cancers

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Article

Are Leading Risk Factors for Cancer and Mental Disorders Multimorbidity Shared by These Two Individual Conditions in Community-Dwelling Middle-Aged Adults?

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Supplementary Materials

Text S1. Classification of Independent Variables

This section describes how the baseline data for independent variables were collected and the classification of these variables.

Participants were classified as current, former and never smokers based on two questions: "Have you ever been a regular smoker?" and "Are you a regular smoker now?". Passive smoking was self-reported in hours per week at home or in other places and was divided in two groups as passive smoking or not.

Alcohol intake was calculated based on two questions: "About how many alcoholic drinks do you have each week?" and "On how many days each week do you usually drink alcohol?". Responses were then categorized according to number of drinks per week (0, 1–4, 5–7, 8–14, or >14) using the National Health and Medical Research Council definitions, with more than two drinks per day (14 drinks/week) considered as consuming "risky" levels of alcohol.

Physical activity was measured using the Active Australia Survey where the total time one spent on walking, moderate-intensity, and vigorous-intensity physical activity (bouts of at least 10 min) in the previous week was assessed [1]. Questions were also asked about number of hours spent on sitting, watching television, and sleep in a typical 24-h day.

Sleep and sitting time were assessed using the following question: "About how many hours in each 24 h day do you usually spend doing the following: sleeping and sitting?". Sleep duration was divided into three groups: <7, 7–9, and >9 h. Sitting time was categorized into two groups as ≤8 or >8 h per day.

Outdoor time per day was assessed using the following question: "About how many hours a day would you usually spend outdoors on a weekday and on the weekend?". An average outdoor time per day in one week in hours was calculated based on the time spent on workdays and weekend days, and it was categorized into five groups according to the quintiles.

Frequency of dietary intakes including vegetable, fruit, breakfast cereal, milk, fish, chicken, red meat, and processed meat per week or per day was recorded based on separate questions. Vegetable intake was divided into five groups according to the quintiles based on the following question: "About how many serves of vegetables do you usually eat each day? A serve is half a cup of cooked vegetables or one cup of salad". Fruit intake was divided into four groups: none, one serving/day, two servings/day, and three or more servings/day based on the following question: "About how many serves of fruit or glasses of fruit juice do you usually have each day? A serve is one medium piece or two small pieces or one cup of diced or canned fruit pieces". Fish intake was divided into three groups: none, one serving per week, and two or more servings per

week based on the following question: "About how many times each week do you eat?". The same question was asked for chicken, red meat, and processed meat. Milk intake was categorized as none, skimmed fat/reduced fat/soy milk, and whole milk based on the following question: "Which type of milk do you mostly have?". Breakfast cereal was defined as non-high-fiber and high-fiber groups based on the following question: "If you eat breakfast cereal, is it usually bran cereal (all bran, bran flakes, etc.), muesli, biscuit cereal (weetbix, shredded wheat etc.), oat cereal (porridge, etc.), or other (cornflakes, rice bubbles, etc.)?".

Socioeconomic status was also assessed using the Index of Relative Socio-economic Disadvantage according to postcode that ranks the income, qualifications, and skilled occupations of residents within an area [2]. Participants were divided into five groups according to the quintiles of Index of Relative Socio-economic Disadvantage, with the lowest quintile representing the greatest socio-economic disadvantage. Health insurance was divided into four groups: private with extras, private no extras, healthcare concession, and none of the above.

Geographic remoteness was divided into four groups including major cities, inner regional area, outer regional area, and remoteness using the Accessibility Remoteness Index of Australia [3].

Psychological distress was accessed using the Kessler-10 scale [4], which provides a global measure of anxiety and depressive symptoms experienced in the preceding month. Scores range from 10 to 50, with the following categories: low (10–11), mild (12–15), moderate (16–21), and high (22–50) psychological distress.

Self-reported quality of life was classified as excellent, very good, good, fair, or poor based on the following question: "In general, how would you rate your quality of life?".

Self-reported overall health was classified as excellent, very good, good, fair, or poor based on the following question: "In general, how would you rate your overall health?".

Four questions from the Duke Social Support Scale asked the respondent how many times per week they spend time with friends or family they do not live with (0, 1–2, and ≥3 were scored as 1, 2, and 3, respectively), talk to someone (friends, relatives or others) on the telephone (0–1, 2–5, and ≥6 were scored as 1, 2, and 3, respectively), spend time at meetings of social clubs, religious/other groups (0–1, 2–5, and ≥6 were scored as 1, 2, and 3, respectively), and how many people outside home, within 1 h of travel they can depend on or feel very close to (0, 1–2 and ≥3 were scored as 1, 2, and 3 respectively) [5]. The total social interaction score ranged from 4–12 and was categorized as low (4–6), moderate (7–9), and high levels (10–12).

Family history of chronic diseases including heart disease, stroke, hypertension, cancer, diabetes, Alzheimer's, Parkinson's disease, depression, arthritis, osteoporosis, and hip fractures was self-reported.

Overall, 48 potential predictors for multimorbidity of cancer and mental disorders were included in the analysis.

Text S2. The Interaction Between the Onsets of Cancer and Mental Disorders

We used Cox proportional regression models to assess the interaction between the onsets of cancer and mental disorders. The incidence of the corresponding primary condition within seven years in all participants at baseline was considered as the reference group. For example, to examine whether cancer as the primary condition would increase the risk of mental disorders as the secondary condition, the comparison was conducted between the incidence of mental disorders as the secondary condition in participants with cancer as the primary condition, and mental disorders as the primary condition in the total population. To enable comparison, the onset of primary and secondary condition was restricted to the cases occurring within the first seven years for this

specific analysis, where participants with follow-up time <7 years for the secondary condition were excluded.

Text S3. Description of Machine Learning Method

This section describes how we applied random forest to evaluate the importance of predictors.

Factorization of Features

The data were factorized into a labeled dataset containing the independent variables (potential predictors were listed in Table 1) and the dependent variable (participants were free of 13 chronic conditions in the nine years following the baseline date) using h2o. We used the whole dataset as both training and testing data as we aimed only to obtain the variable importance metric. We applied the commonly used machine learning method random forest in the analysis.

Random Forest

Random forest is widely applied in research since its creation. The random forest algorithm is a supervised learning algorithm constructing an ensemble of decision trees using randomly bootstrapping sample datasets and averaging predictions of its trees [6]. It applies a bagging method to ensemble multiple decision trees generated from subsets to reduce correlations among the constitute decision trees. A lower correlation between decision tress is associated with a lower forest error rate. Random forest has its robustness to reduce noise and overfitting, given that the datasets are built independently using bagging method [6,7]. The strength of each individual tree in the forest is another determinist factor for the forest error rate. In this study, we used the area under curve to determine the best predicting variable and location for each tree split in our algorithm. We grew the forest with 500 trees. A five-fold cross-validation was conducted to test if the model was overfitting even though random forest is less likely to be overfitting compared with other methods [6]. We implemented grid search to obtain optimal parameters including the number of variables randomly sampled as candidates at each split and the max depth of each tree (effectively the number of interactions are considered in the model) for random forest. A range of values for each hyper-parameter was specified, and all possible combinations of the hyper-parameters were examined, while the combination with the highest cross-validation performance metric was obtained. There are several indices for the model performance, and maximization of the area under the receiver operating characteristic curve was applied in this study. For example, random forest has hyper-parameters specifying the number of trees and the max depth of each tree (effectively how many interactions are considered in the model), whereas the decision rules are the parameters.

We set the parameter nthreads as 1 as to make use of all available cores on the system.

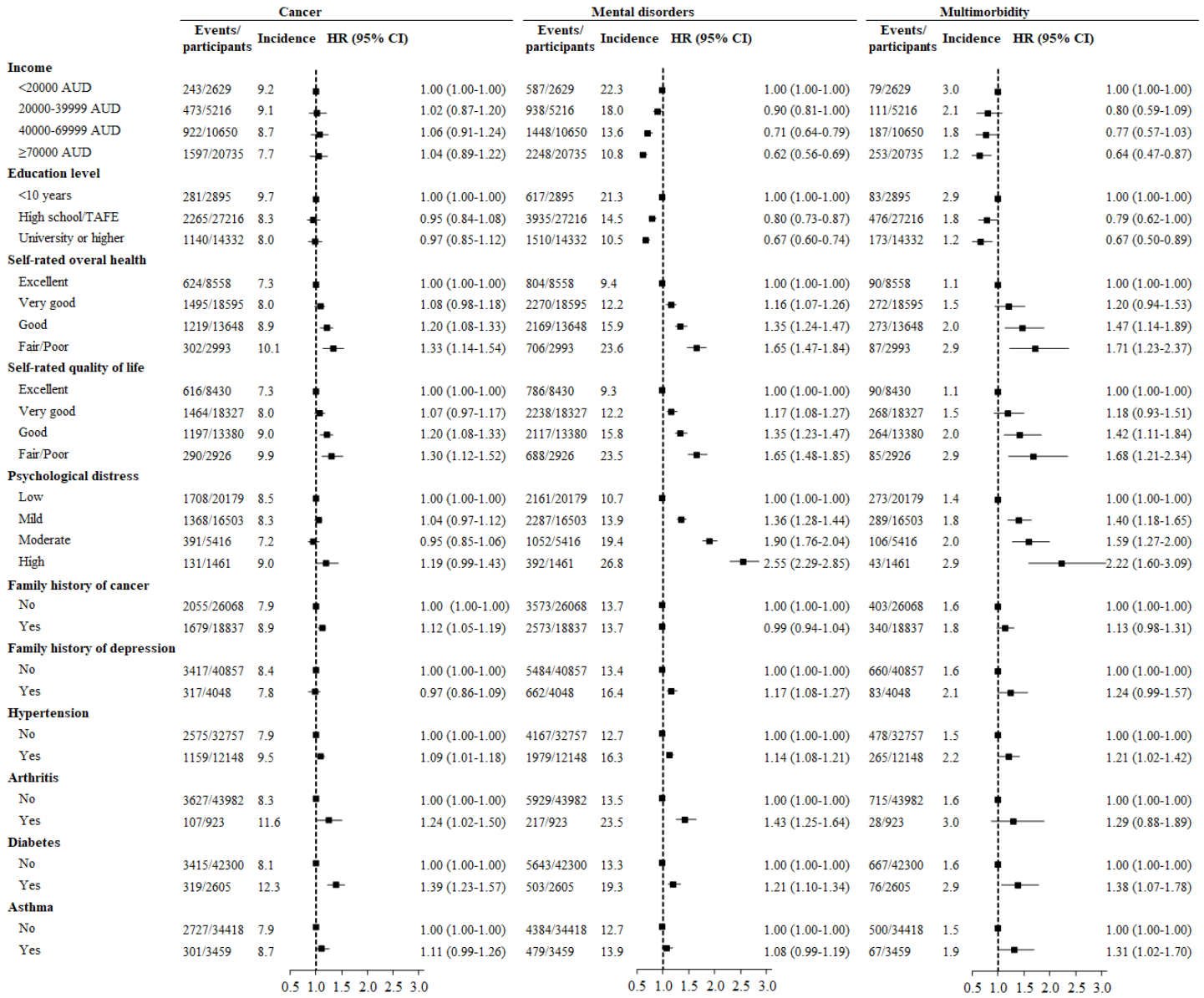
Cancer
Mental disorders
Multimorbidity
Events/ participants
Incidence
HR (95% CI)
Income
<20000 AUD 243/2629 9.2 1.00 (1.00-1.00) 587/2629 22.3 1.00 (1.00-1.00) 79/2629 3.0 1.00 (1.00-1.00)
20000-39999 AUD 473/5216 9.1 1.02 (0.87-1.20) 938/5216 18.0 0.90 (0.81-1.00) 111/5216 2.1 0.80 (0.59-1.09)
40000-69999 AUD 922/10650 8.7 1.06 (0.91-1.24) 1448/10650 13.6 0.71 (0.64-0.79) 187/10650 1.8 0.77 (0.57-1.03)
≥70000 AUD 1597/20735 7.7 1.04 (0.89-1.22) 2248/20735 10.8 0.62 (0.56-0.69) 253/20735 1.2 0.64 (0.47-0.87)
Education level
<10 years 281/2895 9.7 1.00 (1.00-1.00) 617/2895 21.3 1.00 (1.00-1.00) 83/2895 2.9 1.00 (1.00-1.00)
High school/TAFE 2265/27216 8.3 0.95 (0.84-1.08) 3935/27216 14.5 0.80 (0.73-0.87) 476/27216 1.8 0.79 (0.62-1.00)
University or higher 1140/14332 8.0 0.97 (0.85-1.12) 1510/14332 10.5 0.67 (0.60-0.74) 173/14332 1.2 0.67 (0.50-0.89)
Self-rated overal health
Excellent 624/8558 7.3 1.00 (1.00-1.00) 804/8558 9.4 1.00 (1.00-1.00) 90/8558 1.1 1.00 (1.00-1.00)
Very good 1495/18595 8.0 1.08 (0.98-1.18) 2270/18595 12.2 1.16 (1.07-1.26) 272/18595 1.5 1.20 (0.94-1.53)
Good 1219/13648 8.9 1.20 (1.08-1.33) 2169/13648 15.9 1.35 (1.24-1.47) 273/13648 2.0 1.47 (1.14-1.89)
Fair/Poor 302/2993 10.1 1.33 (1.14-1.54) 706/2993 23.6 1.65 (1.47-1.84) 87/2993 2.9 1.71 (1.23-2.37)
Self-rated quality of life
Excellent 616/8430 7.3 1.00 (1.00-1.00) 786/8430 9.3 1.00 (1.00-1.00) 90/8430 1.1 1.00 (1.00-1.00)
Very good 1464/18327 8.0 1.07 (0.97-1.17) 2238/18327 12.2 1.17 (1.08-1.27) 268/18327 1.5 1.18 (0.93-1.51)
Good 1197/13380 9.0 1.20 (1.08-1.33) 2117/13380 15.8 1.35 (1.23-1.47) 264/13380 2.0 1.42 (1.11-1.84)
Fair/Poor 290/2926 9.9 1.30 (1.12-1.52) 688/2926 23.5 1.65 (1.48-1.85) 85/2926 2.9 1.68 (1.21-2.34)
Psychological distress
Low 1708/20179 8.5 1.00 (1.00-1.00) 2161/20179 10.7 1.00 (1.00-1.00) 273/20179 1.4 1.00 (1.00-1.00)
Mild 1368/16503 8.3 1.04 (0.97-1.12) 2287/16503 13.9 1.36 (1.28-1.44) 289/16503 1.8 1.40 (1.18-1.65)
Moderate 391/5416 7.2 0.95 (0.85-1.06) 1052/5416 19.4 1.90 (1.76-2.04) 106/5416 2.0 1.59 (1.27-2.00)
High 131/1461 9.0 1.19 (0.99-1.43) 392/1461 26.8 2.55 (2.29-2.85) 43/1461 2.9 2.22 (1.60-3.09)
Family history of cancer
No 2055/26068 7.9 1.00 (1.00-1.00) 3573/26068 13.7 1.00 (1.00-1.00) 403/26068 1.6 1.00 (1.00-1.00)
Yes 1679/18837 8.9 1.12 (1.05-1.19) 2573/18837 13.7 0.99 (0.94-1.04) 340/18837 1.8 1.13 (0.98-1.31)
Family history of depression
No 3417/40857 8.4 1.00 (1.00-1.00) 5484/40857 13.4 1.00 (1.00-1.00) 660/40857 1.6 1.00 (1.00-1.00)
Yes 317/4048 7.8 0.97 (0.86-1.09) 662/4048 16.4 1.17 (1.08-1.27) 83/4048 2.1 1.24 (0.99-1.57)
Hypertension
No 2575/32757 7.9 1.00 (1.00-1.00) 4167/32757 12.7 1.00 (1.00-1.00) 478/32757 1.5 1.00 (1.00-1.00)
Yes 1159/12148 9.5 1.09 (1.01-1.18) 1979/12148 16.3 1.14 (1.08-1.21) 265/12148 2.2 1.21 (1.02-1.42)
Arthritis
No 3627/43982 8.3 1.00 (1.00-1.00) 5929/43982 13.5 1.00 (1.00-1.00) 715/43982 1.6 1.00 (1.00-1.00)
Yes 107/923 11.6 1.24 (1.02-1.50) 217/923 23.5 1.43 (1.25-1.64) 28/923 3.0 1.29 (0.88-1.89)
Diabetes
No 3415/42300 8.1 1.00 (1.00-1.00) 5643/42300 13.3 1.00 (1.00-1.00) 667/42300 1.6 1.00 (1.00-1.00)
Yes 319/2605 12.3 1.39 (1.23-1.57) 503/2605 19.3 1.21 (1.10-1.34) 76/2605 2.9 1.38 (1.07-1.78)
Asthma
No 2727/34418 7.9 1.00 (1.00-1.00) 4384/34418 12.7 1.00 (1.00-1.00) 500/34418 1.5 1.00 (1.00-1.00)
Yes 301/3459 8.7 1.11 (0.99-1.26) 479/3459 13.9 1.08 (0.99-1.19) 67/3459 1.9 1.31 (1.02-1.70)
0.5 1.0 1.5 2.0 2.5 3.0
0.5 1.0 1.5 2.0 2.5 3.0
0.5 1.0 1.5 2.0 2.5 3.0

Figure S1. Hazard ratios for incident cancer, mental disorders, and multimorbidity associated with age, socioeconomic status, self-rated health and psychological distress, and history and family history of chronic conditions in men. Hazard ratios were assessed using Cox regression models adjusted for age, country of birth, income, education, work status, number of children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

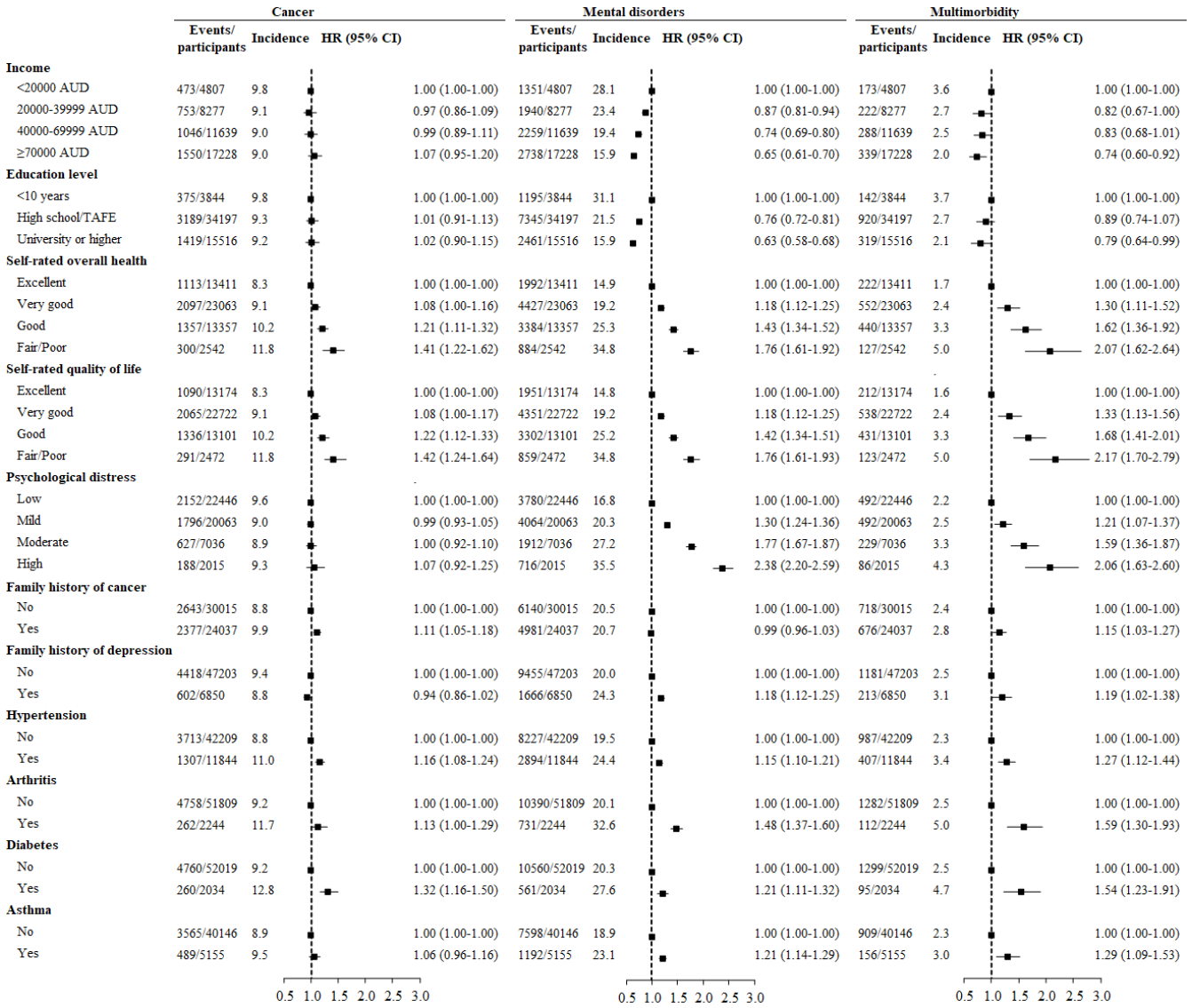
Cancer
Mental disorders
Multimorbidity
Events/ participants
Incidence
HR (95% CI)
Income
<20000 AUD 473/4807 9.8 1.00 (1.00-1.00) 1351/4807 28.1 1.00 (1.00-1.00) 173/4807 3.6 1.00 (1.00-1.00)
20000-39999 AUD 753/8277 9.1 0.97 (0.86-1.09) 1940/8277 23.4 0.87 (0.81-0.94) 222/8277 2.7 0.82 (0.67-1.00)
40000-69999 AUD 1046/11639 9.0 0.99 (0.89-1.11) 2259/11639 19.4 0.74 (0.69-0.80) 288/11639 2.5 0.83 (0.68-1.01)
≥70000 AUD 1550/17228 9.0 1.07 (0.95-1.20) 2738/17228 15.9 0.65 (0.61-0.70) 339/17228 2.0 0.74 (0.60-0.92)
Education level
<10 years 375/3844 9.8 1.00 (1.00-1.00) 1195/3844 31.1 1.00 (1.00-1.00) 142/3844 3.7 1.00 (1.00-1.00)
High school/TAFE 3189/34197 9.3 1.01 (0.91-1.13) 7345/34197 21.5 0.76 (0.72-0.81) 920/34197 2.7 0.89 (0.74-1.07)
University or higher 1419/15516 9.2 1.02 (0.90-1.15) 2461/15516 15.9 0.63 (0.58-0.68) 319/15516 2.1 0.79 (0.64-0.99)
Self-rated overall health
Excellent 1113/13411 8.3 1.00 (1.00-1.00) 1992/13411 14.9 1.00 (1.00-1.00) 222/13411 1.7 1.00 (1.00-1.00)
Very good 2097/23063 9.1 1.08 (1.00-1.16) 4427/23063 19.2 1.18 (1.12-1.25) 552/23063 2.4 1.30 (1.11-1.52)
Good 1357/13357 10.2 1.21 (1.11-1.32) 3384/13357 25.3 1.43 (1.34-1.52) 440/13357 3.3 1.62 (1.36-1.92)
Fair/Poor 300/2542 11.8 1.41 (1.22-1.62) 884/2542 34.8 1.76 (1.61-1.92) 127/2542 5.0 2.07 (1.62-2.64)
Self-rated quality of life
Excellent 1090/13174 8.3 1.00 (1.00-1.00) 1951/13174 14.8 1.00 (1.00-1.00) 212/13174 1.6 1.00 (1.00-1.00)
Very good 2065/22722 9.1 1.08 (1.00-1.17) 4351/22722 19.2 1.18 (1.12-1.25) 538/22722 2.4 1.33 (1.13-1.56)
Good 1336/13101 10.2 1.22 (1.12-1.33) 3302/13101 25.2 1.42 (1.34-1.51) 431/13101 3.3 1.68 (1.41-2.01)
Fair/Poor 291/2472 11.8 1.42 (1.24-1.64) 859/2472 34.8 1.76 (1.61-1.93) 123/2472 5.0 2.17 (1.70-2.79)
Psychological distress
Low 2152/22446 9.6 1.00 (1.00-1.00) 3780/22446 16.8 1.00 (1.00-1.00) 492/22446 2.2 1.00 (1.00-1.00)
Mild 1796/20063 9.0 0.99 (0.93-1.05) 4064/20063 20.3 1.30 (1.24-1.36) 492/20063 2.5 1.21 (1.07-1.37)
Moderate 627/7036 8.9 1.00 (0.92-1.10) 1912/7036 27.2 1.77 (1.67-1.87) 229/7036 3.3 1.59 (1.36-1.87)
High 188/2015 9.3 1.07 (0.92-1.25) 716/2015 35.5 2.38 (2.20-2.59) 86/2015 4.3 2.06 (1.63-2.60)
Family history of cancer
No 2643/30015 8.8 1.00 (1.00-1.00) 6140/30015 20.5 1.00 (1.00-1.00) 718/30015 2.4 1.00 (1.00-1.00)
Yes 2377/24037 9.9 1.11 (1.05-1.18) 4981/24037 20.7 0.99 (0.96-1.03) 676/24037 2.8 1.15 (1.03-1.27)
Family history of depression
No 4418/47203 9.4 1.00 (1.00-1.00) 9455/47203 20.0 1.00 (1.00-1.00) 1181/47203 2.5 1.00 (1.00-1.00)
Yes 602/6850 8.8 0.94 (0.86-1.02) 1666/6850 24.3 1.18 (1.12-1.25) 213/6850 3.1 1.19 (1.02-1.38)
Hypertension
No 3713/42209 8.8 1.00 (1.00-1.00) 8227/42209 19.5 1.00 (1.00-1.00) 987/42209 2.3 1.00 (1.00-1.00)
Yes 1307/11844 11.0 1.16 (1.08-1.24) 2894/11844 24.4 1.15 (1.10-1.21) 407/11844 3.4 1.27 (1.12-1.44)
Arthritis
No 4758/51809 9.2 1.00 (1.00-1.00) 10390/51809 20.1 1.00 (1.00-1.00) 1282/51809 2.5 1.00 (1.00-1.00)
Yes 262/2244 11.7 1.13 (1.00-1.29) 731/2244 32.6 1.48 (1.37-1.60) 112/2244 5.0 1.59 (1.30-1.93)
Diabetes
No 4760/52019 9.2 1.00 (1.00-1.00) 10560/52019 20.3 1.00 (1.00-1.00) 1299/52019 2.5 1.00 (1.00-1.00)
Yes 260/2034 12.8 1.32 (1.16-1.50) 561/2034 27.6 1.21 (1.11-1.32) 95/2034 4.7 1.54 (1.23-1.91)
Asthma
No 3565/40146 8.9 1.00 (1.00-1.00) 7598/40146 18.9 1.00 (1.00-1.00) 909/40146 2.3 1.00 (1.00-1.00)
Yes 489/5155 9.5 1.06 (0.96-1.16) 1192/5155 23.1 1.21 (1.14-1.29) 156/5155 3.0 1.29 (1.09-1.53)
0.5 1.0 1.5 2.0 2.5 3.0
0.5 1.0 1.5 2.0 2.5 3.0
0.5 1.0 1.5 2.0 2.5 3.0

Figure S2. Hazard ratios for incident cancer, mental disorders and multimorbidity associated with age, socioeconomic status, self-rated health and psychological distress, and history and family history of chronic conditions in women. Hazard ratios were assessed using Cox regression models adjusted for age, country of birth, income, education, work status, number of children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

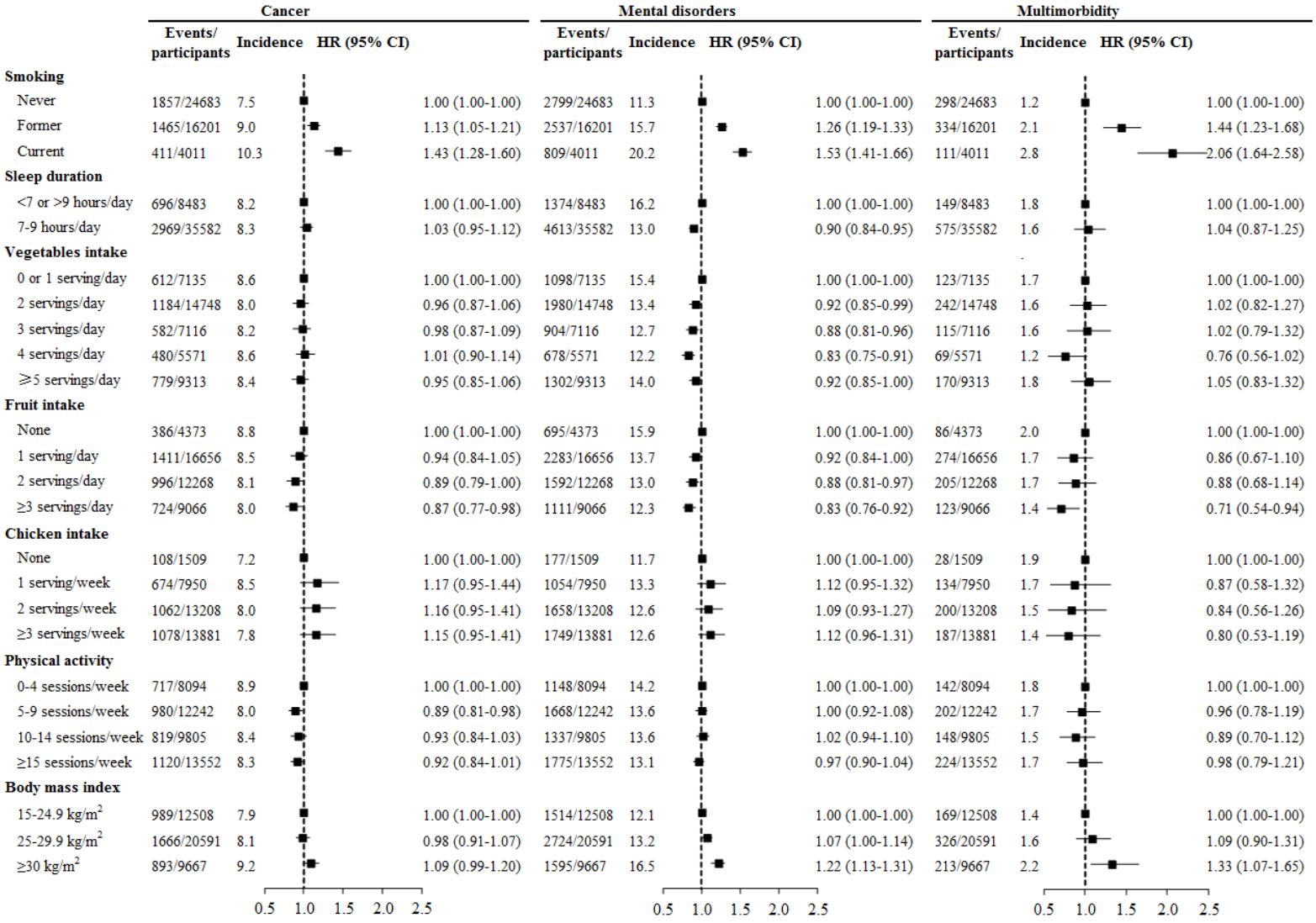
Cancer
Mental disorders
Multimorbidity
Events/ participants
Incidence
HR (95% CI)
Smoking
Never 1857/24683 7.5 1.00 (1.00-1.00) 2799/24683 11.3 1.00 (1.00-1.00) 298/24683 1.2 1.00 (1.00-1.00)
Former 1465/16201 9.0 1.13 (1.05-1.21) 2537/16201 15.7 1.26 (1.19-1.33) 334/16201 2.1 1.44 (1.23-1.68)
Current 411/4011 10.3 1.43 (1.28-1.60) 809/4011 20.2 1.53 (1.41-1.66) 111/4011 2.8 2.06 (1.64-2.58)
Sleep duration
<7 or >9 hours/day 696/8483 8.2 1.00 (1.00-1.00) 1374/8483 16.2 1.00 (1.00-1.00) 149/8483 1.8 1.00 (1.00-1.00)
7-9 hours/day 2969/35582 8.3 1.03 (0.95-1.12) 4613/35582 13.0 0.90 (0.84-0.95) 575/35582 1.6 1.04 (0.87-1.25)
Vegetables intake
0 or 1 serving/day 612/7135 8.6 1.00 (1.00-1.00) 1098/7135 15.4 1.00 (1.00-1.00) 123/7135 1.7 1.00 (1.00-1.00)
2 servings/day 1184/14748 8.0 0.96 (0.87-1.06) 1980/14748 13.4 0.92 (0.85-0.99) 242/14748 1.6 1.02 (0.82-1.27)
3 servings/day 582/7116 8.2 0.98 (0.87-1.09) 904/7116 12.7 0.88 (0.81-0.96) 115/7116 1.6 1.02 (0.79-1.32)
4 servings/day 480/5571 8.6 1.01 (0.90-1.14) 678/5571 12.2 0.83 (0.75-0.91) 69/5571 1.2 0.76 (0.56-1.02)
≥5 servings/day 779/9313 8.4 0.95 (0.85-1.06) 1302/9313 14.0 0.92 (0.85-1.00) 170/9313 1.8 1.05 (0.83-1.32)
Fruit intake
None 386/4373 8.8 1.00 (1.00-1.00) 695/4373 15.9 1.00 (1.00-1.00) 86/4373 2.0 1.00 (1.00-1.00)
1 serving/day 1411/16656 8.5 0.94 (0.84-1.05) 2283/16656 13.7 0.92 (0.84-1.00) 274/16656 1.7 0.86 (0.67-1.10)
2 servings/day 996/12268 8.1 0.89 (0.79-1.00) 1592/12268 13.0 0.88 (0.81-0.97) 205/12268 1.7 0.88 (0.68-1.14)
≥3 servings/day 724/9066 8.0 0.87 (0.77-0.98) 1111/9066 12.3 0.83 (0.76-0.92) 123/9066 1.4 0.71 (0.54-0.94)
Chicken intake
None 108/1509 7.2 1.00 (1.00-1.00) 177/1509 11.7 1.00 (1.00-1.00) 28/1509 1.9 1.00 (1.00-1.00)
1 serving/week 674/7950 8.5 1.17 (0.95-1.44) 1054/7950 13.3 1.12 (0.95-1.32) 134/7950 1.7 0.87 (0.58-1.32)
2 servings/week 1062/13208 8.0 1.16 (0.95-1.41) 1658/13208 12.6 1.09 (0.93-1.27) 200/13208 1.5 0.84 (0.56-1.26)
≥3 servings/week 1078/13881 7.8 1.15 (0.95-1.41) 1749/13881 12.6 1.12 (0.96-1.31) 187/13881 1.4 0.80 (0.53-1.19)
Physical activity
0-4 sessions/week 717/8094 8.9 1.00 (1.00-1.00) 1148/8094 14.2 1.00 (1.00-1.00) 142/8094 1.8 1.00 (1.00-1.00)
5-9 sessions/week 980/12242 8.0 0.89 (0.81-0.98) 1668/12242 13.6 1.00 (0.92-1.08) 202/12242 1.7 0.96 (0.78-1.19)
10-14 sessions/week 819/9805 8.4 0.93 (0.84-1.03) 1337/9805 13.6 1.02 (0.94-1.10) 148/9805 1.5 0.89 (0.70-1.12)
≥15 sessions/week 1120/13552 8.3 0.92 (0.84-1.01) 1775/13552 13.1 0.97 (0.90-1.04) 224/13552 1.7 0.98 (0.79-1.21)
Body mass index
15-24.9 kg/m2 989/12508 7.9 1.00 (1.00-1.00) 1514/12508 12.1 1.00 (1.00-1.00) 169/12508 1.4 1.00 (1.00-1.00)
25-29.9 kg/m2 1666/20591 8.1 0.98 (0.91-1.07) 2724/20591 13.2 1.07 (1.00-1.14) 326/20591 1.6 1.09 (0.90-1.31)
≥30 kg/m2 893/9667 9.2 1.09 (0.99-1.20) 1595/9667 16.5 1.22 (1.13-1.31) 213/9667 2.2 1.33 (1.07-1.65)
0.5 1.0 1.5 2.0 2.5
0.5 1.0 1.5 2.0 2.5
0.5 1.0 1.5 2.0 2.5

Figure S3. Hazard ratios for incident cancer, mental disorders, and multimorbidity associated with behavioral factors in men. Hazard ratios were assessed using Cox regression models adjusted for age, country of birth, income, education, work status, number of children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

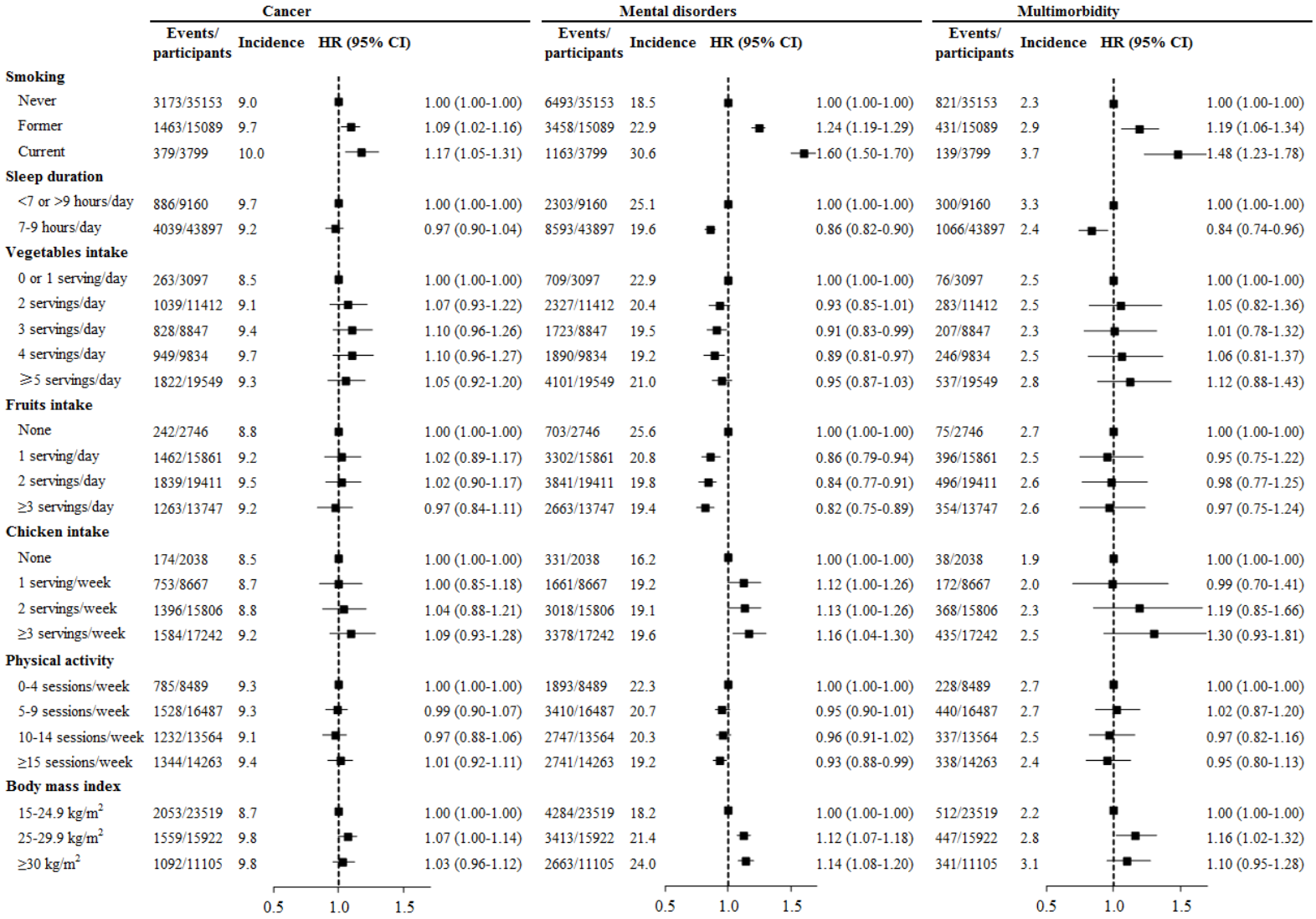
Cancer
Mental disorders
Multimorbidity
Events/ participants
Incidence
HR (95% CI)
Smoking
Never 3173/35153 9.0 1.00 (1.00-1.00) 6493/35153 18.5 1.00 (1.00-1.00) 821/35153 2.3 1.00 (1.00-1.00)
Former 1463/15089 9.7 1.09 (1.02-1.16) 3458/15089 22.9 1.24 (1.19-1.29) 431/15089 2.9 1.19 (1.06-1.34)
Current 379/3799 10.0 1.17 (1.05-1.31) 1163/3799 30.6 1.60 (1.50-1.70) 139/3799 3.7 1.48 (1.23-1.78)
Sleep duration
<7 or >9 hours/day 886/9160 9.7 1.00 (1.00-1.00) 2303/9160 25.1 1.00 (1.00-1.00) 300/9160 3.3 1.00 (1.00-1.00)
7-9 hours/day 4039/43897 9.2 0.97 (0.90-1.04) 8593/43897 19.6 0.86 (0.82-0.90) 1066/43897 2.4 0.84 (0.74-0.96)
Vegetables intake
0 or 1 serving/day 263/3097 8.5 1.00 (1.00-1.00) 709/3097 22.9 1.00 (1.00-1.00) 76/3097 2.5 1.00 (1.00-1.00)
2 servings/day 1039/11412 9.1 1.07 (0.93-1.22) 2327/11412 20.4 0.93 (0.85-1.01) 283/11412 2.5 1.05 (0.82-1.36)
3 servings/day 828/8847 9.4 1.10 (0.96-1.26) 1723/8847 19.5 0.91 (0.83-0.99) 207/8847 2.3 1.01 (0.78-1.32)
4 servings/day 949/9834 9.7 1.10 (0.96-1.27) 1890/9834 19.2 0.89 (0.81-0.97) 246/9834 2.5 1.06 (0.81-1.37)
⩾5 servings/day 1822/19549 9.3 1.05 (0.92-1.20) 4101/19549 21.0 0.95 (0.87-1.03) 537/19549 2.8 1.12 (0.88-1.43)
Fruits intake
None 242/2746 8.8 1.00 (1.00-1.00) 703/2746 25.6 1.00 (1.00-1.00) 75/2746 2.7 1.00 (1.00-1.00)
1 serving/day 1462/15861 9.2 1.02 (0.89-1.17) 3302/15861 20.8 0.86 (0.79-0.94) 396/15861 2.5 0.95 (0.75-1.22)
2 servings/day 1839/19411 9.5 1.02 (0.90-1.17) 3841/19411 19.8 0.84 (0.77-0.91) 496/19411 2.6 0.98 (0.77-1.25)
≥3 servings/day 1263/13747 9.2 0.97 (0.84-1.11) 2663/13747 19.4 0.82 (0.75-0.89) 354/13747 2.6 0.97 (0.75-1.24)
Chicken intake
None 174/2038 8.5 1.00 (1.00-1.00) 331/2038 16.2 1.00 (1.00-1.00) 38/2038 1.9 1.00 (1.00-1.00)
1 serving/week 753/8667 8.7 1.00 (0.85-1.18) 1661/8667 19.2 1.12 (1.00-1.26) 172/8667 2.0 0.99 (0.70-1.41)
2 servings/week 1396/15806 8.8 1.04 (0.88-1.21) 3018/15806 19.1 1.13 (1.00-1.26) 368/15806 2.3 1.19 (0.85-1.66)
≥3 servings/week 1584/17242 9.2 1.09 (0.93-1.28) 3378/17242 19.6 1.16 (1.04-1.30) 435/17242 2.5 1.30 (0.93-1.81)
Physical activity
0-4 sessions/week 785/8489 9.3 1.00 (1.00-1.00) 1893/8489 22.3 1.00 (1.00-1.00) 228/8489 2.7 1.00 (1.00-1.00)
5-9 sessions/week 1528/16487 9.3 0.99 (0.90-1.07) 3410/16487 20.7 0.95 (0.90-1.01) 440/16487 2.7 1.02 (0.87-1.20)
10-14 sessions/week 1232/13564 9.1 0.97 (0.88-1.06) 2747/13564 20.3 0.96 (0.91-1.02) 337/13564 2.5 0.97 (0.82-1.16)
≥15 sessions/week 1344/14263 9.4 1.01 (0.92-1.11) 2741/14263 19.2 0.93 (0.88-0.99) 338/14263 2.4 0.95 (0.80-1.13)
Body mass index
15-24.9 kg/m2 2053/23519 8.7 1.00 (1.00-1.00) 4284/23519 18.2 1.00 (1.00-1.00) 512/23519 2.2 1.00 (1.00-1.00)
25-29.9 kg/m2 1559/15922 9.8 1.07 (1.00-1.14) 3413/15922 21.4 1.12 (1.07-1.18) 447/15922 2.8 1.16 (1.02-1.32)
≥30 kg/m2 1092/11105 9.8 1.03 (0.96-1.12) 2663/11105 24.0 1.14 (1.08-1.20) 341/11105 3.1 1.10 (0.95-1.28)
0.5
1.0
1.5

Figure S4. Hazard ratios for incident cancer, mental disorders, and multimorbidity associated with behavioral factors in women. Hazard ratios were assessed using Cox regression models adjusted for age, country of birth, income, education, work status, number of children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

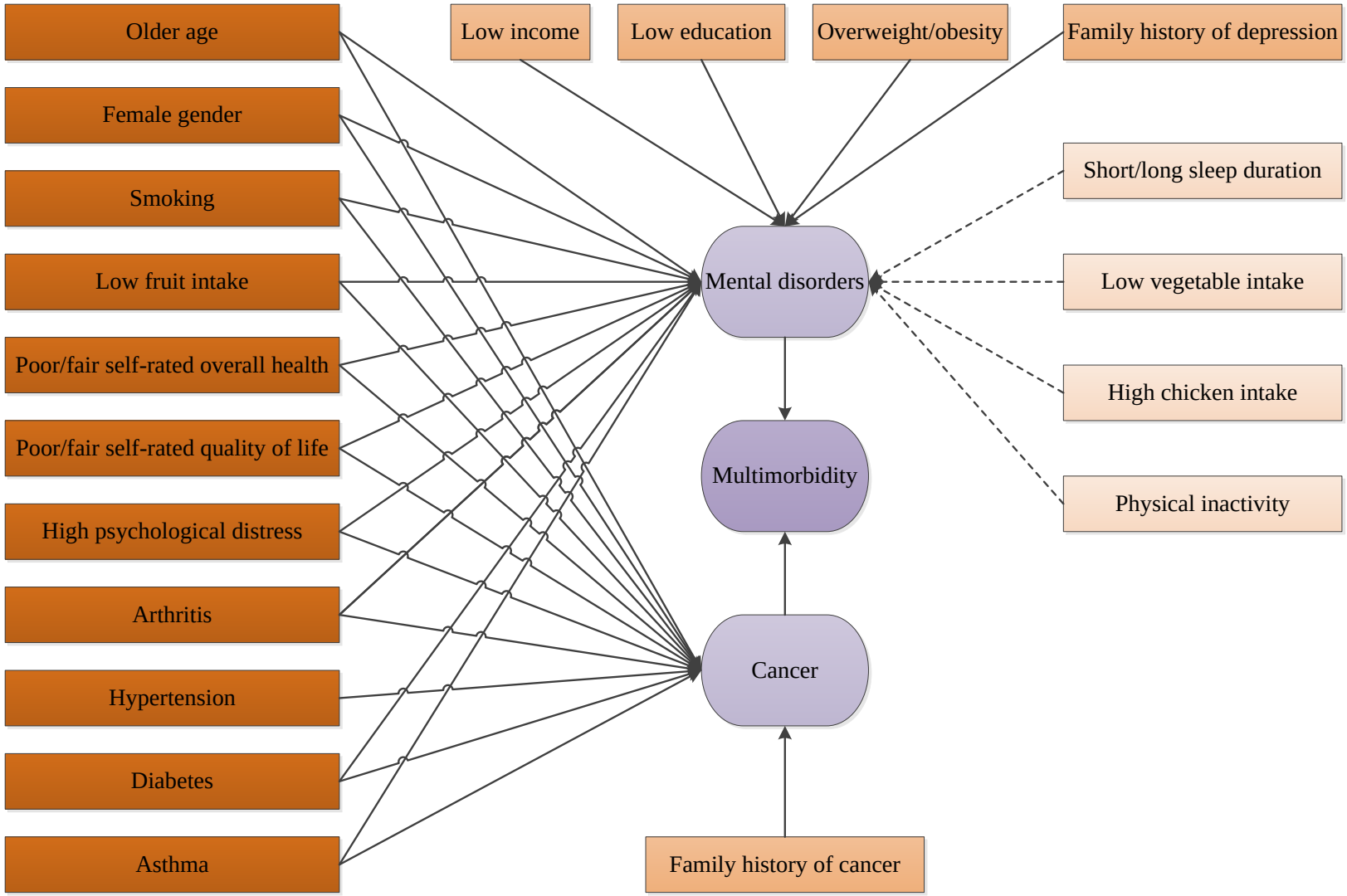
Older age
Female gender
Smoking
Low fruit intake
Poor/fair self-rated overall health
Poor/fair self-rated quality of life
High psychological distress
Arthritis
Hypertension
Diabetes
Asthma
Low income
Low education
Overweight/obesity
Family history of depression
Short/long sleep duration
Low vegetable intake
High chicken intake
Physical inactivity
Mental disorders
Multimorbidity
Cancer
Family history of cancer

Figure S5. Classification of risk factors for incident cancer, mental disorders, and multimorbidity. The risk factors were categorized into four groups according to their relationships with cancer, mental disorders, and multimorbidity presented in Figure 1–4 and Figure S2–S7. Older age, female gender, smoking, low fruit intake, poor/fair self-rated health, poor/fair self-rated quality of life, high psychological distress, hypertension, arthritis, asthma, and diabetes were classified as shared risk factors for cancer and mental disorders as they were associated with an increased risk of incident cancer, mental disorders, and multimorbidity. Low education, low income, overweight/obesity, and family history of depression were classified as risk factors for mental disorders given that they were associated with an increased risk of incident mental disorders but not incident cancer, and their positive association with multimorbidity might depend on mental disorders. Family history of cancer was classified as a risk factor for cancer given that it was associated with an increased risk of incident cancer but not incident mental disorders and its positive association with multimorbidity might depend on cancer. Long/short sleep duration, low vegetable intake, high chicken intake, and physical inactivity were classified as risk factors for mental disorders only since they were associated with an increased risk of incident mental disorders but not incident cancer or multimorbidity.

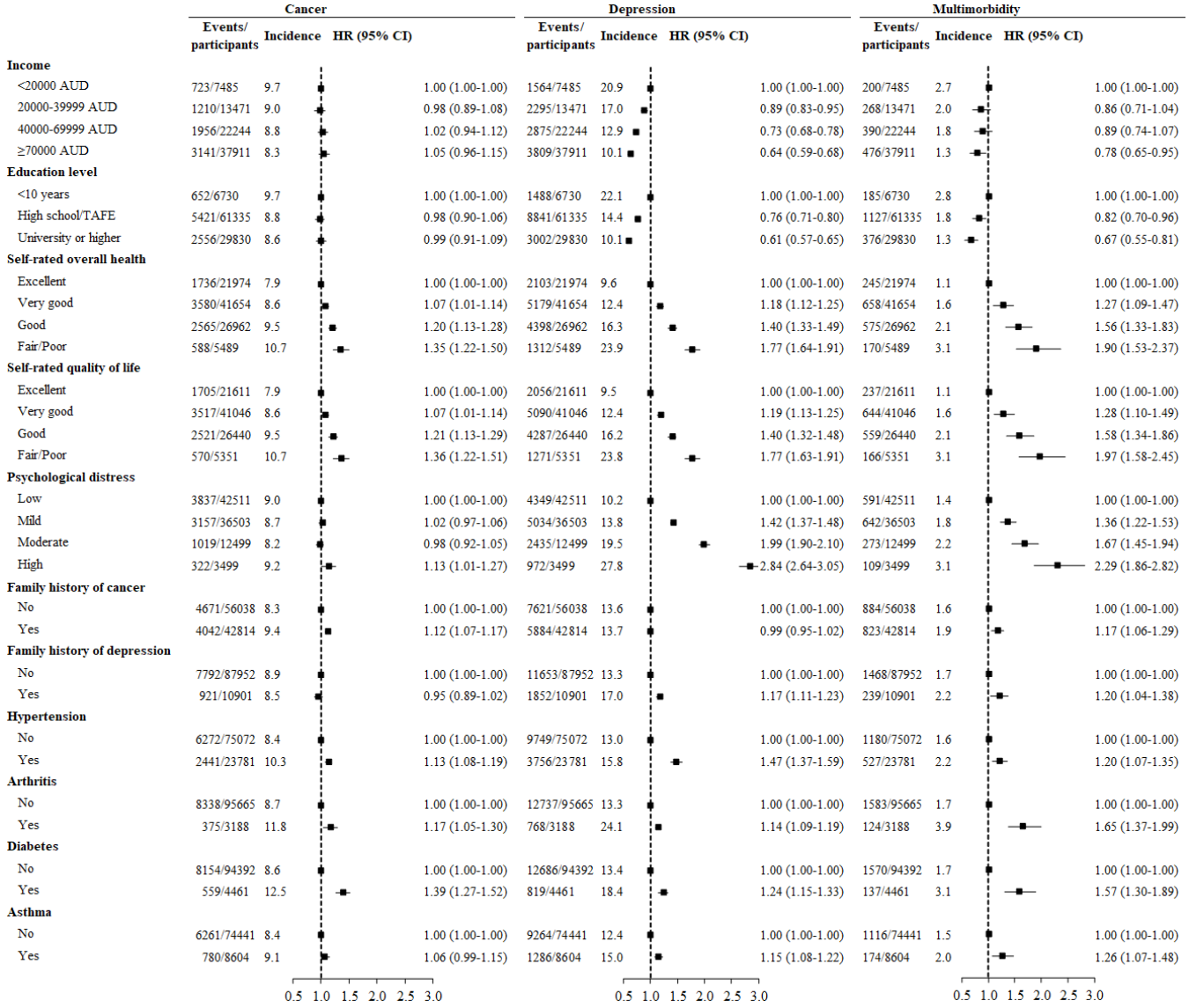
Cancer
Depression
Multimorbidity
Events/ participants
Incidence
HR (95% CI)
Income
<20000 AUD 723/7485 9.7 1.00 (1.00-1.00) 1564/7485 20.9 1.00 (1.00-1.00) 200/7485 2.7 1.00 (1.00-1.00)
20000-39999 AUD 1210/13471 9.0 0.98 (0.89-1.08) 2295/13471 17.0 0.89 (0.83-0.95) 268/13471 2.0 0.86 (0.71-1.04)
40000-69999 AUD 1956/22244 8.8 1.02 (0.94-1.12) 2875/22244 12.9 0.73 (0.68-0.78) 390/22244 1.8 0.89 (0.74-1.07)
≥70000 AUD 3141/37911 8.3 1.05 (0.96-1.15) 3809/37911 10.1 0.64 (0.59-0.68) 476/37911 1.3 0.78 (0.65-0.95)
Education level
<10 years 652/6730 9.7 1.00 (1.00-1.00) 1488/6730 22.1 1.00 (1.00-1.00) 185/6730 2.8 1.00 (1.00-1.00)
High school/TAFE 5421/61335 8.8 0.98 (0.90-1.06) 8841/61335 14.4 0.76 (0.71-0.80) 1127/61335 1.8 0.82 (0.70-0.96)
University or higher 2556/29830 8.6 0.99 (0.91-1.09) 3002/29830 10.1 0.61 (0.57-0.65) 376/29830 1.3 0.67 (0.55-0.81)
Self-rated overall health
Excellent 1736/21974 7.9 1.00 (1.00-1.00) 2103/21974 9.6 1.00 (1.00-1.00) 245/21974 1.1 1.00 (1.00-1.00)
Very good 3580/41654 8.6 1.07 (1.01-1.14) 5179/41654 12.4 1.18 (1.12-1.25) 658/41654 1.6 1.27 (1.09-1.47)
Good 2565/26962 9.5 1.20 (1.13-1.28) 4398/26962 16.3 1.40 (1.33-1.49) 575/26962 2.1 1.56 (1.33-1.83)
Fair/Poor 588/5489 10.7 1.35 (1.22-1.50) 1312/5489 23.9 1.77 (1.64-1.91) 170/5489 3.1 1.90 (1.53-2.37)
Self-rated quality of life
Excellent 1705/21611 7.9 1.00 (1.00-1.00) 2056/21611 9.5 1.00 (1.00-1.00) 237/21611 1.1 1.00 (1.00-1.00)
Very good 3517/41046 8.6 1.07 (1.01-1.14) 5090/41046 12.4 1.19 (1.13-1.25) 644/41046 1.6 1.28 (1.10-1.49)
Good 2521/26440 9.5 1.21 (1.13-1.29) 4287/26440 16.2 1.40 (1.32-1.48) 559/26440 2.1 1.58 (1.34-1.86)
Fair/Poor 570/5351 10.7 1.36 (1.22-1.51) 1271/5351 23.8 1.77 (1.63-1.91) 166/5351 3.1 1.97 (1.58-2.45)
Psychological distress
Low 3837/42511 9.0 1.00 (1.00-1.00) 4349/42511 10.2 1.00 (1.00-1.00) 591/42511 1.4 1.00 (1.00-1.00)
Mild 3157/36503 8.7 1.02 (0.97-1.06) 5034/36503 13.8 1.42 (1.37-1.48) 642/36503 1.8 1.36 (1.22-1.53)
Moderate 1019/12499 8.2 0.98 (0.92-1.05) 2435/12499 19.5 1.99 (1.90-2.10) 273/12499 2.2 1.67 (1.45-1.94)
High 322/3499 9.2 1.13 (1.01-1.27) 972/3499 27.8 2.84 (2.64-3.05) 109/3499 3.1 2.29 (1.86-2.82)
Family history of cancer
No 4671/56038 8.3 1.00 (1.00-1.00) 7621/56038 13.6 1.00 (1.00-1.00) 884/56038 1.6 1.00 (1.00-1.00)
Yes 4042/42814 9.4 1.12 (1.07-1.17) 5884/42814 13.7 0.99 (0.95-1.02) 823/42814 1.9 1.17 (1.06-1.29)
Family history of depression
No 7792/87952 8.9 1.00 (1.00-1.00) 11653/87952 13.3 1.00 (1.00-1.00) 1468/87952 1.7 1.00 (1.00-1.00)
Yes 921/10901 8.5 0.95 (0.89-1.02) 1852/10901 17.0 1.17 (1.11-1.23) 239/10901 2.2 1.20 (1.04-1.38)
Hypertension
No 6272/75072 8.4 1.00 (1.00-1.00) 9749/75072 13.0 1.00 (1.00-1.00) 1180/75072 1.6 1.00 (1.00-1.00)
Yes 2441/23781 10.3 1.13 (1.08-1.19) 3756/23781 15.8 1.47 (1.37-1.59) 527/23781 2.2 1.20 (1.07-1.35)
Arthritis
No 8338/95665 8.7 1.00 (1.00-1.00) 12737/95665 13.3 1.00 (1.00-1.00) 1583/95665 1.7 1.00 (1.00-1.00)
Yes 375/3188 11.8 1.17 (1.05-1.30) 768/3188 24.1 1.14 (1.09-1.19) 124/3188 3.9 1.65 (1.37-1.99)
Diabetes
No 8154/94392 8.6 1.00 (1.00-1.00) 12686/94392 13.4 1.00 (1.00-1.00) 1570/94392 1.7 1.00 (1.00-1.00)
Yes 559/4461 12.5 1.39 (1.27-1.52) 819/4461 18.4 1.24 (1.15-1.33) 137/4461 3.1 1.57 (1.30-1.89)
Asthma
No 6261/74441 8.4 1.00 (1.00-1.00) 9264/74441 12.4 1.00 (1.00-1.00) 1116/74441 1.5 1.00 (1.00-1.00)
Yes 780/8604 9.1 1.06 (0.99-1.15) 1286/8604 15.0 1.15 (1.08-1.22) 174/8604 2.0 1.26 (1.07-1.48)
0.5 1.0 1.5 2.0 2.5 3.0
0.5 1.0 1.5 2.0 2.5 3.0
0.5 1.0 1.5 2.0 2.5 3.0

Figure S6. Hazard ratios for incident cancer, depression, and multimorbidity associated with age, socioeconomic status, self-rated health and psychological distress, and history and family history of chronic conditions. Hazard ratios were assessed using Cox regression models adjusted for age, gender, country of birth, income, education, work status, number of children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

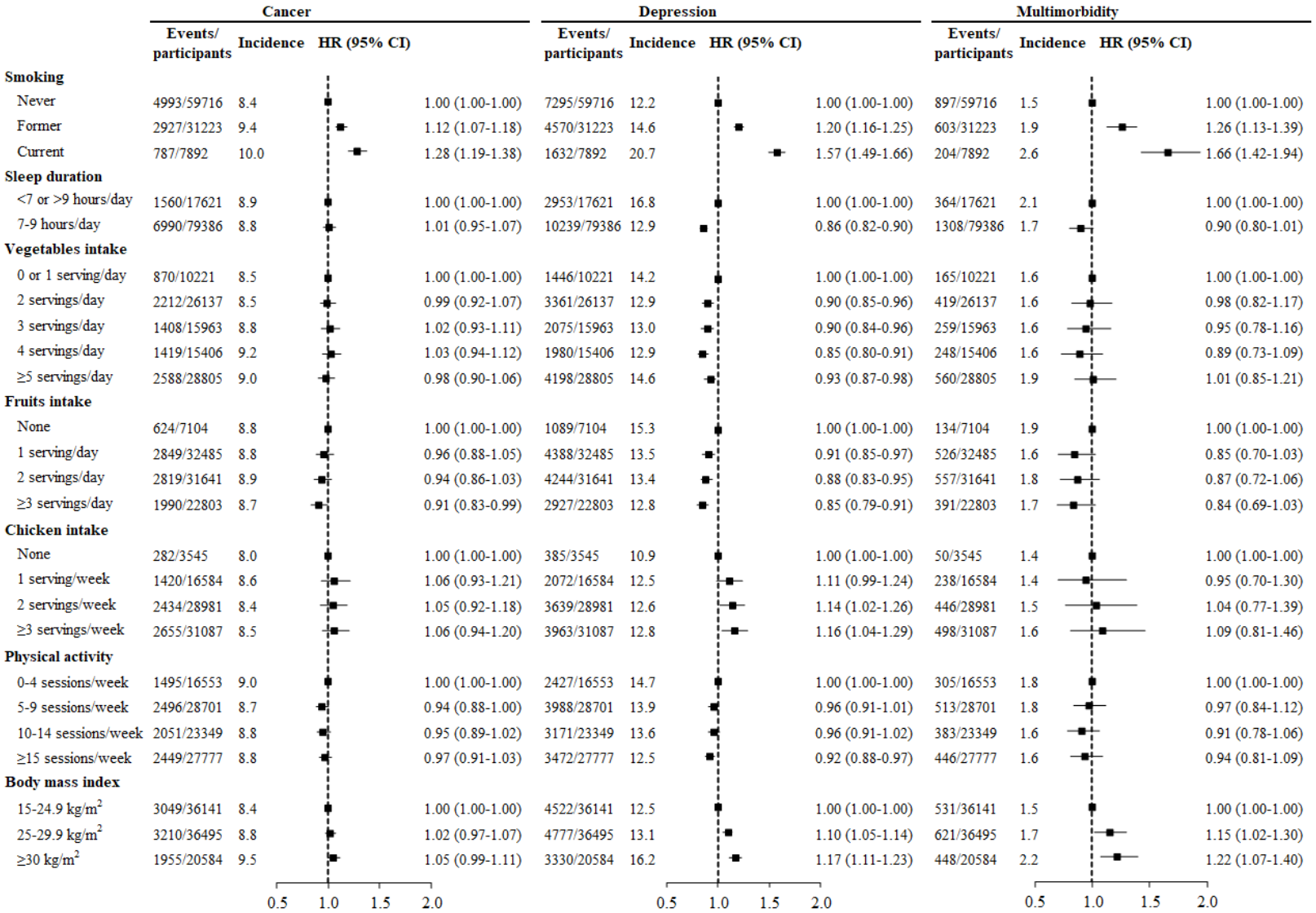
Cancer
Depression
Multimorbidity
Events/ participants
Incidence
HR (95% CI)
Smoking
Never 4993/59716 8.4 1.00 (1.00-1.00) 7295/59716 12.2 1.00 (1.00-1.00) 897/59716 1.5 1.00 (1.00-1.00)
Former 2927/31223 9.4 1.12 (1.07-1.18) 4570/31223 14.6 1.20 (1.16-1.25) 603/31223 1.9 1.26 (1.13-1.39)
Current 787/7892 10.0 1.28 (1.19-1.38) 1632/7892 20.7 1.57 (1.49-1.66) 204/7892 2.6 1.66 (1.42-1.94)
Sleep duration
<7 or >9 hours/day 1560/17621 8.9 1.00 (1.00-1.00) 2953/17621 16.8 1.00 (1.00-1.00) 364/17621 2.1 1.00 (1.00-1.00)
7-9 hours/day 6990/79386 8.8 1.01 (0.95-1.07) 10239/79386 12.9 0.86 (0.82-0.90) 1308/79386 1.7 0.90 (0.80-1.01)
Vegetables intake
0 or 1 serving/day 870/10221 8.5 1.00 (1.00-1.00) 1446/10221 14.2 1.00 (1.00-1.00) 165/10221 1.6 1.00 (1.00-1.00)
2 servings/day 2212/26137 8.5 0.99 (0.92-1.07) 3361/26137 12.9 0.90 (0.85-0.96) 419/26137 1.6 0.98 (0.82-1.17)
3 servings/day 1408/15963 8.8 1.02 (0.93-1.11) 2075/15963 13.0 0.90 (0.84-0.96) 259/15963 1.6 0.95 (0.78-1.16)
4 servings/day 1419/15406 9.2 1.03 (0.94-1.12) 1980/15406 12.9 0.85 (0.80-0.91) 248/15406 1.6 0.89 (0.73-1.09)
≥5 servings/day 2588/28805 9.0 0.98 (0.90-1.06) 4198/28805 14.6 0.93 (0.87-0.98) 560/28805 1.9 1.01 (0.85-1.21)
Fruits intake
None 624/7104 8.8 1.00 (1.00-1.00) 1089/7104 15.3 1.00 (1.00-1.00) 134/7104 1.9 1.00 (1.00-1.00)
1 serving/day 2849/32485 8.8 0.96 (0.88-1.05) 4388/32485 13.5 0.91 (0.85-0.97) 526/32485 1.6 0.85 (0.70-1.03)
2 servings/day 2819/31641 8.9 0.94 (0.86-1.03) 4244/31641 13.4 0.88 (0.83-0.95) 557/31641 1.8 0.87 (0.72-1.06)
≥3 servings/day 1990/22803 8.7 0.91 (0.83-0.99) 2927/22803 12.8 0.85 (0.79-0.91) 391/22803 1.7 0.84 (0.69-1.03)
Chicken intake
None 282/3545 8.0 1.00 (1.00-1.00) 385/3545 10.9 1.00 (1.00-1.00) 50/3545 1.4 1.00 (1.00-1.00)
1 serving/week 1420/16584 8.6 1.06 (0.93-1.21) 2072/16584 12.5 1.11 (0.99-1.24) 238/16584 1.4 0.95 (0.70-1.30)
2 servings/week 2434/28981 8.4 1.05 (0.92-1.18) 3639/28981 12.6 1.14 (1.02-1.26) 446/28981 1.5 1.04 (0.77-1.39)
≥3 servings/week 2655/31087 8.5 1.06 (0.94-1.20) 3963/31087 12.8 1.16 (1.04-1.29) 498/31087 1.6 1.09 (0.81-1.46)
Physical activity
0-4 sessions/week 1495/16553 9.0 1.00 (1.00-1.00) 2427/16553 14.7 1.00 (1.00-1.00) 305/16553 1.8 1.00 (1.00-1.00)
5-9 sessions/week 2496/28701 8.7 0.94 (0.88-1.00) 3988/28701 13.9 0.96 (0.91-1.01) 513/28701 1.8 0.97 (0.84-1.12)
10-14 sessions/week 2051/23349 8.8 0.95 (0.89-1.02) 3171/23349 13.6 0.96 (0.91-1.02) 383/23349 1.6 0.91 (0.78-1.06)
≥15 sessions/week 2449/27777 8.8 0.97 (0.91-1.03) 3472/27777 12.5 0.92 (0.88-0.97) 446/27777 1.6 0.94 (0.81-1.09)
Body mass index
15-24.9 kg/m2 3049/36141 8.4 1.00 (1.00-1.00) 4522/36141 12.5 1.00 (1.00-1.00) 531/36141 1.5 1.00 (1.00-1.00)
25-29.9 kg/m2 3210/36495 8.8 1.02 (0.97-1.07) 4777/36495 13.1 1.10 (1.05-1.14) 621/36495 1.7 1.15 (1.02-1.30)
≥30 kg/m2 1955/20584 9.5 1.05 (0.99-1.11) 3330/20584 16.2 1.17 (1.11-1.23) 448/20584 2.2 1.22 (1.07-1.40)
0.5 1.0 1.5 2.0
0.5 1.0 1.5 2.0
0.5 1.0 1.5 2.0

Figure S7. Hazard ratios for incident cancer, depression, and multimorbidity associated with behavioral factors. Hazard ratios were assessed using Cox regression models adjusted for age, gender, country of birth, income, education, work status, number of children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

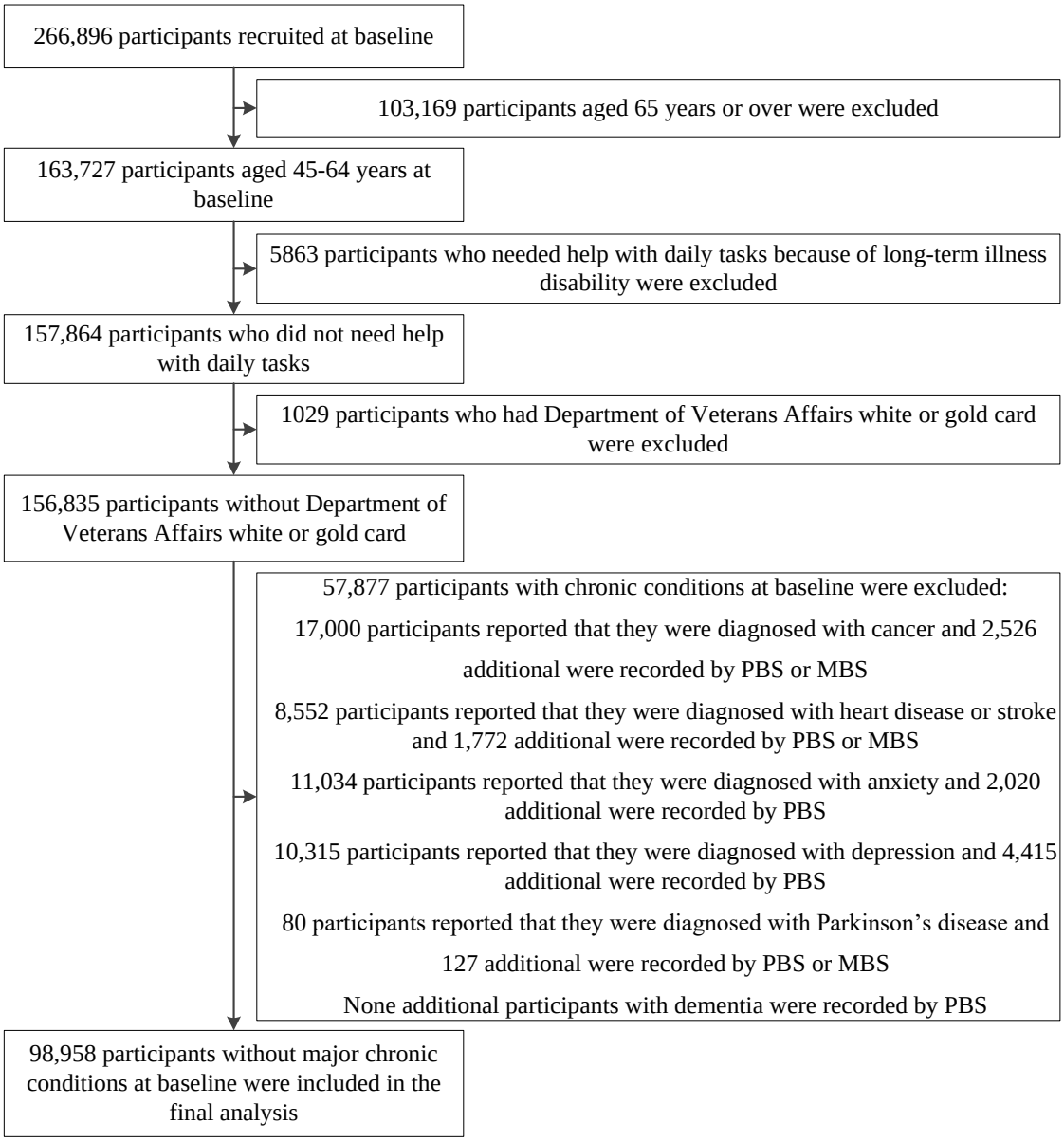

Figure S8. Flowchart of participant selection from the 45 and Up Study for the analysis in this study.

Table S1. List for Pharmaceutical Benefits Scheme and Medicare Benefits Schedule codes[†].

Chronic Conditions	Pharmaceutical Benefits Scheme Codes	ATC Codes for Pharmaceutical Benefits Scheme	Medicare Benefits Schedule Codes	Corresponding ICD Codes
Cancer[*,†]	1031G, 1079T, 1080W, 1134Q, 1144F, 1145G, 1160C, 1161D, 1162E, 1164G, 1265N, 1336H, 1340M, 1342P, 1390E, 1811H, 1929M, 1930N, 1931P, 1932Q, 2198Q, 2199R, 2315W, 2371T, 2372W, 2374Y, 2381H, 2521Q, 2528C, 2548D, 2561T, 2578Q, 2579R, 2580T, 2581W, 2582X, 2583Y, 2585C, 2884T, 2885W, 2904W, 2910E, 3017T, 3026G, 4222F, 4223G, 4309T, 4319H, 4326Q, 4327R, 4357H, 4360L, 4361M, 4364Q, 4394G, 4402Q, 4403R, 4428C, 4429D, 4431F, 4433H, 4439P, 4448D, 4451G, 4502Y, 4512L, 4514N, 4531L, 4567J, 4600D, 4610P, 4613T, 4614W, 4615X, 4618C, 4619D, 4620E, 4632T, 4639E, 4650R, 4703M, 4706Q, 4712B, 4713C, 4725Q, 4732C, 5149B, 5156J, 5270J, 5271K, 5272L, 5273M, 5274N, 5275P, 5428Q, 5429R, 5430T, 5431W, 5432X, 5433Y, 5462L, 5463M, 5464N, 5485Q, 5486R, 5487T, 5488W, 5489X, 5581R, 5582T, 5583W, 5584X, 5585Y, 5586B, 5587C, 5588D, 5589E, 5590F, 5591G, 5592H, 5593J, 5594K, 5595L, 5596M, 5597N, 5598P, 5705G, 5801H, 5804L, 5807P, 5808Q, 5809R, 5810T, 5811W, 5812X, 5813Y, 5814B, 5833B, 5834C, 5835D, 5842L, 5843M, 5844N, 5845P, 5846Q, 5847R, 5852B, 5854D, 5855E, 5856F, 5859J, 5860K, 5861L, 5862M, 5864P, 5865Q, 5866R, 5867T, 5868W, 5869X, 5872C, 5873D, 5874E, 5875F, 5876G, 5879K, 5880L, 5881M, 5882N, 5883P, 5887W, 5889Y, 5891C, 5892D, 5896H, 5897J, 5903Q, 5906W, 5907X, 5908Y, 5909B, 5910C, 5911D, 5912E, 5914G, 5915H, 5916J, 5917K, 5918L, 5919M, 5920N, 5921P, 5922Q, 5925W, 5926X, 5927Y, 5931E, 5932F, 5933G, 5934H, 5935J, 5936K, 5937L, 5943T, 5944W, 5957M, 5958N, 5959P, 5962T, 5963W, 5964X,	L01AA01, L01AA02, L01AA03, L01AA06, L01AB01, L01AX03, L01BA01, L01BA03, L01BA04, L01BB02, L01BB03, L01BB04, L01BC01, L01BC02, L01BC05, L01BC06, L01CA01, L01CA02, L01CA04, L01CB01, L01CD01, L01CD02, L01DB01, L01DB07, L01DC01, L01XA01, L01XA02, L01XC02, L01XC03, L01XE01, L01XE06, L01XE07, L01XX05, L01XX19, L01XX32	32036, 32099, 32102, 32103, 32104, 32106, 32108, 30299, 30300, 30301, 30302, 30303, 42801, 42802, 42803, 42805, 42807, 42809, 31340, 52036, 52039, 52048, 52045, 52042, 31372, 31373, 31374, 31375, 31376, 37227, 35720, 13915, 13918, 13921, 13924, 13927, 13930, 13933, 13936, 13939, 13942, 13945, 13948, 15000, 15003, 15006, 15009, 15012, 15100, 15103, 15106, 15109, 15112, 15115, 15211, 15214, 15215, 15218, 15221, 15224, 15227, 15230, 15233, 15236, 15239, 15242, 15245, 15248, 15251, 15254, 15257, 15260, 15263, 15266, 15269, 15272, 15275, 15303, 15304, 15307, 15308, 15311, 15312, 15315, 15316, 15319, 15320, 15323, 15324, 15327, 15328, 15331, 15332, 15335, 15336, 15339, 15342, 15345, 15348, 15351, 15354, 15357, 15600, 15700, 15705, 15710, 15715, 15900, 16003, 16006, 16009, 16012, 16015, 16018	C00-C97 (excluding C44)

5965Y, 5966B, 5973J, 5974K,
5975L, 5976M, 5977N, 5978P,
5979Q, 5980R, 5981T, 5982W,
5983X, 5988E, 5989F, 5990G,
5991H, 5992J, 5993K, 6007E,
6008F, 6009G, 6010H, 6249X,
6440Y, 6441B, 6444E, 6445F,
6446G, 6447H, 6497Y, 6687Y,
6688B, 6689C, 6690D, 6691E,
6692F, 6693G, 6694H, 6695J,
6696K, 6697L, 6698M, 6699N,
6700P, 6701Q, 6702R, 6703T,
6704W, 6705X, 6706Y, 6707B,
6708C, 6709D, 6710E, 6711F,
6713H, 6714J, 6716L, 6843E,
6844F, 6845G, 6846H, 6847J,
6848K, 6891Q, 6892R, 6893T,
6894W, 6895X, 6896Y, 7050C,
7051D, 7052E, 7053F, 7054G,
7055H, 7086Y, 7087B, 7088C,
7089D, 7222D, 7224F, 7225G,
7226H, 7227J, 7228K, 7229L,
7230M, 7234R, 7235T, 7237X,
7238Y, 7239B, 7244G, 7246J,
7248L, 7249M, 7250N, 7251P,
7252Q, 7254T, 7255W, 7256X,
7257Y, 7258B, 7259C, 7261E,
7262F, 7263G, 7264H, 7265J,
7266K, 7267L, 7268M, 7269N,
7270P, 7271Q, 7272R, 7274W,
7275X, 7281F, 7282G, 7283H,
7284J, 7285K, 8018B, 8033T,
8034W, 8049P, 8050Q, 8071T,
8074Y, 8076C, 8077D, 8120J,
8280T, 8281W, 8284B, 8293L,
8294M, 8360B, 8414W,
8415X, 8515E, 8569B, 8570C,
8665C, 8666D, 8800E, 8809P,
8827N, 8828P, 8850T, 8851W,
8852X, 8863L, 8967Y, 8986Y,
8987B, 8988C, 8989D, 8990E,
8991F, 8992G, 8995K, 8996L,
9005Y, 9117W, 9118X, 9119Y,
9130M, 9131N, 9282M,
9283N, 9284P, 9291B, 9341P,
9401T, 9402W, 9410G, 9414L,
9415M, 9463C, 9689Y, 9690B,
9691C, 9713F, 9729C,
10148D, 10150F, 10158P,
10165B, 10179R, 10193L,
10269L, 10270M, 10296X,
10324J, 10346M, 10362J,
10381J, 10383L, 10391X,
10401K, 10402L, 10423N,
10575N, 10576P, 10581X,
10583B, 10588G, 10589H,
10591K, 10593M, 10595P,
10597R, 10708N, 10710Q,
10720F, 10741H, 10743K,

	10744L, 10811B, 10817H, 10829Y			
Depression†	2418G, 2429W, 2417F, 1561E, 1358L, 1357K, 1012G, 1011F, 1013H, 2420J, 2421K, 2523T, 2522R, 8702B, 8703C, 8220P, 8700X, 8701Y, 10181W, 8270G, 1434L, 8174F, 8512B, 2242B, 2237R, 2236Q, 8837D, 8836C, 2856H, 2444P, 8003F, 1900B, 10234P, 10241B, 9366Y, 10231L, 10245F, 9367B, 9156X, 9155W, 8290H, 3059B, 1628Q, 1627P, 8513C, 8856D, 8883M, 8855C, 9365X, 8857E, 8583R, 8868R, 8302Y, 8301X	N06AA02, N06AA04, N06AA09, N06AA10, N06AA12, N06AA16, N06AB03, N06AB04, N06AB05, N06AB06, N06AB08, N06AB10, N06AB03, N06AF03, N06AF04, N06AG02, N06AX03, N06AX11, N06AX16, N06AX18, N06AX21, N06AX23	–	F32, F33
Anxiety†	3135B, 3134Y, 5355W, 5356X, 5372R, 5371Q, 4144D, 4145E, 3135B, 3134Y, 9432K, 9433L, 10181W, 5357Y, 5358B, 5373T, 5374W, 4150K , 4151L, 4216X, 4522B, 8700X, 8701Y, 8849R	N05BA01, N05BA04, N05BA08, N05BA12, N05BE01	–	F41.1

ATC, Anatomical Therapeutic Chemical Classification; ICT, International Classification of Diseases.

* Non-melanoma skin cancer was excluded in our analysis.

† Pharmaceutical Benefits Scheme (PBS) codes were consistent with the corresponding Anatomical Therapeutic Chemical codes listed in a previous publication based on the 45 and Up Study [8]. We used PBS codes instead of ATC codes for diagnosis detection where each ATC code may include numerous PBS codes. Different PBS codes within one ATC code represent different doses, forms (pill or liquid), intake methods (oral intake or injection), and specific conditions, which helps distinguish the claim purposes for different conditions.

Table S2. Combinations of the hyper-parameters with best performance for random forest*.

Variables	Random Forest
Men	max_depth = 5, mtries = 7, seed = 1, nfolds = 5, ntree = 500
Women	max_depth = 6, mtries = 4, seed = 1, nfolds = 5, ntree = 500
All	max_depth = 6, mtries = 4 seed = 1, nfolds = 5, ntree = 500

* These combinations of the hyper-parameters with best performance would then be separately applied in the machine learning in the final analysis.

Table S3. Area under curve by random forest*.

Variables	Random Forest
Male	0.6597
Female	0.6176
All	0.6592

* We randomly selected 70% to the total population as training data and the remaining 30% as testing data. The testing data were used to evaluate the area under curve for both cross-sectional and longitudinal analysis.

Table S4. Twenty leading predictors by random forest in the longitudinal analysis*.

Ranking	Men		Women		All	
	Predictor	Percentage of variance explained	Predictor	Percentage of variance explained	Predictor	Percentage of variance explained
1	Age	9.0	Smoking	5.4	Age	8.0
2	Relative socioeconomic disadvantage	4.8	Self-rated quality of life	4.7	Self-rated quality of life	5.4
3	Psychological distress	3.8	Self-rated health	4.2	Asthma	4.5
4	Education	3.6	Chicken intake	3.8	Self-rated health	4.4
5	Diabetes	3.5	Red meat intake	3.7	Psychological distress	4.2
6	Smoking	3.5	Psychological distress	3.5	Gender	4.2
7	Self-rated health	3.4	Arthritis	3.3	Red meat intake	3.6
8	Income	3.3	Relative socioeconomic disadvantage	3.2	Smoking	3.6
9	Red meat intake	3.2	Vegetables intake	3.2	Chicken intake	3.4
10	Asthma	2.9	Asthma	3.1	Income	3.3
11	Sleep time	2.9	Alcohol consumption	2.6	Vegetables intake	2.6
12	Sitting time	2.9	Age	2.6	Ancestry	2.4
13	Chicken intake	2.8	Sitting time	2.5	Arthritis	2.4
14	Vegetables intake	2.7	BMI	2.5	BMI	2.4
15	Physical activity	2.6	Income	2.5	Relative socioeconomic disadvantage	2.3
16	Self-rated quality of life	2.5	Working status	2.5	Working status	2.2
17	Fish intake	2.4	Outdoor physical activity	2.4	Alcohol consumption	2.1
18	Rurality	2.3	Milk intake	2.3	Fruit intake	2.1
19	Milk intake	2.2	Fruit intake	2.2	Education	2.0
20	Fruit intake	2.1	Health insurance	2.2	Sitting time	2.0

* Machine learning methods were used to evaluate the importance of predictors in men and women separately and also in the total population.

Table S5. The hazard ratio for incident mental disorders associated with cancer at baseline.

Variable	Events/ Participants	Incidence	HR (95% CI)*	*p*-value
Men	–	–	–	<0.0001
Cancer at baseline	–	–	–	–
No	6016/44,402	13.6	1.00 (1.00–1.00)	–
Yes	840/5077	16.6	1.19 (1.11–1.28)	–
Women	–	–	–	<0.0001
Cancer at baseline	–	–	–	–
No	10,929/53,538	20.4	1.00 (1.00–1.00)	–
Yes	1714/7485	22.9	1.11 (1.05–1.16)	–
All	–	–	–	<0.0001
Cancer at baseline	–	–	–	–
No	16,945/97,940	17.3	1.00 (1.00–1.00)	–
Yes	2554/12,562	20.3	1.15 (1.10–1.20)	–

* Hazard ratios were assessed using Cox regression models adjusted for age, gender, country of birth, income, education, work status, number of parenting children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

Table S6. The hazard ratio for incident cancer associated with mental disorders at baseline.

Variable	Events/Participants	Incidence	HR (95% CI)*	*p* value
Men	–	–	–	0.83
Mental disorders at baseline	–	–	–	–
No	3679/44,402	8.3	1.00 (1.00–1.00)	–
Yes	686/8323	8.2	0.98 (0.90–1.07)	–
Women	–	–	–	–
Mental disorders at baseline	–	–	–	0.39
No	4940/53,538	9.2	1.00 (1.00–1.00)	–
Yes	1759/18,530	9.5	1.03 (0.97–1.10)	–
All	–	–	–	–
Mental disorders at baseline	–	–	–	0.32
No	8619/97,940	8.8	1.00 (1.00–1.00)	–
Yes	2445/26,853	9.1	1.03 (0.98–1.08)	–

* Hazard ratios were assessed using Cox regression models adjusted for age, gender, country of birth, income, education, work status, number of parenting children, BMI, psychological distress, hypertension, dyslipidemia, diabetes, asthma, arthritis, hip replacement, and family history of cancer, depression, heart disease, stroke, diabetes, hypertension, Parkinson's disease, and dementia.

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