Supplemental Online Content

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eAppendix 1. Supplementary Data

eAppendix 2. R Scripts and STATA Do File

eFigure 1. Odds Ratios of Social Isolation for All-Cause Mortality, Cardiovascular Diseases Mortality, and Neoplasms Mortality Among Older People in Japan

eFigure 2. Odds Ratios of Social Isolation for All-Cause Mortality Over Levels of Age at Baseline

eFigure 3. Odds Ratios of Social Isolation for Cardiovascular Diseases Mortality Over Levels of Age at Baseline

eFigure 4. Odds Ratios of Social Isolation for Neoplasms Mortality Over Levels of Age at Baseline

eFigure 5. Odds Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators: Using Population Density That Excluded Nondeveloped Areas (eg, Rivers, Lakes, Forests, and Wasteland) as Well as Nonresidential Land (Such as Farms and Industrial Districts)

eFigure 6. Odds Ratios of Social Isolation for Cardiovascular Diseases Mortality Within All Participants and Subgroups of Moderators: Using Population Density That Excluded Nondeveloped Areas (eg, Rivers, Lakes, Forests, and Wasteland) as Well as Nonresidential Land (Such as Farms and Industrial Districts)

eFigure 7. Odds Ratios of Social Isolation for Neoplasm Diseases Mortality Within All Participants and Subgroups of Moderators: Using Population Density

That Excluded Nondeveloped Areas (eg, Rivers, Lakes, Forests, and Wasteland) as Well as Nonresidential Land (Such as Farms and Industrial Districts)

eFigure 8. Odds Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators: Clustered at Municipal Levels

eFigure 9. Odds Ratios of Social Isolation for Cardiovascular Disease Mortality Within All Participants and Subgroups of Moderators: Clustered at Municipal Levels

eFigure 10. Odds Ratios of Social Isolation for Neoplasm Mortality Within All Participants and Subgroups of Moderators: Clustered at Municipal Levels

eFigure 11. Hazard Ratios of Social Isolation for All-Cause Mortality, Cardiovascular Diseases Mortality, and Neoplasms Mortality With 6-Year Censoring

eFigure 12. Hazard Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators With 6-Year Censoring

eFigure 13. Hazard Ratios of Social Isolation for Cardiovascular Diseases Mortality Within All Participants and Subgroups of Moderators With 6-Year Censoring

eFigure 14. Hazard Ratios of Social Isolation for Neoplasms Mortality Within All Participants and Subgroups of Moderators With 6-Year Censoring

eFigure 15. Hazard Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators Without 6-Year Censoring

eFigure 16. Hazard Ratios of Social Isolation for Cardiovascular Disease Mortality Within All Participants and Subgroups of Moderators Without 6-Year Censoring

eFigure 17. Hazard Ratios of Social Isolation for Neoplasm Mortality Within All Participants and Subgroups of Moderators Without 6-Year Censoring

eFigure 18. Kaplan-Meier Curves for All-Cause Mortality, Cardiovascular Disease Mortality, and Neoplasm Mortality by Social Isolation

eFigure 19. Cumulative Incidence Functions for Cardiovascular Disease Mortality and Neoplasm Mortality by Social Isolation

eTable 1. Number (Percentage) of Missing Values

eTable 2. Baseline Characteristics (Obtained From the 2010 Survey) of Unimputed Data (N = 36 589)

eTable 3. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and All-Cause Mortality Based on Logistic Regression

eTable 4. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Cardiovascular Diseases Mortality Based on Logistic Regression

eTable 5. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Neoplasms Mortality Based on Logistic Regression

eTable 6. Robustness to Unmeasured Confounding (E-Values) of Associations Between Social Isolation and All-Cause Mortality, Cardiovascular Diseases Mortality, and Neoplasms Mortality

eTable 7. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and All-Cause Mortality Based on Survival Regression

eTable 8. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Cardiovascular Diseases Mortality Based on Survival Regression

eTable 9. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Neoplasms Mortality Based on Survival Regression

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Supplementary Data

Definitions of covariates

Socioeconomic status included years of education (9 years or less, 10 years or more), household equivalized income (in JPY), and population density (per km^2) based on Japanese school districts. Household equivalized income was calculated by dividing the annual income by the square root of the number of household members. We defined population density based on Japanese school districts using the 2010 census and Land Utilization Tertiary Mesh Data from the Ministry of Land, Infrastructure, Transport, and Tourism in Japan. These calculations excluded non-developed areas (e.g., rivers, lakes, forests, and wasteland).[1] All spatial calculations were performed using ArcGIS 10.3 software.

Marital status was classified into two categories: married or not married (including single, widowed, divorced, and other). Employment status was categorized as currently working, retired, or never worked. As confounders and potential mediators, we included health behaviors psychological and physiological factors.[2]

Behavioral factors included smoking (never, quit, current), drinking alcohol (never, quit, current), walking (<30min., 30-59, 60-89, ≥90min.), eating meat and fish (every day or not), eating fruit and vegetables (every day or not), and taking health checks (never, more than 4 years ago, 2-3 years, within 1 year).

Psychological factors included depressive symptoms assessed with the short version of the Geriatric Depression Scale (GDS-15), defined as scores of ≥ 5 on the GDS-15 indicating the presence of depressive symptoms (from mild to severe depression).[3]

Physiological factors included body mass index (<18·5, 18·5-25, 25-30, ≥30kg/m2), self-rated health (1=poor; 4=excellent), self-reported hypertension, self-reported diabetes, and self-reported dyslipidemia.

Determining adjusting variables

We built three models. Model 1 included age and gender. In model 2, we added socioeconomic status (education, equivalized income, population density), marital status, and employment status as confounders and potential moderators. In model 3, we included health behaviors psychological and physiological factors as confounders and potential mediators. We were unable to identify the temporal order of the exposure and potential mediators and unable to acquire their values post-baseline assessment. Thus, the variables added to Model 3 may function as both confounders and mediators.[2] Consequently, the fully adjusted model was employed in subsequent analyses.

Sensitivy analysis

We conducted five sensitivity analyses. First, we calculated the E-values for exposure-outcome associations in each moderator stratum (Supplementary Table 6). E-values were used to quantify the minimum strength of association regarding the odds ratio scale that an unmeasured confounder must have with both the exposure and outcome, above and beyond the adjusted covariates, to explain away the observed associations.[4] For example, in the association between social isolation and all-cause mortality among retirees, an unmeasured confounder would need to be associated with both the exposure and outcome by an OR of 1.78-fold each, conditional on the measured covariates, to

fully explain the observed association. An odds ratio of 1.48-fold would be necessary to shift the CI, allowing for the inclusion of the null value. Second, we graphically represented the ORs associated with changes in social isolation across levels of continuous variables (age, household equivalized income, and population density) using restricted cubic splines with three knots (Supplementary Figure 2, 3, 4). Interaction graphs were constructed by using the interactionRCS package of R. However, the CIs of ORs at higher levels of age, household income, and population density were substantially wide. Third, we incorporated a measure of population density that excluded non-developed areas (e.g., rivers, lakes, forests, and wasteland) as well as non-residential land (such as farms and industrial districts) in the logistic model (Supplementary Figure 5, 6, 7). Fourth, we presented the findings with standard errors clustered at the municipality level, reflecting the level at which sampling was conducted and municipal policies were implemented (Supplementary Figure 8, 9, 10). Fifth, we conducted the same analysis applying Cox proportional hazard models for all-cause mortality and competing-risks survival regression based on Fine and Gray's proportional sub-hazards model for CVD mortality and neoplasm mortality with (Supplementary Figure 12, 13, 14) and without (Supplementary Figure 15, 16, 17) 6 year censoring. We also show the Kaplan-Meier Curves and cumulative incidence functions (Supplementary Figure 18, 19).

1. Fujiwara T, Takamoto I, Amemiya A, et al. Is a hilly neighborhood environment associated with diabetes mellitus among older people? Results from the JAGES 2010 study. *Social Science & Medicine*. 2017;182:45-51.
2. Cené CW, Beckie TM, Sims M, et al. Effects of objective and perceived social isolation on cardiovascular and brain health: a scientific statement from the American Heart Association. *Journal of the American Heart Association*. 2022;11(16):e026493.

3. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. *Clinical gerontology*. Routledge; 2014:165-173.
4. VanderWeele TJ. Outcome-wide epidemiology. *Epidemiology (Cambridge, Mass)*. 2017;28(3):399.

eAppendix 2. R Scripts and STATA Do File

```
# Load necessary libraries
library(missForest)
library(doParallel)
library(foreach)
library(dplyr)

#read csv file
data <- read.csv("mydata.csv", header = TRUE, stringsAsFactors = FALSE)

# Perform the imputation
imputed <- missForest(data, verbose = TRUE)
# Extract the OOB error
oob_error <- imputed$OOBerror
print(oob_error)
# Extract the imputed dataset
imputed_data <- imputed$ximp

# Write the imputed dataset back to a new CSV file
write.csv(imputed_data, "imputed_data.csv", row.names = FALSE)
```

STATA do file

```
import delimited "imputed_data.csv", clear

*exclude participants without scode (79 observations deleted, n = 46,065)

drop if scode==.


*exclude people with diseases and impaired ADL

drop if dgns2st10==1

drop if dgns2hd10==1

drop if dgns2ca10==1

drop if adl_3_10!=1


**********Logistic regression analysis**********

*All-cause mortality

*model 1

logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10, cluster(scode)

*model 2

logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10
c.popdens i.marital_bi ib2.empl3pt10, cluster(scode)

*model 3

logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10
c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10
i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re
i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)



*CVD mortality

*model 1

logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10, cluster(scode)

*model 2
```

logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10, cluster(scode)

*model 3

logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*Neoplasms

*model 1

logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10, cluster(scode)

*model 2

logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10, cluster(scode)

*model 3

logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

**Modification_logistic

*All-cause mortality

*effect modification

logistic eve_shibou17_6year i.SI_bi##i.age75 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_shibou17_6year i.SI_bi##i.sex_2_10 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_shibou17_6year i.SI_bi##i.edu2gp age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_shibou17_6year i.SI_bi##i.income_tertile age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_shibou17_6year i.SI_bi##i.popdens_tertile age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_shibou17_6year i.SI_bi##i.marital_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_shibou17_6year i.SI_bi##ib2.empl3pt10 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_shibou17_6year SI_bi age75 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_shibou17_6year SI_bi sex_2_10 age_ysl10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_shibou17_6year SI_bi edu2gp age_ysl10 sex_2_10 c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_shibou17_6year SI_bi income_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d3==0, cluster(scode)

reri logistic eve_shibou17_6year SI_bi income_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d2==0, cluster(scode)

reri logistic eve_shibou17_6year SI_bi popdens_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d3==0, cluster(scode)

reri logistic eve_shibou17_6year SI_bi popdens_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d2==0, cluster(scode)

reri logistic eve_shibou17_6year SI_bi marital_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_shibou17_6year SI_bi empl3pt10_d1 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d3==0, cluster(scode)

reri logistic eve_shibou17_6year SI_bi empl3pt10_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d1==0, cluster(scode)

*subgroup

bysort age75: logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort sex_2_10: logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort edu2gp: logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort income_tertile: logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort popdens_tertile: logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort marital_bi: logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort empl3pt10: logistic eve_shibou17_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*CVD mortality

*effect modification

logistic eve_sibou_IHD_stroke_6year i.SI_bi##i.age75 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_IHD_stroke_6year i.SI_bi##i.sex_2_10 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_IHD_stroke_6year i.SI_bi##i.edu2gp age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_IHD_stroke_6year i.SI_bi##i.income_tertile age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_IHD_stroke_6year i.SI_bi##i.popdens_tertile age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_IHD_stroke_6year i.SI_bi##i.marital_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_IHD_stroke_6year i.SI_bi##ib2.empl3pt10 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*RERI

reri logistic eve_sibou_IHD_stroke_6year SI_bi age75 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi sex_2_10 age_ysl10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi edu2gp age_ysl10 sex_2_10 c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi income_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d3==0, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi income_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d2==0, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi popdens_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d3==0, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi popdens_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d2==0, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi marital_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi empl3pt10_d1 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d3==0, cluster(scode)

reri logistic eve_sibou_IHD_stroke_6year SI_bi empl3pt10_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10

i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d1==0, cluster(scode)

*subgroup

bysort age75: logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort sex_2_10: logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort edu2gp: logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort income_tertile: logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort popdens_tertile: logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort marital_bi: logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort empl3pt10: logistic eve_sibou_IHD_stroke_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10

i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*Cancer mortality

*effect modification

logistic eve_sibou_cancer_6year i.SI_bi##i.age75 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_cancer_6year i.SI_bi##i.sex_2_10 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_cancer_6year i.SI_bi##i.edu2gp age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_cancer_6year i.SI_bi##i.income_tertile age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_cancer_6year i.SI_bi##i.popdens_tertile age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_cancer_6year i.SI_bi##i.marital_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10

i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

logistic eve_sibou_cancer_6year i.SI_bi##ib2.empl3pt10 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*RERI

reri logistic eve_sibou_cancer_6year SI_bi age75 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi sex_2_10 age_ysl10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi edu2gp age_ysl10 sex_2_10 c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi income_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d3==0, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi income_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d2==0, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi popdens_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d3==0, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi popdens_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10

i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d2==0, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi marital_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi empl3pt10_d1 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d3==0, cluster(scode)

reri logistic eve_sibou_cancer_6year SI_bi empl3pt10_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d1==0, cluster(scode)

*subgroup

bysort age75: logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort sex_2_10: logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort edu2gp: logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort income_tertile: logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort popdens_tertile: logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort marital_bi: logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort empl3pt10: logistic eve_sibou_cancer_6year i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

**********Cox regression analysis**********

*All-cause mortality

stset days_sibou_lost2_6year, failure(eve_shibou17_6year ==1) id(samplenumber) scale(365.25)

*model 1

stcox i.SI_bi age_ysl10 sex_2_10, cluster(scode)

*model 2

stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10, cluster(scode)

*model 3

stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*CVD mortality

*competing risk model

stset days_sibou_lost2_6year, failure(eve_sibou_IHD_stroke_6year==1) id(samplenumber) scale(365.25)

*model 1

stcrreg i.SI_bi age_ysl10 sex_2_10, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

*model 2

stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

*model 3

stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

*cancer

*competing risk model

stset days_sibou_lost2_6year, failure(eve_sibou_cancer_6year==1) id(samplenumber) scale(365.25)

*model 1

stcrreg i.SI_bi age_ysl10 sex_2_10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

*model 2

stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

*model 3

stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

*effect modification

*All-cause mortality

stset days_sibou_lost2_6year, failure(eve_shibou17_6year ==1) id(samplenumber) scale(365.25)

stcox i.SI_bi##i.age75 c.age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

stcox i.SI_bi##i.sex_2_10 c.age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

stcox i.SI_bi##i.edu2gp c.age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

stcox i.SI_bi##i.income_tertile c.age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

stcox i.SI_bi##i.popdens_tertile c.age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

stcox i.SI_bi##i.marital_bi c.age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi

i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

stcox i.SI_bi##ib2.empl3pt10 c.age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*RERI

reri stcox SI_bi age75 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri stcox SI_bi sex_2_10 age_ysl10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri stcox SI_bi edu2gp age_ysl10 sex_2_10 c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri stcox SI_bi income_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d3==0, cluster(scode)

reri stcox SI_bi income_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d2==0, cluster(scode)

reri stcox SI_bi popdens_tertile_d2 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d3==0, cluster(scode)

reri stcox SI_bi popdens_tertile_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d2==0, cluster(scode)

reri stcox SI_bi marital_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

reri stcox SI_bi empl3pt10_d1 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d3==0, cluster(scode)

reri stcox SI_bi empl3pt10_d3 age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d1==0, cluster(scode)

*subgroup

bysort age75: stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort sex_2_10: stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort edu2gp: stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort income_tertile: stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort popdens_tertile: stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort marital_bi: stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

bysort empl3pt10: stcox i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, cluster(scode)

*CVD

stset days_sibou_lost2_6year, failure(eve_sibou_IHD_stroke_6year==1) id(samplenumber) scale(365.25)

*effect modification (additive and multiplicative)

*age

gen g = SI_bi

gen e = age75

gen Ige = g*e

stcrreg g e Ige age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1

*gender

drop g e Ige

```
gen g = SI_bi

gen e = sex_2_10

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1


*education

drop g e Ige

gen g = SI_bi

gen e = edu2gp

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1


*income

drop g e Ige

gen g = SI_bi

gen e = income_tertile_d2

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d3==0,
compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1
```

```
drop g e Ige

gen g = SI_bi

gen e = income_tertile_d3

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10
i.dgns2hl10 if income_tertile_d2==0,
compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1



*popdens

drop g e Ige

gen g = SI_bi

gen e = popdens_tertile_d2

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10
i.dgns2hl10 if popdens_tertile_d3==0,
compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1


drop g e Ige

gen g = SI_bi

gen e = popdens_tertile_d3

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10
i.dgns2hl10 if popdens_tertile_d2==0, compete(eve_sibou_IHD_stroke_competing==2)
cluster(scode)
```

```
nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1
```

*marital status

```
drop g e Ige

gen g = SI_bi

gen e = marital_bi

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1
```

*employment

```
drop g e Ige

gen g = SI_bi

gen e = empl3pt10_d1

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d3==0, compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1


drop g e Ige

gen g = SI_bi

gen e = empl3pt10_d3

gen Ige = g*e
```

```
stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10
i.dgns2hl10 if empl3pt10_d1==0, compete(eve_sibou_IHD_stroke_competing==2)
cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1



*subgroup

bysort age75: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens
i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi
i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10
i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2)
cluster(scode)


bysort sex_2_10: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens
i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi
i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10
i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2)
cluster(scode)


bysort edu2gp: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens
i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi
i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10
i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2)
cluster(scode)


bysort income_tertile: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10
c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10
i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re
i.dgns2ht10 i.dgns2dm10 i.dgns2hl10,
compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)


bysort popdens_tertile: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10
c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10
i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re
```

```
i.dgns2ht10 i.dgns2dm10 i.dgns2hl10,
compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)


bysort marital_bi: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens
i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi
i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10
i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_IHD_stroke_6year_comp==2)
cluster(scode)


bysort empl3pt10: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10
c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10
i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re
i.dgns2ht10 i.dgns2dm10 i.dgns2hl10,
compete(eve_sibou_IHD_stroke_6year_comp==2) cluster(scode)



*cancer

stset days_sibou_lost2_6year, failure(eve_sibou_cancer_6year==1) id(samplenumber)
scale(365.25)


*effect modification (additive and multiplicative)

*age

drop g e Ige

gen g = SI_bi

gen e = age75

gen Ige = g*e

stcrreg g e Ige age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10
i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1
```

*gender

```
drop g e Ige

gen g = SI_bi

gen e = sex_2_10

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1
```

*education

```
drop g e Ige

gen g = SI_bi

gen e = edu2gp

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1
```

*income

```
drop g e Ige

gen g = SI_bi

gen e = income_tertile_d2

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if income_tertile_d3==0, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)
```

```
nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1


drop g e Ige

gen g = SI_bi

gen e = income_tertile_d3

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10
i.dgns2hl10 if income_tertile_d2==0, compete(eve_sibou_cancer_6year_comp==2)
cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1



*popdens

drop g e Ige

gen g = SI_bi

gen e = popdens_tertile_d2

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10
i.dgns2hl10 if popdens_tertile_d3==0, compete(eve_sibou_cancer_6year_comp==2)
cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1


drop g e Ige

gen g = SI_bi

gen e = popdens_tertile_d3

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi
ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi
```

ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if popdens_tertile_d2==0, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1

*marital status

drop g e Ige

gen g = SI_bi

gen e = marital_bi

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1

*employment

drop g e Ige

gen g = SI_bi

gen e = empl3pt10_d1

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d3==0, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1

drop g e Ige

gen g = SI_bi

gen e = empl3pt10_d3

gen Ige = g*e

stcrreg g e Ige age_ysl10 i.sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10 if empl3pt10_d1==0, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

nlcom exp(_b[g]+_b[e]+_b[Ige])-exp(_b[g])-exp(_b[e])+1

*subgroup

bysort age75: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

bysort sex_2_10: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

bysort edu2gp: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

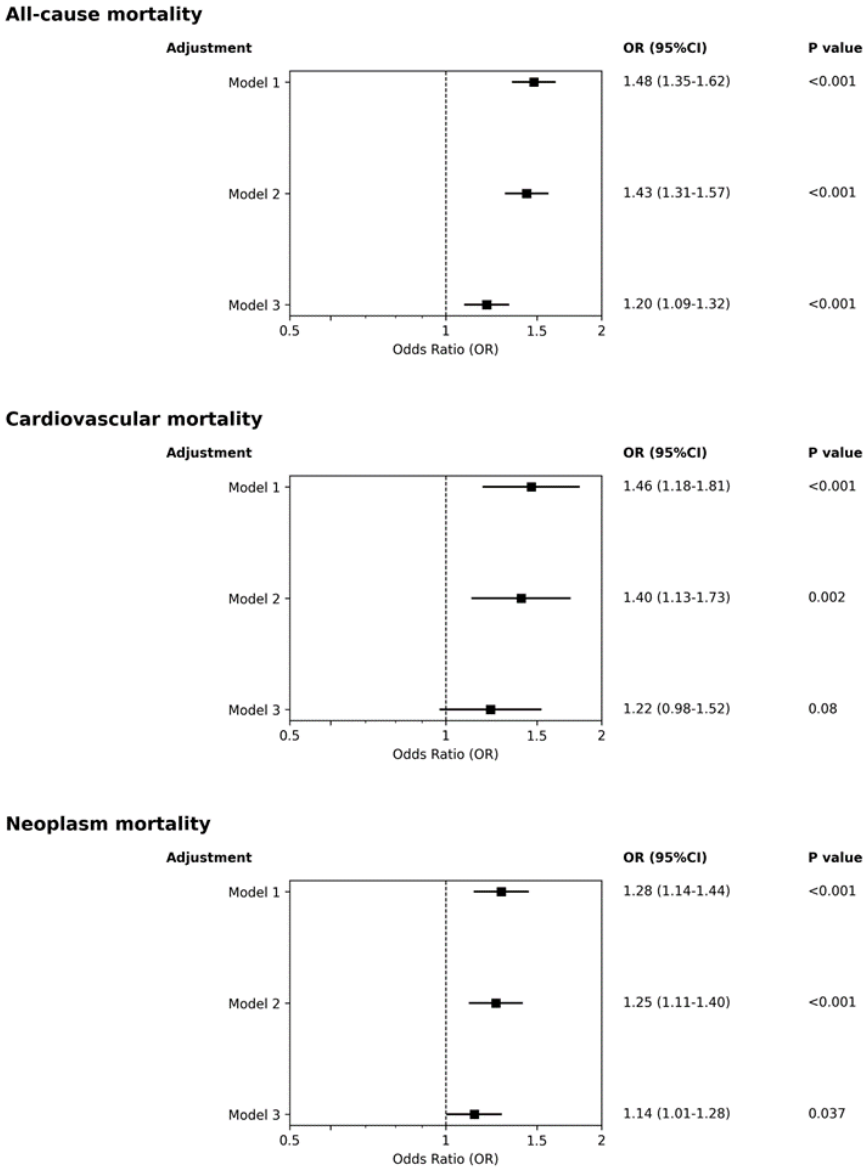
bysort income_tertile: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

bysort popdens_tertile: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)

```
bysort marital_bi: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10 c.popdens
i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10 i.fq7prt10re_bi
i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re i.dgns2ht10
i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2) cluster(scode)
```

```
bysort empl3pt10: stcrreg i.SI_bi age_ysl10 sex_2_10 i.edu2gp c.eqincome10
c.popdens i.marital_bi ib2.empl3pt10 i.smok3_10 i.alcl3_10 i.walk4tm10
i.fq7prt10re_bi i.fq7veg10re_bi ib4.exam4_10re  i.gds5 ib1.bmi4_10 c.srh_4_10re
i.dgns2ht10 i.dgns2dm10 i.dgns2hl10, compete(eve_sibou_cancer_6year_comp==2)
cluster(scode)
```

eFigure 1. Odds Ratios of Social Isolation for All-Cause Mortality, Cardiovascular Diseases Mortality, and Neoplasms Mortality Among Older People in Japan



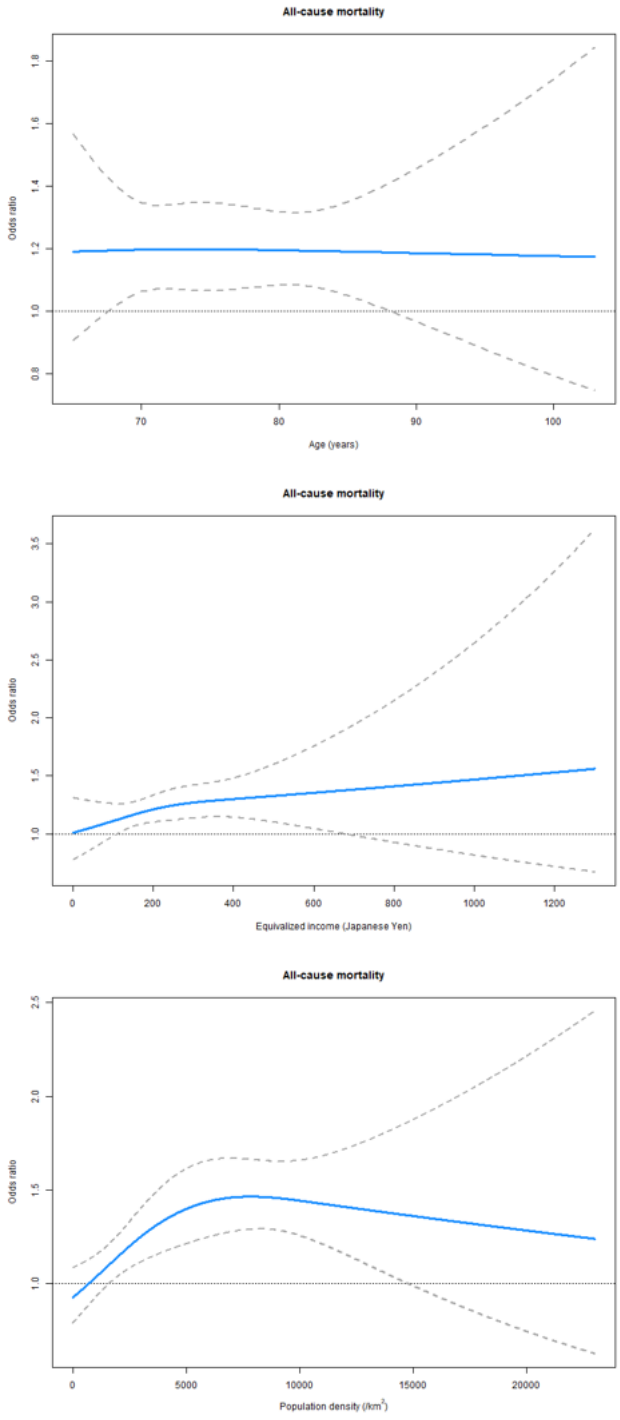
In model 1, age and gender were included.

In model 2, socioeconomic status (education, equivalized income, population density), marital status, and employment status were included.

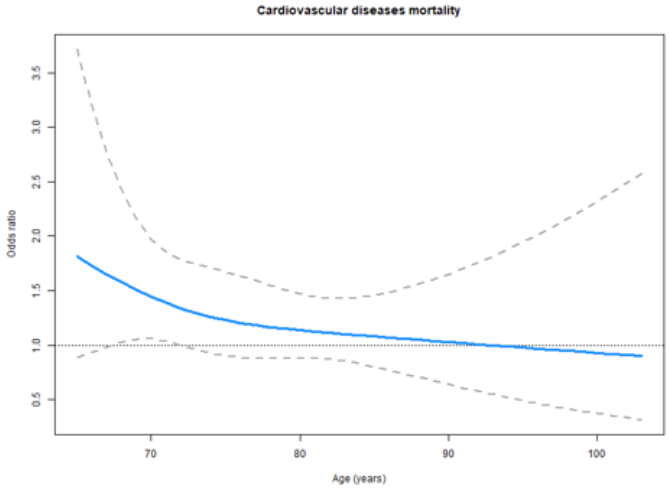
In model 3, health behaviours (smoking, drinking alcohol, walking, frequency of eating meat and fish, frequency of eating fruits and vegetables, taking health check-ups), psychological factors (depressive symptoms), and physiological factors (body mass index, self-rated health, hypertension, diabetes, dyslidemia) were included.

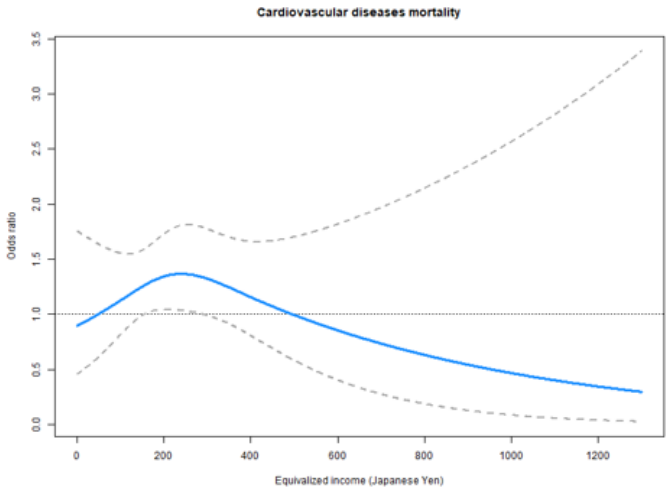
OR: odds ratio; CI: confidence interval.

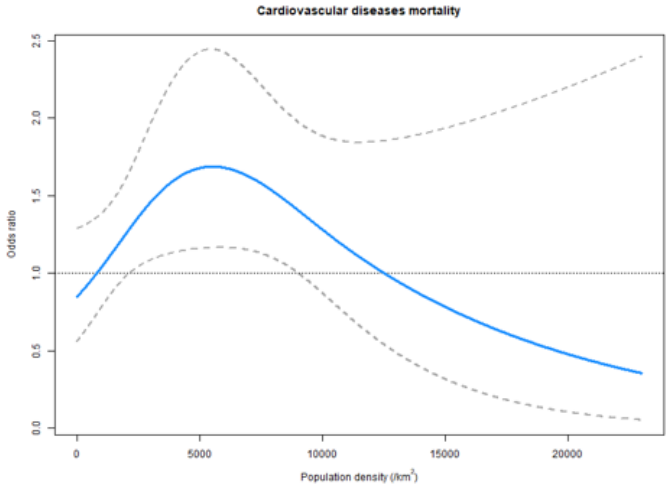
eFigure 2. Odds Ratios of Social Isolation for All-Cause Mortality Over Levels of Age at Baseline



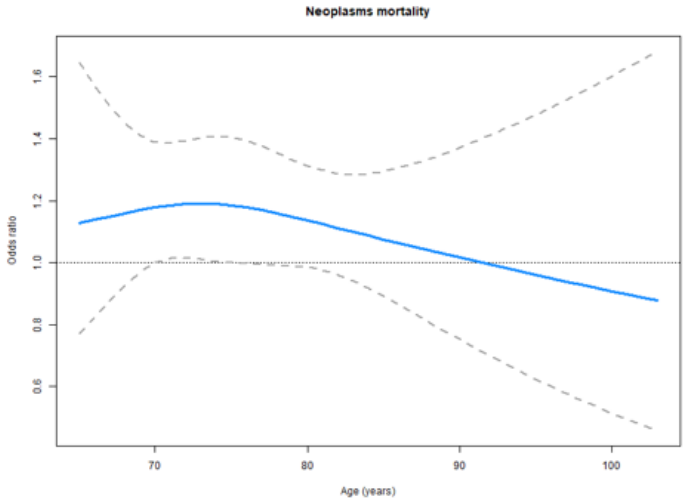
eFigure 3. Odds Ratios of Social Isolation for Cardiovascular Diseases Mortality Over Levels of Age at Baseline

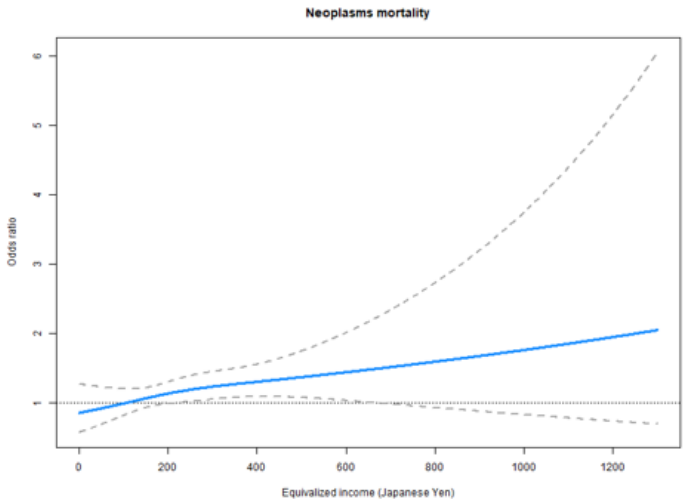


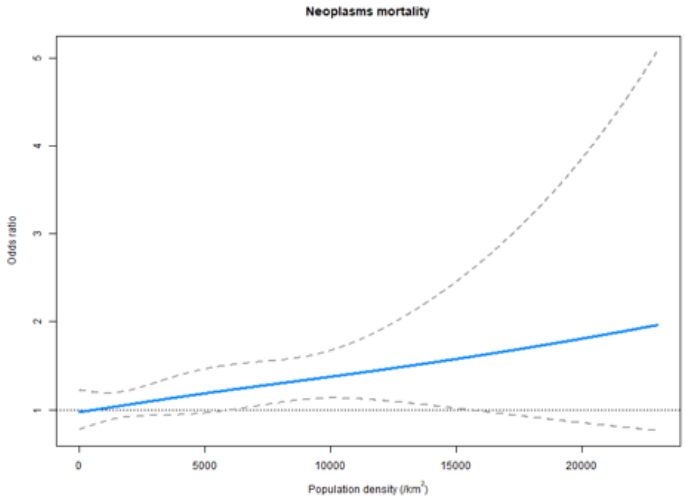




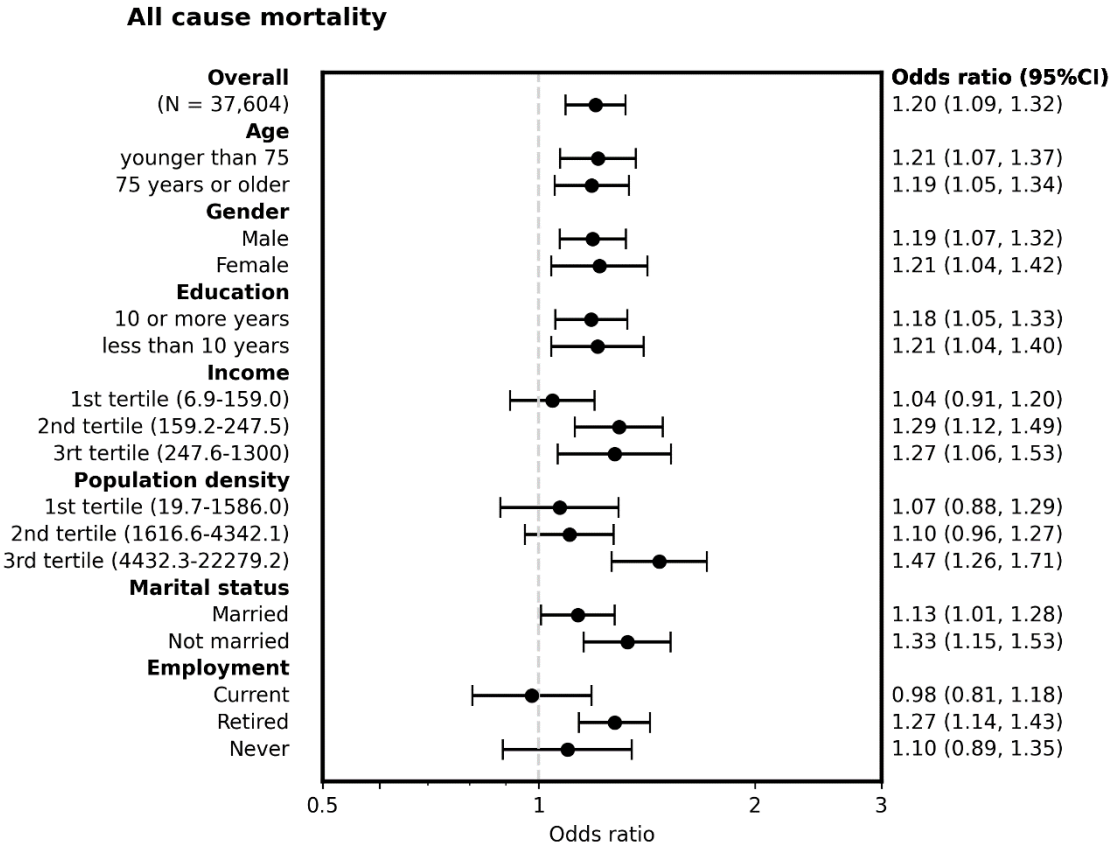
eFigure 4. Odds Ratios of Social Isolation for Neoplasms Mortality Over Levels of Age at Baseline



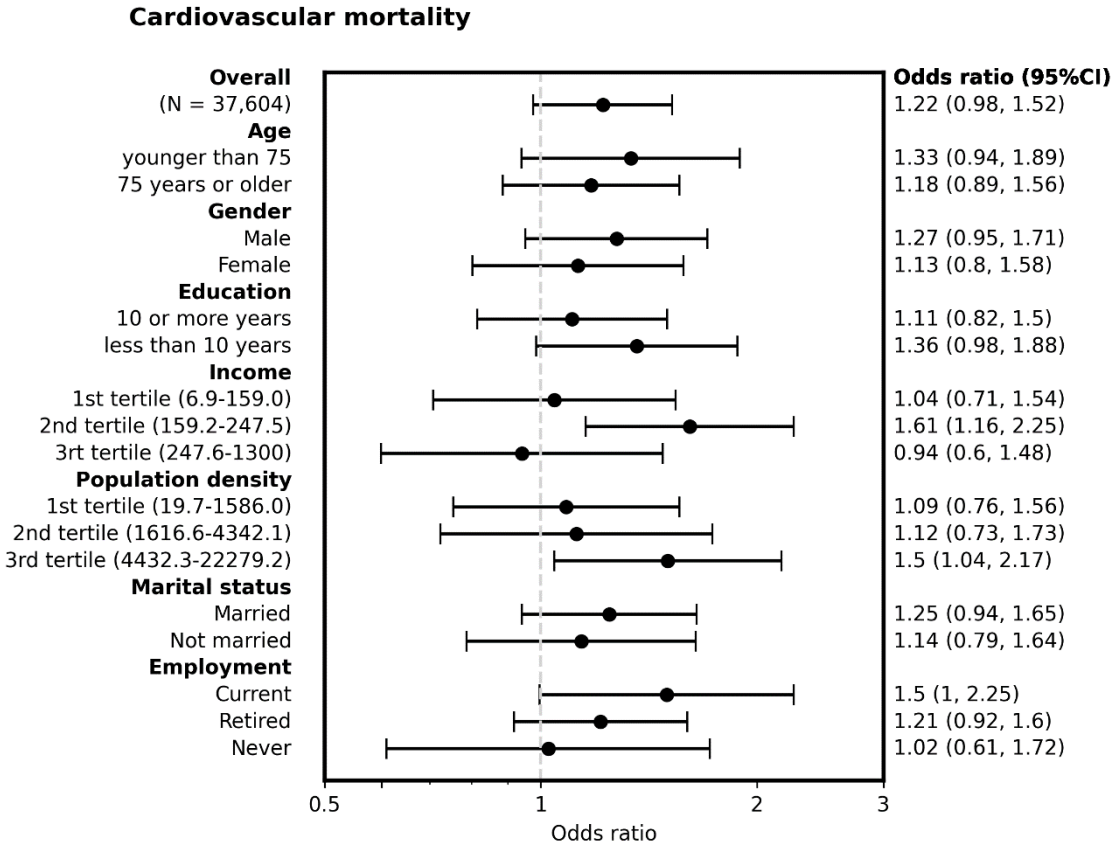




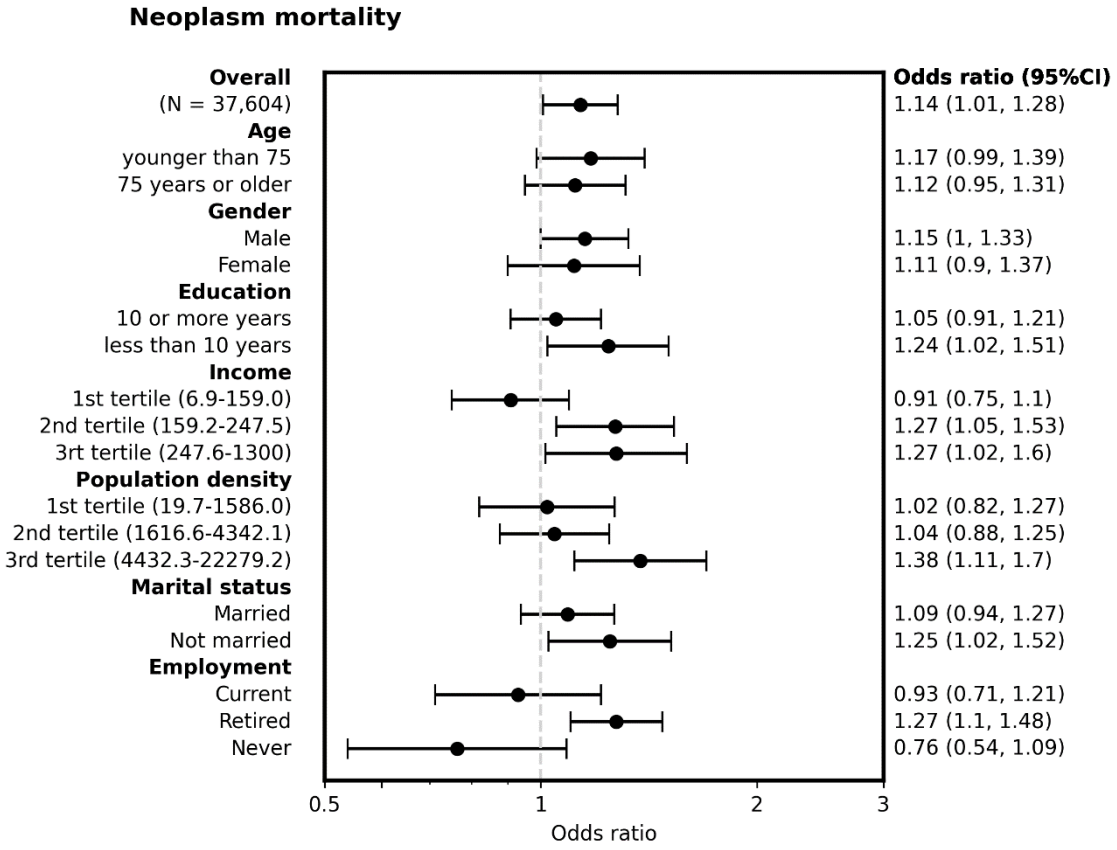
eFigure 5. Odds Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators: Using Population Density That Excluded Nondeveloped Areas (eg, Rivers, Lakes, Forests, and Wasteland) as Well as Nonresidential Land (Such as Farms and Industrial Districts)



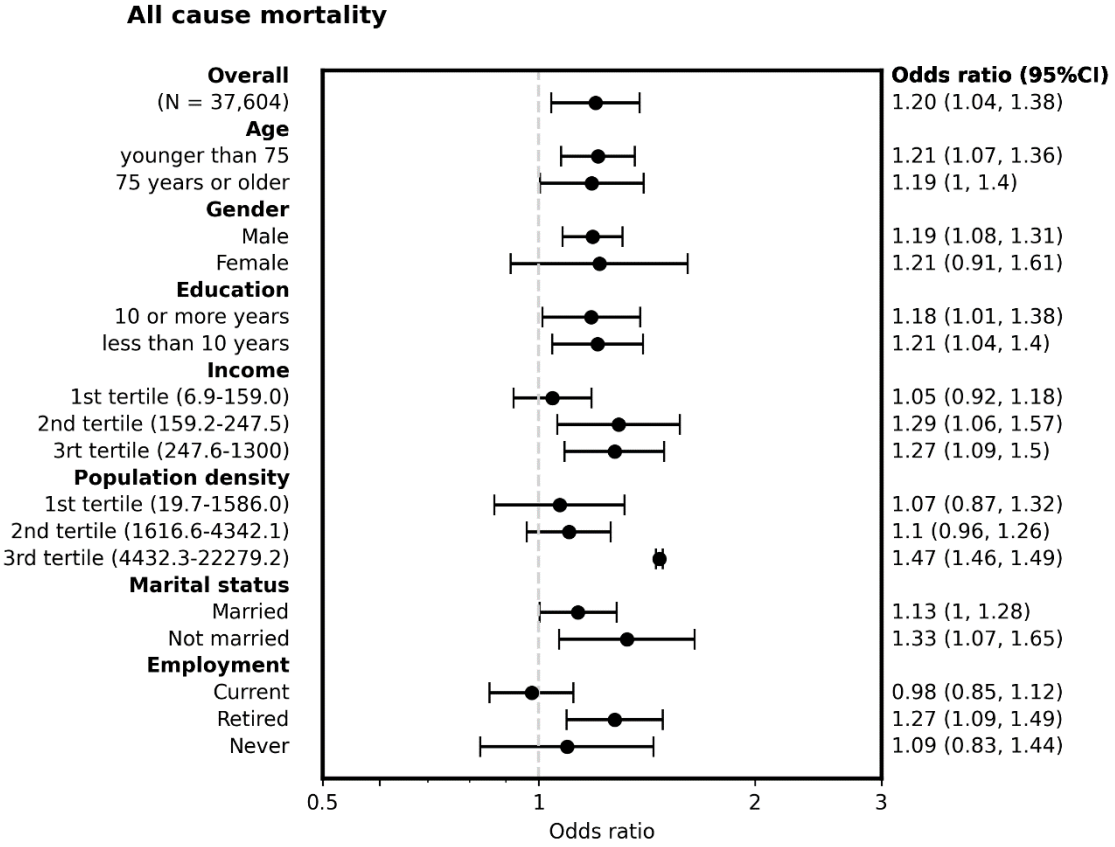
eFigure 6. Odds Ratios of Social Isolation for Cardiovascular Diseases Mortality Within All Participants and Subgroups of Moderators: Using Population Density That Excluded Nondeveloped Areas (eg, Rivers, Lakes, Forests, and Wasteland) as Well as Nonresidential Land (Such as Farms and Industrial Districts)



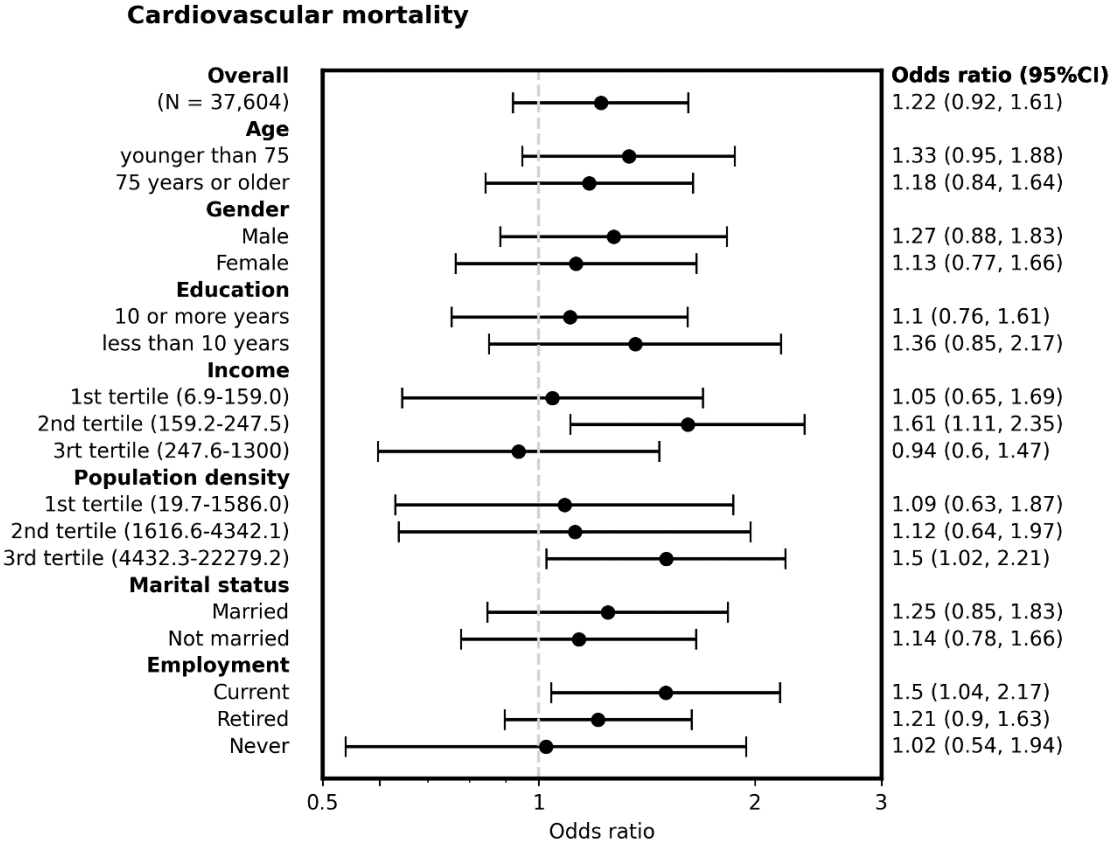
eFigure 7. Odds Ratios of Social Isolation for Neoplasm Diseases Mortality Within All Participants and Subgroups of Moderators: Using Population Density That Excluded Nondeveloped Areas (eg, Rivers, Lakes, Forests, and Wasteland) as Well as Nonresidential Land (Such as Farms and Industrial Districts)



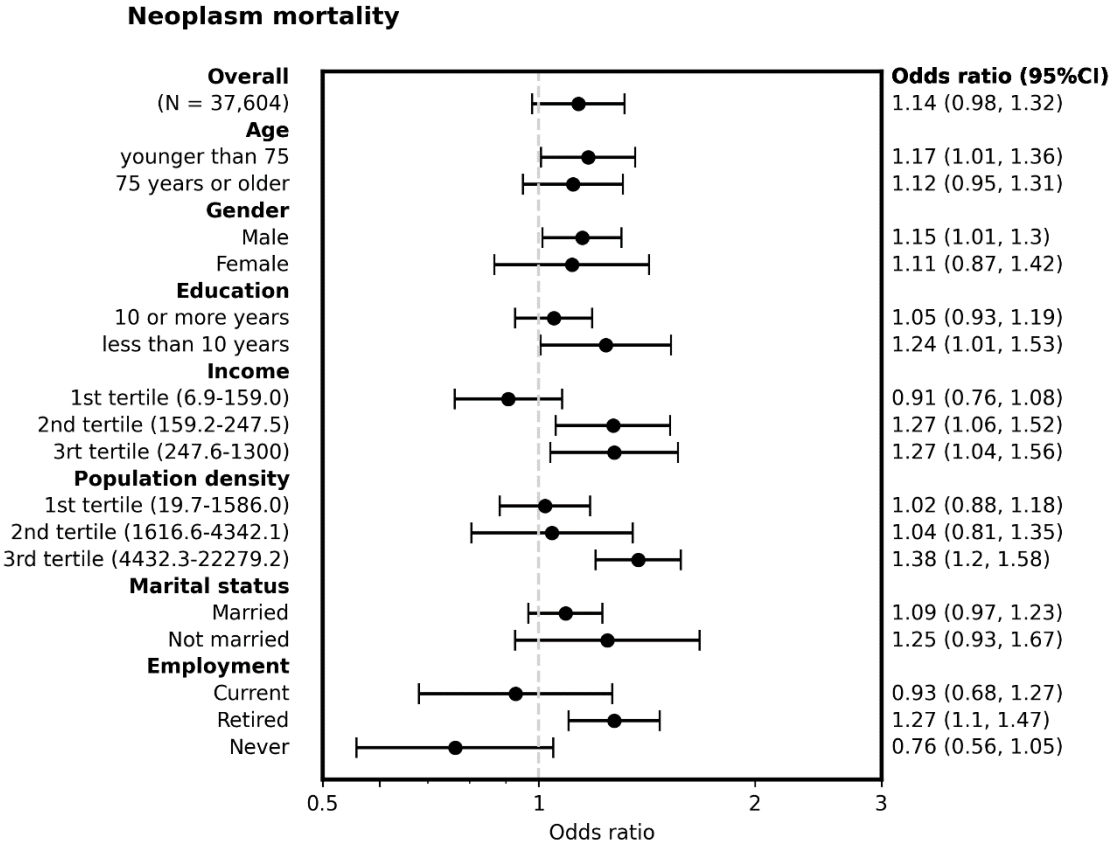
eFigure 8. Odds Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators: Clustered at Municipal Levels



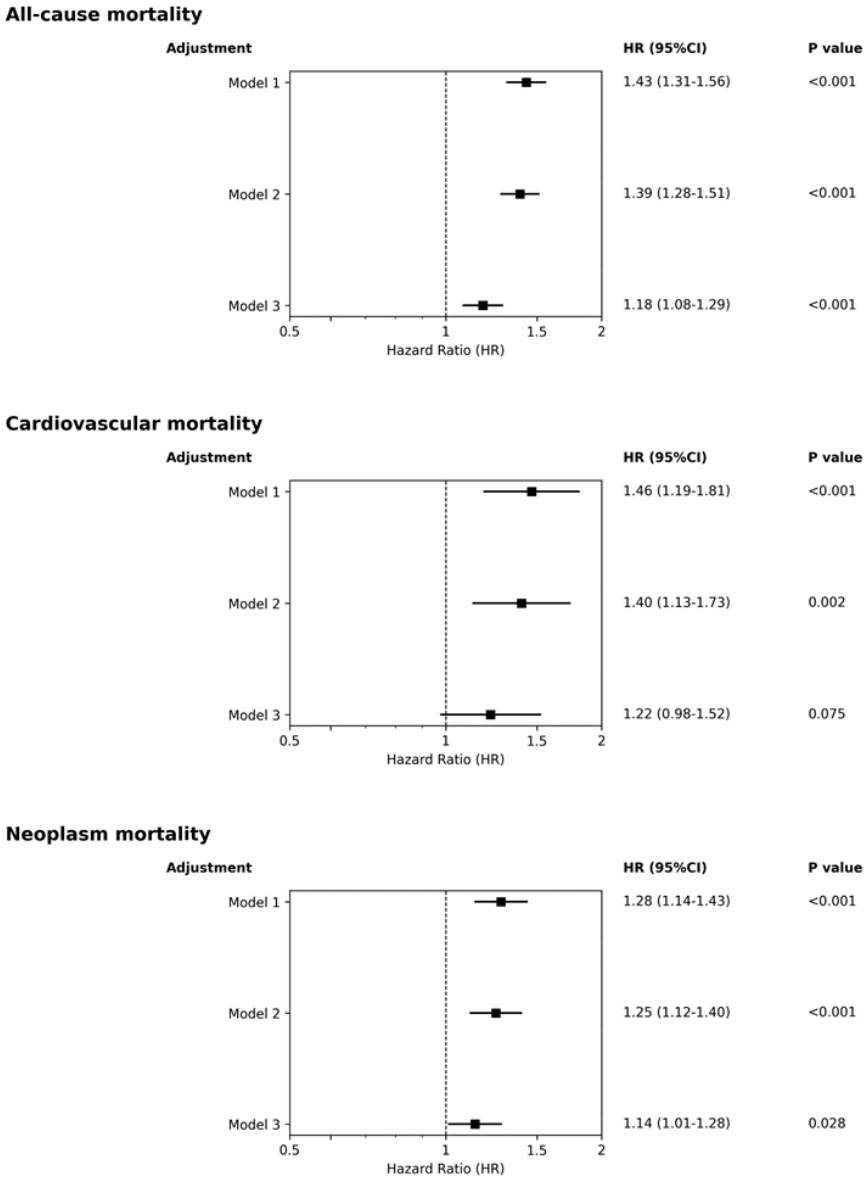
eFigure 9. Odds Ratios of Social Isolation for Cardiovascular Disease Mortality Within All Participants and Subgroups of Moderators: Clustered at Municipal Levels



eFigure 10. Odds Ratios of Social Isolation for Neoplasm Mortality Within All Participants and Subgroups of Moderators: Clustered at Municipal Levels



eFigure 11. Hazard Ratios of Social Isolation for All-Cause Mortality, Cardiovascular Diseases Mortality, and Neoplasms Mortality With 6-Year Censoring



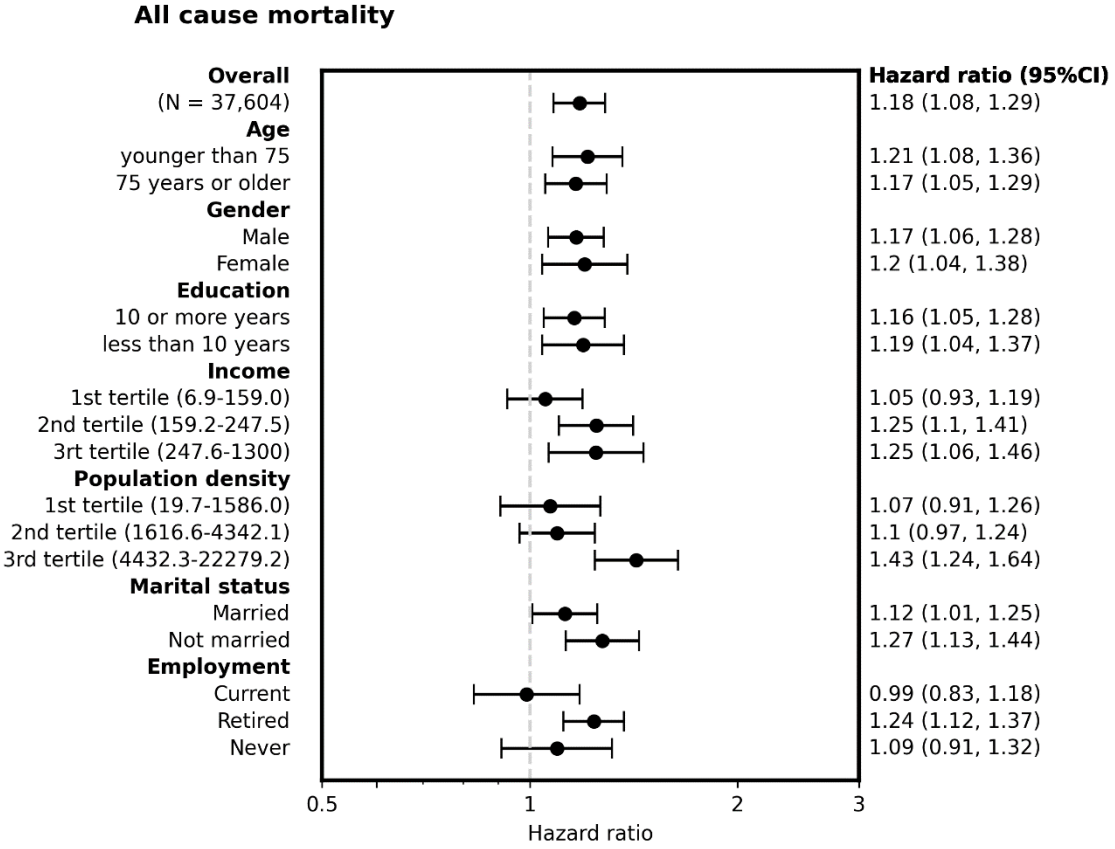
In model 1, age and gender were included.

In model 2, socioeconomic status (education, equivalized income, population density), marital status, and employment status were included.

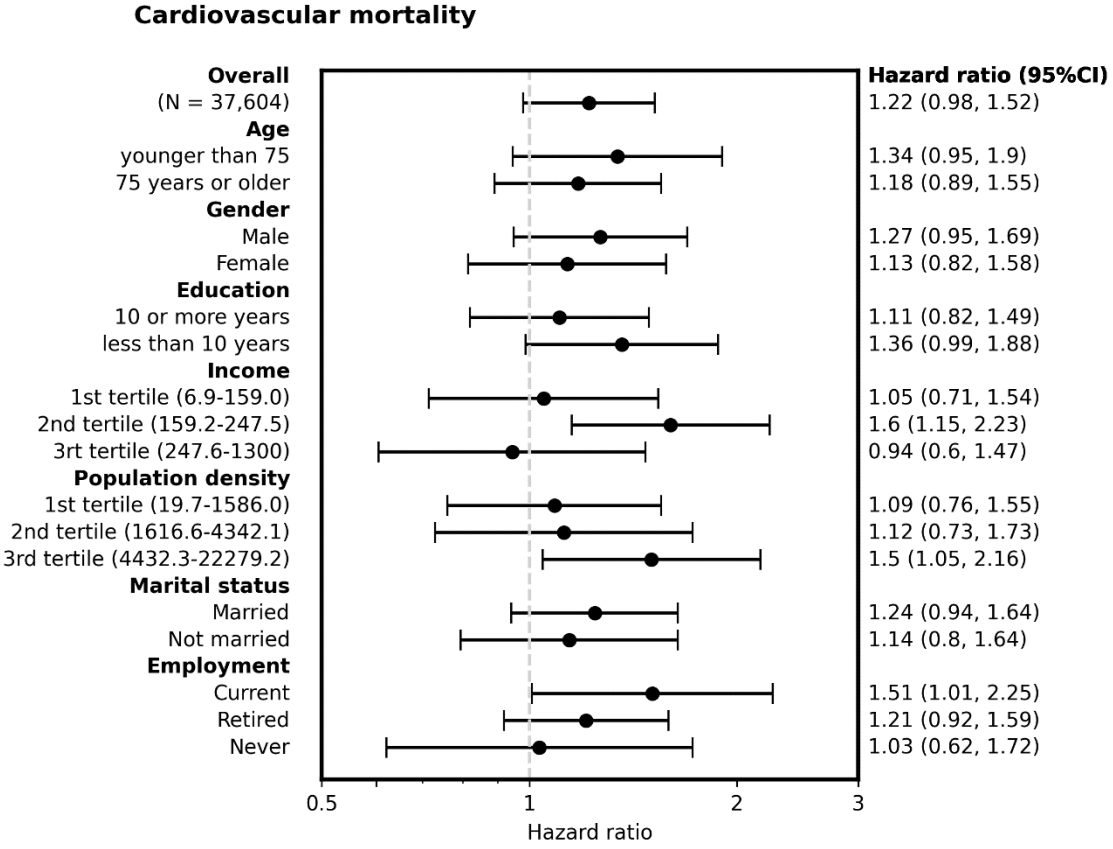
In model 3, health behaviours (smoking, drinking alcohol, walking, frequency of eating meat and fish, frequency of eating fruits and vegetables, taking health check-ups), psychological factors (depressive symptoms), and physiological factors (body mass index, self-rated health, hypertension, diabetes, dyslidemia) were included.

HR: hazard ratio; CI: confidence interval.

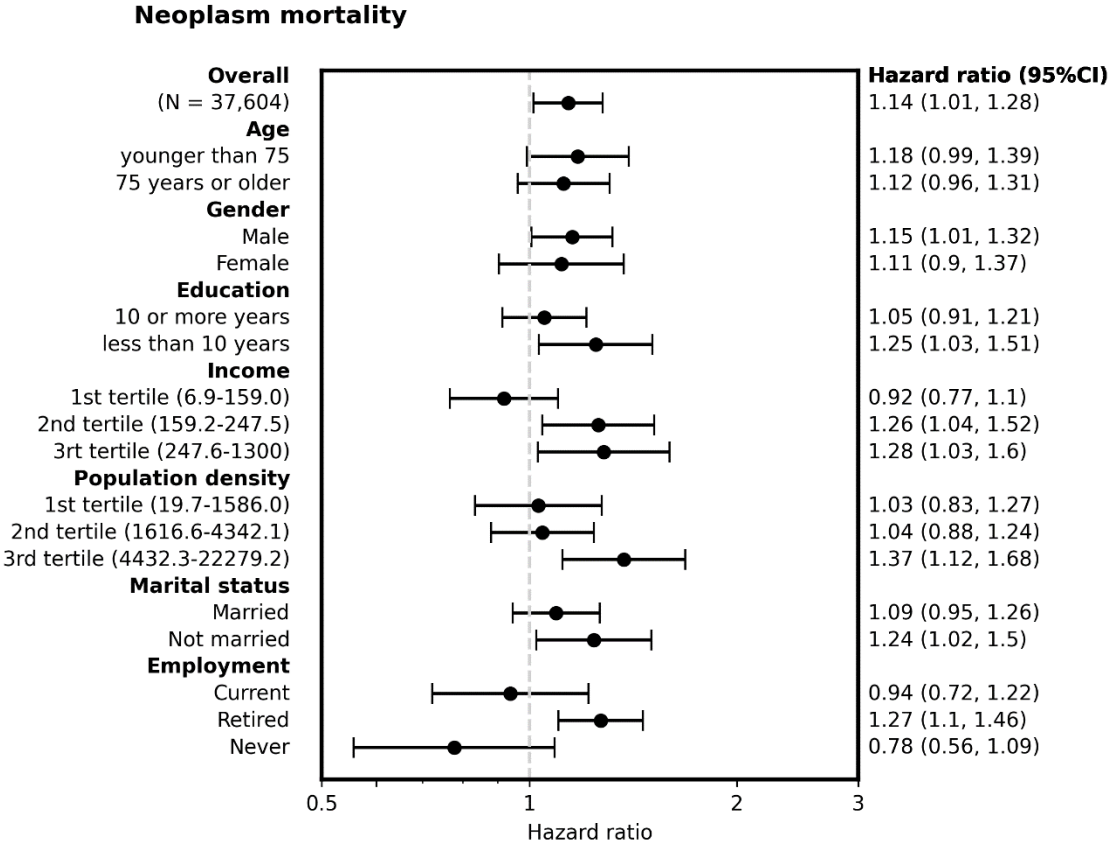
eFigure 12. Hazard Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators With 6-Year Censoring



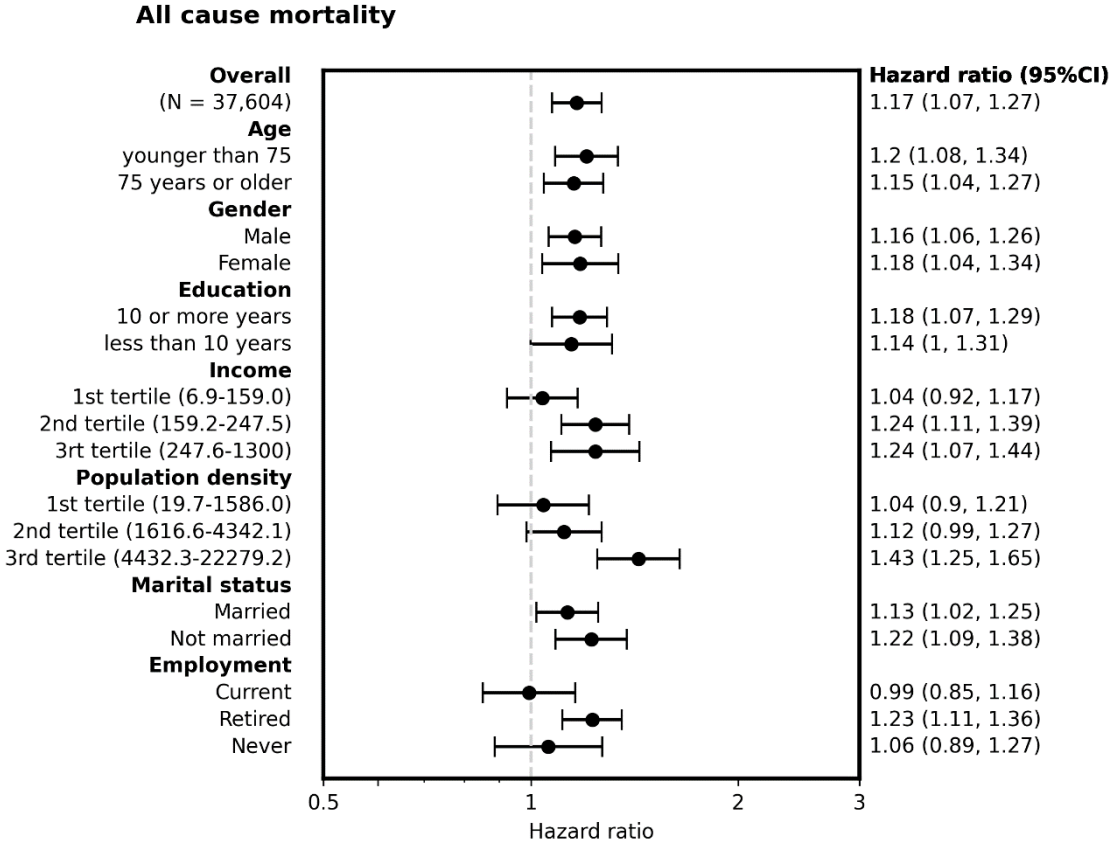
eFigure 13. Hazard Ratios of Social Isolation for Cardiovascular Diseases Mortality Within All Participants and Subgroups of Moderators With 6-Year Censoring



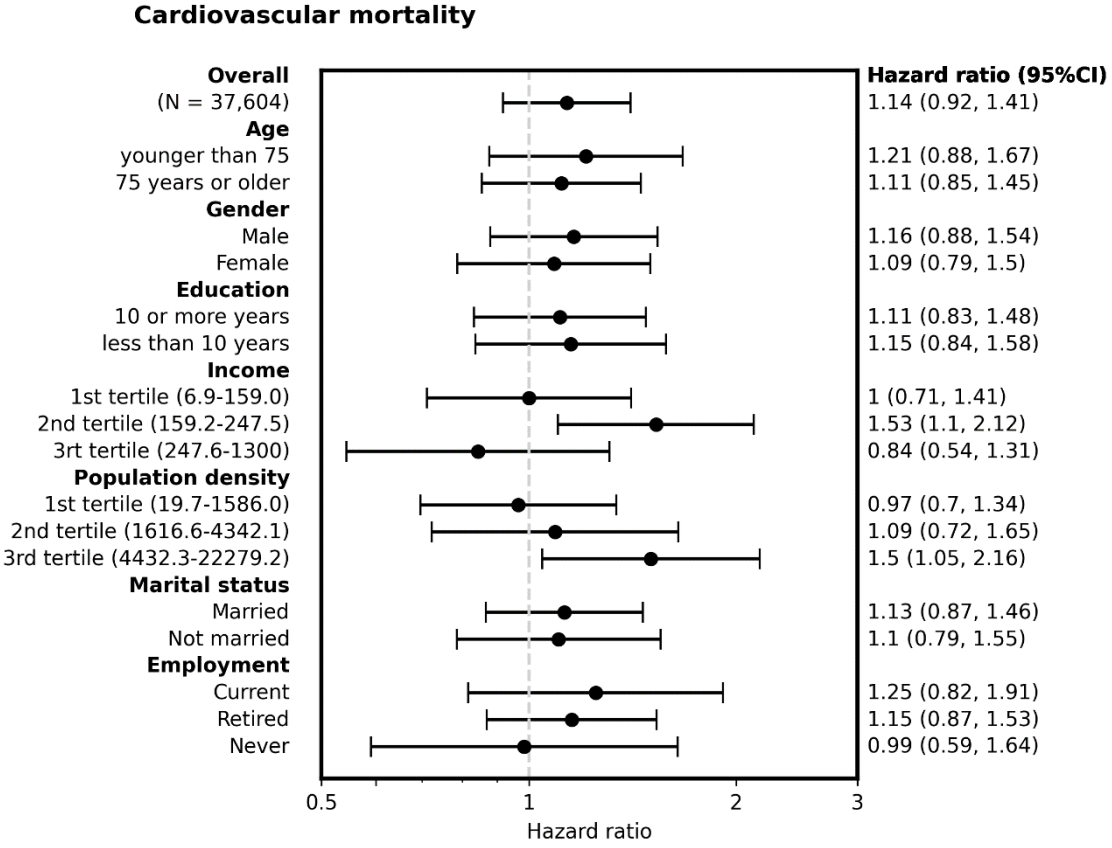
eFigure 14. Hazard Ratios of Social Isolation for Neoplasms Mortality Within All Participants and Subgroups of Moderators With 6-Year Censoring



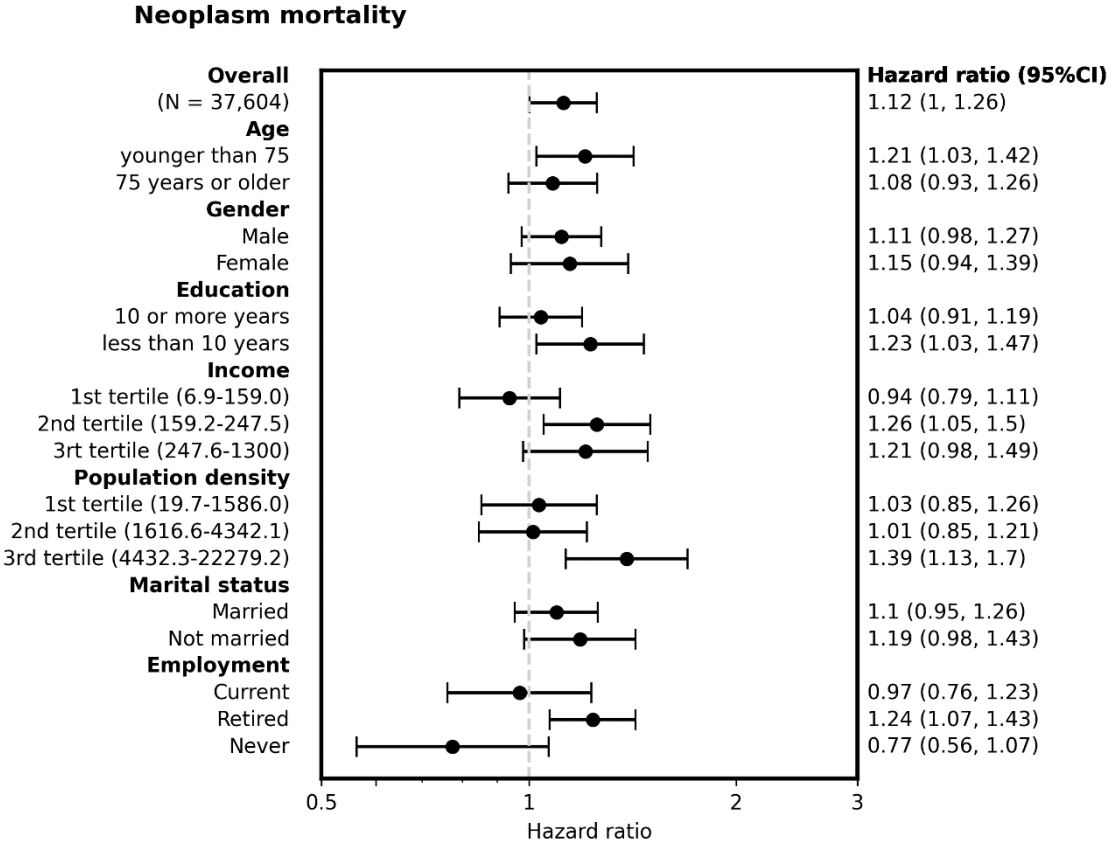
eFigure 15. Hazard Ratios of Social Isolation for All-Cause Mortality Within All Participants and Subgroups of Moderators Without 6-Year Censoring



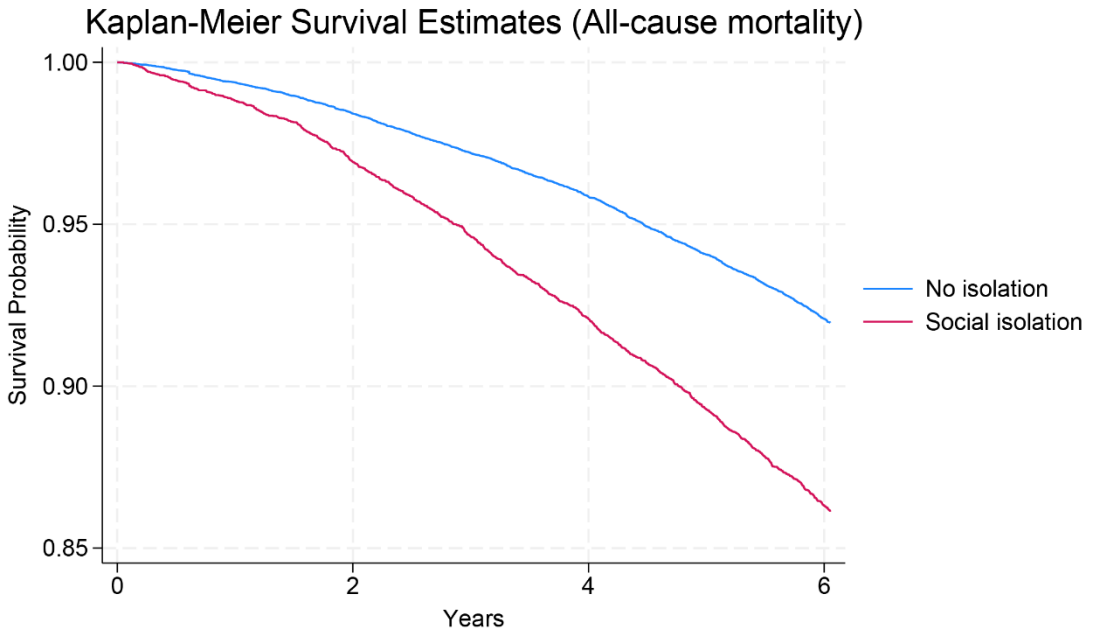
eFigure 16. Hazard Ratios of Social Isolation for Cardiovascular Disease Mortality Within All Participants and Subgroups of Moderators Without 6-Year Censoring

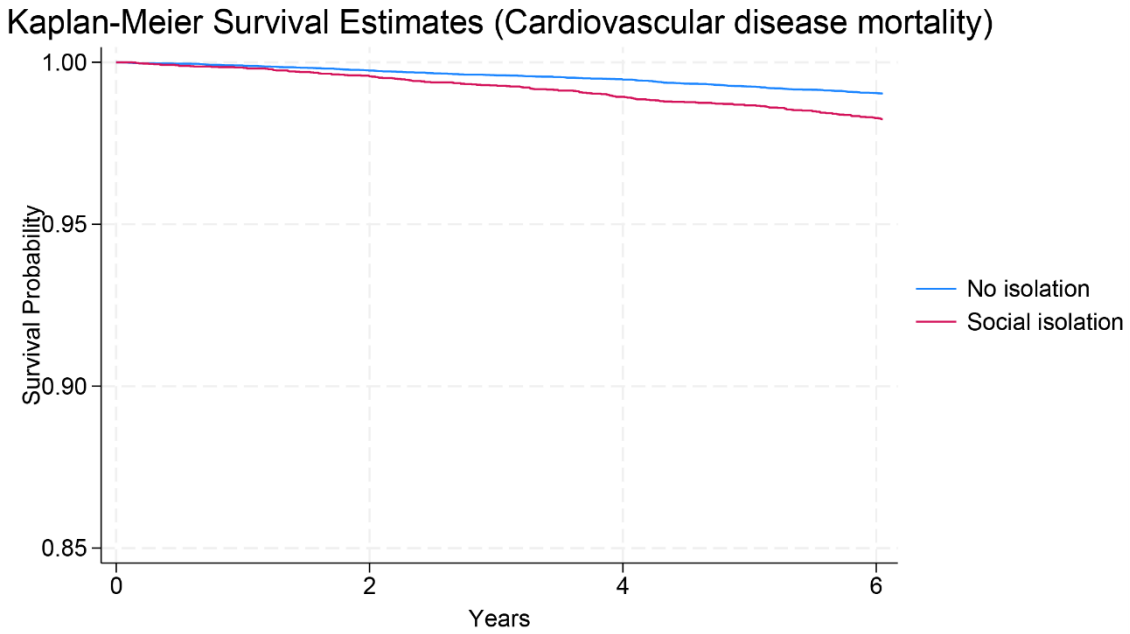


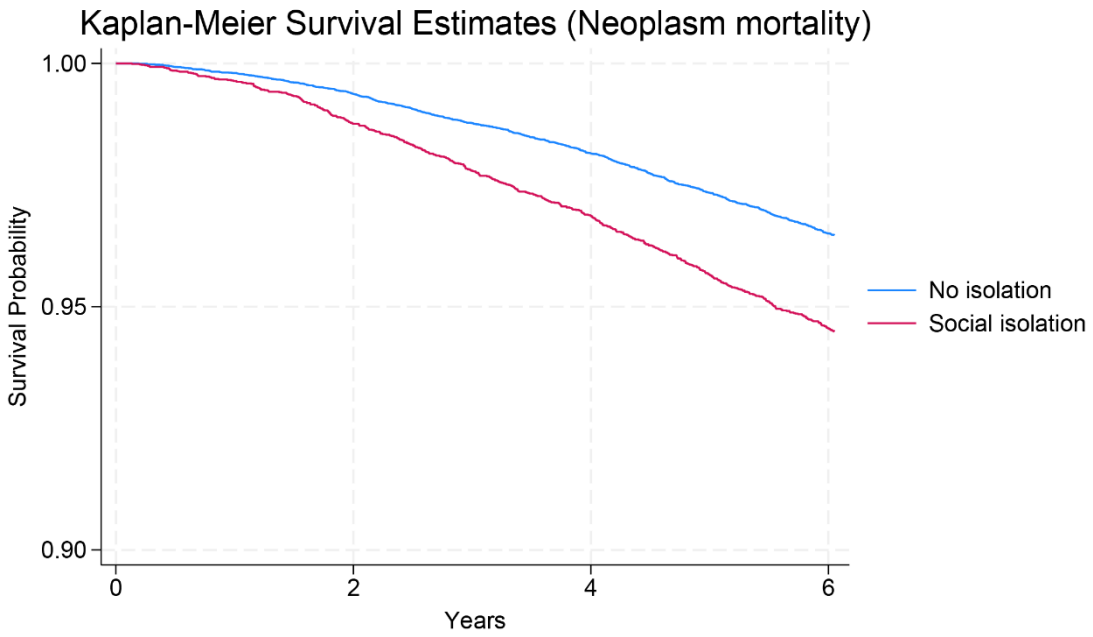
eFigure 17. Hazard Ratios of Social Isolation for Neoplasm Mortality Within All Participants and Subgroups of Moderators Without 6-Year Censoring



eFigure 18. Kaplan-Meier Curves for All-Cause Mortality, Cardiovascular Disease Mortality, and Neoplasm Mortality by Social Isolation

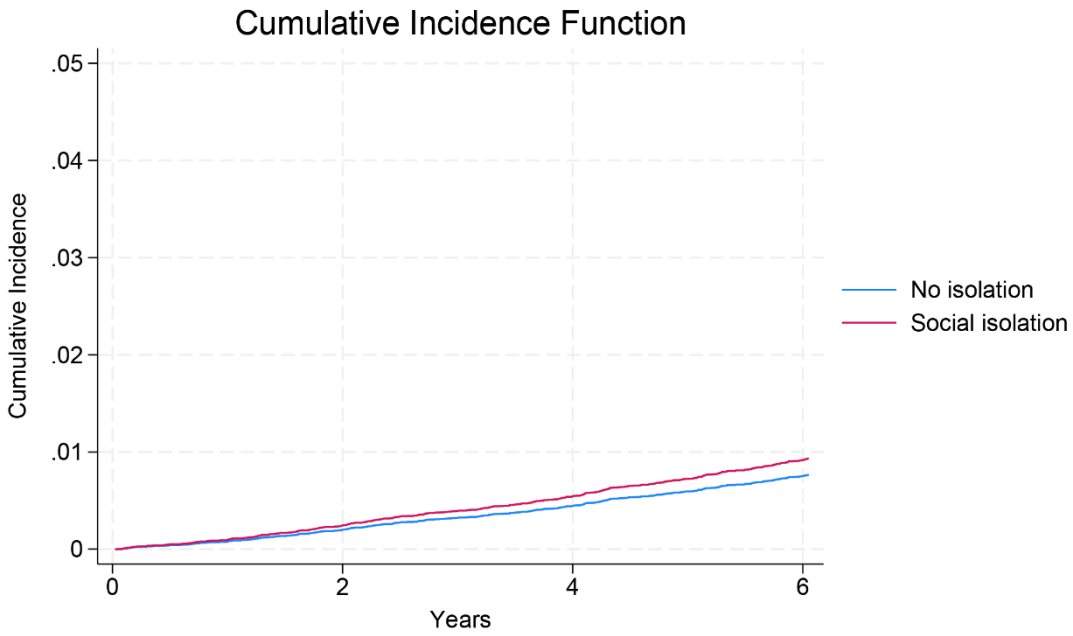




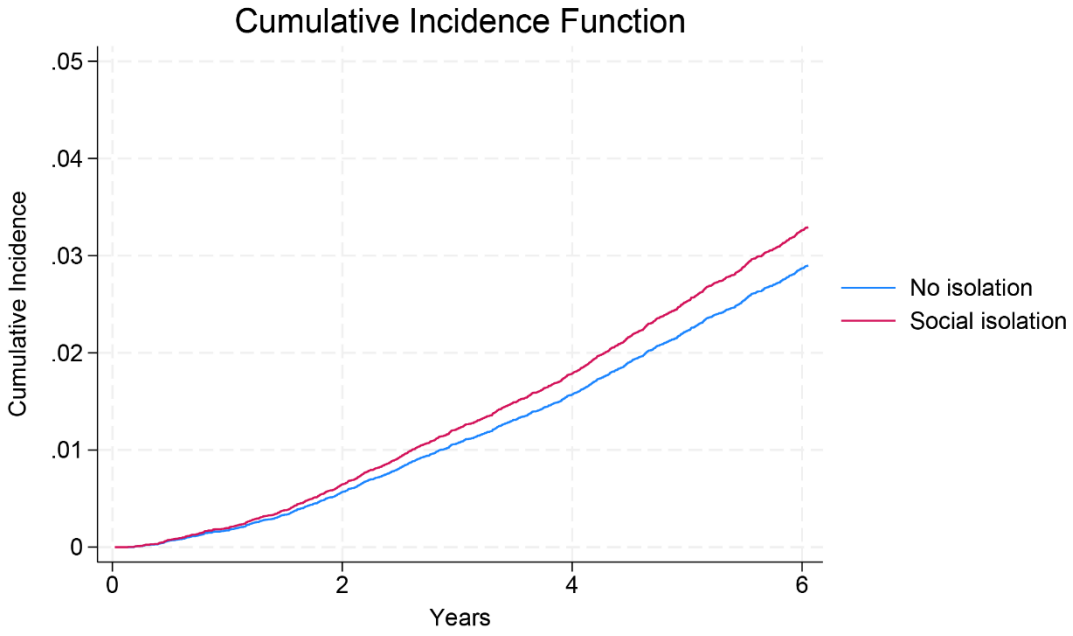


eFigure 19. Cumulative Incidence Functions for Cardiovascular Disease Mortality and Neoplasm Mortality by Social Isolation

Cardiovascular disease mortality



Neoplasm mortality



eTable 1. Number (Percentage) of Missing Values

Varibles	N (%)
Age	0 (0%)
Gender	0 (0%)
Education	620 (1.7%)
Household equivalized income	6457 (17.6%)
Population density	0 (0%)
Marital status	594 (1.6%)
Employment	4392 (12%)
Smoking	3456 (9.4%)
Drinking alcohol	2091 (5.7%)
Walking	2152 (5.9%)
Eating meat and fish every day	2131 (5.8%)
Eating fruits and vegetables every day	1895 (5.2%)
Taking health checks	1473 (4%)
Geriatric Depression Scale	6015 (16.4%)
Body mass index	1419 (3.9%)
Self-rated health	374 (1%)
Self reported hypertension	10367 (28.3%)
Self reported diabetes	10367 (28.3%)
Self reported dislipidemia	10367 (28.3%)
Living alone	569 (1.6%)
Meeting with friends	2450 (6.7%)
Participation in sports groups	7545 (20.6%)
Participation in hobby groups	6444 (17.6%)
Participation in volunteer groups	8988 (24.6%)

eTable 2. Baseline Characteristics (Obtained From the 2010 Survey) of Unimputed Data (N = 36 589)

Baseline characteristics	Total	Social isolation		
		No	Yes	Missing
Number of participants, n (%)	36,589	25,934 (70.9%)	7,742 (21.2%)	2,913 (8.0%)
Age, mean (SD)	73.4 (5.9)	73.2 (5.7)	73.6 (6.3)	75.5 (6.4)
Gender (Female), n (%)	20382 (55.7%)	15055 (58.1%)	3614 (46.7%)	1713 (58.8%)
Socioeconomic status				
Education (10 years or more), n (%)	19542 (54.3%)	14244 (55.6%)	4067 (53.1%)	1231 (45.8%)
Household equivalized income (million JPY), mean (SD)	239.1 (158.1)	245.2 (159.7)	223 (151)	223.3 (158.4)
Population density (/km2), mean (SD)	4213.2 (3932.9)	4152.4 (3897.4)	4381 (4015.4)	4308.2 (4012.1)
Marital status (not married)	10041 (27.9%)	6118 (23.9%)	3044 (39.7%)	879 (32.5%)
Employment				
Current	7829 (24.3%)	5560 (24.2%)	1750 (24.6%)	519 (24.7%)
Retired	20250 (62.9%)	14440 (62.8%)	4513 (63.5%)	1297 (61.6%)
Never	4118 (12.8%)	2983 (13%)	846 (11.9%)	289 (13.7%)
Behavioural factors				
Smoking				
Never, n (%)	20253 (61.1%)	14938 (63.4%)	3803 (53.2%)	1512 (63%)
Quit n (%)	9002 (27.2%)	6169 (26.2%)	2211 (30.9%)	622 (25.9%)
Current, n (%)	3878 (11.7%)	2471 (10.5%)	1140 (15.9%)	267 (11.1%)

Drinking alcohol				
Never, n (%)	12633 (36.6%)	9079 (37%)	2730 (37%)	824 (31.6%)
Quit n (%)	962 (2.8%)	614 (2.5%)	273 (3.7%)	75 (2.9%)
Current, n (%)	20903 (60.6%)	14821 (60.5%)	4372 (59.3%)	1710 (65.5%)
Walking				
<30min. , n (%)	11012 (32%)	7454 (29.7%)	2847 (37.9%)	711 (39.4%)
30-59 min. , n (%)	12227 (35.5%)	9116 (36.3%)	2552 (34%)	559 (31%)
60-89 min. , n (%)	5576 (16.2%)	4269 (17%)	1045 (13.9%)	262 (14.5%)
≥90min. , n (%)	5622 (16.3%)	4293 (17.1%)	1058 (14.1%)	271 (15%)
Eating meat and fish every day	14659 (42.5%)	10802 (44.1%)	2788 (38%)	1069 (40.9%)
Eating fruits and vegetables every day	27802 (80.1%)	20234 (82.1%)	5509 (74.6%)	2059 (77.3%)
Taking health checks				
Never, n (%)	5640 (16.1%)	3482 (13.9%)	1581 (21.1%)	577 (21.9%)
More than 4 years ago, n (%)	3615 (10.3%)	2447 (9.8%)	917 (12.3%)	251 (9.5%)
2-3 years ago, n (%)	4227 (12%)	2983 (11.9%)	934 (12.5%)	310 (11.8%)
Within 1 year, n (%)	21634 (61.6%)	16090 (64.4%)	4044 (54.1%)	1500 (56.9%)
Psychological factors				
Geriatric Depression Scale ≥ 5	7944 (26%)	4892 (22.3%)	2473 (37.1%)	579 (28.7%)
Physiological factors				
Body mass index				

<18.5kg/m^2, n (%)	2495 (6.8%)	1584 (6.1%)	685 (8.8%)	226 (7.8%)
18.5-25kg/m^2, n (%)	25198 (68.9%)	18126 (69.9%)	5213 (67.3%)	1859 (63.8%)
25-30kg/m^2, n (%)	6799 (18.6%)	4936 (19%)	1403 (18.1%)	460 (15.8%)
≥30kg/m^2, n (%)	678 (1.9%)	460 (1.8%)	149 (1.9%)	69 (2.4%)
Self-rated health (1=poor, 4=excellent), mean (SD)	3 (0.6)	3 (0.6)	2.9 (0.6)	2.9 (0.6)
Self reported hypertension, n (%)	14105 (53.8%)	10105 (54.4%)	2886 (52.3%)	1114 (51.9%)
Self reported diabetes, n (%)	4230 (16.1%)	2925 (15.8%)	970 (17.6%)	335 (15.6%)
Self reported dislipidemia, n (%)	3591 (13.7%)	2626 (14.1%)	719 (13%)	246 (11.5%)

eTable 3. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and All-Cause Mortality Based on Logistic Regression

	Odds ratio	Additive (RERI)		Multiplicative (ROR)	
Moderator level	Estimate (95%CI)	Estimate (95%CI)	p value[a]	Estimate (95%CI)	p value[a]
Age					
Younger than 75	1.21 (1.07, 1.36)	Ref.		Ref.	
75 years or older	1.19 (1.05, 1.34)	-0.1 (-0.28, 0.07)	0.31	0.92 (0.79, 1.06)	0.34
Gender					
Male	1.19 (1.07, 1.32)	Ref.		Ref.	
Female	1.21 (1.04, 1.42)	-0.09 (-0.22, 0.05)	0.31	1.01 (0.86, 1.19)	0.87
Education					
10 or more years	1.18 (1.05, 1.33)	Ref.		Ref.	
less than 10 years	1.21 (1.04, 1.4)	0.07 (-0.11, 0.24)	0.44	1.08 (0.91, 1.27)	0.48
Income (10 thousand Japanese yen)					
Tertile 1 (6.9-159.0)	1.05 (0.91, 1.2)	Ref.		Ref.	
Tertile 2 (159.2-247.5)	1.29 (1.12, 1.49)	0.22 (0.03, 0.42)	0.07	1.19 (1, 1.43)	0.13
Tertile 3 (247.6-1300)	1.27 (1.06, 1.53)	0.26 (0.04, 0.49)	0.07	1.25 (1.01, 1.53)	0.12
Population density (/km2)					
Tertile 1 (19.7-1586.0)	1.07 (0.88, 1.29)	Ref.		Ref.	
Tertile 2 (1616.6-4342.1)	1.1 (0.95, 1.27)	0.11 (-0.15, 0.37)	0.44	1.1 (0.87, 1.39)	0.48
Tertile 3 (4432.3-22279.2)	1.47 (1.26, 1.72)	0.34 (0.1, 0.58)	0.03	1.45 (1.16, 1.82)	0.01
Marital status					
Married	1.13 (1.01, 1.28)	Ref.		Ref.	
Not married	1.33 (1.15, 1.53)	0.21 (0.01, 0.4)	0.08	1.15 (0.98, 1.35)	0.16
Employment					
Current	0.98 (0.81, 1.18)	-0.32 (-0.54, -0.11)	0.03	0.75 (0.62, 0.92)	0.03
Retired	1.27 (1.14, 1.43)	Ref.		Ref.	
Never	1.09 (0.89, 1.35)	-0.15 (-0.4, 0.1)	0.31	0.87 (0.71, 1.07)	0.30

CI: confidence interval; RERI: relative excess risk due to interaction (additive interaction estimates); ROR: ratio of odds ratio (multiplicative interaction estimates).

[a]P values are corrected with Benjamini–Hochberg procedure.

eTable 4. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Cardiovascular Diseases Mortality Based on Logistic Regression

Moderator level	Odds ratio	Additive (RERI)		Multiplicative (ROR)	
	Estimate (95%CI)	Estimate (95%CI)	p value[a]	Estimate (95%CI)	p value[a]
Age					
Younger than 75	1.33 (0.94, 1.89)	Ref.		Ref.	
75 years or older	1.18 (0.89, 1.56)	-0.52 (-1.15, 0.11)	0.51	0.66 (0.44, 0.99)	0.23
Gender					
Male	1.27 (0.95, 1.7)	Ref.		Ref.	
Female	1.13 (0.8, 1.58)	-0.08 (-0.51, 0.35)	0.89	0.98 (0.64, 1.49)	0.92
Education					
10 or more years	1.1 (0.81, 1.5)	Ref.		Ref.	
less than 10 years	1.36 (0.99, 1.88)	0.3 (-0.11, 0.72)	0.51	1.39 (0.9, 2.12)	0.34
Income (10 thousand Japanese yen)					
Tertile 1 (6.9-159.0)	1.05 (0.71, 1.54)	Ref.		Ref.	
Tertile 2 (159.2-247.5)	1.61 (1.15, 2.25)	0.56 (0.09, 1.03)	0.19	1.71 (1.09, 2.69)	0.20
Tertile 3 (247.6-1300)	0.94 (0.6, 1.47)	0.07 (-0.45, 0.58)	0.89	1.1 (0.61, 2)	0.84
Population density (/km2)					
Tertile 1 (19.7-1586.0)	1.09 (0.76, 1.56)	Ref.		Ref.	
Tertile 2 (1616.6-4342.1)	1.12 (0.73, 1.73)	0.17 (-0.47, 0.81)	0.87	1.12 (0.67, 1.87)	0.84
Tertile 3 (4432.3-22279.2)	1.5 (1.04, 2.17)	0.38 (-0.23, 1)	0.56	1.47 (0.92, 2.35)	0.34
Marital status					
Married	1.25 (0.94, 1.65)	Ref.		Ref.	
Not married	1.14 (0.79, 1.64)	-0.04 (-0.61, 0.53)	0.89	0.93 (0.61, 1.42)	0.84
Employment					
Current	1.5 (1, 2.26)	0.2 (-0.41, 0.8)	0.87	1.15 (0.71, 1.87)	0.84
Retired	1.21 (0.92, 1.6)	Ref.		Ref.	
Never	1.02 (0.61, 1.72)	-0.29 (-0.96, 0.39)	0.81	0.78 (0.45, 1.33)	0.71

CI: confidence interval; RERI: relative excess risk due to interaction (additive interaction estimates); ROR: ratio of odds ratio (multiplicative interaction estimates).

[a]P values are corrected with Benjamini–Hochberg procedure.

eTable 5. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Neoplasms Mortality Based on Logistic Regression

Moderator level	Odds ratio	Additive (RERI)		Multiplicative (ROR)	
	Estimate (95%CI)	Estimate (95%CI)	p value[a]	Estimate (95%CI)	p value[a]
Age					
Younger than 75	1.17 (0.99, 1.39)	Ref.		Ref.	
75 years or older	1.12 (0.95, 1.31)	-0.06 (-0.33, 0.2)	0.64	0.93 (0.75, 1.16)	0.67
Gender					
Male	1.15 (1, 1.32)	Ref.		Ref.	
Female	1.11 (0.9, 1.37)	-0.08 (-0.26, 0.1)	0.53	0.98 (0.78, 1.22)	0.83
Education					
10 or more years	1.05 (0.91, 1.21)	Ref.		Ref.	
less than 10 years	1.24 (1.02, 1.51)	0.17 (-0.05, 0.4)	0.22	1.2 (0.95, 1.52)	0.21
Income (10 thousands Japanese yen)					
Tertile 1 (6.9-159.0)	0.91 (0.75, 1.09)	Ref.		Ref.	
Tertile 2 (159.2-247.5)	1.27 (1.05, 1.53)	0.31 (0.08, 0.54)	0.04	1.37 (1.07, 1.76)	0.06
Tertile 3 (247.6-1300)	1.27 (1.02, 1.6)	0.35 (0.1, 0.61)	0.04	1.44 (1.09, 1.9)	0.06
Population density (/km2)					
Tertile 1 (19.7-1586.0)	1.02 (0.82, 1.27)	Ref.		Ref.	
Tertile 2 (1616.6-4342.1)	1.04 (0.88, 1.24)	0.07 (-0.23, 0.38)	0.64	1.06 (0.8, 1.4)	0.78
Tertile 3 (4432.3-22279.2)	1.38 (1.11, 1.7)	0.22 (-0.06, 0.49)	0.22	1.35 (1, 1.81)	0.10
Marital status					
Married	1.09 (0.94, 1.27)	Ref.		Ref.	
Not married	1.25 (1.02, 1.52)	0.11 (-0.16, 0.39)	0.53	1.08 (0.86, 1.37)	0.67
Employment					
Current	0.93 (0.71, 1.21)	-0.37 (-0.68, -0.07)	0.05	0.72 (0.55, 0.95)	0.06
Retired	1.27 (1.1, 1.48)	Ref.		Ref.	
Never	0.76 (0.54, 1.09)	-0.41 (-0.76, -0.06)	0.05	0.67 (0.48, 0.95)	0.06

CI: confidence interval; RERI: relative excess risk due to interaction (additive interaction estimates); ROR: ratio of odds ratio (multiplicative interaction estimates).

[a]P values are corrected with Benjamini–Hochberg procedure.

eTable 6. Robustness to Unmeasured Confounding (E-Values) of Associations Between Social Isolation and All-Cause Mortality, Cardiovascular Diseases Mortality, and Neoplasms Mortality

	All-cause mortality		CVD mortality		Neoplasms mortality	
Moderator level	Effect estimate	CI limit	Effect estimate	CI limit	Effect estimate	CI limit
Age						
Younger than 75	1.71	1.35	2.00	1.00	1.62	1.00
75 years or older	1.65	1.29	1.63	1.00	1.48	1.00
Gender						
Male	1.66	1.34	1.86	1.00	1.56	1.00
Female	1.72	1.25	1.50	1.00	1.46	1.00
Education						
10 or more years	1.65	1.29	1.44	1.00	1.28	1.00
less than 10 years	1.71	1.25	2.06	1.00	1.79	1.17
Income (10 thousands Japanese yen)						
Tertile 1 (6.9-159.0)	1.26	1.00	1.26	1.00	1.44	1.00
Tertile 2 (159.2-247.5)	1.91	1.49	2.60	1.58	1.85	1.28
Tertile 3 (247.6-1300)	1.87	1.32	1.33	1.00	1.86	1.14
Population density (/km2)						
Tertile 1 (19.7-1586.0)	1.34	1.00	1.39	1.00	1.16	1.00
Tertile 2 (1616.6-4342.1)	1.44	1.00	1.49	1.00	1.26	1.00
Tertile 3 (4432.3-22279.2)	2.31	1.84	2.37	1.26	2.10	1.47
Marital status						
Married	1.52	1.10	1.80	1.00	1.40	1.00
Not married	1.98	1.58	1.53	1.00	1.80	1.18
Employment						
Current	1.18	1.00	2.37	1.00	1.37	1.00
Retired	1.87	1.53	1.71	1.00	1.86	1.43

Never	1.42	1.00	1.18	1.00	1.94	1.00

Abbreviations: CI, confidence interval; CVD, cardiovascular diseases.

eTable 7. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and All-Cause Mortality Based on Survival Regression

	Hazard ratio	Additive (RERI)		Multiplicative (RHR)	
Moderator level	Estimate (95%CI)	Estimate (95%CI)	p value[a]	Estimate (95%CI)	p value[a]
Age					
Younger than 75	1.21 (1.08, 1.36)	Ref.		Ref.	
75 years or older	1.17 (1.05, 1.29)	-0.15 (-0.32, 0.01)	0.12	0.87 (0.77, 1)	0.11
Gender					
Male	1.17 (1.06, 1.28)	Ref.		Ref.	
Female	1.2 (1.04, 1.38)	-0.04 (-0.16, 0.07)	0.47	1.05 (0.91, 1.22)	0.51
Education					
10 or more years	1.16 (1.05, 1.28)	Ref.		Ref.	
less than 10 years	1.19 (1.04, 1.37)	0.08 (-0.07, 0.24)	0.40	1.09 (0.94, 1.26)	0.35
Income (10 thousands Japanese yen)					
Tertile 1 (6.9-159.0)	1.05 (0.93, 1.19)	Ref.		Ref.	
Tertile 2 (159.2-247.5)	1.25 (1.1, 1.41)	0.17 (0, 0.35)	0.12	1.15 (0.98, 1.35)	0.20
Tertile 3 (247.6-1300)	1.25 (1.06, 1.46)	0.23 (0.04, 0.43)	0.07	1.21 (1.01, 1.45)	0.11
Population density (/km2)					
Tertile 1 (19.7-1586.0)	1.07 (0.91, 1.26)	Ref.		Ref.	
Tertile 2 (1616.6-4342.1)	1.1 (0.97, 1.24)	0.09 (-0.14, 0.32)	0.47	1.07 (0.87, 1.32)	0.51
Tertile 3 (4432.3-22279.2)	1.43 (1.24, 1.64)	0.32 (0.1, 0.53)	0.03	1.4 (1.14, 1.71)	0.01
Marital status					
Married	1.12 (1.01, 1.25)	Ref.		Ref.	
Not married	1.27 (1.13, 1.44)	0.15 (-0.01, 0.32)	0.12	1.11 (0.97, 1.28)	0.24
Employment					
Current	0.99 (0.83, 1.18)	-0.27 (-0.46, -0.08)	0.03	0.79 (0.66, 0.94)	0.05
Retired	1.24 (1.12, 1.37)	Ref.		Ref.	
Never	1.09 (0.91, 1.32)	-0.09 (-0.31, 0.12)	0.47	0.91 (0.76, 1.08)	0.35

CI: confidence interval; RERI: relative excess risk due to interaction (additive interaction estimates); RHR: ratio of hazard ratio (multiplicative interaction estimates).

[a]P values are corrected with Benjamini–Hochberg procedure.

eTable 8. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Cardiovascular Diseases Mortality Based on Survival Regression

Moderator level	Hazard ratio	Additive (RERI)		Multiplicative (RHR)	
	Estimate (95%CI)	Estimate (95%CI)	p value[a]	Estimate (95%CI)	p value[a]
Age					
Younger than 75	1.34 (0.95, 1.9)	Ref.		Ref.	
75 years or older	1.18 (0.89, 1.55)	-0.53 (-1.16, 0.09)	0.47	0.65 (0.44, 0.98)	0.19
Gender					
Male	1.27 (0.95, 1.69)	Ref.		Ref.	
Female	1.13 (0.82, 1.58)	-0.07 (-0.62, 0.49)	0.91	0.99 (0.65, 1.5)	0.96
Education					
10 or more years	1.11 (0.82, 1.49)	Ref.		Ref.	
less than 10 years	1.36 (0.99, 1.88)	0.3 (-0.11, 0.71)	0.50	1.38 (0.91, 2.1)	0.33
Income (10 thousands Japanese yen)					
Tertile 1 (6.9-159.0)	1.05 (0.71, 1.54)	Ref.		Ref.	
Tertile 2 (159.2-247.5)	1.6 (1.15, 2.23)	0.55 (0.09, 1.02)	0.20	1.71 (1.09, 2.67)	0.19
Tertile 3 (247.6-1300)	0.94 (0.6, 1.47)	0.06 (-0.45, 0.57)	0.91	1.08 (0.6, 1.93)	0.89
Population density (/km2)					
Tertile 1 (19.7-1586.0)	1.09 (0.76, 1.55)	Ref.		Ref.	
Tertile 2 (1616.6-4342.1)	1.12 (0.73, 1.73)	0.16 (-0.47, 0.8)	0.88	1.11 (0.67, 1.85)	0.89
Tertile 3 (4432.3-22279.2)	1.5 (1.05, 2.16)	0.39 (-0.23, 1.01)	0.54	1.47 (0.92, 2.34)	0.33
Marital status					
Married	1.24 (0.94, 1.64)	Ref.		Ref.	
Not married	1.14 (0.8, 1.64)	-0.03 (-0.59, 0.53)	0.91	0.93 (0.61, 1.42)	0.89
Employment					
Current	1.51 (1.01, 2.25)	0.2 (-0.4, 0.79)	0.87	1.17 (0.72, 1.88)	0.88
Retired	1.21 (0.92, 1.59)	Ref.		Ref.	
Never	1.03 (0.62, 1.72)	-0.27 (-0.93, 0.39)	0.85	0.79 (0.46, 1.33)	0.75

CI: confidence interval; RERI: relative excess risk due to interaction (additive interaction estimates); RHR: ratio of hazard ratio (multiplicative interaction estimates).

[a]P values are corrected with Benjamini–Hochberg procedure.

eTable 9. Additive and Multiplicative Estimates of Effect Modification for the Associations Between Social Isolation and Neoplasms Mortality Based on Survival Regression

Moderator level	Hazard ratio	Additive (RERI)		Multiplicative (RHR)	
	Estimate (95%CI)	Estimate (95%CI)	p value[a]	Estimate (95%CI)	p value[a]
Age					
Younger than 75	1.18 (0.99, 1.39)	Ref.		Ref.	
75 years or older	1.12 (0.96, 1.31)	-0.07 (-0.33, 0.19)	0.66	0.93 (0.75, 1.15)	0.67
Gender					
Male	1.15 (1.01, 1.32)	Ref.		Ref.	
Female	1.11 (0.9, 1.37)	-0.08 (-0.35, 0.2)	0.66	0.98 (0.8, 1.22)	0.89
Education					
10 or more years	1.05 (0.91, 1.21)	Ref.		Ref.	
less than 10 years	1.25 (1.03, 1.51)	0.18 (-0.04, 0.4)	0.21	1.21 (0.96, 1.52)	0.18
Income (10 thousands Japanese yen)					
Tertile 1 (6.9-159.0)	0.92 (0.77, 1.1)	Ref.		Ref.	
Tertile 2 (159.2-247.5)	1.26 (1.04, 1.52)	0.29 (0.06, 0.52)	0.05	1.35 (1.06, 1.72)	0.07
Tertile 3 (247.6-1300)	1.28 (1.03, 1.6)	0.34 (0.1, 0.59)	0.05	1.44 (1.1, 1.88)	0.07
Population density (/km2)					
Tertile 1 (19.7-1586.0)	1.03 (0.83, 1.27)	Ref.		Ref.	
Tertile 2 (1616.6-4342.1)	1.04 (0.88, 1.24)	0.06 (-0.24, 0.37)	0.68	1.05 (0.8, 1.38)	0.80
Tertile 3 (4432.3-22279.2)	1.37 (1.12, 1.68)	0.21 (-0.06, 0.48)	0.21	1.33 (1, 1.77)	0.11
Marital status					
Married	1.09 (0.95, 1.26)	Ref.		Ref.	
Not married	1.24 (1.02, 1.5)	0.11 (-0.16, 0.38)	0.63	1.08 (0.86, 1.35)	0.67
Employment					
Current	0.94 (0.72, 1.22)	-0.36 (-0.65, -0.06)	0.05	0.72 (0.55, 0.95)	0.07
Retired	1.27 (1.1, 1.46)	Ref.		Ref.	
Never	0.78 (0.56, 1.09)	-0.4 (-0.73, -0.07)	0.05	0.69 (0.49, 0.96)	0.07

CI: confidence interval; RERI: relative excess risk due to interaction (additive interaction estimates); RHR: ratio of hazard ratio (multiplicative interaction estimates).

[a]P values are corrected with Benjamini–Hochberg procedure.