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Original Article

Healthy lifestyle habits, educational attainment, and the risk of 45 age-related health and mortality outcomes in the UK: A prospective cohort study

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ABSTRACT

Objectives: This study aimed to evaluate to what extent lifestyle habits, contribute to associations between EA and various conditions, and test the variability in risk reduction for specific health conditions linked to a healthy lifestyle across different EA levels.

Design, setting, participants, and measurements: Data were analyzed from 341,632 UK Biobank participants without baseline cardiovascular disease or cancer (2006–2010). A healthy lifestyle score (0–5) was created by assigning one point for each of five habits: a healthy diet, sufficient physical activity, non-current smoking, moderate alcohol consumption, and low-risk sleep duration. Baseline data on self-reported and genotype-predicted EA were collected, with 45 health outcomes assessed until January 2021. Logistic regression models were used to assess the relationship between EA and lifestyle habits, and associations between the healthy lifestyle score and health/mortality outcomes were examined using Cox proportional hazards model. Moderation analysis tested whether EA modified the associations between a healthy lifestyle and health outcomes, while mediation analysis estimated the proportion of the association between EA and health outcomes explained by lifestyle habits.

Results: Both self-reported and genotype-predicted EA were associated with a healthy diet, non-current smoking, low-risk sleep duration, and moderate alcohol consumption, but not low-risk physical activity. A healthy lifestyle is inversely linked to risks for 38 of 45 outcomes, including CVD, type 2 diabetes, lung and colon cancer, depression, and chronic kidney disease, as well as overall, CVD, and cancer mortality. Higher EA reduced risk for 25 conditions, such as CVD, certain cancers, chronic liver disease, and fractures; stronger inverse lifestyle-risk associations were observed among less educated individuals. Lifestyle habits explained 47.2% (95% CI: 35.3–59.4%) of the association between genotype-predicted EA and all-cause mortality, mediating a large proportion of associations with CVDs, cancers, dementia, respiratory diseases, and chronic kidney disease.

Conclusions: Higher EA might encourage the adoption of more healthy lifestyle habits, thus promoting healthy aging. Placing greater emphasis on lifestyle modification is essential for individuals with lower EA to effectively address health inequalities associated with EA.

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1. Introduction

It is estimated that major non-communicable diseases (NCDs) including cardiovascular disease (CVD), cancer, diabetes, and neurological diseases accounted for 41.1 million global deaths in 2017 (73.5% of all deaths) [1]. While NCDs are responsible for approximately 89.0% of deaths in the UK [2]. Target 3.4 of the United Nations Sustainable Development Goals, adopted in 2015 as part of a global agenda to promote health and well-being, aims to achieve a one-third reduction in premature mortality caused by NCDs by 2030, using 2015 levels as a baseline [3]. This target aligns with broader efforts to ensure healthy lives and promote well-being for all ages, ultimately contributing to healthy aging and increased life expectancy.

A study utilizing data from the Prospective Urban Rural Epidemiology, a large-scale epidemiological study designed to investigate health determinants, analyzed data from 21 high-, middle-, and low-income countries around the world. The findings demonstrated that behavioral risk factors collectively contributed to 26.3% of total deaths [4]. Evidence shows that adopting a healthy lifestyle was associated with a longer life expectancy [5–7]. Adherence to healthy lifestyle habits was also associated with a reduced risk of CVD [8], certain cancers [9], diabetes [10], mental disorders [11], neurodegenerative diseases [12], and chronic kidney disease (CKD) [13]. However, less is known regarding the association between healthy lifestyle habits and the risk of digestive disorders, respiratory diseases, or ophthalmic conditions. Low educational attainment (EA) was the single largest risk factor for mortality (population attributable risk: 12.5%) [4]. Higher EA has been linked to a reduced risk of some major chronic diseases including CVD, cancer, and depression in both observational [14,15] and genetic analyses [15–17]. Observational analysis has shown higher EA may help promote healthy lifestyle habits thereby mitigating the risk of mortality [18,19].

Recent evidence has demonstrated that multiple organs undergo simultaneous aging [20]. However, a small number of studies have concurrently linked lifestyle habits or EA to a broad spectrum of age-related chronic conditions. The outcome-wide approach is a research framework commonly used in fields such as epidemiology to simultaneously explore the relationships between a single exposure and a broad array of potential outcomes. This evolving approach offers a distinctive opportunity to directly compare connections with various conditions without selective reporting bias [15,21]. Meanwhile, there is limited evidence regarding specific guidelines for preventing individual health conditions among individuals with varying levels of EA.

Using the data from the UK Biobank, we aimed to investigate the associations of healthy lifestyle habits and EA with the risks of a broad spectrum of age-related health conditions and mortality. Additionally, we aimed to test whether the associations between healthy lifestyle habits and risks of health conditions varied among individuals with different EA levels. We then evaluated the degree to which lifestyle habits mediated the relationship between EA and risks of health conditions.

2. Methods

2.1. Study population

The UK Biobank consists of a population cohort of over 500,000 individuals aged between 40 and 73 years at baseline (2006–2010) [22]. From a pool of approximately 9.2 million eligible individuals registered with the National Health Service, demographic information, health-related outcome data, and biomarkers and genetic data was collected from 502,505 individuals at the baseline. The UK Biobank database provides comprehensive health and genetic data, which we utilized in our analysis without additional data collection from participants.

The UK Biobank Study's ethical approval has been granted by the National Information Governance Board for Health and Social Care and the NHS North West Multicenter Research Ethics Committee. All participants provided informed consent through electronic signature at recruitment.

2.2. Ascertainment of chronic conditions and mortality

Individual diseases at baseline were identified using self-reported and inpatient data available in the UK Biobank. A disease was considered present if participants reported that a doctor had informed them of their diagnosis (Field code: Table S1). Inpatient hospital records were obtained through the Hospital Episode Statistics database, the Scottish Morbidity Record, and the Patient Episode Database in England, Scotland, and Wales [22]. The International Classification of Diseases (ICD) codes for each of the 41 diseases can be found in Table S2.

Newly developed cases of those individual diseases were identified using inpatient and mortality data. All-cause and specific-cause mortality (CVD, cancer, and other reasons) were identified using mortality register data. The person-years for each disease were computed starting from the date of the initial assessment until the onset of the condition, date of death, or the conclusion of the follow-up period (December 31, 2020 for England and Wales and January 31, 2021 for Scotland), whichever came first.

2.3. Assessment of lifestyle habits

Lifestyle factors, including diet quality, smoking status, physical activity, alcohol intake, and sleep duration, were self-reported at baseline in the UK Biobank. Based on these responses, we calculated a healthy lifestyle score by assigning one point for each healthy behavior, including a healthy diet, sufficient physical activity, low-risk group for smoking, and optimal sleep duration, as defined below. Diet quality score was computed based on seven commonly eaten food groups with a higher score representing a healthier diet [23]. A diet was categorized as healthy if the diet score was equal to or greater than 4. Low-risk and sufficient physical activity was defined as $\geq$150 min of moderate activity per week or $\geq$75 min of vigorous activity according to the guidelines from the World Health Organization [24]. The low-risk group for smoking was defined as not currently smoking. Low-risk sleep duration was defined as 7−9 hours per day. These factors were selected based on the evidence for their associations with CVD and mortality [5,6].

2.4. Genetic data

The UK Biobank Axiom array, developed by Affymetrix, was employed for genotyping purposes. This array was utilized to perform genotyping on approximately 460,000 out of the total 500,000 participants enrolled in the UK Biobank project. The team at the UK Biobank performed genotype imputation using the Haplotype Reference Consortium reference panel, which was accompanied by rigorous quality control procedures. Genetic variants linked to EA were selected from a Genome-wide associated study involving 3 million individuals, from which 3941 single nucleotide polymorphisms were used to calculate the genetic risk score (GRS) [17]. The summary statistics from this study were used to compute the GRS for EA, and all other statistical analyses were conducted using data from the UK Biobank.

2.5. Covariates

Self-reported data on demographic information (age, sex, EA, ethnicity, and income) was collected using a touchscreen questionnaire. Townsend deprivation index of material deprivation was used to assess neighbourhood-level socioeconomic status. Body mass index (BMI) was calculated using measured weight and height.

2.6. Statistical analysis

Baseline characteristics data were displayed as frequencies (percentages) for categorical variables and as means ± standard deviations for continuous variables across the number of healthy lifestyle habits. We used ANOVA for continuous variables, and Chi-square tests for

categorical variables to test the difference in distribution of characteristics. Logistic regression models were employed to explore the relationship between self-reported and genotype-predicted EA and healthy lifestyle habits.

Cox proportional hazard regression models were used to examine associations between the healthy lifestyle score (quintiles) and risks of 45 health and mortality outcomes. We tested two models for healthy lifestyle score: 1) age, and sex; 2) Model 1 plus ethnicity, EA, income, Townsend index, BMI, dyslipidemia, hypertension, and diabetes at baseline. For the association of self-reported (low: 0–5 years, intermediate: 6–12 years, high: ≥13 years) and genotype-predicted EA (tertiles) with risks of health conditions/mortality, three models were tested: 1) age and sex; 2) Model 1 plus ethnicity, income, Townsend index, BMI, dyslipidemia, hypertension, and diabetes at baseline (additional adjustment for 10 principal components for genotype-predicted EA); 3) Model 2 plus the five individual lifestyle habits.

We investigated whether the associations of the healthy lifestyle score and individual healthy lifestyle habits with the risk of health conditions and mortality were moderated by EA. Mediation analysis was also performed to assess the proportion of associations between self-reported/genotype-predicted EA and the risks of health conditions and mortality explained by lifestyle habits (details in the Supplemental materials).

Sensitivity analyses were carried out to explore the association between the healthy lifestyle score/EA and the risks of health conditions/mortality, excluding individuals who developed the corresponding condition within the first five years of follow-up.

The percentages of participants with missing values on income, and BMI, were 0.3%, 11.1%, and 1.4%, respectively. Multiple imputations for missing data in covariates were conducted to create 10 imputed datasets. For multiple comparisons, Benjamin–Hochberg's procedure was used to control the false discovery rate (FDR) at a 5% level [25]. Significant associations were identified when consistent directions were observed across different models. Data analyses were conducted using SAS 9.4 for Windows (SAS Institute Inc.) and all P values were two-sided with statistical significance set at <0.05.

3. Results

3.1. Population selection

Of 502505 participants with baseline data, those with missing data on diet (n = 6048), physical activity (n = 97809), smoking (n = 1104), alcohol consumption (n = 192), or sleep duration (n = 55), or those with CVDs (n = 27566), or cancer (n = 28099) at baseline were excluded from the analysis. We included 341632 participants (52.8% females) aged 55.7 (SD = 8.1) years in the analysis of the association between lifestyle and risk of health conditions (Figure S1).

3.2. Healthy lifestyle habits

63.5% had a healthy diet, 54.6% engaged in low-risk physical activity, 89.8% were non-smokers, 44.0% consumed alcohol moderately, and 74.5% had low-risk sleep. Only 12.4% maintained all five healthy habits (Figure S2). Men were less likely than women to have a healthy diet, be non-smokers, and have low-risk sleep, but more likely to consume alcohol moderately and engage in low-risk physical activity (Figure S3). Older individuals were more likely than younger ones to have healthy habits, particularly in sleep and physical activity (Figure S4).

More educated individuals were more likely to have a healthy diet, be non-smokers, have low-risk sleep, and consume alcohol moderately, but were less physically active. These patterns were confirmed by genotype-predicted EA analysis (Fig. 1).

3.3. Baseline characteristics

Individuals with more healthy lifestyle habits were more likely to be females, older, whites, and have higher income and lower Townsend deprivation. A higher healthy lifestyle score was associated with a lower prevalence of hypertension, diabetes, and dyslipidemia (Table S3).

3.4. Incidence of health conditions and mortality

Over an average follow-up period of 11.7 years, the number of incident cases of specific diseases ranged from 592 cases for Meniere's disease to 34,375 cases for diverticulitis. The overall mortality rate was 4.20 cases per 1,000 person-years.

3.5. Healthy lifestyle habits and health conditions and mortality

The healthy lifestyle score was inversely associated with the risk of all CVDs and metabolic disorders. The HR (95% CI) for CVD associated with each healthy lifestyle habit increment was 0.89 (0.88−0.90). The risk reduction (95% CI) associated with each healthy lifestyle habit increment ranged from 5% (3–7%) for atrial fibrillation to 22% (20–25%) for peripheral vascular disease.

Individuals with a higher healthy lifestyle score had a lower risk of all cancers (HR (95% CI) for each healthy lifestyle habit increment: 0.93 (0.92−0.94)). A higher lifestyle score was associated with a lower risk of lung cancer, stomach cancer, oesophageal cancer, colon cancer, breast cancer, and other cancers, and a higher risk of melanoma in the full model.

Healthy lifestyle score was inversely associated with the risk of all neurological disorders and psychological disorders. The risk reduction (95% CI) ranged from 6% (1–10%) for Parkinson's disease to 22% (20–23%) for depression.

A higher healthy lifestyle score was associated with a lower risk of all digestive disorders, respiratory disorders, CKD, musculoskeletal disorders, and ophthalmic conditions. The risk reduction (95% CI) for overall mortality, CVD mortality, and cancer mortality associated with each healthy lifestyle habit was 21% (20–22%), 22% (19–25%), and 18% (16–19%), respectively.

In summary, a higher healthy lifestyle score was associated with a reduced risk of 34 health conditions and all four mortality outcomes and an increased risk of two diseases (melanoma and prostate cancer) (Fig. 2). Similar results were observed when the healthy lifestyle score was analyzed as a categorical variable in quintiles (Table S4).

Men had higher incidence rates of CVDs, metabolic disorders, cancers, CKD, neurological disorders, and mortality, while women had higher incidence rates of psychological and musculoskeletal disorders (Figure S5). The inverse associations between healthy lifestyle score and incident CVDs, chronic obstructive pulmonary disease (COPD), pernicious anaemia, and osteoporosis were stronger in women than in men (Figure S6).

As shown in Figure S7, a healthy diet was inversely associated with the risk of 30 individual health conditions and not positively associated with the risk of any condition. Low-risk physical activity was inversely associated with the risk of 32 individual health conditions and positively associated with the risk of two conditions (rectal cancer and osteoporosis). Non-current smoking was inversely associated with the risk of 34 individual health conditions and positively associated with the risk of four conditions (melanoma, prostate cancer, prostate disorders, and Parkinson's disease).

3.6. Educational attainment and health conditions and mortality

In the age- and sex-adjusted model, a higher EA was associated with a lower risk of 31 and a higher risk of two (prostate cancer, breast cancer) out of 41 individual health conditions tested. After adjustment for socioeconomic and metabolic indicators, 24 of the inverse associations remained significant. This number was reduced to 23 after further adjustment for lifestyle habits. EA was inversely associated with the risk of all-cause mortality and mortality caused by cancer or other reasons, but not CVD in the full model (Fig. 3).

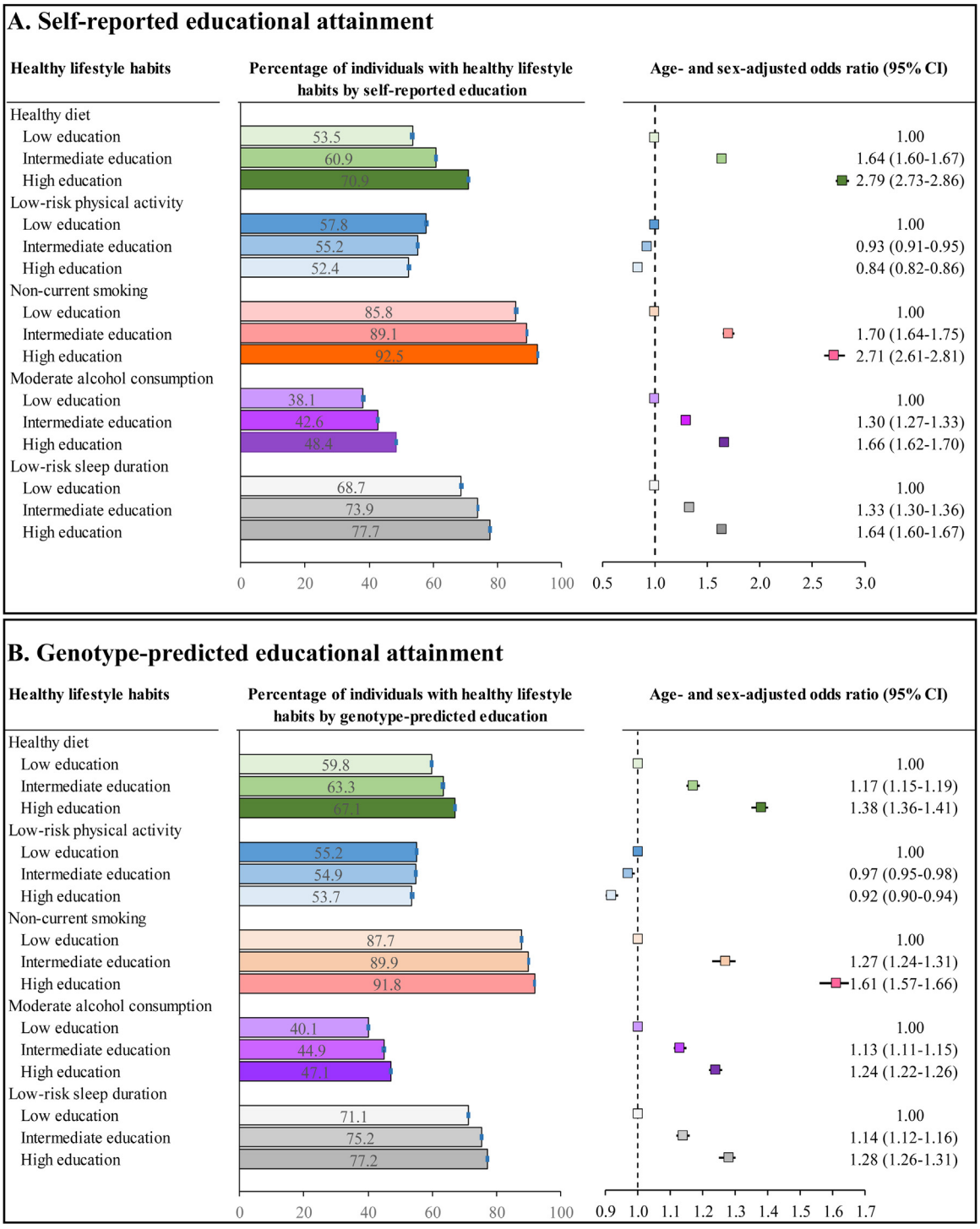

Fig. 1. The association of self-reported and genotype-predicted educational attainment with healthy lifestyle habits.
Self-reported educational attainment falling within the ranges of 0–5, 6–12, and ≥13 years were categorized as low, intermediate, and high levels, respectively. Tertiles 1, 2, and 3 of genotype-predicted educational attainment were categorized as low, intermediate, and high levels, respectively. Logistic regression model was used to examine the associations of self-reported and genotype-predicted educational attainment with healthy lifestyle habits. For self-reported educational attainment, the model was adjusted for age and sex. For genotype-predicted educational attainment, the model was adjusted for age, sex, and 10 genetic principal components.
The vertical dash lines represent the odds ratio of 1. Squares represent the odds ratios. Horizontal lines indicate the range of the 95% confidence interval.

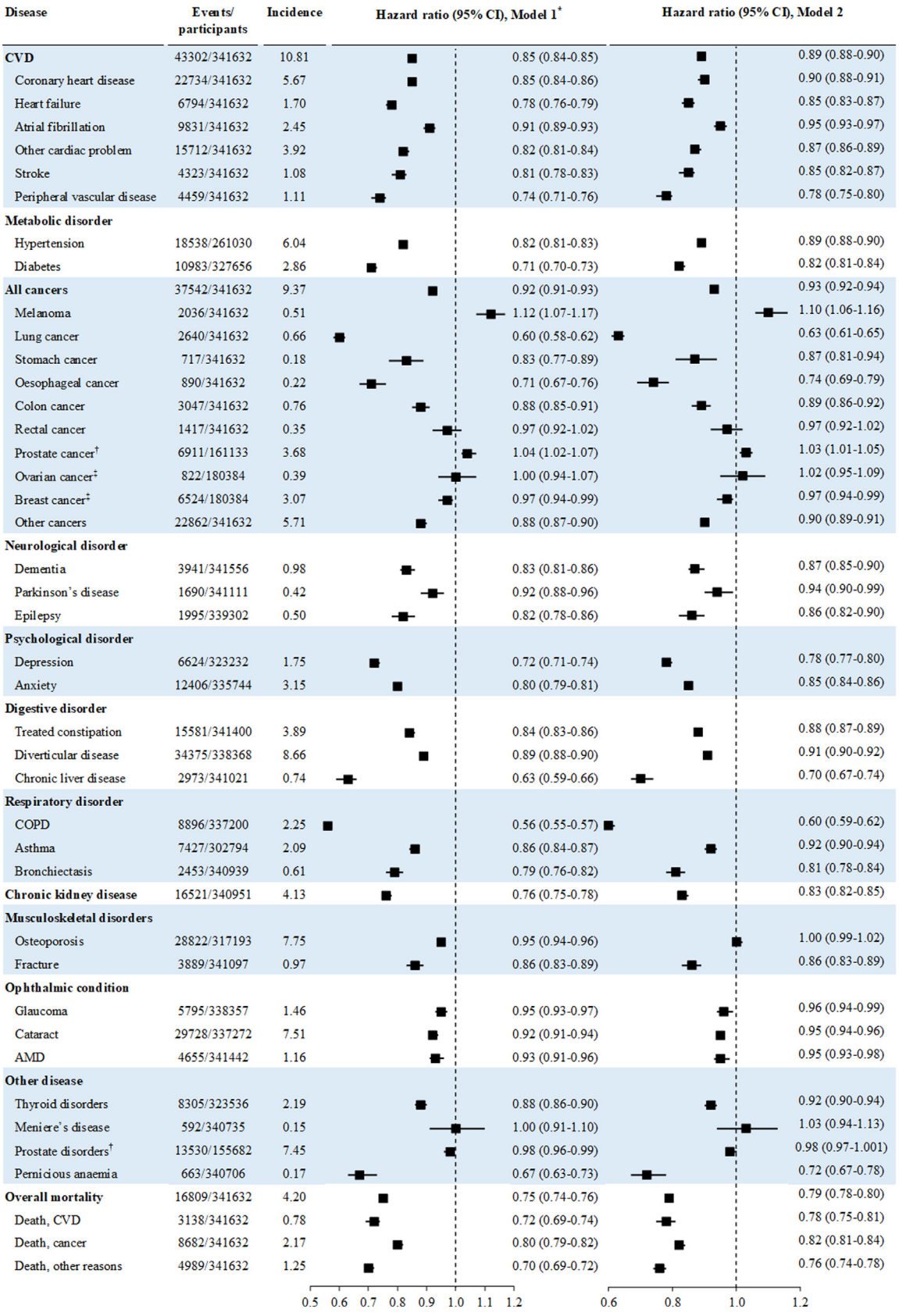

Fig. 2. The association between healthy lifestyle score and the risk of individual health conditions and mortality.
AMD, age related macular degeneration; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease.
The incidence refers to the number of event cases per 1000 person-years. Cardiovascular disease includes coronary heart disease, heart failure, atrial fibrillation, other cardiac disease, stroke, and peripheral vascular disease. All cancers encompass any type of cancer except for non-melanoma skin cancer. The vertical dash lines represent the hazard ratio of 1. Squares represent the hazard ratios. Horizontal lines indicate the range of the 95% confidence interval.

Similar results for the associations with the risk of health conditions and mortality were seen when genotype-predicted EA was analyzed (Figure S8).

3.7. Moderation analysis

The HRs (95% CIs) for mortality associated with each healthy lifestyle habit increment among individuals with low, intermediate, and high EA were 0.76 (0.74−0.78), 0.79 (0.78−0.81), and 0.83 (0.80−0.85), respectively. Similarly, the risk reduction for CVD, certain cancers, chronic liver disease, digestive disorders, and fracture associated with healthy lifestyle score was more pronounced among individuals with low EA (Figure S9).

The inverse associations between healthy diet and risks of some CVDs, lung cancer, asthma, and all-cause and cancer mortality were stronger among individuals with low EA (Figure S10). The inverse associations between low-risk physical activity and the risk for some CVDs, asthma, and mortality were more prominent among less educated individuals (Figure S11). Similarly, the inverse associations between non-current smoking and risks of some CVDs, certain cancers, CKD, some digestive disorders, and mortality were stronger among less educated individuals (Figure S12). In contrast, the associations between moderate alcohol consumption and the risk of atrial fibrillation were more evident among those with high EA (Figure S13). The inverse associations between low-risk sleep duration and the risk of colon cancer and bronchiectasis were stronger among less educated individuals (Figure S14).

3.8. Mediation analysis

The links between EA, lifestyle habits, and risks of health and mortality outcomes are shown in Figure S15. The proportion (95% CI) of the association between self-reported EA and risk of all mortality explained by five lifestyle habits combined was 41.4% (32.4–51.0%). The corresponding number for CVDs, all cancers, dementia, COPD, and CKD was 16.7% (14.5–19.2%), 27.9% (17.8–40.9%), 21.5% (11.7–36.1%), 27.7% (24.5–31.0%), 17.2% (14.6–20.3%), respectively (Fig. 4). Lifestyle habits were significant mediators for the association between genotype-predicted EA and risks of health and mortality outcomes (Figure S16).

3.9. Sensitivity analysis

Similar results for the association between healthy lifestyle score (Figure S17)/EA (Figure S18) and risks of individual diseases were observed among individuals by excluding those developed the corresponding disease in the first 5 years of follow-up.

4. Discussion

In this large cohort study, we found individuals with higher EA were more likely to accommodate four healthy lifestyle habits except for low-risk physical activity. Healthy lifestyle score was inversely associated with the risks of 38 out of the 45 health and mortality outcomes. Whist higher EA was independently associated with a lower risk of 25 health and mortality outcomes in both observational and genetic analyses. The inverse association between healthy lifestyle score and the risk of mortality and major diseases including CVDs, certain cancers, CKD, and chronic liver disease was stronger among individuals with low EA. Attaining higher education might encourage the adoption of healthy lifestyle habits, such as a healthy diet, non-current smoking, low-risk sleep duration, and moderate alcohol consumption, thereby contributing to healthy aging.

Recent evidence has underscored the importance of healthy lifestyle for promoting a longer life expectancy free of major chronic diseases [6,7]. Likely, our study showed that a healthy lifestyle is linked to a lower risk of most age-related chronic diseases across multiple organ systems. Clear guidelines for adopting lifestyle behaviors that prevent CVDs, along with cancers, neurodegenerative disorders, COPD, and renal disease, have been established [13]. However, there is a necessity to broaden the scope to encompass a broader range of health conditions, including digestive disorders, ophthalmic conditions, thyroid disorders, and pernicious anemia. Our findings provide more evidence on these less studied chronic diseases. We further found that men were more incident in most physical diseases whereas a healthy lifestyle yielded a larger risk reduction for CVDs, COPD, and certain cancers in women. This is in line with the previous research indicating that the increased projected life expectancy linked to healthier lifestyle habits was more pronounced in women than in men [5]. This also aligns with the observation that females tend to exhibit greater longevity. For individual lifestyle habits, non-smoking yielded the largest risk reduction for most health and mortality outcomes in our study. However, our study is consistent with earlier research indicating that smoking was linked to a reduced risk of melanoma, prostate cancer, and Parkinson's disease [26–28]. Our findings are also line with some studies indicating that short sleep duration was associated with a lower risk of melanoma [29], and alcohol drinking was associated with a lower risk of prostate disorders [30]. Adopting a healthy lifestyle has the potential to facilitate the regulation of oxidative stress, inflammation, endothelial function, hemostatic factors, and epigenetic processes [31–33], which is linked to a reduced risk of chronic diseases. Our study provides evidence on lifestyle guidelines for the prevention of specific chronic conditions and the promotion of healthy ageing.

Higher EA may have positive effects on lifestyle habits thus preventing or delaying the development of age-related chronic diseases [16]. Several previous studies have linked EA to health outcomes using Mendelian Randomization analyses [15–17], but this is limited by analyzing a small number of health/mortality conditions (10 or less). We expanded to 45 health and mortality outcomes and found EA was inversely associated with the risk of 25 conditions in both observational and genetic analyses. Meanwhile, we found EA was not significantly associated with the risk of Parkinson's disease in the age- and sex-adjusted model whereas this association was strengthened to be inversely significant when socioeconomic and metabolic disorders or lifestyle was further adjusted for. Consistent with numerous prior observational studies [34,35], our genetic analysis demonstrated that higher EA might increase the risk of Parkinson's disease. Individuals with higher EA may be more likely to accommodate healthy behaviors [16], and seek health care, which partly explains the favorable effects of EA on the prevention of chronic diseases. However, our findings regarding mechanisms for the causal benefits of higher EA on the prevention of digestive disorders, respiratory disorders, CKD, pernicious anaemia, and thyroid disorders need to be explored in further research.

Higher EA may promote lifestyle modification thus minimizing the risk of age-related health conditions and mortality. A recent cohort study has demonstrated 13.9% (95% CI: 12.0–16.0%) of the association between EA and the risk of mortality was attributed to behavioural factors [18]. We found individuals with higher EA were more likely to accommodate healthy lifestyle habits including healthy diet, non-current

*Cox proportional hazard regression models were used to examine associations of healthy lifestyle score (each healthy lifestyle habit increment) with the risk of individual health conditions and mortality. Model 1 was adjusted for age and sex; Model 2 was adjusted for Model 1 plus ethnicity, educational attainment, income, Townsend index, BMI, dyslipidemia, hypertension, and diabetes at baseline. Healthy lifestyle score was analyzed as a continuous variable (each healthy lifestyle habit increment).
†The analysis for prostate cancer and prostate disorders (excluding prostate cancer) was conducted among men only.
‡The analysis for ovarian cancer and breast cancer was conducted among women only.

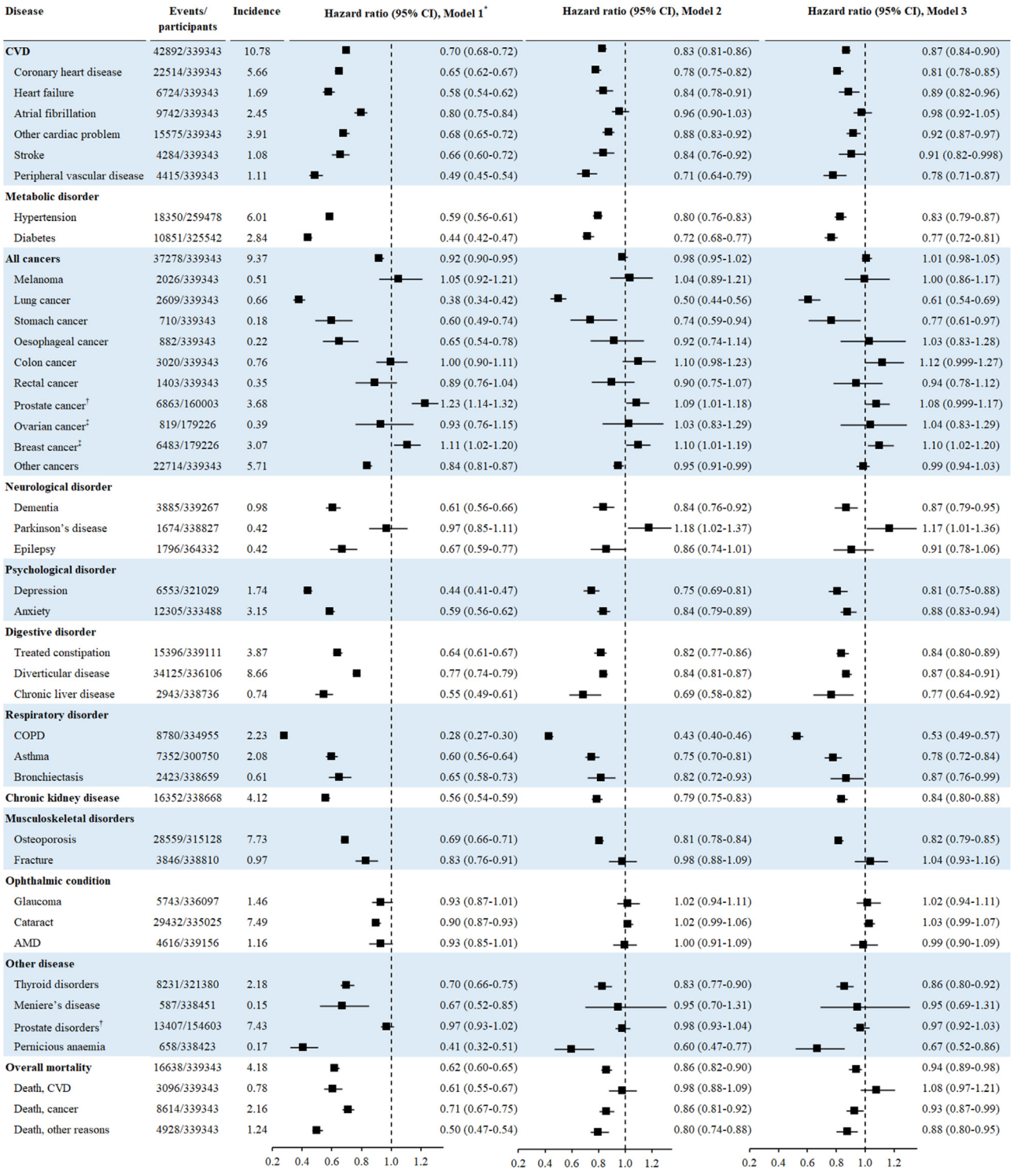

Fig. 3. The association between self-reported educational attainment and the risk of individual health conditions and mortality.
AMD, age related macular degeneration; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease.
The incidence refers to the number of event cases per 1000 person-years. Cardiovascular disease includes coronary heart disease, heart failure, atrial fibrillation, other cardiac disease, stroke, and peripheral vascular disease. All cancers encompass any type of cancer except for non-melanoma skin cancer. The vertical dash lines represent the hazard ratio of 1. Squares represent the hazard ratios. Horizontal lines indicate the range of the 95% confidence interval.
*Cox proportional hazard regression models were used to examine associations of educational attainment with the risk of individual health conditions and mortality. Self-reported educational attainment falling within the ranges of 0–5, 6–12, and ≥13 years were categorized as low, intermediate, and high levels, respectively. This figure illustrates the hazard ratios comparing high educational attainment to low educational attainment. Model 1 was adjusted for age and sex; Model 2 was adjusted for Model 1 plus ethnicity, income, Townsend index, BMI, dyslipidemia, hypertension, and diabetes at baseline; Model 3 was adjusted for Model 2 plus diet, smoking, physical activity, alcohol consumption, and sleep duration at baseline. The hazard ratios (95% CIs) refer to the high versus low educational attainment.
†The analysis for prostate cancer and prostate disorders (excluding prostate cancer) was conducted among men only.
‡The analysis for ovarian cancer and breast cancer was conducted among women only.

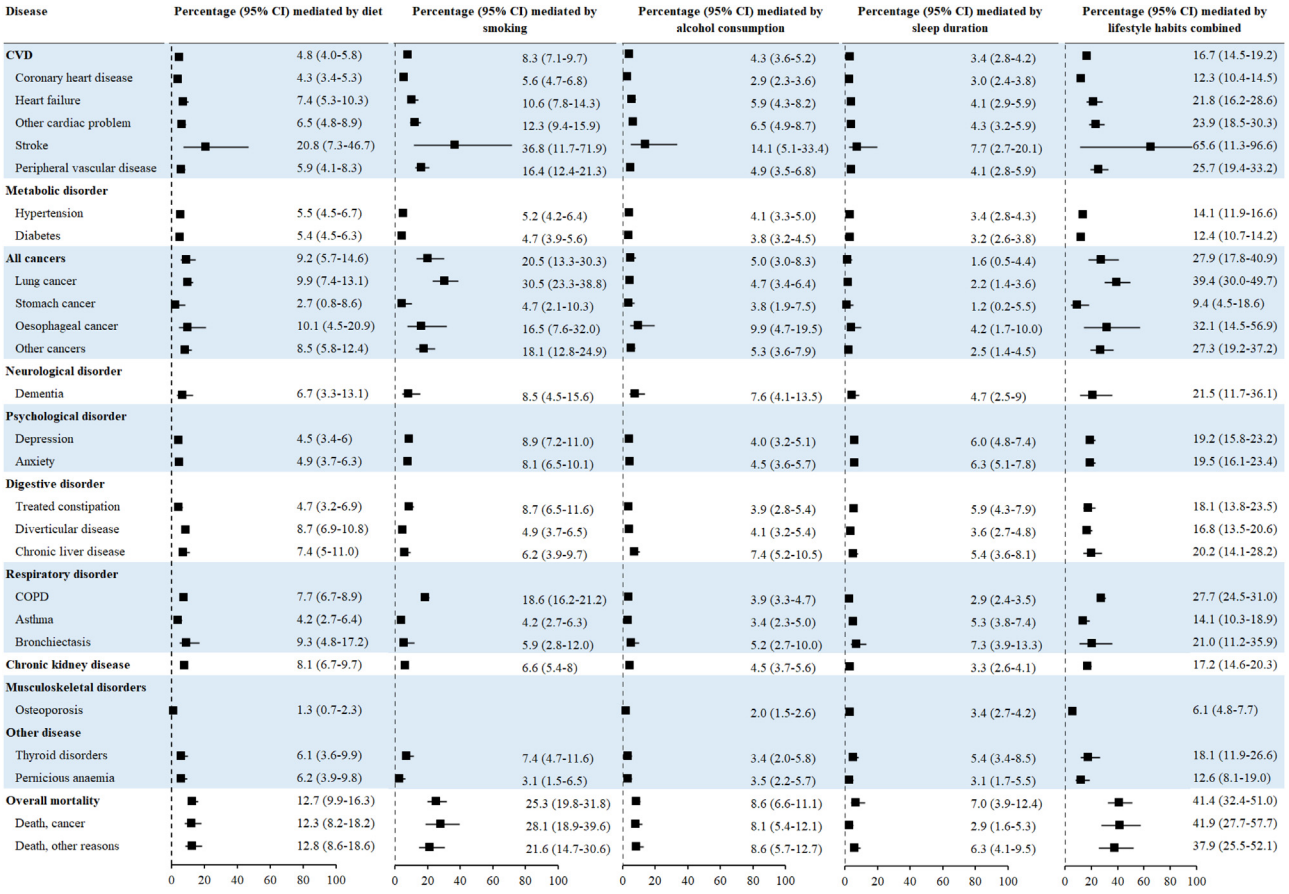

Fig. 4. Proportion of the association between self-reported educational attainment and risks of individual age-related health and mortality outcomes mediated by lifestyle habits.

Cardiovascular disease includes coronary heart disease, heart failure, atrial fibrillation, other cardiac disease, stroke, and peripheral vascular disease. All cancers encompass any type of cancer except for non-melanoma skin cancer.

We used the following criteria to establish mediation: (1) the mediator was significantly associated with educational attainment; (2) educational attainment was significantly associated with the health or mortality outcome; (3) the mediator was significantly associated with the health or mortality outcome; and (4) the association between educational attainment and with the corresponding health or mortality outcome was attenuated by the mediator. We examined the mediation effect of individual lifestyle habits and these factors combined. Only the health and mortality outcomes significantly associated with both self-reported and genotype-predicted educational attainment were analyzed.

smoking, low-risk sleep duration, and moderate alcohol consumption but less likely to be physically active. These findings have been confirmed in both observational and genetic analyses. These lifestyle habits explained a large proportion of the association between EA and risks of mortality and health conditions. For individual lifestyle habits, we found that educational inequalities (assessed through both self-reported and genotype-predicted data) in mortality and major chronic diseases were driven most by current smoking and unhealthy diet followed by alcohol consumption and high-risk sleep duration. In our study, a healthier lifestyle score yielded a larger risk reduction for mortality and major chronic diseases including CVDs, and certain cancers, and some respiratory disorders among individuals with lower EA. It is possible that individuals with lower EA are less likely to seek health care and more likely to develop age-related health conditions. Individuals with lower EA are less informed [36], and may respond more positively to lifestyle modifications, such that targeting lifestyle interventions within this population subset could prove more effective in reducing health and mortality disparities related to EA.

This is the first cohort study to link lifestyle/EA (both self-reported and genotype-predicted EA) to a wide range of health conditions and mortality. Our study also uniquely examined whether the association between lifestyle and risks of health conditions differed between individuals with different EA levels and the proportion of the association between EA and health conditions explained by lifestyle habits. The present study has several potential limitations. Firstly, it is important to acknowledge the possibility of measurement errors in lifestyle habits due to their self-reported nature. However, these measurement errors are inclined to reduce the true associations. Secondly, our study indicates that certain chronic diseases, such as melanoma or breast cancer, may be harmfully influenced by healthy lifestyle habits or higher educational attainment in our study. The findings need to be confirmed by further research. Thirdly, UK Biobank participants are more likely to exhibit good general health; however, a preceding study has shown that conclusions pertaining to the links between exposure and disease can be generalized to other populations. Finally, given that a majority of participants in our study were of Caucasian ethnicity, it should be cautious to extend our findings to other ethnic groups.

In conclusion, adopting to a higher lifestyle score or achieving higher EA yielded lower risks of most age-related health conditions across multiple organ systems as well as mortality. Higher EA might promote healthier lifestyle habits thus mitigating the risk of health conditions and promoting healthy ageing. Greater emphasis on lifestyle modification is essential for individuals with lower EA to effectively tackle health inequalities related to EA.

CRediT authorship contribution statement

XS, MH conceived and designed the study. ZZ, WW performed data curation. XS conducted data analysis and drafted the initial manuscript. XS, YH, SW, LT, XLZ, SL, ZZ, JL, WW, XYZ, ST, YH, ZG, HY, and MH made a critical revision to the manuscript for important intellectual content. All authors read the manuscript and approved the final draft. XS and MH are study guarantors. The corresponding authors attest that all listed aubthors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethics approval

The North West Multicenter Research Ethics Committee in the United Kingdom (reference: 16/NW/0274) approved the study protocol. Written consent for participation was obtained from all individuals involved in the UK Biobank.

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Data statement

All the analyses are conducted based on the UK Biobank data. The UK Biobank dataset used in this study is not publicly available but can be obtained by application through the data-access protocol (https://www.ukbiobank.ac.uk/). The typical duration from submitting an application to the release of data is approximately 15 weeks for the UK Biobank. The UK Biobank application number for this study is 101032.

Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jnha.2025.100525.

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