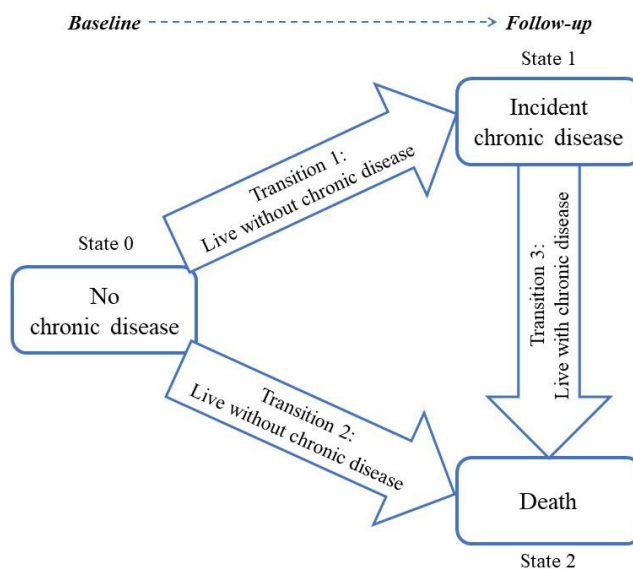


## Supplementary Methods

### Statistical method used for estimating the difference in life expectancy.

To calculate the life expectancy free of chronic diseases, we considered three health status, state 0 (free of disease), state 1 (presence of disease), and state 2 (death). Between health states, three possible transitions were evaluated, transition 1 (from non-disease to incident disease), transition 2 (from non-disease to death), and transition 3 (from disease diagnosis to death)<sup>1</sup>. As shown in Diagram 1 below, all participants started from state 0 (free of disease) at baseline.

**Diagram 1**, Schematic diagram for three transitions over the time of follow-up.



We integrated information from three sources to build multistate lifetable and calculated the differences in life expectancy between combined categories of loneliness and social isolation (henceforth “exposure groups”), **Diagram 2:**

#### ***For each transition:***

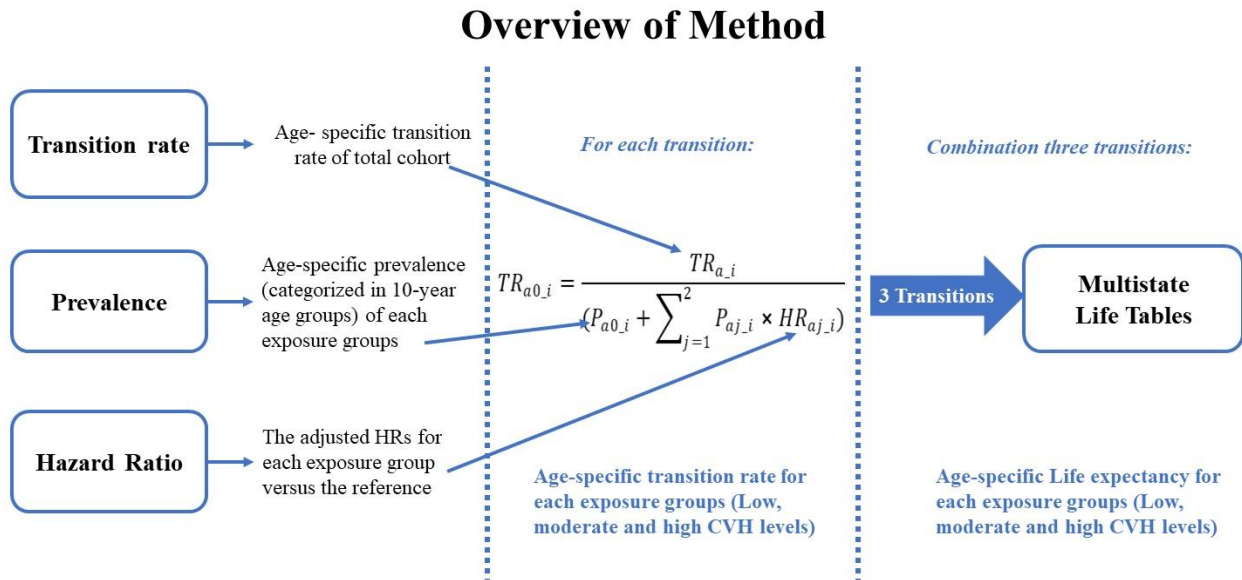
- (1) Transition rate by a single year of age (from 50 to 100 years old) for total cohort.

(2) The multiple adjusted Hazard Ratio (HR) in each exposure group (loneliness only, social isolation only, and both loneliness and social isolation) versus the reference (non-loneliness or social isolation).

(3) The age-specific population prevalence (categorized in 10-year age groups) of each exposure group.

Age-specific transition rates for each exposure groups ( $TR_{aj_i}$ ) were calculated by weighting the (1) transition rate of total cohort with the corresponding (2) HR and (3) prevalence. To be specific, we inferred the age-specific transition rate appropriate for our reference group  $TR_{a0_i}$  as<sup>2</sup>:

$$TR_{a0_i} = \frac{TR_{a_i}}{(P_{a0_i} + \sum_{j=1}^2 P_{aj_i} \times HR_{aj_i})}$$



**Diagram 2.** An overview of multistate lifetable method.

For transition  $i$ , where  $TR_{a_i}$  is the transition rate of total cohort for age group  $a$ ,  $P_{aj_i}$  is the prevalence of exposure group  $j$ , and  $HR_{aj_i}$  is the adjusted hazard ratio in comparison of exposure

group  $j$  versus reference group ( $j = 0$ ). The age-specific transition rates in each of the non-reference exposure groups were then inferred in turn by multiplying the age-specific transition rate for the reference group  $TR_{a0_i}$  by the hazard ratios  $HR_{aj_i}$ :

$$TR_{aj_i} = TR_{a0_i} \times HR_{aj_i} (j>0)$$

For each of the exposure groups, a set of age-specific transition rates (from 3 transitions) were calculated and were subsequently combined to build a multistate lifetable. For the main analysis in this study, we created a total of 4 multistate lifetables for combined categories of loneliness and social isolation in men and women, respectively.

We built the multistate lifetable starting at age 50 years and ending at 100 years by single-year age intervals. Probability of survival between ages  $x$  and  $x + 1$  was calculated based on probability of transitions (transition rates) between ages  $x$  and  $x + 1$  assuming that survivor function declines linearly between ages  $x$  and  $x + 1$ <sup>3,4</sup>. The life expectancy at any given age was derived by dividing the total person-years that would be lived beyond age  $x$  by the number of people who survived to that age interval.

## **Lifestyle assessment and definition**

Healthy lifestyle score was created based on information about 5 modifiable lifestyle factors<sup>5-7</sup>, including smoking, body mass index, physical activity, diet and sleep hours. A touch-screen questionnaire was used to collect self-reported information on smoking (never, former, and current), physical activity (minutes of moderate or vigorous physical activity or an equivalent combination per week), diet, and sleep hours. No current smoking (former and never) was defined as healthy or at low risk. Participants who spent at least 150 min/week doing moderate or vigorous activity or an equivalent combination were defined as healthy or at low risk, according to guidelines for physical activity in adults<sup>8</sup>. Healthy diet was assessed based on 7 food groups, including vegetable intake ( $\geq 3$  servings/day), fruit intake ( $\geq 3$  servings/day), fish intake ( $\geq 2$  servings/week), processed meat intake ( $\leq 1$  serving/week), unprocessed red meats ( $\leq 1.5$  servings/week), whole grains ( $\geq 3$  servings/day) and refined grains ( $\leq 1.5$  servings/day). Participants who consumed at least 4 of 7 food factors were defined as healthy or at low risk<sup>9</sup>. Participants who slept 7–8 h per day were defined as healthy or at low risk. Height and weight were measured during the assessment visit, and body mass index was calculated as weight in kilograms divided by height in meters squared ( $\text{kg}/\text{m}^2$ ). We defined a low risk or normal weight as a body mass index greater than  $18.5 \text{ kg}/\text{m}^2$  and lower than  $25 \text{ kg}/\text{m}^2$ .

**Supplementary Table 1. Codes used in the UK Biobank study to identify diseases.**

| <b>Major Chronic diseases</b> | <b>ICD-10 (incidence and baseline)</b>                                                                                                 | <b>ICD-9 (baseline)</b>                                                                                                     | <b>Self-reported UK Biobank field code (baseline)</b> |
|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| Cardiovascular disease        | Coronary heart disease: I20-I25<br>Stroke: I60, I61, I63, I64<br>Heart failure: I11.0, I13.0, I13.2, I50.X<br>Atrial fibrillation: I48 | Coronary heart disease: 410-414<br>Stroke: 430, 431, 434, 436<br>Heart failure: 402, 404, 428<br>Atrial fibrillation: 427.3 | 20002, 6150                                           |
| Diabetes                      | Type 2 diabetes: E11<br>Type 1 diabetes at baseline: E10                                                                               | 250                                                                                                                         | 20002, 2443                                           |
| Cancer                        | C00-C97, except C44 (non-melanoma skin cancer)                                                                                         | 140–209 except 173 (non-melanoma skin cancer)                                                                               | 20001, 2453                                           |
| Neurodegenerative disease     | Dementia: F00, F01, F02, F03, F05.1, F10.6, G30, G31, A81.0, I67.3<br>Parkinson's disease: G20                                         | Dementia: 290.2, 290.3, 290.4, 291.2, 294.1, 331.0, 331.1, 331.2, 331.5<br>Parkinson's disease: 332.0                       | 20002                                                 |
| Chronic respiratory disease   | Asthma: J45, J56<br>Chronic obstructive pulmonary disease: J43, J44                                                                    | Asthma: 493<br>Chronic obstructive pulmonary disease: 492, 492.0, 492.8, 496.X                                              | 20002, 6152                                           |
| Depression <sup>a</sup>       | F32, F33, F34, F38, F39                                                                                                                | 319.9                                                                                                                       | 20002, 2050, 2060                                     |
| Anxiety <sup>b</sup>          | F40, F41                                                                                                                               | 300.0, 300.2                                                                                                                | 20002, 2070, 2080                                     |

ICD-10, International Classification of Diseases, Tenth Revision; ICD-9, International Classification of Diseases, Ninth Revision.

<sup>a</sup>, 2050 and 2060 were PHQ-2 questions used to define a depression score; participants with a score equal to or higher than 3 were identified as having depression and excluded from baseline<sup>10</sup>.

<sup>b</sup>, 2070 and 2080 were used to define an anxiety score; participants with a score equal to or higher than 3 were identified as having anxiety and excluded from baseline<sup>11</sup>.

**Supplementary Table 2.** Sample size for the joint categories of loneliness or social isolation status and levels of healthy lifestyle.

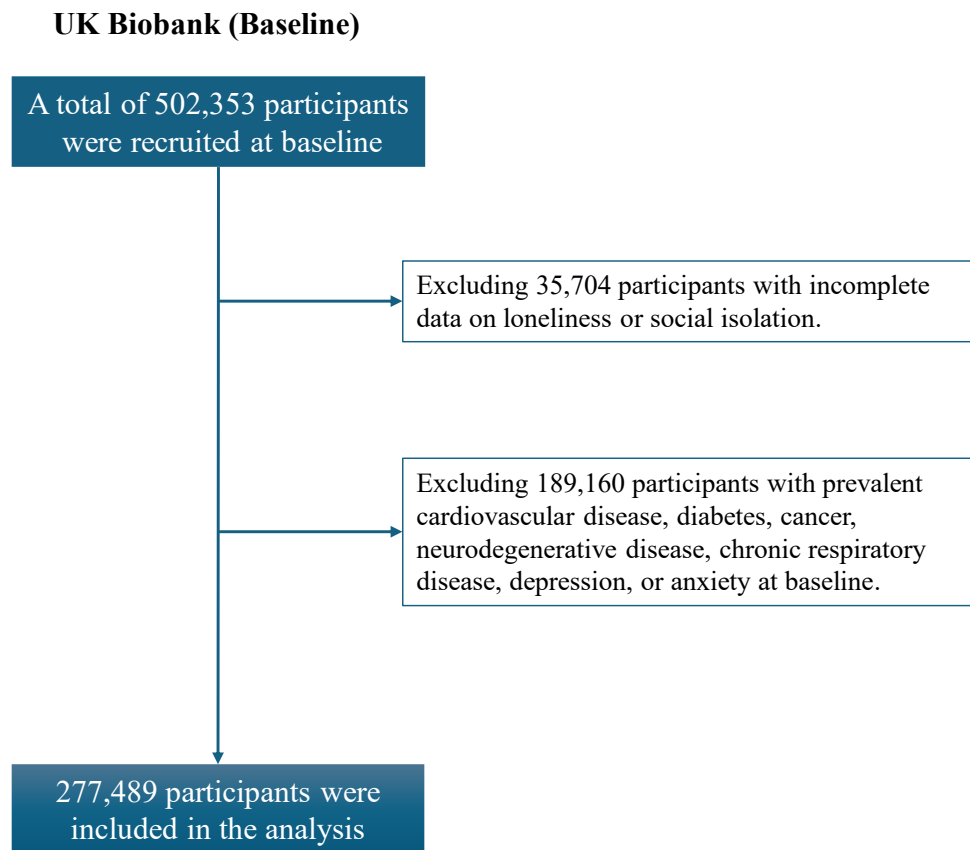
| Healthy Lifestyles                | Women                      |                        | Men                        |                        |
|-----------------------------------|----------------------------|------------------------|----------------------------|------------------------|
|                                   | <i>Non-loneliness</i>      | <i>Loneliness</i>      | <i>Non-loneliness</i>      | <i>Loneliness</i>      |
| Unhealthy (0-2 favorable factors) | 32032                      | 2012                   | 24318                      | 1430                   |
| Medium (3 favorable factors)      | 39291                      | 1713                   | 41351                      | 1769                   |
| Healthy (4-5 favorable factors)   | 41597                      | 1420                   | 67100                      | 2153                   |
|                                   | <i>Non-social isolated</i> | <i>Social isolated</i> | <i>Non-social isolated</i> | <i>Social isolated</i> |
| Unhealthy (0-2 favorable factors) | 30531                      | 3513                   | 23070                      | 2678                   |
| Medium (3 favorable factors)      | 37865                      | 3139                   | 39787                      | 3333                   |
| Healthy (4-5 favorable factors)   | 40154                      | 2863                   | 65679                      | 3574                   |

**Supplementary Table 3.** Baseline characteristics of low or high-risk lifestyle factors by combined categories of loneliness and SI status.

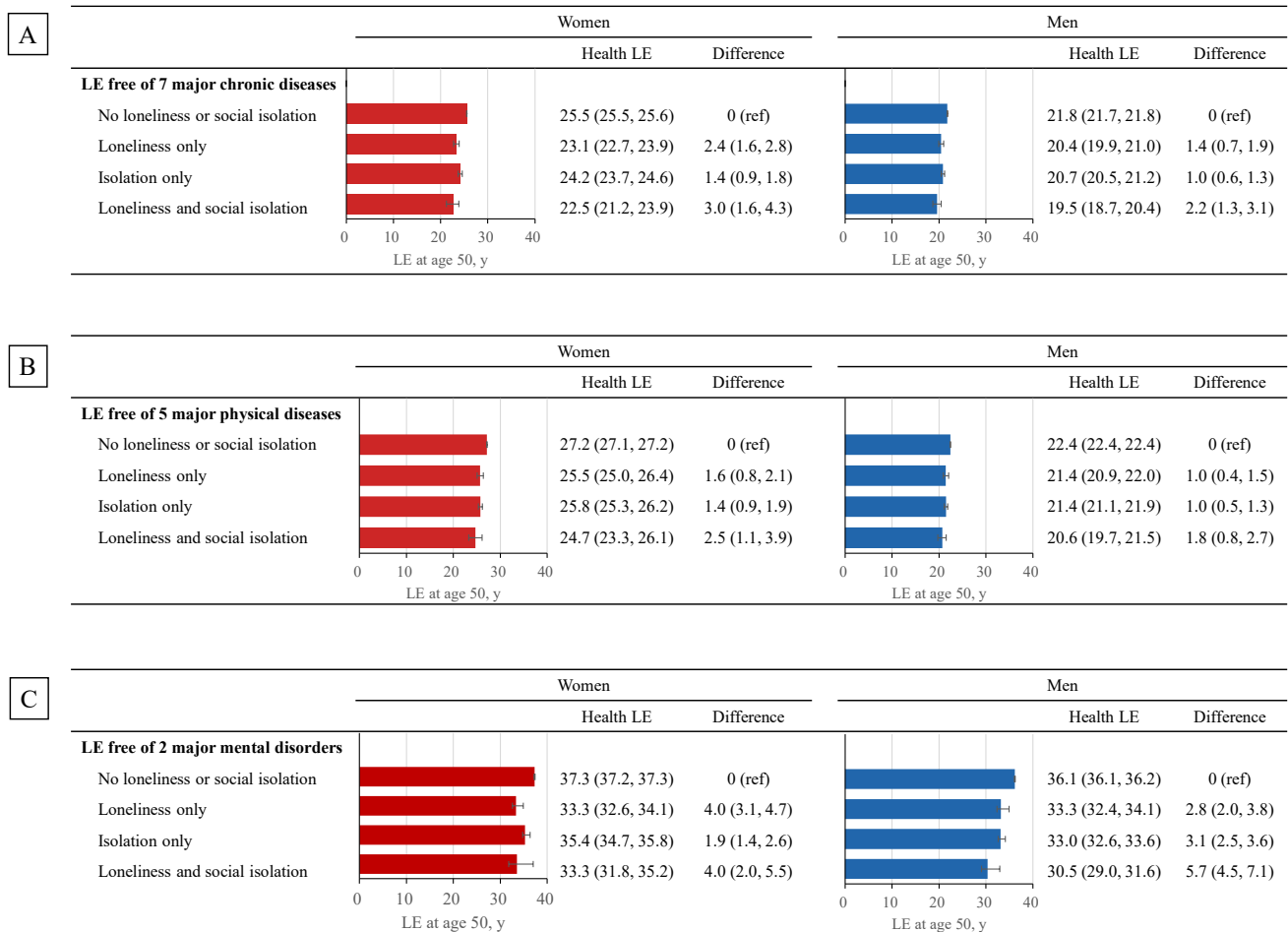
| Characteristic                  | No loneliness or SI | Loneliness only | SI only      | Loneliness and SI |
|---------------------------------|---------------------|-----------------|--------------|-------------------|
| <b>Smoking, n (%)</b>           |                     |                 |              |                   |
| Non-current smoking             | 214208 (91.4)       | 7652 (87.9)     | 14860 (84.6) | 1687 (81.5)       |
| Current smoking                 | 20063 (5.6)         | 1053 (12.1)     | 2702 (15.4)  | 384 (18.5)        |
| <b>Body Mass Index, n (%)</b>   |                     |                 |              |                   |
| Normal Body Mass Index          | 84497 (36.1)        | 2828 (32.5)     | 6249 (35.6)  | 703 (33.9)        |
| Abnormal Body Mass Index        | 149774 (63.9)       | 5877 (67.5)     | 11313 (64.4) | 1368 (66.1)       |
| <b>Physical activity, n (%)</b> |                     |                 |              |                   |
| Regular physical activity       | 144466 (61.7)       | 5071 (58.3)     | 8465 (48.2)  | 955 (46.1)        |
| Irregular physical activity     | 89805 (38.3)        | 3634 (41.8)     | 9097 (51.8)  | 1116 (53.9)       |
| <b>Diet, n (%)</b>              |                     |                 |              |                   |
| Healthy diet                    | 159315 (68.0)       | 5320 (61.1)     | 11644 (66.3) | 1206 (58.2)       |
| Unhealthy diet                  | 74956 (32.0)        | 3385 (38.9)     | 5918 (33.7)  | 865 (41.8)        |
| <b>Sleep, n (%)</b>             |                     |                 |              |                   |
| Sleep 7- < 9 hours              | 170670 (72.9)       | 5561 (63.9)     | 11637 (66.3) | 1228 (59.3)       |
| Sleep < 7 or ≥ 8 hours          | 63601 (27.2)        | 3144 (36.1)     | 5925 (33.7)  | 843 (40.7)        |

SI, social isolation

**Supplementary Figure 1.** The flow chat of sample selection.

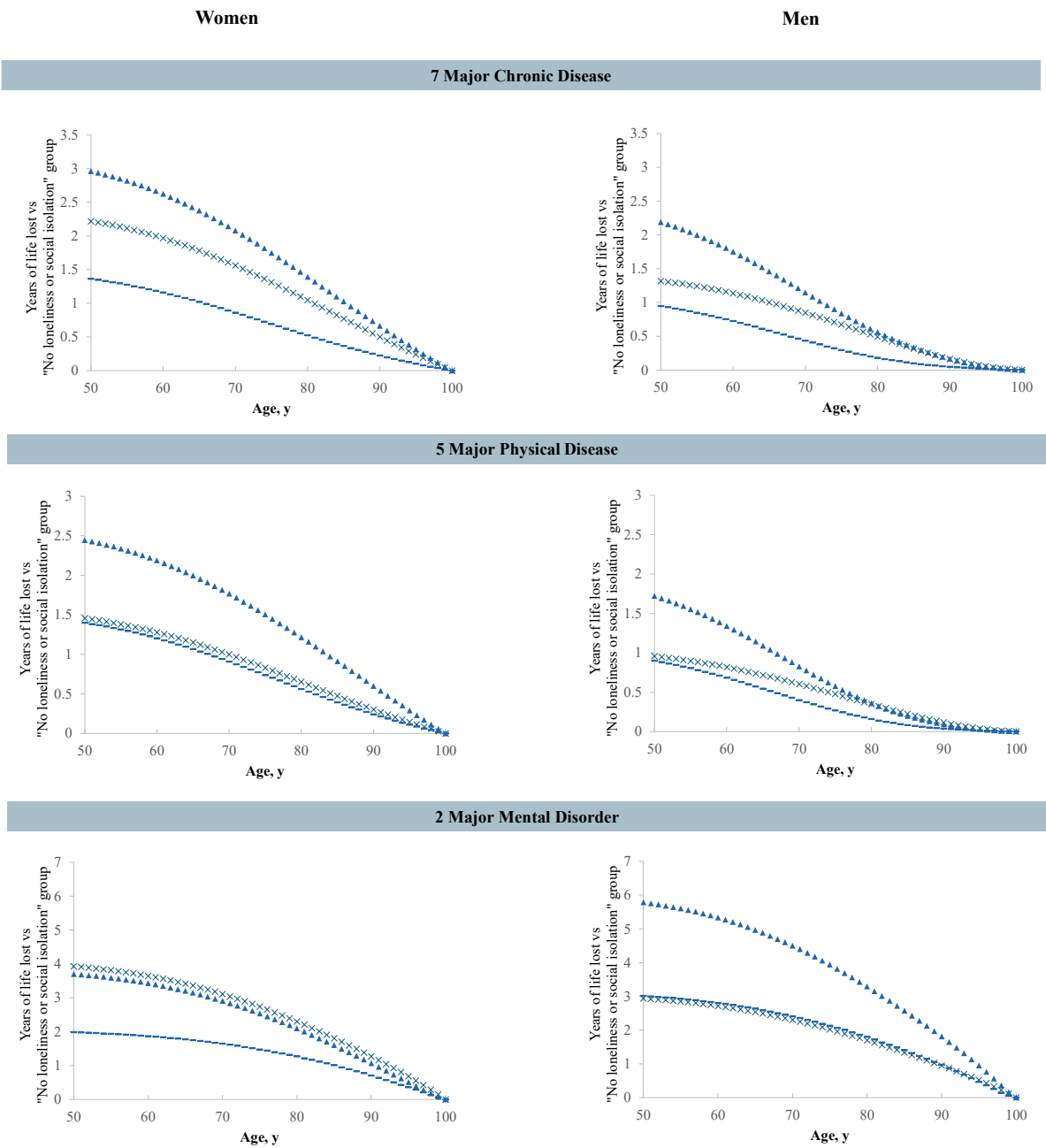


**Supplementary Figure 2.** The Estimated Life Expectancy Free of Chronic Diseases According to the Combined Categories of Loneliness and Social Isolation at Age 50 Years, excluding participants who became ill or died within two years.

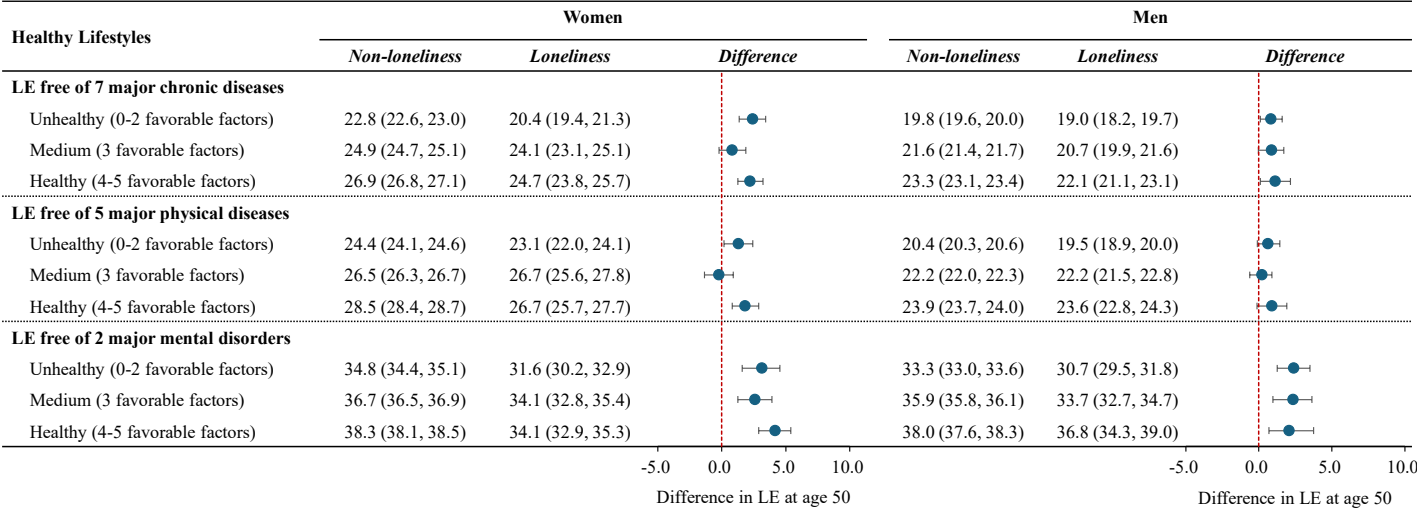


A. Life expectancy free of 7 chronic diseases for each exposure groups in women and man. B. Life expectancy free of 5 physical diseases for each exposure groups in women and man. C. Life expectancy free of 2 mental disorders for each exposure groups in women and man. The sample size used to estimate life expectancy is n=134,318 for women and n=143,171 for men. Data are presented as life expectancy and 95% Confidence intervals (CI). LE, life expectancy. Red color represents the life expectancy for women, and blue color represent the life expectancy for men. Life expectancy was calculated by multistate life tables. Source data are provided as a Source Data file.

**Supplementary Figure 3.** The Estimates of Cumulative Survival Time from 50 Years of age Onward Among Participants with Combined Categories of Loneliness and Social Isolation.

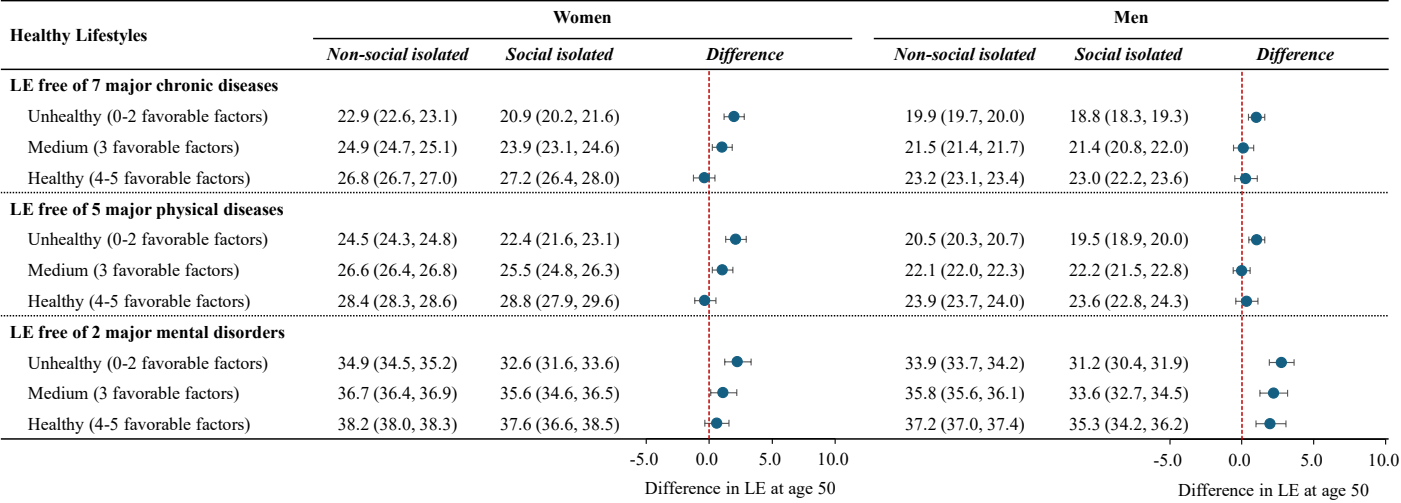


**Supplementary Figure 4.** Association of Loneliness and Healthy Lifestyle with Estimated Life Expectancy Free of Chronic Diseases at Age 50 Years.



LE, life expectancy

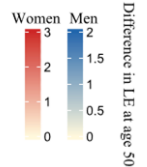
**Supplementary Figure 5.** Association of Social Isolation and Healthy Lifestyle with Estimated Life Expectancy Free of Chronic Diseases at Age 50 Years.



LE, life expectancy

**Supplementary Figure 6.** Association of Loneliness, Social Isolation and Healthy Lifestyle with Estimated Life Expectancy Free of Chronic Diseases at Age 50 Years.

| Lifestyle Behaviors               | Women             |                   |                 | Men               |                   |                 |
|-----------------------------------|-------------------|-------------------|-----------------|-------------------|-------------------|-----------------|
|                                   | Non-loneliness    | Loneliness        | Difference      | Non-loneliness    | Loneliness        | Difference      |
| <b>Loneliness</b>                 |                   |                   |                 |                   |                   |                 |
| <b>Smoking</b>                    |                   |                   |                 |                   |                   |                 |
| Current                           | 19.9 (19.5, 20.3) | 18.9 (17.3, 20.3) | 1.0 (-0.5, 2.8) | 18.0 (17.8, 18.3) | 16.8 (15.8, 17.8) | 1.2 (0.2, 2.3)  |
| Former                            | 24.6 (24.5, 24.8) | 22.7 (21.7, 23.7) | 1.9 (0.9, 2.9)  | 21.3 (21.1, 21.4) | 20.1 (19.3, 20.9) | 1.1 (0.3, 1.9)  |
| Never                             | 26.6 (26.4, 26.7) | 24.4 (23.6, 25.2) | 2.2 (1.3, 2.9)  | 23.0 (22.9, 23.1) | 22.2 (21.4, 22.9) | 0.8 (0.0, 1.6)  |
| <b>Body Mass Index</b>            |                   |                   |                 |                   |                   |                 |
| ≥ 30 kg/m <sup>2</sup>            | 22.2 (22.0, 22.5) | 21.2 (20.1, 22.2) | 1.1 (0.0, 2.2)  | 19.2 (19.0, 19.4) | 18.4 (17.5, 19.2) | 0.8 (-0.1, 1.8) |
| ≥ 25 and < 30 kg/m <sup>2</sup>   | 25.7 (25.5, 25.8) | 23.3 (22.1, 24.4) | 2.2 (1.2, 3.1)  | 22.0 (21.9, 22.1) | 20.8 (20.2, 21.6) | 1.2 (0.4, 1.8)  |
| ≥ 18.5 and < 25 kg/m <sup>2</sup> | 27.1 (26.9, 27.3) | 24.6 (23.6, 25.6) | 2.5 (1.5, 3.6)  | 23.4 (23.2, 23.6) | 21.9 (20.8, 22.9) | 1.5 (0.5, 2.6)  |
| <b>Physical Activity</b>          |                   |                   |                 |                   |                   |                 |
| 0 minute                          | 24.1 (23.8, 24.4) | 21.5 (20.2, 22.6) | 2.6 (1.4, 4.0)  | 20.5 (20.3, 20.8) | 18.5 (17.3, 19.5) | 2.1 (1.0, 3.3)  |
| > 0 and < 150 minutes             | 25.1 (24.9, 25.4) | 23.3 (22.1, 24.4) | 1.9 (0.8, 3.1)  | 21.4 (21.2, 21.6) | 20.9 (19.9, 21.8) | 0.6 (-0.4, 1.6) |
| ≥ 150 minutes                     | 25.9 (25.8, 26.0) | 24.1 (23.3, 24.9) | 1.8 (1.0, 2.6)  | 22.0 (21.9, 22.1) | 20.9 (20.3, 21.6) | 1.1 (0.4, 1.7)  |
| <b>Healthy Diet Score</b>         |                   |                   |                 |                   |                   |                 |
| ≤ 3 favorable items               | 24.3 (24.0, 24.5) | 22.4 (21.3, 23.5) | 1.8 (0.7, 3.0)  | 20.9 (20.8, 21.0) | 19.9 (19.2, 20.5) | 1.0 (0.3, 1.7)  |
| 4 favorable items                 | 25.3 (25.0, 25.5) | 24.0 (22.6, 25.3) | 1.3 (-0.1, 2.7) | 21.7 (21.5, 21.9) | 20.5 (19.4, 21.6) | 1.1 (0.0, 2.4)  |
| ≥ 5 favorable items               | 26.0 (25.9, 26.1) | 23.6 (22.8, 24.4) | 2.4 (1.6, 3.2)  | 22.5 (22.3, 22.6) | 21.2 (20.4, 22.2) | 1.3 (0.3, 2.1)  |
| <b>Sleep hours</b>                |                   |                   |                 |                   |                   |                 |
| < 6 or ≥ 10 hours                 | 23.5 (23.0, 24.0) | 21.6 (19.8, 23.2) | 1.9 (0.2, 3.8)  | 19.5 (19.1, 20.0) | 18.3 (16.9, 19.6) | 1.3 (-0.2, 2.8) |
| ≥ 6 and < 7 or ≥ 9 and < 10 hours | 24.9 (24.7, 25.2) | 22.6 (21.6, 23.7) | 2.3 (1.2, 3.4)  | 21.2 (21.0, 21.4) | 19.8 (19.0, 20.7) | 1.4 (0.5, 2.2)  |
| ≥ 7 and < 9 hours                 | 25.8 (25.7, 25.9) | 23.9 (23.2, 24.7) | 1.9 (1.1, 2.6)  | 22.0 (21.9, 22.1) | 21.1 (20.5, 21.8) | 0.9 (0.2, 1.5)  |
| <b>Social Isolation</b>           |                   |                   |                 |                   |                   |                 |
| <b>Smoking</b>                    |                   |                   |                 |                   |                   |                 |
| Current                           | 20.2 (19.8, 20.6) | 17.9 (17.1, 18.8) | 2.2 (1.3, 3.2)  | 18.1 (17.8, 18.4) | 17.1 (16.4, 17.8) | 1.0 (0.2, 1.8)  |
| Former                            | 24.6 (24.4, 24.8) | 23.9 (23.1, 24.6) | 0.7 (0.0, 1.5)  | 21.3 (21.1, 21.4) | 20.7 (20.1, 21.3) | 0.6 (-0.1, 1.2) |
| Never                             | 26.5 (26.4, 26.6) | 26.3 (25.6, 27.0) | 0.2 (-0.6, 1.0) | 23.0 (22.9, 23.1) | 22.7 (22.1, 23.2) | 0.3 (-0.3, 1.0) |
| <b>Body Mass Index</b>            |                   |                   |                 |                   |                   |                 |
| ≥ 30 kg/m <sup>2</sup>            | 22.2 (22.0, 22.5) | 21.7 (20.9, 22.5) | 0.5 (-0.4, 1.4) | 19.2 (19.0, 19.4) | 18.7 (18.0, 19.4) | 0.5 (-0.2, 1.2) |
| ≥ 25 and < 30 kg/m <sup>2</sup>   | 25.7 (25.6, 25.9) | 23.9 (23.2, 24.6) | 1.8 (1.0, 2.6)  | 22.0 (21.9, 22.2) | 21.2 (20.6, 21.7) | 0.9 (0.3, 1.5)  |
| ≥ 18.5 and < 25 kg/m <sup>2</sup> | 27.1 (26.9, 27.2) | 26.1 (25.3, 26.9) | 1.0 (0.1, 1.8)  | 23.4 (23.2, 23.6) | 22.5 (21.8, 23.2) | 0.8 (0.1, 1.6)  |
| <b>Physical Activity</b>          |                   |                   |                 |                   |                   |                 |
| 0 minute                          | 24.1 (23.8, 24.4) | 22.8 (21.9, 23.6) | 1.3 (0.4, 2.2)  | 20.4 (20.1, 20.7) | 20.1 (19.3, 20.8) | 0.3 (-0.5, 1.2) |
| > 0 and < 150 minutes             | 25.2 (24.9, 25.4) | 24.0 (23.1, 24.7) | 1.2 (0.4, 2.1)  | 21.4 (21.2, 21.6) | 21.4 (20.7, 22.0) | 0.1 (-0.7, 0.9) |
| ≥ 150 minutes                     | 25.9 (25.7, 26.0) | 25.0 (24.3, 25.7) | 0.9 (0.1, 1.5)  | 22.0 (21.9, 22.1) | 21.1 (20.6, 21.6) | 0.9 (0.4, 1.4)  |
| <b>Healthy Diet Score</b>         |                   |                   |                 |                   |                   |                 |
| ≤ 3 favorable items               | 24.3 (24.1, 24.6) | 22.6 (21.7, 23.4) | 1.7 (0.9, 2.6)  | 20.9 (20.8, 21.1) | 20.1 (19.3, 20.8) | 0.9 (0.4, 1.5)  |
| 4 favorable items                 | 25.4 (25.1, 25.7) | 23.1 (22.1, 23.9) | 2.3 (1.4, 3.4)  | 21.7 (21.5, 21.9) | 20.5 (19.7, 21.2) | 1.2 (0.4, 2.0)  |
| ≥ 5 favorable items               | 25.9 (25.8, 26.0) | 25.4 (24.7, 26.0) | 0.5 (-0.1, 1.3) | 22.5 (22.3, 22.6) | 22.3 (21.7, 22.9) | 0.2 (-0.5, 0.9) |
| <b>Sleep hours</b>                |                   |                   |                 |                   |                   |                 |
| < 6 or ≥ 10 hours                 | 23.6 (23.1, 24.1) | 21.4 (19.9, 22.8) | 2.2 (0.6, 3.8)  | 19.6 (19.2, 20.1) | 18.3 (17.1, 19.4) | 1.3 (0.1, 2.6)  |
| ≥ 6 and < 7 or ≥ 9 and < 10 hours | 24.9 (24.7, 25.2) | 23.4 (22.6, 24.2) | 1.5 (0.7, 2.4)  | 21.2 (21.0, 21.4) | 20.5 (19.9, 21.1) | 0.8 (0.1, 1.4)  |
| ≥ 7 and < 9 hours                 | 25.8 (25.7, 25.9) | 24.8 (24.3, 25.4) | 0.9 (0.3, 1.6)  | 22.0 (21.9, 22.1) | 21.5 (21.0, 21.9) | 0.5 (0.0, 1.0)  |



Data are presented as life expectancy and 95% Confidence intervals (CI). LE, life expectancy. Red color represents the magnitude of life expectancy for women, and blue color represent the magnitude of life expectancy for men. Life expectancy was calculated by multistate life tables. Source data are provided as a Source Data file.

## Supplementary References

1. Peeters A, Mamun AA, Willekens F, Bonneux L. A cardiovascular life history. *Eur Heart J*. 2002;23(6):458.
2. Woloshin S, Schwartz LM, Welch HG. The risk of death by age, sex, and smoking status in the United States: putting health risks in context. *J Natl Cancer Inst*. 2008;100(12):845.
3. Arias E, Xu J. United States Life Tables, 2019. *National Vital Statistics Reports: From the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System*. 2022;70(19):1.
4. Chiang CL, Organization WH. Life table and mortality analysis. 1979.
5. Guasch-Ferré M, Li Y, Bhupathiraju SN, et al. Healthy lifestyle score including sleep duration and cardiovascular disease risk. *Am J Prev Med*. 2022. 63(1): 33.
6. Song Z, Yang R, Wang W, et al. Association of healthy lifestyle including a healthy sleep pattern with incident type 2 diabetes mellitus among individuals with hypertension. *Cardiovasc Diabetol*. 2021. 20: 1.
7. Lloyd-Jones DM, Allen NB, Anderson CAM, et al. Life's essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a presidential advisory from the American Heart Association. *CIRCULATION*. 2022;146(5):e18-e43.
8. Piercy KL, Troiano RP, Ballard RM, et al. The physical activity guidelines for Americans. *JAMA*. 2018. 320(19): 2020.
9. Lourida I, Hannon E, Littlejohns TJ, et al. Association of lifestyle and genetic risk with incidence of dementia. *JAMA*. 2019;322(5):430.
10. Xu X, Feng C, Han H, et al. Prospective study of depressive symptoms and incident cardiovascular diseases in people with type 2 diabetes. *J Affect Disord*. 2024;345:427.
11. Gao X, Geng T, Jiang M, et al. Accelerated biological aging and risk of depression and anxiety: evidence from 424,299 UK Biobank participants. *Nat Commun*. 2023;14(1):2277.