

Sociodemographic heterogeneity in the association between social isolation and all-cause mortality among Japanese older adults: JAGES longitudinal panel study



Frances Rom Lunar,^a Naoki Kondo,^{a,*} Yukiko Honda,^a Atsushi Nakagomi,^b Toshiaki Komura,^c Kosuke Inoue,^{a,d} and Koichiro Shiba^e

^aDepartment of Social Epidemiology, Graduate School of Medicine and School of Public Health, Kyoto University, Kyoto, Japan

^bDepartment of Social Preventive Medical Sciences, Center for Preventive Medical Sciences, Chiba University, Chiba, Japan

^cDepartment of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA, USA

^dHakubi Center, Kyoto University, Kyoto, Japan

^eDepartment of Epidemiology, Boston University School of Public Health, Boston, MA, USA



Summary

Background Social isolation has been linked to higher mortality; however, it remains unknown how this association varies across individuals and social groups.

Methods We used a nationwide cohort study of ~20,000 older adults with a 9.4-year follow-up period (Japan Gerontological Evaluation Study, 2013–2022), adjusting for 60 pre-baseline covariates. We also used a national insurance database to ascertain 4299 all-cause deaths. Using a causal machine-learning method, we estimated the heterogeneous association between social isolation and mortality.

Findings Social isolation was more prevalent among those with lower education and income and associated on average with 69.5-day shorter survival time (restricted mean survival time [RMST] difference; 95% CI: –111, –28.4). There was evidence of heterogeneity where social isolation was associated with even shorter survival days in some subgroups (e.g., –205 days among the bottom quintile of the estimated RMST differences [95% CI: –321, –87.8]). These subgroups tended to be older, men, and have lower education. The adverse association of social isolation and mortality was particularly stronger when lower education was combined with higher income, especially among women. Individuals with lower levels of education accounted for a larger share of deaths attributable to social isolation (58.5% of excess deaths).

Interpretation Social isolation may be more harmful among those from socially disadvantaged backgrounds, and a combination of some characteristics can synergistically amplify its effects on mortality. Proper population-level interventions informed with the evidence of effect heterogeneity might not only improve health on average but also mitigate existing health disparities.

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Introduction

Social isolation, or “the objective state of having a small network of kin and non-kin relationships and thus few

or infrequent interactions with others,” is an urgent public health concern among older adults.¹ It is experienced by approximately 25.0% of community-

*Corresponding author. School of Public Health, Kyoto University, Floor 2, Science Frontier Laboratory, Yoshida-konoe-cho, Sakyo-ku, Kyoto-shi, Kyoto, 606-8315, Japan.

E-mail address: kondo.naoki.0s@kyoto-u.ac.jp (N. Kondo).

Research in context

Evidence before this study

We searched PubMed for English observational and review studies published from inception up to June 30, 2025, using a combination of terms such as: "Social Isolation" [Mesh], social networks, social relations, social integration, "Mortality" [Mesh], all-cause mortality, "Aged" [Mesh], older adult, and elderly. Based on a systematic review of studies published until October 2022, the association between social isolation association and mortality only varied by country and not according to gender, follow-up time, education, depression, smoking, drinking, body mass index, ethnicity, chronic diseases, and assessment method of social isolation. One study published after this review found effect modification by population density and employment while another did not find a difference according to age, gender, education, and income. However, the evidence from these studies on the heterogeneous effects of social isolation on mortality is limited because they examined only a narrow set of potential effect modifiers and used analytic approaches that considered those modifiers individually rather than estimating synergistic interactions arising from multiple effect modifiers simultaneously.

Added value of this study

To overcome these limitations, we used a novel causal machine-learning approach that estimated how the

association between social isolation and all-cause mortality varied across the values of a high-dimensional set of effect modifiers. After categorizing our sample into quintiles of the estimated conditional average effect of social isolation, we found that the subgroup most vulnerable to the adverse effects of social isolation were more likely to be older, men, with fewer school years, retired or never had a job, smokers, people who did not participate in annual physical examinations, and socially isolated pre-baseline. Moreover, we found that the combination of low education and being in the middle- and high-income tertiles was associated with the greatest reduction in survival days due to social isolation, with this pattern being stronger among women. Lastly, our simulation showed that education- and income-based class disparities in survival would decrease if social isolation were eliminated.

Implications of all the available evidence

Social isolation may be associated with shorter survival time and this relationship is heterogeneous and varies across individuals. A combination of some social disadvantages could synergistically amplify the adverse effects of social isolation on mortality. Population-level interventions reducing social isolation would not only improve health on average but also mitigate existing health disparities.

dwelling older adults globally² and adversely affects health through increased risks of cardiovascular diseases, mental health problems, diabetes, limitations in activities of daily living, and worsened quality of life.¹

Social isolation and its link with all-cause mortality is well-supported, with the most recent meta-analysis reporting a 35% increased risk.³ The mechanisms underlying this relationship include: 1) lack of social supports, decreasing health-promoting behaviors (e.g., smoking cessation and physical activity) and access to healthcare, 2) increased psychological distress, and 3) biological changes.⁴

While population-average relationships are useful, it is also critical to assess how the effects of social isolation might differ across social groups (i.e., within-population effect heterogeneity). Such evidence can help identify individuals for whom social isolation may be more harmful and, hence, might need prioritization for interventions.⁵ It also informs whether population-level interventions that affect all members (e.g., policies) might disproportionately affect the health of some subgroups by reducing or increasing existing health disparities. For example, social isolation may be more health-damaging among individuals with low education as they tend to have limited resources to offset increased distress due to isolation. Moreover, socially marginalized and disadvantaged (e.g., lower education/

income) groups are more likely to experience social isolation. If population-level interventions reducing social isolation can disproportionately improve the health of these vulnerable individuals, class-based health disparities in the population might be mitigated.

The association between social isolation with all-cause mortality has been shown to differ by income, population density and employment status⁶ but not by age, gender, and education.⁷ A meta-analysis also found a statistically significant difference by country (i.e., US versus non-US) but no evidence of effect modification by education, depression, smoking, drinking, body mass index, ethnicity, chronic disease, follow-up duration, and social isolation measurement.⁸ While these provide promising preliminary evidence, two limitations remain unsolved. First, studies have considered only narrow sets of effect modifiers. Second, their analytic approaches (e.g., subgroup analysis or adding and an interaction term for a treatment and a modifier of interest) have not considered multiple effect modifiers simultaneously. A combination of multiple modifiers (e.g., gender*poverty*educational attainment) can interact with each other and alter the effects of social isolation synergistically.

Thus, this study aimed to comprehensively examine heterogeneous associations between social isolation and mortality using data from a cohort study of

Japanese older adults, identify subpopulations that experience a greater impact of social isolation on mortality, and determine how this could influence health disparities. To do this, we used a novel machine-learning-based approach that allowed flexible modeling of effect heterogeneity by high-dimensional effect modifiers,⁹ thereby overcoming the limitations of previous studies.

Methods

Data

We used data from the Japan Gerontological Evaluation Study (JAGES), a nationwide cohort of physically and cognitively independent community dwelling older adults (≥ 65 years old). We used the 2010 and 2013 waves containing data from 13 municipalities that could be linked to the mortality database. Of the participants enrolled in 2010 ($n = 68,564$), we included those who responded to both the 2010 ($n = 40,039$; response rate: 58.4%) and 2013 waves ($n = 27,143$; follow-up rate: 67.8%). After excluding those with incomplete social isolation data ($n = 7749$), our analytic sample consisted of 19,664 individuals ([Supplementary Figure S1](#)).

Exposure

Our main exposure was social isolation in 2013 (2013/10/01–2013/12/2). We created composite scores for social isolation (range: 0–3) by summing three criteria: 1) living alone, 2) less than monthly contact with friends, and 3) less than weekly participation in social activities (i.e., sports, hobbies, or volunteering). This measure of social isolation has been used previously.⁶ Individuals were classified as socially isolated if their score was two or three; otherwise, they were considered not socially isolated.

Outcome

All-cause mortality was quantified as time to deaths due to all causes. This was obtained from the National Long Term Insurance database—a registry with information on all-cause deaths. The completeness of death-linkage data ranged from 96.1–99.6% and the follow-up period was from the 2013 survey date to the administrative censoring (2022/11/01–2023/03/14) (maximum time: 3431 days, ~ 9.4 years; average time: 3019 days, ~ 8.27 years).

Covariates

We selected 60 pre-baseline covariates measured in 2010 (2010/8/10–2011/3/28) to ensure temporal order between the covariates and social isolation and avoid adjusting for potential mediators.¹⁰ These included demographics (age, gender, years of formal education, employment, income, pension type), health and well-being (body mass index [BMI], number of existing

conditions, health conditions [e.g., hypertension, diabetes mellitus, hyperlipidemia, heart disease, stroke, etc.], instrumental activities of daily living, ability to walk without stopping for about 15 min, depressive symptoms, life satisfaction, looking up phone numbers and making phone calls by themselves, forgetfulness, forgetting the date), health behaviors (smoking, alcohol, protein, fruit and vegetable consumption, walking, frequency of going out, annual physical examination), cognitive social capital (trust, reciprocity, attachment), and environmental characteristics ([Online Appendix 1](#)). These covariates were selected because they are likely to be confounders, effect modifiers, or both. Furthermore, we included pre-baseline social isolation from the 2010 wave status to mitigate the risk of reverse causality.¹⁰

Data analysis

First, we estimated the average treatment effect (ATE) of social isolation on all-cause mortality for the entire sample by computing for the restricted mean survival time (RMST) differences between those who were socially isolated and those who were not, adjusting for pre-baseline covariates. RMST differences can be interpreted as the difference in average time to death and negative values imply that social isolation was associated with shorter survival time. Using survival time differences might be useful for health policy development because it provides more intuitive interpretation in comparison with conventional effect measures for time-to-event data (e.g., hazard ratio as a ratio of instantaneous rate of event onsets conditional on survival to the prior time point).¹¹ For this analysis, we used the *rmst2* function of the *survRM2* package in RStudio (version 2025-05-1 + 513). Second, to examine heterogeneous effects, we estimated conditional average treatment effects (CATEs) of social isolation on all-cause mortality. In this study, CATEs refer to the average effect of social isolation on all-cause mortality among individuals with identical covariates. We used the causal survival forest method—an algorithm that estimates heterogeneous associations for a time-to-event outcome with right censoring.¹² The causal survival forest was built using the *causal_survival_forest* function of the *grf* 2.3.2 package in RStudio. We also used a technique called “honesty” to reduce the risk of overfitting.⁹ Within the causal survival forest algorithm, all 60 pre-baseline covariates were considered as confounders prior to building the survival forest through residualization. They were also accounted for when building the survival forest via sample splitting as potential sources of effect heterogeneity. The algorithm does not involve hypothesis testing and thus, no *p*-values were produced for the splits. Furthermore, CATE estimates were obtained as weighted averages across all trees and not only those who captured effect heterogeneity. We then evaluated how well the model captured heterogeneity using a calibration plot of

RMST differences according to five quintiles determined by ranking CATEs. Additional details and the code of our causal survival forest analysis is provided in [Online Appendix 2](#). Third, to assess social patterning in effect heterogeneity, we compared the two most extreme tails of the quintiles. The first quintile (Q1) was labeled as the “high impact” group because their estimated CATEs were the furthest from the null (i.e., social isolation was associated with even shorter survival time compared to other quintiles). On the other hand, the fifth quintile (Q5) was labeled as the “low impact” group because their estimated CATEs were close to the null or even in the opposite direction (i.e. social isolation has no effect or was associated with slightly longer survival time). To account for multiple comparisons, we used the Benjamini-Hochberg approach¹³ to update p-values for the comparison of pre-baseline characteristics between the high-impact versus low-impact groups. Fourth, to assess differential patterns in effect heterogeneity by the direction of change in the exposure (i.e., becoming isolated/ceasing to be isolated), we stratified the comparison of quintiles by social isolation at the pre-baseline. We also assessed patterns in effect heterogeneity through a heatmap showing estimated CATE means by combinations of years of education, standardized income tertiles, and gender. These covariates were chosen as they capture aspects of socioeconomic status and social stratification in a Japanese population.¹⁴

We then simulated how eliminating social isolation in the population might change education- and income-based disparities in mortality by: 1) estimating observed class-based disparities (i.e., RMST differences across categories of education and income), 2) predicting counterfactual levels of disparities had social isolation been eliminated based on their estimated CATEs, and 3) estimating change in disparities comparing the observed versus counterfactual scenarios. We used the most advantaged category for education (13 years or more) and income (highest tertile) as the reference for estimating disparities. Finally, we examined the population-level impact of social isolation using the Population Attributable Fraction (PAF). PAF captures the fraction of deaths attributable to social isolation and was calculated via Levin’s formula:

$$PAF = \frac{Pe \times (RR - 1)}{Pe \times (RR - 1) + 1}$$

where RR corresponds to the risk ratio for the association between social isolation and mortality from Modified Poisson Regression, and Pe corresponds to the prevalence of social isolation. We estimated PAF by levels of education and income. We then applied these estimated PAFs to the 2013–2022 full JAGES cohort data (n = 52,320) and determined the distribution of education and income groups among deaths

attributable and not attributable to social isolation. Details of these analyses are provided in [Online Appendix 3](#).

Imputation of missing covariate values was done using *missRanger* function from the *ranger* package in R, utilizing a random forest that used other variables as predictors.

Ethics approval

Nihon Fukushi University (application no. 10-05, July 27, 2010 and application no. 13–14, August 6, 2013).

Role of the funding source

The funders had no role in study design, collection, analysis, and interpretation of data, writing of the report, and the decision to submit the paper for publication.

Results

At pre-baseline, socially isolated individuals tended to be men (55% vs 46%), smokers (12% vs 8·7%), had lower years of education (nine or less years: 47·1% vs 39·9%), lower mean annual household income (22,860 USD vs 27,280 USD), lower self-rated health (poor/fair: 19·8% vs 13·4%), and less likely to participate in annual physical examination (34·9% vs 25·8%) ([Table 1](#) for selected characteristics and [Supplementary Table S1](#) for all characteristics). Within the follow-up period, 4299 (21·9%) individuals died. Proportions of missing data were generally low (<10%) except for pre-baseline social isolation status (20%) and missingness rates were comparable between exposed and unexposed groups ([Supplementary Table S2](#)). While pre-baseline characteristics between all participants in 2010 (n = 40,039) and the analytic sample (n = 19,664) were mostly comparably distributed (one to five percentage points difference), excluded individuals due to loss-to-follow-up and lack of social isolation data (n = 20,375) tended to have lower socioeconomic backgrounds (education/income), and poorer baseline health (e.g., increased depressive symptoms and chronic conditions) ([Supplementary Table S3](#)).

The ATE indicated social isolation was associated with 69·5 days shorter survival time (95% CI for RMST difference: –111 to –28·4) ([Fig. 1A](#)). Around this ATE, estimated CATEs were widely distributed (mean: –55·4; minimum/maximum: –387/140; median: –49·0; SD: 65·8) ([Supplementary Table S4](#)). Rank-specific RMST differences implied good fit of our causal survival forest model, showing a monotonic increase ([Fig. 1B](#)). The high impact group showed the greatest reduction in survival time associated with social isolation (RMST difference = –204·7; 95% CI: –321·5 to –87·8) and this association attenuated with increasing CATE quintiles (e.g., RMST difference for the low impact group = 59·8; 95% CI: –5·8 to 125·4) ([Supplementary Table S4](#)).

Compared to the low impact group, the high impact group tended to be older (mean [SD]: 78.0 [6.03] vs 70.1 [3.70]), men (65% vs 44%), with fewer school years (nine or less years: 47.1% vs 40.9%), retired/never had a job (85% vs 74%), current smokers (13% vs 7.2%), do not participate in annual physical examinations (33.8% vs 27.9%), and socially isolated in 2010 (32% vs 21%) (Table 2). This group was also characterized by lower BMI, functional independence, self-rated health, and depressive symptoms. Supplementary Table S5 shows all the covariate characteristics across all quintiles. After stratifying by social isolation at pre-baseline, we observed similar patterns (Supplementary Table S6).

Mean CATEs based on combinations of education, income, and gender were overall the greatest in the lowest education subgroup (less than six years) (−88 to −125). This education-based gradient in the estimated CATEs was particularly salient when low education was coupled with middle ($n = 67$) and highest ($n = 55$) income tertiles (range: −115 to −125). This trend appeared stronger among women (lowest education + highest income tertile in men: −115 vs women: −125) (Supplementary Figure S2).

The magnitude of education- and income-based disparities in mortality under the observed and counterfactual scenarios suggested class-based disparities except for ten to 12 years of education (Fig. 2). All class-based disparities in mortality decreased under the counterfactual scenario (e.g., change in RMST difference: less than six vs ≥ 13 years of education = 37.32 [95% CI: 26.1, 49.0], lowest vs highest income tertile: 8.66 [95% CI: 6.94, 10.3]. Moreover, more survival days were gained in the counterfactual scenario among the more disadvantaged subgroups (lowest education: +56 days; lowest income: +25 days) (Supplementary Figure S3). PAF calculation showed that a larger proportion of deaths attributable to social isolation came from the lower levels of education ($\leq$ nine years: 58.5%). On the other hand, middle- and highest-income subgroups comprised a larger percentage of deaths attributable to social isolation (77.1%) (Fig. 3).

Discussion

In this nationwide 9-year cohort study of older adults in Japan, we examined the heterogeneous impacts of social isolation on mortality. There are three key findings. First, social isolation appeared more harmful to individuals who were older, men, and had lower education, with a 265-day difference on the impact of social isolation on survival time between the high and low impact subgroups. Second, the adverse association of social isolation appeared particularly strong when lower education was combined with higher income, especially among women by around twice compared to men with high education and high income. Third, our simulation showed that eliminating social isolation in the

	Overall, $n = 19,664^a$	Social isolation status in 2013	
		Not socially isolated, $n = 13,964^a$	Socially isolated, $n = 5700^a$
Demographic characteristics			
Age	72 (5)	72 (5)	73 (6)
Gender			
Men	9617 (49%)	6480 (46%)	3137 (55%)
Women	10,047 (51%)	7484 (54%)	2563 (45%)
Years of formal education			
Less than 6 years	250 (1.3%)	128 (0.9%)	122 (2.1%)
6–9 years	7979 (41%)	5441 (39%)	2538 (45%)
10–12 years	7647 (39%)	5658 (41%)	1989 (35%)
13 years or more	3788 (19%)	2737 (20%)	1051 (18%)
Pretax household income (USD)	26,000 (16,690)	27,280 (16,905)	22,860 (15,720)
Standardized household income^b	0.00 (1.00)	0.08 (1.01)	−0.19 (0.94)
Employment status			
I have a paid job	4340 (22%)	3120 (22%)	1220 (21%)
I am retired from my job	13,099 (67%)	9288 (67%)	3811 (67%)
I have never had a job	2225 (11%)	1556 (11%)	669 (12%)
Pre-baseline social isolation			
Socially isolated in 2010	4920 (25%)	1359 (9.7%)	3561 (62%)
Health and wellbeing			
Body Mass Index	23.04 (2.98)	23.08 (2.92)	22.95 (3.14)
Self-rated health			
Excellent	2513 (13%)	1954 (14%)	559 (9.8%)
Good	14,173 (72%)	10,183 (73%)	3990 (70%)
Fair	2626 (13%)	1632 (12%)	994 (17%)
Poor	352 (1.8%)	195 (1.4%)	157 (2.8%)
Number of existing medical conditions	1.46 (1.40)	1.41 (1.34)	1.59 (1.55)
IADL total score	11.79 (1.66)	12.07 (1.40)	11.10 (2.01)
GDS total score	3.14 (2.98)	2.77 (2.74)	4.06 (3.31)
Health behaviors			
Smoking status			
I have never smoked	11,901 (61%)	8744 (63%)	3157 (55%)
I stopped smoking 5 or more years ago	4953 (25%)	3422 (25%)	1531 (27%)
I stopped smoking within the past 4 years	896 (4.6%)	583 (4.2%)	313 (5.5%)
I am currently a smoker	1914 (9.7%)	1215 (8.7%)	699 (12%)
Alcohol consumption			
Yes	7874 (40%)	5652 (40%)	2222 (39%)
I used to drink	573 (2.9%)	365 (2.6%)	208 (3.6%)
No	11,217 (57%)	7947 (57%)	3270 (57%)
Recent physical examination			
I had one within a year	14,051 (71%)	10,362 (74%)	3689 (65%)
I had one within 2–3 years	1900 (9.7%)	1321 (9.5%)	579 (10%)
I had one more than 4 years ago	1555 (7.9%)	991 (7.1%)	564 (9.9%)
I've never had one	2158 (11%)	1290 (9.2%)	868 (15%)

IADL: Instrumental Activities of Daily Living; GDS: Geriatric Depression Scale. ^aMean (SD) for continuous variables; n (%) for categorical/binary variables. ^bStandardized income was computed using the formula: (household income—mean household income/standard deviation).

Table 1: Pre-baseline characteristics of the analytic sample in 2010.

population might decrease education- and income-related health disparities in survival by as much as 37 days on average. Moreover, 58.5% of excess deaths due to social isolation came from lower education subgroups.

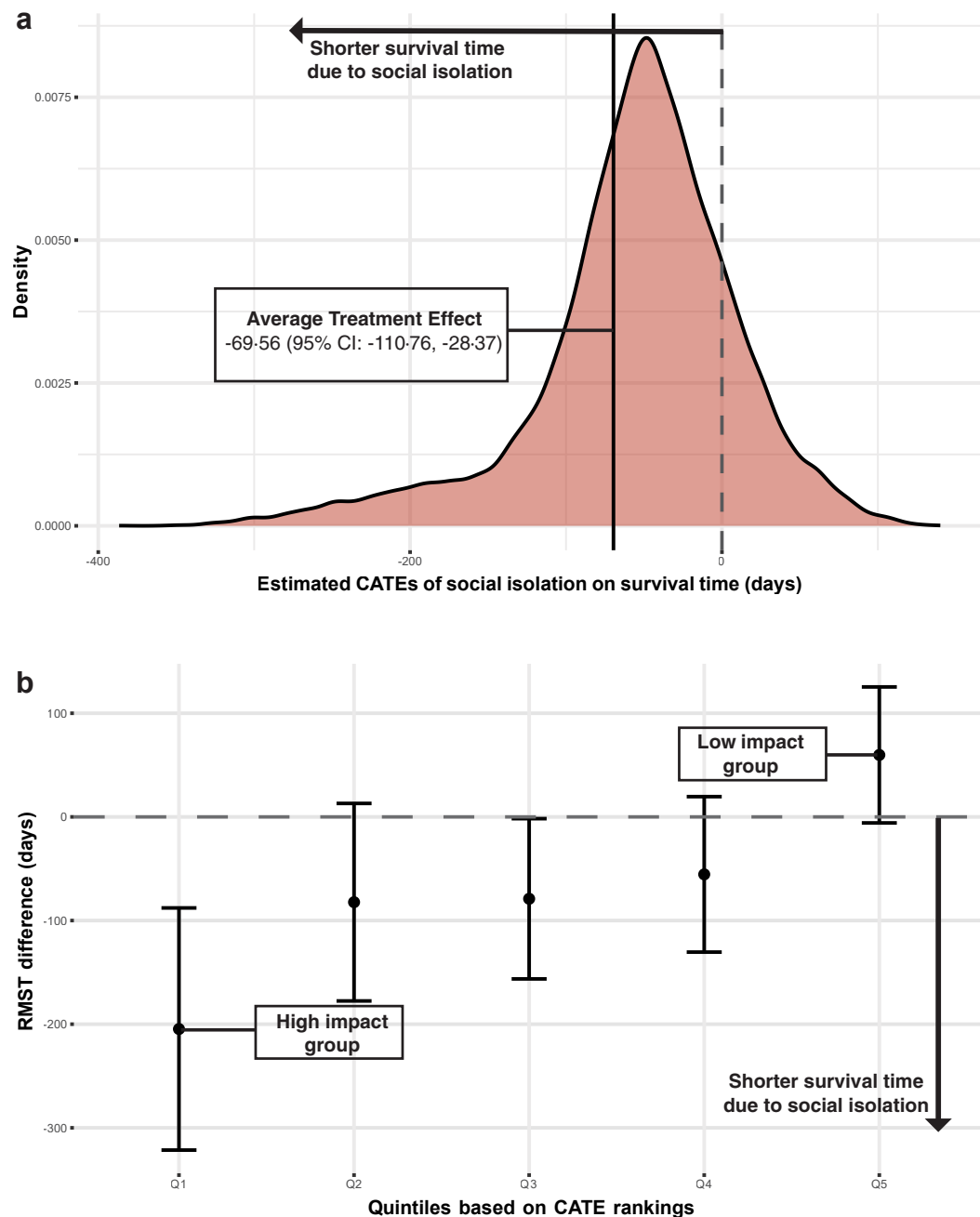


Fig. 1: (a) Estimated conditional average treatment effects of social isolation on survival times (days) by subgroups identified through the causal survival forest, and (b) Calibration plot showing the restricted survival time difference (i.e. average effect of social isolation) by CATE-based quintiles. CATE: Conditional Average Treatment Effects; RMST: Restricted Mean Survival Time. For both figures, the dashed line indicates the null where social isolation has no effect on survival time.

To our knowledge, this is the first study that: 1) examined the heterogeneity in the association of social isolation and mortality inductively using machine learning, and 2) determined the magnitude of this heterogeneity in terms of survival time. Furthermore, our study presented evidence of effect modification

according to age, gender, and education in contrast with previous studies.^{6–8} By using a rich set of covariates, we also showed that this association additionally varied according to factors such as employment, health behaviors and prior social isolation. Thus, we have expanded what is currently known in this area by

	Q1 (High impact) n = 3,940 ^a	Q5 (Low impact) n = 3,934 ^a	p-value ^b
Estimated average treatment effect for the quintile group^c	-204.67 (-321.50, -87.84)	59.78 (-5.82, 125.39)	<0.001***
Demographic characteristics			
Age at 2010	77.96 (6.03)	70.13 (3.70)	<0.001***
Gender			<0.001***
Men	2561 (65%)	1721 (44%)	
Women	1374 (35%)	2214 (56%)	
Years of formal education			<0.001***
Less than 6 years	122 (3.1%)	35 (0.9%)	
6–9 years	1712 (44%)	1577 (40%)	
10–12 years	1404 (36%)	1525 (39%)	
13 years or more	697 (18%)	798 (20%)	
Standardized household income for 2009 ^d	0.08 (1.05)	0.09 (1.06)	0.97
Employment status			<0.001***
I have a paid job	617 (16%)	1012 (26%)	
I am retired from my job	2743 (70%)	2493 (63%)	
I have never had a job	575 (15%)	430 (11%)	
Pre-baseline social isolation			
Socially isolated in 2010			<0.001***
No	2659 (68%)	3109 (79%)	
Yes	1276 (32%)	826 (21%)	
Health and wellbeing			
Body Mass Index	21.48 (2.27)	26.47 (2.53)	<0.001***
Self-rated health			<0.001***
Excellent	392 (10%)	544 (14%)	
Good	2779 (71%)	2911 (74%)	
Fair	657 (17%)	434 (11%)	
Poor	107 (2.7%)	46 (1.2%)	
Number of existing medical conditions	1.66 (1.55)	1.56 (1.36)	0.13
IADL total score	11.18 (2.11)	12.21 (1.16)	<0.001***
GDS total score	3.41 (2.95)	2.47 (2.56)	<0.001***
Health behaviors			
Smoking status			<0.001***
I have never smoked	1848 (47%)	2581 (66%)	
I stopped smoking 5 or more years ago	1320 (34%)	915 (23%)	
I stopped smoking within the past 4 years	255 (6.5%)	157 (4.0%)	
I am currently a smoker	512 (13%)	282 (7.2%)	
Alcohol consumption			<0.001***
Yes	1650 (42%)	1564 (40%)	
I used to drink	177 (4.5%)	90 (2.3%)	
No	2108 (54%)	2281 (58%)	
Recent physical examination			<0.001***
I had one within a year	2622 (67%)	2836 (72%)	
I had one within 2–3 years	386 (9.8%)	386 (9.8%)	
I had one more than 4 years ago	418 (11%)	280 (7.1%)	
I've never had one	509 (13%)	433 (11%)	

IADL: Instrumental Activities of Daily Living; GDS: Geriatric Depression Scale; CATE: Conditional Average Treatment Effects. We estimated conditional average treatment effects (CATEs) of social isolation on all-cause mortality using the causal survival forest algorithm. We estimated restricted mean survival time differences conditional on the pre-baseline covariates as CATEs. The first quantile (Q1) was determined as the “high impact” group because their estimated CATEs were the furthest away from the null value (i.e., social isolation was associated with even shorter survival time in this group compared to other quintile groups). On the other hand, the fifth quantile (Q5) was labeled as the “low impact” group because their estimated CATEs were close to the null or even in the opposite direction (i.e. social isolation has no effect or was associated with slightly longer survival time). ^aMean (SD/95% CI); n (%). ^bp < 0.05; **p < 0.01; ***p < 0.001, we accounted for multiple comparisons using the Benjamini-Hochberg correction. ^cEstimated as a difference in restricted mean survival times. ^dStandardized income was computed using the formula: (household income – mean household income)/standard deviation.

Table 2: The average treatment effect of social isolation on all-cause mortality and pre-baseline characteristics of the high impact (quintile 1) versus low impact (quintile 5) groups.

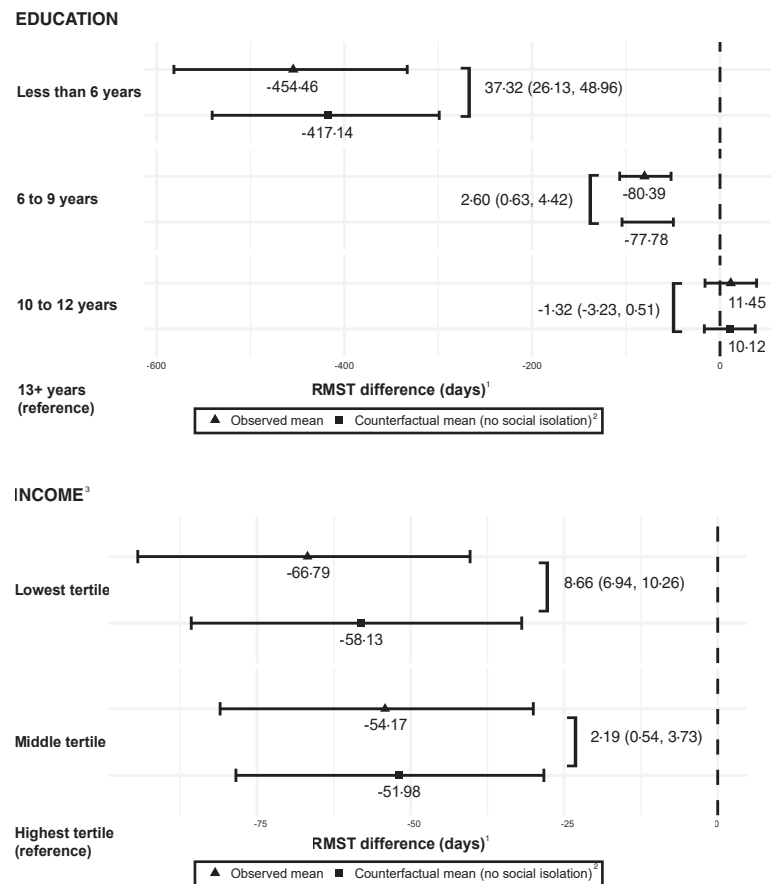


Fig. 2: Simulated changes in survival time according to education and income when removing social isolation. RMST: Restricted Mean Survival Time. ¹We used RMST difference between each education/income category and the reference category (13+ years of education and highest income tertile) to represent disparity in survival time. A change in this RMST difference towards zero implies reduced disparity. ²The counterfactual represents the magnitude of disparity in survival time that would have been observed had a hypothetical intervention eliminated social isolation in the population. This was computed by subtracting the conditional average treatment effects from the observed RMST if the individual was socially isolated at baseline. ³Income tertiles (lowest, middle, highest) were determined by sorting the standardized household income and assigning tertiles based on ranking.

identifying sources of heterogeneity that have been previously missed.

Regarding the combined effect of low education with higher income, while higher income is generally protective, this counterintuitive trend has also been reported previously in the association between disaster-related home loss and functional limitations.¹⁵ The discordance between educational attainment and income may magnify the adverse effects of social isolation on health. Such discrepancies between the position a person holds in one social domain comparative to another, referred to as status inconsistency, may lead to frustration and increased stress.^{16,17} This concept has been linked with lower mental and self-rated health as well as increased risk of stroke and heart disease.¹⁸ Also, higher income may backfire among those with lower education and lead to increased use of unhealthy coping

methods (e.g., alcohol). Moreover, because people with high income tend to have rich social networks, lacking connections may be especially stressful due to social comparisons with well-connected peers or their previous status. Furthermore, the greater vulnerability of those with high income and low education was more salient among women. This may be explained by their higher likelihood to engage in harmful behaviors and coping strategies.¹⁹ Moreover, societal expectations for Japanese women to adhere to traditional roles may have limited their ability to change their social circumstances.²⁰ However, these are all speculative, and future research is warranted to understand underlying mechanisms.

Our simulation also showed that eliminating social isolation among Japanese older adults might decrease education- and income-related health disparities in



Fig. 3: Distribution of education and income groups among deaths attributable and not attributable to social isolation. Note: We calculated for the distribution of education and income subgroups (in percentages) within each type of death (attributable and not attributable to social isolation).

survival. In our study, socially isolated individuals were likely to have lower education and income. Furthermore, our PAF analysis found evidence of more harmful effects of social isolation among those with lower education, with more deaths attributable to social isolation coming from these subgroups. In contrast, the higher proportion of deaths attributable to social isolation coming from higher income subgroups does not necessarily mean resilience of lower income subgroups to mortality risks due to social isolation, as our causal survival forest showed that income did not differ between the low-impact versus high-impact groups. Rather, because low-income groups are more vulnerable to other risk factors for mortality such as smoking,²¹ they may have died due to these other risk factors before experiencing the effects of social isolation. Future research may confirm this. Furthermore, it is still worthwhile to address social isolation in these subgroups as our simulation revealed that they may experience the greatest benefit in terms of survival time upon elimination of social isolation. To further illustrate, a study using JAGES found around 19,000 annual older adult deaths due to social isolation.²² Extrapolating this to our PAF results, addressing social isolation is estimated to save around 11,000 Japanese older adults from lower education subgroups annually.

Our study has some limitations. While we adjusted for 60 pre-baseline characteristics, residual confounding due to unmeasured factors is still possible due to our observational design. For example, the JAGES 2010 wave lacked information on personality traits, genetic predispositions as well as physical activity data. These are known risk factors of mortality and/or predictors of social isolation^{23–25}; which may have confounded the association between social isolation and mortality. We also could not consider the impact of wealth beyond annual income due to data unavailability. Disasters such as the Great East Japan Earthquake (2011) and the COVID-19 pandemic (2020) may have also influenced our data. For example, although the majority of our participants (85.72%) were not from the site directly affected by the earthquake (Iwanuma City), it may have altered pre-baseline covariate values after the 2010 data collection, leading to residual confounding. The earthquake may have also increased baseline social isolation. Similarly, the pandemic and resulting social distancing regulations may have increased social isolation among those who were not socially isolated at baseline. These changes in the exposure over time would lead to underestimation of the effects of baseline social isolation.²⁶ Moreover, considering the characteristics of excluded participants, there might have been a selective attrition of susceptible individuals, leading to selection bias that potentially underestimated the effects of baseline social isolation as well. Future studies might consider these in their analyses. Our results are also unable to determine

which pre-baseline characteristics should be intervened on to mitigate the effects of social isolation as these were included in the analysis mainly to adjust for confounding between social isolation and mortality and not between each modifier and the outcome. Furthermore, we imputed missing data, which may be inaccurate and induce some biases. While multiple imputation is a common approach to address these issues, the random forest approach we employed is computationally more efficient and has been shown in simulation studies to have reasonable performance.²⁷ Considering the mean age of our sample (72 ± 5), our follow-up (~8 years) may have also been insufficient to incur sufficient death events. Also, our data came from 13 municipalities that participated in JAGES, which may not represent the whole Japanese older adult population. Finally, our results are specific to Japanese older adults. Future studies should use data from different populations and investigate how the patterns we have identified might differ.

Our results serve as a good starting point in understanding which subpopulations are at a higher risk of experiencing social isolation and more vulnerable to the adverse effect of social isolation. Public health interventions may consider removing barriers to social connections among individuals from socially disadvantaged backgrounds (e.g., lower education/income). For example, Ide and colleagues reported that participating in community gathering places was longitudinally associated with improved social connectedness among older adults in Japan, such as more frequent social participation and volunteering.²⁸ Such public spaces can act as social hubs that are accessible regardless of social class and improve social connectedness particularly among those who lack personal resources to establish social ties.²⁹ Moreover, a recent systematic review of social isolation interventions among older adults emphasized the need to use a person-centered approach.³⁰ Therefore, future research should focus on clarifying the effects of a wide range of interventions that allow tailor-fitting.

Contributors

Conceptualization: NK, KS.

Data curation: FRL, KS.

Formal analysis and visualization: FRL, NK, AN, TK, KI, KS.

Analysis validation: FRL, NK, KS.

Writing (original draft): KS, FRL.

Writing (review and editing): FRL, NK, YH, AN, TK, KI, KS.

Supervision: NK, YH, KS.

All authors had access to the data, have read and approved the final version of the manuscript, and accept responsibility for the submission.

Data sharing statement

The dataset supporting the conclusions of the article is available upon request to the JAGES committee. Details of how to access the Japan Gerontological Evaluation Study data is available at <https://www.jages.net>. JAGES datasets have ethical or legal restrictions for public distribution due to inclusion of sensitive information from human

participants. The code for the heterogeneous treatment effects analysis is provided in the supplementary. The rest of the codes used for analyses are available upon request.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lanwpc.2025.101691>.

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