

Annual Review of Public Health

Social Connection as a Public Health Issue: The Evidence and a Systemic Framework for Prioritizing the “Social” in Social Determinants of Health

Julianne Holt-Lunstad

Department of Psychology, Brigham Young University, Provo, Utah, USA;
email: julianne_holt-lunstad@byu.edu

ANNUAL
REVIEWS **CONNECT**

www.annualreviews.org

- Download figures
- Navigate cited references
- Keyword search
- Explore related articles
- Share via email or social media

Annu. Rev. Public Health 2022. 43:193–213

First published as a Review in Advance on
January 12, 2022

The *Annual Review of Public Health* is online at
publhealth.annualreviews.org

<https://doi.org/10.1146/annurev-publhealth-052020-110732>

Copyright © 2022 by Annual Reviews. This work is licensed under a Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See credit lines of images or other third-party material in this article for license information



Keywords

social connection, loneliness, social support, social isolation, mortality, morbidity, health, public health, policy

Abstract

There is growing interest in and renewed support for prioritizing social factors in public health both in the USA and globally. While there are multiple widely recognized social determinants of health, indicators of social connectedness (e.g., social capital, social support, social isolation, loneliness) are often noticeably absent from the discourse. This article provides an organizing framework for conceptualizing social connection and summarizes the cumulative evidence supporting its relevance for health, including epidemiological associations, pathways, and biological mechanisms. This evidence points to several implications for prioritizing social connection within solutions across sectors, where public health work, initiatives, and research play a key role in addressing gaps. Therefore, this review proposes a systemic framework for cross-sector action to identify missed opportunities and guide future investigation, intervention, practice, and policy on promoting social connection and health for all.

Loneliness:

a subjective indicator of social deficits marked by a distressing feeling of aloneness or isolation from others; the discrepancy between one's actual and desired level of connection

Social isolation:

an objective indicator of social deficits marked by having few social relationships and roles, and infrequent social contact; a structural indicator of low social connection

Social connection:

an umbrella term that encompasses the structure, function, and quality of social relationships represented in the scientific literature; social connection is a multifactorial construct on a continuum of risk, when social connection is low, to protection, when social connection is high

INTRODUCTION

Interest in the potential relevance to health of social connectedness or lack thereof (e.g., isolation and loneliness) has been growing globally (2, 30, 41, 57, 69), amid a backdrop of long-standing public health research suggesting that anywhere from 40% to more than 80% of health and wellness can be directly or indirectly attributed to social factors (44). This increasing interest may be the result of a confluence of the growing body of scientific evidence demonstrating short- and long-term effects on health outcomes, societal trends (e.g., aging population, advancements in technology, remote working, inequality, political polarization) that have direct social implications, and pivotal events such as the coronavirus 2019 (COVID-19) pandemic that led to the implementation of policies and practices to reduce social contact across every sector of society on a global scale.

Population estimates within the USA prior to the pandemic suggest that a significant portion of the adult population was isolated, lonely, or both (22, 48, 73), and data synthesized from 32 longitudinal studies show increases in both the prevalence and severity of loneliness during the pandemic (M. Ernst, A.M. Werner, D. Niederer, E. Brähler & M. Beutel, manuscript under revision). These longitudinal studies rigorously demonstrate changes in loneliness; however, because the studies use different measurement tools and classification criteria, it is challenging to estimate the exact prevalence of social isolation and loneliness within the population. There is currently no standardized measurement approach within the USA, nor is loneliness systematically included within national population health surveys in order to gather data, despite clear mechanisms by which to assess population needs and trends.

Despite a complex literature, decades of research across multiple scientific disciplines and methodological approaches have extensively documented compelling evidence of the health relevance of social connection, isolation, and loneliness, including both long-term health effects and the biological and behavioral basis of these effects (37, 57, 69, 75, 105). Yet, this evidence has been underrecognized and neglected within medicine and public health (69). The United Kingdom and Japan have appointed ministers of loneliness, and local, national, and global initiatives are beginning to address social isolation and loneliness or foster greater social connection. However, within the USA, national-level approaches to public health and policy lag in comparison to other countries and relative to many other behavioral risk factors and other social determinants of health (SDoH). Indeed, addressing social connectedness is noticeably absent from most ongoing health objectives, such as those of the Healthy People 2030 program, and initiatives, such as community-based interventions aimed at ameliorating health risks in the USA.

The relevance of social connection to public health has received only scant attention to date, possibly because for decades the scientific evidence had emerged in disciplinary silos such as epidemiology, psychology, and sociology. However, recent reviews and meta-analyses have begun to synthesize this evidence, leading to the conclusion that a lack of social connection has significant adverse health consequences. This article summarizes the current state of the scientific evidence to justify the prioritization of social connection in health promotion and prevention, simultaneously signaling public health implications and gaps in evidence across and within sectors. Given the current chasm between evidence-based knowledge and its application, I offer a novel systemic framework of cross-sector action to advocate and guide future scientific investigation, intervention, practice, and policy on promoting social connection and health.

EVIDENCE OF SOCIAL CONNECTION AS A DETERMINANT OF HEALTH

It is widely accepted across scientific disciplines that humans are fundamentally a social species and that social connections are vital for development, reproduction, and survival. Thus, it

naturally follows that social factors would be influential and perhaps even critical for human health and well-being. Social influences on health and well-being have been systematically examined using varying scientific approaches, including large-scale prospective epidemiological research, cross-sectional and cohort studies, large-scale network analysis, randomized clinical trials, and tightly controlled experiments. Converging evidence has documented effects on mental, cognitive, and physical health outcomes, with the strongest evidence demonstrating associations with risk for premature mortality (69). An umbrella review of social connection and health that focused exclusively on social deficits (social isolation, loneliness, and living alone) identified 10 meta-analyses on physical health, including 276 independent studies, and 15 meta-analyses on mental health, including 416 independent studies, confirming and establishing the public health importance of social connections (65). Nonetheless, despite the clear relevance of social connection for health, the evidence is complex, and there remain several important unanswered questions that require greater attention and prioritization.

Social support: the actual or perceived availability of resources, advice, understanding, or acceptance (e.g., tangible support, informational support, emotional support, belonging support); a functional indicator of social connection

Multifactorial Conceptualization and Measurement Within the Evidence

The converging evidence of robust associations with physical health outcomes is particularly noteworthy, given that there is some variability in how social influence is measured across different scientific disciplines (37, 43). For example, several related but distinct concepts have been represented in the literature, including social capital, social isolation, loneliness, social support, social networks, social participation, and relationship strain and conflict. Some measurement approaches assess social assets, while others assess social deficits; however, with a few exceptions, these are conceived and treated analytically as poles on a continuum, suggesting a continuum of risk to protection. Generally, the approaches represented in the larger body of evidence on social relationships and health can be stratified into three major conceptual components: relationship structure, function, and quality (**Figure 1**).

The structural component encompasses our connection to others via the existence of social relationships, roles, and interactions. The structure of one's social connections is often measured quantitatively by assessing the size or diversity of one's social network, social group membership or participation, living arrangements (e.g., living alone), and frequency of social interactions. The

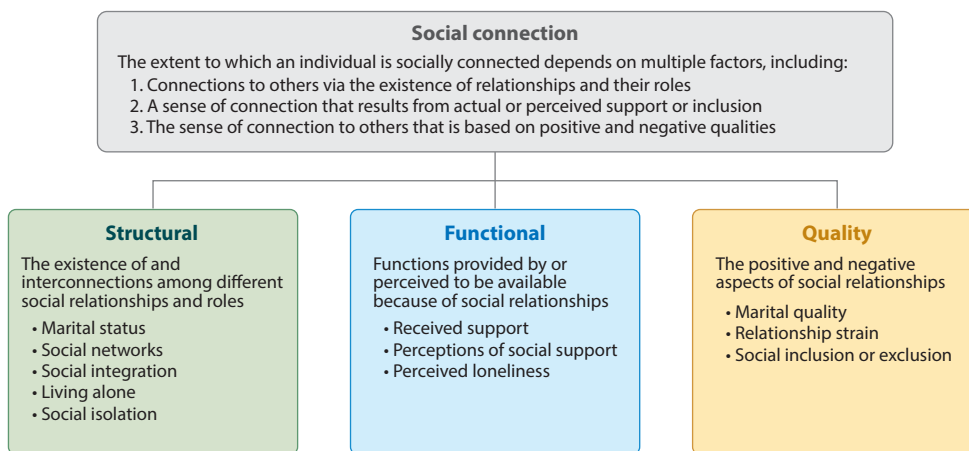


Figure 1

Conceptual model of social connection as a continuous multifactorial construct based on cumulative evidence across disciplines. Figure reprinted from Reference 37.

functional component acknowledges our connection to others via the resources provided or available to meet various needs, including emotional, physical, tangible, informational, and belonging needs. Measurement of the functional component of social connection typically assesses whether support from one's social relationships is received or is perceived to be available to meet these needs (e.g., social support, loneliness). The quality component acknowledges positive and negative affective qualities in our social connections and is measured by assessing these qualities (e.g., relationship satisfaction, cohesion, intimacy, closeness, strain, conflict). While there is some variability in effect sizes, each of these various measurement types has been linked to health outcomes (41, 43, 57). Correlations between these social measures are not large, reinforcing the distinction among these related concepts (20, 75). This consistency across measures has important implications for public health because it suggests that each component may contribute to health in unique ways and that no single component is sufficient to adequately capture risk when deficits exist.

Variability in the measurement and conceptualization of social connection may have been an impediment to the prioritization of social relationship factors in public health in the past. To address this barrier, scholars recently proposed a unifying umbrella term, social connection, to provide structure to the multifactorial continuum of influence that social relationships have on health (**Figure 1**). This multifactorial conceptual approach may help guide public health efforts, since a narrower approach that focuses on only one component or measurement type may leave gaps of unaddressed social deficits and/or untapped assets for health prevention and promotion. When a multifactorial approach is applied to other complex health risk factors, such as type 2 diabetes (80), obesity (100), or cardiovascular disease (3), prognosis improves dramatically; thus, such an approach to social connection could potentially improve the prognosis across a range of health issues. Also supporting this multifactorial conceptualization is evidence on mortality, morbidity, and biomarkers of health that underscores the importance of addressing social connection in public health.

Social Connection and Mortality

Some of the strongest and most rigorous evidence supporting the public health relevance of social connection comes from research on mortality. Systematic investigations of social factors date back to Durkheim's classic 1897 study on suicide, which demonstrated that socially isolated individuals were at a significantly increased risk of death by suicide (31). While suicide is a significant public health outcome itself, there is also compelling evidence for disease-related mortality. In a classic 1988 review by House et al. (46), five large-scale epidemiological studies demonstrated strong age-adjusted mortality risk among people who were less socially integrated; in 2010, a meta-analysis of 148 prospective studies showed that social connections significantly influence the risk of premature death from all causes (43).

Over the past couple of decades, the number, quality, and sample size of studies have grown exponentially, replicating these findings and providing greater confidence in these effects. For example, UK Biobank data alone include nearly half a million people and have demonstrated that social isolation significantly predicts risk for earlier all-cause mortality even after adjusting for a robust set of demographic, lifestyle, biological, and health risk factors (25). The cumulative evidence makes a compelling case that social connection increases the odds of survival (43), whereas a lack of social connections (social isolation, loneliness, and living alone) is a significant predictor of risk of premature death from all causes (42, 68, 76).

Several meta-analyses have documented a prospective association between some aspect of social connection and mortality (74, 76, 78, 81, 85–87). While the strength of the effect varies across measurement type, the magnitude of these effects is comparable to and in some cases exceeds the

risk of other well-known mortality risk factors, including lifestyle factors (e.g., obesity, excessive alcohol consumption, physical inactivity), environmental factors (e.g., air pollution) (41), and traditional clinical risk factors (e.g., smoking, elevated blood pressure, high cholesterol) (70). These studies consistently control for the effects of age and initial health status and frequently include other known risk factor variables, including biological (e.g., body mass index, blood pressure), behavioral (e.g., smoking, alcohol consumption, physical activity), socioeconomic (education, income), and psychological (e.g., depression, anxiety, cognitive functioning) risk factors. Thus, these studies provide strong evidence that social connection, or lack thereof, is an independent risk factor for premature mortality from all causes.

Despite strong meta-analytic evidence of the effects of social connection on mortality risk, gaps remain. For example, meta-analyses find remarkable consistency across countries, but most evidence comes from North America, the United Kingdom and Europe, Asia, and Australia, with fewer studies conducted in developing countries. There are also fewer prospective studies that begin examining people at younger ages due to the feasibility constraints of following individuals over long periods of time to capture mortality, limiting our understanding of how early risk emerges. Furthermore, while there is evidence of significant associations with mortality risk among each of the different measurement and conceptual approaches, few studies examine multiple aspects within the same sample, thereby limiting the ability to examine independent, additive, or synergistic effects across components of social connection. Perhaps most notably, longitudinal evidence that has accumulated in recent decades began to be collected prior to the widespread use of many tech-mediated means of social interaction. The degree of equivalency among means of connecting socially, and how it might influence subsequent long-term risk, is unclear.

Social Connection and Morbidity

Data on nonfatal health outcomes also present compelling evidence in support of associations between social connection and physical, mental, and cognitive health outcomes. Because nonfatal outcomes may be bidirectional, it is important to distinguish study methodologies that can determine directionality. For example, poorer social connections may lead to poorer health, but it is also plausible that poorer health influences social connection (e.g., isolation, loneliness). For example, chronic health conditions may make it more difficult for a person to engage socially, leading to greater isolation and loneliness. Both the bidirectional and directional associations between social connection and health outcomes point to significant public health implications. However, longitudinal studies establish the level of social connection prior to any health outcome and thus offer stronger evidence of a directional effect of social connection on health.

For the physical health outcomes associated with social connection, some of the strongest evidence comes from cardiovascular outcomes. For example, data from 16 longitudinal studies show that poor social relationships predict a 29% increased risk of coronary heart disease and a 32% increased risk of stroke (101). Data synthesized from 13 longitudinal studies show that poor social connection among patients with heart failure is associated with a 55% increased risk of hospital readmission (35). Several meta-analyses also document associations between components of social connection and other physical health outcomes, including diabetes self-management (90), malnutrition (4), frailty in older men (51), and vaccine uptake (49). While the vast majority of clinical studies focused on older adults, one meta-analysis demonstrated that poor social connection is associated with greater chronic physical complaints among children and adolescents with chronic physical conditions (61). A review of 35 years of experimental viral-challenge studies showed that persons with greater social connection (social networks, social support) are less susceptible to upper respiratory infectious illness (19). These findings were replicated across multiple respiratory

viruses and included younger samples ranging from 18 to 55 years of age. Overall, this body of evidence shows associations with several significant physical health indicators, with robust longitudinal data on cardiovascular outcomes [cardiovascular disease is the leading chronic disease in the USA among both men and women (21)], and promising but limited data on other health outcomes.

Mental health is also strongly related to social connectedness and has received considerable attention in public health. Meta-analyses synthesizing these data have found that various components of poor social connection are associated with social anxiety in both adolescents (60, 62) and adults (94), as well as with depression (16, 26, 62, 104, 106), psychosis (17, 64), and suicidal ideation (15, 24), while greater social connection is associated with better overall mental health among aging populations in long-term care residential settings (5). However, many of these data are cross-sectional, and substantial evidence points to bidirectional effects between mental health and social connection. Overall, these studies show that better social connection is associated with better mental health, with longitudinal data demonstrating an increased risk of depression due to poor social connection (16, 106).

Cognitive health is of particular concern for population health as our aging population continues to grow. Meta-analyses demonstrate longitudinal associations between social connections and cognitive health outcomes, including cognitive functioning and risk of dementia. For example, data across 51 studies indicate that better social engagement and large social networks are associated with better global cognitive function, memory, and executive function (27). Multiple meta-analyses demonstrate the longitudinal influence of social connection on risk of dementia (53, 54, 72). For example, data from 31 studies with more than 3.2 million participants demonstrate that having a poor social network increases risk by 59% and poor social support by 28%, whereas greater social engagement is a protective factor (72). These data suggest that social connection may play a protective and central role in maintaining better cognitive function and preventing dementia.

Biological and Behavioral Pathways by Which Social Connectedness Influences Health

In addition to the evidence that social connection influences health, there is growing evidence of plausible biological and behavioral pathways that explain these associations. Several reviews have documented evidence of plausible biological mechanisms (e.g., 10, 45, 71, 96). Social experiences, and our perceptions of them, can influence health through central processing that in turn influences peripheral health-relevant biology (18). Reviews of this evidence have found that social connection factors influence specific biological pathways, including chronic allostatic load (82), cardiovascular reactivity (95), blood pressure (29), oxidative stress (59), neuroendocrine dysregulation (10), immune functioning (19, 58, 63, 67, 77), inflammation (98), and gut-microbiome interactions (92). Because chronic inflammation is implicated in many chronic illnesses, including cardiovascular disease, depression, and dementia, this may be a common mechanism that could explain the diverse health effects of social connections or lack thereof.

Similarly, social connections may influence health outcomes via psychological and behavioral factors. One widely examined psychological pathway is the role of social connections (social support) and perceived stress (45). Social relationships help us cope with stress, thereby buffering the health effects of stress (23, 71), or conversely may be sources of interpersonal stress, thereby exacerbating biological stress responses and potentially downstream health effects (6, 93). Several reviews have documented the influence of aspects of social connection on behavioral factors such as sleep quality and quantity, obsessive behavior, physical activity, and smoking (10, 50, 84). Social

connection has also been associated with other public health issues, including opioid misuse (11) and smoking in adolescents (83).

Importance Across the Life Span

Because humans are fundamentally social, it is unlikely that there is any stage of development where social connection would be irrelevant (33). Early infant–caregiver relationships not only are essential to survival, given that humans are one of the most vulnerable species at birth, but also are thought to become the first social safety net, forming the basis on which relationships are judged as reliable sources of support and protection (7). Some of the earliest public health policies stemmed from research demonstrating that infants and young children in custodial care who are deprived of human contact fail to thrive and, in some cases, die (91, 99). Similarly, studies demonstrating the effectiveness of early contact between mother and infant on subsequent health and development outcomes (9) have led to maternity care practices and policies for skin-to-skin contact within 1 hour of birth (12). Several studies show that early childhood experiences affect cognitive, behavioral, and physical development, significantly predicting health (56, 102).

Social connection, or conversely isolation and loneliness, is often assumed to be more relevant to health in older age, with a significant number of studies and reviews focused primarily or entirely on older adults. However, emerging evidence suggests that it is relevant across the life span (33), and some data indicate that younger age groups could be at the same or greater risk. For example, regarding the prevalence rates of indicators of deficits of social connection (e.g., loneliness), some surveys have found that loneliness occurs across ages, but several national surveys have found the highest prevalence rates among young adults (1). One study suggests that loneliness may peak at age 19 (88). Analyses of data from 75 longitudinal studies from Asia, Australia, Europe, and North America found evidence of an inverted-U-shaped trajectory for loneliness across the life span (66). On average, loneliness decreases throughout childhood and remains relatively stable from adolescence to the oldest old age, suggesting its relevance across the life span (66). Within a US sample, the nonlinear association with age was consistent with that of other samples; however, some variables were predictors of loneliness across all ages, while others were relevant to specific age groups (32).

Evidence of who may be at greatest risk of adverse health outcomes further prescribes a life-span approach. For example, in a meta-analysis of 70 prospective studies, isolation, loneliness, and living alone were significant predictors of premature mortality across ages, and the effect was stronger among younger individuals than among those above 65 years of age (42). Furthermore, in another recent study, loneliness predicted a significantly increased risk of earlier mortality among young and middle-aged adults but not among older adults (55). There is significant evidence of the importance of social connection across developmental stages for health-relevant biological processes. For example, a review of evidence documenting the relevance of social connection to the innate immune system during development demonstrates the importance of warmth and rejection in the social environment for childhood immune processes, including inflammation regulation (77). Beyond childhood, an analysis of four nationally representative studies representing the life course (adolescence and early, middle, and late adulthood) documented dose–response effects of the structure, function, and quality of social connections on multiple health-relevant biomarkers, including C-reactive protein, systolic and diastolic blood pressure, waist circumference, and body mass index, across each stage of life (105). However, the elevated risk associated with lacking social connection was much stronger at some stages of life. For example, the effects of social isolation were more strongly associated with inflammation during adolescence than physical inactivity.

Research also indicates the potential for unique antecedent processes in perceived and received social support across the life span (97), suggesting that a life span approach may have implications for intervention efforts. Overall, this evidence suggests that social connection is relevant to health across the life span and may help identify unique features, triggers, and targets that are relevant to health across the life course.

Social Connection as a Causal Determinant of Health

Cumulative evidence supports the possibility of a causal association between social connection and health (39, 47). Although causality is difficult to establish for many public health issues, given that most epidemiological data are observational rather than experimental, drawing causal inferences for disease is a critical step toward preventive action. When determining what criteria to use to draw causal inference from epidemiological research, the Bradford Hill guidelines are frequently cited as a standard to apply (36). These criteria can be applied to evaluate social connection as a causal determinant of health. The criteria for causation include the strength of the association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy. While no single factor is sufficient to establish causation, if all or most of the guidelines are met, then the necessary evidence exists to sustain a greater likelihood of a causal relationship than simply an association. **Table 1** summarizes the supporting evidence across the nine Bradford Hill criteria; more detailed analyses applying these criteria to social connection have been published elsewhere (39, 47). There is enough evidence to support each criterion except for specificity, given that social connection has been linked to multiple health outcomes—which is also true of smoking.

Critics of the Bradford Hill guidelines argue that they rely too heavily on epidemiological data and that a data integration framework is preferable for determining causality (28). A data integration framework incorporates data from multiple scientific disciplines, not just epidemiology,

Table 1 Bradford Hill guidelines and summary of supporting evidence for social connection

| Bradford Hill criteria | | Summary of supporting evidence |
|------------------------|--|---|
| Strength | How large is the association? | Effect size is comparable to or exceeds that of other clinical and mortality risk factors |
| Consistency | Is there consistency or replicability across varying types of studies and populations? | Ten meta-analyses, 276-plus studies using a variety of locations, populations, and methods |
| Specificity | Does exposure give rise to only a single outcome? | Exposure gives rise to multiple health-related outcomes Some evidence of mechanistic specificity |
| Temporality | Does exposure precede the outcome? | Prospective epidemiological studies |
| Biological gradient | Is there evidence of a dose–response curve? | Demonstrated in nationally representative samples across development stages |
| Plausibility | Are there plausible biological mechanisms? | Several plausible biological mechanisms have been documented |
| Coherence | Is there parallel evidence? Does it fit within what is known? | Fits within the framework of social determinants of health |
| Experiment | Is there experimental evidence? | Nonhuman animal studies of isolation Human social RCT interventions Laboratory manipulations of social situations |
| Analogy | Is the evidence consistent across measurement types? | Consistency across multiple conceptualizations and measurement approaches |

Abbreviation: RCT, randomized controlled trial.

Table adapted from Reference 39 (copyright 2021 Sage Publications).

into evaluations of causation, and it can be applied to evaluate social connection as a causal determinant of health. Notably, evidence spanning psychology, neuroscience, genetics, molecular biology, and immunology, among other disciplines, has documented plausible biological mechanisms between social connection and health (for reviews, see 10, 45, 96). Furthermore, evidence of a dose–response effect of the structure, function, and quality of social connection on multiple health-relevant biomarkers across the life span (105) supports a biological gradient. Based on the Bradford Hill guidelines and the data integration framework, the cumulative evidence supports the likelihood of a causal link between strong social connections and both better health and longer life (47).

OPPORTUNITIES FOR INCLUSION IN PUBLIC HEALTH INITIATIVES

With a wealth of evidence documenting both short- and long-term health outcomes, spanning both chronic and infectious diseases, policy makers should consider prioritizing social connection within public health agendas. Specific resources and activities must be identified to facilitate these objectives. Emphasis on social connections within SDoH is a logical approach.

Emphasis Within the Social Determinants of Health

Over the past 15–20 years, SDoH have received increasing attention from public health and non-profit organizations (8), including the World Health Organization (WHO) Commission on the Social Determinants of Health. Estimates suggest that SDoH factors are a major contributor to population health, with medicine and medical care accounting for only around 20% of population health (44).

According to the US Centers for Disease Control and Prevention (CDC), SDoH are the “conditions in the places where people live, learn, work, and play that affect a wide range of health and quality-of-life-risks and outcomes” (13). Healthy People 2030 comprises five key domains, including economic stability, access to education and quality, health care access and quality, neighborhood and built environment, and social and community context (34). The domain of social and community context within SDoH clearly aligns with social connection. For example, social and community context is described as follows (34):

People’s relationships and interactions with family, friends, coworkers, and community members can have a major impact on their health and well-being. Healthy People 2030 focuses on helping people get the social support they need in the places where they live, work, learn, and play.

This description corresponds to how social connection has been defined, conceptualized, and measured in interdisciplinary health research. However, at present no SDoH objectives focus directly on promoting interactions or relationships with family, friends, coworkers, and community members, or on social support—all components of social connectedness. Moreover, social connection is not identified as a health indicator and is not well represented within many existing public health initiatives (e.g., Healthy People 2030) or population health surveys to gather data related to social connection (e.g., Behavioral Risk Factor Surveillance System, National Health Interview Survey, National Health and Nutrition Examination Survey). Thus, the SDoH domain of social and community context is inadequately represented in national public health objectives and national health surveys in the USA.

Emphasis Within Social Determinants of Health Initiatives

What resources are needed to facilitate the inclusion of social connection within SDoH objectives? The overarching goal of Healthy People 2030 related to SDoH is to “create social, physical, and

economic environments that promote attaining the full potential for health and well-being for all” (34). To accomplish this goal, it is critical to ensure adequate representation of expertise on social connection within the CDC’s Social Determinants of Health Workgroup. Another critical resource is an adequate measurement model. The Healthy People 2030 framework provides a vision for a national health agenda and a strategy for improving health and health equity by identifying measurable objectives and targets that should be achieved by the end of the decade. This requires tracking data-driven outcomes to monitor progress and to motivate, guide, and focus action. Existing data sources (e.g., the Health and Retirement Study) can be used as a proxy to gather national-level social connection data to sustain the baseline development and monitor it throughout the decade. Other data sources already identified by the Healthy People 2030 program could provide data for the rest of the US population (adults <50 years); nonetheless, there may be additional opportunities for improving surveillance systems (at the national or state level) to capture population health data. Given that Healthy People 2030 objectives are aimed at the most pressing public health issues and that the social isolation accompanying the COVID-19 pandemic exacerbated an existing public health crisis (40), the absence of objectives is both notable and problematic.

Many opportunities exist to advance public health through greater inclusion of social connection and related social factors within existing efforts at national, state, and local levels. For example, the Administration for Community Living has established Commit to Connect, a national clearinghouse of community-based interventions to address social isolation and loneliness that will also serve as a resource for older adults and people with disabilities. National efforts such as Commit to Connect provide evidence-based resources and best practices that can also be utilized at a local level.

While it is critical to reach the most vulnerable groups, preventive efforts need to be implemented across the risk trajectory of the population to impact public health more comprehensively. National health guidelines, such as those for nutrition, physical activity, and sleep, provide the basis for which factors are recognized and implemented in health prevention. These guidelines serve as an evidence-based foundation for health policies and programs across the USA to help health care professionals and policy makers guide Americans in making healthy lifestyle choices. National health guidelines have been helpful in raising awareness and providing benchmarks for what individuals should be striving for in their daily behavior. Members of the public are looking for guidance on what they can personally do to reduce their risk—for example, guidelines for sleep, nutrition, and physical activity. Just as guidelines for nutrition consider both quantity and quality and those for physical activity consider both frequency and intensity, social guidelines similarly need to represent the complexity of the evidence. Social health guidelines need to be established by expert consensus and periodically updated on the basis of current evidence (41).

Given the strength of the evidence documenting sizable health effects associated with social connection, there are glaring missed opportunities for population health. In light of the COVID-19 global pandemic and what many researchers have also referred to as a double pandemic of isolation and loneliness (40), the time is ripe to establish a more systematic and strategic public health approach to advancing social connection within health promotion and prevention.

INTEGRATING SOCIAL CONNECTION INTO EXISTING PUBLIC HEALTH FRAMEWORKS

Due to its complexity, addressing social connection in public health may seem daunting; thus, a systemic framework of action is needed to guide this work. More specifically, the framework should

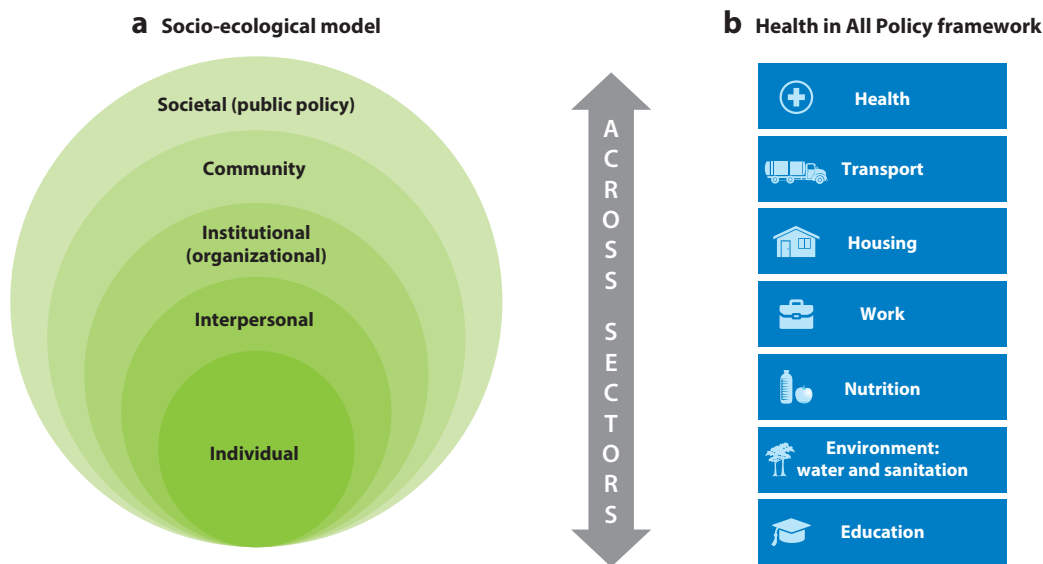


Figure 2

The socio-ecological model of health and the Health in All Policy framework are traditionally applied separately in public health. Panel *a* adapted from a public domain diagram by the Centers for Disease Control and Prevention. Panel *b* adapted from a diagram published by the World Health Organization.

guide and foster future scientific investigation, intervention, practice, and policy on promoting social connection as a means of improving public health.

Several frameworks or models have already been widely adopted and are guiding public health efforts. For example, the CDC (12) has adopted the socio-ecological model of prevention (14), which acknowledges that individuals are situated within interpersonal relationships, neighborhoods and communities, organizations and institutions, and society and culture (Figure 2). The socio-ecological model has been widely applied to understand various factors that contribute to health risk and protection (e.g., violence prevention) (14); however, less research has applied this model to social connection. A systems approach using the socio-ecological model has been proposed to identify both the underlying causal factors that may contribute to health at each level (e.g., individual, interpersonal, community, society) and potential solutions across these levels (37). Given that much research to date has focused primarily on the individual level, the socio-ecological model could substantially advance evidence and practice by drawing attention to interpersonal-, community-, and societal-level influences on social connection and their roles as potential targets for solutions. For example, reviews of the existing literature reveal that most interventions focus on the individual (e.g., maladaptive cognition or social skills) or relationship (e.g., dyadic or peer support) and to a lesser extent on community-level (e.g., social programs or clubs) or societal-level (e.g., policy) approaches. Consideration of the full socio-ecological model suggests that there are important missed opportunities to prevent and promote health that take a broader societal and population health perspective, including approaches that address the built environment, normative practices, and public policy.

The WHO has proposed a Health in All Policy framework (HiAP) (103), which suggests that every sector of society can potentially influence health and, therefore, that policies within every sector should consider the health implications of those policies (Figure 2). The CDC's National Prevention Strategy adopted the HiAP, recognizing that health is influenced by various factors

beyond medicine and health care and, in some cases, traditional public health (79). Adapted versions of the HiAP have been applied to well-being (52) and social connection (38). The Social in All Policy framework argues that policies across sectors have social implications (38). The social relevance of these sectors was widely evident during the COVID-19 pandemic, when policies were implemented to reduce social contact and every sector of society had to adapt. Indeed, the public health implications of social connections go beyond the health sector. Nearly every sector, and almost every governmental department, can play a role. This framework illustrates powerfully how every sector of society can potentially contribute to risk or protection via policies that limit or facilitate social connection (38).

While each of these frameworks can substantially advance public health by more carefully considering social connection, there may be limitations. For example, the HiAP acknowledges key sectors as potential levers of action but focuses exclusively on policy. In contrast, the socio-ecological model suggests that policy is only one of several levels at which to truly understand and intervene to promote social connection and health. Given the evidence summarized above, each of these models could also benefit from adopting a life span approach.

A MORE COMPREHENSIVE PUBLIC HEALTH FRAMEWORK

A SOCIAL Framework: The Systemic Framework of Cross-Sector Integration and Action Across the Life Span

The proposed **Systemic Framework of Cross-Sector Integration and Action Across the Life Span (SOCIAL)** aims to facilitate and accelerate progress within public health. This framework illustrates untapped opportunities to significantly influence population health, many of which are not adequately addressed in US public health programming today. Drawing upon, merging, and expanding upon the socio-ecological model and the HiAP, a scientific advisory council of interdisciplinary experts created the SOCIAL (**Figure 3**).

This framework aims to illustrate the intersectionality of several selected factors relevant to health. At its most basic level, it contains two primary axes: the level of influence across the socio-ecological model and a selection of sectors from the HiAP. The former includes individual, interpersonal relationship, institutional/organizational, community, and society levels within the socio-ecological model. The latter includes clinical and population health, transportation, housing, employment, nutrition, environment and sanitation, education, and leisure.

In this model (**Figure 4**), the intersection between each socio-ecological system level and each sector is represented by a cell. On the basis of this model, we can systematically identify and evaluate the evidence and application opportunities as well as gaps by numbering each level and sector. Much of the evidence and many of the intervention efforts are within cell 1.1 (**Figure 4**), which is the intersection of the health sector and the individual level. For example, a meta-analysis of 106 randomized controlled trials of interventions aimed at patients (individuals) within clinical settings (the health care sector) found that patients randomized to receive some kind of psychosocial support in addition to standard treatment had a 20% increased odds of survival relative to controls (89). Furthermore, the National Academy of Sciences consensus report (69) on social isolation and loneliness focused on the health sector (**Figure 4**, row 1), though it also noted gaps beyond the individual level and made recommendations for community-based and policy-based approaches.

Notably, this model is explicitly flexible, dynamic, and designed to expand upon previous models in important ways. Within the context of the definition of SDoH, some sectors are not well represented—for instance, where people play. Therefore, to address the absence of this sector in previous models, leisure, including arts and entertainment, is included as a sector with the potential

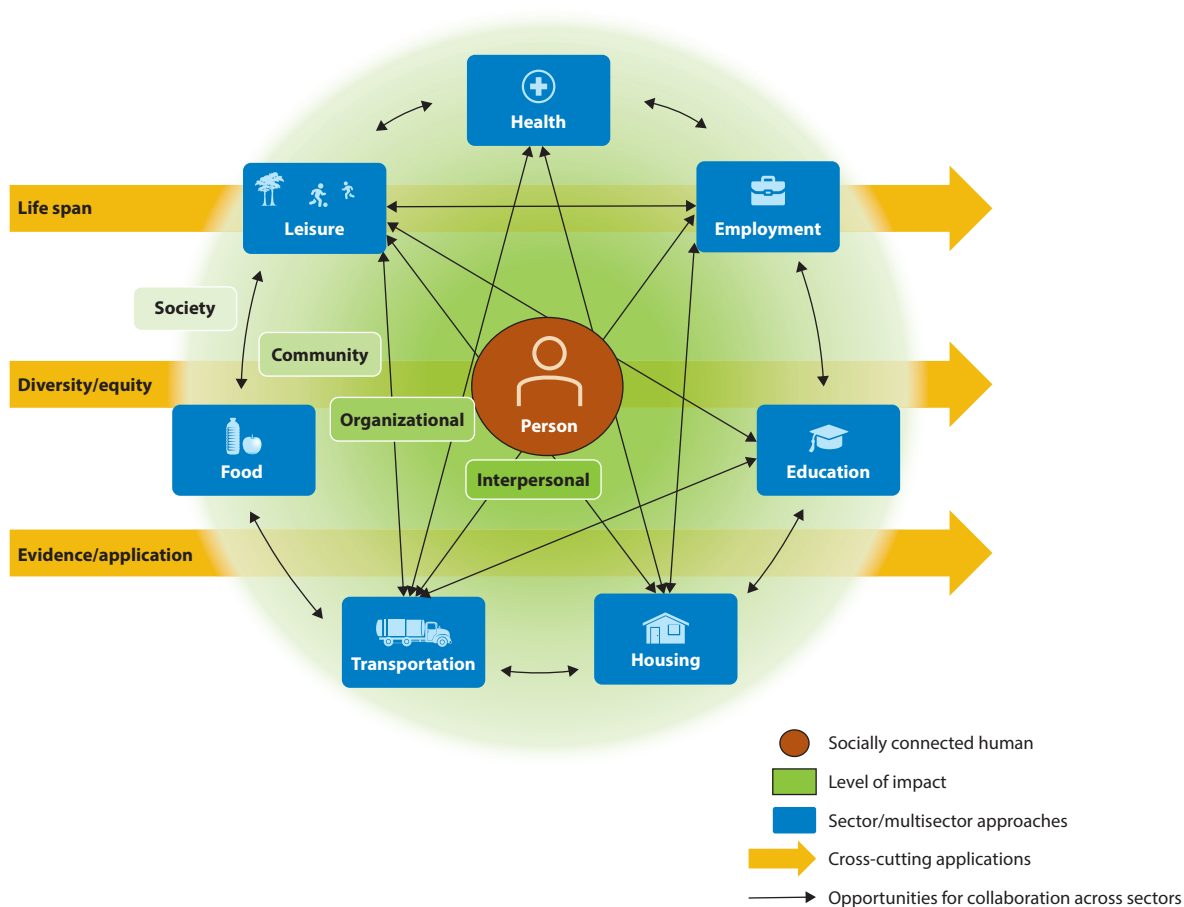


Figure 3

The **Systemic Framework of Cross-Sector Integration and Action Across the Life Span (SOCIAL)** is a conceptual model that combines and extends traditional public health models to more holistically guide public health.

Erratum >

to influence health through its impact on social connection. During the global pandemic, leisure was one of the sectors influenced by policies that limited social contact in an effort to reduce the spread of the virus. For example, theaters and museums were closed and sporting and other social events were canceled. In some cases, leisure activities were resumed in isolation or remotely. Like other sectors represented in the HiAP, leisure may be both a contributor to health through its impact on social connection and an opportunity for prevention and intervention across levels.

Another way in which this model improves upon previous models is by integrating a life span approach. Because many definitions of SDoH include the recognition of how we age, this framework explicitly acknowledges a life span approach within each intersection between socio-ecological levels and sectors. For example, the life span could be broken down into six stages (infancy, childhood, adolescence, young adulthood, middle age, and older adulthood), each stage could be numbered, and each cell could then be expanded into six subcells (e.g., 1. Infancy, 2. Childhood, 3. Adolescence, 4. Young Adulthood, 5. Middle Age, 6. Older Adulthood). Social connection is critical at every stage of life, with research demonstrating dose-response effects on biomarkers and mortality at adolescence, young adulthood, middle adulthood, and older age (105). While

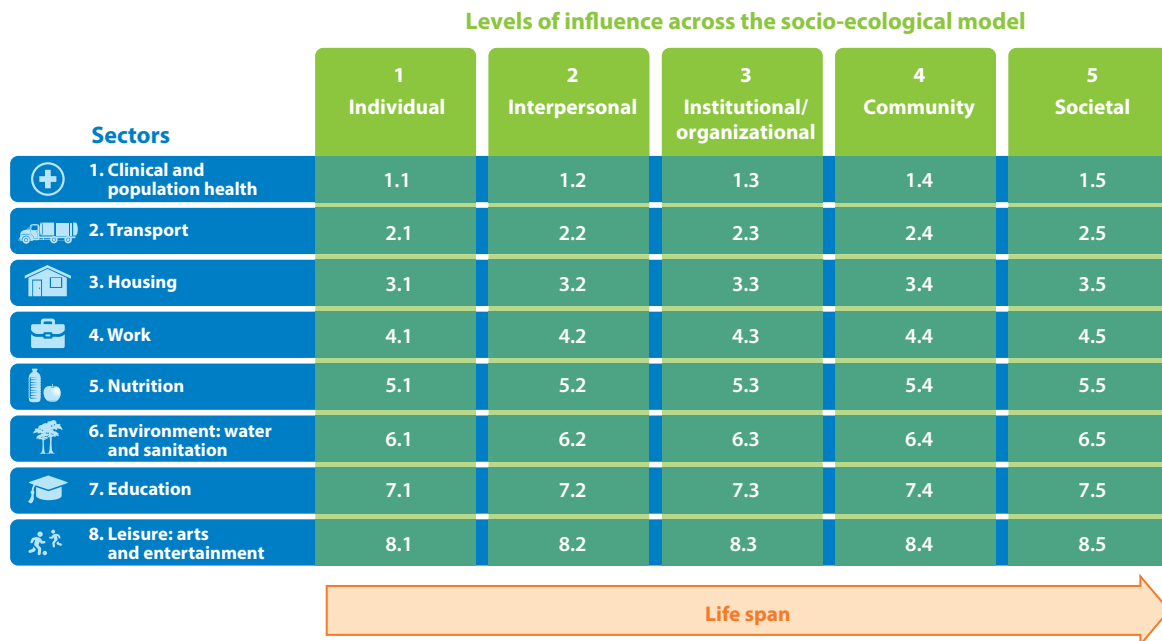


Figure 4

The Systemic Framework of Cross-Sector Integration and Action Across the Life Span (SOCIAL), which combines and extends traditional public health models, can be used to identify intersections among levels of the socio-ecological model and the sectors of the Health in All Policy model. The horizontal axis (*green boxes*) reflects a systems approach, including individual, interpersonal relationship, institutional/organizational, community, and society levels within the socio-ecological model. The sectors identified in the Health in All Policy framework are along the vertical axis (*blue boxes*) and include clinical and population health; transport; housing; work; nutrition; environment, including water and sanitation; education; and leisure, including arts and entertainment. Each cell represents an area of focus for evidence and application.

there is compelling evidence of health effects across major developmental stages throughout the life span, less is known about biological mechanisms and effective prevention and intervention efforts. This framework can help elucidate where there are gaps in the evidence. For example, educational policy efforts (**Figure 4**, cell 7.5) could be expanded to determine policies appropriate across each developmental stage. These could include programs focused on a specific developmental stage, such as prenatal and postnatal education programs focused on bonding and attachment for early healthy development (**Figure 4**, e.g., subcell 7.5.1), the inclusion of social connection in elementary and secondary public health education to focus on childhood and adolescence (**Figure 4**, e.g., subcells 7.5.2 and 7.5.3), or education programs among Medicare beneficiaries (**Figure 4**, e.g., subcell 7.5.6). Alternatively, these could be programs that are explicitly meant to cut across ages, such as educational programs focused on national health guidelines (**Figure 4**, cell 7.5).

Furthermore, collaboration between sectors and levels could create efficiencies to accelerate progress. Traditional boundaries between sectors and levels can be crossed in both evidence and application. For example, individually focused interventions could target ridesharing transportation for older adults in order to facilitate community engagement and medical appointment adherence; if successful, institutions could create policy to cover the associated costs. Thus, as represented by the bidirectional arrows between sectors (**Figure 3**), we could create collaborative partnerships to capitalize on overlapping avenues of investigation and application.

The Framework as an Evidence Gap Map

While the systemic framework of cross-sector action can provide a conceptual lens through which to address the chasm between evidence and application, it is also critical for advancing the science and relevant evidence within each of these cells. Cross-sector action needs to be evidence based. This framework can facilitate the identification of evidence gaps within each level that can guide funding priorities.

This framework may guide the development of an evidence gap map. In its most basic form, the framework identifies 40 cells based on the intersections between the five levels included within the socio-ecological model and the eight sectors within the HiAP (**Figure 4**). Yet, most of the evidence is only in one or two cells, suggesting we have tapped into only one-fortieth to one-twentieth of what can and should be done to affect public health by addressing social connection (**Figure 4**). If the model were expanded to encompass the life span approach, this fraction would be much smaller. If we assume that each of these cells contributes equally to population health, and that two of these cells were adequately and fully addressed, then we have focused our efforts on only 5% of the issue. If we can systematically begin to address the other 95%, the potential for change in population health would rise exponentially.

A Flexible Framework

The current representation of the systemic framework for cross-sector action is meant to be illustrative and not exhaustive, as the framework is purposely designed to be flexible. Just as there are variations on the socio-ecological model and the WHO HiAP sectors, additional levels may be added to the systems and sectors for more fine-grained analysis and application within the systemic framework. Similarly, the life span approach could be divided into more incremental stages from conception to death. Thus, the number of intersections (represented by cells) could grow as additional levels of analysis are needed.

To advance both evidence and solutions, this framework can be adapted to include additional factors. At least four factors may be particularly relevant. First, each cell could be expanded by specifying targets within the public health approach of primary, secondary, and tertiary prevention. Second, the framework could be expanded by explicitly identifying evidence and solutions within each cell for each component (i.e., structure, function, and quality) of social connection. Third, as social contact is increasingly tech-mediated, we need to better understand explicitly its role across each of these cells. Fourth, this framework should advance greater health equity and reduce health disparities by explicitly identifying disparities within each cell. Importantly, mapping of potential gaps in the intersections between relevant factors is not unique to social connection, and there is potential for application to other SDoH factors and other public health issues.

CONCLUSION

Cumulative evidence clearly demonstrates that a lack of social connection is associated with poorer health, pointing to the clear public health relevance of social connections. This evidence spans a range of physical and mental health outcomes, has been replicated across different populations and contexts, is independent of a range of potentially confounding factors, and demonstrates that the magnitude of effect rivals other risk factors for health and mortality. Despite this wealth of evidence, social connection is not adequately recognized or prioritized in many national public health efforts. Given the high prevalence within the population of persons who may lack adequate social connection and the severity of the health consequences, greater prioritization of social connection within public health and within efforts aiming to address SDoH is warranted. The global

COVID-19 pandemic has provided greater awareness of how social contact cuts across sectors and the urgency to address this issue within public health policy. Using the proposed SOCIAL framework, we can systematically map out gaps in evidence and solutions to accelerate progress focused on social connection within public health.

SUMMARY POINTS

1. Decades of accumulated interdisciplinary evidence on the relationship between social connections and health document associations, pathways, and biological mechanisms and provide a scientific foundation for prioritizing social connection for health both in the USA and globally.
2. Research across multiple scientific disciplines and methodological approaches has extensively documented compelling evidence of both the long-term health effects and the biological and behavioral basis of these effects; however, this evidence has been under-recognized within medicine and public health.
3. Current evidence suggests that the prevalence of poor social connection (e.g., loneliness, isolation) within the population is high and has increased during the COVID-19 pandemic, pointing to a potential major public health concern.
4. Given both short- and long-term health outcomes, spanning both chronic and infectious diseases, it is critical to identify the objectives that must be accomplished to achieve the overall goal of elevating social connections into the realm of a public health priority nationally.
5. National health objectives are aimed at the most pressing public health issues, and the social isolation accompanying the COVID-19 pandemic exacerbated an existing public health crisis; therefore, national objectives focused on social connection are needed.
6. Systematic approaches to identifying opportunities to address gaps in the evidence and apply the evidence to practice, across levels and sectors, will accelerate progress in addressing social connection within public health.

DISCLOSURE STATEMENT

The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

ACKNOWLEDGMENTS

I acknowledge the contributions to the conceptualization of the systemic framework by the members of the Scientific Advisory Council of the Foundation for Social Connection: Juan Albertorio, Thomas Cudjoe, Kelli Harding, Louise Hawkey, Eden Litt, Matthew Pantell, Carla Perissinotto, and Matthew Smith; Edward Garcia, Executive Director of the Foundation for Social Connection; and Matthew Itzkowitz, Policy Director.

LITERATURE CITED

1. AARP Found., United Health Found. 2020. *The pandemic effect: a social isolation report*. Slides, Oct. 6, AARP Found./United Health Found., Washington, DC
2. Albers C. 2020. Loneliness—a risk to health we can no longer ignore. *Occup. Health Wellbeing* 72:18–21

3. Alvarez-Bueno C, Caverro-Redondo I, Martinez-Andres M, Arias-Palencia N, Ramos-Blanes R, Salcedo-Aguilar F. 2015. Effectiveness of multifactorial interventions in primary health care settings for primary prevention of cardiovascular disease: a systematic review of systematic reviews. *Prev. Med.* 76(Suppl.):S68–75
4. Besora-Moreno M, Llauradó E, Tarro L, Solà R. 2020. Social and economic factors and malnutrition or the risk of malnutrition in the elderly: a systematic review and meta-analysis of observational studies. *Nutrients* 12(3):737
5. Bethell J, Aelick K, Babineau J, Bretzlaff M, Edwards C, et al. 2021. Social connection in long-term care homes: a scoping review of published research on the mental health impacts and potential strategies during COVID-19. *J. Am. Med. Dir. Assoc.* 22:228–37.e25
6. Birmingham WC, Holt-Lunstad J. 2018. Social aggravation: understanding the complex role of social relationships on stress and health-relevant physiology. *Int. J. Psychophysiol.* 131:13–23
7. Bowlby J. 1982. Attachment and loss: retrospect and prospect. *Am. J. Orthopsychiatry* 52:664–78
8. Braveman P, Egerter S, Williams DR. 2011. The social determinants of health: coming of age. *Annu. Rev. Public Health* 32:381–98
9. Bystrova K, Ivanova V, Edhborg M, Matthiesen AS, Ransjö-Arvidson AB, et al. 2009. Early contact versus separation: effects on mother–infant interaction one year later. *Birth* 36:97–109
10. Cacioppo JT, Cacioppo S, Capitanio JP, Cole SW. 2015. The neuroendocrinology of social isolation. *Annu. Rev. Psychol.* 66:733–67
11. Cance JD, Saavedra LM, Wondimu B, Scaglione NM, Hairgrove S, Graham PW. 2021. Examining the relationship between social connection and opioid misuse: a systematic review. *Subst. Use Misuse* 56:1493–507
12. CDC (Cent. Dis. Control Prev.). 2021. *Overview: maternity care practices*. Data Stat., CDC, Washington, DC. <https://www.cdc.gov/breastfeeding/data/mpinc/maternity-care-practices.htm#:~:text=Immediate%20skin%2Dto%2Dskin%20contact,baby%20to%20start%20breastfeeding%20well>
13. CDC (Cent. Dis. Control Prev.). 2021. *Social determinants of health: know what affects health*. Fact Sheet, CDC, Washington, DC. <https://www.cdc.gov/socialdeterminants/index.htm>
14. CDC (Cent. Dis. Control Prev.). 2021. *The social-ecological model: a framework for prevention*. Fact Sheet, CDC, Washington, DC. <https://www.cdc.gov/violenceprevention/about/social-ecologicalmodel.html>
15. Chang Q, Chan CH, Yip PSF. 2017. A meta-analytic review on social relationships and suicidal ideation among older adults. *Soc. Sci. Med.* 191:65–76
16. Chatterjee A, Banerjee S, Stein C, Kim M-H, DeFerio J, Pathak J. 2018. Risk factors for depression among civilians after the 9/11 World Trade Center terrorist attacks: a systematic review and meta-analysis. *PLOS Curr. Disasters*. <https://doi.org/10.1371/currents.dis.6a00b40c8ace0a6a0017361d7577c50a>
17. Chau AKC, Zhu C, So SH. 2019. Loneliness and the psychosis continuum: a meta-analysis on positive psychotic experiences and a meta-analysis on negative psychotic experiences. *Int. Rev. Psychiatry* 31:471–90
18. Coan JA, Sbarra DA. 2015. Social baseline theory: the social regulation of risk and effort. *Curr. Opin. Psychol.* 1:87–91
19. Cohen S. 2021. Psychosocial vulnerabilities to upper respiratory infectious illness: implications for susceptibility to coronavirus disease 2019 (COVID-19). *Perspect. Psychol. Sci.* 16:161–74
20. Cohen S, Underwood LG, Gottlieb BH. 2000. *Social Support Measurement and Intervention: A Guide for Health and Social Scientists*. Oxford, UK: Oxford Univ. Press
21. Dalen JE, Alpert JS, Goldberg RJ, Weinstein RS. 2014. The epidemic of the 20th century: coronary heart disease. *Am. J. Med.* 127:807–12
22. DiJulio B, Hamel L, Muñana C, Brodie M. 2018. *Loneliness and social isolation in the United States, the United Kingdom, and Japan: an international survey*. Res. Rep., Kaiser Family Found., San Francisco
23. Ditzen B, Heinrichs M. 2014. Psychobiology of social support: the social dimension of stress buffering. *Restor. Neurol. Neurosci.* 32:149–62

24. Du L, Shi HY, Qian Y, Jin XH, Li Y, et al. 2021. Association between social support and suicidal ideation in patients with cancer: a systematic review and meta-analysis. *Eur. J. Cancer Care* 30:e13382
25. Elovainio M, Hakulinen C, Pulkki-Råback L, Virtanen M, Josefsson K, et al. 2017. Contribution of risk factors to excess mortality in isolated and lonely individuals: an analysis of data from the UK Biobank cohort study. *Lancet Public Health* 2:e260–66
26. Erzen E, Cikrikci O. 2018. The effect of loneliness on depression: a meta-analysis. *Int. J. Soc. Psychiatry* 64:427–35
27. Evans IEM, Martyr A, Collins R, Brayne C, Clare L. 2019. Social isolation and cognitive function in later life: a systematic review and meta-analysis. *J. Alzheimer's Dis.* 70:S119–44
28. Fedak KM, Bernal A, Capshaw ZA, Gross S. 2015. Applying the Bradford Hill criteria in the 21st century: how data integration has changed causal inference in molecular epidemiology. *Emerg. Themes Epidemiol.* 12:14
29. Fortmann AL, Gallo LC. 2013. Social support and nocturnal blood pressure dipping: a systematic review. *Am. J. Hypertens.* 26:302–10
30. Fried L, Prohaska T, Burholt V, Burns A, Golden J, et al. 2020. A unified approach to loneliness. *Lancet* 395:114
31. Hassan R. 1998. One hundred years of Emile Durkheim's *Suicide: A Study in Sociology*. *Aust. N. Z. J. Psychiatry* 32:168–71
32. Hawkey L, Buecker S, Kaiser T, Luhmann M. 2020. Loneliness from young adulthood to old age: explaining age differences in loneliness. *Int. J. Behav. Dev.* <https://doi.org/10.1177/0165025420971048>
33. Hawkey LC, Capitanio JP. 2015. Perceived social isolation, evolutionary fitness and health outcomes: a lifespan approach. *Philos. Trans. R. Soc. B* 370(1669):20140114
34. Healthy People 2030. *Social determinants of health*. Fact Sheet, Off. Dis. Prev. Health Promot., Washington, DC. <https://health.gov/healthypeople/objectives-and-data/social-determinants-health>
35. Heidari Gorji MA, Fatahian A, Farsavian A. 2019. 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* 60:27–36
36. Hill AB. 1965. The environment and disease: association or causation? *Proc. R. Soc. Med.* 58:295–300
37. Holt-Lunstad J. 2018. Why social relationships are important for physical health: a systems approach to understanding and modifying risk and protection. *Annu. Rev. Psychol.* 69:437–58
38. Holt-Lunstad J. 2020. Social isolation and health. *Health Aff.* <https://doi.org/10.1377/hpb20200622.253235>
39. Holt-Lunstad J. 2021. The major health implications of social connection. *Curr. Dir. Psychol. Sci.* 30:251–59
40. Holt-Lunstad J. 2021. A pandemic of social isolation? *World Psychiatry* 20:55–56
41. Holt-Lunstad J, Robles TF, Sbarra DA. 2017. Advancing social connection as a public health priority in the United States. *Am. Psychol.* 72:517–30
42. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. 2015. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect. Psychol. Sci.* 10:227–37
43. Holt-Lunstad J, Smith TB, Layton JB. 2010. Social relationships and mortality risk: a meta-analytic review. *PLOS Med.* 7:e1000316
44. Hood CM, Gennuso KP, Swain GR, Catlin BB. 2016. County health rankings: relationships between determinant factors and health outcomes. *Am. J. Prev. Med.* 50:129–35
45. Hostinar CE. 2015. Recent developments in the study of social relationships, stress responses, and physical health. *Curr. Opin. Psychol.* 5:90–95
46. House JS, Landis KR, Umberson D. 1988. Social relationships and health. *Science* 241:540–45
47. Howick J, Kelly P, Kelly M. 2019. Establishing a causal link between social relationships and health using the Bradford Hill guidelines. *SSM Popul. Health* 8:100402
48. HRSA (Health Resour. Serv. Adm.). 2019. *The “loneliness epidemic.”* eNewsletter, HRSA, Rockville, MD. <https://www.hrsa.gov/enews/past-issues/2019/january-17/loneliness-epidemic>
49. Jain A, van Hoek AJ, Boccia D, Thomas SL. 2017. Lower vaccine uptake amongst older individuals living alone: a systematic review and meta-analysis of social determinants of vaccine uptake. *Vaccine* 35:2315–28

50. Kent de Grey RG, Uchino BN, Trettenvik R, Cronan S, Hogan JN. 2018. Social support and sleep: a meta-analysis. *Health Psychol.* 37:787–98
51. Kojima G, Taniguchi Y, Kitamura A, Fujiwara Y. 2020. Is living alone a risk factor of frailty? A systematic review and meta-analysis. *Ageing Res. Rev.* 59:101048
52. Kottke TE, Stiefel M, Pronk NP. 2016. “Well-being in all policies”: promoting cross-sectoral collaboration to improve people’s lives. *Prev. Chronic Dis.* 13:E52
53. Kuiper JS, Zuidersma M, Oude Voshaar RC, Zuidema SU, van den Heuvel ER, et al. 2015. Social relationships and risk of dementia: a systematic review and meta-analysis of longitudinal cohort studies. *Ageing Res. Rev.* 22:39–57
54. Lara E, Martin-Maria N, De la Torre-Luque A, Koyanagi A, Vancampfort D, et al. 2019. Does loneliness contribute to mild cognitive impairment and dementia? A systematic review and meta-analysis of longitudinal studies. *Ageing Res. Rev.* 52:7–16
55. Lara E, Moreno-Agostino D, Martin-Maria N, Miret M, Rico-Uribe LA, et al. 2020. Exploring the effect of loneliness on all-cause mortality: Are there differences between older adults and younger and middle-aged adults? *Soc. Sci. Med.* 258:113087
56. Larkin H, Shields JJ, Anda RF. 2012. The health and social consequences of adverse childhood experiences (ACE) across the lifespan: an introduction to prevention and intervention in the community. *J. Prev. Interv. Community* 40:263–70
57. Leigh-Hunt N, Baggeley D, Bash K, Turner V, Turnbull S, et al. 2017. An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health* 152:157–71
58. Leschak CJ, Eisenberger NI. 2019. Two distinct immune pathways linking social relationships with health: inflammatory and antiviral processes. *Psychosom. Med.* 81:711–19
59. Li H, Xia N. 2020. The role of oxidative stress in cardiovascular disease caused by social isolation and loneliness. *Redox Biol.* 37:101585
60. Maes M, Nelemans SA, Danneel S, Fernandez-Castilla B, Van den Noortgate W, et al. 2019. Loneliness and social anxiety across childhood and adolescence: multilevel meta-analyses of cross-sectional and longitudinal associations. *Dev. Psychol.* 55:1548–65
61. Maes M, Van den Noortgate W, Fustolo-Gunnink SF, Rassart J, Luyckx K, Goossens L. 2017. Loneliness in children and adolescents with chronic physical conditions: a meta-analysis. *J. Pediatr. Psychol.* 42:622–35
62. Mahon NE, Yarcheski A, Yarcheski TJ, Cannella BL, Hanks MM. 2006. A meta-analytic study of predictors for loneliness during adolescence. *Nurs. Res.* 55:308–15
63. Mattos dos Santos R. 2020. Isolation, social stress, low socioeconomic status and its relationship to immune response in Covid-19 pandemic context. *Brain Behav. Immun. Health* 7:100103
64. Michalska da Rocha B, Rhodes S, Vasilopoulou E, Hutton P. 2018. Loneliness in psychosis: a meta-analytical review. *Schizophr. Bull.* 44:114–25
65. Morina N, Kip A, Hoppen TH, Priebe S, Meyer T. 2021. 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. *BMJ Open* 11:e042335
66. Mund M, Freuding MM, Mobius K, Horn N, Neyer FJ. 2020. The stability and change of loneliness across the life span: a meta-analysis of longitudinal studies. *Personal. Soc. Psychol. Rev.* 24:24–52
67. Muscatell KA. 2021. Social psychoneuroimmunology: understanding bidirectional links between social experiences and the immune system. *Brain. Behav. Immun.* 93:1–3
68. Naito R, Leong DP, Bangdiwala SI, McKee M, Subramanian SV, et al. 2021. Impact of social isolation on mortality and morbidity in 20 high-income, middle-income and low-income countries in five continents. *BMJ Glob. Health* 6(3):e004124
69. NASEM (Nat. Inst. Sci. Eng. Med.). 2020. *Social isolation and loneliness in older adults: opportunities for the health care system*. Consens. Study Rep., NASEM, Washington, DC
70. Pantell M, Rehkopf D, Jutte D, Syme SL, Balmes J, Adler N. 2013. Social isolation: a predictor of mortality comparable to traditional clinical risk factors. *Am. J. Public Health* 103:2056–62
71. Peen NF, Duque-Wilckens N, Trainor BC. 2021. Convergent neuroendocrine mechanisms of social buffering and stress contagion. *Horm. Behav.* 129:104933

72. Penninkilampi R, Casey AN, Singh MF, Brodaty H. 2018. The association between social engagement, loneliness, and risk of dementia: a systematic review and meta-analysis. *J. Alzheimer's Dis.* 66:1619–33
73. Perissinotto CM, Stijacic Cenzer I, Covinsky KE. 2012. Loneliness in older persons: a predictor of functional decline and death. *Arch. Intern. Med.* 172:1078–83
74. Pinquart M, Duberstein PR. 2010. Associations of social networks with cancer mortality: a meta-analysis. *Crit. Rev. Oncol. Hematol.* 75:122–37
75. Prohaska T, Burholt V, Burns A, Golden J, Hawkey L, et al. 2020. Consensus statement: loneliness in older adults, the 21st century social determinant of health? *BMJ Open* 10:e034967
76. Rico-Urbe LA, Caballero FF, Martin-Maria N, Cabello M, Ayuso-Mateos JL, Miret M. 2018. Association of loneliness with all-cause mortality: a meta-analysis. *PLOS ONE* 13:e0190033
77. Robles TF. 2021. Social relationships and the immune system during development. *J. Child Psychol. Psychiatry* 62:539–59
78. Roelfs DJ, Shor E, Kalish R, Yogev T. 2011. The rising relative risk of mortality for singles: meta-analysis and meta-regression. *Am. J. Epidemiol.* 174:379–89
79. Rudolph L, Caplan J, Ben-Moshe K, Dillon L. 2013. *Health in All Policies: A Guide for State and Local Governments*. Washington, DC/Oakland, CA: Am. Public Health Assoc./Public Health Inst.
80. Ryden L, Ferrannini G, Mellbin L. 2019. Risk factor reduction in type 2 diabetes demands a multifactorial approach. *Eur. J. Prev. Cardiol.* 26:81–91
81. Sharra DA, Law RW, Portley RM. 2011. Divorce and death: a meta-analysis and research agenda for clinical, social, and health psychology. *Perspect. Psychol. Sci.* 6:454–74
82. Seeman TE, Singer BH, Ryff CD, Dienberg Love G, Levy-Storms L. 2002. Social relationships, gender, and allostatic load across two age cohorts. *Psychosom. Med.* 64:395–406
83. Seo D-C, Huang Y. 2012. Systematic review of social network analysis in adolescent cigarette smoking behavior. *J. Sch. Health* 82:21–27
84. Shankar A, McMunn A, Banks J, Steptoe A. 2011. Loneliness, social isolation, and behavioral and biological health indicators in older adults. *Health Psychol.* 30:377–85
85. Shor E, Roelfs DJ. 2015. Social contact frequency and all-cause mortality: a meta-analysis and meta-regression. *Soc. Sci. Med.* 128:76–86
86. Shor E, Roelfs DJ, Bugyi P, Schwartz JE. 2012. Meta-analysis of marital dissolution and mortality: reevaluating the intersection of gender and age. *Soc. Sci. Med.* 75:46–59
87. Shor E, Roelfs DJ, Curreli M, Clemow L, Burg MM, Schwartz JE. 2012. Widowhood and mortality: a meta-analysis and meta-regression. *Demography* 49:575–606
88. Shovelstul B, Han J, Germine L, Dodell-Feder D. 2020. Risk factors for loneliness: the high relative importance of age versus other factors. *PLOS ONE* 15:e0229087
89. Smith TB, Workman C, Andrews C, Barton B, Cook M, et al. 2021. Effects of psychosocial support interventions on survival in inpatient and outpatient healthcare settings: a meta-analysis of 106 randomized controlled trials. *PLOS Med.* 18:e1003595
90. Song Y, Nam S, Park S, Shin IS, Ku BJ. 2017. The impact of social support on self-care of patients with diabetes: What is the effect of diabetes type? Systematic review and meta-analysis. *Diabetes Educ.* 43:396–412
91. Spitz RA. 1945. Hospitalism: an inquiry into the genesis of psychiatric conditions in early childhood. *Psychoanal. Study Child* 1:53–74
92. Sylvia KE, Demas GE. 2018. A gut feeling: microbiome-brain-immune interactions modulate social and affective behaviors. *Horm. Behav.* 99:41–49
93. Takahashi A, Flanigan ME, McEwen BS, Russo SJ. 2018. Aggression, social stress, and the immune system in humans and animal models. *Front. Behav. Neurosci.* 12:56
94. Teo AR, Lerrigo R, Rogers MA. 2013. The role of social isolation in social anxiety disorder: a systematic review and meta-analysis. *J. Anxiety Disord.* 27:353–64
95. Teoh AN, Hilmert C. 2018. Social support as a comfort or an encouragement: a systematic review on the contrasting effects of social support on cardiovascular reactivity. *Br. J. Health Psychol.* 23:1040–65
96. Uchino BN. 2006. Social support and health: a review of physiological processes potentially underlying links to disease outcomes. *J. Behav. Med.* 29:377–87

97. Uchino BN. 2009. What a lifespan approach might tell us about why distinct measures of social support have differential links to physical health. *J. Soc. Pers. Relatsh.* 26:53–62
98. Uchino BN, Trettenvik R, Kent de Grey RG, Cronan S, Hogan J, Baucom BRW. 2018. Social support, social integration, and inflammatory cytokines: a meta-analysis. *Health Psychol.* 37:462–71
99. UNICEF. 1997. *Children at risk in Central and Eastern Europe: perils and promises*. Reg. Monit. Rep., Int. Child Dev. Cent., Florence, Italy
100. Valavanis IK, Mougiakakou SG, Grimaldi KA, Nikita KS. 2010. A multifactorial analysis of obesity as CVD risk factor: use of neural network based methods in a nutrigenetics context. *BMC Bioinform.* 11:453
101. Valtorta NK, Kanaan M, Gilbody S, Ronzi S, Hanratty B. 2016. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. *Heart* 102:1009–16
102. von Soest T, Luhmann M, Gerstorf D. 2020. The development of loneliness through adolescence and young adulthood: its nature, correlates, and midlife outcomes. *Dev. Psychol.* 56:1919–34
103. WHO (World Health Organ.). 2014. *Helsinki statement on health in all policies*. Conf. Statem., WHO, Geneva. https://www.who.int/healthpromotion/conferences/8gchp/8gchp_helsinki_statement.pdf
104. Xiu-Ying H, Qian C, Xiao-Dong P, Xue-Mei Z, Chang-Quan H. 2012. Living arrangements and risk for late life depression: a meta-analysis of published literature. *Int. J. Psychiatry Med.* 43:19–34
105. Yang YC, Boen C, Gerken K, Li T, Schorpp K, Harris KM. 2016. Social relationships and physiological determinants of longevity across the human life span. *PNAS* 113:578–83
106. Yuan MZ, Fang Q, Liu GW, Zhou M, Wu JM, Pu CY. 2019. Risk factors for post-acute coronary syndrome depression: a meta-analysis of observational studies. *J. Cardiovasc. Nurs.* 34:60–70