are socially isolated or lonely or both and that social isolation and  
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26 loneliness may occur unequally across age groups. For example, Hawkley and  
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28 colleagues<sup>6</sup> reported that loneliness decreased with age through the early 70s and then  
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30 increased again. Several studies indicate that at least a fifth of adults report frequent  
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32 loneliness,<sup>7,8</sup> and that more than 40 percent of adults aged 60 and older report feeling  
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34 lonely.<sup>9</sup>  
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39 The extent to which individuals are socially isolated can have a profound  
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41 impact on both physical and psychological well-being.<sup>2</sup> Social connection is thought  
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43 to influence health through behavioral and biological pathways.<sup>10</sup> Several studies  
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45 demonstrate that social connection is associated with health-relevant behaviors, such  
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47 as lack of physical activity, poorer sleep, obsessive behavior, as well as  
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49 neuroendocrine dysregulation,<sup>10</sup> chronic allostatic load,<sup>11</sup> high blood pressure and  
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51 poor immune functioning.<sup>2,12,13</sup> Furthermore, the magnitude of the effect of social  
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53 connection on mortality may be equivalent to or exceed the impacts of deleterious  
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55 behaviors such as excessive drinking or obesity.<sup>4</sup>  
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3 Physical distancing may increase lack of social connection and therefore have  
4 a negative impact on physical and mental health. For weighing up this potential  
5 impact in policy decisions, the existing evidence needs to be considered. Against this  
6 background, we conducted a systematic umbrella review to synthesize the evidence  
7 on the association between social connection and physical and mental health  
8 outcomes. As recommended by the World Health Organization (WHO), we explored  
9 relevant meta-analyses by means of a rapid review of evidence.<sup>14</sup>  
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## 21 **Methods**

22 To select relevant meta-analyses on the association between social connection and  
23 physical or mental health outcomes we conducted a systematic search on 6<sup>th</sup> April  
24 2020 using the databases Medline, PsycINFO, and Web of Science. We conducted  
25 multi-field searches (in titles, abstracts, and key concepts) using the following terms:  
26 social isolation, loneliness, living alone, and meta-analy\*, which we combined using  
27 the Boolean operators “or” plus “and”. The full search string for Medline and  
28 PsycINFO was "( ( TI Loneliness OR AB loneliness OR SU Loneliness ) OR ( TI  
29 social isolation OR AB social isolation OR SU social isolation ) OR ( TI living alone  
30 OR AB living alone OR SU living alone ) ) AND ( TI meta-analy\* OR AB meta-  
31 analy\* OR SU meta-analy\* )".  
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47 Relevant outcomes included any sort of physical or mental health outcome. We  
48 applied no restrictions on age of participants, applied research designs (i.e., cross-  
49 sectional, longitudinal), or publication language. Furthermore, we did not apply any  
50 limits. We first inspected the title and abstract of all hits and then read full texts of the  
51 hits that seemed to meet the aforementioned inclusion criteria. The Preferred  
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3 Reporting Items for Systematic Reviews and Meta-analyses reporting standards were  
4 followed to document the process of systematic review selection.<sup>15</sup>  
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### 7 **Coding of trial characteristics**

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10 Systematic reviews with a quantitative synthesis of trial results (meta-analysis) were  
11 retained. Two reviewers (NM & THH) coded and extracted from each meta-analysis  
12 several objectively verifiable characteristics: Authors and year of publication,  
13 inclusion criteria, number of included primary studies, number of participants and  
14 their composition by age and health conditions, study design, type of social  
15 connection (social isolation/living alone/loneliness) evaluated, clinical outcome,  
16 length of follow-up, number of databases searched, and search areas. Furthermore, we  
17 extracted the main findings on the association between social isolation/living  
18 alone/loneliness and health outcomes (correlation values, odds ratios, or hazard ratios,  
19 and the corresponding 95% confidence intervals). With respect to the 95% confidence  
20 intervals, both values greater than one (or both values less than one) represent a  
21 significant increase (or decrease) as a function of social connection.  
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### 37 **Quality Assessment**

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40 The quality of included systematic meta-analyses was independently assessed by two  
41 reviewers (AK & TM) using A Measurement Tool to Assess Systematic Reviews – 2  
42 (AMSTAR-2).<sup>16</sup> Following the tool's guidelines, the raters assigned one of four  
43 global quality ratings (i.e., high, moderate, low, or critically low) after consideration  
44 of 16 potential critical and non-critical weaknesses. Items addressing the following  
45 criteria were considered as critical: Clear research question including definitions of  
46 population, intervention, control group, and outcomes (PICO), adequacy of the  
47 literature search, and adequate assessment and/or consideration of risk of bias in the  
48 primary studies. Typically, high and moderate ratings reflect the presence of one or  
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3 more non-critical weakness, while low and critically low ratings indicate one or more  
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5 critical weaknesses. Any discrepancies among the independent raters were discussed  
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7 until consensus was reached.  
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## 13 **Results**

### 14 Selection and characteristics of included studies

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17 Figure 1 displays a PRISMA<sup>15</sup> flow diagram of the publication selection process.

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20 After reading 530 abstracts, 89 full text publications were reviewed. The final review  
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22 resulted in 25 meta-analyses. Relevant characteristics of these meta-analyses are  
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24 summarized in Table 1.  
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**Table 1:** Overview of the included meta-analyses

Publication	Social connection	Clinical outcome	Study design	Age: <i>M (SD)</i> , range, or cut-off	Literature search: timespan	Range of follow-up	<i>N</i> data-bases searched	Quality score
↳ Results:								
<i>Studies on physical health:</i>								
Besora-Moreno et al., 2020	Living alone	Malnutrition/ malnutrition risk	Cross-sectional	60+	01.2000 - 12.2018	n.a.	2	L
Results:	Living alone		Combined effect			<b>OR=1.92</b> (95% CI: 1.73–2.14); <i>k</i> =10; <i>N</i> =9,042		
Heidari Gorji et al., 2019	Living alone, social isolation, loneliness	Hospital readmission in heart failure patients	Longitudinal	70.87 (8.62)	up to 11.2018	13 months	6	H
Results:	Any type of poor social connection		Combined effect			<b>OR=1.55</b> (95% CI: 1.39–1.73); <i>k</i> =13; <i>N</i> =6,468		
	Living alone or social isolation		Combined effect			<b>OR=1.52</b> (95% CI: 1.24–1.86); <i>k</i> =6; <i>N</i> =3,812		
	Loneliness		Combined effect			<b>OR=1.63</b> (95% CI: 1.31–2.01); <i>k</i> =7; <i>N</i> =2,656		
Holt-Lunstad et al., 2015	Living alone, social isolation, loneliness	Early mortality	Longitudinal	66.00 (n.r.)	01.1980 - 02.2014	7.1 years	5	L
Results:	Living alone		Unadjusted studies			<b>OR=1.51</b> (95% CI: 1.32–1.74); <i>k</i> =20; <i>N</i> =n.r.		
	Living alone		Studies with multiple covariates			<b>OR=1.32</b> (95% CI: 1.14–1.53); <i>k</i> =25; <i>N</i> =n.r.		
	Social isolation		Unadjusted studies			<b>OR=1.83</b> (95% CI: 1.27–2.63); <i>k</i> =3; <i>N</i> =n.r.		
	Social isolation		Studies with multiple covariates			<b>OR=1.29</b> (95% CI: 1.06–1.56); <i>k</i> =14; <i>N</i> =n.r.		
	Loneliness		Unadjusted studies			<b>OR=1.49</b> (95% CI: 1.22–1.84); <i>k</i> =8; <i>N</i> =n.r.		
	Loneliness		Studies with multiple covariates			<b>OR=1.26</b> (95% CI: 1.04–1.53); <i>k</i> =13; <i>N</i> =n.r.		
Jain et al., 2017	Living alone	Reduced vaccine uptake in older adults	Cross-sectional <sup>a,b</sup>	60+	up to 02.2016	n.r.	2	M
Results:	Living alone		Seasonal influenza vaccine			<b>OR=1.39</b> (95% CI: 1.16–1.68); <i>k</i> =9; <i>N</i> =40,551		
	Living alone		Pneumococcal vaccine			<b>OR=1.71</b> (95% CI: 1.20–2.46); <i>k</i> =1; <i>N</i> =1,702		



Kojima et al., 2020	Living alone	Frailty in older adults	Cross-sectional <sup>b</sup> & longitudinal <sup>b</sup>	60+	2000 - 02.2019	n.r.	1	L
Results:	Living alone		Cross-sectional studies Sub-analysis: only men Sub-analysis: only women Sub-analysis: >=60, <70 years old Sub-analysis: >=80 years old					<b>OR=1.28</b> (95% CI: 1.13–1.45); <i>k</i> =44; <i>N</i> =113,374 <b>OR=1.71</b> (95% CI: 1.49–1.96); <i>k</i> =20; <i>N</i> =n.r. OR=1.00 (95% CI: 0.83–1.20); <i>k</i> =22; <i>N</i> =n.r. <b>OR=1.67</b> (95% CI: 1.51–1.86); <i>k</i> =4; <i>N</i> =n.r. OR=0.96 (95% CI: 0.69–1.31); <i>k</i> =6; <i>N</i> =n.r.
	Living alone		Longitudinal studies					OR=0.88 (95% CI: 0.76–1.03); <i>k</i> =6; <i>N</i> =38,549
Maes et al., 2017	Loneliness	Chronic physical conditions in children/adolescents	Cross-sectional <sup>a</sup>	children < 12 and adolescents < 21	1987 – 06.2016	n.r.	4	L
Results:	Loneliness		Combined effect (excl. 3 outliers) Sub-analysis: control group studies Sub-analysis: hearing/visual problems					<b>g=0.17</b> (95% CI: 0.03–0.30); <i>k</i> =40; <i>N</i> =3,981 <b>g=0.13</b> (95% CI: 0.01–0.26); <i>k</i> =23; <i>N</i> =2,995 <b>g=0.43</b> (n.r.); <i>k</i> =8; <i>N</i> =770
Rico-Uribe et al., 2018	Loneliness	Early mortality	Longitudinal <sup>b</sup>	Mainly 50+	up to 06.2016	n.r.	4	H
Results:	Loneliness		Combined effect Sub-analysis: only men Sub-analysis: only women					<b>HR=1.22</b> (95% CI: 1.10–1.35); <i>k</i> =31; <i>N</i> =77,220 <b>HR=1.44</b> (95% CI: 1.19–1.76); <i>k</i> =7; <i>N</i> =5,815 <b>HR=1.26</b> (95% CI: 1.07–1.48); <i>k</i> =7; <i>N</i> =10,248
Smith et al, 2020	Social isolation, loneliness	Inflammation markers	Cross-sectional <sup>a</sup>	16+	up to 07.2019	n.r.	5	H
Results:	Social isolation		C-reactive protein: unadjusted studies C-reactive protein: adjusted studies Fibrinogen: unadjusted studies Fibrinogen: adjusted studies Interleukin-6: unadjusted studies Interleukin-6: adjusted studies					<b>r=.186</b> (95% CI: .063–.303); <i>k</i> =7; <i>N</i> =41,126 <i>r</i> =.021 (95% CI: .051–.092); <i>k</i> =11; <i>N</i> =41,911 <b>r=.103</b> (95% CI: .043–.163); <i>k</i> =6; <i>N</i> =15,421 <b>r=.039</b> (95% CI: .011–.067); <i>k</i> =6; <i>N</i> =22,161 <i>r</i> =.267 (95% CI: -.341–.718); <i>k</i> =4; <i>N</i> =12,291 <i>r</i> =-.003 (95% CI: -.148–.141); <i>k</i> =6; <i>N</i> =14,243
	Loneliness		C-reactive protein: unadjusted studies C-reactive protein: adjusted studies Fibrinogen: unadjusted studies					<i>r</i> =.047 (95% CI: -.003–.098); <i>k</i> =8; <i>N</i> =17,835 <i>r</i> =.023 (95% CI: -.018–.065); <i>k</i> =6; <i>N</i> =19,292 <i>r</i> =.006 (95% CI: -.057–.070); <i>k</i> =3; <i>N</i> =1,806

									Fibrinogen: adjusted studies Interleukin-6: unadjusted studies Interleukin-6: adjusted studies	$r=.037$ (95% CI: -.015–.089); $k=4$ ; $N=7,672$ $r=.082$ (95% CI: -.001–.163); $k=4$ ; $N=4,219$ $r=.070$ (95% CI: .015–.124); $k=2$ ; $N=1,451$
6	7	8	9	10	11	12	13	14	15	16
Step toe & Kivimäki, 2013	Social isolation, loneliness	Cardiovascular disease	Longitudinal <sup>b</sup>	n.r.	up to 2011	n.r.	n.r.	CL		
Results:	Social isolation or loneliness		Combined effect		<b>RR=1.51</b> (95% CI: 1.21–1.88); $k=7$ ; $N=n.r.$					
Valtorta et al., 2016	Social isolation, loneliness	Coronary heart disease and stroke	Longitudinal <sup>b</sup>	18+	up to 05.2015	3 to 21 years	16	H		
Results:	Social isolation or loneliness Social isolation		Coronary heart disease Stroke incidence		<b>RR=1.29</b> (95% CI: 1.04–1.59); $k=11$ ; $N=n.r.$ <b>RR=1.32</b> (95% CI: 1.04–1.68); $k=9$ ; $N=n.r.$					
<b>Studies on mental health:</b>										
Chang et al., 2017	Living alone, loneliness	Late-life suicidal ideation	Cross-sectional <sup>a,c</sup>	50+	01.2000 - 11.2016	n.r.	7	L		
Results:	Living alone Loneliness		Combined effect Combined effect		<b>OR=1.38</b> (95% CI: 1.19–1.61); $k=8$ ; $N=102,401$ <b>OR=2.24</b> (95% CI: 1.73–2.90); $k=3$ ; $N=58,482$					
Chatterjee et al., 2018	Social isolation, loneliness	Depression in civilians after 9/11	Longitudinal	43.78 (n.r.)	09.2001 - 07.2016	n.r.	3	L		
Results:	Social isolation or loneliness		Combined effect		<b>OR=1.68</b> (99.5% CI:1.13–2.49); $k=4$ ; $N=27,395$					
Chau et al., 2019	Loneliness	Psychosis	Cross-sectional <sup>a,c</sup>	Adults (mainly)	up 10.2018	n.r.	5	M		
Results:	Loneliness		Positive symptoms		$r=.302$ (95% CI: .243–.359); $k=30$ ; $N=17,832$					
			Sub-analysis: clinical populations		$r=.149$ (95% CI: .057–.238); $k=14$ ; $N=n.r.$					
			Sub-analysis: non-clinical populations		$r=.389$ (95% CI: .232–.526); $k=5$ ; $N=n.r.$					
			Sub-analysis: mixed populations		$r=.366$ (95% CI: .308–.422); $k=12$ ; $N=n.r.$					
			Sub-analysis: Paranoia		$r=.448$ (95% CI: .371–.519); $k=7$ ; $N=n.r.$					
			Sub-analysis: Hallucinations		$r=.201$ (95% CI: .101–.297); $k=10$ ; $N=n.r.$					
	Loneliness		Negative psychotic symptoms		$r=.347$ (95% CI: .239–.446); $k=15$ ; $N=5,567$					
			Sub-analysis: clinical populations		$r=.127$ (95% CI: .029–.223); $k=9$ ; $N=n.r.$					
			Sub-analysis: non-clinical populations		$r=.479$ (95% CI: .351–.589); $k=4$ ; $N=n.r.$					
			Sub-analysis: mixed populations		$r=.547$ (95% CI: .464–.620); $k=2$ ; $N=n.r.$					

Choi & Smith, 2013	Social isolation	Adolescents' smoking behaviors	Cross-sectional	< 19	n.r.	n.a.	3	CL
Results:	Social isolation					Network position: isolate vs. member Network position: isolated vs. liaison	<b>OR=1.55</b> (95% CI: 1.32–1.81); <i>k</i> =8; <i>N</i> =5,067 <b>OR=1.49</b> (95% CI: 1.07–2.07); <i>k</i> =8; <i>N</i> =5,067	
Erzen & Çikrikci, 2018	Loneliness	Depression	Cross-sectional <sup>a</sup>	Adults	up to 01.2018	n.r.	2	CL
Results:	Loneliness					Combined effect Sub-analysis: clinical populations Sub-analysis: other populations	<i>r</i> =.50 (95% CI: .44–.55); <i>k</i> =88; <i>N</i> =40,068 <i>r</i> =.54 (95% CI: .38–.67); <i>k</i> =10; <i>N</i> =n.r. <i>r</i> =.44 (95% CI: .16–.66); <i>k</i> =12; <i>N</i> =n.r.	
Evans et al., 2018	Social isolation	Cognitive functioning	Longitudinal	50+	up to 01.2018	2-24 years	4	M
Results:	Social isolation					Combined effect Sub-analysis: global measures Sub-analysis: memory Sub-analysis: executive functioning	<i>r</i> =.054 (95% CI: .043–.065); <i>k</i> =51; <i>N</i> =102,035 <i>r</i> =.061 (95% CI: .044–.079); <i>k</i> =43; <i>N</i> =74,933 <i>r</i> =.050 (95% CI: .028–.072); <i>k</i> =13; <i>N</i> =35,230 <i>r</i> =.031 (95% CI: .015–.047); <i>k</i> =7; <i>N</i> =30,528	
Kuiper et al., 2015	Social isolation, loneliness	Risk of dementia	Longitudinal <sup>b</sup>	60+	up to 07.2012	2 to 15 years	3	M
Results:	Social isolation Social isolation Social isolation Loneliness Loneliness					Low social network size Low level of participation Low frequency of contacts Feeling lonely Low satisfaction with social network	RR=1.17 (95% CI: 0.92–1.48); <i>k</i> =5; <i>N</i> =7,749 <b>RR=1.41</b> (95% CI: 1.13–1.75); <i>k</i> =6; <i>N</i> =7,687 <b>RR=1.57</b> (95% CI: 1.32–1.85); <i>k</i> =8; <i>N</i> =15,762 <b>RR=1.58</b> (95% CI: 1.19–2.09); <i>k</i> =3; <i>N</i> =3,252 RR=1.25 (95% CI: 0.96–1.62); <i>k</i> =4; <i>N</i> =6,207	
Lara et al., 2019	Loneliness	Dementia & mild cognitive impairment	Longitudinal <sup>b</sup>	50+	up to 11.2018	n.r.	6	H
Results:	Loneliness					Combined effect	<b>RR=1.26</b> (95% CI: 1.14–1.40); <i>k</i> =8; <i>N</i> =33,555	
Maes et al., 2019	Loneliness	Social anxiety in children/adolescents	Cross-sectional & longitudinal	15.59 (4.27)	1981 - 06.2016	1.25 to 72 months	4	CL
Results:	Loneliness Loneliness					Cross-sectional effects Longitudinal/cross-lagged effects	<i>r</i> =.46 (95% CI: .43–.48); <i>k</i> =98; <i>N</i> =41,776 <i>r</i> =.12 (95% CI: .04–.21); <i>k</i> =10; <i>N</i> =3,995	
Mahon et al., 2006	Loneliness	Depression & social anxiety in adolescence	Cross-sectional <sup>a</sup>	Adolescents (11 to 23)	1980 - 2004	n.r.	4	CL

	Results: Loneliness		Depression			$r=.61$ (n.r.); $k=30$ ; $N=17,691$		
			Sub-analysis: outliers removed			$r=.55$ (n.r.); $k=18$ ; $N=6,058$		
	Loneliness		Anxiety			$r=.41$ (n.r.); $k=12$ ; $N=3,853$		
			Sub-analysis: outliers removed			$r=.35$ (n.r.); $k=10$ ; $N=2,705$		
Michalska da Rocha et al., 2018	Loneliness	Psychosis	Cross-sectional <sup>a,c</sup>	Adults	up to 02.2016	n.r.	4	H
	Results: Loneliness		Combined effect			$r=.32$ (95% CI: 0.20–0.44); $k=13$ ; $N=15,647$		
Penninkilampi et al., 2018	Living alone, social isolation, loneliness	Risk of dementia	Longitudinal & case-control	60+	01.2012 – 05.2017	5.9 years	8	L
	Results: Any type of poor social connection		Combined effect			<b>RR=1.41</b> (95% CI: 1.21–1.65); $k=15$ ; $N=2,330,163$		
	Social isolation		Combined effect			<b>RR=1.59</b> (95% CI: 1.31–1.93); $k=6$ ; $N=25,373$		
	Living alone		Combined effect			<b>RR=1.41</b> (95% CI: 1.07–1.84); $k=4$ ; $N=5,401$		
	Loneliness		Combined effect			<b>RR=1.38</b> (95% CI: 0.98–1.94); $k=4$ ; $N=4,698$		
Teo et al., 2013	Living alone	Social anxiety disorder	Cross-sectional <sup>a</sup>	Adults (mainly)	01.1980 - 02.2011	n.r.	4	M
	Results: Living alone		Combined effect			<b>OR=1.73</b> (95% CI: 1.34–2.24); $k=4$ ; $N=12,831$		
			Sub-analysis: large survey studies			<b>OR=1.70</b> (95% CI: 1.38–2.10); $k=3$ ; $N=12,773$		
Xiu-Ying et al., 2012	Living alone	Late life depression	Cross-sectional & longitudinal	55+	1966 - 08.2007	n.r.	3	CL
	Results: Living alone		Cross-sectional effects			<b>OR=1.44</b> (95% CI: 1.04–1.99); $k=16$ ; $N=34,090$		
			Sub-analysis: vs. living with family			<b>OR=2.59</b> (95% CI: 1.60–4.20); $k=5$ ; $N=12,537$		
	Living alone		Longitudinal/cross-lagged effects			<b>RR=1.27</b> (95% CI: 0.89–1.80); $k=4$ ; $N=1,345$		
Yuan et al., 2019	Living alone	Post-acute coronary syndrome depression	Longitudinal & case-control	19+	01.1996 - 03.2018	n.r.	4	L
	Results: Living alone		Combined effect			<b>OR=1.17</b> (95% CI: 1.12–1.22); $k=11$ ; $N=n.r.$		

Note: For each result, we specify the type of social connection, the focus of the (sub-)analysis, followed by the reported effect size (in brackets: confidence intervals), as well as included numbers of independent studies and participants. Most meta-analyses included studies both with adjusted and unadjusted effect

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2 sizes (typically controlling for potential confounders like age, sex, education, socioeconomic status, chronic conditions, depression or anxiety). Unless specified  
3 in the table, the authors did not indicate a preference for adjusted or for unadjusted effect sizes. Note that adequate consideration of confounding is also in part  
4 reflected in the quality scores. Effect sizes printed in boldface are statistically significant at  $\alpha = 0.05$ . Abbreviations: n.a.: not applicable; n.r.: not reported;  
5 H: High; M: Moderate; L: Low; CL: Critically low.  
6

7 <sup>a</sup> These studies included different study designs and extracted cross-sectional data or aggregated longitudinal and cross-sectional data.

8 <sup>b</sup> Effect sizes with adjustment for confounders were preferred in this meta-analysis.

9 <sup>c</sup> Effect sizes with no or minimal adjustment were preferred in this meta-analysis.  
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For peer review only

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3 All publications were journal articles in English. Ten meta-analyses reported  
4 associations of social isolation, living alone, and loneliness with physical health  
5 outcomes, and 15 with mental health outcomes. Different indicators of social  
6 connection were measured in the included studies. We considered as structural  
7 indicators of social connection: *social isolation* defined as an objectively quantifiable  
8 variable of one's social network ties irrespective of its perceived quality and *living*  
9 *alone* as an objective characteristic of the living situation. Furthermore, we defined  
10 *loneliness* as a quality indicator representing the subjective emotional appraisal of the  
11 extent and quality of social relationships.<sup>2</sup> The meta-analyses differed with respect to  
12 whether they kept these three measures of social connection separate of whether they  
13 combined them (see Tab. 1).  
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#### 29 Figure 1 & Table 1

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31 A total of 276 primary studies were included in the 10 meta-analyses on  
32 physical health. However, there was some overlap in samples in meta-analyses that  
33 examined cardiovascular disease<sup>17,18</sup> and early mortality.<sup>4,19</sup> Steptoe and Kivimäki<sup>17</sup>  
34 and Valtorta et al.<sup>18</sup> shared one primary study. In addition, Holt-Lunstad et al.<sup>4</sup> and  
35 Rico-Urbe et al.<sup>19</sup> shared 12 primary studies. The reported results in Table 1 were  
36 based on sample sizes ranging from 1,451<sup>20</sup> to 113,374<sup>21</sup> participants, with three  
37 meta-analyses not reporting on the sample size. Five meta-analyses were based on  
38 longitudinal studies only, one on cross-sectional studies only, and the remaining four  
39 on a pooled combination of both cross-sectional and longitudinal studies.  
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41 Furthermore, social isolation and living alone were examined in 5 meta-analyses on  
42 physical health, respectively. Loneliness, on the other hand, was examined in 7 meta-  
43 analyses on mental health. Only one of these studies was conducted with children and  
44 adolescents.<sup>22</sup> The meta-analyses based on cross-sectional studies revealed a  
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3 significant association between social connection and the following health problems:  
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5 chronic physical complaints in children and adolescents,<sup>22</sup> coronary heart disease and  
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7 stroke,<sup>18</sup> and frailty in older male (but not female) adults.<sup>21</sup> Additionally, social  
8  
9 connection was associated with malnutrition<sup>23</sup> and vaccine uptake amongst older  
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11 adults.<sup>24</sup> One meta-analysis<sup>20</sup> reported mostly non-significant results on a positive  
12  
13 association between social connection and inflammation (acute-phase C-reactive  
14  
15 protein and fibrinogen). The meta-analyses conducted with longitudinal studies  
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17 indicate that social connection is associated with increased risk of cardiovascular  
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19 disease,<sup>17</sup> early mortality,<sup>4,19</sup> and hospital readmission in heart failure patients.<sup>25</sup>  
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24 The 15 meta-analyses on mental health were based on a total of 416 primary  
25  
26 studies. The reported results are based on sample sizes ranging from 1,345<sup>26</sup> to  
27  
28 2,330,163<sup>27</sup> participants, with one meta-analysis failing to report on the sample size.  
29  
30 There was some overlap in samples in the four meta-analyses focusing on cognitive  
31  
32 functioning or risk of dementia.<sup>27-30</sup> Kuiper et al.<sup>29</sup> shared two primary studies with  
33  
34 Evans et al.<sup>28</sup>, four with Lara et al.<sup>30</sup>, and three with Penninkilampi et al.<sup>27</sup>  
35  
36 Penninkilampi et al.<sup>27</sup> further shared two primary studies Lara et al.<sup>30</sup> Four of the 15  
37  
38 meta-analyses provided longitudinal data only, one provided cross-sectional data  
39  
40 only, and the remaining ten meta-analyses reported on both cross-sectional and  
41  
42 longitudinal studies. In addition, social isolation, living alone, and loneliness were  
43  
44 examined in 5, 5, and 10 meta-analyses on mental health, respectively. Three meta-  
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46 analyses focused on studies with children and adolescents.<sup>31-33</sup> The included meta-  
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48 analyses based on cross-sectional designs reported a significant positive association  
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50 between social connection and late-life suicidal ideation,<sup>34</sup> depression in adults,<sup>35</sup> late  
51  
52 life depression,<sup>26</sup> psychosis,<sup>31,36,37</sup> smoking behavior in adolescents,<sup>32</sup> depression and  
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54 social anxiety in childhood and adolescence,<sup>31,33</sup> and social anxiety disorder in  
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3 adults.<sup>38</sup> The meta-analyses based on longitudinal studies suggest that social  
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5 connection is associated with higher risk of depression in adults,<sup>39</sup> post-acute  
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7 coronary syndrome depression,<sup>40</sup> and dementia and cognitive impairment in later  
8  
9 life.<sup>27,28,30,29</sup> See Table 1 for detailed information.

### 12 Study quality

13  
14 The Intraclass Correlation Coefficient (ICC) of the global quality ratings among the  
15  
16 two raters was .83, 95% CI = .62 – .93, indicating good inter-rater reliability. Study  
17  
18 quality was very heterogeneous among meta-analyses both on physical and mental  
19  
20 health (see Tab. 1). With respect to the meta-analyses on physical health, the global  
21  
22 rating was high in 40%, medium in 10%, low in 40%, critically low in 10% of the  
23  
24 meta-analyses. In the 15 meta-analyses on mental health, study quality was rated as  
25  
26 high in 13%, medium in 27%, low in 27%, and critically low in 33% of the meta-  
27  
28 analyses. Among the AMSTAR-2 criteria, inadequate assessment of risk of bias  
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30 and/or lack of consideration of risk of bias represented the most frequent critical  
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32 weaknesses of included meta-analyses.  
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### 40 Discussion

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42 The review clearly demonstrates that lack of social connection is associated with  
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44 poorer health. This applies to a range of physical and mental health outcomes and has  
45  
46 been found in different populations and contexts. The evidence based on both cross-  
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48 sectional and longitudinal data is substantial for physical health outcome and even  
49  
50 more extensive for mental health outcomes. More specifically, social connection is  
51  
52 linked with chronic physical symptoms, frailty, coronary heart disease, stroke, early  
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54 mortality, malnutrition, hospital readmission in heart failure patients, and vaccine  
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56 uptake. With respect to mental health, social connection is linked with depression in  
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3 young and adult populations, social anxiety, psychosis, dementia and cognitive  
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5 impairment in later life, and late-life suicidal ideation.  
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## 10 Strengths and limitations

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12 This is, to our knowledge, the first review to synthesize the existing evidence that has  
13  
14 been reported in meta-analyses on the link between social connection and physical  
15  
16 and mental health outcomes. The findings reflect a reasonable number of meta-  
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18 analyses. Thus, the overall conclusions of this umbrella review are based on an  
19  
20 extensive body of empirical evidence.  
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24 However, the review also has several limitations. Firstly, we considered  
25  
26 different indicators of social connection, and our method did not allow us to identify  
27  
28 whether one indicator is more relevant than another. Secondly, half of the included  
29  
30 meta-analyses for both physical and mental health outcomes had an overall quality  
31  
32 rated on AMSTAR-2 as low or critically low, with inadequate consideration of risk of  
33  
34 bias being the most frequent critical flaw. Thirdly, the quality of the primary research  
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36 studies that went into the included meta-analyses also varied and their different  
37  
38 methodological shortcomings cannot be adequately considered in this review.  
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40 Fourthly, the results on the association between living alone and health outcomes  
41  
42 need to be interpreted with caution. As reported above, living alone is not necessarily  
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44 indicative of feeling lonely.<sup>3</sup> Finally, the review included a wide range of health  
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46 outcomes and did not quantify the strength of the associations for different outcomes.  
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## 54 Implications

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56 The review leaves little doubt that social connection is linked with poorer physical  
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58 and mental health. The findings are strengthened by the fact that several meta-  
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3 analyses were conducted with longitudinal studies. In particular, longitudinal data  
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5 indicate that social connection is associated with increased risk of several physical  
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7 and mental health outcomes, cardiovascular disease, hospital readmission in heart  
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9 failure patients, early mortality, cognitive impairment, and  
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11 depression.<sup>4,17,19,25,27,39,40,28,30,29</sup> However, the findings are all based on observational  
12  
13 studies and do not provide evidence on the causal direction of the association. Poor  
14  
15 physical and mental health can lead to lack of social connection, and lack of social  
16  
17 connection can lead to poorer health. For establishing a causal relationship and  
18  
19 examining the strength of the predictive relationship of social isolation and loneliness  
20  
21 with health outcomes experimental studies are required, which were not the subject of  
22  
23 this review.<sup>5,41</sup> Experimental research with animals, however, suggests that lack of  
24  
25 social connection increases mortality.<sup>42</sup> Furthermore, experimental studies with  
26  
27 humans indicate that randomly inducing loneliness or exclusion leads to different  
28  
29 health relevant physiological responses than being randomly assigned to a support  
30  
31 condition.<sup>42</sup> For most of the considered outcomes in this review, a causal effect of  
32  
33 social connection is plausible and likely to explain at least part of the identified  
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35 associations. The casual direction is definite in case of the greater risk of isolated  
36  
37 people to die early.<sup>4</sup> For an explanation of the damaging effect of social connection on  
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39 health outcomes, one may refer to different theoretical models. Theorists from  
40  
41 different perspectives have postulated that the impact of social connection on health is  
42  
43 mediated by impairments in social capital,<sup>43</sup> social control,<sup>44</sup> social identification,<sup>45</sup>  
44  
45 and social support.<sup>46</sup>

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47 Furthermore, some evidence from randomized controlled trials, however,  
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49 suggests that expanding the social connections of individuals, e.g., through  
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51 befriending programs, may indeed improve different health outcomes.<sup>47</sup> Altogether,  
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3 the literature on interventions to reduce loneliness and social isolation indicates that a  
4 policy focus on social connection is a cost-effective strategy for enhancing health at  
5 the population level due to the potential pay-offs in health care costs that would  
6 otherwise occur. Existing volunteer friendly visiting programs or psychosocial group  
7 interventions<sup>48</sup> may need to be redesigned to the point that they can be readily  
8 implemented in accordance with existing rules of physical distancing. Creative  
9 programs and interventions to foster social connections, including technology-based  
10 social networking programs, are needed.<sup>49</sup> Furthermore, existing policies should  
11 ensure that populations at greater risk, such as the poor, receive most support.<sup>1</sup>  
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24 All the included studies assessed social connection as it occurs in a normal  
25 societal context. Physical distancing as part of measures to limit the spread of  
26 COVID-19 is different from the situations considered in the research synthesized in  
27 this review. Firstly, for the vast majority of the population, the required physical  
28 distancing leads to a much more pronounced lack of social connection than what they  
29 have experienced before. Secondly, physical distancing is externally imposed and not  
30 due to individual life style decisions, lack of material means, poor social skills or  
31 other barriers to socialize. And thirdly, physical distancing is requested from people  
32 in an overall context of uncertainty that comes with further stressors, health risks, and  
33 often a reduced accessibility of health care.  
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47 It is important to note that physical distancing is a broad umbrella term that  
48 incorporates a wide range of potential measures, with highly divergent implications  
49 for social routines. It can include a full lock down and curfew, specific guidelines for  
50 meetings and gatherings of people, physical distancing in public, and a recommended  
51 or mandatory wearing of face masks. The type, degree, and duration of physical  
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3 distancing measures have been variable across countries and will affect how isolated  
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5 different groups in the population become.  
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8 One can only speculate as to whether and, if so, to what extent the increased  
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10 lack of social connections resulting from physical distancing measures in the current  
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12 situation will have an even greater impact on health outcomes than has been  
13  
14 suggested in this review. Arguably, an even greater impact can be expected for certain  
15  
16 risk groups, such as socially disadvantaged groups (e.g., individuals in need of mental  
17  
18 or physical health care or individuals with low income) who often face even more  
19  
20 economic adversity than before the pandemic. Further research is required to identify  
21  
22 which populations are at particular risk to suffer health problems as a result of  
23  
24 physical distancing and to explore whether the resulting lack of social connections  
25  
26 may – at least to some extent and in some people – be compensated through positive  
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28 effects of the pandemic, such as strengthened local communities and increased  
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30 options for online social activities.<sup>47,50</sup>  
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### 38 Conclusions

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40 In governmental decisions about future physical distancing measures, a potential  
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42 negative impact of the resulting physical isolation on the health of the population  
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44 needs to be considered. The existing literature suggests that social isolation and  
45  
46 loneliness may affect both physical and mental health outcomes and include an excess  
47  
48 mortality. However, the potential impact of physical distancing on social isolation and  
49  
50 loneliness and ultimately on physical and mental health outcomes need to be  
51  
52 thoroughly examined. In addition, the existing knowledge on the association between  
53  
54 social connection and physical and mental health should be considered in clinical  
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56 practice. Finally, more experimental research is needed to increase our understanding  
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3 of the causal relationship between social connection and physical and psychological  
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5 well-being.  
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3 **Figure Captions:** Fig.1. Flow diagram of study selection process.  
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9

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11 reviews and meta-analyses included in our overview.  
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14  
15 **Authors' Contributions:** NM had full access to all of the data in the study and takes  
16 responsibility for the integrity of the data and the accuracy of the data analysis.  
17 NM designed the search strategy with input from AK and TM. NM and AK carried  
18 out the literature searches and screening. NM, THH, and TM carried out the data  
19 extraction. AK and TM assessed the quality of the included meta-analyses. NM and  
20 SP wrote the first draft of the manuscript and all authors contributed to and have  
21 approved the final manuscript.  
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37 are included in this published article and supplementary material.  
38  
39 **Ethics approval and consent to participate:** This study did not require ethical approval.  
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43 **Consent for publication:** Not applicable.  
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46 **Patient and Public Involvement statement:** Not applicable.  
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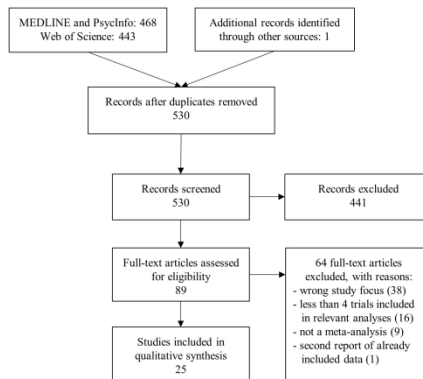


Fig. 1. Flow diagram of study selection process

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## MOOSE (Meta-analyses Of Observational Studies in Epidemiology) Checklist

A reporting checklist for Authors, Editors, and Reviewers of Meta-analyses of Observational Studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Reporting Criteria	Reported (Yes/No)	Reported on Page No.
<b>Reporting of Background</b>		
Problem definition		
Hypothesis statement		
Description of Study Outcome(s)		
Type of exposure or intervention used		
Type of study design used		
Study population		
<b>Reporting of Search Strategy</b>		
Qualifications of searchers (eg, librarians and investigators)		
Search strategy, including time period included in the synthesis and keywords		
Effort to include all available studies, including contact with authors		
Databases and registries searched		
Search software used, name and version, including special features used (eg, explosion)		
Use of hand searching (eg, reference lists of obtained articles)		
List of citations located and those excluded, including justification		
Method for addressing articles published in languages other than English		
Method of handling abstracts and unpublished studies		
Description of any contact with authors		
<b>Reporting of Methods</b>		
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested		
Rationale for the selection and coding of data (eg, sound clinical principles or convenience)		
Documentation of how data were classified and coded (eg, multiple raters, blinding, and interrater reliability)		
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)		

Reporting Criteria	Reported (Yes/No)	Reported on Page No.
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results		
Assessment of heterogeneity		
Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated		
Provision of appropriate tables and graphics		
<b>Reporting of Results</b>		
Table giving descriptive information for each study included		
Results of sensitivity testing (eg, subgroup analysis)		
Indication of statistical uncertainty of findings		
<b>Reporting of Discussion</b>		
Quantitative assessment of bias (eg, publication bias)		
Justification for exclusion (eg, exclusion of non-English-language citations)		
Assessment of quality of included studies		
<b>Reporting of Conclusions</b>		
Consideration of alternative explanations for observed results		
Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)		
Guidelines for future research		
Disclosure of funding source		

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