

**Management of Social Isolation and Loneliness in Community Dwelling Older Adults: Protocol
for a Network Meta-analysis of Randomized Controlled Trials**

Supplementary Files

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Supplementary file 1: PRISMA NMA checklist

Table A.1: PRISMA NMA checklist of items to include when reporting a systematic review involving a network meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review <i>incorporating a network meta-analysis (or related form of meta-analysis)</i> .	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: Background: main objectives Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal; and <i>synthesis methods, such as network meta-analysis</i> . Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; <i>treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.</i> Discussion/Conclusions: limitations; conclusions and implications of findings. Other: primary source of funding; systematic review registration number with registry name.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, <i>including mention of why a network meta-analysis has been conducted.</i>	5-6
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. <i>Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).</i>	8-12 Additional file 2

Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	12-13
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	12-13 Additional file 3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	13-15
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	13-15
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	13-15
Geometry of the network	S1	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	16
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	15-16
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). <i>Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.</i>	16-18
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: <ul style="list-style-type: none"> • <i>Handling of multi-arm trials;</i> • <i>Selection of variance structure;</i> • <i>Selection of prior distributions in Bayesian analyses; and</i> • <i>Assessment of model fit.</i> 	17-18
Assessment of Inconsistency	S2	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	17-18

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	15
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: <ul style="list-style-type: none"> • Sensitivity or subgroup analyses; • Meta-regression analyses; • <i>Alternative formulations of the treatment network; and</i> • <i>Use of alternative prior distributions for Bayesian analyses (if applicable).</i> 	19-20
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	n/a
Presentation of network structure	S3	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	n/a
Summary of network geometry	S4	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	n/a
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	n/a
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	n/a
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. <i>Modified approaches may be needed to deal with information from larger networks.</i>	n/a
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. <i>In larger networks, authors may focus on comparisons versus a particular comparator (e.g.</i>	n/a

		<i>placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.</i>	
Exploration for inconsistency	S5	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, <i>P</i> values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	n/a
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, <i>alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth</i>).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	21
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). <i>Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).</i>	21-22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	22
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	23

PICOS = population, intervention, comparators, outcomes, study design.

* Text in italics indicateS wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.

† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

Supplementary file 2: PICOS statement

PICOS	Inclusion	Exclusion
Participants	<ul style="list-style-type: none"> <input type="checkbox"/> Community-dwelling older adults ≥ 60 years of age (If mean or median age of participants is 60 year or older, it can be included.) <input type="checkbox"/> Healthy or have a chronic disease, but mobile (i.e., older adults are able to walk independently with or without gait aid, or can self-propel wheelchair.) <input type="checkbox"/> A mild or moderate dementia or cognitive dysfunction 	<ul style="list-style-type: none"> <input type="checkbox"/> Adults < 60 years of age <input type="checkbox"/> Not community residing (inpatients, nursing home, hospital wards, or long-term care facilities) <input type="checkbox"/> Dementia or moderate to severe cognitive dysfunction (Mini-Mental State Examination (MMSE)<24, Montreal Cognitive Assessment (MoCA) <26, or Short Portable Mental Status Questionnaire (SPMSQ)>6) <input type="checkbox"/> Chronic diseases related to death or serious risk: cancer, AIDS (HIV), chronic heart failure, recent surgery or transplant or intractable rare disease <input type="checkbox"/> Unstable diseases such as bipolar disorder, active psychosis, or suicidal plans <input type="checkbox"/> Caregivers
Interventions	<ol style="list-style-type: none"> 1) Social activities (with others) and social/recreational services: social engagement (also, social involvement, social participation), social facilitation, social support (including emotional instrumental and informational support), psychotherapy (e.g., counselling therapy, music, art or animal intervention, etc.), and education program 2) Exercise programs: group exercise (e.g., tai-chi, aerobic or yoga class) and one-to-one/individual exercise (in gym, outdoor, home, web, telephone- 	<ul style="list-style-type: none"> <input type="checkbox"/> Pharmaceutical interventions including medications and nutritional supplements (vit D, calcium, or protein) for mental health, anxiety, or depression

	based, and etc.)	
	3) Health services: health care provision (e.g., care management, home visits from nurses or other professionals) and etc.	
	4) Befriending interventions: peer or partnership program, charity-funded friendship clubs and etc.	
	5) Leisure/skill development intervention: gardening programs, computer/internet use, voluntary work, holidays and sports (for hobby), productive activities (e.g., reading or engaging in hobbies), passive consumptive activities (e.g., watching TV or listening to radio) and etc.	
	6) Multicomponent/ Multifaced interventions: any combination of intervention (e.g., social activity combined with exercise programs or social/health service)	
Comparison intervention	<input type="checkbox"/> Usual care, a control, or placebo	
Outcomes	1) Loneliness (e.g., De Jong Gierveld Loneliness Scale, UCLA Loneliness Scale Version #, other (such as Italian) Loneliness Scale or loneliness from The Philadelphia Geriatric Morale Scale (PGMS))	<input type="checkbox"/> Social or family wellbeing <input type="checkbox"/> Happiness <input type="checkbox"/> Satisfaction with life <input type="checkbox"/> Depression
	2) Social isolation (e.g., the Turkish version of the Nottingham Health Profile questionnaire)	
	3) Social support (e.g., Revised Social Support Questionnaire, Multidimensional Scale of Perceived Social Support (MSPSS), Duke Social Support Index-10, the	

short version of the Medical Outcomes Study ¹⁷ Social Support Survey, or the Chinese version of the Inventory of Social Supportive Behaviours)

4) Social network (size) including frequency of contact with network members (e.g., Lubben Social Network Scale-6)

5) Social functioning as a sub-domain of health-related quality of life

6) Social participation (e.g., Subjective Social Participation Index)

7) Health quality of life (e.g., EQ-5D by the EuroQol Group, The Short Form (SF-36) Health Survey, The World Health Organization Quality of Life Assessment questionnaire (WHOQOL-BREF), or the 12-item Short Form Health Survey)

Although it is the same trial number, if there are different outcomes in each study, it will be included respectively.

Study design	<input type="checkbox"/> All RCTs or quasi-RCTs regardless of sample size	<input type="checkbox"/> Non-RCTs <input type="checkbox"/> Observational studies (prospective, retrospective cohort, case-control, nested case-control, case cohort, cross-sectional, and simulation studies), comments, editorials, letters to the editor, case series, conference abstract, and animal studies
Setting	<input type="checkbox"/> Community settings	
Language	<input type="checkbox"/> English	<input type="checkbox"/> Non-English

Supplementary file 3: Search strategy

Table A.3.1: MEDLINE via OVID from 1946 to Nov 20, 2019

Searches	Search Terms
1	loneliness/
2	social isolation/
3	social alienation/
4	social support/
5	community networks/
6	social distance/
7	interpersonal relations/
8	friends/
9	psychosocial deprivation/
10	social participation/
11	(lonely or loneliness or solitude).ti,ab.
12	((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti,ab.
13	(social wellbeing or social health or social capital).ti,ab.
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15	randomized controlled trial.pt.
16	randomized.mp.
17	controlled clinical trial.pt.
18	placebo.mp.
19	15 or 16 or 17 or 18
20	14 and 19
21	exp aged/ or older aged/
22	(aged or elder* or geriatric* or gerontol* or nonagenarian* or octogenarian* or older or "oldest old" or senior* or septuagenarian* or sexagenarian* or "very old").ti.
23	21 or 22
24	20 and 23

Table A.3.2: EMBASE from 1974 to Nov 20, 2019

Searches	Search Terms
1	loneliness/
2	social isolation/
3	social alienation/
4	social support/
5	community networks.mp.
6	social distance/
7	human relation/
8	friend/
9	psychosocial deprivation.mp.
10	social participation/
11	(lonely or loneliness or solitude).ti,ab.
12	((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti,ab.
13	(social wellbeing or social health or social capital).ti,ab.
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15	random:.tw.
16	placebo:.mp.
17	double-blind:.tw.
18	15 or 16 or 17
19	14 and 18
20	exp aged/ or older aged/
21	(aged or elder* or geriatric* or gerontol* or nonagenarian* or octogenarian* or older or "oldest old" or senior* or septuagenarian* or sexagenarian* or "very old").ti.
22	20 or 21
23	19 and 22

Table A.3.3: PsycINFO from 1806 to Nov 20, 2019

Searches	Search Terms
1	exp loneliness/
2	exp social deprivation/
3	exp social support/
4	exp alienation/
5	exp friendship/
6	exp social networks/
7	exp interpersonal relationships/
8	(lonely or loneliness or solitude).ti,ab.
9	((social* or societ* or perce* or person*) adj3 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*)).ti,ab.
10	(social wellbeing or social health or social capital).ti,ab.
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	double-blind.tw.
13	control.tw.
14	random: assigned:.tw.
15	12 or 13 or 14
16	11 and 15
17	exp aged/ or older aged.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measure, mesh]
18	(aged or elder* or geriatric* or gerontol* or nonagenarian* or octogenarian* or older or "oldest old" or senior* or septuagenarian* or sexagenarian* or "very old").ti.
19	17 and 18
20	16 and 19

Table A.3.4: CENTRAL from - to Nov 20, 2019

Searches	Search Terms
1	loneliness
2	social isolation
3	social alienation
4	social support
5	community networks
6	social distance
7	interpersonal relations
8	friends
9	psychosocial deprivation
10	social participation
11	lonely or loneliness or solitude
12	MeSH descriptor: [Social Isolation] explode all trees
13	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
14	MeSH descriptor: [Aged] in all MeSH products
15	senior* OR elder*
16	#14 OR #15
17	#13 AND #16

Table A.3.5: CINAHL from - to Nov 20, 2019

Searches	Search Terms
1	(MH "Loneliness")
2	(MH "Social Isolation")
3	(MH "Social Alienation")
4	(MH "Support, Psychosocial")
5	(MH "Community networks")
6	(MH "Interpersonal Relations")
7	(MH "Social Networks")
8	(MH "Psychosocial Deprivation")
9	(MH "Social Participation")
10	TI lonely or loneliness or solitude
11	AB lonely or loneliness or solitude
12	TI ((social* or societ* or perce* or person*) N2 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*))
13	AB ((social* or societ* or perce* or person*) N2 (isolation or isolated or alienation or alienated or relation* or detachment or detached or contact or link or ties or support* or network* or participation or activ* or engage* or connect* or disconnect* or cohesion or cohesive or embedded* or vulnerab* or interact*))
14	TI (social wellbeing or social health or social capital)
15	AB (social wellbeing or social health or social capital)
16	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15
17	TI randomized
18	AB randomized
19	TI placebo
20	AB placebo
21	"placebo"
22	TI double-blind
23	AB double-blind
24	17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23
25	16 AND 26
26	(MH "Aged")
27	TI aged or elder* or geriatric* or gerontol*

28	26 OR 27
29	25 AND 28
