# Age- and sex-specific modifiable risk factor profiles of dementia: evidence from the UK Biobank

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# Abstract

**Background**: To inform targeted preventive strategies of dementia, systematic investigation in its age- and sex-specific modifiable risk factor profiles in the general adult population is warranted.

**Methods**: We used data of 372,867 adults free from dementia at baseline (2006-2010) in the UK Biobank, and followed them up until March 2021. We assigned participants into five groups according to their age and into two groups according to their sex. We estimated the age- and sex-specific hazard ratios (HRs) using Cox proportional hazard models and calculated the corresponding population attributable fractions (PAFs) for dementia attributable to three major categories of modifiable risk factors, including socioeconomic (low education level, high Townsend deprivation index), lifestyle (non-moderate alcohol intake, current smoking, suboptimal diet, non-regular physical exercise, and sleep duration <=6 or >=8 hrs/d), and health condition (hypertension, diabetes, cardiovascular diseases, and depressive symptom) risk factors.

**Findings**: During 4,338,030 person-years of follow-up, 113, 146, 360, 1,087, and 2,002 of participants across five increasing age groups (40-<50, 50-<55, 55-<60, 60-<65, or >=65 y), respectively, were newly diagnosed with dementia. Five out of eleven modifiable risk factors showed significantly stronger associations with dementia among younger adults than in relatively older adults (P-interactions < 0.05), including non-moderate alcohol intake (HR [95% confidence interval, CI]=1.90 [1.35, 2.68] for participants 50-<55 y vs. 1.22 [1.11, 1.35] for participants > 65 y), suboptimal diet (1.86 [1.26, 2.74] for participants 40-< 50 y vs. 0.96 [0.86, 1.06] for participants > 65 y), hypertension (1.52 [0.96, 2.42] vs. 1.08 [0.99, 1.19]), CVD (4.20 [2.15, 8.22] vs. 1.64 [1.45, 1.85]), and diabetes (3.09 [1.60, 6.00] vs. 1.73 [1.51, 2.00]). We observed no significant difference in dementia risk factor profiles between women and men. Dementia cases attributable to three categories of risk factors all decreased with age, with the PAFs (95% CI) for sociodemographic, lifestyle, and health condition risk factors being 52.56% (22.98%, 82.15%), 46.57% (8.08%, 85.06%), and 35.42% (24.09%, 46.75%) for participants aged 40-<50 y, and 12.29% (3.82%, 20.75%), 13.01% (2.53%, 23.49%), and 15.85% (11.81%, 19.90%) for those over 65 y.

**Interpretation**: This study identified stronger association and greater attributable risk of several modifiable risk factors for dementia among younger adults, underscoring the importance of preventive strategies from an earlier age across adult life course to reduce the risk of dementia.


# 1. Introduction

Dementia is constituting an increasing challenge to public health [1]. Worldwide, about 55.2 million people had prevalent dementia in 2019, with the number being expected to triple by 2050[2]. The expanding dementia population also means heavier economic burdens for individuals and health systems. A previous study estimated that the worldwide economic costs of dementia were US$280 billion in 2000, and surged to $948 billion in 2016[3]. Since its underlying mechanism is largely unknown, and

there is currently no effective curative treatments for dementia[1], it is crucial to identify the risk factors, especially modifiable ones, of dementia for prevention measures.

Emerging studies have suggested several modifiable risk factors of dementia, e.g., low education[4], smoking[5], suboptimal dietary patterns[6], hypertension[7], diabetes[8], and depression[9]. The Lancet Commission on dementia prevention, intervention, and care pooled results of prospective studies and concluded that 40 percent of dementia cases could be prevented or delayed by targeting 12 modifiable risk factors[10]. However, considering the potential interactions between sex differences, physical changes associated with aging, and the modifiable risk factors, whether these risk factors were consistently related to dementia across sex and age groups remained largely unknown. Although numerous studies have conducted subgroup analyses when investigating the relation of individual risk factors, few studies have characterized the disparities of risk factors across sex and age groups in sufficient detail, which, on the other hand, is vital for effective prevention of dementia in specific populations. Specifically, the population-specific risk factor profiles may serve as evidence for prioritizing particular risk factors for different populations.

To address this research gap, the current study assessed the relations of potentially modifiable risk factors with incident dementia across five age groups and two sex groups in the UK Biobank, a nationwide cohort study in the UK.

# 2. Methods

### 2.1 Study population

This study was based on the UK Biobank (UKB), a large multicentre cohort study in the UK[11]. From 2006 to 2010, UKB recruited over 500,000 UK residents aged >=40 y at 22 assessment centers, as described in details on the UK Biobank website (http://www.ukbiobank.ac.uk/resources/). Ethical approval was granted by the North West-Haydock Research Ethics Committee (REC reference: 16/NW/0274).

We included participants aged >= 40 y at baseline in the UKB. Participants were excluded in further analyses if they: 1) had prevalent dementia at baseline; 2) had missing data in any of the risk factors; or 3) requested to exit the program before March 2021. A total of 372,867 participants were included in the analyses. The inclusion flowchart is shown in **Figure S1**. We assigned participants into five age groups (40-<50, 50-<55, 55-<60, 60-<65, or >=65 y) and into two sex groups (female or male). We selected potential risk factors in the UK Biobank that are relatively prevalent, considered causally associated with dementia, and can be directly or indirectly modified, according to previous evidence in observational or interventional studies. These factors included two socioeconomic, five lifestyle, and four health condition risk factors.

### 2.2 Socioeconomic risk factors

In the UK Biobank, participants were asked whether they had a college or university degree at baseline. Townsend deprivation index (TDI) is an area-based proxy measure of socioeconomic status composed of ownership and employment as a state of observable and demonstrable disadvantage relative to local community[12]. A higher TDI indicates a higher level of deprivation. This study considered education level below high school and high TDI (above median value) as socioeconomic risk factors, according to previous studies [4,10,13,14]. A composite socioeconomic risk score was calculated by summing the two items, ranging from 0 to 2.

### 2.3 Lifestyle risk factors

At baseline, all participants were asked to finish a web-based lifestyle questionnaire, in which they reported their alcohol drinking behaviour, smoking status, dietary habits, physical activity, and sleep duration. In this study, lifestyle risk factors included non-moderate alcohol intake[15] (defined as no alcohol intake or daily alcohol intake over 28 g or two drink equivalences for men and over 14 g or one drink equivalence for women[16]), current smoking, suboptimal diet (insufficient consumption of at least 4 of 7 commonly eaten food groups following the American Heart Association recommendations[17]), non-regular physical exercise (not meeting the American Heart Association recommendations[18] of >= 150 minutes of moderate activity per week or 75 minutes of vigorous activity per week or an equivalent combination or engaging in moderate physical activity at least 5 days a week or vigorous activity once a week), and sleep duration [19]<=6 or >=8 hrs/d, as in prior findings[5,6,10,15,19–21]. A composite lifestyle risk score was calculated by summing the five items, ranging from 0 to 5.

### 2.4 Health condition risk factors

The UK Biobank incorporated a multi-source health condition identification system. The current study identified hypertension, diabetes, and cardiovascular diseases (CVD, e.g., stroke and coronary heart disease) from International Classification of Diseases (ICD) codes (Version 9 and 10) of hospital inpatient admission data or self-reports. The depressive symptom was identified using the two-item Patient Health Questionnaires (PHQ-2)[22]. All these conditions have been suggested as risk factors of dementia in previous researches[7–10,23–25]. Obesity was not considered a risk factor but only adjusted for in this study because previous findings on the relation of obesity to dementia were inconsistent[26]. A composite health condition risk score was calculated by summing the four items, ranging from 0 to 4.

### 2.5 Dementia ascertainment

Dementia cases in the UK Biobank were linked to hospital inpatient admissions and death registries. We identified Alzheimer's Dementia (AD), vascular dementia (VaD), and other types or undefined dementia from ICD codes, according to a validated algorithm-based indentifying method with a positive predictive value over 80%[27]. In this study, health conditions were updated in the linkage to the healthcare system to March 2021.

### 2.6 Statistical analyses

Participants' baseline characteristics were presented by their age and sex. Continuous variables were displayed as means (standard deviations, SDs), and categorical variables were shown as numbers (percentages). Cox proportional hazard models were used to estimate the hazard ratios (HRs) and confidence intervals (CIs) for incident dementia associated with modifiable risk factors across subgroups of participants, with person-years being calculated to the diagnosis of dementia, the ascertainment of death, end of follow-up, or loss to follow-up, whichever came first. Proportional hazard assumption was tested and verified by Schoenfeld residual methods. In this study, we included several covariates for confounding adjustment, including race and body mass index (BMI) categorized into underweight (BMI<=20.0 kg/$m^2$), normal weight (BMI >20.0 but <=25.0 kg/$m^2$), or overweight (BMI >25.0 kg/$m^2$). Missing values for BMI were assigned to a separate class. Risk factors are mutually adjusted in the Cox models. We tested the potential effect modifications of age and sex by entering the main effect terms and the corresponding cross-product term into the models.

In the secondary analysis, we investigated the association of the three composite risk scores (socioeconomic risk score, lifestyle risk score, and health condition risk score) with incident dementia. The risk scores were all included in the same model as continuous variables. The HRs represented the relative risk for each unit increment in these scores adjusted for race, BMI categories, and other risk scores. We further calculated the adjusted population-attributable fractions (PAFs) and 95% CIs of dementia attributable to each risk factor using R package "AF"[28]. The PAFs estimated the percentage of cases of a disease (in this case dementia) that would be prevented, supposing the particular risk factor being eliminated[29].

To test the robustness of the main findings, we performed the following sensitivity analyses: 1) given that APOE genotype was strongly associated dementia, we further adjusted the models for APOE genotype (only available among European-ancestry participants); 2) to further reduce potential reverse causation, we removed participants who were consored or developed dementia within the first two years after baseline; 3) to reduce the potential confounding by stroke, we excluded participants with baseline stroke; 4) given that mortality might be a competing risk for dementia, we replicated the primary analysis using Fine & Gray competing risk model[30]; 5) to validate the definition of non-moderate alcohol intake, we separated zero intake and heavy intake (> 14g/d for women and >28 g/d for men) and assessed their relations to dementia and tested the potential non-linearity between them.

Statistical analyses were performed using R 3.6.0, and two-sided P-values below 0.05 were considered statistically significant.

# 3. Results

## 3.1 Participant Characteristics

Of the 372,867 dementia-free participants, the mean (SD) age at baseline was 55.61 (8.06) years old. Among them, 202,166 (54.2%) were female, and 354,601 (95.1%) had white racial/ethnic background

(**Table 1**). Older participants were more likely to be less educated, higher in TDI, non-current smokers, to sleep too much or too less, to have hypertension, diabetes, and CVD. Female participants were less likely to be current smokers, to have sufficient physical activity, moderate alcohol intake, hypertension, CVD, and diabetes.

### 3.2 Sex- and age-specific modifiable risk factors of dementia

During 4,338,030 person-years (mean = 9.5 y) of follow-up, a total of 3,078 dementia cases were reported, among whom 113, 146, 360, 1,087, and 2,002 were from participants with baseline age of 40-<50, 50-<55, 55-<60, 60-<65, and >=65 y, respectively.

In the overall participants, all risk factors, except for suboptimal diet, were associated with a significant higher risk of later-life dementia (**Figure 1 & Table S1**). The adjusted HRs (95% CI) were generally higher for health condition risk factors, being 1.99 (1.73, 2.28) for depressive symptom, 1.93 (1.74, 2.14) for diabetes, 1.81 (1.65, 1.99) for CVD, and 1.16 (1.08, 1.25) for hypertension. Additionally, lifestyle factors were significantly associated with increased risk of dementia, with HR being 1.31 (1.17, 1.46) for current smoking, 1.29 (1.20, 1.39) for non-moderate alcohol intake, 1.16 (1.08, 1.24) for sleep duration <=6 or >=8 hrs, and 1.13 (1.06, 1.22) for insufficient physical activity. Socioeconomic risk factors, including low education level (1.14 [1.07, 1.23]) and high TDI (1.13 [1.06, 1.21]), were also related to higher risk of dementia.

We observed different associations between several risk factors and incident dementia by age groups (**Figure 1)**. For suboptimal diet, a significantly elevated risk of dementia was mainly observed in younger participants aged 40-<50 y (HR [95%CI] = 1.86 [1.26, 2.74], P-interaction = 0.006). Non-moderate alcohol intake was associated with higher risk of dementia across almost all age groups, with the strongest association in the age group of 50-<55 y (1.90 [1.35, 2.68], P-interaction = 0.049). The associations of chronic diseases, including hypertension, CVD, and diabetes, were all stronger in younger participants than in older adults. For example, CVD was associated with a 4.2-fold hazard of dementia (4.20 [2.15, 8.22]) for the youngest participants (aged 40-< 50 y), but the relation was relatively weaker in older adults (1.64 [1.45, 1.85]). Although the statistical interactions between age groups and other risk factors were non-significant, the trend of stronger assocations in younger participants persisted (**Table S1**).

Overall, the composite health condition risk score demonstrated the strongest association with dementia (HR [95%CI] = 1.50 [1.44, 1.56] for per unit increment), followed by the lifestyle risk score (1.15 [1.11, 1.19]) and the socioeconomic risk score (1.14 [1.09, 1.20]) (**Figure 2 & Table S2**). The corresponding associations were similar in men as in women, while stronger associations were consistently observed among younger participants. For socioeconomic risk score, the HRs (95% CI) for per unit increment were 1.74 (1.28, 2.35) for participants age 40-<50 y, and 1.11 (1.04, 1.19) for participants >=65 y. For lifestyle risk score, the HRs (95% CI) were 1.56 (1.33, 1.84) for participants <50 y, and 1.11 (1.07, 1.16) for participants >=65 y. The elevated hazard of dementia associated with health condition risk score was much higher in participants <50 y (2.36 [1.90, 2.95]) than in older adults (1.37 [1.29, 1.45]).

When further adjusted for the APOE genotype, we observed similar results as in primary analysis (**Table S3**). After excluding participants who developed dementia or died within the first two years after baseline assessment, the magnitudes of the associations between risk factors and dementia was slightly attenuated but remained significant (**Table S4**). The relations remained similar when excluding participants with stroke history at baseline (**Table S5**). Taking mortality of other causes into consideration, the estimated HRs were not substantially affected by competing risk of mortality (**Table S6**). Further, we observed a significant non-linear association (P<0.001) between alcohol intake and dementia (**Figure S2**), confirming the validity of the definition of non-moderate alcohol intake in this study population.

### 3.3 Sex- and age-specific population attributable fractions (PAFs)

In the overall participants, the dementia risk were mostly attributable to lifestyle factors (PAF [95% CI]=21.90% [13.33%, 30.04%]), with the leading factors being non-moderate alcohol intake (8.73% [6.19%, 11.40%] and insufficient or excessive sleep (8.65% [4.52%, 12.44%]) (**Figure S3**). The corresponding PAFs for socioeconomic and health conditions risk factors were 13.39% (6.83%, 20.49%), and 14.31% (10.40%, 18.42%), respectively.

The PAFs for each individual risk factor showed different patterns across sex and age groups (**Figure 3 & Table S7**). For female participants, non-moderate alcohol intake was the leading factors (11.14% [6.69%, 15.59%]), followed by inadequate or excessive sleep duration (9.25% [3.07%, 15.43%]). For male participants, suboptimal sleep duration (9.13% [3.59%, 14.67%]), CVD (9.12% [7.01%,11.22%]), and education below high school (8.67% [3.19%, 14.15%]) were three primary population attributable factors for dementia. For participants with a baseline age below 50, the risk were mostly attributable to socioeconomic and lifestyle risk factors, including high deprivation (28.25% [6.54%, 49.97%]), lower education (34.67% [11.95%, 57.38%]), suboptimal diet (27.80% [11.26%, 44.35%]), and suboptimal sleep duration (25.77% [3.66%, 47.87%]). In older participants (>=65 y), the leading factors were suboptimal sleep duration (8.97% [3.22%, 14.71%]), lower education(7.11% [1.06%, 13.17%]), and CVD (6.90% [4.95%, 8.86%]).

The PAFs for each risk factor category also demonstrated a specific pattern according to sex and age. Compared to female participants, PAF for health conditions was higher in the male participants (**Figure 4A & Table S8**). Overall, the PAFs for these factors decreased as the age increased, with the risk attributable to socioeconomic and lifestyle factors decreasing more rapidly (**Figure 4B**). The PAFs of health conditions were generally constant across age groups and became dominant in older adults.

## 4. Discussion

In this large cohort of UK adults followed from different life stages, specific patterns in the association and attributable risk of several socioeconomic, lifestyle, and health condition risk factors for dementia were observed across age subgroups. In general, five out of eleven modifiable risk factors had stronger associations with dementia among younger adults than in relatively older adults, including suboptimal

diet, non-moderate alcohol intake, hypertension, CVD, and diabetes. Consequently, the corresponding PAFs were consistently greater among younger adults. Although we did not observe a significant difference in dementia risk factors between women and men, the PAF of health conditions was higher in the male participants due to their higher prevalences. Overall, we observed stronger association and greater attributable risk of several modifiable risk factors for dementia among younger adults.

To the best of our knowledge, this is one of the few studies to systematically capture the age and sex disparities in risk factors of dementia. Although subgroup analyses are frequently conducted, most prior studies did not look into the age disparities in sufficient depth. Among overall adult participants, the magnitudes of the associations between risk factors and dementia were, in general, comparable with those in previous studies. For example, we observed that smoking was associated with approximately 30% increased dementia risk in the overall population (HR [95%CI] = 1.31 [1.17, 1.46]), which was close to results in a previous meta-analysis[13] (1.37 [1.23, 1.52]). Similarly, our study found that diabetes (1.93 [1.74, 2.14]) conferred a 1.9-fold hazard of incident dementia, aligning with the pooled results of the previous findings[8]. Different from the risk factor profiles of other diseases, such as CVD[31], diabetes[32], and heart failure[33], we do not consider obesity as an established risk factor for dementia because previous evidence was conflicting [26, 34].

Notably, we observed significant effect modifications on these risk factors by age. This finding potentially represented differences in susceptibilities of the risk factors across adult life stage and benefits to be brought about by controlling them. The HRs were higher for most modifiable risk factors in younger participants, although the disparities were not all statistically significant. The attenuated associations acrossing increasing age groups were similar to previous studies investigating individual risk factors, such as diabetes[35] and hypertension[36].We additionally reported stronger assocations of several other modifiable risk factors, especiallay suboptimal diet, non-moderate alcohol intake and CVD. In particular, suboptimal diet was significianlty associated with a increased dementia risk among participants aged 40-55 years but not in older adults. While it may be subjective to potential measurement error, this finding suggested that dietary factors from early adult life and over long preiods may be needed to have benefits in preventing late-life dementia. Nonetheless, more research is needed to understand the long-term developmental course, its associated factors and biological mechanisms of dementia. On the other hand, we detected no significant interaction between the risk factors and sex, suggesting that targeting modifiable risk factors are equally important for both men and women.

Taking into account the differences in the subgroup prevalence of these risk factors, we also estimated the corresponding PAFs in our study population to represent the propotion of preventable dementia cases by a variety of risk factors. Specifically, the dementia risk attributable to health conditions was higher in men than in women, mainly due to the higher prevalence of diabetes, CVD, and hypertension in male participants. It is noteworthy that the overall PAF was lower in older participants than in younger participants, suggesting that percentage of incident dementia that could be prevented by controlling these risk factors are less among older participants. Taken together, our findings provided timely and

essential public health implications to design targeted prevention strategies with sex- and age-specific considerations for different populations according to their specific modifiable risk factor profiles.

The current study has several strengths. The large well-characterized cohort study with large variations in age at baseline enabled us to examine a wide range of modifiable risk factors in diversified age subgroups. The definition of dementia based on clinical diagnosis and death information increased the accuracy of our analysis. The relatively long follow-up time, low rate of loss-to-follow-up, and careful control for potential confounders also increased the validity of the study results. However, our findings should be interpreted with caution due to a few limitations. First, the population distributions in our study may not be highly representative of the UK residents as the dominant European-ancestery population in the cohort may have limited the racial representation. Second, because of potential residual confounding and the observational nature of this study, our findings may not fully reflect causal relationships, even though we carefully controlled for potential confounders and selected risk factors identified by meta-analyses. Third, the null association between overall dietary quality and dementia in elderly adults might be a result of measurement error in the dietary assessment method. Although previous studies also reported inconsistent associations between dietary factors and dementia [39–41], reverse causality could exist considering the long-term nature of dementia and that participants with preclinical symptoms tended to alter their dietary behaviour. Furthermore, the underreporting of milder dementia cases is possible when patients did not acquire medical assistance and were thus not recorded in the registry.

# 5. Conclusions

In conclusion, this study identified age-specific modifiable risk factor profiles for incident dementia in a large cohort of UK participants. Our observational findings supported the stronger association and greater attributable risk of major modifiable risk factors for dementia among younger adults, indicating the importance of targeted preventive strategies from an earlier age across adult life course to reduce the risk of dementia in the aging population.

# Declarations


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**Declarations of interest**: None


**Author contributions**: HC, GZ, and CY designed the study; HC performed the statistical analyses; HC drafted and YM, YC, and GZ revised the manuscript; CY supervised the data analysis and interpretation; CY had the primary responsibility for the final content. All authors critically reviewed the manuscript and approved the final draft.

**Patient and Public Involvement:** Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research

**Data share statement**: This research was conducted using the UK Biobank Resource: application number 55005. Data used in this study from the UK Biobank and codebooks are all available upon application (www.ukbiobank.ac.uk/). The authors thank the participants of the UK Biobank for their contributions to this work.

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**DATA AVAILABILITY:** Data used in this study from the UK Biobank are all available upon application (www.ukbiobank.ac.uk/).

# Abbreviations

body mass index, BMI; hazard ratio, HR; confidence interval, CI; population attributable fraction, PAF; Townsend deprivation index, TDI; UK Biobank, UKB; cardiovascular disease, CVD.

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# Table 1

**Table 1**. Baseline characteristics of UK Biobank participants by age and sex

| | Overall | By Age | | | | | By Sex | |
|---|---|---|---|---|---|---|---|---|
| | | 40-<50 | 50-<55 | 55-<60 | 60-<65 | >=65 | Female | Male |
| **n** | 372867 | 99665 | 61292 | 69472 | 84449 | 57989 | 202166 | 170701 |
| **Female (%)** | 202166 (54.2) | 55253 ( 54.4) | 35012 ( 57.1) | 38446 ( 55.3) | 44892 (53.1) | 28626 (49.4) | 0 ( 0.0) | 170701 (100.0) |
| **White ethnicity (%)** | 354601 (95.1) | 91687 ( 92.0) | 57801 ( 94.3) | 66642 ( 95.9) | 82186 (97.3) | 56285 (97.1) | 192166 ( 95.1) | 162435 ( 95.2) |
| **age, mean (SD)** | 55.61 (8.06) | 44.95 (2.74) | 52.03 (1.41) | 57.05 (1.42) | 61.90 (1.39) | 66.86 (1.48) | 55.34 (7.96) | 55.93 (8.17) |
| **Sociodemographic risk factors** | | | | | | | | |
| High deprivation (%) | 186391 (50.0) | 56411 ( 56.6) | 31757 ( 51.8) | 33898 ( 48.8) | 38505 (45.6) | 25820 (44.5) | 102107 ( 50.5) | 84284 ( 49.4) |
| Below High School (%) | 223972 (60.1) | 57523 ( 57.7) | 35587 ( 58.1) | 40207 ( 57.9) | 52758 (62.5) | 37897 (65.4) | 124458 ( 61.6) | 99514 ( 58.3) |
| **Lifestyle risk factors** | | | | | | | | |
| Current smoking (%) | 34875 ( 9.4) | 12545 ( 12.6) | 6354 ( 10.4) | 6101 ( 8.8) | 6305 ( 7.5) | 3570 ( 6.2) | 15972 ( 7.9) | 18903 ( 11.1) |
| Insufficient physical activity (%) | 106652 (28.6) | 25732 ( 25.8) | 17791 ( 29.0) | 21324 ( 30.7) | 24941 (29.5) | 16864 (29.1) | 61408 ( 30.4) | 45244 ( 26.5) |
| Suboptimal diet (%) | 120953 (32.4) | 39221 ( 39.4) | 20943 ( 34.2) | 21124 ( 30.4) | 23782 (28.2) | 15883 (27.4) | 50116 ( 24.8) | 70837 ( 41.5) |
| Non-moderate alcohol intake (%) | 122990 (33.0) | 35822 ( 35.9) | 20167 ( 32.9) | 22161 ( 31.9) | 26230 (31.1) | 18610 (32.1) | 86365 ( 42.7) | 36625 ( 21.5) |
| Sleep <=6 or >=8 hrs (%) | 220629 (59.2) | 56292 ( 56.5) | 34769 ( 56.7) | 40317 ( 58.0) | 52118 (61.7) | 37133 (64.0) | 122268 ( 60.5) | 98361 ( 57.6) |
| **Health condition risk factors** | | | | | | | | |
| Hypertension (%) | 91764 (24.6) | 12467 ( 12.5) | 12418 ( 20.3) | 18048 ( 26.0) | 26791 (31.7) | 22040 (38.0) | 43604 ( 21.6) | 48160 ( 28.2) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Caridovascular Diseases (%) | 16695 ( 4.5) | 1170 ( 1.2) | 1559 ( 2.5) | 2707 ( 3.9) | 5259 ( 6.2) | 6000 (10.3) | 4991 ( 2.5) | 11704 ( 6.9) |
| Diabetes (%) | 15499 ( 4.2) | 1905 ( 1.9) | 2013 ( 3.3) | 2976 ( 4.3) | 4501 ( 5.3) | 4104 ( 7.1) | 5424 ( 2.7) | 10075 ( 5.9) |
| Depressive symptoms (%) | 15877 ( 4.3) | 5833 ( 5.9) | 3421 ( 5.6) | 2926 ( 4.2) | 2350 ( 2.8) | 1347 ( 2.3) | 9668 ( 4.8) | 6209 ( 3.6) |
| **Obesity (%)** | 84126 (22.6) | 21122 ( 21.2) | 14618 ( 23.8) | 16432 ( 23.7) | 19442 (23.0) | 12512 (21.6) | 43684 ( 21.6) | 40442 ( 23.7) |
| **Incident dementia (%)** | 3708 ( 1.0) | 113 ( 0.1) | 146 ( 0.2) | 360 ( 0.5) | 1087 ( 1.3) | 2002 ( 3.5) | 1674 ( 0.8) | 2034 ( 1.2) |
| Alzheimer's Disease (%) | 1057 ( 0.3) | 13 ( 0.0) | 29 ( 0.0) | 82 ( 0.1) | 330 ( 0.4) | 603 ( 1.0) | 530 ( 0.3) | 527 ( 0.3) |
| vascular dementia (%) | 503 ( 0.1) | 6 ( 0.0) | 16 ( 0.0) | 33 ( 0.0) | 139 ( 0.2) | 309 ( 0.5) | 204 ( 0.1) | 299 ( 0.2) |

# Figures

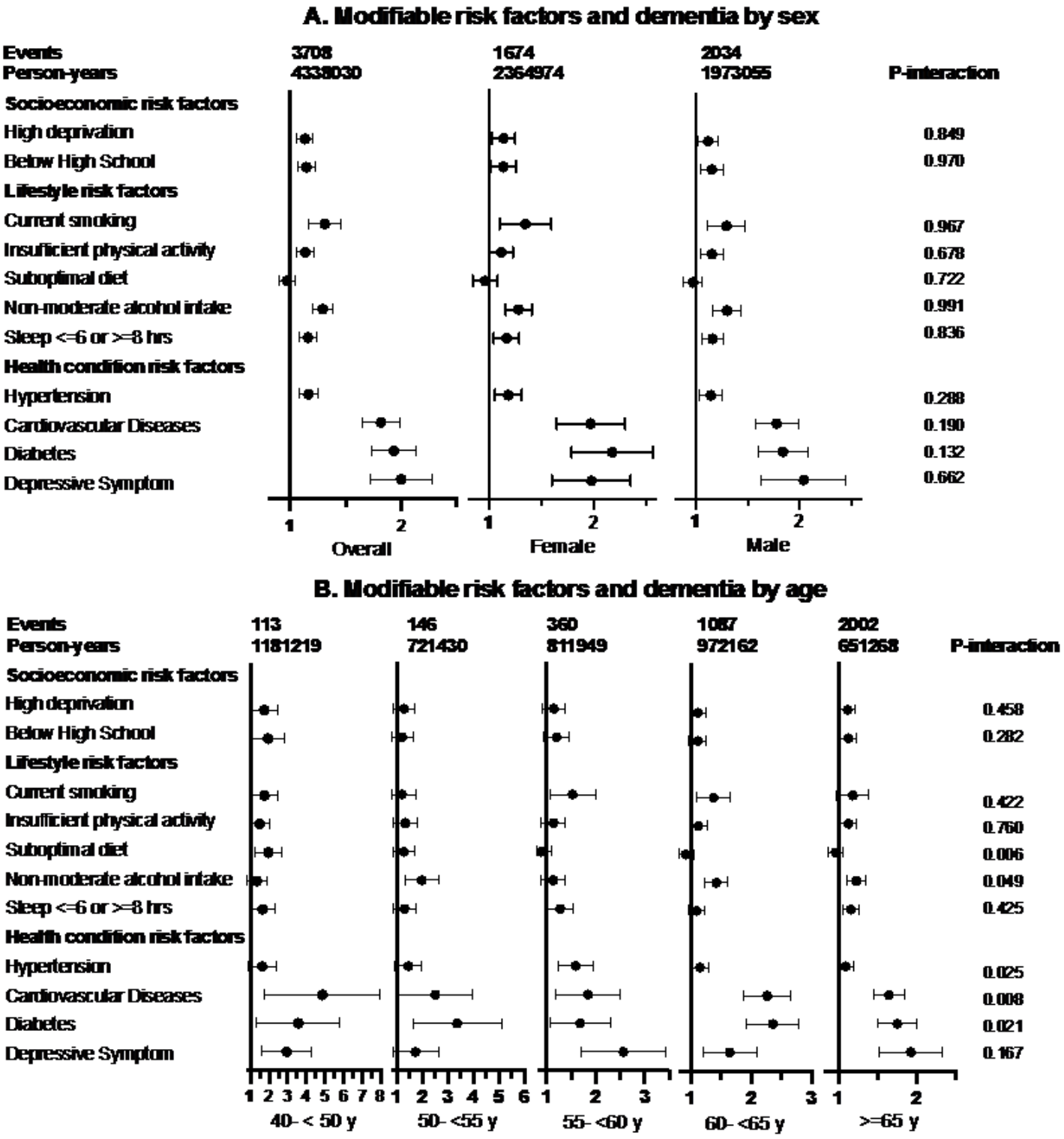
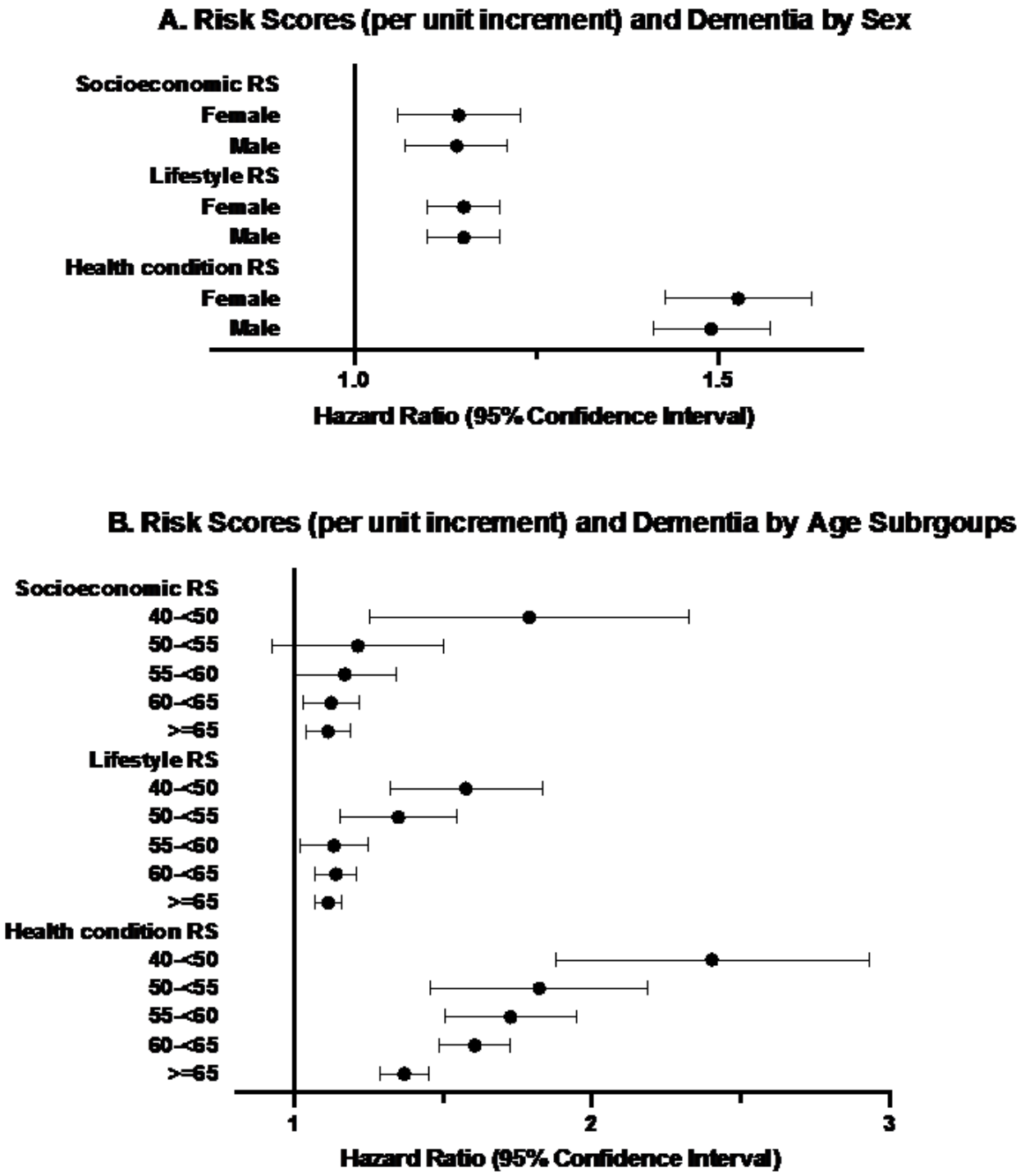



Figure 1

Hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between modifiable risk factors and dementia by age and sex. Models were adjusted for age (not in the age-stratified models), sex (not in the sex-stratified models), and mutually adjusted for individual risk factors. P-interaction was calculated as the significance of the multiplication term of individual risk factors and sex or age ine the overall population.




## Figure 2

Hazard ratios (HRs) and 95% confidence intervals (CIs) of incident dementia associated with each 1-point increment in risk scores (RSs) by age and sex. Socioeconomic risk factors included education below high school and high Townsend deprivation index, with the risk score ranging from 0 to 2. Lifestyle risk factors included non-moderate alcohol intake, current smoking behaviour, suboptimal diet, non-regular physical exercise, and sleep duration <=6 or >=8 hrs/d, with the risk score ranging from 0 to 5. Health condition risk factors included hypertension, diabetes, cardiovascular diseases, and depressive symptom, with the risk

score ranging from 0 to 4. Models were adjusted for age (not in the age-stratified models), sex (not in the sex-stratified models), and mutually adjusted for risk scores of other categories.

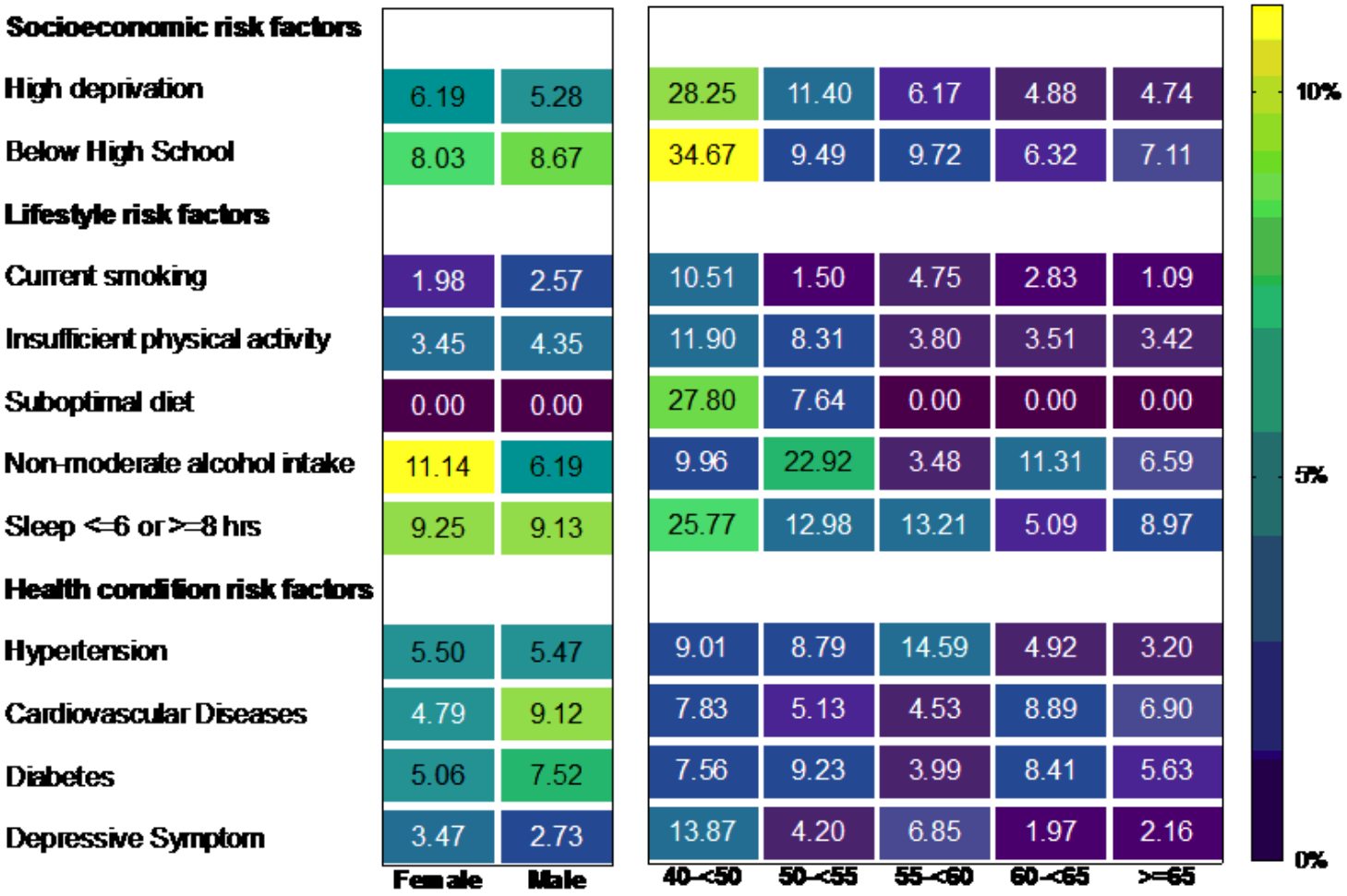



Figure 3

Population-attributable fractions (PAFs) for incident dementia associated with individual risk factors by sex and age. PAFs were calculated using adjusted hazard ratios (HRs) of each individual risk factors. Risk factors with a PAF below 0 were truncated at 0.

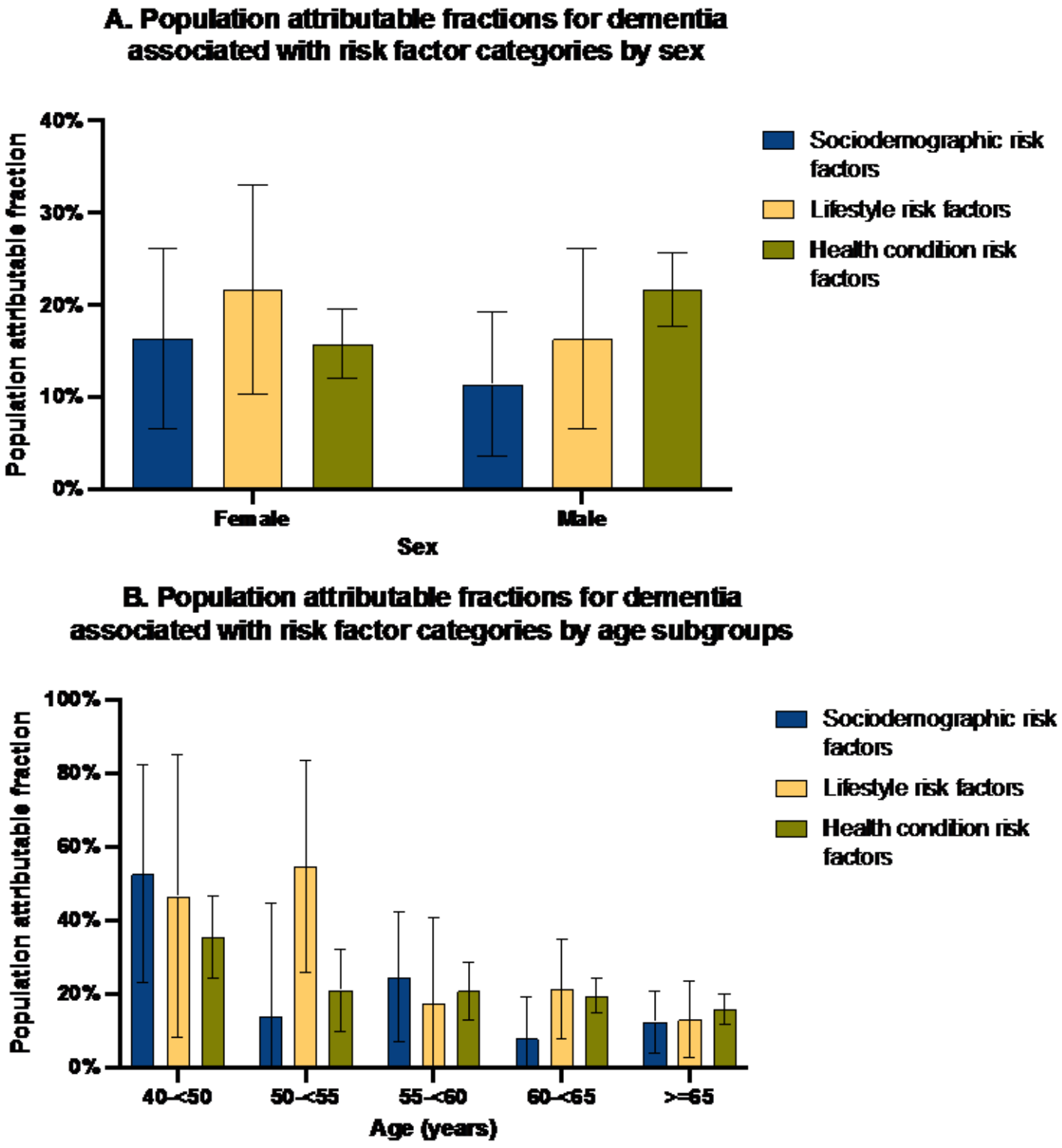



Figure 4

Population-attributable fractions for incident dementia associated with categories of risk factors by age and sex. PAFs were calculated using adjusted hazard ratios (HRs) of each categories of risk factors. Risk factor categories with a PAF below 0 were truncated at 0.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SIRFPdementia1107.docx