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Longitudinal Analyses Indicate Bidirectional Associations between Loneliness and Health

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Abstract

Objectives: To evaluate temporal dynamics between loneliness and both objective and subjective health (i.e., functional impairment and self-rated health) in mid- to late-adulthood.

Method: We applied Bivariate Dual-Change-Score Models to longitudinal data from 3 Swedish twin studies (N = 1,939) to explore dynamic associations between loneliness and health across 3 age ranges (50-70, 70-82, and >82 years) to investigate whether associations between loneliness and health change with age due to increasing incidence of chronic health conditions and bereavement.

Results: Results showed bidirectional associations between loneliness and both objective and subjective health, with adverse impacts of loneliness observed on subsequent subjective and objective health beginning at age 70. Associations between health and subsequent loneliness were observed after age 82 and varied for subjective and objective health, with subjective health associated with less loneliness and objective health associated with greater loneliness.

Conclusions: Our results indicate dynamic associations between loneliness and health with age in midto late-adulthood, with earlier impacts of loneliness on health and later impacts of health on loneliness that vary for objective and subjective measures of health. These findings suggest impacts of health on loneliness may arise later in life when worsening health or mobility interfere with social interaction.

Keywords: Loneliness; self-rated health; functional impairment; dynamic associations; dual-change-score model, age-based analysis, aging

Longitudinal Analyses Indicate Bidirectional Associations between Loneliness and Health

Loneliness is a potent stressor that increases in prevalence in late life (Hajek & König, 2020; Nicolaisen & Thorsen, 2014; Qualter et al., 2015) and has been associated with poorer self-rated health and many adverse health outcomes including cardiovascular disease, lung disease, diabetes, and functional limitations (Christensen et al., 2021; Jessen et al., 2018; Luo et al., 2012; Ong et al., 2015; National Academies of Sciences, Engineering, and Medicine, 2020; Petitte et al., 2015; Richard et al., 2017). Loneliness results from the perception that the quality or quantity of a person's social relationships does not adequately meet their social needs (Hawkley & Cacioppo, 2010). Older adults may be increasingly vulnerable to experiencing feelings of loneliness as they get older due to experiencing the death of family and friends that occurs with greater frequency in older age (Nicolaisen & Thorsen, 2014; Pinguart, 2003; Qualter et al., 2015; Smith, 2012). Indeed, the prevalence of loneliness has been shown to increase non-linearly with age after age 75 (Luhmann & Hawkley, 2016). The association between loneliness and health appears to be bidirectional—loneliness may adversely impact health through a variety of behavioral and physiological pathways (Hawkley & Cacioppo, 2003; Cacioppo et al., 2014) while poor or worsening health may impose barriers to social interaction that lead to onset or intensification of feelings of loneliness (Hajek & König, 2020; Havens et al., 2004; Ong et al., 2015; Pinguart, 2003; Smith, 2012).

Stress associated with the experience of loneliness may result in physiological changes that negatively impact health over time (Cacioppo et al., 2003; Christiansen et al., 2016). Indeed, loneliness correlates with higher cortisol levels indicative of hypothalamic-pituitary-adrenal (HPA) axis dysregulation, heightened inflammation, worse immune function, and an altered pattern of gene expression in blood leukocytes characterized by increased expression of pro-inflammatory genes and reduced expression of genes involved in the immune response (Cole et al., 2007; Cole, 2013; Creswell et al., 2012; Hawkley & Cacioppo, 2010; Hawkley & Capitanio, 2015). Further, loneliness has been linked

with reduced engagement in health behaviors (e.g., healthy diet; exercise) and reduced sleep quality (Christiansen et al., 2016; Hawkley & Cacioppo, 2007; Hawkley & Cacioppo, 2010; Segrin & Passalacqua, 2010), which have both been observed to mediate the relation between loneliness and health outcomes (Christiansen et al., 2016; Segrin & Passalacqua, 2010).

Worsening health or mobility may contribute to increases in loneliness in older adults by limiting opportunities for social interaction (Hajek & König, 2020; Havens et al., 2004; Ong et al., 2015; Pinquart, 2003; Smith, 2012). Moreover, they may increase need for social support, but in ways that contravene other social needs such as friendship and supporting others (Pinquart, 2003). Older adults with poor or worsening health or mobility may also feel like a burden to members of their social network and consequently withdraw from social interaction, increasing the likelihood of experiencing loneliness (Pinquart, 2003).

Collectively, prior work on loneliness and both objective and subjective health outcomes has indicated bidirectional association; however, little longitudinal work has examined temporal dynamics between loneliness and health. Luo et al. (2012) used cross-lagged models to explore reciprocal associations between loneliness and self-rated health and loneliness and functional limitations in adults \geq 50 years of age across 3 time points/4 years of follow-up in the Health and Retirement Study and found a reciprocal association between loneliness and functional limitations—higher baseline loneliness predicted greater functional limitations after two years of follow-up, which in turn predicted higher loneliness after four years of follow-up. More functional limitations at baseline also predicted greater loneliness after two years of follow-up which then predicted more functional limitations after four years of follow-up. Earlier self-rated health was more strongly associated with later loneliness than vice versa and the association between earlier loneliness and later self-rated health only reached trend significance. Tsur et al. (2019) used cross-lagged models to investigate associations between loneliness and self-rated health across 3 time points/24 years of follow-up in a sample of war veterans and found

that loneliness at baseline was associated with self-rated health at the second time point 17 years later which in turn was associated with loneliness 7 years later. In contrast, self-rated health at baseline was not associated with loneliness at the second time point which in turn was not associated with self-rated health at the third time point.

Clarifying the directional relationship of health and loneliness requires longitudinal modeling of repeated evaluations of the variables across the second half of the lifespan. To address the question of cause and effect, it is necessary to evaluate the extent to which each component (health and loneliness) predicts subsequent changes in the other component over age using structural equation models that allow for dynamic interaction between the two components. The development of dual-change-score models (DCSMs) to characterize age changes has facilitated specification and testing of dynamic agerelated hypotheses about temporal dynamics (McArdle, 2001; McArdle et al., 2000). There is consensus that strong and often bidirectional associations are observed between loneliness and a number of health outcomes (Blazer et al., 2020), albeit fewer findings are available with respect to functional mobility. We address calls to advance understandings of the mechanisms by which loneliness and health may be associated (Blazer et al., 2020) by evaluating how temporal dynamics between loneliness and objective and subjective health unfold. Specifically, we explored dynamic associations between change in loneliness and changes in self-rated health and functional impairment in mid- to late-adulthood. This analysis enabled assessment of directionality of associations between loneliness and measures of both objective and subjective health, and temporal dynamics of changes in loneliness and health with age using data from 3 longitudinal studies of aging with up to 25 years of follow-up. As individuals tend to be relatively healthier and experience less bereavement in mid-adulthood than in later life when chronic health conditions and bereavement become increasingly common, we reasoned that dynamic associations between loneliness and health may not be consistent across the second half of the lifespan

and therefore explored changes in the bidirectional relationship across 3 age ranges or "contexts of aging" (ages 50-70, 70-82, and >82).

Method

Participants

Data came from three studies: Swedish Adoption/Twin Study of Aging (SATSA; Finkel & Pedersen, 1994), Origins of Variance in the Oldest Old (OCTO-Twin; McClearn et al., 1997), and Aging in Women and Men: A Longitudinal Study of Gender Differences in Health Behavior and Health among the Elderly (GENDER; Gold et al., 2002). Recruitment and testing procedures for the three studies have been described previously. In brief, all three samples were drawn independently from the population-based Swedish Twin Registry (Lichtenstein et al., 2002), resulting in non-overlapping samples that were evaluated utilizing similar protocols. In-person testing (IPT) took place in locations convenient to participants, such as district nurses' offices, health-care schools, long-term care clinics, or at the participant's home. IPT intervals across the studies ranged from two to four years. Both health and loneliness data were available from at least one testing occasion for 1939 individuals: 799 from SATSA, 645 from OCTO-Twin, and 495 from GENDER. All participants were of European ancestry and 59.4% of the sample was female. Although the proportion female was slightly higher for participants older than 65 (60.0%) versus younger than 65 (57.4%), the difference was not statistically significant. Three or more waves of data were available for 76% of the sample. As shown in Table 1, the sample ranged in age from 40 to 98 at intake and mean age at intake was 74.6 (SD = 9.37). Longitudinal follow-up ranged from 0 to 25 years, with a mean of 7.6 years. Among the three studies, the shortest interval between testing waves was 2 years. Therefore, to support statistical modeling and to maximize the age range available for study inclusion, data were divided into 23 two-year age intervals from 50 to 96 years: e.g., everyone with data (regardless of IPT wave) at ages 50 – 51.9 was included in the first age interval. Thus, each

participant was included in as many different age intervals as possible, consistent with the number of waves of data available for the participant (see Supplemental Table 1).

Institutional Review Board (IRB) approval was obtained for this research at the coordinating site for the Consortium on Interplay of Genes and Environment across Multiple Studies (IGEMS), University of Southern California (USC; project title: Gene-Social Environment Interplay; protocol number UP-16-00315-CR003) and the institution of the corresponding author, University of California Riverside (UCR; project title: Effects of Gene-Social Environment Interplay on Health; protocol number HS-11-004).

Original IRB approval for the SATSA, OCTO-Twin, and GENDER studies was obtained at Karolinska Institutet (document numbers 84:61, 98:380, and 93:226, respectively).

Measures

Loneliness

As part of the Interplay of Genes and Environment across Multiple Studies (IGEMS) consortium (Pedersen et al., 2013, 2019), a harmonized measure of loneliness was created (Phillips et al., 2019). Nine items assessing loneliness were collected by at least one of the three studies included in the current analyses: I feel/felt lonely, do you suffer from/are troubled by feelings of loneliness, have you got friends you can talk to, do you feel part of a set of friends, do you lack company, do you feel abandoned, and do you feel lonely even when with others. The SATSA, OCTO-Twin and Gender studies administered 3, 6, and 7 of these items, respectively. Items were combined using Rasch measurement analysis, for which data from the 3 studies were pooled with data from a crosswalk sample (n = 888) who were given all study items and a 10-item version of the UCLA Loneliness Scale. The Rasch analysis yielded a single loneliness score for each participant based on how they responded to each of the loneliness items they were asked at each in-person testing wave (Phillips, 2020). Finally, the composite was translated to the T-score metric (mean = 50, SD = 10); higher scores indicate more loneliness.

Self-Rated Health (SRH)

The number of response options for the SRH item (how would you rate your overall health?) varied among studies from 3 to 7 options. Based on an earlier analysis of various harmonization methods within IGEMS (Gatz et al., 2015), the most parsimonious and effective approach to harmonization was standardizing the variable within study, transforming to a T-score metric, and then combining data across studies (Finkel et al., 2020). Higher scores indicated poorer subjective health.

Functional Aging Index (FAI)

We designed FAI to complement existing measures of biological aging and frailty indexes by focusing on functional capacity (Finkel et al., 2019). We included measures of 5 functional biomarkers: self-reported vision and hearing, peak expiratory lung flow, grip strength, and gait speed. Before calculation of FAI, grip strength was regression-adjusted for sex and peak expiratory flow was adjusted for body volume through dividing it by the individual's squared height in meters. The five variables were standardized separately based on intake means and standard deviations, and grip strength and peak expiratory flow were reverse scored to ensure that higher scores indicated poorer performance. Finally, the composite score was translated to the T-score metric; higher scores on FAI indicate poorer functioning.

Statistical Method

We used age-based (rather than time-based) bivariate dual change score models (DCSM) to examine the dynamic relationships between Loneliness (L) and the Health variables (H). DCSM models have been well-characterized in previous work (McArdle, 2001; McArdle et al., 2004; Ghisletta & deRibaupierre, 2005; Lövdén et al., 2005). As presented in Figure 1, the model is based on latent difference scores that create a growth curve reflecting change from one age to another age (i.e., Δ L and Δ H), rather than performance at a single age, which is modeled as a function of both constant change (α L and α H) that accumulates over time in an additive fashion as well as proportional change (β L and β H) based on the previous score. In the full DCSM model, α L and α H are set to 1, reflecting the time

interval between assessments, and the magnitude of the βL and βH parameters reflect the extent to which the longitudinal change is nonlinear. The bivariate DCSM allows for a coupling mechanism (γH) where change in Loneliness depends on the previous value of the Health measures, and vice versa (γL).

A variety of hypotheses about the nature of changes with age can be tested. First, multiple values of β can be estimated, testing for different rates of change at different age intervals. Previous analyses in these samples indicated different rates of change in middle age (ages 50-70), early aging (ages 70-82), and after age 82 (e.g., Emery et al., 2020). The correlations between Loneliness and the Health variables were similar for SRH and FAI at ages 50-69 and 70-81, with slight increases in the correlations from the first to second age range (see Table 2). However, the correlations differed after age 82, with continued increase in correlation between Loneliness and SRH but a drop in correlation between Loneliness and FAI. Therefore, we tested nested DCSMs that progressively added additional complexity to the estimated aging trajectories: 1 beta across the entire age range, 1 flexion point yielding 2 betas (ages 50-69, 70+), and two flexion points yielding 3 betas (ages 50-69, 70-81, 82+). Additionally, the bivariate model evaluates dynamic hypotheses about temporal order of changes in variables. As we added flexion points to estimated Loneliness and Health trajectories (betas), we also tested models that recognized different dynamics between them at the flexion points (gamma parameters). Having identified the best-fitting model within variables, additional models tested the nature of the relationship between the two variables. In the most reduced model, we included no dynamic coupling between Loneliness and Health (i.e., all g set to zero). Next, models of unidirectional dynamic relation functions were tested, either with Loneliness as a leading indicator of change in the Health variable (i.e., $y_H = 0$), or with the Health variable as a leading indicator of change in Loneliness (i.e., $\gamma_L = 0$).

One of the fundamental assumptions of DCSM is that data are missing at random. In longitudinal studies, drop-out is rarely random but results instead from increasing sample selectivity; in aging studies

morbidity or mortality are common sources. In SATSA, a maximum of 8 waves of longitudinal participation was possible, but on average individuals participated in 4 waves. SATSA participants aged 50 to 64 at intake participated in 4.5 waves on average, but participants aged 65 and older participated in only 2.6 waves on average. The benefit of combining SATSA with OCTO-Twin (5 waves of data collection) and Gender (3 waves of data collection) was to ensure sufficient waves of longitudinal data after age 65 to model aging trajectories because they had older intake ages. Their sampling was somewhat more selective, however, as they required that both members of twin pairs participate.

We fit DCSMs using Mplus (Muthén & Muthén, 2012-2015). Model fit was indicated by the log-likelihood (-2LL), Akaike Information Criterion (AIC; Akaike, 1987), and the root mean square error of approximation (RMSEA; Browne & Cudeck, 1993). Adequate fit of the model to the data is indicated when the RMSEA is less than or equal to 0.10 and an RMSEA of .05 or less indicates "close" fit. We tested hypotheses by comparing model fit indices and compared nested models using the likelihood ratio test obtained by taking the difference between the obtained model -2LLs, and their degrees of freedom difference. We controlled co-twin relationship in all models (i.e., co-twin status was coded and models were bi-level).

Results

To investigate the longitudinal relationships between Loneliness and SRH and Loneliness and FAI, we tested 5 bivariate DCSMs to estimate the shapes of the aging trajectories, followed by 3 models to estimate the natures of the dynamic relations between variables. Table 3 presents the loglikelihood fit statistics for each model and the likelihood ratio tests (LRT) comparing model fits. Model 1 was the simplest model: 1 beta estimating nonlinear change for each variable and 1 gamma estimating cross-variable cross-time dynamics over the entire age range. Model 2 included 2 betas to estimate Loneliness and Health trajectories: β 1 for ages 50-69 and β 2 for ages 70 and over. LRT of model 2 vs. model 1 indicated a significantly improved fit to the data for both the Loneliness-SRH and the Loneliness-FAI

relations. Model 3 included 2 betas and 2 gammas. LRT comparing model 3 to model 2 indicated that adding additional complexity between variables did not improve model fit. Model 4 included 3 betas within variables, modeling the three age ranges (50-69, 79-81, 82-96); comparison with model 2 indicated significantly improved fit for both Loneliness-SRH and Loneliness-FAI, suggesting different rates of change with age in the three age ranges. Finally, model 5 added 3 gammas, which resulted in a significant improvement in model fit for Loneliness-FAI, but not Loneliness-SRH. Moreover, model 5 minimized AIC and RMSEA for both pairs of variables. The RMSEA for model 5 was .015 for Loneliness-SRH and .023 for Loneliness-FAI which suggests a close fit. Parameter estimates and estimated dynamic trajectories differed little between models 4 and 5 for Loneliness-SRH; therefore, to support comparison between Loneliness-SRH and Loneliness-FAI results, model 5 was selected to represent the shapes of aging trajectories for both pairs of variables.

In the next phase of model fitting, we tested the directions of the relations between Loneliness and the Health variables by dropping parameters instead of adding them. Model 6 dropped all coupling parameters (γ) between variables and resulted in a significantly reduced model fit for both Loneliness-SRH and Loneliness-FAI, indicating significant dynamic coupling between variables. With models 7 and 8 we tested the directions of the dynamic relations by dropping the 3 gamma parameters from the Health variable to Loneliness (model 7) and from Loneliness to the Health variable (model 8). Both models resulted in significant reductions in model fit, indicating dynamic bidirectional relations for both Loneliness-SRH and Loneliness-FAI.

Estimates of the coupling parameters (γ) from model 5 are presented in Table 4 (see Supplemental Table 2 for complete model parameters). All coupling parameters were significantly different from zero. The impact of Loneliness on subsequent changes in both SRH and FAI tended to diminish over the age ranges. In contrast, the impact of SRH and FAI on subsequent Loneliness varied across age ranges, with the highest value for SRH \rightarrow Loneliness in the 82-96 age range and the highest

value for FAI Doneliness in the 70-81 age range. The estimated bivariate trajectories for the full coupling and no coupling models for Loneliness and the Health variables are presented in Figure 2. The overall trajectories for subjective health (SRH) and FAI differed: poorer SRH ratings increased with age up to age 82 and then either plateau or improve somewhat, whereas FAI showed consistent increases across the age range. When coupled with Loneliness, values for both SRH and FAI were higher (worse) than in the non-coupling models and the difference between full-coupling and non-coupling trajectories was evident beginning at age 70. Including the influences of previous scores on Loneliness in the model resulted in a plateau for SRH after age 70 instead of improvement. FAI values increased faster after age 70 in the full-coupling model than in the no coupling model, although trajectories converged somewhat by age 94. The impact of Health on Loneliness differed in two ways from the impact of Loneliness on Health. First, the impact was evident later: after age 82 instead of age 70. Second, the influences of worse SRH and FAI on Loneliness differed. Including the influences of previous waves on SRH resulted in less Loneliness whereas Including the influences of previous waves on FAI resulted in more Loneliness.

Discussion

This study provides an initial exploration of the temporal dynamics of loneliness and objective and subjective health with age in mid and late adulthood. Bivariate dual change score models of longitudinal data on loneliness and measures of health indicated that loneliness and health affect each other in later adulthood, but their relative impacts vary with age with different associations for subjective and objective health. Loneliness negatively influenced subsequent subjective and objective health beginning at age 70. Poorer subjective health (SRH) was associated with less loneliness, but poorer objective health (FAI) was associated with greater loneliness, but not until age 82.

Our results were consistent with existing research indicating associations between greater loneliness and poor or worsening objective and subjective health in older age (Christensen et al., 2021; Hawkley & Cacioppo, 2010; Jessen et al., 2018; Nummela et al., 2011; Ong et al., 2015; Petitte et al.,

2015; Richard et al., 2017) and with work showing links between poor or worsening health and loneliness (Nicolaisen & Thorsen, 2014; Smith, 2012). They suggested that stress associated with loneliness may adversely impact both SRH and FAI beginning at age 70, while declining health after age 82 may reduce ability to participate in social activities, increasing perception of unmet social needs (Pinquart, 2003). The plateau or improvement seen in the SRH trajectory after age 70 (refer to Figure 2) may reflect sample attrition: adults who were still participating in this age range are likely to have been healthier than adults who dropped out. FAI continued to deteriorate in the same age range, but this is normal throughout the health distribution among older adults. It is also possible that those who were still participating after age 70 perceived their health as relatively good because they compared themselves to others their age who may be in poorer health (e.g., dead or disabled) as opposed to general adult medical standards or comparisons younger adults make among their same-aged peers (Andersen et al., 2007; Jylhä, 2009). Evidence suggests that the discordance between objective and subjective health increases in late adulthood (Henchoz, Cavalli, and Girardin, 2008), possibly as a result of greater emphasis on psychological rather than physical components of subjective health assessments by older adults (Araújo, Teixeira, Ribiero, & Paúl, 2018).

Our observation that earlier loneliness predicted later FAI and vice versa was consistent with those from the only other study, to the best of our knowledge, to explore dynamic associations between loneliness and objective health. Luo et al. (2012) similarly reported reciprocal dynamic associations across a 4-year period for loneliness and functional limitations. For subjective health, our observation that higher loneliness predicted worse SRH after age 70 while worse SRH predicted less loneliness after age 82 only partially aligned with findings from prior studies of dynamic associations between loneliness and subjective health. While we observed a significant association between earlier loneliness and later SRH, Luo et al. (2012) found this association to be marginal and Tsur et al. (2019) found it to be inconsistent over time (i.e., with significant associations between one set of adjacent time points and

not another). Our observation that worse SRH predicted decreases in loneliness was inconsistent with prior observations showing that worse SRH predicted later increases in loneliness (Luo et al., 2012; Tsur et al., 2019) although this association has also been observed to be inconsistent across time (Tsur et al., 2019). A partial explanation may be the apparent de-coupling of subject health assessments from physical health, per se, with an increased emphasis on psychological aspects of experience (Araújo et al., 2018; Henchoz et al., 2008). Older adults may normalize their current health status by shifting their expectations of health, with an associated shift in their expectations of social interactions (Puvill, Lindenberg, Gussekloo, de Craen, Slaets, & Westendorp, 2016).

Such inconsistent associations between loneliness and SRH over time suggest that modeling dynamic associations between health and loneliness across age may aid in elucidation of how and why loneliness and health affect each other throughout mid- and late-life. Age-based analyses using the DCSM offer an advantage over the crossed-lagged approach used in previous research because both cross-lagged relationships and longitudinal trajectories are modeled simultaneously, thus allowing examination of impacts on change with age (McArdle, 2001). The three age ranges were selected based on prior analyses in these samples that indicated different rates of change across age for related measures of physical and emotional health: BMI and depression (Emery et al., 2020). However, these age ranges can also be conceptualized as different contexts or phases of the lifespan, with 50-70 years of age reflecting aging most people experience that does not tend to impact lifestyle very much, 70-82 years of age reflecting normally increasing physical limitations that increasingly intrude on lifestyle, and 82+ years of age reflecting selective survival, contrasting with mortality processes and terminal decline (Birren & Cunningham, 1985). The relations between loneliness and health may require different interpretations within these phases. For example, impacts of loneliness on health may be more pronounced after age 82 when declining health is more common and financial, social, and physical resources may be comparatively diminished relative to those at ages 50-70. Impacts of health on

loneliness may also change with age, as health problems that do not drastically alter one's lifestyle or social relationships likely would not impact loneliness as much as health problems that do, and these become increasingly prevalent with age in late life.

This study had several strengths including availability of a harmonized measure of loneliness that used all available loneliness information for each participant in each subsample, inclusion of measures of both objective and subjective health, use of longitudinal data with up to 25 years of followup, and use of a pooled sample with data spanning a wide age range. Modeling associations with age rather than assessment also allowed a novel exploration of how dynamic relations between loneliness and health unfold across mid and late life. Limitations of this study included lack of inclusion of potentially important covariates such as measures of objective social isolation and depressive symptoms which may have roles in associations between loneliness and health, lack of ethnic diversity within the primarily Caucasian sample, and sample selectivity in participation criteria. Moreover, no participant in our pooled sample had data spanning the entire age range examined—the trajectories of loneliness and health across age were determined by different individuals within the sample rather than within individuals in the sample. The self-rated health measure also consisted of a single item and left the reference base completely open to participant interpretation (e.g., past self, age peers, objective standards, own expectations, etc.); however, single item measures of subjective health are used extensively in research on aging. The self-rated health measure may also be limited in terms of distribution, especially for the SATSA and OCTO-Twin studies which only offered 3 response options.

Overall, our observations indicate dynamic associations between loneliness and health with age in mid- to late-life with loneliness predicting decline in both objective and subjective health after age 70, and objective and subjective health predicting greater and less loneliness after age 82, respectively.

These observations, together with other work exploring temporal dynamics between loneliness and health, suggest that it is important to consider the dynamic interplay between these variables over

time/age in studies of loneliness and health in greater detail and other samples to understand these associations more fully. Our observation that poorer objective health predicted greater loneliness after age 82 supported the notion that worsening health or mobility with age in late life increases risk of loneliness by restricting opportunities for social interaction (Hajek & König, 2020; Havens et al., 2004; Ong et al., 2015; Pinquart, 2003; Smith, 2012). Further, our observations that loneliness predicted poorer subsequent health beginning at age 70 support that at these ages, loneliness may have long-term health effects that might occur via numerous pathways including but not limited to adverse physiological changes (e.g., altered viral immune response, increased inflammation) and altered sleep patterns/quality (Cole, 2013; Hawkley & Cacioppo, 2010). We advocate future research on loneliness and health that explores dynamic associations between loneliness and measures of both objective and subjective health given apparent bidirectional associations between these variables and our observed differences in associations across age for loneliness and subjective versus objective health. Investigations of how associations between loneliness, social isolation, depression and objective and subjective health unfold across age in greater detail, especially within individuals, will be important for furthering understanding of the dynamic relations between loneliness and health within the context of aging over mid- and late-life and developing ways of remediating them.

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DECLARATION OF INTEREST STATEMENT

The authors of this paper do not have any conflicts of interest.

References

- Akaike, H. (1987). Factor analysis and aic. Psychometrika, 52, 317-332.
- Andersen, F. K., Christensen, K., & Frederiksen, H. (2007). Self-rated health and age: A cross-sectional and longitudinal study of 11,000 Danes aged 45-102. *Scandinavian Journal of Public Health*, *35*, 164-171.
- Araújo, L., Teixeira, L., Ribeiro, O., & Paúl, C. (2018). Objective vs. subjective health in very advanced ages: Looking for discordance in centenarians. *Frontiers in Medicine*, *5*, 189.
- Birren, J. E., & Cunningham, W. R. (1985). *Research on the psychology of aging: Principles, concepts and theory.* In J. E. Birren & K. W. Schaie (Eds.), *The handbooks of aging. Handbook of the psychology of aging* (p. 3–34). Van Nostrand Reinhold Co.
- Blazer, D. (2020). Social isolation and loneliness in older adults: A mental health/public health challenge. *JAMA Psychiatry*, 77(10), 990-991.
- Browne, M., & Cudeck, R. (1993). Alternative ways of assessing model fit. In *Testing structural equation models* (pp. 136-62), ed. K. Bollen, S. Long. Beverly Hills, CA: Sage.
- Cacioppo, S., Capitanio, J. P., & Cacioppo, J. T. (2014). Toward a neurology of loneliness. *Psychological Bulletin*, *140*(6), 1464.
- Cacioppo, J. T., Hawkley, L. C., & Berntson, G. G. (2003). The anatomy of loneliness. *Current Directions in Psychological Science*, *12*(3), 71-74.
- Cacioppo, J. T., Hawkley, L. C., Crawford, L. E., Ernst, J. M., Burleson, M. H., Kowalewski, R. B., ... & Berntson, G. G. (2002). Loneliness and health: Potential mechanisms. *Psychosomatic Medicine*, *64*(3), 407-417.
- Christiansen, J., Larsen, F. B., & Lasgaard, M. (2016). Do stress, health behavior, and sleep mediate the association between loneliness and adverse health conditions among older people?. *Social Science & Medicine*, *152*, 80-86.

Christiansen, J., Lund, R., Qualter, P., Andersen, C. M., Pedersen, S. S., & Lasgaard, M. (2021). Loneliness, social isolation, and chronic disease outcomes. *Annals of Behavioral Medicine*, *55*(3), 203-215.

- Cole, S. W. (2013). Social regulation of human gene expression: mechanisms and implications for public health. *American Journal of Public Health*, *103*(S1), S84-S92.
- Cole, S. W., Hawkley, L. C., Arevalo, J. M., Sung, C. Y., Rose, R. M., & Cacioppo, J. T. (2007). Social regulation of gene expression in human leukocytes. *Genome Biology*, 8(9), R189.
- Creswell, J. D., Irwin, M. R., Burklund, L. J., Lieberman, M. D., Arevalo, J. M., Ma, J., ... & Cole, S. W. (2012). Mindfulness-based stress reduction training reduces loneliness and pro-inflammatory gene expression in older adults: A small randomized controlled trial. *Brain, Behavior, and Immunity*, 26(7), 1095-1101.
- Emery, C. F., Finkel, D., Gatz, M., & Dahl Aslan, A. K. (2020). Evidence of Bidirectional Associations

 Between Depressive Symptoms and Body Mass Among Older Adults. *The Journals of Gerontology: Series B*, 75(8), 1689-1698.
- Finkel, D., & Pedersen, N. L. (2004). Processing speed and longitudinal trajectories of change for cognitive abilities: The Swedish Adoption/Twin Study of Aging. *Aging, Neuropsychology, and Cognition*, *11*, 325-45. doi.10.1080/13825580490511152
- Finkel, D., & Franz, C. E., Christensen, K., Reynolds, C. A., Pedersen, N. L., for the IGEMS consortium (2020). Longitudinal twin study of subjective health: Differences in genetic and environmental components of variance across age and sex. *Journals of Gerontology: Psychological Sciences, 75*, 1-10. doi.org/10.1093/geronb/gby030.
- Finkel, D., Sternäng, O., Jylhävä, J., Bai, G., & Pedersen, N. L. (2019). Functional aging index complements frailty in prediction of entry into care and mortality. *The Journals of Gerontology: Series*A, 74(12), 1980-1986. doi: 10.1093/gerona/glz155
- Gatz, M., Reynolds, C. A., Finkel, D., Hahn, C., Zhou, Y., Zavala, C., for the IGEMS Consortium (2015). Data harmonization in aging research: Not so fast. *Experimental Aging Research*, *14*, 475-495.

Ghisletta, P., & de Ribaupierre, A. (2005). A dynamic investigation of cognitive dedifferentiation with control for retest: Evidence from the Swiss Interdisciplinary Longitudinal Study of the Oldest Old.

*Psychology and Aging, 20, 671-82. doi.10.1037/0882-7974.20.4.671

- Gold, C. H., Malmberg, B., McClearn, G. E., Pedersen, N. L., & Berg, S. (2002). Gender and health: A study of unlike-sex twins. *Journal of Gerontology: Social Sciences, 57B*, S168-S176. doi.10.1093/geronb/57.3.S168
- Hajek, A., & König, H. H. (2020). Which factors contribute to loneliness among older Europeans? Findings from the Survey of Health, Ageing and Retirement in Europe: Determinants of loneliness. *Archives of Gerontology and Geriatrics*, 89, 104080.
- Havens, B., Hall, M., Sylvestre, G., & Jivan, T. (2004). Social isolation and loneliness: Differences between older rural and urban Manitobans. *Canadian Journal on Aging/La Revue canadienne du vieillissement*, 23(2), 129-140.
- Hawkley, L. C., & Cacioppo, J. T. (2003). Loneliness and pathways to disease. *Brain, Behavior, and Immunity*, 17(1), 98-105.
- Hawkley, L. C., & Cacioppo, J. T. (2007). Aging and loneliness: Downhill quickly? *Current Directions in Psychological Science*, *16*(4), 187-191.
- Hawkley, L. C., & Cacioppo, J. T. (2010). Loneliness matters: A theoretical and empirical review of consequences and mechanisms. *Annals of Behavioral Medicine*, 40(2), 218-227.
- Hawkley, L. C., & Capitanio, J. P. (2015). Perceived social isolation, evolutionary fitness and health outcomes: a lifespan approach. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *370*(1669), 20140114.
- Henchoz, K., Cavalli, S., & Girardin, M. (2008). Health perception and health status in advanced old age:

 A paradox of association. *Journal of Aging Studies*, 22(3), 282-290

Jessen, M. A. B., Pallesen, A. V. J., Kriegbaum, M., & Kristiansen, M. (2018). The association between loneliness and health—a survey-based study among middle-aged and older adults in Denmark. *Aging & Mental Health*, 22(10), 1338-1343.

- Jylhä., M. (2009). What is self-rated health and why does it predict mortality? Towards a unified conceptual model. *Social Science & Medicine*, *69*, 307-316.
- Lichtenstein, P., Floderus, B., Svartengren, M., Svedberg, P., & Pedersen, N. L. (2002). The Swedish Twin Registry: a unique resource for clinical, epidemiological and genetic studies. *Journal of Internal Medicine*, 252(3), 184-205. doi:10.1046/j.1365-2796.2002.01032.x
- Lövdén, M., Ghisletta, P., & Lindenberger, U. (2005). Social participation attenuates decline in perceptual speed in old and very old age. *Psychology and Aging, 20*, 423-34. doi.10.1037/0882-7974.20.3.423
- Luhmann, M., & Hawkley, L. C. (2016). Age differences in loneliness from late adolescence to oldest old age. *Developmental Psychology*, *52*(6), 943-959.
- Luo, Y., Hawkley, L. C., Waite, L. J., & Cacioppo, J. T. (2012). Loneliness, health, and mortality in old age:

 A national longitudinal study. *Social Science & Medicine*, *74*(6), 907-914.
- McArdle, J. J. (2001). A latent difference score approach to longitudinal dynamic structural analyses. In *Structural equation modeling: Present and future* (pp. 342-80), ed. R. Cudeck, S. duToit, D. Sorbom, Lincolnwood, IL: Scientific Software International.
- McArdle, J. J., Hamagami, F., Jones, K., Jolesz, F., Kikinis, R., Spiro A. III., & Albert, M. S. (2004). Structural modeling of dynamic changes in memory and brain structure using longitudinal data from the normative aging study. *Journal of Gerontology: Psychological Sciences, 59B*, P294-P304. doi.10.1093/geronb/59.6.P294
- McArdle, J. J., Hamagami, F., Meredith, W., & Bradway, K. P. (2000). Modeling the dynamic hypotheses of Gf–Gc theory using longitudinal life-span data. *Learning and Individual Differences*, *12*(1), 53-

79.

- McClearn, G. E., Johansson, B., Berg, S., Pedersen, N. L., Ahern, F., Petrill, S. A., & Plomin, R. (1997).

 Substantial genetic influence on cognitive abilities in twins 80 or more years old. *Science*, *276*, 1560–1563. doi.10.1126/science.276.5318.1560
- Muthén, L. K., & Muthén, B. O. (2012-2015). *Mplus User's Guide* (4th ed.). Los Angeles, CA: Muthén & Muthén.
- National Academies of Sciences, Engineering, and Medicine. (2020). *Social isolation and loneliness in older adults: Opportunities for the health care system*. National Academies Press.
- Nicolaisen, M., & Thorsen, K. (2014). Who are lonely? Loneliness in different age groups (18–81 years old), using two measures of loneliness. *The International Journal of Aging and Human Development*, 78(3), 229-257.
- Nummela, O., Seppänen, M., & Uutela, A. (2011). The effect of loneliness and change in loneliness on self-rated health (SRH): A longitudinal study among aging people. *Archives of Gerontology and Geriatrics*, *53*(2), 163-167.
- Ong, A. D., Uchino, B. N., & Wethington, E. (2015). Loneliness and health in older adults: A mini-review and synthesis. *Gerontology*, *62*(4), 443-449.
- Pedersen, N. L., Christensen, K., Dahl, A., Finkel, D., Franz, C. E., Gatz, M., Horwitz, B. N., Johansson, B., Johnson, W., Kremen, W. S., Lyons, M. J., Malmberg, B., McGue, M., Neiderhiser, J. M., Petersen, I., and Reynolds, C. A. (2013). IGEMS: The Consortium on Interplay of Genes and Environment across Multiple Studies. *Twin Research and Human Genetics*, *16*, 481-489.
- Pedersen, N. L., Gatz, M., Finch, B. K., Finkel, D., Butler, D. A., Aslan, A. D., Franz, C. E., Kaprio, J., Lapham, S., McGue, M., Mosing, M. A., Niederhiser, J., Nygaard, M., Panizzon, M., Prescott, C. A., Reynolds, C. A., Sachdev, P., Whitfield, K., for the IGEMS Consortium (2019). IGEMS: The Consortium on Interplay of Genes and Environment across Multiple Studies: An update. *Twin*

- Research and Human Genetics, 22, 809-816.
- Petitte, T., Mallow, J., Barnes, E., Petrone, A., Barr, T., & Theeke, L. (2015). A systematic review of loneliness and common chronic physical conditions in adults. *The Open Psychology Journal*, 8(Suppl 2), 113.
- Phillips, D. M. (2020). Longitudinal Loneliness and Cognitive Aging in Mid and Late Life: Patterns of

 Associations and Epigenetic Pathways (Doctoral dissertation, UC Riverside).
- Phillips, D. M., Wang, Y., Pedersen, N. L., Hägg, S., & Reynolds, C. A. (2019). Loneliness and DNA methylation of variants in the conserved transcriptional response to adversity pathway. Poster presented at the 49th annual meeting of the Behavior Genetics Association, Stockholm, Sweden.

 Abstract published in *Behavior Genetics*, 49.
- Pinquart, M. (2003). Loneliness in married, widowed, divorced, and never-married older adults. *Journal of Social and Personal Relationships*, *20*(1), 31-53.
- Puvill, T., Lindenberg, J., Gussekloo, J., de Craen, A. J., Slaets, J. P., & Westendorp, R. G. (2016).

 Associations of various health-ratings with geriatric giants, mortality and life satisfaction in older people. *PLoS One*, *11*(9), e0163499.
- Qualter, P., Vanhalst, J., Harris, R., Van Roekel, E., Lodder, G., Bangee, M.,...Verhagen, M. (2015).

 *Perspectives on Psychological Science, 10(2), 250-264.
- Richard, A., Rohrmann, S., Vandeleur, C. L., Schmid, M., Barth, J., & Eichholzer, M. (2017). Loneliness is adversely associated with physical and mental health and lifestyle factors: Results from a Swiss national survey. *PloS One*, *12*(7), e0181442.
- Segrin, C., & Passalacqua, S. A. (2010). Functions of loneliness, social support, health behaviors, and stress in association with poor health. *Health Communication*, *25*(4), 312-322.
- Smith, J. M. (2012). Toward a better understanding of loneliness in community-dwelling older adults. *The Journal of Psychology*, *146*(3), 293-311.

Tsur, N., Stein, J. Y., Levin, Y., Siegel, A., & Solomon, Z. (2019). Loneliness and subjective physical health among war veterans: Long term reciprocal effects. *Social Science & Medicine*, *234*, 112373.