



### **Research Article**

## Loneliness in Later Life and Reaching Longevity: Findings From the Longitudinal Aging Study Amsterdam

# Lloyd Brandts, PhD,<sup>1,\*</sup> Theo G. van Tilburg, PhD,<sup>2,</sup> Hans Bosma, PhD,<sup>3</sup> Martijn Huisman, PhD,<sup>2,4</sup> and Piet A. van den Brandt, PhD<sup>1,5,</sup>

<sup>1</sup>Department of Epidemiology, GROW - School for Oncology and Developmental Biology, Maastricht University Medical Centre, the Netherlands. <sup>2</sup>Department of Sociology, Vrije Universiteit, Amsterdam, the Netherlands. <sup>3</sup>Department of Social Medicine, CAPHRI - School for Public Health and Primary Care, Maastricht, the Netherlands. <sup>4</sup>Department of Epidemiology and Biostatistics, Amsterdam Public Health Research Institute, VU University Medical Center, the Netherlands. <sup>5</sup>Department of Epidemiology, CAPHRI - School for Public Health and Primary Care, Maastricht, the Netherlands.

\*Address correspondence to: Lloyd Brandts, PhD, Department of Epidemiology, Maastricht University Medical Centre, PO Box 616, 6200 MD Maastricht, the Netherlands. E-mail: Lloyd.brandts@maastrichtuniversity.nl

Received: January 9, 2020; Editorial Decision Date: August 20, 2020

Decision Editor: Deborah S. Carr, PhD, FGSA

#### Abstract

**Objectives:** There is an increasing research interest in factors that characterize those who reach exceptionally old ages. Although loneliness is often associated with an increased risk for premature mortality, its relationship with reaching longevity is still unclear. We aimed to quantify the association between (social/emotional) loneliness and the likelihood of reaching the age of 90 years in men and women separately.

**Methods:** For these analyses, data from the Longitudinal Aging Study Amsterdam (LASA) were used. Loneliness, social loneliness, and emotional loneliness were assessed at baseline using the 11-item De Jong-Gierveld scale in 1992–1993 (at age 64–85 years). Follow-up for vital status information until the age of 90 years was 99.5% completed. Multivariable-adjusted Cox regression analyses with a fixed follow-up time were based on 1,032 men and 1,078 women to calculate risk ratios (RR) of reaching 90 years.

**Results:** No significant associations were observed between loneliness and reaching 90 years in both men (RR, 0.90; 95% confidence interval [CI], 0.70–1.14) and women (RR, 0.98; 95% CI, 0.83–1.14). Social loneliness was significantly associated with a reduced chance of reaching 90 years in women (RR, 0.82; 95% CI, 0.67–0.99).

**Discussion:** The current analyses did not show support for the existence of a meaningful effect of loneliness on reaching longevity in both sexes. When investigating specific dimensions of loneliness, we observed that reporting social loneliness was associated with reaching 90 years in women. This indicates that, for women, a large and diverse personal network at an older age could increase the probability of reaching longevity. However, replication of our findings in other cohorts is needed.

Keywords: Aging, Life span, Loneliness, Longevity, Prospective cohort study

With an increasing number of individuals reaching exceptionally old ages, there is an increasing research interest in identifying factors that characterize this group of long-lived individuals. Apart from the added years to life, human longevity has also been associated with delayed morbidity (Andersen et al., 2012). Therefore, identifying

© The Author(s) 2020. Published by Oxford University Press on behalf of The Gerontological Society of America.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (http://creativecommons.org/ licenses/by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

factors that are associated with reaching longevity might contribute to the understanding of promoting both longer and healthier life spans. Human longevity is mostly defined as reaching a specific age that exceeds the life expectancy (U.S. Department of Health and Human Services, 2001). To date, several studies have identified genetic and lifestylerelated factors that are associated with reaching longevity, mostly defined as reaching the age of 90 years (Brandts & van den Brandt, 2018, 2019; Edjolo et al., 2013; Rantanen et al., 2012; Revelas et al., 2018; Wilhelmsen et al., 2011; Yates et al., 2008). Few studies investigated the relationship between psychosocial factors and longevity. Recently, two prospective cohort analyses reported a positive association between optimism and social integration and reaching the age of 85 years (Lee et al., 2019; Trudel-Fitzgerald et al., 2019). While these positive psychosocial traits seem to increase the probability of reaching longevity, analyses on negative psychosocial traits, such as loneliness, in relation to the probability of reaching longevity have not yet been performed.

Loneliness is defined as a perceived lack of social relationships and unfulfilled intimacy (de Jong-Gierveld, 1989). Additionally, loneliness can be further distinguished by emotional loneliness and social loneliness. Emotional loneliness refers to a perceived lack of intimacy or close emotional attachment in relationships, whereas social loneliness refers perceived lack of a broader group of contacts or engaging in a social network (de Jong-Gierveld et al., 2018).

Loneliness is common among older individuals, and the prevalence seems to increase with age, especially at older ages (75+ years; Luhmann & Hawkley, 2016). Based on surveys, it is estimated that around 25% of individuals aged 45-79 years report moderate or serious loneliness. In individuals aged 80+ years, this is estimated to be around 43% (de Jong Gierveld, 1998; Pinquart & Sorensen, 2001). Loneliness has often been linked to an increased chance of premature death. In a meta-analysis on loneliness and mortality, loneliness was associated with all-cause mortality in both men and women (Rico-Uribe et al., 2018). Another meta-analysis indicated that the association between loneliness and mortality risk was similar to other well-established risk factors for mortality (Holt-Lunstad et al., 2015). Berkman et al. (2000) have presented a conceptual model on how (a lack of) social interaction might influence health (Berkman et al., 2000). They describe three downstream pathways through which these psychosocial mechanisms may influence health and longevity namely, via health behavioral-, psychological-, and physiologic pathways (Berkman et al., 2000). In line with this conceptual model, other researchers have suggested that loneliness is associated with a reduced capacity of self-regulation (Hawkley & Cacioppo, 2010) and unhealthy lifestyle habits (Hawkley et al., 2009; Lauder et al., 2006. Although several studies observed a positive association between loneliness and mortality, this does not necessarily mean that loneliness will

be associated with a decreased probability of reaching longevity as well. During the aging process, different contextual conditions might influence the survival curve, the effect that relevant factors might have the risk of mortality might converge or crossover across different stages of life, and the role of chance on mortality is substantial (McDonald & Ruhe, 2011; Salaris, 2015). Therefore, studies on mortality are more suitable for identifying factors that are associated with premature mortality, which occurs at every stage of the life course, rather than identifying factors that are associated with reaching exceptionally high ages. In terms of causality, inspired by the causal pie model of Kenneth Rothman (Rothman, 1976; Rothman & Greenland, 2005), studies on mortality might hint toward factors that act as a component cause for reaching longevity. However, these factors do not necessarily add up to a sufficient cause for reaching longevity because the outcome (longevity) is not yet known. As a result, a factor might be associated with premature mortality and not with longevity and vice versa. In addition, it has been observed that the relationship between loneliness and mortality became weaker with increasing age of the participants (Holt-Lunstad et al., 2015), which could indicate that long-lived individuals are more resilient to the harmful effects of loneliness. Using data from the Longitudinal Aging Study Amsterdam (LASA) cohort, we aimed to quantify the relationship between loneliness and the likelihood of reaching the age of 90 years. Because men and women follow different survival patterns (e.g., women have a higher overall probability of reaching 90 years compared to men), all analyses were stratified by sex.

#### Method

#### Study Design and Population

The LASA is a prospective cohort study initiated in 1992 to study the physical, emotional, cognitive, and social functioning of individuals aged 55-84 years in the Netherlands. In 1992, a sample was recruited from 11 municipal registries within three representative geographic regions in the Netherlands for the Living Arrangements and Social Networks of Older Adults program (LSN). Participants recruited for this study were born between 1908 and 1937, with an oversampling of older individuals and males. The initial response rate was 62% (n = 3,805). From this sample, 3,677 surviving participants were contacted for the first LASA cycle (1992-1993) on average 11 months after the LSN interview, with a response rate of 85%. Examinations were performed at the participants' homes, and re-examinations took place about every 3 years. Trained interviewers conducted interviews, and additional data were obtained using a questionnaire. During the interviews, the participants were also asked for permission to participate in a separate medical interview. Clinical measurements were taken during the medical interview, and the interviewer asked additional questions. Detailed information on the

data collection procedures has been described elsewhere (Huisman et al., 2011).

Mortality follow-up was done by record linkage to the municipal population registries, Basisregistratie Personen (BRP). The last date of mortality follow-up for this study was August 1, 2018. Because only a part of the full cohort was "at risk" of reaching the age of 90 years at this date, the analyses were restricted to participants born before August 2, 1928 (Figure 1). Of these, follow-up for mortality was 99.5% completed. After exclusion of participants with missing data information on loneliness (n = 62), 1,032 men and 1,078 women were included for the analyses (Figure 1).

#### Exposure Assessment and Outcome

Loneliness has been assessed at baseline by using a validated 11-item De Jong-Gierveld scale (de Jong-Gierveld & Kamphuls, 1985) in 1992–1993. De Jong-Gierveld scale was proved to have good psychometric properties, in previous studies in the Netherlands (van Tilburg & Leeuw, 1991). Items scores have been computed into an overall measure of loneliness ranging from 0 (no loneliness) to 11 (severe loneliness). Loneliness was also computed into a dichotomous variable, in which a participant is considered mildly or severely lonely at a cutoff score of  $\geq$ 3 on the loneliness scale, as has been done in other studies before (van Tilburg & de Jong, 1999).

Two dimension of loneliness can be further distinguished from the overall loneliness scale items, namely emotional loneliness (range 0–6) and social loneliness (range 0–5). Participants who scored  $\geq 2$  out of six emotional loneliness items were considered emotionally lonely. Those scoring  $\geq 2$  out of five social loneliness items were considered socially lonely (van Tilburg & de Jong, 1999). Reaching the age of 90 years (yes/no) was used as an outcome measure.

#### **Statistical Analyses**

Baseline characteristics were presented with mean values for continuous variables and with percentages for categorical variables. Characteristics were presented by survival status at age 90 years and experienced loneliness at baseline, both stratified by sex. The association between loneliness and the likelihood of reaching 90 years was assessed using age- and multivariable-adjusted Cox regression models with a fixed follow-up time (Breslow, 1974; Nijem et al., 2005). Huber-White sandwich estimator was used to calculate standard errors to account for underdispersion (Barros & Hirakata, 2003). For the multivariable-adjusted analyses, a priori confounders were selected based on literature and directed acyclic graphs. Baseline age (years, continuous), educational level (primary/lower vocational, junior/senior high school, and higher vocational/university), and marital status (never married, married, divorced, and widowhood) were selected as confounders for our main analyses. Additional adjustments were made for number of (selected) chronic diseases at baseline (0, 1, 2, 3, or more from nonspecific lung diseases, cardiac diseases, peripheral artery disease, diabetes mellitus, stroke, arthritis, and malignancies) and the Mini-Mental State Examination (MMSE) score (0–30, continuous) in Model 3, and smoking status (never, former, current, and missing), body mass index (BMI; <18.5, 18.5-<25, 25-<30, 30+

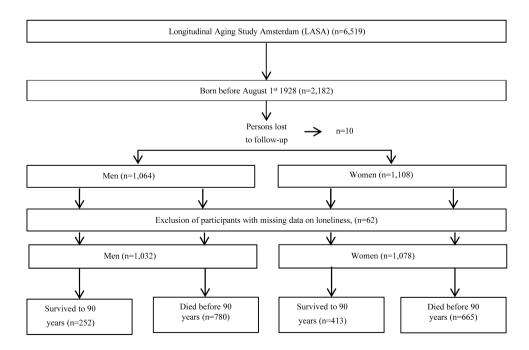


Figure 1. Flow diagram on analyses between loneliness and longevity in an older cohort (aged 64-85 years) of the Longitudinal Aging Study Amsterdam (LASA) (1992-2018).

kg/m<sup>2</sup>, and missing), total minutes of nonoccupational physical activity per day(<30, 30–<60, 60–<90, 90–<120,  $\geq$ 120, and missing), and number of alcohol beverages per week (0, >0–<1, 1–<5, 5–<10, 10+, and missing) in Model 4. Although we consider these additional variables as potential confounders, these factors might also act as a mediator, making it more difficult to interpret the additionally adjusted results. All analyses were stratified by sex.

After evaluation of the confounding variables, we observed missing values (n = 548) on confounding lifestyle factors including smoking status, BMI, physical activity, alcohol intake, educational level, and MMSE (Tables 1 and 2). To limit bias that might occur due to this dropout, a multiple imputation approach with 20 iterations was performed, based on linear (for continuous variables) and logistic (for categorical variables) regression models. Information on loneliness, marital status, number of selected disease, smoking status, BMI, nonoccupational physical activity, alcohol consumption, education level, sex, and reaching the age of 90 (yes/no) were used as predictors for the imputed data.

#### Results

In this study, the average probability of reaching the age of 90 years was 0.24 in men and 0.38 in women (Table 1). Having a higher vocational or university degree, and reporting no (selected) diseases at baseline was more common in those who survived to 90 years, compared to those who died before this age (Table 1).

Regarding lifestyle factors, men who survived to 90 years were less often current smokers (19.4% vs. 30.0%), were less often obese ( $\geq$ 30 kg/m<sup>2</sup>; 7.5% vs. 8.9%), had a somewhat higher average level of physical activity (150 vs. 131 min/day), and drank less alcoholic beverages per week (8.3 vs. 9.2 drinks/week). Women who survived to 90 years were also less often current smokers (7.3% vs. 14.3%), but drank more alcoholic beverages per week (4.1 vs. 3.5 drinks/week). However, it has to be noted that both men and women who died before 90 years were more likely to have missing information on lifestyle characteristics, compared with those who survived to 90 years (Table 1).

In Table 2, we observed that both men and women who experienced loneliness were less often married and had more often at least one (selected) chronic disease at baseline. Those who experienced loneliness were also more likely to have missing information on lifestyle characteristics (Table 2).

In both men and women, no significant associations were observed between loneliness and reaching longevity in dichotomous and continuous analyses (Table 3). In the main analyses (Model 2), we observed a nonsignificant inverse association between loneliness (yes vs. no) and reaching 90 years in men (risk ratio [RR], 0.90; 95% confidence interval [CI], 0.70–1.14), and in women (RR, 0.98; 95% CI, 0.83–1.15).

Point estimates of effect showed that emotional loneliness was not associated with reaching 90 years in both men (RR, 0.86; 95% CI, 0.66–1.12), and women (RR, 0.90; 95% CI, 0.76–1.05), in the main analyses (Model 2). In the main analyses, social loneliness was significantly inversely associated with reaching 90 years in women (RR, 0.82; 95% CI, 0.67–0.99), and nonsignificantly inverse in men (RR, 0.93; 95% CI, 0.73–1.18). Additional adjustment for disease and lifestyle factors attenuated the effect estimates to RR, 0.91 and 95% CI, 0.75–1.11 in women and RR, 1.02 and 95% CI, 0.80–1.30 in men (Table 3).

#### Discussion

Based on the data from the LASA cohort, we observed that loneliness was not significantly associated with reaching the age of 90 years in both men and women. When we distinguished different dimensions of loneliness, we observed that social loneliness was significantly associated with a reduced chance of reaching the age of 90 years in women.

In the current analyses, no significant associations were observed between loneliness and reaching longevity. Although the literature on loneliness and longevity is scarce, several studies studied the relationship between loneliness and premature mortality. In a meta-analyses of 35 articles investigating the relationship between loneliness and all-cause mortality, a pooled HR of 1.44 (95% CI, 1.19-1.76) in men and a pooled HR of 1.26 (95% CI, 1.10–1.35) in women was observed (Rico-Uribe et al., 2018). Furthermore, loneliness was also significantly associated with an increased mortality risk in an earlier analvsis of the LASA cohort (Holwerda et al., 2016). However, this analysis on mortality also included participants who were younger at baseline (aged 55-63 years). It is known that feelings of loneliness increase during aging due to the decline in social contacts and are even common among the very old (Dykstra et al., 2005; Pinquart & Sorensen, 2001). Because of the inherent decline of social contacts at older ages, aging might also be accompanied with changing strategies to cope with loneliness. For instance, reflection and acceptance have been found to be important strategies to reduce distress caused by loneliness (Rokach, 2018). This strategy has found to be more common in older individuals and in those who have experienced long-term loneliness (Kharicha et al., 2020). It is believed that these strategies are more common in older individuals because they are more likely to attribute loneliness to stable, irreversible factors (Pinquart & Sorensen, 2001). In contrast, younger individuals who experience loneliness might experience that their situation is culturally divergent, which could pose an additional threat to their self-esteem and mental well-being (Holt-Lunstad et al., 2010). This could indicate that the effect of loneliness on mortality differs throughout the life course and might explain why the results of our study differed from the results observed in the earlier analyses within the LASA cohort (Holwerda et al.,

Table 1. Baseline Characteristics of the Cohort Members Overall and by Survival Status in an Older Cohort (aged 64–85 years)
of the LASA (1992–2018)

	Men			Women		
	Total	Survived to 90 years	Died before age 90 years	Total	Survived to 90 years	Died before age 90 years
N (%) <sup>a</sup>	1,032	252 (24.4)	780 (75.6)	1,078	413 (38.3)	665 (61.7)
Age at baseline, mean $\pm$ SD	75.4 ± 5.9	$76.2 \pm 6.2$	75.1 ± 5.8	$75.2 \pm 6.1$	$76.0 \pm 6.3$	74.6 ± 5.9
Loneliness scale $(0-11)$ , mean $\pm SD$	$2.1 \pm 2.5$	$2.1 \pm 2.4$	$2.2 \pm 2.5$	$2.5 \pm 2.8$	$2.4 \pm 2.7$	$2.5 \pm 2.8$
Loneliness (≥3 pt), (%)	32.6	31.8	32.8	37.9	38.0	37.7
Emotional loneliness scale $(0-6)$ , mean $\pm SD$	1.1 ± 1.6	$1.0 \pm 1.5$	1.1 ± 1.6	1.5 ± 1.9	$1.5 \pm 1.9$	1.5 ± 1.9
Emotional loneliness ( $\geq 2$ pt), (%)	26.3	25.0	26.7	38.3	36.8	39.3
Social loneliness scale $(0-5)$ , mean $\pm SD$	$1.1 \pm 1.4$	1.1 ± 1.4	1.1 ± 1.4	$0.9 \pm 1.4$	$0.9 \pm 1.3$	$1.0 \pm 1.4$
Social loneliness ( $\geq 2$ pt), (%)	28.0	27.4	28.2	23.3	20.3	25.1
Educational level (%)						
Primary/lower vocational	61.4	57.1	62.8	74.0	68.8	77.3
Junior/senior high school	25.2	27.0	24.6	19.1	23.0	16.7
Higher vocational/university	13.4	15.9	12.6	6.9	8.2	6.0
Marital status (%)						
Never married	4.6	5.2	4.4	6.9	7.3	6.6
Married	75.1	73.0	75.8	42.3	39.0	44.4
Divorced	4.2	5.6	3.7	5.1	5.8	4.7
Widowhood	16.2	16.3	16.2	45.7	47.9	44.4
Number of chronic (selected) diseases (%)	10.2	10.0	10.2	1017	17.5	
0	36.3	46.4	33.1	30.0	34.4	27.2
1	35.3	36.1	35.0	36.9	37.3	36.7
2	18.8	12.7	20.8	21.8	21.3	22.1
3 or more	9.6	4.8	11.2	11.3	7.0	14.0
Mini-Mental State Examination score	$26.5 \pm 3.2$	$27.1 \pm 2.6$	$26.4 \pm 3.3$	$26.4 \pm 3.3$	26.9 ± 2.6	$26.1 \pm 3.6$
(0-30), mean ± <i>SD</i>	20.3 ± 3.2	27.1 ± 2.0	20.1 ± 5.5	20.1 ± 3.3	20.7 ± 2.0	20.1 ± 5.0
Smoking status (%)			4.0			
Never	5.9	9.1	4.9	48.9	54.7	45.3
Former	53.4	61.5	50.8	23.0	24.2	22.3
Current	27.4	19.4	30.0	11.6	7.3	14.3
Missing	13.3	9.9	14.3	16.5	13.8	18.2
BMI (kg/m <sup>2</sup> ) <sup>b</sup> , mean ± <i>SD</i> BMI (kg/m <sup>2</sup> ), (%)	25.8 ± 3.3	25.8 ± 3.1	25.9 ± 3.3	27.8 ± 4.7	27.7 ± 4.5	27.9 ± 4.8
<18.5 kg/m <sup>2</sup>	0.9	0.4	1.0	1.0	0.2	1.5
18.5-<25 kg/m <sup>2</sup>	33.6	36.1	32.8	21.7	23.5	20.6
25-<30 kg/m <sup>2</sup>	41.3	44.8	40.1	33.5	36.8	31.4
≥30 kg/m²	8.5	7.5	8.9	23.6	22.3	24.4
Missing	15.7	11.1	17.2	20.2	17.2	22.1
Total physical activity $(min/day)^b$ , mean $\pm SD$	$136 \pm 106$	$150 \pm 110$	131 ± 105	$176 \pm 106$	$179 \pm 106$	174 ± 106
Total physical activity (min/day), (%)						
<30 min/day	10.9	6.8	12.2	5.0	2.9	6.3
30–<60 min/day	10.5	8.7	11.0	5.0	5.1	5.0
60-<90 min/day	12.9	15.9	11.9	8.0	8.0	8.0
90-<120 min/day	14.4	13.9	14.6	8.9	10.4	8.0
120+ min/day	44.3	48.0	43.1	64.5	67.3	62.7
Missing	7.1	6.8	7.2	8.6	6.3	10.1
Number of alcoholic beverages per week <sup>b</sup> ,	9.0 ± 10.4	8.3 ± 8.6	9.2 ± 10.9	$3.7 \pm 6.5$	4.1 ± 6.4	$3.5 \pm 6.5$
mean $\pm SD$						2.2 - 0.0
Number of alcoholic beverages per week (%)						
0 (Abstainers)	15.9	13.9	16.5	26.4	23.5	28.2
>0–<1 drink/week	7.1	6.8	7.2	13.5	13.6	13.5

#### Table 1. Continued

	Men			Women		
	Total	Survived to 90 years	Died before age 90 years	Total	Survived to 90 years	Died before age 90 years
1-<5 drinks/week	15.7	17.5	15.1	21.8	24.5	20.2
5-<10 drinks/week	19.9	23.8	18.6	12.2	12.6	11.9
10+ drinks/week	27.7	27.8	27.7	9.2	11.1	8.0
Missing	13.8	10.3	14.9	16.9	14.8	18.2

Note: BMI = Body mass index; LASA = Longitudinal Aging Study Amsterdam.

<sup>a</sup>Number of participants with complete information on loneliness, emotional loneliness, social loneliness, and confounders including: baseline age, educational level, marital status, number of (selected) disease at baseline, and MMSE-score. <sup>b</sup>Excluding participants with missing data.

2016). One meta-analysis did report that the effect estimates between loneliness and mortality became weaker with increasing ages of the participants (Holt-Lunstad et al., 2015). However, this hypothesis remains speculative, and replication of our findings in other cohorts is needed. Some evidence suggests that the use of coping strategies to deal with loneliness seems to differ between cultures as well (Rokach et al., 2004). Therefore, the relationship between loneliness and longevity we did observe in our Dutch cohort might not be generalizable to other cultures.

Although no significant association was observed between loneliness and longevity, we did find a significant association between social loneliness and a decreased chance of reaching 90 years in women. An individual might experience social loneliness when there is an absence of a broader group of contacts or engaging in a social network (de Jong-Gierveld et al., 2018). In previous studies, it has been observed that a larger size and diversity of the social network were more strongly associated with a reduced risk for mortality in older individuals, compared to functional characteristics like emotional support (Barefoot et al., 2005; Ellwardt et al., 2015). Furthermore, there is evidence that, with aging, men receive and provide more emotional support, whereas women seem to receive more tangible support (Shaw et al., 2007). This could indicate that, at least for women, the size and diversity of a personal network might be more important for reaching longevity. However, additional adjustment for number of selected diseases at baseline and other lifestyle factors did attenuate the results. This could indicate that the presence of a chronic disease or an unhealthy lifestyle limits the possibility of having a large diverse personal network, explaining the observed relationship. Given these uncertainties, the exact mechanism on how social and emotional loneliness is associated with reaching longevity in both sexes needs to be further explored and replicated in other longitudinal cohort studies as well.

As in studies on mortality, the causal direction between loneliness and unfavorable lifestyle characteristics and disease occurrence remains questionable. In this study, adjustments were made for history of chronic (selected) diseases at baseline and lifestyle characteristics. In these analyses, the effect estimates between (the different dimensions of) loneliness became weaker, which might indicate that these factors partially explain the unfavorable association between loneliness and longevity. However, because adjustment for mediating factors might introduce bias toward the null, we consider the effect estimates with adjustment for pre-exposure covariates (e.g., marital status and educational level) less biased than the fully-adjusted effect estimates (Rothman et al., 2008).

The strengths of this study are the large sample size and the long and complete follow-up for mortality (99.5%). The prospective study design limits the risk for information bias and selection bias due to differential follow-up. Furthermore, loneliness was assessed using a reliable and valid measurement instrument (de Jong-Gierveld & Kamphuls, 1985).

A limitation that should be considered is that information on loneliness and covariables was only based on the observation at baseline (in 1992-1993). Furthermore, residual confounding by baseline age might have influenced our results. It is known that individuals report more loneliness with increasing age. The ages at which the participants were included in the study were broad (ages 64-85 years). While older individuals are more likely to report loneliness, they also have a higher (conditional) chance of reaching 90 years of age at baseline, which might have led to an underestimation of the association between loneliness and longevity. We did account for this potential confounding effect by adjusting for baseline age in the multivariable-adjusted models. Despite this measure, we should not rule out the possibility of residual confounding by baseline age. Even though the sample size of the current analyses was not sufficient to provide age-stratified analyses, we suggest that future studies should prefer stratification by age groups when the sample size allows for that. Furthermore, the participants in this study already survived to older ages, which could have led to survivorship bias. The association

Table 2. Baseline Characteristics of the Cohort Members by Sex and Loneliness Status in an Older Cohort (aged 64–85 years)	
of the LASA (1992–2018)	

	Men		Women	
	Not lonely	Lonely (≥3pt)	Not lonely	Lonely (≥3pt)
$\overline{N^a}$	696	336	670	408
Age at baseline, mean $\pm$ SD	$74.6 \pm 5.8$	76.9 ± 5.9	$74.6 \pm 6.2$	$76.1 \pm 5.8$
Educational level, <i>n</i> (%)				
Primary/lower vocational	59.9	64.6	72.2	77.0
Junior/senior high school	26.6	22.2	19.9	17.9
Higher vocational/university	13.5	13.2	7.9	5.2
Marital status, $n$ (%)				
Never married	2.6	8.6	6.7	7.1
Married	84.3	56.0	51.0	27.9
Divorced	3.2	6.3	4.6	5.9
Widowhood	9.9	29.2	37.6	59.1
Number of (selected) diseases at baseline, $n$ (%)				
0	38.1	32.7	32.8	25.3
1	35.2	35.4	38.5	34.3
2	17.0	22.6	19.1	26.2
3 or more	9.8	9.2	9.6	14.2
Mini-Mental State Examination score $(0-30)$ , mean $\pm$ SD	$26.8 \pm 2.7$	$25.9 \pm 4.0$	$26.7 \pm 3.0$	$25.9 \pm 3.7$
Smoking status (%)	20.0 2 2.7	23.72 1.0	20.7 2 3.0	20.7 2 0.7
Never	6.5	4.8	50.1	45.8
Former	55.5	49.1	23.1	22.8
Current	25.6	31.3	10.9	12.8
Missing	12.5	14.9	15.2	18.6
BMI $(kg/m^2)^b$ , mean $\pm SD$	12.5 25.9 ± 3.1	25.7 (3.6)	13.2 28.0 ± 4.5	27.5 (5.1)
BMI (kg/m <sup>2</sup> ), (%)	$23.9 \pm 3.1$	23.7 (3.6)	$20.0 \pm 4.5$	27.5 (3.1)
<18.5 kg/m <sup>2</sup>	0.6	1.5	0.6	1.7
-	34.2	32.4	20.0	
$18.5 - 25 \text{ kg/m}^2$	42.1	32.4 39.6		24.5
25-<30 kg/m <sup>2</sup>			37.0	27.7
$\geq$ 30 kg/m <sup>2</sup>	8.5	8.6	24.5	22.1
Missing	14.7	17.9	17.9	24.0
Total physical activity $(min/day)^b$ , mean $\pm SD$	$137 \pm 105$	$134 \pm 110$	$186 \pm 107$	$159 \pm 103$
Total physical activity (min/day), (%)				
<30 min/day	9.3	14.0	3.0	8.3
30-<60 min/day	10.5	10.4	4.5	5.9
60–<90 min/day	13.8	11.0	8.2	7.6
90-<120 min/day	16.2	10.7	8.4	9.8
120+ min/day	44.8	43.2	68.4	58.1
Missing	5.3	10.7	7.6	10.3
Number of alcoholic beverages per week <sup>b</sup> , mean ± SD	8.8 ± 9.9	$9.3 \pm 11.3$	$3.8 \pm 6.6$	$3.6 \pm 6.3$
Number of alcoholic beverages per week (%)				
0 (Abstainers)	15.1	17.6	27.2	25.3
>0–<1 drink/week	7.3	6.6	12.2	15.7
1–<5 drinks/week	15.0	17.3	22.5	20.6
5–<10 drinks/week	21.6	16.4	13.1	10.5
10+ drinks/week	28.0	27.1	9.3	9.1
Missing	13.1	15.2	15.7	18.9

Note: BMI = Body mass index; LASA = Longitudinal Aging Study Amsterdam.

<sup>a</sup>Number of participants with complete information on loneliness, emotional loneliness, social loneliness, baseline age, educational level, marital status, number of (selected) disease at baseline, and MMSE-score. <sup>b</sup>Excluding participants with missing data.

	Males				Females			
	Model 1 <sup>a</sup>	Model 2 <sup>b</sup>	Model 3 <sup>c</sup>	Model 4 <sup>d</sup>	Model 1 <sup>a</sup>	Model 2 <sup>b</sup>	Model 3 <sup>c</sup>	Model 4 <sup>d</sup>
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Loneliness (0–11) Dichotomous								
No (<3 pt)	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Yes (≥3 pt)	0.91 (0.72 - 1.15)	0.90(0.70 - 1.14)	0.95 (0.75-1.21)	0.99 (0.78-1.26)	0.98(0.83 - 1.14)	0.98 (0.83-1.15)	1.04(0.89 - 1.22)	1.10(0.94 - 1.29)
Continuous (per 1pt	0.98 (0.94–1.02)	0.98 (0.93-1.02)	0.99(0.95 - 1.04)	1.00 (0.96–1.05)	0.99(0.96 - 1.01)	0.98 (0.96–1.01)	1.00 (0.97-1.03)	1.01 (0.98–1.04)
increment)								
Emotional loneliness								
(00)								
Dichotomous								
No (<2pt)	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Yes (≥2 pt)	0.87 (0.68 - 1.11)	$0.86\ (0.66 - 1.12)$	0.92 (0.71-1.20)	0.95 (0.73-1.24)	0.91(0.77 - 1.06)	0.90 (0.76-1.05)	0.97 (0.82 - 1.14)	1.01(0.86 - 1.19)
Continuous (per 1pt	0.96 (0.90-1.03)	0.96(0.89 - 1.03)	0.98 (0.91-1.06)	1.00(0.92 - 1.08)	0.99 (0.95-1.03)	1.00 (0.96-1.04)	1.01(0.97 - 1.06)	1.03 (0.99–1.07)
increment)								
Social loneliness								
(0-5)								
Dichotomous								
No (<2pt)	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Yes (≥2 pt)	0.94 (0.74-1.20)	0.93 (0.73-1.18)	0.96 (0.76-1.23)	1.02 (0.80-1.30)	$0.82\ (0.68 - 1.00)$	0.82 (0.67-0.99)	0.84 (0.70-1.02)	0.91 (0.75-1.11)
Continuous (per 1pt	0.99(0.92 - 1.06)	0.98 (0.91–1.06)	1.00 (0.92-1.07)	1.01 (0.94–1.09)	$0.96\ (0.90-1.01)$	0.95(0.90 - 1.01)	0.97(0.91 - 1.03)	0.99(0.94 - 1.05)
increment)								

and widowhood). 'Additionally adjusted for number of (selected) diseases at baseline (0, 1, 2, 3, or more), and MMSE-score (0–30; continuous). 'Additionally adjusted for smoking status (never, formet, and missing), body mass index (<18.5–-25, 25–<30 30+ kg/m<sup>2</sup>, and missing), total physical activity per day (<30, 30–<60, 60–<90, 90–<120, 110 min/day, and missing), and number of alcoholic beverages per week (0, >0–<1, 1–<5, 5–<10, 10+ drinks/week, and missing).

between loneliness and longevity might potentially be stronger if younger baseline ages were considered.

In conclusion, we did not observe a significant association between loneliness and longevity in both men and women. Strongest support was observed for an association of social loneliness with longevity in women, which might indicate that in women the quantity of relationships might be more important than the quality of relationship in terms of reaching longevity.

#### Funding

This work was supported by "Longitudinal Aging Study Amsterdam" (LASA; www.lasa-vu.nl), largely funded by the Dutch Ministry of Health, Welfare and Sport.

#### **Author Contributions**

L. Brandts planned the analyses, performed the statistical analyses, and wrote the paper. T. G. van Tilburg provided substantial feedback during the data analysis and revised the manuscript. M. Huisman provided substantial feedback during the data analysis and revised the manuscript. H. Bosma critically revised the manuscript. P.A. van den Brandt planned the analyses, provided substantial feedback during the data analysis, and revised the manuscript.

#### **Conflict of Interest**

None declared.

#### References

- Andersen, S. L., Sebastiani, P., Dworkis, D. A., Feldman, L., & Perls, T. T. (2012). Health span approximates life span among many supercentenarians: Compression of morbidity at the approximate limit of life span. *Journals of Gerontology, Series A: Biomedical Sciences and Medical Sciences*, 67(4), 395–405. doi:10.1093/gerona/glr223
- Barefoot, J. C., Grønbæk, M., Jensen, G., Schnohr, P., & Prescott, E. (2005). Social network diversity and risks of ischemic heart disease and total mortality: Findings from the Copenhagen City Heart Study. American Journal of Epidemiology, 161(10), 960– 967. doi:10.1093/aje/kwi128
- Barros, A. J. D., & Hirakata, V. N. (2003). Alternatives for logistic regression in cross-sectional studies: An empirical comparison of models that directly estimate the prevalence ratio. *BMC Medical Research Methodology*, 3(1), 21. doi:10.1186/1471-2288-3-21
- Berkman, L. F., Glass, T., Brissette, I., & Seeman, T. E. (2000). From social integration to health: Durkheim in the new millennium. Social Science & Medicine, 51(6), 843–857. doi:10.1016/ s0277-9536(00)00065-4

- Brandts, L., & van den Brandt, P. A. (2018). Sex-specific associations between smoking habits and reaching longevity: Netherlands Cohort Study. *Geriatrics & Gerontology International*, 18(8), 1249–1258. doi:10.1111/ggi.13468
- Brandts, L., & van den Brandt, P. A. (2019). Body size, nonoccupational physical activity and the chance of reaching longevity in men and women: Findings from the Netherlands Cohort Study. *Journal of Epidemiology and Community Health*, 73(3), 239–249. doi:10.1136/jech-2018-211410
- Breslow, N. (1974). Covariance analysis of censored survival data. *Biometrics*, **30**(1), 89–99.
- de Jong-Gierveld, J. (1989). Personal relationships, social support, and loneliness. *Journal of Social and Personal Relationships*, 6(2), 197-221.
- de Jong Gierveld, J. (1998). A review of loneliness: Concept and definitions, determinants and consequences. *Reviews in Clinical Gerontology*, 8(1), 73–80.
- de Jong-Gierveld, J., & Kamphuls, F. (1985). The development of a Rasch-type loneliness scale. *Applied Psychological Measurement*, 9(3), 289–299.
- de Jong-Gierveld, J., van Tilburg, T. G., & Dykstra, P. A. (2018). New ways of theorizing and conducting research in the field of loneliness and social isolation. In A. L. Vangelisti & D. Perlman (Eds.), *The Cambridge handbook of personal relationships* (pp. 391–404). Cambridge University Press.
- Dykstra, P. A., van Tilburg, T. G., & Gierveld, J. D. J. (2005). Changes in older adult loneliness: Results from a seven-year longitudinal study. *Research on Aging*, 27(6), 725–747. doi:10.1177/0164027505279712
- Edjolo, A., Helmer, C., Barberger-Gateau, P., Dartigues, J. F., Maubaret, C., & Pérès, K. (2013). Becoming a nonagenarian: Factors associated with survival up to 90 years old in 70+ men and women. Results from the PAQUID longitudinal cohort. *The Journal of Nutrition, Health & Aging*, 17(10), 881–892. doi:10.1007/s12603-013-0041-8
- Ellwardt, L., van Tilburg, T., Aartsen, M., Wittek, R., & Steverink, N. (2015). Personal networks and mortality risk in older adults: A twenty-year longitudinal study. *PLoS One*, 10(3), e0116731. doi:10.1371/journal.pone.0116731
- 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. doi:10.1007/ s12160-010-9210-8
- Hawkley, L. C., Thisted, R. A., & Cacioppo, J. T. (2009). Loneliness predicts reduced physical activity: Cross-sectional & longitudinal analyses. *Health Psychology*, 28(3), 354. doi:10.1037/ a0014400
- Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality: A meta-analytic review. *Perspectives on Psychological Science*, 10(2), 227–237. doi: 10.1177/1745691614568352
- Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: a meta-analytic review. *PLoS Medicine*, 7(7), e1000316. doi:10.1371/journal.pmed.100316
- Holwerda, T. J., Van Tilburg, T. G., Deeg, D. J. H., Schutter, N., Van, R., Dekker, J., Stek, M. L., Beekman, A. T., & Schoevers, R. A. (2016). Impact of loneliness and depression on mortality:

Results from the longitudinal ageing study Amsterdam. *The British Journal of Psychiatry*, 209(2), 127–134. doi:10.1192/bjp.bp.115.168005

- Huisman, M., Poppelaars, J., van der Horst, M., Beekman, A. T., Brug, J., van Tilburg, T. G, & Deeg, D. J. (2011). Cohort profile: The longitudinal aging study Amsterdam. *International Journal* of Epidemiology, 40(4), 868–876. doi:10.1093/ije/dyq219
- Kharicha, K., Manthorpe, J., Iliffe, S., Chew-Graham, C. A., Cattan, M., Goodman, C., Kirby-Barr, M., Whitehouse, J. H., & Walters, K. (2020). Managing loneliness: A qualitative study of older people's views. *Aging & Mental Health*, 1–8. doi:10.1080/ 13607863.2020.1729337
- Lauder, W., Mummery, K., Jones, M., & Caperchione, C. (2006). A comparison of health behaviours in lonely and non-lonely populations. *Psychology, Health & Medicine*, 11(2), 233– 245. doi:10.1080/13548500500266607
- Lee, L. O., James, P., Zevon, E. S., Kim, E. S., Trudel-Fitzgerald, C., Spiro, A., III, Grodstein, F., & Kubzansky, L. D. (2019). Optimism is associated with exceptional longevity in 2 epidemiologic cohorts of men and women. *Proceedings of the National Academy* of Sciences of the United States of America, 116(37), 18357– 18362. doi:10.1073/pnas.1900712116
- Luhmann, M., & Hawkley, L. C. (2016). Age differences in loneliness from late adolescence to oldest old age. *Developmental Psychology*, 52(6), 943. doi:10.1037/dev0000117
- McDonald, R. B., & Ruhe, R. C. (2011). Aging and longevity: Why knowing the difference is important to nutrition research. *Nutrients*, 3(3), 274–282. doi:10.3390/nu3030274
- Nijem, K., Kristensen, P., Al-Khatib, A., & Bjertness, E. (2005). Application of different statistical methods to estimate relative risk for self-reported health complaints among shoe factory workers exposed to organic solvents and plastic compounds. *Norsk Epidemiologi*, 15(1). doi:10.5324/nje.v15i1.233
- Pinquart, M., & Sorensen, S. (2001). Influences on loneliness in older adults: A meta-analysis. *Basic and Applied Social Psychology*, 23(4), 245–266. doi:10.1207/153248301753225702
- Rantanen, T., Masaki, K., He, Q., Ross, G. W., Willcox, B. J., & White, L. (2012). Midlife muscle strength and human longevity up to age 100 years: A 44-year prospective study among a decedent cohort. Age (Dordrecht, Netherlands), 34(3), 563–570. doi:10.1007/s11357-011-9256-y
- Revelas, M., Thalamuthu, A., Oldmeadow, C., Evans, T-J., Armstrong, N. J, Kwok, J. B, Brodaty, H., Schofield, P. R., Scott, R. J., Sachdev, P. S., Attia, J. R., & Mather, K. A. (2018). Review and meta-analysis of genetic polymorphisms associated with exceptional human longevity. *Mechanisms of Ageing and Development*, 175, 24–34. doi:10.1016/j.mad.2018.06.002
- Rico-Uribe, L. A., Caballero, F. F., Martín-María, N., Cabello, M., Ayuso-Mateos, J. L., & Miret, M. (2018). Association of

loneliness with all-cause mortality: A meta-analysis. *PLoS One*, 13(1), e0190033. doi:10.1371/journal.pone.0190033

- Rokach, A. (2018). Effective coping with loneliness: A review. Open Journal of Depression, 7(4), 61–72. doi:10.4236/ojd.2018.74005
- Rokach, A., Orzeck, T., & Neto, F. (2004). Coping with loneliness in old age: A cross-cultural comparison. *Current Psychology*, 23(2), 124. doi:10.1007/BF02903073
- Rothman, K. J. (1976). Causes. American Journal of Epidemiology, 104(6), 587–592. doi:10.1093/oxfordjournals.aje.a112335
- Rothman, K. J., & Greenland, S. (2005). Causation and causal inference in epidemiology. *American Journal of Public Health*, 95(Suppl. 1), S144–S150. doi:10.2105/AJPH.2004.059204
- Rothman, K. J., Greenland, S., & Lash, T. L. (2008). Modern epidemiology. Lippincott Williams & Wilkins.
- Salaris, L. (2015). Differential mortality in a long-living community in Sardinia (Italy): A cohort analysis. *Journal of Biosocial Science*, 47(4), 521–535. doi:10.1017/S0021932014000224
- Shaw, B. A., Krause, N., Liang, J., & Bennett, J. (2007). Tracking changes in social relations throughout late life. *The Journals* of Gerontology, Series B: Psychological Sciences and Social Sciences, 62(2), S90–S99. doi:10.1093/geronb/62.2.s90
- Trudel-Fitzgerald, C., Zevon, E. S., Kawachi, I., Tucker-Seeley, R. D., Grodstein, F., & Kubzansky, L. D. (2019). The prospective association of social integration with lifespan and exceptional longevity in women. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, 75(10), 2132–2141. doi:10.1093/geronb/gbz116
- U.S. Department of Health and Human Services. (2001). Report of the National Institute on Aging Advisory Panel on Exceptional Longevity (APEL) (Public Health Service, National Institute of Health & National Institute on Aging, Trans.) (pp. 47).
- van Tilburg, T. G., & de Jong, G. J. (1999). [Reference standards for the loneliness scale]. *Tijdschrift voor Gerontologie en Geriatrie*, 30(4), 158–163.
- van Tilburg, T. G., & Leeuw, E. (1991). Stability of scale quality under various data collection procedures: A mode comparison on the 'De Jong-Gierveld loneliness scale. *International Journal of Public Opinion Research*, 3(1), 69–85. doi:10.1093/ ijpor/3.1.69
- Wilhelmsen, L., Svärdsudd, K., Eriksson, H., Rosengren, A., Hansson, P. O., Welin, C., Odén, A., & Welin, L. (2011). Factors associated with reaching 90 years of age: A study of men born in 1913 in Gothenburg, Sweden. *Journal of Internal Medicine*, 269(4), 441–451. doi:10.1111/j.1365-2796.2010.02331.x
- Yates, L. B., Djoussé, L., Kurth, T., Buring, J. E., & Gaziano, J. M. (2008). Exceptional longevity in men: Modifiable factors associated with survival and function to age 90 years. *Archives of Internal Medicine*, 168(3), 284–290. doi:10.1001/ archinternmed.2007.77