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Are loneliness and social isolation equal threats to health and well-being? An outcome-wide longitudinal approach

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ABSTRACT

The detrimental effects of loneliness and social isolation on health and well-being outcomes are well documented. In response, governments, corporations, and community-based organizations have begun leveraging tools to create interventions and policies aimed at reducing loneliness and social isolation at scale. However, these efforts are frequently hampered by a key knowledge gap: when attempting to improve specific health and well-being outcomes, decision-makers are often unsure whether to target loneliness, social isolation, or both. Filling this knowledge gap will inform the development and refinement of effective interventions. Using data from the Health and Retirement Study (13,752 participants (59% women and 41% men, mean [SD] age = 67 [10] years)), we examined how changes in loneliness and social isolation over a 4-year follow-up period (from t0:2008/2010 to t1:2012/2014) were associated with 32 indicators of physical-, behavioral-, and psychosocial-health outcomes 4-years later (t2:2016/2018). We used multiple logistic-, linear-, and generalized-linear regression models, and adjusted for sociodemographic, personality traits, pre-baseline levels of both exposures (loneliness and social isolation), and all outcomes (t0:2008/2010). We incorporated data from all participants into the overall estimate, regardless of whether their levels of loneliness and social isolation changed from the pre-baseline to baseline waves. After adjusting for a wide range of covariates, we observed that both loneliness and social isolation were associated with several physical health outcomes and health behaviors. However, social isolation was more predictive of mortality risk and loneliness was a stronger predictor of psychological outcomes. Loneliness and social isolation have independent effects on various health and well-being outcomes and thus constitute distinct targets for interventions aimed at improving population health and well-being.

1. Introduction

COVID-19 has heightened our awareness of loneliness and social isolation's detrimental effects on health and well-being outcomes (Berg-Weger & Morley, 2020). Loneliness is the *subjective* perception of feeling socially disconnected (Perlman et al., 1981), whereas social isolation is the *objective* lack of social interactions (e.g., smaller social network) (Cacioppo et al., 2014). Mounting research shows that loneliness and social isolation are each associated with an elevated risk of: psychological distress (e.g., depression) (Courtin & Knapp, 2017), dysregulated biologic functioning (e.g., allostatic loads) (Seeman et al., 2002), chronic conditions (e.g., cardiovascular disease) (Valtorta et al., 2016), and premature mortality (Holt-Lunstad et al., 2015; Shor & Roelfs, 2015). Further, the economic burden of weaker social connections is substantial and rising (e.g., ~$7 billion extra in Medicare spending annually) (Flowers et al., 2017). Thus, loneliness and social

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isolation are increasingly recognized as urgent public health threats.

In response, governments, corporations, and community-based organizations have begun leveraging tools to create interventions and policies aimed at reducing loneliness (e.g., cognitive behavioral therapy) (Masi et al., 2011; National Academies of Sciences, Engineering, and Medicine, 2020a) and social isolation (e.g., programs aimed at increasing social interactions) (Cattan et al., 2005) at-scale (Fried et al., 2020). However, these efforts are frequently hampered by a key knowledge gap: when attempting to improve specific health and well-being outcomes, decision-makers are unsure whether to target loneliness, social isolation, or both (Holt-Lunstad et al., 2015). Filling this knowledge gap is important for the development of effective interventions.

A growing number of studies have begun examining loneliness and social isolation simultaneously, which has helped understand how they are differentially related to health and well-being outcomes (Beller & Wagner, 2018; Beridze et al., 2020; Bu et al., 2020; Cassie et al., 2020; Christiansen et al., 2021; Coyle & Dugan, 2012; Fiordelli et al., 2020; Gale et al., 2018; Ge et al., 2017; Golden et al., 2009; Hakulinen et al., 2018; Holwerda et al., 2014; Hoogendijk et al., 2020; Hsu, 2020; Müller et al., 2021; Schrempft et al., 2019; Schutter et al., 2021; Shankar et al., 2013, 2017; Smith & Victor, 2019; Tomaka et al., 2006; Valtorta et al., 2018; Ward et al., 2021; Xia & Li, 2018). For example, loneliness and social isolation often show similar associations with some health outcomes (e.g., mortality) (Holt-Lunstad et al., 2015). However, loneliness appears to be a stronger risk factor for depression (Ge et al., 2017; Taylor et al., 2018; Teo et al., 2013), whereas social isolation appears to be a stronger risk factor for physical activity and cognitive decline (Schrempft et al., 2019; Yu et al., 2021). Despite increasing research examining loneliness and social isolation concurrently, many studies have yet to examine many other outcomes that are also important for healthy aging (e.g., optimism, various chronic health conditions). Further, some studies have yielded mixed results even when examining a more narrow set of outcomes (Holwerda et al., 2014; Kobayashi & Steptoe, 2018; Lara et al., 2019; Shankar et al., 2011). The underlying reasons for diverging results remain unclear, but might be due to differences in: 1) study designs (e.g., cross-sectional vs. longitudinal data), 2) populations, 3) covariate-adjustment, 4) key moderators (e.g., gender) (Liu et al., 2020), 5) exposure and/or outcomes measurement tools. Further, existing studies examined the cumulative effects of loneliness/social isolation over the life span on health and well-being outcomes rather than the effects of changes in loneliness and social isolation. In this era of translational research, interventionists and policy makers are seeking answers to a different question that most past studies have not addressed. What changes in health and well-being outcomes might we observe if loneliness or social isolation were intervened upon?

To begin addressing this question and help addressing limitations of previous research, we used an outcome-wide analytic approach (Hsu, 2020) and examined how *changes* in loneliness and social isolation are associated with 32 subsequent outcomes in a large, prospective, and nationwide sample of adults aged >50. This outcome-wide analytic approach can holistically capture potential heterogenous effects across a range of outcomes using a standardized: 1) study design, 2) population, 3) set of covariates, 4) exposure, and 5) outcomes. Further, this approach controls for the following factors all in the pre-baseline wave: the exposure (loneliness/social isolation), a robust range of potential confounders, and all outcomes. Controlling for the pre-baseline exposure helps us condition on (i.e., take into consideration the pre-baseline levels of social isolation or loneliness, effectively adjusting our analysis to acknowledge these initial conditions) or remove the potential accumulating effects that past loneliness or social isolation had on health/well-being in the past, thus allowing us to evaluate the effects of changes in loneliness or social isolation and provide better estimates of the outcomes we might expect to observe if loneliness or social isolation were intervened upon. Without such adjustment for the pre-baseline exposure, our estimates would capture not only the effects of "change," but also the potentially lingering effects of the past exposure on the outcomes (i.e., cumulative effects). Outcome-wide analyses are a hypothesis-generating, data-driven approach aimed at discovering promising health and well-being outcomes associated with exposures (loneliness and social isolation in this study), which may then undergo further investigation in future studies. The outcomes in this study were chosen because they are often included in the conceptualization of key gerontological models that characterize the antecedents, processes, and outcomes that foster healthy aging (Aldwin & Igarashi, 2015; Depp & Jeste, 2006; Reich et al., 2010; Rowe & Kahn, 1987; Ryff & Singer, 2009).

2. Methods

2.1. Study population

We used data from the Health and Retirement Study (HRS), an ongoing nationwide panel study of U.S. adults aged >50 years. In 2008, a randomly selected 50% of the participants completed an enhanced face-to-face interview. It was also the first year that an expanded loneliness measure was administered in HRS. The remaining half were interviewed in 2010. Following the interview, respondents completed a psychosocial questionnaire (response rates: 84% for the 2008 sub-cohort and 73% for the 2010 sub-cohort) (Smith et al., 2017, p. 72). To increase the sample size, we ensured the compatibility and combined data from both sub-cohorts as the pre-baseline wave.

We used three waves of data. All covariates were first measured (pre-baseline wave: $t_{0,}$ 2008/2010), the exposures (loneliness/social isolation) were measured four years later (baseline wave: $t_{1,}$ 2012/2014), and all outcomes were measured another four years later (outcomes wave: $t_{2,}$ 2016/2018). The ethics review board at the University of British Columbia exempted the study from human subjects review because it used de-identified and publicly available data. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

3. Measures

3.1. Loneliness

Loneliness was measured using an 11-item revised UCLA Loneliness Scale. Positively-worded items were reverse-coded, and all 11 items were averaged. The average score was transformed into z-scores for standardization (higher scores indicated greater loneliness; α in 2008 = 0.88; α in 2010 = 0.87). To examine potential non-linear associations, scores were categorized into three groups: 1) "least lonely" (<1 SD below the mean (=1.03), 2) "somewhat lonely" (within 1 SD of the mean (=1.50), and 3) "lonely" (>1 SD above the mean (=2.22).

3.2. Social isolation

We created a 8-item social isolation measure that assessed five domains of a social network (Berkman & Syme, 1979; Cornwell & Waite, 2009). *Domain 1* assessed information about participants' most intimate ties: 1) marital status (0 = married, 1 = not married), 2) whether participants live with a spouse/partner (0 = live with spouse/partner, 1 = do not live with spouse/partner). *Domain 2* assessed participants' relationships with children/other family: 1) number of close children/other family (reverse-coded such that higher value indicates fewer ties), 2) how often they meet/speak on the phone/write/email with children/other family (1=≥3x/week, 7=<1x/year/never). *Domain 3* assessed participants' friendships: 1) number of close friends (reverse--coded so that higher values indicate fewer ties), 2) how often they meet/speak on the phone/write/email friends (1=≥3x/week, 7=<1x/year/never). *Domain 4* assessed participants' engagement in various social activities: how often they volunteer, do charity work,

attend educational courses/social clubs/non-religious organizations (1 = daily, 7 = never/not relevant). *Domain 5* assessed religious service attendance (1=>1x/week, 5 = not at all).

To standardize the measure, we first created z-scores for each of the 8 items. Then, since Domains 1–3 had two items each, we took the average z-score of both items to create a single score for each of those domains. Finally, we created a composite social isolation score by averaging z-scores for all 5 Domains (higher scores indicated greater social isolation). To evaluate potential non-linear associations, scores were categorized into three groups (Shaw et al., 2017): 1) "least isolated" (<1 SD below the mean), 2) "somewhat isolated" (within 1 SD of the mean) and, 3) "socially isolated" (>1 SD above the mean).

3.3. Outcomes

In 2016/2018(t_2), four years after the exposure assessment, 32 outcomes were assessed including: physical health (all-cause mortality, number of chronic conditions, diabetes, hypertension, stroke, cancer, heart disease, lung disease, arthritis, overweight/obesity, physical functioning limitations, cognitive impairment, chronic pain, self-rated health), health behaviors (heavy drinking, smoking, exercise, and sleep problems), psychological well-being (positive affect, life satisfaction, optimism, purpose in life, mastery, health mastery, and financial mastery), psychological distress (depression, depressive symptoms, hopelessness, negative affect, constraints), and social factors (loneliness and social isolation; see Table 3's footnote for further rationale on including these outcomes).

3.4. Covariates

Covariates included 1) sociodemographic factors (age, sex, race/ethnicity [White, African-American, Hispanic, and Other], 2) annual household income (<$50,000, $50,000–$74,999, $75,000–$99,999, ≥$100,000), 3) total wealth (based on quintiles of the score distribution in the current sample), 4) education (no degree, GED/high school diploma, ≥college degree), 5) employment status (yes/no), 6) health insurance (yes/no), 7) geographic regions (Northeast, Midwest, South, and West), 8) childhood abuse (yes/no), and 9) personality traits (openness, conscientiousness, extraversion, agreeableness, and neuroticism). We also adjusted for all outcome variables in the pre-baseline wave. The HRS documentation (Fisher et al., 2005; Jenkins et al., 2008; Smith et al., 2017, p. 72) and Supplemental Text 1 provide additional information about the covariates and outcome variables. In all models, we adjusted for loneliness and social isolation in the pre-baseline wave.

3.5. Statistical analysis

The outcome-wide analytic approach implements analytic decisions not commonly used in disciplines outside of causal inference (VanderWeele et al., 2020a). Thus, we summarize these analytic decisions here with one of the exposures: loneliness (the same analyses were also conducted with social isolation). First, we adjust for covariates in the pre-baseline wave (t_0, 2008/2010), assessed prior to the exposure, since if covariates are measured at the same timepoint as the exposure (t_1, 2012/2014), it is unclear if the covariates are confounders or mediators (VanderWeele et al., 2020a). Second, all outcomes in the pre-baseline wave (t_0, 2008/2010) were adjusted for in each model to reduce potential reverse causality. Third, to evaluate change in loneliness, we adjust for loneliness in the pre-baseline wave (t_0, 2008/2010). This helps us "hold constant" pre-baseline levels of loneliness. Thus, this method allows us to evaluate how *changes* in loneliness (between t_0 and t_1) are associated with subsequent outcomes (at t_2; see Supplemental Text 2 for further details). We incorporated data from all participants into the overall estimate, regardless of whether their levels of loneliness and social isolation changed from the pre-baseline to baseline waves. Adjusting for pre-baseline loneliness (t_0) also has additional advantages: 1) helps reduce potential unmeasured confounding since an unmeasured confounding variable would have to be substantially associated with present loneliness pathways independent of past loneliness; 2) helps reduce the risk of reverse causality by "removing" the potential accumulating effects that loneliness might have already had on health and well-being outcomes in the past ("prevalent exposure") (VanderWeele, 2021).

We examined loneliness and social isolation as separate independent variables in each model, and further examined each outcome in separate models. Depending on the nature of the outcome, we used different analytic approaches: 1) logistic regression models for binary outcomes with <10% prevalence, 2) modified Poisson regression models (Zou, 2004) for binary outcomes with ≥10% prevalence, or 3) linear regression models for continuous outcomes. We standardized (mean = 0, SD = 1) all continuous outcomes for more accurate interpretation of the outcome effect sizes. Bonferroni correction was used to account for multiple testing (VanderWeele & Mathur, 2019).

3.6. Additional analyses

First, we calculated *E*-values as a sensitivity analysis for potential unmeasured confounding which assessed the minimum strength of association that an unmeasured confounder must have on the risk ratio scale (with both loneliness/social isolation and the outcome), conditional on the observed covariates, to explain away the observed associations between the loneliness/social isolation-health and well-being (Haneuse et al., 2019; VanderWeele & Ding, 2017). Second, we re-analyzed all models with fewer covariates that are more conventional in the literature.

We also conducted sensitivity analyses using the social isolation measure. First, we examined how each domain (Domains 1–5) was independently associated with 32 outcomes across five separate sets of analyses. Additionally, we examined how the "behavioral" vs. "network" characteristics of the social isolation measure were associated with the outcomes. Behavioral characteristics capture the quantity of active social actions/engagement (social contact frequency, social activity participation, religious service attendance), and the network characteristics capture the size/quantity of the social network (marital/living status, number of close ties). We used continuous z-scores (vs. three groups) for all supplementary analyses using the social isolation measure. Finally, we conducted analyses that "pit" loneliness and social isolation against each other in the same model.

3.7. Multiple imputation

In our data, the total proportion of missing values across all variables were as follows: 1.2% of loneliness, 0.2% of social isolation, 16.7% of covariates, and 29.6% of outcomes were missing. Thus, we imputed all missing exposure, covariates, and outcome data using imputation by chained equations which produced 5 datasets (Asendorpf et al., 2014; Harel et al., 2018; Moons et al., 2006). A missing at random mechanism for the missing values was evaluated by our team and others (Lu & Shelley, 2022). Additionally, we used an inclusive approach when selecting auxiliary items for imputing missing data, instead of a restrictive approach (VanderWeele et al., 2020b).

4. Results

At the pre-baseline wave (t_0:2008/2010), participants were average 67 years-old, and more likely to be women (59%) and married (63%). Tables 1 and 2 summarize participant characteristics by loneliness and social isolation in the pre-baseline wave. Supplementary Table 1 describes the *changes* in loneliness and social isolation from the pre-baseline (t_0) wave to baseline wave (t_1).

Table 3 summarizes the estimated associations with subsequent

Table 1
Characteristics of participants at pre-baseline by groups of loneliness (N = 10,450)[a,b,c].

Participant Characteristics	Loneliness					
	Group 1 (n = 2615)		Group 2 (n = 6011)		Group 3 (n = 1824)	
	No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)
Sociodemographic factors						
Age (yr; range: 48–96)		67.2 (9.0)		67.4 (9.6)		64.9 (9.3)
Female (%)	1646 (62.9)		3572 (59.4)		1064 (58.3)	
Race/Ethnicity (%)						
White	2162 (82.7)		4455 (74.1)		1282 (70.3)	
Black	262 (10.0)		835 (13.9)		287 (15.7)	
Hispanic	143 (5.5)		561 (9.3)		202 (11.1)	
Other	47 (1.8)		158 (2.6)		53 (2.9)	
Married (%)	1941 (74.2)		3804 (63.3)		971 (53.3)	
Annual Household Income (%)						
<$50,000	1191 (45.5)		3424 (57.0)		1227 (67.3)	
$50,000–$74,999	484 (18.5)		970 (16.1)		252 (13.8)	
$75,000–$99,999	298 (11.4)		592 (9.9)		139 (7.6)	
≥$100,000	642 (24.6)		1025 (17.1)		206 (11.3)	
Total Wealth (%)						
1st Quintile	269 (10.3)		1093 (18.2)		567 (31.1)	
2nd Quintile	396 (15.1)		1209 (20.1)		428 (23.5)	
3rd Quintile	547 (20.9)		1221 (20.3)		348 (19.1)	
4th Quintile	649 (24.8)		1248 (20.8)		266 (14.6)	
5th Quintile	754 (28.8)		1240 (20.6)		215 (11.8)	
Education (%)						
<High School	243 (9.3)		960 (16.0)		393 (21.6)	
High School	1411 (54.2)		3366 (56.1)		1015 (55.8)	
≥College	951 (36.5)		1671 (27.9)		412 (22.6)	
Employed (%)	1149 (44.0)		2517 (42.9)		744 (40.8)	
Health Insurance (%)	2521 (96.5)		5632 (93.8)		1637 (89.9)	
Geographic Region (%)						
Northeast	375 (14.3)		858 (14.3)		276 (15.2)	
Midwest	681 (26.0)		1623 (27.0)		448 (24.6)	
South	1043 (39.9)		2337 (38.9)		742 (40.8)	
West	516 (19.7)		1186 (19.8)		354 (19.5)	
Childhood Abuse (%)	145 (5.6)		433 (7.3)		218 (12.1)	
Physical Health						
Diabetes (%)	373 (14.3)		1222 (20.4)		428 (23.5)	
Hypertension (%)	1384 (53.0)		3363 (56.0)		1094 (60.0)	
Stroke (%)	120 (4.6)		361 (6.0)		142 (7.8)	
Cancer (%)	380 (14.5)		832 (13.9)		216 (11.9)	
Heart Disease (%)	485 (18.6)		1280 (21.3)		415 (22.8)	
Lung Disease (%)	147 (5.6)		479 (8.0)		205 (11.2)	
Arthritis (%)	1416 (54.2)		3549 (59.1)		1092 (59.9)	
Overweight/Obesity (%)	1806 (70.0)		4368 (73.3)		1348 (75.1)	
Physical Function Limitations (%)	329 (12.6)		1150 (19.1)		571 (31.3)	
Cognitive impairment (%)	238 (9.2)		881 (14.8)		363 (20.1)	
Chronic Pain (%)	680 (26.0)		2127 (35.4)		845 (46.3)	
Self-Rated Health (range: 1–5)		3.6 (0.9)		3.3 (1.0)		2.8 (1.1)
Health Behaviors						
Heavy Drinking (%)	189 (8.9)		365 (7.5)		122 (8.4)	
Smoking (%)	241 (9.3)		723 (12.1)		341 (18.8)	
Frequent Physical Activity (%)	2095 (80.2)		4458 (74.2)		1190 (65.3)	
Sleep Problems (%)	478 (33.5)		1348 (39.7)		532 (52.6)	
Religious Service Attendance (%)						
More than once a week	566 (21.66)		961 (16.0)		208 (11.4)	
Once a week	763 (29.2)		1635 (27.2)		366 (20.1)	
2–3 times a month	292 (11.2)		707 (11.8)		227 (12.5)	
One or more times a year	506 (19.4)		1215 (20.2)		407 (22.3)	
Not at all	486 (18.6)		1489 (24.8)		614 (33.7)	
Psychological Well-Being						
Positive Affect (range: 1–5)		4.1 (0.6)		3.6 (0.7)		2.9 (0.8)
Life Satisfaction (range: 1–7)		5.8 (1.2)		5.0 (1.4)		3.9 (1.6)
Optimism (range: 1–6)		5.1 (0.8)		4.5 (0.9)		3.8 (1.0)
Purpose in Life (range: 1–6)		5.2 (0.7)		4.7 (0.9)		4.1 (1.0)
Mastery (range: 1–6)		5.2 (0.9)		4.8 (1.0)		4.3 (1.1)
Health Mastery (range: 1–10)		8.1 (1.8)		7.4 (2.2)		6.5 (2.6)
Financial Mastery (range: 1–10)		8.0 (2.0)		7.3 (2.5)		5.9 (3.0)
Psychological Distress						
Depression (%)	98 (3.8)		684 (11.4)		563 (30.9)	
Depressive Symptoms (range: 0–8)		0.5 (1.0)		1.2 (1.7)		2.5 (2.5)
Hopelessness (range: 1–6)		1.6 (0.8)		2.3 (1.2)		3.3 (1.3)
Negative Affect (range: 1–5)		1.4 (0.4)		1.7 (0.5)		2.2 (0.8)
Perceived Constraints (range: 1–6)		1.5 (0.8)		2.1 (1.1)		3.0 (1.3)
Social Factors						

(*continued on next page*)

Table 1 (*continued*)

Participant Characteristics	Loneliness					
	Group 1 (n = 2615)		Group 2 (n = 6011)		Group 3 (n = 1824)	
	No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)
Social Isolation		−0.2 (0.4)		0.03 (0.5)		0.3 (0.5)
Personality						
Openness (range: 1–4)		3.1 (0.5)		2.9 (0.5)		2.7 (0.6)
Conscientiousness (range: 1–4)		3.6 (0.4)		3.4 (0.4)		3.2 (0.5)
Extraversion (range: 1–4)		3.5 (0.5)		3.2 (0.5)		2.7 (0.6)
Agreeableness (range: 1–4)		3.7 (0.4)		3.5 (0.5)		3.3 (0.6)
Neuroticism (range: 1–4)		1.7 (0.5)		2.0 (0.6)		2.4 (0.7)

[a] This table was created based on non-imputed data.
[b] All variables in Table 1 were used as covariates, and assessed in the pre-baseline wave (t_0;2008/2010).
[c] The percentages in some sections may not add up to 100% due to rounding.

Table 2
Characteristics of participants at pre-baseline by groups of social isolation (N = 10,577)[a,b,c].

Participant Characteristics	Social Isolation					
	Group 1 (n = 1593)		Group 2 (n = 7184)		Group 3 (n = 1800)	
	No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)
Sociodemographic factors						
Age (yr; range: 48–96)		68.0 (8.9)		66.9 (9.5)		66.1 (9.9)
Female (%)	996 (62.5)		4347 (60.5)		1022 (56.8)	
Race/Ethnicity (%)						
White	1176 (73.8)		5457 (76.0)		1330 (74.0)	
Black	243 (15.3)		935 (13.0)		233 (13.0)	
Hispanic	140 (8.8)		618 (8.6)		182 (10.1)	
Other	34 (2.1)		173 (2.4)		53 (3.0)	
Married (%)	1430 (89.8)		4802 (66.9)		538 (29.9)	
Annual Household Income (%)						
<$50,000	764 (48.0)		3875 (53.9)		1299 (72.2)	
$50,000–$74,999	276 (17.3)		1207 (16.8)		235 (13.1)	
$75,000–$99,999	184 (11.6)		741 (10.3)		109 (6.1)	
≥$100,000	369 (23.2)		1361 (18.9)		157 (8.7)	
Total Wealth (%)						
1st Quintile	148 (9.3)		1198 (16.7)		622 (34.6)	
2nd Quintile	274 (17.2)		1361 (18.9)		429 (23.8)	
3rd Quintile	330 (20.72)		1484 (20.7)		323 (17.9)	
4th Quintile	391 (24.5)		1544 (21.5)		246 (13.7)	
5th Quintile	450 (28.3)		1597 (22.2)		180 (10.0)	
Education (%)						
<High School	191 (12.0)		1079 (15.1)		372 (20.7)	
High School	799 (50.3)		4008 (56.0)		1042 (58.0)	
≥College	600 (37.7)		2076 (29.0)		382 (21.3)	
Employed (%)	642 (40.3)		3091 (43.0)		716 (39.8)	
Health Insurance (%)	1523 (95.7)		6743 (94.0)		1631 (90.7)	
Geographic Region (%)						
Northeast	192 (12.1)		1043 (14.5)		293 (16.3)	
Midwest	449 (28.2)		1899 (26.5)		433 (24.1)	
South	683 (42.9)		2824 (39.4)		673 (37.4)	
West	267 (16.8)		1410 (19.7)		399 (22.2)	
Childhood Abuse (%)	96 (6.1)		512 (7.2)		197 (11.1)	
Physical Health						
Diabetes (%)	283 (17.8)		1352 (18.8)		418 (23.2)	
Hypertension (%)	884 (55.5)		3975 (55.4)		1052 (58.5)	
Stroke (%)	72 (4.5)		415 (5.8)		142 (7.9)	
Cancer (%)	207 (13.0)		999 (13.9)		237 (13.2)	
Heart Disease (%)	309 (19.4)		1508 (21.0)		389 (21.7)	
Lung Disease (%)	88 (5.5)		532 (7.4)		223 (12.4)	
Arthritis (%)	929 (58.4)		4149 (57.8)		1056 (58.8)	
Overweight/Obesity (%)	1165 (73.8)		5181 (72.9)		1268 (71.6)	
Physical Function Limitations (%)	220 (13.8)		1335 (18.6)		535 (29.7)	
Cognitive impairment (%)	181 (11.5)		989 (13.9)		348 (19.6)	
Chronic Pain (%)	479 (30.1)		2445 (34.1)		772 (42.9)	
Self-Rated Health (range: 1–5)		3.5 (1.0)		3.3 (1.0)		2.9 (1.1)
Health Behaviors						
Heavy Drinking (%)	64 (4.8)		477 (8.3)		138 (9.4)	
Smoking (%)	70 (4.4)		811 (11.4)		439 (24.5)	
Frequent Physical Activity (%)	1299 (81.6)		5414 (75.5)		1118 (62.2)	
Sleep Problems (%)	320 (36.0)		1505 (38.9)		555 (49.3)	
Religious Service Attendance (%)						
More than once a week	772 (48.5)		953 (13.3)		28 (1.6)	

(*continued on next page*)

Table 2 (*continued*)

Participant Characteristics	Social Isolation					
	Group 1 (n = 1593)		Group 2 (n = 7184)		Group 3 (n = 1800)	
	No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)
Once a week	605 (38.0)		2100 (29.3)		101 (5.6)	
2–3 times a month	115 (7.2)		983 (13.7)		144 (8.0)	
One or more times a year	76 (4.8)		1668 (23.2)		408 (22.7)	
Not at all	25 (1.6)		1473 (20.5)		1117 (62.1)	
Psychological Well-Being						
Positive Affect (range: 1–5)		3.9 (0.7)		3.6 (0.8)		3.2 (0.8)
Life Satisfaction (range: 1–7)		5.5 (1.4)		5.0 (1.5)		4.2 (1.6)
Optimism (range: 1–6)		4.8 (0.9)		4.6 (0.9)		4.0 (1.0)
Purpose in Life (range: 1–6)		5.05 (0.8)		4.8 (0.9)		4.3 (1.0)
Mastery (range: 1–6)		5.0 (1.0)		4.8 (1.1)		4.6 (1.2)
Health Mastery (range: 1–10)		7.8 (2.0)		7.4 (2.2)		7.0 (2.6)
Financial Mastery (range: 1–10)		7.6 (2.2)		7.3 (2.5)		6.7 (3.0)
Psychological Distress						
Depression (%)	113 (7.1)		851 (11.9)		409 (22.7)	
Depressive Symptoms (range: 0–8)		0.8 (1.5)		1.2 (1.8)		2.0 (2.3)
Hopelessness (range: 1–6)		1.9 (1.0)		2.2 (1.2)		2.9 (1.4)
Negative Affect (range: 1–5)		1.6 (0.5)		1.7 (0.6)		1.9 (0.7)
Perceived Constraints (range: 1–6)		1.9 (1.0)		2.1 (1.1)		2.5 (1.3)
Social Factors						
Loneliness (range: 1–3)		1.3 (0.3)		1.5 (0.4)		1.8 (0.5)
Personality						
Openness (range: 1–4)		3.1 (0.5)		2.9 (0.5)		2.8 (0.6)
Conscientiousness (range: 1–4)		3.5 (0.4)		3.4 (0.5)		3.3 (0.5)
Extraversion (range: 1–4)		3.4 (0.5)		3.2 (0.5)		2.9 (0.6
Agreeableness (range: 1–4)		3.7 (0.4)		3.5 (0.5)		3.4 (0.5)
Neuroticism (range: 1–4)						

[a] This table was created based on non-imputed data.
[b] All variables in Table 1 were used as covariates, and assessed in the pre-baseline wave (t_0;2008/2010).
[c] The percentages in some sections may not add up to 100% due to rounding.

health and well-being outcomes for the highest level (versus lowest) of loneliness/social isolation, conditional on pre-baseline levels of loneliness and social isolation. For physical health outcomes, greater loneliness and social isolation were both associated with increased risk of all-cause mortality and physical functioning limitations. For example, participants in the highest (versus lowest) level of loneliness, conditional on prior loneliness, had 43% higher risk of all-cause mortality (95% CI [1.17, 1.76]), and those in the highest (versus lowest) group of social isolation, conditional on prior social isolation, had a 74% higher risk of all-cause mortality (95% CI [1.25, 2.42]). For other physical health outcomes, different associations were observed for loneliness and social isolation. Greater loneliness was associated with a 25% increased risk of lung disease (95% CI [1.04, 1.51]), 13% increased risk of chronic pain (95% CI [1.02, 1.25]), and worse self-rated health ($\beta = -0.12$, 95% CI [−0.20, −0.05]). However, greater social isolation was associated with a 30% greater risk of stroke (95% CI [1.01, 1.67]) and a 22% higher risk of cognitive impairment (95% CI [1.02, 1.46]).

When considering health behaviors, those in the highest (versus lowest) group of loneliness, had a 16% increased risk of subsequent sleep problems (95% CI [1.04, 1.29]). Those in the highest (versus lowest) group of social isolation, had a 13% decreased likelihood of subsequent frequent physical activity (95% CI [0.77, 0.97]).

For psychological outcomes, greater loneliness was associated with worse outcomes for all psychological well-being and distress factors. Greater social isolation was associated with a subset of these including decreased subsequent positive affect, life satisfaction, optimism, purpose in life, and increased subsequent depression, depressive symptoms, hopelessness, and perceived constraints.

4.1. Additional analyses

First, *E*-values suggested that many of the observed associations were at least moderately robust to potential unmeasured confounding (Tables 4 and 5). For example, for the association between social isolation and mortality, an unmeasured confounder that was associated with both increased mortality and higher social isolation by risk ratios of 2.87-fold each (above and beyond the measured covariates) could explain away the association between social isolation and mortality, but weaker joint unmeasured confounder associations could not. To shift the confidence interval to include the null, risk ratio confounder associations of 1.8-fold each could suffice, but weaker joint associations could not. Second, models adjusting for conventional covariates showed larger estimates compared to fully-adjusted models (Supplementary Table 2). Third, domain-specific analyses suggested that Domain 4 (social activity participation) and Domain 5 (religious service attendance) are more strongly associated with various outcomes compared to Domains 1–3 (Supplementary Table 3). Fourth, separate results evaluating social behaviors versus network characteristics suggested that behavioral social isolation domains (vs. network characteristics) are more predictive of most outcomes (Supplementary Table 4). Fifth, results from analyses that "pit" loneliness and social isolation against each other in the same model were largely similar to results from the main analyses (Supplementary Table 5).

5. Discussion

5.1. Summary of findings

In this large, prospective nationwide study of U.S. adults aged >50 years, greater loneliness and social isolation were both associated with worse physical health outcomes and health behaviors. Social isolation showed a slightly larger effect size than loneliness for all-cause mortality, and both loneliness and social isolation were associated with a similar number of physical health outcomes and health behaviors. However, the effect sizes between social isolation and physical health outcomes were somewhat stronger than the effect sizes between loneliness and physical health outcomes. In contrast, loneliness was associated with a greater number of psychological well-being and distress

Table 3
Loneliness, social isolation and subsequent health and well-being; (N = 13,752)[a,b,c,d,e,f].

	Loneliness and Social Isolation		
	Group 1 (Reference)	Loneliness Group 3 vs. Bottom Group 1 (n = 1824) RR/ OR/β (95% CI)	Social Isolation Group 3 vs. Bottom Group 1 (n = 1800) RR/ OR/β (95% CI)
Physical Health			
All-cause mortality	1.00	1.43 (1.17, 1.76)***	1.74 (1.25, 2.42)**
Number of chronic conditions	0.00	0.03 (−0.02, 0.09)	0.00 (−0.05, 0.05)
Diabetes	1.00	0.99 (0.87, 1.14)	0.92 (0.79, 1.08)
Hypertension	1.00	1.02 (0.94, 1.10)	1.00 (0.91, 1.11)
Stroke	1.00	1.11 (0.90, 1.36)	1.30 (1.01, 1.67)*
Cancer	1.00	1.04 (0.89, 1.22)	0.88 (0.73, 1.07)
Heart disease	1.00	1.01 (0.90, 1.14)	1.00 (0.86, 1.16)
Lung disease	1.00	1.25 (1.04, 1.51)*	1.20 (0.93, 1.55)
Arthritis	1.00	1.03 (0.94, 1.11)	1.02 (0.92, 1.12)
Overweight/obesity	1.00	0.97 (0.90, 1.05)	0.95 (0.86, 1.06)
Physical functioning limitations	1.00	1.26 (1.11, 1.45)***	1.38 (1.18, 1.62)***
Cognitive impairment	1.00	1.10 (0.94, 1.29)	1.22 (1.02, 1.46)*
Chronic pain	1.00	1.13 (1.02, 1.25)*	1.05 (0.92, 1.20)
Self-rated health	0.00	−0.12 (−0.20, −0.05)**	−0.05 (−0.12, 0.02)
Health Behaviors			
Heavy drinking	1.00	0.89 (0.62, 1.27)	0.95 (0.57, 1.59)
Smoking	1.00	0.99 (0.81, 1.21)	1.28 (0.87, 1.88)
Frequent physical activity	1.00	0.94 (0.85, 1.03)	0.87 (0.77, 0.97)*
Sleep problems	1.00	1.16 (1.04, 1.29)**	1.03 (0.90, 1.17)
Psychological Well-being			
Positive affect	0.00	−0.39 (−0.48, −0.31)***	−0.27 (−0.35, −0.20)***
Life satisfaction	0.00	−0.38 (−0.46, −0.30)***	−0.21 (−0.30, −0.11)***
Optimism	0.00	−0.38 (−0.49, −0.26)***	−0.20 (−0.31, −0.10)**
Purpose in life	0.00	−0.37 (−0.43, −0.31)***	−0.21 (−0.29, −0.13)***
Mastery	0.00	−0.28 (−0.34, −0.22)***	−0.04 (−0.12, 0.04)
Health mastery	0.00	−0.10 (−0.17, −0.02)*	−0.09 (−0.20, 0.01)
Financial mastery	0.00	−0.24 (−0.31, −0.16)***	−0.12 (−0.24, 0.00)
Psychological Distress			
Depression	1.00	2.65 (2.00, 3.51)***	1.36 (1.04, 1.78)*
Depressive symptoms	0.00	0.34 (0.27, 0.41)***	0.13 (0.03, 0.23)*
Hopelessness	0.00	0.35 (0.24, 0.46)***	0.18 (0.08, 0.28)***
Negative affect	0.00	0.39 (0.29, 0.50)***	0.07 (−0.02, 0.17)
Perceived constraints	0.00	0.33 (0.24, 0.42)***	0.12 (0.03, 0.22)*
Social Factors			
Loneliness	0.00	0.95 (0.90, 1.01)***	0.38 (0.27, 0.49)***
Social Isolation	0.00	0.15 (0.13, 0.18)***	0.57 (0.52, 0.62)***

Abbreviations: CI, confidence interval; OR, odds ratio; RR, risk ratio.
*p < 0.05 before Bonferroni correction; **p < 0.01 before Bonferroni correction; ***p < 0.05 after Bonferroni correction (the p-value cut-off for Bonferroni correction is p = 0.05/32 outcomes = $p < 0.0015625$).We marked multiple p-value cutoffs in the table and confidence intervals, because multiple testing practices vary widely, and this is an evolving area of research.

[a] If the reference value is "1," the effect estimate is OR or RR; if the reference value is "0," the effect estimate is β.

[b] The analytic sample was restricted to those who had participated in the baseline wave (t_1;2012 or 2014). Multiple imputation was performed to impute missing data on the exposure, covariates, and outcomes. All models adjusted for sociodemographic characteristics (age, sex, race/ethnicity, annual household income, total wealth, level of education, employment status, health insurance, geographic region), pre-baseline childhood abuse, pre-baseline values of the outcome variables (diabetes, hypertension, stroke, cancer, heart disease, lung disease, arthritis, overweight/obesity, physical functioning limitations, cognitive impairment, chronic pain, self-rated health, heavy drinking, current smoking status, physical activity, sleep problems, positive affect, optimism, purpose in life, mastery, health mastery, financial mastery, depressive symptoms, hopelessness, negative affect, perceived constraints), and personality factors (openness, conscientiousness, extraversion, agreeableness, neuroticism). These variables were adjusted for in the pre-baseline wave (t_1;2012 or 2014).

[c] We used an outcome-wide analytic approach and ran a separate model for each outcome. We also ran a different type of model depending on the nature of the outcome: 1) for each binary outcome with a prevalence of ≥10%, we ran a generalized linear model with a log link and Poisson distribution to estimate a RR; 2) for each binary outcome with a prevalence of <10%, we ran a logistic regression model to estimate an OR; and 3) for each continuous outcome, we ran a linear regression model to estimate a β.

[d] All continuous outcomes were standardized (mean = 0, standard deviation = 1), and β was the standardized effect size.

[e] Without reference points and benchmarks, it is difficult to interpret effect sizes. Thus, we included loneliness and social isolation as outcomes so that readers can use the effect sizes as mental reference points to evaluate the effect sizes between loneliness and social isolation with the other health and well-being outcomes.

[f] Loneliness and social isolation were examined as separate independent variables in all models. Thus, they were not included simultaneously in the same model.

outcomes, and it also had larger effect sizes with those outcomes than social isolation.

5.2. Results in the context of past research

Our results converge with previous studies, which observed that both loneliness and social isolation are associated with some physical health outcomes (e.g., increased risk of all-cause mortality, functional limitations) (Holt-Lunstad et al., 2015; Shankar et al., 2017; Steptoe et al., 2013), and psychological factors (e.g., lower life satisfaction, depression, mental health) (Beridze et al., 2020; Coyle & Dugan, 2012; Domènech-Abella et al., 2019; Ge et al., 2017; Van den Brink et al., 2018). Our findings also converge with prior studies, which observed that loneliness and social isolation have different magnitudes of association with some outcomes. For example, in line with prior research (Hakulinen et al., 2018; Holt-Lunstad et al., 2015; Kraav et al., 2021;

Table 4
Robustness to Unmeasured Confounding (E-Values) for the Associations Between Loneliness (3rd Group vs. 1st Group) and Subsequent Health and Well-Being (N = 13,752)[a].

	Effect Estimate[b]	Confidence Interval Limit[c]
Physical Health		
All-cause mortality	2.22	1.62
Number of chronic conditions	1.20	1.00
Diabetes	1.09	1.00
Hypertension	1.15	1.00
Stroke	1.45	1.00
Cancer	1.25	1.00
Heart disease	1.13	1.00
Lung disease	1.81	1.25
Arthritis	1.19	1.00
Overweight/obesity	1.20	1.00
Physical functioning limitations	1.84	1.45
Cognitive impairment	1.43	1.00
Chronic pain	1.52	1.18
Self-rated health	1.49	1.28
Health Behaviors		
Heavy drinking	1.51	1.00
Smoking	1.10	1.00
Frequent physical activity	1.34	1.00
Sleep problems	1.59	1.24
Psychological Well-being		
Positive affect	2.21	2.00
Life satisfaction	2.18	1.98
Optimism	2.17	1.90
Purpose in life	2.14	1.98
Mastery	1.91	1.75
Health mastery	1.41	1.17
Financial mastery	1.79	1.60
Psychological Distress		
Depression	4.74	3.42
Depressive symptoms	2.06	1.88
Hopelessness	2.10	1.84
Negative affect	2.21	1.96
Constraints	2.04	1.82
Social Factors		
Loneliness	4.18	3.95
Social isolation	1.57	1.50

[a] See VanderWeele and Ding (2017) for the formula for calculating E-values.
[b] The E-values for effect estimates are the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to fully explain away the observed association between the exposure and outcome, conditional on the measured covariates.
[c] The E-values for the limit of the 95% confidence interval (CI) closest to the null denote the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to shift the confidence interval to include the null value, conditional on the measured covariates.

Table 5
Robustness to Unmeasured Confounding (E-Values) for the Associations Between Social Isolation (3rd Group vs. 1st Group) and Subsequent Health and Well-Being (N = 13,752)[a].

	Effect Estimate[b]	Confidence Interval Limit[c]
Physical Health		
All-cause mortality	2.87	1.80
Number of chronic conditions	1.04	1.00
Diabetes	1.38	1.00
Hypertension	1.06	1.00
Stroke	1.92	1.12
Cancer	1.51	1.00
Heart disease	1.06	1.00
Lung disease	1.69	1.00
Arthritis	1.15	1.00
Overweight/obesity	1.27	1.00
Physical functioning limitations	2.10	1.63
Cognitive impairment	1.74	1.17
Chronic pain	1.28	1.00
Self-rated health	1.27	1.00
Health Behaviors		
Heavy drinking	1.28	1.00
Smoking	1.88	1.00
Frequent physical activity	1.58	1.22
Sleep problems	1.19	1.00
Psychological Well-being		
Positive affect	1.88	1.69
Life satisfaction	1.71	1.46
Optimism	1.70	1.44
Purpose in life	1.70	1.50
Mastery	1.24	1.00
Health mastery	1.39	1.00
Financial mastery	1.47	1.11
Psychological Distress		
Depression	2.06	1.24
Depressive symptoms	1.51	1.24
Hopelessness	1.64	1.40
Negative affect	1.34	1.00
Constraints	1.49	1.22
Social Factors		
Loneliness	2.17	1.90
Social isolation	2.75	2.62

[a] See VanderWeele and Ding (2017) for the formula for calculating E-values.
[b] The E-values for effect estimates are the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to fully explain away the observed association between the exposure and outcome, conditional on the measured covariates.
[c] The E-values for the limit of the 95% confidence interval (CI) closest to the null denote the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome to shift the confidence interval to include the null value, conditional on the measured covariates.

Lennartsson et al., 2021; Nakagomi et al., 2023; Steptoe et al., 2013; Stokes et al., 2021; Tanskanen & Anttila, 2016), we observed that social isolation has a stronger association with physical health outcomes such as increased mortality risk (74% increased risk of mortality), compared to loneliness (43% increased risk of mortality). We also observed that social isolation, compared to loneliness, had somewhat stronger associations with other physical health outcomes including: stroke, cognitive impairment, and physical functioning limitations. This observation might be explained by several hypothesized mechanisms (Cohen, 1988), including how socially isolated people (an objective dearth of social contact and network size) have less: 1) instrumental support (e.g., reduced access to healthcare facilities where people can receive preventive visits when healthy and limited access to adequate care when sick, reduced access to assistance with grocery shopping and food preparation), 2) informational support (e.g., reduced dissemination of health information, such as knowledge about which healthcare providers in the area are excellent at treating specific health conditions, and reduced knowledge about health-promoting behaviors), 3) opportunity to interact with others who can provide positive social influence (e.g. social learning, maintenance of healthy norms through informal social control, such as discouraging substance misuse and encouraging physical activity and diets).

However, we observed that loneliness, compared to social isolation, often had stronger effect sizes with psychological outcomes. At times, the effect sizes were two times larger (e.g., life satisfaction, optimism, purpose in life, depression, hopelessness), or even three to four times larger (e.g., sense of mastery, depressive symptoms, negative affect, perceived constraints). These larger associations were observed despite adjusting for the same psychological outcomes in the pre-baseline wave. These results might be partially explained by several hypothesized mechanisms, including how lonely people (a subjective emotional state): 1) experience decreased social and psychological support (e.g., decreased perceptions of support received during stressful life periods), 2) experience decreased appraisal support (e.g., decreased experiences of receiving feedback about how to navigate stressful family situations or transitions into retirement). These mechanisms might be shared by

both social isolation and loneliness, thus, further research should characterize the shared and unique ways in which social isolation and loneliness influence health and well-being outcomes.

Although our results mostly converged with results from prior work, there were some discrepancies. As illustrative examples, one meta-analysis observed a 26% and 29% increased risk of mortality for loneliness and social isolation, respectively (Holt-Lunstad et al., 2015). We observed larger associations with mortality in our results for both loneliness (43%) and social isolation (74% increased mortality risk). Another meta-analysis observed that poor social relationships (an umbrella term that grouped together loneliness and social isolation studies) were associated with a 29% increase in incident coronary heart disease risk and a 32% increase in stroke risk (Valtorta et al., 2016). In our study, there were no associations with heart disease, and only social isolation was associated with an elevated risk of stroke (30%).

Methodologically, the underlying reasons for diverging results between our study and past studies may stem from a range of reasons including, differences in: 1) study population (e.g., nationally representative vs. non-generalizable samples, younger vs. older samples), 2) study design (e.g., cross-sectional vs. longitudinal), 3) measurement of the exposure (e.g., 1-, 3-, 11-, or 20-item UCLA loneliness scale, and different social isolation measures), 4) measurement of the outcome (some studies used specific measures of physical health outcomes such as stroke, while others used more general measures like heart disease), 5) covariates controlled for, 6) control for prior loneliness or social isolation measures.

5.3. Study limitations

Our study had several limitations. First, our study may be subject to confounding by unmeasured third variables. However, we mitigated this potential concern by 1) using a longitudinal study design, 2) adjusting for a robust set of covariates, including pre-baseline values of the outcomes and exposures, and 3) reporting E-values to assess the robustness of observed associations to unmeasured confounding. Second, many physical health and health behavior outcomes were self-reported and thus are vulnerable to self-report bias and common method bias. However, to mitigate potential bias, we controlled for a wide range of psychological variables (e.g., big-5 personality factors, hopelessness, depression, optimism, etc.) that might impact how different exposure groups (i.e., people who are lonely vs. not lonely) report their experiences, and control for prior self-report outcomes likewise helps mitigate this. Future studies should use objective measures of physical and behavioral health outcomes to help address these limitations. Third, we used a relatively short follow-up length (4 years). For certain health and well-being outcomes (e.g., dementia), a longer follow-up length may be needed (VanderWeele et al., 2016). Fourth, to assess social isolation, we used an updated version of the Berkman-Syme index; however this newer version has not been psychometrically evaluated. We did not use the original version of the scale because the literature on social isolation has advanced substantially since the creation of the scale. Thus, we updated the scale and operationalized it using the data we had available to us in HRS. Future studies should evaluate the psychometric properties of this scale.

6. Conclusion

Our results indicate that changes in both loneliness and social isolation are associated with several health and well-being outcomes. Depending on the outcome being targeted (e.g., mortality vs. psychosocial outcomes), policy makers or interventionists might consider targeting different factors (social isolation vs. loneliness, respectively). However, broadly speaking, both loneliness and social isolation are associated with a range of important outcomes. Growing evidence suggests that loneliness and social isolation can be reduced through interventions (Bickerdike et al., 2017; Masi et al., 2011; National Academies of Sciences, Engineering, and Medicine, 2020a), and others have described practical ways in which these types of interventions can be deployed through various systems at-scale (e.g., healthcare system) (Hong et al., 2022; National Academies of Sciences, Engineering, and Medicine, 2020b; The U.S. Surgeon General' s Office, 2023). Our results highlight how continued efforts to develop, refine, and deploy scalable loneliness and social isolation interventions may be a promising and innovative way to increase a wide range of health and well-being outcomes in older adults, though the magnitude of the effects of these respective interventions will vary by outcome.

Author contributions

J.H.H. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis; all authors contributed to the study concept and design; J.H.H. and E.S.K. contributed to the acquisition, analysis, or interpretation of data; J.H.H. and E.S.K. contributed to drafting the original manuscript; all authors contributed to critical revision of the manuscript for important intellectual content.

Declaration of competing interest

Tyler J. VanderWeele has received personal fees from Flerish and Flourishing Metrics.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2023.101459.

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