BMJ Open

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

Nexhmedin Morina ,[1] Ahlke Kip,[1] Thole Hilko Hoppen ,[1] Stefan Priebe,[2] Thomas Meyer[1]

¹Institute of Psychology, University of Münster, Münster, Germany
²Unit of Social and Community Psychiatry, Queen Mary University of London, Faculty of Medicine and Dentistry, London, UK

Correspondence to
Dr Nexhmedin Morina;
morina@uni-muenster.de

ABSTRACT

Background The imperative for physical distancing (mostly referred to as social distancing) during COVID-19 pandemic may deteriorate physical and mental health. We aimed at summarising 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 summarised 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.

BACKGROUND

The 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 types of physical distancing (mostly referred to as social distancing) making it impossible for people to maintain their normal social life.

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 standardised measure.
► Different indicators of social connection were included.
► The used method did not allow for a quantitative comparison of associations with health outcomes.

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 reimposed 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. While 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 a range of health outcomes.

A recent general population survey revealed that physical distancing can increase the lack of social connection.[1] 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.[2] Three indicators of social connection are commonly used in research: social isolation, living alone and loneliness.[3–5] Social isolation is a behavioural measure of a person's social network that can—at least in theory—be objectively quantified. Living alone describes a basic characteristic of an individual's social situation that can be associated with reduced social relationships but is not necessarily so.[2] Loneliness, on the other hand, is an individual's subjective assessment of the quality and quantity of their social relationships, reflecting a belief that they have too few or too poor relationships or both. Accordingly, social isolation and living alone represent structural indicators, whereas loneliness represents a quality measure of social connections.[2 5]

Although these three indicators capture distinct aspects of social connection, they commonly overlap and are associated with each other. Literature suggests that many individuals are socially isolated or lonely or both and that social isolation and loneliness may occur unequally across age groups. For example, Hawkley and colleagues[6] reported that loneliness decreased with age through the early 70s and then increased again. Several studies indicate that at least a fifth of adults report frequent loneliness,[7 8] and that more than 40% of adults aged 60 and older report feeling lonely.[9]

The extent to which individuals are socially isolated can have a profound impact on both physical and psychological well-being.[2] Social connection is thought to influence health through behavioural and biological pathways.[10] Several studies demonstrate that social connection is associated with health-relevant behaviours such as lack of physical activity, poorer sleep, obsessive behaviour as well as neuroendocrine dysregulation,[10] chronic allostatic load,[11] high blood pressure and poor immune functioning.[2 12 13] Furthermore, the magnitude of the effect of social connection on mortality may be equivalent to or exceed the impacts of deleterious behaviours such as excessive drinking or obesity.[4]

Physical distancing may increase lack of social connection and, therefore, have a negative impact on physical and mental health. For weighing up this potential impact in policy decisions, the existing evidence needs to be considered. Against this background, we conducted a systematic umbrella review to synthesise the evidence on the association between social connection and physical and mental health outcomes. As recommended by the WHO, we explored relevant meta-analyses by means of a rapid review of evidence.[14]

METHODS
To select relevant meta-analyses on the association between social connection and physical or mental health outcomes, we conducted a systematic search on 6 April 2020 using the databases Medline, PsycINFO and Web of Science. We conducted multifield searches (in titles, abstracts and key concepts) using the following terms: social isolation, loneliness, living alone, and meta-analy*, which we combined using the Boolean operators "or" plus "and". The full search string for Medline and PsycINFO was "((TI Loneliness OR AB loneliness OR SU Loneliness) OR (TI social isolation OR AB social isolation OR SU social isolation) OR (TI living alone OR AB living alone OR SU living alone)) AND (TI meta-analy* OR AB meta-analy* OR SU meta-analy*)".

Relevant outcomes included any sort of physical or mental health outcome. We applied no restrictions on age of participants, applied research designs (ie, cross-sectional, longitudinal) or publication language. Furthermore, we did not apply any limits. We first inspected the title and abstract of all hits and then read full texts of the hits that seemed to meet 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.[15]

Coding of trial characteristics
Systematic reviews with a quantitative synthesis of trial results (meta-analysis) were retained. Two reviewers (NM and 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 (social isolation/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 social isolation/living alone/loneliness and health outcomes (correlation values, ORs or HRs and the corresponding 95% CIs). With respect to the 95% CIs, both values greater than one (or both values less than one) represent a significant increase (or decrease) as a function of social connection.

Quality assessment
The quality of included systematic meta-analyses was independently assessed by two reviewers (AK and TM) using A Measurement Tool to Assess Systematic Reviews—2 (AMSTAR-2).[16] Following the tool's guidelines, the raters assigned one of four global quality ratings (ie, high, moderate, low or critically low) after consideration of 16 potential critical and noncritical weaknesses. Items addressing the following criteria were considered as critical: clear research question including definitions of population, intervention, control group and outcomes, adequacy of the literature search and adequate assessment and/or consideration of risk of bias in the primary studies. Typically, high and moderate ratings reflect the presence of one or more noncritical weakness, while low and critically low ratings indicate one or more critical weaknesses. Any discrepancies among the independent raters were discussed until consensus was reached.
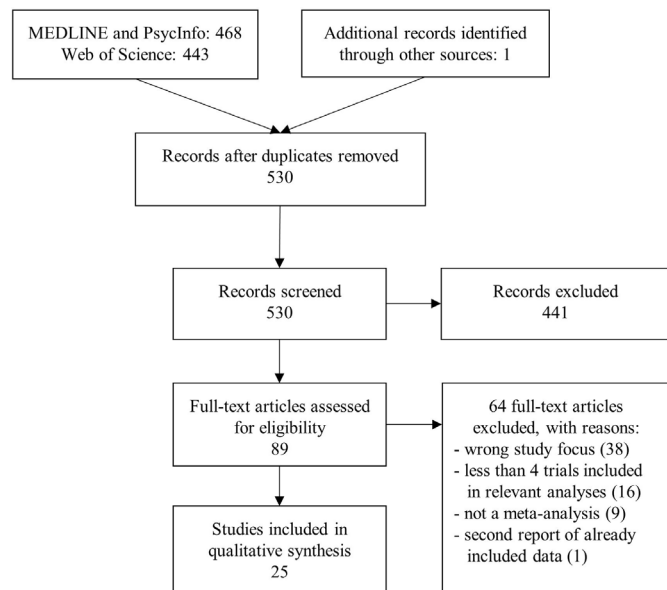
Figure 1 Flow diagram of study selection process.

RESULTS

Selection and characteristics of included studies

Figure 1 displays a PRISMA[15] flow diagram of the publication selection process. After reading 530 abstracts, 89 full-text publications were reviewed. The final review resulted in 25 meta-analyses. Relevant characteristics of these meta-analyses are summarised in table 1.

All publications were journal articles in English. Ten meta-analyses reported associations of social isolation, living alone and loneliness with physical health outcomes and 15 with mental health outcomes. Different indicators of social connection were measured in the included studies. We considered as structural indicators of social connection: *social isolation* defined as an objectively quantifiable variable of one's social network ties irrespective of its perceived quality and *living alone* as an objective characteristic of the living situation. Furthermore, we defined *loneliness* as a quality indictor representing the subjective emotional appraisal of the extent and quality of social relationships.[2] The meta-analyses differed with respect to whether they kept these three measures of social connection separate of whether they combined them (see table 1).

A total of 276 primary studies were included in the 10 meta-analyses on physical health; however, there was some overlap in samples in meta-analyses that examined cardiovascular disease[17 18] and early mortality.[4 19] Steptoe and Kivimäki[17] and Valtorta et al[18] shared one primary study. In addition, Holt-Lunstad et al[4] and Rico-Uribe et al[19] shared 12 primary studies. The reported results in table 1 were based on sample sizes ranging from 1451[20] to 113,374[21] participants, with three meta-analyses not reporting on the sample size. Five meta-analyses were based on longitudinal studies only, one on cross-sectional studies only and the remaining four on a pooled combination of both cross-sectional and longitudinal studies. Furthermore, social isolation and living alone were examined in five

meta-analyses on physical health, respectively. Loneliness, on the other hand, was examined in seven meta-analyses on mental health. Only one of these studies was conducted with children and adolescents.[22] The meta-analyses based on cross-sectional studies revealed a significant association between social connection and the following health problems: chronic physical complaints in children and adolescents,[22] coronary heart disease and stroke[18] and frailty in older male (but not female) adults.[21] Additionally, social connection was associated with malnutrition[23] and vaccine uptake among older adults.[24] One meta-analysis[20] reported mostly nonsignificant results on a positive association between social connection and inflammation (acute-phase C reactive protein and fibrinogen). The meta-analyses conducted with longitudinal studies indicate that social connection is associated with increased risk of cardiovascular disease,[17] early mortality[4 19] and hospital readmission in patients with heart failure.[25]

The 15 meta-analyses on mental health were based on a total of 416 primary studies. The reported results are based on sample sizes ranging from 1345[26] to 2,330,163[27] participants, with one meta-analysis failing to report on the sample size. There was some overlap in samples in the four meta-analyses focusing on cognitive functioning or risk of dementia.[27–30] Kuiper et al[29] shared two primary studies with Evans et al,[28] four with Lara et al[30] and three with Penninkilampi et al.[27] Penninkilampi et al[27] and Lara et al[30] further shared two primary studies. Four of the 15 meta-analyses provided longitudinal data only, one provided cross-sectional data only and the remaining 10 meta-analyses reported on both cross-sectional and longitudinal studies. In addition, social isolation, living alone and loneliness were examined in 5, 5 and 10 meta-analyses on mental health, respectively. Three meta-analyses focused on studies with children and adolescents.[31–33] The included meta-analyses based on cross-sectional designs reported a significant positive association between social connection and late-life suicidal ideation,[34] depression in adults,[35] late life depression,[26] psychosis,[31 36 37] smoking behaviour in adolescents,[32] depression and social anxiety in childhood and adolescence[31 33] and social anxiety disorder in adults.[38] The meta-analyses based on longitudinal studies suggest that social connection is associated with higher risk of depression in adults,[39] postacute coronary syndrome depression[40] and dementia and cognitive impairment in later life.[27–30] See table 1 for detailed information.

Study quality

The intraclass correlation coefficient of the global quality ratings among the two raters was 0.83, 95% CI 0.62 to 0.93, indicating good inter-rater reliability. Study quality was very heterogeneous among meta-analyses both on physical and mental health (see table 1). With respect to the meta-analyses on physical health, the global rating was high in 40%, medium in 10%, low in 40%, critically low in 10% of the meta-analyses. In the 15 meta-analyses on mental health, study quality was rated as high in 13%,

Table 1 Overview of the included meta-analyses

Publication results:	Social connection	Clinical outcome	Study design	Age: M (SD), range, or cut-off	Literature search: timespan	Range of follow-up	N databases searched	Quality score
Studies on physical health								
Besora-Moreno et al[23]	Living alone	Malnutrition/ malnutrition risk	Cross-sectional	60+	01.2000–12.2018	n.a.	2	L
Results:	Living alone		Combined effect			OR=1.92 (95% CI: 1.73 to 2.14); k=10; N=9042		
Heidari Gorji et al[25]	Living alone, social isolation, loneliness	Hospital readmission in patients with heart failure	Longitudinal	70.87 (8.62)	Up to 11.2018	13 months	6	H
Results:	Any type of poor social connection		Combined effect			OR=1.55 (95% CI: 1.39 to 1.73); k=13; N=6468		
	Living alone or social isolation		Combined effect			OR=1.52 (95% CI: 1.24 to 1.86); k=6; N=3812		
	Loneliness		Combined effect			OR=1.63 (95% CI: 1.31 to 2.01); k=7; N=2656		
Holt-Lunstad et al[4]	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			OR=1.51 (95% CI: 1.32 to 1.74); k=20; N=n.r.		
	Living alone		Studies with multiple covariates			OR=1.32 (95% CI: 1.14 to 1.53); k=25; N=n.r.		
	Social isolation		Unadjusted studies			OR=1.83 (95% CI: 1.27 to 2.63); k=3; N=n.r.		
	Social isolation		Studies with multiple covariates			OR=1.29 (95% CI: 1.06 to 1.56); k=14; N=n.r.		
	Loneliness		Unadjusted studies			OR=1.49 (95% CI: 1.22 to 1.84); k=8; N=n.r.		
	Loneliness		Studies with multiple covariates			OR=1.26 (95% CI: 1.04 to 1.53); k=13; N=n.r.		
Jain et al[24]	Living alone	Reduced vaccine uptake in older adults	Cross-sectional*†	60+	Up to 02.2016	n.r.	2	M
Results:	Living alone		Seasonal influenza vaccine			OR=1.39 (95% CI: 1.16 to 1.68); k=9; N=40 551		
	Living alone		Pneumococcal vaccine			OR=1.71 (95% CI: 1.20 to 2.46); k=1; N=1702		
Kojima et al[21]	Living alone	Frailty in older adults	Cross-sectional† and longitudinal†	60+	2000–02.2019	n.r.	1	L
Results:	Living alone		Cross-sectional studies			OR=1.28 (95% CI: 1.13 to 1.45); k=44; N=1 13374		
			Subanalysis: only men			OR=1.71 (95% CI: 1.49 to 1.96); k=20; N=n.r.		
			Subanalysis: only women			OR=1.00 (95% CI: 0.83 to 1.20); k=22; N=n.r.		
			Subanalysis:≥60,<70 years old			OR=1.67 (95% CI: 1.51 to 1.86); k=4; N=n.r.		
			Subanalysis:≥80 years old			OR=0.96 (95% CI: 0.69 to 1.31); k=6; N=n.r.		
	Living alone		Longitudinal studies			OR=0.88 (95% CI: 0.76 to 1.03); k=6; N=38549		
Maes et al[22]	Loneliness	Chronic physical conditions in children/ adolescents	Cross-sectional*	Children<12 and adolescents<21	1987–06.2016	n.r.	4	L

Table 1 Continued

Publication results:	Social connection	Clinical outcome	Study design	Age: M (SD), range, or cut-off	Literature search: timespan	Range of follow-up	N databases searched	Quality score
Results:	Loneliness		Combined effect (excluding three outliers)			g=0.17 (95% CI: 0.03 to 0.30); k=40; N=3981		
			Subanalysis: control group studies			g=0.13 (95% CI: 0.01 to 0.26); k=23; N=2995		
			Subanalysis: hearing/visual problems			g=0.43 (n.r.); k=8; N=770		
Rico-Uribe et al[19]	Loneliness	Early mortality	Longitudinal†	Mainly 50+	Up to 06.2016	n.r.	4	H
Results:	Loneliness		Combined effect			HR=1.22 (95% CI: 1.10 to 1.35); k=31; N=77220		
			Subanalysis: only men			HR=1.44 (95% CI: 1.19 to 1.76); k=7; N=5815		
			Subanalysis: only women			HR=1.26 (95% CI: 1.07 to 1.48); k=7; N=10248		
Smith et al[20]	Social isolation, loneliness	Inflammation markers	Cross-sectional*	16+	Up to 07.2019	n.r.	5	H
Results:	Social isolation		C reactive protein: unadjusted studies			r=0.186 (95% CI: .063 to 0.303); k=7; N=41126		
			C reactive protein: adjusted studies			r=0.021 (95% CI: .051 to 0.092); k=11; N=41911		
			Fibrinogen: unadjusted studies			r=0.103 (95% CI: 0.043 to 0.163); k=6; N=15421		
			Fibrinogen: adjusted studies			r=0.039 (95% CI: 0.011 to 0.067); k=6; N=22161		
			Interleukin-6: unadjusted studies			r=0.267 (95% CI: -0.341 to 0.718); k=4; N=12291		
			Interleukin-6: adjusted studies			r=-.003 (95% CI: -0.148 to 0.141); k=6; N=14243		
Results:	Loneliness		C reactive protein: unadjusted studies			r=0.047 (95% CI: -0.003 to 0.098); k=8; N=17835		
			C reactive protein: adjusted studies			r=0.023 (95% CI: -0.018 to 0.065); k=6; N=19292		
			Fibrinogen: unadjusted studies			r=0.006 (95% CI: -0.057 to 0.070); k=3; N=1806		
			Fibrinogen: adjusted studies			r=0.037 (95% CI: -0.015 to 0.089); k=4; N=7672		
			Interleukin-6: unadjusted studies			r=0.082 (95% CI: -0.001 to 0.163); k=4; N=4219		
			Interleukin-6: adjusted studies			r=0.070 (95% CI: .015 to 0.124); k=2; N=1451		
Steptoe and Kivimäki[17]	Social isolation, loneliness	Cardiovascular disease	Longitudinal†	n.r.	Up to 2011	n.r.	n.r.	CL
Results:	Social isolation or loneliness		Combined effect			RR=1.51 (95% CI: 1.21 to 1.88); k=7; N=n.r.		
Valtorta et al[18]	Social isolation, loneliness	Coronary heart disease and stroke	Longitudinal†	18+	Up to 05.2015	3 to 21 years	16	H
Results:	Social isolation or loneliness	Coronary heart disease				RR=1.29 (95% CI: 1.04 to 1.59); k=11; N=n.r.		
	Social isolation	Stroke incidence				RR=1.32 (95% CI: 1.04 to 1.68); k=9; N=n.r.		

Continued

Table 1 Continued

Publication results:	Social connection	Clinical outcome	Study design	Age: M (SD), range, or cut-off	Literature search: timespan	Range of follow-up	N databases searched	Quality score
Studies on mental health								
Chang et al[34]	Living alone, loneliness	Late-life suicidal ideation	Cross-sectional*‡	50+	01.2000–11.2016	n.r.	7	L
Results:	Living alone		Combined effect			OR=1.38 (95% CI: 1.19 to 1.61); k=8; N=102401		
	Loneliness		Combined effect			OR=2.24 (95% CI: 1.73 to 2.90); k=3; N=58482		
Chatterjee et al[39]	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			OR=1.68 (99.5% CI:1.13 to 2.49); k=4; N=27395		
Chau et al[37]	Loneliness	Psychosis	Cross-sectional*‡	Adults (mainly)	Up 10.2018	n.r.	5	M
Results:	Loneliness		Positive symptoms			r=0.302 (95% CI: 0.243 to 0.359); k=30; N=17832		
			Subanalysis: clinical populations			r=0.149 (95% CI: 0.057 to 0.238); k=14; N=n.r.		
			Subanalysis: non-clinical populations			r=0.389 (95% CI: 0.232 to 0.526); k=5; N=n.r.		
			Subanalysis: mixed populations			r=0.366 (95% CI: 0.308 to 0.422); k=12; N=n.r.		
			Subanalysis: Paranoia			r=0.448 (95% CI: 0.371 to 0.519); k=7; N=n.r.		
			Subanalysis: Hallucinations			r=0.201 (95% CI: 0.101–.297); k=10; N=n.r.		
	Loneliness		Negative psychotic symptoms			r=0.347 (95% CI: 0.239–.446); k=15; N=5567		
			Subanalysis: clinical populations			r=0.127 (95% CI: 0.029 to 0.223); k=9; N=n.r.		
			Subanalysis: non-clinical populations			r=0.479 (95% CI: 0.351 to 0.589); k=4; N=n.r.		
			Subanalysis: mixed populations			r=0.547 (95% CI: 0.464 to 0.620); k=2; N=n.r.		
Choi and Smith[32]	Social isolation	Adolescents' smoking behaviours	Cross-sectional	<19	n.r.	n.a.	3	CL
Results:	Social isolation		Network position: isolate vs member			OR=1.55 (95% CI: 1.32 to 1.81); k=8; N=5067		
			Network position: isolated vs liaison			OR=1.49 (95% CI: 1.07 to 2.07); k=8; N=5067		
Erzen and Çıkrıkçı[35]	Loneliness	Depression	Cross-sectional*	Adults	Up to 01.2018	n.r.	2	CL
Results:	Loneliness		Combined effect			r=0.50 (95% CI: 0.44 to 0.55); k=88; N=40068		
			Subanalysis: clinical populations			r=0.54 (95% CI: 0.38 to 0.67); k=10; N=n.r.		
			Subanalysis: other populations			r=0.44 (95% CI: 0.16 to .66); k=12; N=n.r.		
Evans et al[28]	Social isolation	Cognitive functioning	Longitudinal	50+	Up to 01.2018	2–24 years	4	M

Continued

Table 1 Continued

Publication results:	Social connection	Clinical outcome	Study design	Age: M (SD), range, or cut-off	Literature search: timespan	Range of follow-up	N databases searched	Quality score
Results:	Social isolation		Combined effect			r=0.054 (95% CI: 0.043 to 0.065); k=51; N=102035		
			Subanalysis: global measures			r=0.061 (95% CI: 0.044 to 0.079); k=43; N=74933		
			Subanalysis: memory			r=0.050 (95% CI: 0.028 to 0.072); k=13; N=35230		
			Subanalysis: executive functioning			r=0.031 (95% CI: 0.015 to 0.047); k=7; N=30528		
Kuiper et al[29]	Social isolation, loneliness	Risk of dementia	Longitudinal†	60+	Up to 07.2012	2 to 15 years	3	M
Results:	Social isolation		Low social network size			RR=1.17 (95% CI: 0.92 to 1.48); k=5; N=7749		
	Social isolation		Low level of participation			**RR=1.41** (95% CI: 1.13 to 1.75); k=6; N=7687		
	Social isolation		Low frequency of contacts			**RR=1.57** (95% CI: 1.32 to 1.85); k=8; N=15762		
	Loneliness		Feeling lonely			**RR=1.58** (95% CI: 1.19 to 2.09); k=3; N=3252		
	Loneliness		Low satisfaction with social network			RR=1.25 (95% CI: 0.96 to 1.62); k=4; N=6207		
Lara et al[30]	Loneliness	Dementia and mild cognitive impairment	Longitudinal†	50+	Up to 11.2018	n.r.	6	H
Results:	Loneliness		Combined effect			**RR=1.26** (95% CI: 1.14 to 1.40); k=8; N=33555		
Maes et al[31]	Loneliness	Social anxiety in children/adolescents	Cross-sectional and longitudinal	15.59 (4.27)	1981–06.2016	1.25 to 72 months	4	CL
Results:	Loneliness		Cross-sectional effects			r=0.46 (95% CI: 0.43 to 0.48); k=98; N=41776		
	Loneliness		Longitudinal/cross-lagged effects			r=0.12 (95% CI: 0.04 to 0.21); k=10; N=3995		
Mahon et al[33]	Loneliness	Depression and social anxiety in adolescence	Cross-sectional*	Adolescents (11–23) 1980–2004		n.r.	4	CL
Results:	Loneliness		Depression			r=0.61 (n.r); k=30; N=17691		
	Loneliness		Subanalysis: outliers removed			r=0.55 (n.r); k=18; N=6058		
	Loneliness		Anxiety			r=0.41 (n.r); k=12; N=3853		
	Loneliness		Subanalysis: outliers removed			r=0.35 (n.r); k=10; N=2705		
Michalska da Rocha et al[36]	Loneliness	Psychosis	Cross-sectional*‡	Adults	Up to 02.2016	n.r.	4	H
Results:	Loneliness		Combined effect			r=0.32 (95% CI: 0.20 to 0.44); k=13; N=15647		
Penninkilampi et al[27]	Living alone, social isolation, loneliness	Risk of dementia	Longitudinal and case-control	60+	01.2012–05.2017	5.9 years	8	L

Continued

Table 1 Continued

Publication results:	Social connection	Clinical outcome	Study design	Age: M (SD), range, or cut-off	Literature search: timespan	Range of follow-up	N databases searched	Quality score
Results:	Any type of poor social connection		Combined effect			RR=1.41 (95% CI: 1.21 to 1.65); k=15; N=2330163		
	Social isolation		Combined effect			RR=1.59 (95% CI: 1.31 to 1.93); k=6; N=25373		
	Living alone		Combined effect			RR=1.41 (95% CI: 1.07 to 1.84); k=4; N=5401		
	Loneliness		Combined effect			RR=1.38 (95% CI: 0.98 to 1.94); k=4; N=4698		
Teo et al[38]	Living alone	Social anxiety disorder	Cross-sectional*	Adults (mainly)	01.1980–02.2011	n.r.	4	M
Results:	Living alone		Combined effect			OR=1.73 (95% CI: 1.34 to 2.24); k=4; N=12831		
	Living alone		Subanalysis: large survey studies			OR=1.70 (95% CI: 1.38 to 2.10); k=3; N=12773		
Xiu-Ying et al[26]	Living alone	Late life depression	Cross-sectional and longitudinal	55+	1966–08.2007	n.r.	3	CL
Results:	Living alone		Cross-sectional effects			OR=1.44 (95% CI: 1.04 to 1.99); k=16; N=34090		
	Living alone		Subanalysis: versus living with family			OR=2.59 (95% CI: 1.60 to 4.20); k=5; N=12537		
	Living alone		Longitudinal/cross-lagged effects			RR=1.27 (95% CI: 0.89 to 1.80); k=4; N=1345		
Yuan et al[40]	Living alone	Postacute coronary syndrome depression	Longitudinal and case-control	19+	01.1996–03.2018	n.r.	4	L
Results:	Living alone		Combined effect			OR=1.17 (95% CI: 1.12 to 1.22); k=11; N=n.r.		

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

*These studies included different study designs and extracted cross-sectional data or aggregated longitudinal and cross-sectional data.

†Effect sizes with adjustment for confounders were preferred in this meta-analysis.

‡Effect sizes with no or minimal adjustment were preferred in this meta-analysis.

CL, critically low; H, high; L, low; M, moderate; n.a., not applicable; n.r., not reported.

medium in 27%, low in 27% and critically low in 33% of the meta-analyses. Among the AMSTAR-2 criteria, inadequate assessment of risk of bias and/or lack of consideration of risk of bias represented the most frequent critical weaknesses of included meta-analyses.

DISCUSSION

The review clearly demonstrates that lack of social connection 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 based on both cross-sectional and longitudinal data is substantial for physical health outcome and even more extensive for mental health outcomes. More specifically, social connection is linked with chronic physical symptoms, frailty, coronary heart disease, stroke, early mortality, malnutrition, hospital readmission in patientswith heart failure and vaccine uptake. With respect to mental health, social connection 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 synthesise the existing evidence that has been reported in meta-analyses on the link between social connection and physical and mental health outcomes. The findings reflect a reasonable number of meta-analyses. Thus, the overall conclusions of this umbrella review are based on an extensive body of empirical evidence.

However, the review also has several limitations. First, we considered different indicators of social connection, and our method did not allow us to identify whether one indicator is more relevant than another. Second, 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. Third, the quality of the primary research studies that went into the included meta-analyses also varied and their different methodological shortcomings cannot be adequately considered in this review. Fourth, the results on the association between living alone and health outcomes need to be interpreted with caution. As reported above, living alone is not necessarily indicative of feeling lonely.[3] Finally, the review included a wide range of health outcomes and did not quantify the strength of the associations for different outcomes.

Implications

The review leaves little doubt that social connection is linked with poorer physical and mental health. The findings are strengthened by the fact that several meta-analyses were conducted with longitudinal studies. In particular, longitudinal data indicate that social connection is associated with increased risk of several physical and mental

health outcomes, cardiovascular disease, hospital readmission in patientswith heart failure, early mortality, cognitive impairment and depression.[4 17 19 25 27–30 39 40] However, the findings are all based on observational studies and do not provide evidence on the causal direction of the association. Poor physical and mental health can lead to lack of social connection, and lack of social connection can lead to poorer health. For establishing a causal relationship and examining the strength of the predictive relationship of social isolation and loneliness with health outcomes experimental studies are required, which were not the subjects of this review.[5 41] Experimental research with animals, however, suggests that lack of social connection increases mortality.[42] Furthermore, experimental studies with humans indicate that randomly inducing loneliness or exclusion leads to different health-relevant physiological responses than being randomly assigned to a support condition.[42] For most of the considered outcomes in this review, a causal effect of social connection is plausible and likely to explain at least part of the identified associations. The casual direction is definite in case of the greater risk of isolated people to die early.[4] For an explanation of the damaging effect of social connection on health outcomes, one may refer to different theoretical models. Theorists from different perspectives have postulated that the impact of social connection on health is mediated by impairments in social capital,[43] social control,[44] social identification[45] and social support.[46]

Furthermore, some evidence from randomised controlled trials, however, suggests that expanding the social connections of individuals, for example, through befriending programmes, may indeed improve different health outcomes.[47] Altogether, the literature on interventions to reduce loneliness and social isolation indicates that a policy focus on social connection is a cost-effective strategy for enhancing health at the population level due to the potential pay-offs in healthcare costs that would otherwise occur. Existing volunteer friendly visiting programmes or psychosocial group interventions[48] may need to be redesigned to the point that they can be readily implemented in accordance with existing rules of physical distancing. Creative programmes and interventions to foster social connections, including technology-based social networking programmes, are needed.[49] Furthermore, existing policies should ensure that populations at greater risk, such as the poor, receive most support.[1]

All the included studies assessed social connection as it occurs in a normal societal context. Physical distancing as part of measures to limit the spread of COVID-19 is different from the situations considered in the research synthesised in this review. First, for the vast majority of the population, the required physical distancing leads to a much more pronounced lack of social connection than what they have experienced before. Second, physical distancing is externally imposed and not due to individual lifestyle decisions, lack of material means, poor social skills or other barriers to socialise. And third, physical distancing is

requested from people in an overall context of uncertainty that comes with further stressors, health risks and often a reduced accessibility of healthcare.

It is important to note that physical distancing is a broad umbrella term that incorporates a wide range of potential measures, with highly divergent implications for social routines. It can include a full lock down and curfew, specific guidelines for meetings and gatherings of people, physical distancing in public and a recommended or mandatory wearing of face masks. The type, degree and duration of physical distancing measures have been variable across countries and will affect how isolated different groups in the population become.

One can only speculate as to whether and, if so, to what extent the increased lack of social connections resulting from physical distancing measures in the current situation will have an even greater impact on health outcomes than has been suggested in this review. Arguably, an even greater impact can be expected for certain risk groups such as socially disadvantaged groups (eg, individuals in need of mental or physical healthcare or individuals with low income) who often face even more economic adversity than before the pandemic. Further research is required to identify which populations are at particular risk to suffer health problems as a result of physical distancing and to explore whether the resulting lack of social connections may—at least to some extent and in some people—be compensated through positive effects of the pandemic, such as strengthened local communities and increased options for online social activities.[47 50]

CONCLUSIONS

In governmental decisions about future physical distancing measures, a potential negative impact of the resulting physical isolation on the health of the population needs to be considered. The existing literature suggests that social isolation and loneliness may affect both physical and mental health outcomes and include an excess mortality. However, the potential impact of physical distancing on social isolation and loneliness and ultimately on physical and mental health outcomes need to be thoroughly examined. In addition, the existing knowledge on the association between social connection and physical and mental health should be considered in clinical practice. Finally, more experimental research is needed to increase our understanding of the causal relationship between social connection and physical and psychological well-being.

ORCID iDs
Nexhmedin Morina http://orcid.org/0000-0002-2331-9140
Thole Hilko Hoppen http://orcid.org/0000-0002-6050-8696

REFERENCES

1 Holmes EA, O'Connor RC, Perry VH, et al. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *Lancet Psychiatry* 2020;7:547–60.
2 Holt-Lunstad J. Why social relationships are important for physical health: a systems approach to understanding and modifying risk and protection. *Annu Rev Psychol* 2018;69:437–58.
3 Perissinotto CM, Covinsky KE, alone L. Living alone, socially isolated or Lonely—What are we measuring? *J Gen Intern Med* 2014;29:1429–31.
4 Holt-Lunstad J, Smith TB, Baker M, et al. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect Psychol Sci* 2015;10:227–37.
5 National Academies of Sciences, Engineering, and Medicine. *Social isolation and loneliness in older adults: opportunities for the health care system*. Washington, DC: National Academies Press, 2020.
6 Hawkley LC, Wroblewski K, Kaiser T, et al. Are U.S. older adults getting lonelier? age, period, and cohort differences. *Psychol Aging* 2019;34:1144–57.
7 DiJulio B, Hamel L, Muñana C. *Loneliness and social isolation in the United States, the United Kingdom, and Japan: an international survey*. The Economist & Kaiser Family Foundation, 2018.
8 Anderson GO, Thayer CE. *Loneliness and social connections: a national survey of adults 45 and older*. Washington, DC: AARP Foundation, 2018.
9 Perissinotto CM, Stijacic Cenzer I, Covinsky KE. Loneliness in older persons: a predictor of functional decline and death. *Arch Intern Med* 2012;172:1078–84.
10 Cacioppo JT, Cacioppo S, Capitanio JP, et al. The neuroendocrinology of social isolation. *Annu Rev Psychol* 2015;66:733–67.
11 Seeman TE, Singer BH, Ryff CD, et al. Social relationships, gender, and allostatic load across two age cohorts. *Psychosom Med* 2002;64:395–406.
12 Hawkley LC, Capitanio JP, isolation Psocial. Perceived social isolation, evolutionary fitness and health outcomes: a lifespan approach. *Philos Trans R Soc Lond B Biol Sci* 2015;370:20140114.
13 Grant N, Hamer M, Steptoe A. Social isolation and stress-related cardiovascular, lipid, and cortisol responses. *Ann Behav Med* 2009;37:29–37.
14 Tricco AC, Langlois EV, Straus SE others. *Rapid reviews to strengthen health policy and systems: a practical guide*. Geneva: World Health Organization, 2017.
15 Moher D, Liberati A, Tetzlaff J. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;151:264–9.
16 Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;358:j4008.

17 Steptoe A, Kivimäki M. Stress and cardiovascular disease: an update on current knowledge. *Annu Rev Public Health* 2013;34:337–54.

18 Valtorta NK, Kanaan M, Gilbody S, *et al*. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. *Heart* 2016;102:1009–16.

19 Rico-Uribe LA, Caballero FF, Martín-María N, *et al*. Association of loneliness with all-cause mortality: a meta-analysis. *PLoS One* 2018;13:e0190033.

20 Smith KJ, Gavey S, RIddell NE, *et al*. The association between loneliness, social isolation and inflammation: a systematic review and meta-analysis. *Neurosci Biobehav Rev* 2020;112:519–41.

21 Kojima G, Taniguchi Y, Kitamura A, *et al*. Is living alone a risk factor of frailty? A systematic review and meta-analysis. *Ageing Res Rev* 2020;59:101048.

22 Maes M, Van den Noortgate W, Fustolo-Gunnink SF, *et al*. Loneliness in children and adolescents with chronic physical conditions: a meta-analysis. *J Pediatr Psychol* 2017;42:622–35.

23 Besora-Moreno M, Llauradó E, Tarro L, *et al*. Social and economic factors and malnutrition or the risk of malnutrition in the elderly: a systematic review and meta-analysis of observational studies. *Nutrients* 2020;12:737.

24 Jain A, van Hoek AJ, Boccia D, *et al*. Lower vaccine uptake amongst older individuals living alone: a systematic review and meta-analysis of social determinants of vaccine uptake. *Vaccine* 2017;35:2315–28.

25 Heidari Gorji MA, Fatahian A, Farsavian A. The impact of perceived and objective social isolation on hospital readmission in patients with heart failure: a systematic review and meta-analysis of observational studies. *Gen Hosp Psychiatry* 2019;60:27–36.

26 Xiu-Ying H, Qian C, Xiao-Dong P, *et al*. Living arrangements and risk for late life depression: a meta-analysis of published literature. *Int J Psychiatry Med* 2012;43:19–34.

27 Penninkilampi R, Casey A-N, Singh MF, *et al*. The association between social engagement, loneliness, and risk of dementia: a systematic review and meta-analysis. *JAD* 2018;66:1619–33.

28 Evans IEM, Martyr A, Collins R, *et al*. Social isolation and cognitive function in later life: a systematic review and meta-analysis. *J Alzheimers Dis* 2019;70:S119–44.

29 Kuiper JS, Zuidersma M, Oude Voshaar RC, *et al*. Social relationships and risk of dementia: a systematic review and meta-analysis of longitudinal cohort studies. *Ageing Res Rev* 2015;22:39–57.

30 Lara E, Martín-María N, De la Torre-Luque A, *et al*. Does loneliness contribute to mild cognitive impairment and dementia? A systematic review and meta-analysis of longitudinal studies. *Ageing Res Rev* 2019;52:7–16.

31 Maes M, Nelemans SA, Danneel S, *et al*. Loneliness and social anxiety across childhood and adolescence: multilevel meta-analyses of cross-sectional and longitudinal associations. *Dev Psychol* 2019;55:1548–65.

32 Choi HJ, Smith RA, Members SRA. Members, isolates, and liaisons: meta-analysis of adolescents' network positions and their smoking behavior. *Subst Use Misuse* 2013;48:612–22.

33 Mahon NE, Yarcheski A, Yarcheski TJ, *et al*. A meta-analytic study of predictors for loneliness during adolescence. *Nurs Res* 2006;55:308–15.

34 Chang Q, Chan CH, Yip PSF. A meta-analytic review on social relationships and suicidal ideation among older adults. *Soc Sci Med* 2017;191:65–76.

35 Erzen E, Çikrikci Özkan, Ö Çikrikci. The effect of loneliness on depression: a meta-analysis. *Int J Soc Psychiatry* 2018;64:427–35.

36 Michalska da Rocha B, Rhodes S, Vasilopoulou E, *et al*. Loneliness in psychosis: a Meta-analytical review. *Schizophr Bull* 2018;44:114–25.

37 Chau AKC, Zhu C, So SH-W. Loneliness and the psychosis continuum: a meta-analysis on positive psychotic experiences and a meta-analysis on negative psychotic experiences. *Int Rev Psychiatry* 2019;31:471–90.

38 Teo AR, Lerrigo R, Rogers MAM. The role of social isolation in social anxiety disorder: a systematic review and meta-analysis. *J Anxiety Disord* 2013;27:353–64.

39 Chatterjee A, Banerjee S, Stein C, *et al*. Risk factors for depression among civilians after the 9/11 world Trade center terrorist attacks: a systematic review and meta-analysis. *PLoS Curr* 2018;10:ecurrents. dis.6a00b40c8ace0a6a0017361d7577c50a.

40 Yuan M-Z, Fang Q, Liu G-W, *et al*. Risk factors for post-acute coronary syndrome depression: a meta-analysis of observational studies. *J Cardiovasc Nurs* 2019;34:60–70.

41 Ong AD, Uchino BN, Wethington E. Loneliness and health in older adults: a mini-review and synthesis. *Gerontology* 2016;62:443–9.

42 Howick J, Kelly P, Kelly M. Establishing a causal link between social relationships and health using the Bradford Hill guidelines. *SSM Popul Health* 2019;8:100402.

43 Szreter S, Woolcock M. Health by association? social capital, social theory, and the political economy of public health. *Int J Epidemiol* 2004;33:650–67.

44 Craddock E, vanDellen MR, Novak SA, *et al*. Influence in relationships: a meta-analysis on health-related social control. *Basic Appl Soc Psych* 2015;37:118–30.

45 Postmes T, Wichmann LJ, van Valkengoed AM, *et al*. Social identification and depression: a meta-analysis. *Eur J Soc Psychol* 2019;49:110–26.

46 Uchino BN, Bowen K, de GRK. Social support and physical health: Models, mechanisms, and opportunities. In: *Principles and concepts of behavioral medicine*. Springer, 2018: 341–72.

47 Siette J, Cassidy M, Priebe S. Effectiveness of befriending interventions: a systematic review and meta-analysis. *BMJ Open* 2017;7:e014304.

48 Fakoya OA, McCorry NK, Donnelly M. Loneliness and social isolation interventions for older adults: a scoping review of reviews. *BMC Public Health* 2020;20:1–14.

49 Czaja SJ, Boot WR, Charness N, *et al*. Improving social support for older adults through technology: findings from the prism randomized controlled trial. *Gerontologist* 2018;58:467–77.

50 Steffens NK, LaRue CJ, Haslam C, *et al*. Social identification-building interventions to improve health: a systematic review and meta-analysis. *Health Psychol Rev* 2021;15:85–112.