Topic Brief: Loneliness and Well-Being

Date: 8/22/2019
Nomination Number: 0856

Purpose: This document summarizes the information addressing a nomination submitted on 5/7/2019 through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: Loneliness and social isolation are associated with a variety of health conditions and increased mortality[1]. No guidelines exist on how to screen or intervene to reduce the detrimental effects of loneliness and social isolation on health.

Program Decision:

- The EPC Program will not develop a new systematic review because systematic reviews were identified that addressed the majority of the nomination. For those components that were not fully addressed, there were limited and diverse primary studies that would not be amenable to synthesis.

Key Findings

- We identified systematic reviews that fully addressed the relationship between loneliness and health, and did not identify any systematic reviews or primary studies that addressed screening for loneliness. We identified systematic reviews that covered most of the characteristics associated with loneliness, and interventions for loneliness. A search for primary studies for the relationship between race/ethnicity and loneliness yielded only six studies and primarily addressed loneliness in immigrant populations, and a search for primary studies for healthcare-based interventions yielded only three studies of varied interventions. The estimated number of primary studies would be 17.

Background

Social isolation has been conceptualized as a state of limited contact with others, while loneliness is defined by a subjective experience unrelated to degree of contact with others[2]. Loneliness and social isolation are demonstrated risk factors for all-cause mortality[1], and may be linked to health conditions such as coronary heart disease and stroke[3], high blood pressure[4], and depression[5]. The financial burden of social isolation in older adults is estimated to be $6.7 billion in U.S. federal expenditures annually[6], while the evidence for the cost of social isolation and loneliness in younger persons is limited [7]. A survey conducted in 2018 reported that the U.S. and the U.K. identified similar proportions of loneliness and social isolation, at 22% and 23%, respectively, which was twice that of in Japan (9%)[8].

Government organizations are recognizing the need to address loneliness given the prevalence and risk factors for poor health outcomes. Specifically, the U.K. appointed a Minister of Loneliness in 2018 to lead interventions such as social prescribing, which allows general practitioners to direct patients to community resources to address loneliness[9]. In the U.S., the Health Resources & Services Administration has labeled loneliness an "epidemic"[6], but the U.S. Preventive Services Task Force cautions against widespread screening for health-related social determinants of health ahead of the establishment of accurate screening tests, effective treatment, and meaningful health outcome improvement[10]. For loneliness and social isolation, guidelines for screening and treatment do not exist.

Scope

1) What is the relationship between loneliness/social isolation and physical and mental health?
2) What characteristics are associated with loneliness/social isolation?
3) What is the comparative validity of screening tools for loneliness/social isolation?
4) What is the effectiveness of interventions to reduce loneliness/social isolation?

Table 1. Questions and PICO (population, intervention, comparator, outcome)

Questions	1) Loneliness and health	2) Characteristics associated with loneliness	3) Screening for loneliness	4) Interventions for loneliness
	Adolescents and adults with loneliness or social isolation	Adolescents and adults with loneliness and social isolation Age, Gender, Rural/urban, SES, Race/ethnicity, Veteran status, Homelessness, LGBT, Physical/mental disabilities (e.g., intellectual or developmental disabilities), Substance use disorder	Adolescents and adults	Adolescents and adults diagnosed with loneliness or social isolation
	N/A	N/A	Any screening tools for social isolation/ loneliness	Any intervention aimed at reducing loneliness
	N/A	N/A	Clinical judgment, Other screening tools for social isolation /loneliness	No treatment Usual care Other active treatment
	Physical health outcomes. Mental health outcomes such as	Measures of loneliness/ social isolation	Measurement of loneliness- diagnostic accuracy	Levels of loneliness/ social isolation,

	depression or substance abuse.			levels of social connectedness Clinical outcomes such as suicide, depression, physical health outcomes, etc.

Abbreviations: LGBT=Lesbian, Gay, Bisexual, Transgender; SES= Socioeconomic status; N/A= not applicable

Assessment Methods

See Appendix A.

Summary of Literature Findings

- We identified systematic reviews that covered much of the nomination. For components of the nomination for which there were not sufficient systematic reviews, we found too few studies for a new systematic review.
- Specifically, we identified relevant systematic reviews on the relationship between loneliness and physical and mental health (Question 1), including an overview of reviews that addressed the relationship of loneliness with both physical and mental health[11].
- For the question of characteristics associated with loneliness (Question 2), we identified reviews that evaluated the relationship between loneliness and intellectual and developmental disability[12], age group [13], and substance dependence [14]. Since the nominator was also interested in the relationship between loneliness and race/ethnicity and it was not addressed in the available reviews, we conducted a search for primary studies and identified six studies that assessed loneliness in immigrant groups in regions including Canada, New Zealand, and the Netherlands[15-20].
- For the question regarding screening for loneliness (Question 3), we did not identify any systematic reviews or primary studies.
- For interventions for loneliness (Question 4), we identified a total of nine reviews, including an overview of reviews evaluating a range of interventions for loneliness in individuals across the lifespan[21]. Because the nominator was particularly interested in healthcare-initiated interventions such as social prescribing which was not included in the available reviews, we conducted a search for primary studies and only identified three, which evaluated the use of omega-3 supplementation[22], social prescribing[23], and community paramedicine[24].
- The estimated number of primary studies would be 17.

Table 2. Literature identified for each Question

Question	Systematic reviews (6/2016-9/2019)	Primary studies (7/2014-7/2019)
Question 1: Loneliness and health	Total: 6 • Cochrane: 0 • AHRQ: 0 • Other: 4[11, 25-27] (one overview of reviews) • Protocol: 2[28, 29]	N/A
Question 2: Characteristics associated with loneliness	Total: 4 • Cochrane: 0 • AHRQ: 0 • Other: 1[12]	Total: 6 • RCT: 0 • Observational: 6[15-20]

Question	Systematic reviews (6/2016-9/2019)	Primary studies (7/2014-7/2019)
	• Protocol: 2[13, 14]	Clinicaltrials.gov • Recruiting: 0
Question 3: Screening for loneliness	Total: 0 • Cochrane: 0 • AHRQ: 0 • Other: 0	Total: 0 • RCT: 0 • Observational: 0 Clinicaltrials.gov • Recruiting: 0
Question 4: Interventions for loneliness	Total: 9 • Cochrane: 0 • AHRQ: 1[30] (rapid review) • Other: 3[21, 31, 32] (1 review of reviews) • Protocol: 6[33-38]	Total: 3 • RCT: 1[22] • Observational: 1[23] Clinicaltrials.gov • Recruiting: 1[24]

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; NA=not applicable; RCT=randomized controlled trial

See Appendix B for detailed assessments of all EPC selection criteria.

Summary of Selection Criteria Assessment

- This nomination did not meet all of the selection criteria. There were systematic reviews identified that addressed the majority of the nomination. Where systematic reviews did not exist to address the nomination, there were too few studies for a new systematic review.

Please see Appendix B for detailed assessments of individual EPC Program selection criteria.

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Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years 6/19/2016-6/19/2019 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
  - AHRQ Evidence Reports https://www.ahrq.gov/research/findings/evidence-based-reports/index.html
  - EHC Program https://effectivehealthcare.ahrq.gov/
  - US Preventive Services Task Force https://www.uspreventiveservicestaskforce.org/
  - AHRQ Technology Assessment Program https://www.ahrq.gov/research/findings/ta/index.html
- US Department of Veterans Affairs Products publications
  - Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
  - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program https://www.healthquality.va.gov/
- Cochrane Systematic Reviews https://www.cochranelibrary.com/
- University of York Centre for Reviews and Dissemination database https://www.crd.york.ac.uk/CRDWeb/
- PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
- PubMed https://www.ncbi.nlm.nih.gov/pubmed/
- Campbell Collaboration http://www.campbellcollaboration.org/
- Health Systems Evidence https://www.healthsystemsevidence.org/?lang=en
- PDQ Evidence https://www.pdq-evidence.org/
- PsychINFO https://www.apa.org/pubs/databases/psycinfo/

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a limited literature search in PubMed and PsycInfo for the last five years 7/2014-7/2019. We reviewed all identified titles and abstracts for inclusion for Questions 2 and 3. Because a large number of articles were identified for Question 4, we reviewed a random sample of 200 titles and abstracts for inclusion. We calculated the total number of included studies based

on the total number of studies from Questions 2 and 3, plus the calculated projected number of studies included from the random sample for Question 4.

Search strategy

Feasibility Question 2	
MEDLINE(PubMed) searched on August 1st, 2019	
Concept	
loneliness/isolation	((((("Social Alienation"[Mesh]) OR "Loneliness"[Mesh]) OR "Social Isolation"[Mesh])) OR ((loneliness[Title] OR "social isolation"[Title]))
AND	
population characteristics	"Population Characteristics"[Majr]) OR "Risk Factors"[Majr]
Limits:	Filters activated: published in the last 5 years, Humans, English, Adolescent: 13-18 years, Adult: 19+ years.
SR N=2	systematic[sb]
RCT N=69	(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])
Observational N=59 (Because of the nature of this question I pulled out observational studies as a group to examine)	(((((("Cohort Studies"[Mesh]) OR "Controlled Clinical Trial"[Publication Type]) OR "Case-Control Studies"[Mesh])) OR (("Evaluation Studies"[Publication Type]) OR "Comparative Study"[Publication Type])) OR (("Comparative Study"[Publication Type]) OR "Follow-Up Studies"[Mesh])
Other N=207	

Feasibility Question 3	
MEDLINE(PubMed) searched on August 1st, 2019	
Concept	
loneliness/isolation	((((("Social Alienation"[Mesh]) OR "Loneliness"[Mesh]) OR "Social Isolation"[Mesh])) OR ((loneliness[Title] OR "social isolation"[Title]))
AND	
Screening tools	((validity[Title] OR reliability[Title] OR measurement[Title])) OR (("Mass Screening"[Mesh]) OR "Reproducibility of Results"[Mesh])
Limits:	Filters activated: published in the last 5 years
SR N=0	systematic[sb]
RCT N=15	(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR

	(controlled clinical trial[pt])) OR (randomized controlled trial[pt])
Other N=55	

Feasibility Question 4	
MEDLINE(PubMed) searched on August 1st, 2019	
Concept	
loneliness/isolation	((((("Social Alienation"[Mesh]) OR "Loneliness"[Mesh]) OR "Social Isolation"[Mesh])) OR ((loneliness[Title] OR "social isolation"[Title]))
AND	
Interventions	(((((((address[Title/Abstract]) OR program[Title/Abstract]) OR intervention*[Title/Abstract]) OR reduce[Title/Abstract]) OR eliminate[Title/Abstract])))) OR ("therapy"[Subheading] OR "Therapeutics"[Mesh])
Limits:	Filters activated: published in the last 5 years
SR N=17	systematic[sb]
RCT N=206	(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])
Other N=545	

Appendix B. Selection Criteria Assessment

Selection Criteria	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes
1b. Is the nomination a request for an evidence report?	Yes
1c. Is the focus on effectiveness or comparative effectiveness?	Yes
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes
2a. Represents a significant disease burden; large proportion of the population	A survey conducted in 2018 reported that the U.S. and the U.K. had similar proportions of reported loneliness and social isolation, at 22% and 23%, respectively, which was twice that of in Japan (9%)[8].
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes. Loneliness has been demonstrated to be a risk factor for all-cause mortality[1].
2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes. Data from a recent systematic review indicates a strong inverse relationship between strength of social relationships and readmission to the hospital[39].
3. A recent high-quality systematic review or other evidence review is not available on this topic	We found systematic reviews that fully address Question 1 and parts of Questions 2 and 4. No reviews address Question 3. Question 1: Four systematic reviews: One that addresses both physical and mental health associations with loneliness[11], one on the relationship between loneliness and dementia[25], one on the relationship between loneliness and stress reactivity[26], and one on loneliness and mental health[27]. Two protocols for in-process systematic reviews: One on the relationship between cardiovascular and metabolic health and loneliness[28], and one on the relationship between suicidal behavior and loneliness[29]. Question 2: One systematic review in a population of individuals with intellectual and developmental disorders[12]. Two protocols for in-process systematic reviews: One on prevalence of loneliness by age group[13], and one in populations experiencing substance dependence[14]. Existing or in-process systematic reviews did not adequately address the relationship between loneliness and race/ethnicity.

	Question 3: We did not identify any existing or in-process systematic reviews for Question 3. Question 4: Four systematic reviews: One rapid review examining interventions in older adults[30], one review of reviews for interventions across ages[21], one on electronic interventions in older persons[31], and an integrative review on interventions for older people[32]. Five protocols for in-process systematic reviews for the following interventions: digital technology interventions[34], psychological interventions[35], community-based group interventions[36], mind and body practice interventions[37], and any interventions in adolescents[38]. Existing or in-process systematic reviews did not adequately address healthcare-initiated interventions.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes. No guidelines exist on screening and interventions for loneliness and social isolation.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	No. No guidelines exist on screening and interventions for loneliness and social isolation.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	Question 2: We searched for studies on the relationship between loneliness/social isolation and race/ethnicity and identified six observational studies[15-20]. Question 3: We searched for studies on the comparative validity of screening tools for loneliness/social isolation and did not identify any. Question 4: We searched for studies on healthcare-initiated interventions and identified one RCT[22], one observational studies[23], and one clinical trial[24]. Due to the high yield of studies for Question 4, the reported included studies were identified from a sample of the total yield. The total number of primary studies is estimated to be 17.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality