Peer Review File

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Reviewer A:

Comment 1: Line 97: should read 'enrollment' not enrolment.

Reply 1: Thank you for your careful review and pointing out the error. We have examined all the spelling errors throughout the manuscript and corrected them carefully. And we do apologize for these errors.

Changes in the text: *(In "Methods", Page 6, paragraph 2,* **Participants***)*

This study recruited participants randomly selected from the Services Australia (formerly the Australian Government Department of Human Services) Medicare enrollment database, accounted for an estimated 10% of the NSW population.

Comment 2: Line 132: should read 'or' not of

Reply 2: Thank you for your suggestions and we have corrected this error accordingly.

Changes in the text: *(In "Methods", Page 8, paragraph 2,* **Covariates***)*

The highest level of education attained was classified into three groups: <10 years, high school, and university or higher.

Comment 3: Line 232: please elaborate or explain 'U-shape' association

Reply 3: Thanks for your comments. In the present study, we observed that the consumption of 5-7 alcoholic drinks per week may be beneficial for participants with a BMI between certain range. However, no significant associations were observed in participants with a smaller or larger alcoholic consumption. The U-shape association between alcohol intake and clinical disorders in epidemiologic studies means that moderate consumption may be protective, whereas heavy alcohol consumption becomes a significant risk factor. For example, in a review of 84 studies of alcohol consumption and cardiovascular disease, alcohol consumption about ≤1 drink a day

was consistently associated with a 14-25% reduction in the risk of all outcomes assessed compared with abstaining from alcohol, but consumption of larger amounts of alcohol was associated with higher risks for stroke incidence and mortality.

Changes in the text: *(In "Discussion", Page 14, paragraph 1)*

An U-shape association, which usually refers to the nonlinear relationship, between alcohol intake and clinical disorders is often observed in epidemiologic studies, for example, the relationship between alcohol and cardiovascular diseases. Similar results regarding the association between BMI and cataracts were found in a meta-analysis. Moderate consumption may be protective, whereas heavy alcohol consumption becomes a significant risk factor of ARC, which is consistent with our results.

Reviewer B:

Comment 1: It is one of very few reports on the subject if not the only one. As with analysis like that it is important to list the limitations, which obviously authors did. Please stress that fact in the abstract.

Reply 1: Thank you for your comments. We have tried to search the literature, and there were no exact studies evaluating the association between BMI and early-onset cataract. A number of studies investigated the relationship between BMI and age-related cataract, and the participants in these studies differed with those in our study. Hoping this addresses your concerns.

Changes in the text:

(In "Abstract")

Body mass index (BMI) has been reported to be associated with age-related cataract, whereas its impact on early onset cataract (EOC) remains unknown.

(In "Discussion", Page 12, paragraph 2)

Numerous previous studies have been conducted to investigate the impact of BMI on cataracts, however these have been conducted in the context of ARC, and no studies have done so on the subset of EOC.

Reviewer C:

Comment 1: Owing to the fact that BMI changes over time and the method for the assessment of the association used was the Cox proportional hazards ratio, it would be of benefit to know if the study assessed for proportionality. If this assessment was done, please consider stating this in the methods. If this assessment was not done, please consider doing so and then including a statement that recognizes that proportionality was assessed and was confirmed for this study.

Reply 1: Thank you for your valuable suggestion. The multivariate-adjusted cox regression analyses were assessed for proportionality, using a BMI of 20.0-22.49 kg/m^2 as the reference. (Table 3) In the original version, this was stated in "Methods" (Statistical analysis): "*Hazard ratios (HRs) with 95% confidence intervals (CI) were estimated for all categories of BMI, using a BMI of 20.0-22.49 kg/m^2 as the reference."*

Changes in the text: *None.*

Comment 2: In the section titled "Exposures" please consider testing for the interactions between physical activity and body mass index as well as the interaction of body mass index and alcohol intake for each of the described subgroups.

Reply 2: Thank you for your suggestions. We have investigated the association between BMI categories and EOC stratified by physical activity as well as alcohol consumption. We observed the consumption of 5–7 alcoholic drinks per week may be a protective factor against EOC for participants with a BMI of 18.5–19.99 kg/m^2 or 25.0–27.49 kg/m^2, whereas no significant associations were found between physical activity and BMI.

Changes in the text: *(In "Table 3").*

Table 3 Multivariate-adjusted cox regression analyses stratified by covariates.

Subgroup	BMI (20.0-22.49 kg/m^2 as reference, HR(95% CI))						P for interaction
	18.5-19.99	22.5-24.99	25.0-27.49	27.5-29.99	30.0-32.49	32.5-50	
Alcohol intake (drinks/week)							0.784
0	0.89(0.52-1.53)	1.13(0.81-1.57)	1.10(0.78-1.54)	0.90(0.61-1.31)	1.00(0.67-1.50)	1.08(0.75-1.55)	
1-4	1.45(0.89-2.36)	0.84(0.60-1.18)	0.93(0.67-1.30)	0.91(0.63-1.30)	1.10(0.75-1.61)	0.83(0.56-1.25)	
5-7	0.27(0.10-0.74)	0.75(0.50-1.11)	0.63(0.41-0.96)	0.71(0.45-1.13)	0.71(0.40-1.26)	0.69(0.39-1.23)	
7-14	1.11(0.61-2.01)	0.79(0.55-1.12)	0.83(0.57-1.20)	0.94(0.64-1.39)	0.99(0.63-1.56)	0.91(0.56-1.48)	
≥15	0.68(0.23-1.96)	0.82(0.50-1.36)	0.80(0.49-1.32)	0.91(0.55-1.50)	1.32(0.77-2.25)	0.67(0.35-1.28)	
Physical activity, min/wk							0.048*
0	1.76(0.80-3.88)	1.13(0.66-1.94)	0.83(0.48-1.46)	1.20(0.69-2.09)	1.29(0.73-2.29)	1.14(0.65-2.00)	
1-149	0.95(0.51-1.78)	1.07(0.73-1.57)	1.12(0.77-1.64)	1.26(0.86-1.86)	1.22(0.79-1.88)	1.03(0.67-1.58)	
150-299	0.62(0.28-1.39)	0.67(0.44-1.01)	0.84(0.56-1.26)	0.65(0.41-1.04)	0.86(0.52-1.40)	0.64(0.37-1.11)	
300-539	1.07(0.55-2.08)	1.02(0.70-1.48)	0.73(0.49-1.09)	0.74(0.48-1.15)	1.09(0.69-1.74)	0.93(0.58-1.51)	
≥540	0.77(0.47-1.25)	0.75(0.56-1.00)	0.84(0.63-1.13)	0.80(0.58-1.12)	0.92(0.62-1.35)	0.77(0.52-1.14)	

Min/wk = minutes per week

Comment 3: In the aforementioned "Exposures" section, please consider providing a justification for the rationale of the subgroups.

Reply 3: Thank you for your comments. According to the World Organization Health (WHO) weight classification, BMI was divided into six status including underweight (below 18.5), normal weight (18.5-24.9 kg/m^2), Pre-obesity (25.0-29.9 kg/m^2), Obesity class I (30.0-34.9 kg/m^2), Obesity class II (35.5-39.9 kg/m^2), and Obesity class III (above 40 kg/m^2). In this study, participants with extreme measures of BMI (<15 kg/m^2 or BMI>50 kg/m^2) were excluded due to the increased probability of measurement error. Considering the distribution of participants, BMI was further divided into seven categories including 18.5–19.99, 20–22.49, and 22.5–24.99 kg/m^2 (normal weight); 25–27.49 and 27.5–29.99 kg/m^2 (overweight); and 30–32.49 and 32.5–50 kg/m^2 (obese). Hoping this addresses your concern.

Changes in the text: *(In "Methods", Page 8, paragraph 1, **Exposures**).*

According to the body weight classification by World Health Organization(WHO) and the distribution of participants in the present study, BMI was divided into seven categories including 18.5-19.99, 20-22.49, and 22.5-24.99 kg/m^2 (normal weight); 25-27.49 and 27.5-29.99 kg/m^2 (overweight); and 30-32.49 and 32.5-50 kg/m^2 (obese).

Comment 4: The paper also mentions many covariates that are assessed for, such as: physical activity, alcohol intake, etc. however these topics are not mentioned until much later in the paper. Please consider briefly introducing these topics in the introduction.

Reply 4: Thank you for your valuable suggestion. We have added these information accordingly.

Changes in the text: *(In "Introduction", Page 6, paragraph 1).*

Moreover, the impact of other lifestyle factors like alcohol consumption and physical activity, which might have interactions with BMI, remains unclear.

Comment 5: In the section titled "Covariates" please consider providing a rationale for the stratification of the variables mentioned. It is not clearly understood why the stratifications that were used. For example, it would be beneficial to the reader to

present the poverty income when discussing income in order to provide a better understanding of the level of income of the individuals involved in the study as well as the social determinants of health that these individuals may or may not be exposed to. It would also be of benefit to make the addition of a Zero category for the categories of alcohol intake as I find it highly unlikely that a study of over 73,000 individuals did not have a single person who did not partake in alcohol consumption. It would also be of benefit to discuss the rationale behind the categorization of physical activity per week, considering that given the standard week of 7 days, it would be incredibly difficult for the average individual to participate in greater than 14 sessions or 2 sessions of physical activity every day. It would be of benefit to show the amount of individuals who fall into each category and adjust the categories accordingly to provide a better stratification for this variable.

Reply 5: Thank you for your valuable suggestion. The classifications of covariates referred to the baseline questionnaire and the distributions of participants. We have added a zero category for alcohol consumption, as well as changed the categories of physical activity in the unit of minutes per week, based on the question " If you add up all the time you spent doing activity LAST WEEK, how much time did you spend ALTOGETHER?". The Table 1 has been updated in the revised version of manuscript according to your suggestions.

Changes in the text: *(In "Methods", Page 8, paragraph 2,* ***Covariates;*** *In "****Table 1****").*

The covariates included self-reported baseline responses for age, gender, ethnicity (whites or non-whites), household income, education level, smoking status, alcohol intake, physical activity (PA), history of cardiovascular disease (yes/no), history of diabetes (yes/no), and history of hypertension (yes/no). The classifications of covariates referred to the baseline questionnaire and the distributions of participants. Household income was classified into four groups: <$20,000, $20,000 to 39,999, $40,000-69,999, and >$70,000, measured in Australian dollars (AUD). The highest level of education attained was classified into three groups: <10 years, high school, and university or higher. Smoking was categorized into the three groups: never smoker, former smoker, and current smoker. Alcohol intake was classified into five groups organized by the number of drinks per week: 0, 1-4, 5-7, 8-14, or ≥15 drinks. The PA in minutes per week was classified into five groups: 0, 1-149, 150-299, 300-539, and ≥540 minutes per week.

Table 1 Baseline characteristics of eligible participants stratified by BMI categories.

Characteristics	**Normal weight**			**Overweight**		**Obese**		***P* Value**
BMI (kg/m^2)	**18.5-19.99**	**20-22.49**	**22.5-24.99**	**25-27.49**	**27.5-29.99**	**30-32.49**	**32.5-50**	
No. of participants (%)	3096(4.2)	10337(14.2)	16128(22.1)	15845(21.7)	11896(16.3)	7240(9.9)	8465(11.6)	-
Male (%)	485(15.7)	2270(22.0)	6134(38.0)	8216(51.9)	6545(55.0)	3609(49.8)	3229(38.1)	< 0.001*
Mean age (SD), years	50.6±3.0	50.7±2.9	50.9±2.9	50.9±2.9	51.1±2.9	51.0±3.0	50.9±3.0	< 0.001*
Born in Australia (%)	2138(69.1)	7432(71.9)	11964(74.2)	12255(77.3)	9509(79.9)	5945(82.1)	7103(83.9)	< 0.001*
Ethnicity								< 0.001*
Whites(%)	2138(69.1)	7432(71.9)	11964(74.2)	12255(77.3)	9509(79.9)	5945(82.1)	7103(83.9)	
Non-whites(%)	942(30.4)	2868(27.7)	4101(25.4)	3530(22.3)	2329(19.6)	1266(17.5)	1329(15.7)	
Missing(%)	16(0.5)	37(0.4)	63(0.4)	60(0.4)	58(0.5)	29(0.4)	33(0.4)	
Private health insurance (%)	1913(61.8)	6930(67)	11093(68.8)	11050(69.7)	8341(70.1)	4878(67.4)	5312(62.8)	0.010*
Household income (AUD/years)								0.864
<20000	353(11.4)	708(6.8)	979(6.1)	876(5.5)	635(5.3)	454(6.3)	702(8.3)	
20000-39999	453(14.6)	1357(13.1)	1820(11.3)	1726(10.9)	1251(10.5)	814(11.2)	1034(12.2)	
40000-69999	618(20.0)	2235(21.6)	3413(21.2)	3360(21.2)	2648(22.3)	1700(23.5)	1969(23.3)	
>70000	1101(35.6)	4323(41.8)	7493(46.5)	7687(48.5)	5650(47.5)	3207(44.3)	3319(39.2)	
Missing	571(18.4)	1714(16.6)	2423(15.0)	2196(13.9)	1712(14.4)	1065(14.7)	1441(17.0)	
Education								< 0.001*
<10 years	177(5.7)	457(4.4)	707(4.4)	834(5.3)	682(5.7)	526(7.3)	830(9.8)	
High school	1779(57.5)	5786(56.0)	9249(57.3)	9518(60.1)	7449(62.6)	4669(64.5)	5551(65.6)	
University or higher	1116(36.1)	4015(38.8)	6061(37.6)	5403(34.1)	3695(31.1)	1981(27.4)	2008(23.7)	
Smoking status								< 0.001*
Never smoker	1886(60.9)	6407(62.0)	9712(60.2)	9284(58.6)	6717(56.5)	3907(54.0)	4606(54.4)	
Former smoker	727(23.5)	2749(26.6)	4849(30.1)	5100(32.2)	4114(34.6)	2610(36.0)	3039(35.9)	
Current smoker	481(15.5)	1179(11.4)	1561(9.7)	1456(9.2)	1062(8.9)	721(10.0)	818(9.7)	

Alcoholic intake (±SD), drinks/wk								< 0.001*
0	1070 (34.6)	2935(28.4)	4124(25.6)	3734(23.6)	2887(24.3)	2075(28.7)	3232(38.2)	
1-4	672(21.7)	2525(24.4)	3632(22.5)	3663(23.1)	2750(23.1)	1692(23.4)	1976(23.3)	
5-7	505(16.3)	1720(16.6)	2518(15.6)	2342(14.8)	1597(13.4)	889(12.3)	879(10.4)	
8-14	528(17.1)	1990(19.3)	3412(21.2)	3225(20.4)	2338(19.7)	1266(17.5)	1162(13.7)	
≥ 15	281(9.1)	1063(10.3)	2298(14.2)	2735(17.3)	2234(18.8)	1261(17.4)	1125(13.3)	
Missing	40(1.3)	104(1.0)	144(0.9)	146(0.9)	90(0.8)	57(0.8)	91(1.1)	
Physical activity (±SD), min/wk								< 0.001*
0	377(12.2)	1065(10.3)	1821(11.3)	1944(12.3)	1666(14.0)	1148(15.9)	1667(19.7)	
1-149	635(20.5)	2043(19.8)	3329(20.6)	3415(21.6)	2798(23.5)	1785(24.7)	2178(25.7)	
150-299	493(15.9)	1763(17.1)	2824(17.5)	2797(17.7)	2098(17.6)	1254(17.3)	1351(16.0)	
300-539	568(18.3)	2063(20.0)	3238(20.1)	3174(20.0)	2210(18.6)	1259(17.4)	1337(15.8)	
≥ 540	942(30.4)	3209(31.0)	4635(28.7)	4221(26.6)	2882(24.2)	1640(22.7)	1684(19.9)	
Missing	81(2.6)	194(1.9)	281(1.7)	294(1.9)	242(2.0)	154(2.1)	248(2.9)	
Comorbidities								
Cardiovascular disease (%)	64(2.1)	248(2.4)	369(2.3)	477(3.0)	455(3.8)	282(3.9)	393(4.6)	< 0.001*
Diabetes (%)	45(1.5)	155(1.5)	329(2.0)	409(2.6)	467(3.9)	412(5.7)	920(10.9)	< 0.001*
Hypertension (%)	232(7.5)	952(9.2)	2071(12.8)	2949(18.6)	2927(24.6)	2251(31.1)	3449(40.7)	< 0.001*

BMI=Body mass index; SD=Standard deviation; AUD= Australian dollars; min/wk= Minutes per week.

Comment 6: In the section titled "Outcome" please consider acknowledging the mentioned MBS claims records assumption as a part of the limitations due to the fact that the decreased number of individuals who experienced the desired outcome being lower, due to the lack of claims records, would decrease the risk that was estimated for the study from the actual risk.

Reply 6: Thanks for your suggestion. We have added this accordingly.

Changes in the text: *(In "Discussion", Page 15, paragraph 1).*

The possible underestimation of the actual risk should be noted in this population, considering the above-mentioned limitations.

Comment 7: In the section titled "Statistical Analysis" please consider including more detail as to the variables that were adjusted for in each of the models.
Reply 7: Thank you for your valuable suggestion. We have added this accordingly.

Changes in the text: *(In "Methods", Page 9, paragraph 1, **Statistical Analysis**).*

Two regression models were used in the analysis: a first regression model adjusted for age and gender only, and a second model with further adjustment for all potential confounding factors including age, gender, ethnicity, income, education level, lifestyle factors (smoking, alcohol drinking and physical activity), and systematic diseases (hypertension, cardiovascular disease and diabetes).

Comment 8: In the aforementioned section, Line 149 mentions "A univariate model" being used for the first model, however this is inaccurate. For a model to be described as univariable, it should not include any covariates included in it and instead should just be a model of the exposure.

Reply 8: Thanks for your comments. We do apologize for this error and have corrected it accordingly.

Changes in the text: *(In "Methods", Page 9, paragraph 1, **Statistical Analysis**).*

Two regression models were used in the analysis: a first regression model adjusted for age and gender only, and a second model with further adjustment for all potential confounding factors including age, gender, ethnicity, income, education level, lifestyle factors (smoking, alcohol drinking and physical activity), and systematic diseases

(hypertension, cardiovascular disease and diabetes).

Comment 9: In the results section, please consider expanding the hazards ratios into percentages.

Reply 9: Thank you for your valuable suggestion. We have modified the related results.

Changes in the text: *(In "Results", Page 10, paragraph 3).*

Among participants who drank 5 to 7 alcoholic drinks per week, a 73% and 27% reduction in the risk of EOC was observed in participants with a BMI of 18.5–19.99 kg/m^2 and 25.0–27.49 kg/m^2 , respectively, compared to those with a BMI of 20.0-22.49 kg/m^2.

Comment 10: In the section titled "Exposures" please consider providing a rationale for the separation of BMI into the seven categories

Reply 10: Thank you for your comments. According to the World Organization Health (WHO) weight classification, BMI was divided into six status including underweight (below 18.5), normal weight (18.5-24.9 kg/m^2), Pre-obesity (25.0-29.9 kg/m^2), Obesity class I (30.0-34.9 kg/m^2), Obesity class II (35.5-39.9 kg/m^2), and Obesity class III (above 40 kg/m^2). In this study, participants with extreme measures of BMI (<15 kg/m^2 or BMI>50 kg/m^2) were excluded due to the increased probability of measurement error. Considering the distribution of participants, BMI was further divided into seven categories including 18.5–19.99, 20–22.49, and 22.5–24.99 kg/m^2 (normal weight); 25–27.49 and 27.5–29.99 kg/m^2 (overweight); and 30–32.49 and 32.5–50 kg/m^2 (obese). Hoping this addresses your concern.

Changes in the text: *(In "Methods", Page 8, paragraph 1, **Exposures**).*

According to the body weight classification by World Health Organization(WHO) and the distribution of participants in the present study, BMI was divided into seven categories including 18.5-19.99, 20-22.49, and 22.5-24.99 kg/m^2 (normal weight); 25-27.49 and 27.5-29.99 kg/m^2 (overweight); and 30-32.49 and 32.5-50 kg/m^2 (obese).

Comment 11: In the section titled “Results” please consider describing the results of the tables more quantitatively

Reply 11: Thank you for your valuable suggestion. We have modified the results section.

Changes in the text: *(In “Results”, Page 10, paragraph 2-3).*

Table 2 shows the HR and 95% CI of EOC risk related to BMI categories. There were no significant associations between BMI and EOC adjusted for age and gender. Males with a BMI of 30.0-32.49 kg/m^2 showed a 54% higher risk of EOC compared with those with a BMI of 20.0-22.49 kg/m^2. When further adjustments were made for all potential confounding factors (Model 2), no statistically significant associations were observed between BMI and EOC in total, and in analyses stratified by gender.
Table 3 shows the associations between BMI and EOC stratified by gender, ethnicity, education level, smoking status, alcohol consumption, PA, and systematic diseases (hypertension, cardiovascular disease and diabetes). Among participants who drank 5 to 7 alcoholic drinks per week, a 73% and 27% reduction in the risk of EOC was observed in participants with a BMI of 18.5–19.99 kg/m^2 and 25.0–27.49 kg/m^2, respectively, compared to those with a BMI of 20.0-22.49 kg/m^2. No significant associations were observed between the incidence of EOC and BMI after data were stratified by other confounding factors.

Reviewer D:

Comment 1: This is a very good analysis of multiple factors associated with early onset cataract. I consider this study to have valuable data but there are some concerns that need to be addressed. Specific: However, earlier studies have suggested that early onset cataract may be associated with diabetes mellitus, sedentary lifestyle, atopy, high myopia, long term corticosteroid use and smoking, these data are inconsistent between studies. So the authors should consider to change the title of the manuscript into "Ocular comorbodities of Early Onset Cataract in the 45 and Up cohort study" and add to analysis other factors like cardiovascular diseases, stroke, diabetes and hypertension. Publishing only analysis of BMI without co-existing diseases may lead to misconclusions. The other important limitation of the present study is the Cox regression analysis. The authors should stratify BMI with other factors like level of education and physical activity in my opinion. After that the results, discussion and

conclusions sections should be adjusted

Reply 1: Thanks for your comments. The present study was to evaluate the association between BMI and the incidence of EOC after adjusting for a number of confounding factors, not to investigate the ocular comorbodities of patients with EOC, thus we could not use the title “Ocular comorbodities of Early Onset Cataract in the 45 and Up cohort study” as you suggested. According to your suggestions, we have added the analysis on the relationship between BMI and EOC stratifies by gender, ethnicity, education level, smoking status, alcohol consumption, physical activity, and systematic diseases (hypertension, cardiovascular disease and diabetes). Among participants who drank 5 to 7 alcoholic drinks per week, a relatively 73% and 27% reduction in the risk of EOC was observed in participants with a BMI of 18.5-19.99 kg/m^2 and 25.0-27.49 kg/m^2 , respectively, compared to those with a BMI of 20.0-22.49 kg/m^2. No statistically significant associations were observed between the incidence of EOC and BMI after data were stratified by other confounding factors. Hoping this addresses your concern.

Changes in the text: *(In “Table 3”).*

Table 3 Multivariate-adjusted cox regression analyses stratified by covariates.

Subgroup	BMI (20.0-22.49 kg/m^2 as reference, HR(95% CI))						P for interaction
	18.5-19.99	22.5-24.99	25.0-27.49	27.5-29.99	30.0-32.49	32.5-50	
Gender							0.369
Females	1.13(0.53-2.41)	0.91(0.64-1.31)	0.92(0.65-1.30)	0.97(0.68-1.38)	1.22(0.84-1.77)	1.00(0.67-1.50)	
Males	0.87(0.64-1.18)	0.88(0.73-1.07)	0.88(0.72-1.08)	0.86(0.69-1.08)	0.94(0.73-1.21)	0.83(0.65-1.06)	
Ethnicity							0.821
Whites	0.88(0.62-1.23)	0.88(0.73-1.07)	0.82(0.68-1.00)	0.83(0.68-1.03)	1.02(0.81-1.28)	0.81(0.64-1.02)	
Non-whites	1.00(0.61-1.66)	0.85(0.61-1.18)	1.08(0.78-1.49)	1.08(0.75-1.56)	1.09(0.71-1.68)	1.14(0.75-1.72)	
Education							0.799
<10 years	0.32(0.04-2.56)	0.79(0.32-1.93)	1.00(0.43-2.33)	1.17(0.51-2.72)	1.14(0.47-2.77)	1.35(0.60-3.06)	
High school	0.87(0.59-1.27)	0.90(0.73-1.13)	0.87(0.69-1.08)	0.91(0.72-1.15)	1.03(0.80-1.34)	0.86(0.66-1.12)	
University or higher	1.03(0.68-1.56)	0.80(0.62-1.05)	0.81(0.62-1.07)	0.79(0.59-1.08)	0.95(0.67-1.34)	0.76(0.53-1.10)	
Smoking status							0.999
Never smoker	1.10(0.79-1.53)	0.90(0.73-1.11)	0.87(0.70-1.08)	0.84(0.66-1.06)	0.97(0.75-1.26)	0.88(0.68-1.14)	
Former smoker	0.74(0.41-1.33)	0.82(0.61-1.11)	0.78(0.58-1.06)	0.91(0.67-1.25)	1.06(0.75-1.49)	0.84(0.59-1.20)	
Current smoker	0.28(0.07-1.23)	0.79(0.42-1.49)	1.31(0.72-2.37)	0.92(0.46-1.82)	1.22(0.61-2.47)	0.75(0.35-1.59)	
Alcohol intake (drinks/week)							0.784
0	0.89(0.52-1.53)	1.13(0.81-1.57)	1.10(0.78-1.54)	0.90(0.61-1.31)	1.00(0.67-1.50)	1.08(0.75-1.55)	
1-4	1.45(0.89-2.36)	0.84(0.60-1.18)	0.93(0.67-1.30)	0.91(0.63-1.30)	1.10(0.75-1.61)	0.83(0.56-1.25)	
5-7	0.27(0.10-0.74)	0.75(0.50-1.11)	0.63(0.41-0.96)	0.71(0.45-1.13)	0.71(0.40-1.26)	0.69(0.39-1.23)	
7-14	1.11(0.61-2.01)	0.79(0.55-1.12)	0.83(0.57-1.20)	0.94(0.64-1.39)	0.99(0.63-1.56)	0.91(0.56-1.48)	
≥15	0.68(0.23-1.96)	0.82(0.50-1.36)	0.80(0.49-1.32)	0.91(0.55-1.50)	1.32(0.77-2.25)	0.67(0.35-1.28)	
Physical activity, min/wk							0.048*
0	1.76(0.80-3.88)	1.13(0.66-1.94)	0.83(0.48-1.46)	1.20(0.69-2.09)	1.29(0.73-2.29)	1.14(0.65-2.00)	

1-149	0.95(0.51-1.78)	1.07(0.73-1.57)	1.12(0.77-1.64)	1.26(0.86-1.86)	1.22(0.79-1.88)	1.03(0.67-1.58)	
150-299	0.62(0.28-1.39)	0.67(0.44-1.01)	0.84(0.56-1.26)	0.65(0.41-1.04)	0.86(0.52-1.40)	0.64(0.37-1.11)	
300-539	1.07(0.55-2.08)	1.02(0.70-1.48)	0.73(0.49-1.09)	0.74(0.48-1.15)	1.09(0.69-1.74)	0.93(0.58-1.51)	
≥540	0.77(0.47-1.25)	0.75(0.56-1.00)	0.84(0.63-1.13)	0.80(0.58-1.12)	0.92(0.62-1.35)	0.77(0.52-1.14)	
Cardiovascular disease							0.772
No	0.87(0.65-1.15)	0.86(0.73-1.02)	0.86(0.72-1.02)	0.86(0.72-1.04)	1.00(0.82-1.22)	0.85(0.70-1.05)	
Yes	7.09(1.37-36.61)	1.62(0.41-6.37)	1.75(0.46-6.65)	1.79(0.48-6.64)	2.75(0.71-10.63)	1.52(0.38-6.12)	
Diabetes							0.594
No	0.91(0.69-1.21)	0.87(0.73-1.03)	0.85(0.72-1.01)	0.88(0.73-1.05)	1.00(0.82-1.23)	0.89(0.72-1.10)	
Yes	0.62(0.07-5.39)	0.92(0.32-2.69)	1.26(0.46-3.42)	0.93(0.33-2.63)	1.37(0.50-3.78)	0.80(0.30-2.12)	
Hypertension							0.670
No	0.83(0.61-1.12)	0.86(0.72-1.03)	0.84(0.70-1.01)	0.83(0.68-1.02)	1.00(0.80-1.27)	0.89(0.69-1.13)	
Yes	1.87(0.87-4.04)	1.04(0.64-1.68)	1.07(0.68-1.69)	1.15(0.72-1.82)	1.22(0.76-1.95)	1.00(0.63-1.59)	

BMI=Body mass index; HR=Hazard ratio; 95% CI=95% Confidence interval; min/wk= minutes per week.