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ORIGINAL RESEARCH

Association of Age-Related Eye Diseases with Comorbidity of Coronary Heart Disease and Depression in a Population-Based Cohort Study

Xue He[1,*], Cong Li[1,2,*], Yan Wang[1,3,*], Zhenchao Du[1,4], Jianrong Jiang[1,5], Wenli Zhang[1,4], Jingyan Peng[1,5], Zhishen Peng[1,5], Tengda Huang[1,3], Heng Li[1,4], Yu Kuang[1], Honghua Yu[1], Lei Liu[1], Xiaohong Yang[1,3]

[1]Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, People's Republic of China; [2]Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Sciences, Guangzhou, People's Republic of China; [3]School of Medicine, South China University of Technology, Guangzhou, People's Republic of China; [4]School of Medicine, Shantou University Medical College, Shantou, People's Republic of China; [5]The Second School of Clinical Medicine, Southern Medical University, Guangzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xiaohong Yang; Lei Liu, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, People's Republic of China, Email syyangxh@scut.edu.cn; liulei@gdph.org.cn

Background: Coronary heart disease (CHD) and depression are highly comorbid and increase mortality risk. Although age-related eye diseases (AREDs) are independently associated with CHD and depression, their link to comorbidity remains unknown. Therefore, we aim to investigate the association between AREDs and the comorbidity of CHD and depression.

Methods: Using UK Biobank data, we conducted a prospective cohort analysis with baseline assessments from March 2006 to December 2010 and follow-up until July 2021. AREDs include age-related macular degeneration, glaucoma, cataract, and diabetes-related eye diseases (DRED). Incident cases were identified via self-reports and hospital records. Multivariable Cox proportional hazard regression models were applied to investigate the association between AREDs and comorbidity risk.

Results: Among 116,501 participants free of CHD and depression at baseline, 7,750 (6.65%), 3,682 (3.16%), and 741 (0.64%) developed CHD, depression, and their comorbidity over a mean of 11.82 years (inter-quartile range: 11.51–13.11) of follow-up. After adjusting for confounders, individuals with AREDs had a higher risk of developing CHD (hazard ratio [HR] 1.10, 95% confidence interval [CI]: 1.03–1.17), depression (HR 1.28, 95% CI: 1.16–1.42), and comorbidity (HR 1.37, 95% CI: 1.12–1.67). Compared to those without AREDs, individuals with cataract were associated with increased risks of comorbidity (HR 1.57, 95% CI: 1.23–2.03) and depression (HR 1.26, 95% CI: 1.10–1.43), while those with DRED had an increased risk of incident CHD (HR 1.33, 95% CI: 1.13–1.56).

Conclusion: The study found that individuals with AREDs had a higher risk of comorbid CHD and depression than of either condition independently. Our findings highlighted the importance of screening for the comorbidity of CHD and depression in the longitudinal management of AREDs.

Keywords: age-related eye diseases, coronary heart disease, depression, comorbidity

Introduction

Coronary heart disease (CHD) is the leading cause of mortality and disability worldwide.[1–3] Among individuals with CHD, depression is highly comorbid, with a prevalence of approximately 15–30%.[4,5] Depression is a risk factor for CHD and patients combined with CHD and depression have a worse prognosis than those with only one of the conditions.[5–9] Based on the above evidence, it can be concluded that CHD and depression are strongly linked and early screening and management of patients with a comorbidity of diseases is necessary.

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Growing evidence has supported that age-related eye diseases (AREDs) are related to an increased risk of both CHD and depression.[10–14] For example, a study from the Korean National Health Insurance System database found that age-related macular degeneration (AMD) was associated with an increased risk of myocardial infarction (MI).[15] Another study from Australia reported that individuals with AREDs have a higher risk of depression compared to those without.[16] As AREDs are major causes of vision impairment and blindness, they have garnered increasing attention.[17,18] With advancements in eye health screening, AREDs can now be detected earlier. The chronic ocular inflammation in AREDs promotes systemic endothelial dysfunction while simultaneously disrupting neurotransmitter metabolism through shared inflammatory pathways.[19,20] Furthermore, retinal microvascular abnormalities often parallel cerebral and coronary microcirculation defects, and vision-related circadian rhythm disturbances may concurrently impair cardiovascular and mood regulation.[13,21] Given these potential mechanistic links and the clinical significance of comorbidity of CHD and depression burden, AREDs could disproportionately increase comorbidity risk compared to their effects on either disease individually. Understanding the precise relationship between AREDs and the future risk of comorbidities such as CHD and depression may enhance early diagnosis and enable timely intervention, potentially preventing the full onset of these clinical syndromes. However, to our knowledge, it is unclear whether the AREDs are associated with an increased risk of comorbidity of CHD and depression.

Therefore, we specifically investigates whether AREDs confer differential risk for comorbidity of CHD and depression compared to their individual occurrences, which could reveal novel pathways for preventing multi-morbidity in aging populations. This study aims to examine the relationship between AREDs and the co-occurrence of CHD and depression in a population-based cohort.

Methods

Study Design and Population

The UK Biobank is a population-based cohort of more than 500,000 people, aged 40–70 years, recruited between March 2006 and December 2010 at 22 assessment centers throughout the UK. At baseline assessment, participants completed a touch-screen questionnaire covering demographic, socioeconomic and lifestyle, and had physical measurements taken. Participants provided written informed consent to participate in research as previously described. Further information about the study protocols is available online (https://www.ukbiobank.ac.uk/).

In the present study, 174,575 participants with complete information on eye diseases were included. Of which, participants diagnosed with CHD (n=10,877) or depression (n=10,687) at baseline were excluded. Those who had missing data on key variables required to define covariates were also excluded (n=36,510). Eventually, 116,501 subjects were included in the final analysis (Figure 1).

Ethics Statement

This research has been conducted using the UK Biobank Resource under Application Number 82906. This study was in accordance with the principles of the Declaration of Helsinki. The ethical approval was given by the National Information Governance Board for Health (headquartered at Skipton House, London SE1, UK) and Social Care and the NHS North West Multicentre Research Ethics Committee (based in Haydock, UK; reference number: 11/NW/0382). All participants had completed a written informed consent before enrolment. This study was exempt from approval by the institutional review board of the Guangdong Provincial People's Hospital because it used publicly available data (registration number: KY-Q-2022-495-01).

AREDs

AREDs were defined as individuals with only one of the eye conditions, which include AMD, glaucoma, cataract, and diabetes-related eye disease (DRED). Those conditions were ascertained using the participants' self-reported previous diagnosis and International Classification of Diseases (ICD) diagnosis codes (10th Revision, ICD-10, or 9th Revision, ICD-9). The Hospital Episode Statistics records (England and Wales) and the Scottish Morbidity Records (Scotland) were linked to the UK Biobank to determine the date and diagnosis for hospital admissions. Information on eye problems

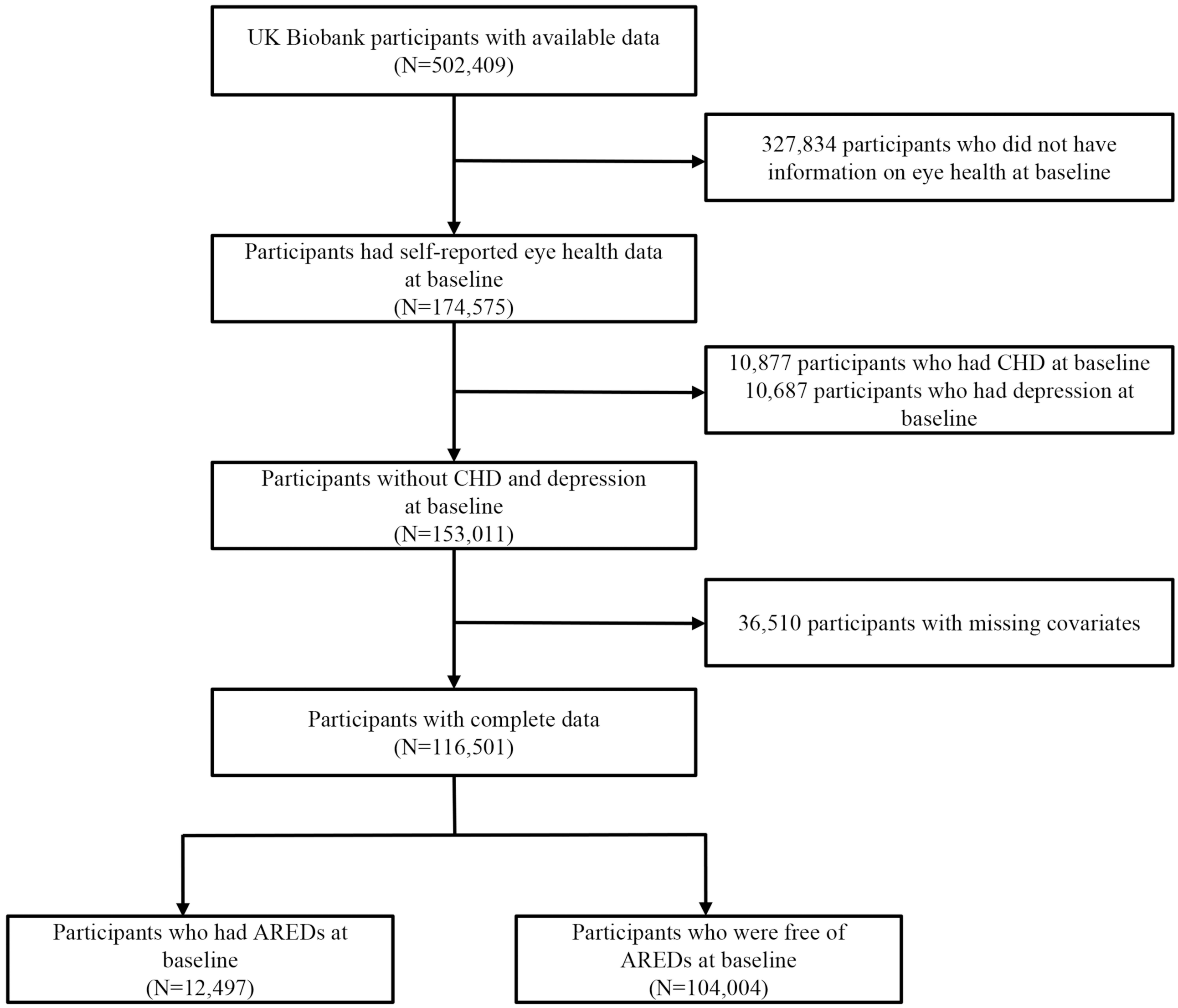

Figure 1 Selection process of the study population.
Abbreviations: AREDs, age-related eye diseases; CHD, coronary heart disease.

was assessed in the baseline questionnaire by asking "Has a doctor told you that you have any of the following problems with your eyes?". The participants were classified into AMD, glaucoma, cataract, and DRED based on their choice of answers to the corresponding question. DERD includes DR, diabetic AMD, diabetes-related glaucoma, and diabetes-related cataract. The control group included patients without any diagnosis of AREDs, CHD, or depression during the baseline investigation. Detailed information on ICD codes and self-reported fields for each condition are described in Table S1.

Ascertainment of Outcomes

Incident of comorbidity of CHD and depression was defined as individuals diagnosed with angina or MI and with depression between January 2011 and July 2021,[22,23] regardless of the order in which the conditions were diagnosed. The outcomes were identified according to self-reported information and hospital inpatient records. The time at risk of comorbidity of CHD and depression was defined to start on the individual's index date and end on the date when both conditions were first documented in the medical records or on the date of the study data extraction (August 10, 2021).

Covariates

In the UK Biobank, covariates were collected from standardized questionnaires, physical measurements, and biochemical measurements. Factors known to be associated with CHD and depression were included in the analyses as confounders.[24–27] We assessed the following covariates: age at recruitment, sex (male, female), ethnicity (White, non-White), education level (college or university degree, other), Townsend deprivation, smoking status (former/current, never), alcohol consumption (former/current, never), physical activity (above moderate/ vigorous/ walking recommendation, and not), body mass index (BMI), history of hypertension, history of hyperlipidemia, history of diabetes, and diabetes duration (detailed information are described in Table S1).

Statistical Analysis

The comparison of baseline characteristics stratified by the presence of AREDs was conducted using *t*-test for continuous variables and the $\chi 2$ test for categorical variables. The Cox regression hazard models were used to estimate the hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) of the association between AREDs and CHD, depression, and their comorbidity. Three models were used. Model 1 was crude; model 2 was adjusted for age and sex, and model 3 was adjusted for age, sex, ethnicity, education, Townsend Deprivation Index, smoking status, alcohol consumption, total physical activity level, BMI, history of hypertension, and history of hyperlipidemia and diabetes. The association between DRED and the outcomes was additionally adjusted for diabetes duration. Stratified analyses according to age (40–49 years, 50–59 years or ≥60 years),[25] sex (female or male), smoking status (never or former/current), and drinking status (never or former/current) were further performed. We also conducted stratified analyses according to diabetes duration (<5 years, ≥5 to <10 years, or ≥10 years) for patients with DRED.[28] We employed the Benjamini–Hochberg (BH) procedure for controlling the false discovery rate (FDR) which entailed the correction of p-values in the stratified multiple analyses, thereby facilitating efficient control of the FDR.[29] To minimize the possibility of including prevalent cases in the present analysis, a sensitivity analysis was conducted to exclude individuals who developed CHD or depression within the first 2 years of follow-up. While our primary analysis focused on individuals with single eye conditions, we recognized that multiple coexisting eye diseases are clinically common. Therefore, we performed additional analyses in individuals with multiple ocular comorbidities to assess the robustness of our findings. To evaluate potential selection bias from missing data, we also performed a sensitivity analysis in the original dataset with missing data (153,011 participants). Multiple imputation by chained equations (MICE) with 5 imputations was performed to impute missing data, as the missingness rate was below 30%.[30] All analyses were conducted using Stata version 16 (StataCorp LLC, College Station, Texas, USA).

Results

Baseline Characteristics

The characteristics of participants according to AREDs status are summarized in Table 1. Participants with age-related eye diseases (AREDs) were significantly older, more likely to be male, predominantly of White ethnic background, and had lower educational attainment. They also had higher income levels, were more frequently former or current smokers, had a higher body mass index, were more likely to meet recommended physical activity levels, and had higher prevalence of diabetes mellitus, hypertension, and hyperlipidemia. The baseline characteristics stratified by outcomes are illustrated in Table S2.

Association of AREDs with Incident Comorbidity of CHD and Depression

During a mean of 11.82 years (IQR=11.51–13.11) of follow-up, CHD, depression, and their comorbidity were observed in 7,750 (6.65%), 3,682 (3.16%), and 741 (0.64%) participants, respectively.

The association of AREDs with comorbidity of CHD and depression is shown in Table 2 and Figure 2. In the crude model (model 1), participants with AREDs had a greater risk of developing comorbidity (HR=1.66, 95% CI: 1.36–2.01). Specifically, cataract and DRED were significantly associated with the outcome. After adjusting for age and gender (model 2), the presence of any AREDs (HR=1.42, 95% CI: 1.17–1.73), cataract (HR=1.42, 95% CI: 1.11–1.82), and

Table 1 Baseline Characteristics of Study Participants, According to the Presence of AREDs

Variables	Total	AREDs	Control group	P value
N	116,501	12,497	104,004	
Age, mean (SD), years	57.00(8.08)	61.20(6.51)	56.50(8.11)	<0.001*
Sex, n (%)				<0.001*
Female	63,457(54.47)	6,589(52.72)	56,868(54.68)	
Male	53,044(45.53)	5,908(47.28)	47,136(45.32)	
Ethnicity, n (%)				<0.001*
White	107,065(91.90)	11,596(92.79)	95,469(91.79)	
Non-White	9,436(8.10)	901(7.21)	8,535(8.21)	
Townsend index, mean (SD)	−1.12(3.02)	−1.31(3.04)	−1.09(3.02)	<0.001*
BMI, kg/m^2, mean (SD)	27.30(4.73)	27.53(4.78)	27.28(4.72)	<0.001*
Education level, n (%)				0.001*
College or university degree	40,314(34.60)	4,161(33.30)	36,153(34.76)	
Others	76,187(65.40)	8,336(66.70)	67,851(65.24)	
Smoking status, n (%)				<0.001*
Never	65,244(56.00)	6,666(53.34)	58,578(56.32)	
Former/current	51,257(44.00)	5,831(46.66)	45,426(43.68)	
Alcohol assumption, n (%)				0.515
Never	5,762(4.95)	633(5.07)	5,129(4.93)	
Former/current	110,739(95.05)	11,864(94.93)	98,875(95.07)	
Physical activity, n (%)				<0.001*
Not meeting recommendation	38,209(32.80)	2,284(18.28)	35,925(34.54)	
Meeting recommendation	78,292(67.20)	10,213(81.72)	68,079(65.46)	
Diabetes mellitus, n (%)	7,409 (6.36)	1,692 (13.54)	5,717 (5.50)	<0.001*
Hypertension, n (%)	64,037(54.97)	8,217(65.75)	55,820(53.67)	<0.001*
Hyperlipidemia, n (%)	54,831(47.06)	6,895(55.17)	47,936(46.09)	<0.001*

Notes: Data are mean (SD) or n (%); * Value with P < 0.05 are considered as statistically significant for the differences between the two groups.
Abbreviations: AREDs, age-related eye diseases; BMI, body mass index.

Table 2 Associations of AREDs with the Risk of Incident Comorbidity of CHD and Depression

Ocular Conditions	Events/Total	Model 1		Model 2		Model 3	
		HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
With any AREDs	125/12,497	1.66(1.36–2.01)	<0.001*	1.42(1.17–1.73)	<0.001*	1.37(1.12–1.67)	0.002*
Only AMD	12/1,574	1.15(0.65–2.03)	0.632	1.01(0.57–1.79)	0.969	1.17(0.66–2.07)	0.599
Only glaucoma	16/2,924	0.82(0.50–1.35)	0.434	0.70(0.43–1.16)	0.166	0.77(0.47–1.26)	0.298
Only cataract	72/6,989	1.65(1.30–2.11)	<0.001*	1.42(1.11–1.82)	0.005*	1.57(1.23–2.03)	<0.001*
Only DRED†	25/1,010	4.35(2.92–6.48)	<0.001*	3.91(2.62–5.83)	<0.001*	1.43(0.90–2.25)	0.129

Note: * Statistical significance (P<0.05); †Among participants with DRED, model 3 additionally adjusted for diabetes duration. Model 1 was the unadjusted model; Model 2 was adjusted for age and gender; Model 3 was adjusted for age, gender, ethnicity, education, Townsend Deprivation Index, smoking status, alcohol consumption, total physical activity level, BMI, history of diabetes, hypertension, and hyperlipidemia.
Abbreviations: AREDs, age-related eye diseases; CHD, coronary heart disease; AMD, age-related macular degeneration; DRED, diabetes-related eye diseases; HR, hazard ratio; CI, confidence interval.

DRED (HR=3.91, 95% CI: 2.62–5.83) were significantly associated with comorbidity. After multivariate adjustment (model 3), the presence of AREDs remained significantly associated with comorbidity (HR = 1.37, 95% CI: 1.12–1.67). Notably, among the specific AREDs, only cataract remained significantly associated with comorbidity after multivariate adjustment (HR = 1.57, 95% CI: 1.23–2.03). However, after adjusting for the diabetes duration of DRED patients, no significant association was observed between AREDs and comorbidity. We further investigate the relationship between AREDs and incident CHD and depression (Tables S3 and S4). After multivariate adjustment (model 3), the presence of

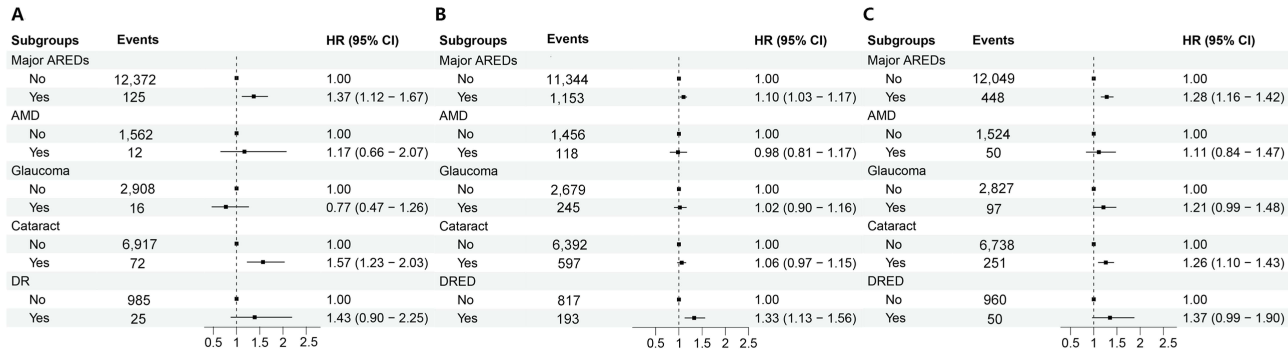

Figure 2 The association of age-related eye diseases with comorbidity of CHD and depression (**A**), CHD (**B**), and depression (**C**).
Abbreviations: The multivariable model was adjusted for age, gender, ethnicity, education, Townsend Deprivation Index, smoking status, alcohol consumption, total physical activity level, body mass index, history of diabetes, hypertension, and hyperlipidemia, and diabetes duration (only in the corresponding analysis). AREDs, age-related eye diseases; AMD, age-related macular degeneration; DRED, diabetes-related eye diseases; CHD, coronary heart disease; HR, hazard ratio; CI, confidence interval.

any AREDs was significantly associated with incident CHD (HR=1.10, 95% CI: 1.03–1.17) and depression (HR=1.28, 95% CI: 1.16–1.42). Specifically, patients with DRED had a higher risk of incident CHD (HR=1.33, 95% CI: 1.13–1.56), while patients with cataract had a higher risk of incident depression (HR=1.26, 95% CI: 1.10–1.43).

Stratified Analysis and Sensitivity Analysis

Figure 3 shows the associations of AREDs with the risk of comorbidity of CHD and depression stratified by age, sex, smoking, and drinking status. The adjusted HR of comorbidity was higher among individuals aged ≥ 60 years, female, ever smoked or drank alcohol. No significant interaction effects were observed between comorbidity and subgroup factors related to AREDs or diabetes duration (P for interaction > 0.05). After FDR adjustment, the original statistically

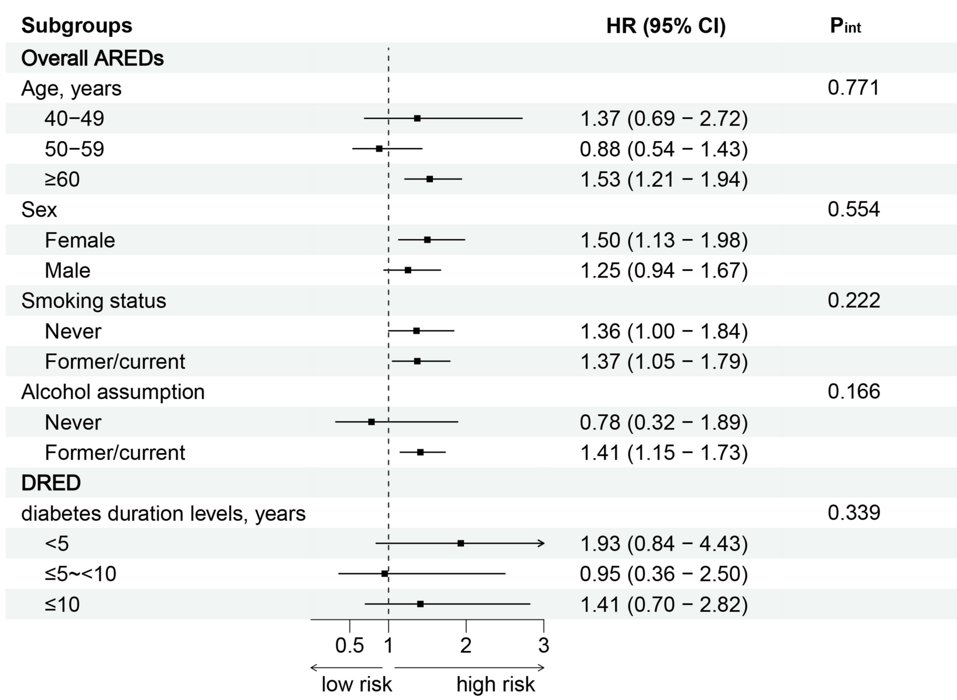

Figure 3 Stratified analysis for the Association of AREDs with Incidence of Comorbidity of CHD and depression.
Abbreviations: The multivariable model was adjusted for age, gender, ethnicity, education, Townsend Deprivation Index, smoking status, alcohol consumption, total physical activity level, body mass index, history of diabetes, hypertension, and hyperlipidemia, and diabetes duration (only in the corresponding analysis). AREDs, age-related eye diseases; CHD, coronary heart disease; DRED, diabetes-related eye diseases; HR, hazard ratio; CI, confidence interval; Pint, P value for interaction.

significant findings remained significant (q < 0.05), reinforcing their robustness (Table S5). The stratified analyses of the associations between AREDs and independent CHD and independent depression are also presented in Table S5.

The sensitivity analyses excluding the first 2 years of follow-up revealed no substantial changes in the associations identified from the main analyses, suggesting the robustness of the findings (Table S6). Similar results were observed after additionally analysed individuals with more than one than one eye problems (Table S7). Additionally, the results remained consistent with the primary analysis after using multiple imputation, suggesting minimal bias from missing data (Table S8).

Discussion

To our knowledge, this is a novelty study to mainly examine the association of AREDs with comorbidity of CHD and depression. In this population-based longitudinal study, we found that individuals with AREDs overall had a 37% higher risk of developing comorbid CHD and depression compared to those without AREDs. Furthermore, AREDs patients were associated with a higher risk of comorbidity than the risk of either CHD or depression occurring independently. Our findings indicated that AREDs might be a potential marker of comorbidity of CHD and depression that can be early detected, thus highlighting the importance of monitoring the CHD and depression risks in AREDs patients.

We found that individuals with AREDs have a 37% higher risk of developing comorbidity of CHD and depression. Our findings were in agreement with previous studies. A cross-sectional study using the National Health and Nutrition Exanimation Surveys data[31] and a prospective study from Canadian Longitudinal Study[32] demonstrated that eye diseases were significantly associated with independent CHD and independent depression. The comorbidity was considered to be a more severe condition than with independent CHD or depression.[5–7] However, the association of AREDs with comorbidity is unknown. Our finding suggested a higher risk of incident comorbidity of CHD and depression in AREDs patients, especially cataract patients, with a 57% higher risk of comorbidity. Our study further verified that individuals with AREDs have a higher risk of comorbidity of CHD and depression compared to the risk of either condition occurring independently. This result indicated that the comorbidity may be a more noteworthy problem than independent CHD or depression.

Prior studies have reported that cataract has been associated with a high risk of depression. A 16-year nationwide population-based longitudinal study[33] and a meta-analysis[34] have suggested that patients with cataract have higher risks of developing depression despite adjusting for possible confounders. Our findings showed the same results that cataract was associated with a 26% increased risk of depression. Of note, we also found a 57% higher risk of comorbidity of CHD and depression. Depression is a known risk factor for the development of CHD.[35] The possible explanation for the results is that patients with cataract have been shown to be more likely to develop depression, which may influence cardiovascular health and in turn could lead to higher risks of developing the comorbidity.[33,36]

In addition, we found that DRED was associated with a 33% increased risk of independent CHD. Being considered one of the traditional cardiovascular risk factors, DRED has been reported to have a significant association with CHD in previous studies.[37–39] Notably, previous studies have demonstrated conflicting results on the relationship between DRED and depression. A few studies reported that DRED was associated with an increased risk of depression,[14,40,41] whereas some studies showed that DRED is an independent risk factor for depression.[42,43] The deviation of these results may be due to differences in the composition of the study populations, study design, as well as definitions. An implication is that there is a need for additional studies to investigate the relationship between DRED and depression, as well as the comorbidity.

Notably, our findings showed that AMD and glaucoma were not associated with an increased risk of CHD or depression after multivariable adjustment. Findings from previous research on the association of AMD with CHD have reported conflicting results.[15,44,45] A prospective study from US populations demonstrated that the presence of early AMD was associated with an increased risk of incident CHD, but late AMD was not associated with incident CHD.[10] A study reported that glaucoma was associated with an increased risk of CVD in the UK population,[46] while another study found those with glaucoma had a nonsignificant increased risk of cardiovascular death.[47] Additionally, most studies reported that patients with AMD or glaucoma are linked to a high risk of depressive symptoms.[13,45] A possible explanation for these results is that our study determined depression outcomes based on hospital admission records.

Typically, patients who are hospitalized may have moderate to severe depressive symptoms.[48] Thus, AMD and glaucoma patients with milder levels of depression may not be detected in this study. Another potential reason for the discrepancy is that both AMD and glaucoma tend to be present with no discernible symptoms until they have significantly advanced, complicates early detection.[49] This underascertainment may have reduced our statistical power to detect significant associations with the comorbidity of CHD and depression. Furthermore, differences in pathophysiology and systemic involvement across AREDs may partly explain the findings. Cataract and DRED are more strongly associated with systemic dysfunction, while AMD and glaucoma may have weaker systemic ties,[50,51] reducing their association with comorbidity. Further studies are needed to investigate whether AMD and glaucoma are associated with CHD or depression risk.

Interestingly, in stratified analyses, we found that AREDs patients aged ≥60 years, female, ever smoker or consumed alcohol had a higher risk of developing comorbidity of CHD and depression. However, interaction tests for stratified analyses were not statistically significant, indicating these observed differences may reflect random variation or unmeasured confounding rather than genuine effect modification. The relationship between AREDs and CHD and depression in different subgroups was not consistent. A 3-year prospective cohort study showed that patients with eye diseases were more likely to develop depression in males and younger than 65 years subgroup.[32] Another study showed that the association between AMD and CHD was more evident in females, but no significant interaction according to age groups.[15] Therefore, further studies are needed to robust the findings.

The underlying mechanisms of a higher risk of comorbidity of CHD and depression in people with major AREDs may be multifactorial. There have been a few hypotheses postulated to explain the association of major AREDs with CHD and depression. First, inflammaging is a key driver of pathogenesis in AREDs.[52–54] The increased levels of inflammatory factors in AREDs, such as C-reactive protein, interleukin-6, and Nucleotide-binding leucine-rich repeat containing receptor 3, were also associated with the occurrence of CHD and depression.[55,56] Therefore, the inflammatory markers may be a major pathway leading to CHD and depression in AREDs. Second, oxidative stress is an important pathomechanism found in numerous ocular degenerative diseases and also has been implicated in the pathogenesis of both atherosclerosis and depression.[57,58] The presence of comorbidity of CHD and depression may be an indicator of the high level of cumulative oxidative damage resulting from physiological and pathological ageing.[59] Besides, the profound overlap in risk factors of AREDs, CHD, and depression could lead to the result of increasing risk of comorbidity, which also provides the opportunity for prevention of both CHD and depression.[60–62]

To our knowledge, this is the first study to innovatively report the association between AREDs and comorbidity of CHD and depression, as previous studies only discussed the single link between AREDs and independent CHD or depression. Our study revealed a higher risk of comorbidity in AREDs patients, which emphasizes the importance of management of AREDs patients. Given the increasing awareness of the high prevalence of comorbidity of CHD and depression, earlier recognition and adequate therapy of the comorbidity could help maintain the quality of life. Ophthalmic examination is easily accessible and low-cost, which can be early detected the presence of AREDs. Therefore, the presence of AREDs may be a more visible signal of a high risk of comorbidity of CHD and depression and assist physicians in screening for cardiovascular and psychological disorders in these patients.

The strengths of this study include its prospective design, large sample size cohort, and long-term follow-up duration. In addition, our findings may provide new directions for the mechanisms linking CHD and depression. Several limitations should be considered in interpreting our results. First, ophthalmic diagnoses and outcomes relied on self-reported and inpatient record data, milder or subclinical cases might be under-ascertained, which could result in significant variation or misclassification. However, this may partially explain the null association between some of the AREDs and CHD or depression observed in our study. The true association between AMD and the risk of depression might be stronger than in the current study. Second, as an observational study, it can only suggest associations between AREDs and comorbid CHD and depression; causal relationships cannot be established. Validation of these findings in external cohorts may be necessary. Third, the UK Biobank participants were relatively healthy and might not represent the whole population. This could introduce selection bias and affect the generalization of the results to other population groups. Fourth, we could not fully adjust for the systemic diseases that aged patients may have, which may be potential confounders and contribute to the development of both CHD and depression. Fifth, excluding individuals with missing data may cause selection bias, but the low missing rate and consistent imputation results suggest minimal impact on conclusions. Lastly, the number of incident comorbidity of CHD and depression was relatively small, which might have led to an underestimation of the association between AREDs and the comorbidity. Although our definition intentionally captured comorbid conditions regardless of the order of diagnosis to maximize case inclusion, this approach cannot distinguish whether CHD preceded depression or depression preceded CHD. Recent evidence suggests that the temporal order of disease onset may influence prognosis and care needs.[63] Future prospective studies with larger samples are needed to clarify the impact of the temporal order of CHD and depression on outcomes in patients with comorbid conditions. Overall, the findings of this study suggested that AREDs were significantly associated with the increasing risk of comorbidity of CHD or depression, highlighting the potential need to investigate cardiovascular health and depressive symptoms among patients with eye diseases.

Conclusion

The current study found that AREDs were associated with an increased risk of comorbidity of CHD and depression. Our findings highlighted the importance of screening for CHD and depression in the longitude development of AREDs. Patients with AREDs, especially cataract and DRED, should be targeted for risk factor management and disease prevention for CHD and depression.

Abbreviation

CHD, stands for coronary heart disease; AREDs, age-related eye diseases; DRED, diabetes-related eye diseases; AMD, age-related macular degeneration; MI, myocardial infarction; ICD, International Classification of Diseases; HR, hazard ratio; CI, confidence intervals.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

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