Association of red and processed meat consumption with cardiovascular morbidity and mortality in participants with and without obesity: A prospective cohort study

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Abstract

Objective

There is increasing evidence that red and processed meat consumption is associated with increased risk of cardiovascular (CV) disease. However, little literature reported the association among people with obesity versus those without obesity. We sought to investigate this using the UK Biobank data.

Methods

In this large prospective population-based cohort study, the red and processed meat consumption was assessed through the UK Biobank touch-screen questionnaire at baseline. The estimated hazards ratios (HRs) with 95% confidence intervals (CIs) were obtained from the Cox proportional hazard models to assess the association between red and processed meat consumption and the risk of CV death, cerebrovascular, and ischemic heart diseases in participants with and without obesity.

Results

Of 428,070 participants, 100,175 (23.4%) were obese with the mean age of 56 (SD: 7.9) years old and 54% were female. Participants without obesity, the mean age was 56 (SD: 5.2) years old and 55% were female. The overall median follow-up was 7.2 (IQR: 6.5-7.8) years. red and processed meat consumption had increased risk of CV death (HR (95%CI):1.04 (1.01-1.08) per week serve for participants with obesity and 1.04 (1.02-1.07) for those without obesity) after adjusted for age, sex, ethnicity, education, smoking and alcohol status and overall health. The moderate positive association between red and processed meat consumption and ischemic heart disease was only observed in participants without obesity (HR (95%CI): 1.15 (1.00-1.31) for the highest versus lowest terciles of red and processed meat consumption). No association was found with cerebrovascular disease in the participants regardless of obesity.

Conclusions

Consumption frequency of red and processed meat is associated with higher risk of CV death regardless of obesity. The risk of ischemic heart disease associated with red and processed meat consumption may be higher in participants without obesity. Further studies are needed to understand the full extent of the mechanism of the association.

Keywords: Red meat consumption; obesity; cardiovascular death; cardiovascular disease; general population with UK.

Introduction

Cardiovascular disease (CVD) is a leading cause of death globally [1]. Studies have revealed that obesity is one of the contributing factors of CV disease [2-5] and particularly associated with risk of developing heart failure (HF) and coronary heart disease [6-8]. In the USA, about 40% of the population are classified as obese [2, 9]. The number of people with obesity is growing in the UK [10, 11] and worldwide [5, 12]. In the UK, obesity levels in adults increased from approximately 15% in 1993 to 26% in 2016 [13]. Worldwide, around 11% of men and 15% of women were obese in 2016 and the prevalence of obesity nearly tripled between 1975 and 2016 [14]. This has an effect on people's quality of life and represent a major and growing socioeconomic burden. Some research suggests that change in the structure and function of the heart due to obesity may be the main cause of CVD [15, 16]. Recent evidence indicates that obesity could be beneficial in patients with CVD. In patients with HF mild-to-moderate obesity is associated with a lower mortality, the so-called obesity paradox [4].

There is increasing evidence that red and processed meat consumption is associated with increased risk of CV disease and mortality [17-25] because of possible high level of cholesterol, saturated fatty acid and haem iron from red and processed meat consumption [21, 22]. A recent dose-response meta-analysis revealed that higher consumption of red and processed meat is associated with increased risk of CV mortality [17]. A large prospective study showed red and processed meat consumption was associated with a modest increase in CVD mortality [20]. On the other hand, this positive association between red and processed meat consumption and CV mortality was not found in the studies conducted by other researchers [23, 26, 27].

Possibly, people with obesity consume more red and processed meat and have higher risk of CV disease [28]. Some studies suggested that high meat consumption was correlated with

prevalence of obesity [28, 29]. A recent systematic review and meta-analysis observed that red and processed meat consumption is directly associated with risk of obesity [30]. While Lee et al [31], in addition, found in the Asian countries, red meat consumption had decreased risk of CVD mortality in men, which may be due to cultural, socioeconomic status, levels of physical activity and genetic differences between men and women in the Asian.

The association between red and processed meat consumption and CV disease in people with obesity and without obesity are unclear. There is lack of an existing study to link them all together in one study. Clarifying and understanding these associations can be of value when advising patients on how to modify their cardiovascular risk factors. Using data from the UK Biobank, we aim to examine and quantify the association of red and processed meat consumption with CV death, cerebrovascular and ischemic heart diseases (IHD) in participants with and without obesity in the general population.

Methods

Study population

The UK Biobank [32, 33] is a large general population-based prospective cohort study conducted from 22 assessment centres across the UK taken between 2006 and 2010 for the adults aged between 40-69 years at the point of recruitment. The data include detailed information on participant demographic, social, lifestyle, physical activity, medical history, hospital records and mortality data. The UK Biobank protocol is available online (http://www.ukbiobank.ac.uk/wp-content/uploads/ 2011/11/UK-Biobank-Protocol.pdf). In this study, participants with cardiovascular disease such as angina, myocardial infarction and stroke at baseline were excluded. Participants with cancer (malignant neoplasms) were also

excluded. All participants provided electronic informed consent. All participants with information on red and processed meat consumption were used.

This study was based on the UK Biobank resource. Details of patients and public involvement in the UK Biobank are available online (http://www.ukbiobank.ac.uk/about-biobank-uk/ and https://www.ukbiobank.ac.uk/wp-content/uploads/2011/07/Summary-EGFconsultation.pdf?phpMyAdmin=trmKQlYdjjnQIgJ%2CfAzikMhEnx6).

Red and processed meat consumption

Red and processed meat consumption was assessed through the UK Biobank touch-screen questionnaire at baseline. The touchscreen questionnaire is available on the UK Biobank website(http://biobank.ndph.ox.ac.uk/showcase/showcase/docs/TouchscreenQuestionsMainFinal.pdf). The variables related to red and processed meat consumption in the questionnaire have been shown reasonable validity and reliability [34].

In this study, red meat consisted of beef, pork and lamb/mutton. Each participant was asked their frequency of consumption, which is "how often do you eat each of them". A response could be "Never", this was coded it as 0, "Less than once a week", coded as 0.5, "Once a week" coded as 1, "2-4 times a week" coded as 3, "5-6 times a week " coded as 5.5, and "Once or more daily" was coded it 7. Processed meat consisted of any consumption of bacon, ham, sausages, meat pies, kebabs, burgers and nuggets. The similar coding method was applied for assessing processed meat. A total score of red and processed meat consumption was calculated by summing up all the coded numbers from the above. The minimum total score of red and processed meat consumption frequencies was 0 and 28 was the maximum score for each week. In this study, we assume that participants' dietary habits are stable for a long time.

Other variables

The following baseline variables were measured when the participants attended the assessment centre, such as age (years), gender (male and female), ethnicity, weight (kg) and height (m). Smoking status (prefer not to answer, never, previous and current), alcohol status (prefer not to answer, never, previous and current), duration of moderate activity (minutes) on a typical day, overall health rating (excellent, good, fair, poor, do not know and prefer not to answer) and qualification were obtained from touchscreen questionnaire. Diet iron was estimated intake based on food and beverage consumption yesterday excluding any supplements.

Obesity

Obesity is defined based on a body mass index (BMI (kg/m^2)) that is equal or over 30, which is recommended by the National Institutes of Health. The BMI is calculated based on body weight (kg) and height (m) measured at the baseline.

Endpoints

The main study endpoints were CV death, cerebrovascular disease and ischemic heart disease. The cause of death was defined according to the 10th edition of the International Classification of Diseases (ICD-10), and cardiovascular death is coded as I00-I99. Cerebrovascular disease (first hospitalization) was defined as ICD-10: I60-I69 and ischemic heart disease (first hospitalization) as ICD-10: I20-I25. The study period for participants is the date of their attendance at the recruitment centre until the 1st March 2016, the date of CV death or the date of the first relevant CV events. The date of the outcome was taken from hospital admissions data.

Statistical analysis

Baseline characteristics were described by terciles of the total score of red and processed meat consumption frequencies in participants with and without obesity respectively. Continuous variables were expressed as mean with standard deviation (SD) or median with inter-quartile range (IQR) depending on the distribution of the data and categorical variables as frequency and proportion. Univariate and multivariable Cox proportional hazard regression models were used to assess association between red and processed meat consumption and the time of CV death, cerebrovascular disease and ischemic heart disease. red and processed meat consumption was used as a continuous variable in the models. The terciles of red and processed meat consumption were also investigated. The results were presented as hazard ratio (HR) with the 95% confidence intervals (CI). The proportional hazards assumption was checked based on Schoenfeld residuals.

The multivariable models were developed for adjusting for age and sex first, and then were additionally adjusted for ethnicity, education, smoking status, alcohol status, and overall health (main model). Several separate multivariable analyses were performed. First, the associations between red and processed meat consumption frequency and CV outcomes were investigated separately by men and women (Supplementary Table 5). Second, we evaluated individual effect of red meat unprocessed and red meat processed consumption frequency (Supplementary Table 6). Moreover, the associations were investigated in participants who were overweight (BMI>25 kg/m2) and those were not (Supplementary Table 7). In addition, the intake of poultry, fish, fruit and vegetables were included in the main model to consider their possible impact on the association (Supplementary Table 8). Furthermore, we added diabetes as a covariate (n= 327,142 participants available) to the main model to study the potential impact on the association (Supplementary Table 9).

We did not include the variables with a large number of missing values, such as physical activity. Median imputation was used to impute the missing values for the continuous variables with missing values less than 3%, as they were not normally distributed. In addition, association between diet iron and red and processed meat and CVD was examined.

Statistical analyses were conducted using STATA version 14.2. The level of significance was set at alpha=0.05 with two tails.

Results

Baseline characteristics

Of the 502,543 participants in the dataset, we excluded 67,926 due to severe CV events (such as angina, heart attack or stroke) and cancer at baseline, 6,547 participants were excluded as they did not have red and processed meat consumption records. The study included 428,070 participants in total.

In this study, the median age was 57 with the IQR: 49-63 years and 54.9% of the participants were female. 88.3% of the participants were from white background including British, Irish and any other white background. 23.4% of the participants were obese. Compared with the obesity group, participants without obesity had a higher percentage of higher education (35.7%), particularly among those who had lower red and processed meat consumption frequency (37.8%). Participants without obesity had higher overall excellent health rate (82.2%) (Table 1) and they were more likely to be current alcohol drinkers (93.9%) but were less likely to be previous smokers (32.2%). They also reported higher levels of activity. The average dietary iron intake was higher in participants without obesity than those who were obese and it appears that there was positive relationship between red and processed meat consumption and dietary iron intake. Women had less red and processed meat consumption

frequency whatever obesity or not (Table 1). Overall, participants with obesity had higher frequencies of consumption red and processed meat compared to those without obesity (Supplementary Table 1).

Baseline characteristics by CV death and CV disease for each tercile of red and processed meat consumption in participants with obesity and without obesity were described in Supplementary Table 2 and Supplementary Table 3 respectively. The rate of CV death in those with obesity per 10,000 person years of observation time was significantly higher than participants without obesity (8.41, 95%CI: 7.76-9.11 for obese group, and 5.22, 95%CI: 4.95-5.52 for non-obese group, $p<0.001$). The rates of cerebrovascular disease and IHD in those with obesity were also higher than participants without obesity (Supplementary Table 4).

Association between red and processed meat consumption and CV death, cerebrovascular and ischemic heart diseases

Non-obesity: Of the 327,895 participants without obesity (Obesity is defined as a BMI equal or over 30 (kg/m^2)) during a median follow-up period of 7.16 (IQR: 6.5-7.8) years, 1,237 died due to cardiovascular disease, 682 had cerebrovascular disease and 1,308 had ischemic heart disease. The total consumption of red and processed meat had increase the risk of CV death (the full adjusted hazard ratio (HR) with 95% confidence intervals (CI) was 1.04 (1.02-1.07) per week serve), and was associated with the development of ischemic heart disease (HR (95%CI) was 1.03 (1.00-1.05) adjusted for age and sex). No association was observed between red and processed meat consumption and cerebrovascular disease (Table 2). The assumptions of linearity of the models were tested and the results showed satisfaction (Table 3). Compared to tercile 1, tercile 3 of red and processed meat consumption frequency were associated with increased risk of CV death (the full adjusted HR (95%CI) was: 1.20 (1.05-1.38)). Compared with tercile 1, tercile 2 and 3 had higher risk of ischemic heart disease (the

full adjusted HR (95%CI) were: 1.14 (1.00-1.31) for tercile 2, and for tercile 3: 1.15 (1.00-1.31)).

Obesity: Of the 100,175 participants with obesity during a median follow-up period of 7.1 (IQR: 6.4 -7.9) years, 600 died due to cardiovascular, 149 had cerebrovascular disease and 552 had ischemic heart disease. Consumption frequency of red and processed meat had increased risk of CV death (the full adjusted HR (95%CI): 1.04 (1.01-1.08) per week serve). No associations were found between red and processed meat consumption frequency and either cerebrovascular disease and ischemic heart disease (Table 2). Similar results obtained using the data based on terciles of red and processed meat consumption (Table 3).

Diet iron: Of the 61,190 participants who had diet iron measurements (diet iron was estimated intake based on food and beverage consumption yesterday excluding any supplements) at baseline, we evaluated the association between diet iron and CV events in subgroups of obesity and red and processed meat consumption frequency. Diet iron was found to be linked with CV death in participants with non-obesity (HR (95%CI): 1.04 (1.01-1.07) and high red and processed meat consumption (1.07 (1.03-1.10)). A negative association was observed between diet iron and cerebrovascular disease for participants without obesity. No relationship was found between diet iron and ischemic heart disease regardless participants with obesity and amount of red and processed meat consumption (Supplementary Table 10).

Discussion

In this study, we examined the associations of consumption frequency of red and processed meat with CV death, cerebrovascular and ischemic heart diseases in participants with and without obesity. The finding suggested that red and processed meat consumption increased

risk of CV death by 4% per week serving irrespective of obesity. Among non-obese participants, those in the highest tercile of red and processed meat consumption had significantly higher risk of cardiovascular death (HR (95%CI): 1.20 (1.05-1.38)) and higher risk of ischemic heart disease (HR (95%CI): 1.15 (1.00-1.31)) compared to the first tercile of red and processed meat consumption frequency. The association of ischemic heart disease with red and processed meat consumption was not observed in participants with obesity. We found no significant association between red and processed meat consumption frequency and cerebrovascular disease in those with and without obesity.

It is widely observed that red and processed meat consumption is associated with CV death [35]. The current study demonstrated positive association of CV death with red and processed meat consumption among all participants and the participants with obesity and non-obesity. The observed association was in agreement with the results reported in the recent dose-response meta-analysis included nine studies [17]. The association was also aligned with the study conducted from two prospective cohort studies [18] and the most recent study of 29,682 adults from USA [35], however, those studies did not evaluate the participants in regards of obesity. Further study conducted by Bellavia et al [19] considered only red meat consumption for 74,645 Swedish population with mean BMI of 25.5 (SD: 3.6) and showed that participants in the highest quintile of red meat consumption had a 21% increased risk of all-cause mortality compared to those in the lowest quintile. In addition, the Netherlands cohort study [36] reported that processed meat other than red meat consumption was positively associated with CV death. These results might be influenced by the fact that the models used to assess the association were adjusted additionally for comorbidity, such as hypertension and diabetes in addition to the major lifestyle and social status that most studies included. In contrast, a negative association between moderate meat consumption and IHD death was observed in men whose BMI>=25 (HR (95%CI): 0.36 (0.15-0.83) for highest vs

lowest quintile) in a study based on Japanese cohort, however, the number of IHD deaths were small (range: 9-25 events).

We observed that red and processed meat consumption was positively associated with a small increased risk of ischemic heart disease (IHD) for the participants without obesity. The results were consistent with the most recent findings reported by Key et al [37], which included 409,885 participants (mean of BMI: 25.8 (SD: 4.0)). On the other hand, a systematic review and meta-analysis of previous studies of red and processed meat consumption showed that coronary heart disease was linked to the consumption of processed meat and not red meat [38]. It is worth noting that the present study showed a positive association between red and processed meat consumption and IHD. In fact, this association was mainly contributed due to the participants without obesity, not in participants with obesity.

Results of the meta-analysis of prospective studies published in the year 2012 with 329,495 participants and 10,630 cases of stroke showed that red and processed meat consumption is associated with increased risk of total stroke and ischemic stroke. However, the association is not observed in the participants with haemorrhagic stroke [39]. A most recent dose-response meta-analysis performed on seven prospective cohort studies and found no association between red and processed meat consumption and haemorrhagic stroke [40]. The current study found no association of cerebrovascular disease with red and processed meat consumption in participants with and without obesity, this is similar to the previous systematic review and meta-analysis study regardless of obesity [38].

There were no studies designated to evaluate the association separately in people with and without obesity. One study [26] conducted from a Japanese cohort, in which the association between moderate red and processed meat consumption and CV death was investigated using stratified BMI with less or more than 25 kg/m^2, however, there were very limited number of

events. In patients with CVD, an “obesity paradox” relationship has been described between BMI and CV events [4]. In the current study, no association was observed between red and processed meat consumption and IHD in participants with obesity. One of the explanations for this may be due to the fact that obesity might be protective in patients with CV disease. Fat might provide an energy reserve that helps a patient from CV disease cope with the metabolic costs of illness, protecting muscle and bone from the catabolic effects of worsening of CV disease. Fat might also provide protection against endotoxins [41, 42]. It is unclear whether this association is causal. In addition, obesity can be a risk factor for developing CV disease. In this study, we assumed that dietary habits were relatively stable over time. We recognise this is a potential limitation as dietary habits can vary especially in obese participants who may be trying to lose weight. Further study is needed to understand the pathophysiology of both red and processed meat consumption and obesity, and its effects on CVD.

During the current coronavirus disease 2019 (COVID-19) pandemic, increasing number of studies have found the link between obesity, CV diseases and severity of COVID-19. Cardiovascular disease was associated with worse outcomes in patients with COVID-19 and obesity appears to be a risk factor for severity of COVID-19 infection.

To the best of our knowledge, this is the first study to evaluate consumption of red and processed meat with CV death, IHD and cerebrovascular disease in people with and without obesity. The main strength of the study is that the associations between red and processed meat consumption and CV outcomes were evaluated based on a large middle-aged population, this allowed us to separate the participants into those with obesity and without obesity groups. In addition, the models were adjusted for a number of lifestyle variables, such as, smoking status and alcohol consumption.

This study analysed observational data from the UK Biobank, which, like any observational study, has certain limitations. First, the confounding variables, such as, the presence of diabetes, physical activity and dietary iron intake were not included in the main analysis due to limited numbers in the dataset. However, we performed the separate analysis for including diabetes variable. Second, we did not consider that a high consumption of red meat could be associated with an increase in the consumption of other "bad" processed foods such as processed carbohydrates. Next, consumption frequency of red and processed meat was obtained from questionnaire, and the assumption that dietary habits were relatively stable over time, which may be subject to bias. In addition, the obesity was defined by BMI, which is not the most accurate measurement of fat mass. BMI does not differentiate between lean muscle and fat mass [43, 44] and the possibility of residual confounding by the typical fluctuations in BMI during follow-up exists.

In conclusion, this study suggested that red and processed meat consumption frequency was associated with CV death in the participants with and without obesity. Consumption frequency of red and processed meat was associated with increased risk of developing ischemic heart disease in participants with non-obesity. Association was not observed between red and processed meat consumption frequency and cerebrovascular disease regardless of obesity. However, further studies are needed to validate of the current results.

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Ethics approval

This study was conducted based on the UK Biobank resource. The ethics approval was not necessary. Details of patients and public involvement in the UK Biobank are available online (http://www.ukbiobank.ac.uk/about-biobank-uk/ and https://www.ukbiobank.ac.uk/wp-content/uploads/2011/07/Summary-EGF-consultation.pdf?phpMyAdmin=trmKQlYdjjnQIgJ%2CfAzikMhEnx6).

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Disclosure

The authors declared no conflict of interest.

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Table 1

Baseline characteristics by terciles of red and processed meat consumptions in participants with and without obesity (n=428,070).

	All participants (n=428,070)				Obese (n=100,175)				Non-obese (n=327,895)			
	Tercile 1 (n=187,711)	Tercile 2 (n=128,740)	Tercil 3 (n = 111,619)	All	Tercile 1 (n=37,263)	Tercile 2 (n=31,609)	Tercil 3 (n = 31,303)	All	Tercile 1 (n=150,448)	Tercile 2 (n=97,131)	Tercil 3 (n =80,316)	All
Age (yrs)	57 (49-62)	57 (49-63)	57 (49-63)	57 (49-63)	57 (50-62)	57 (50-57)	57 (50-63)	57 (50-63)	57 (49-62)	57 (49-63)	57 (49-63)	57 (49-63)
<60 years	114,524 (61.0)	76,411 (59.4)	65,821 (59.0)	256,756 (60.0)	22,539 (60.5)	18,839 (59.6)	18,386 (58.7)	59,764 (59.7)	91,985 (61.1)	57,572 (59.3)	47,435 (59.1)	169,992 (60.1)
>=60 years	73,187 (39.0)	52,329 (40.7)	45,798 (41.0)	171,314 (40.0)	14,724 (39.5)	12,770 (40.4)	12,917 (41.3)	40,411 (40.3)	58,463 (38.9)	39,559 (40.7)	32,881 (40.9)	130,903 (39.9)
Female (%)	124,092 (66.1)	66,731 (51.8)	44,132 (39.5)	234,955 (54.9)	24,846 (66.7)	16,425 (52.0)	12,306 (39.3)	53,577 (53.5)	99,246 (66.0)	50,306 (51.8)	31,826 (39.6)	181,378 (55.3)
Ethnicity-White (%)												
White	163,059 (86.9)	115,921 (90.0)	98,952 (88.7)	377,932 (88.3)	31,931 (85.7)	28,354 (89.7)	27,708 (88.5)	87,993 (87.8)	131,128 (87.2)	87,567 (90.1)	71,244 (88.7)	289,939 (88.4)
others	24,652 (13.1)	12,819 (10.0)	12,667 (11.3)	50,138 (11.7)	5,332 (14.3)	3,255 (10.3)	3,595 (11.5)	12,182 (12.2)	19,320 (12.8)	9,564 (9.8)	9,072 (11.3)	37,956 (11.6)
Body mass index (kg/m^2)	26.1 (23.6-29.1)	26.9 (24.3-29.9)	27.4 (24.7-30.5)	26.6 (24.1-29.7)	32,7 (31.1-35.3)	32.7 (31.1-35.4)	32.8 (31.2-32.8)	32.7 (31.1-35.4)	25.1 (23.0-27.1)	25.6 (23.6-27.5)	25.9 (23.9-27.7)	25.5 (23.4-27.4)
Education												
College or University	67,069 (35.7)	40,567 (31.5)	34,897 (31.3)	142,533 (33.3)	10,146 (27.2)	7,661 (24.2)	7,754 (24.8)	25,561 (25.5)	56,923 (37.8)	32,906 (33.9)	27,143 (33.8)	116,972 (35.7)
Others	117,434 (62.6)	86,005 (66.8)	74,811 (67.0)	278,250 (65.0)	26,357 (70.0)	23,369 (73.9)	22,964 (73.4)	72,690 (72.6)	91,077 (60.5)	62,636 (64.5)	51,847 (64.6)	205,560 (62.7)
Prefer not to answer	3,208 (1.7)	2,168 (1.7)	1,911 (1.7)	7,287 (1.7)	760 (2.0)	579 (1.8)	585 (1.9)	1,924 (1.9)	2,448 (1.6)	1,589 (1.6)	1,326 (1.6)	5,363 (1.6)
Red meat and processed meat intake (per week serve)	2.0(1.5-2.5)	3.5 (3.0-4.5)	6.0 (5.0-7.5)	3.0 (2.0-5.0)	2.0 (1.5-2.5)	4.0 (3.0-4.5)	6.0 (5.0-7.5)	3.5 (2.5-5.0)	2.0 (1.5-2.5)	3.5 (3.0-4.5)	6.0 (5.0-7.5)	3.0 (2.0-4.5)
Dietary iron (mg)	12.9 (9.7-16.4)	13.1 (10.1-16.5)	13.6 (10.5-17.1)	13.1 (10.0-16.6)	12.2 (9.1-15.9)	12.8 (9.7-16.2)	13.4 (10.8-17.1)	12.7 (9.6-16.4)	13.0 (9.9-16.5)	13.2 (10.2-16.6)	13.7 (10.6-17.1)	13.2 (10.1-16.7)
Smoking status (%)												

Never	109,139 (58.1)	71,720 (55.7)	58,553 (52.5)	239,412 (55.9)	20,720 (55.6)	16,641 (52.6)	15,450 (49.4)	52,811 (52.8)	88,419 (58.8)	55,079 (56.7)	43,103 (53.7)	186,601 (56.9)
Previous	61,795 (32.9)	43,122 (33.5)	37,919 (34.0)	142,836 (33.4)	13,333 (35.8)	11,886 (37.6)	12,169 (38.9)	37,388 (37.3)	48,462 (32.2)	31,236 (32.2)	25,750 (32.1)	105,448 (32.2)
Current	16,165 (8.6)	13,481 (10.5)	14,789 (12.3)	44,435 (10.4)	3,051 (8.2)	2,946 (9.3)	3,571 (11.4)	9,568 (9.5)	13,114 (8.7)	10,535 (10.8)	11,218 (14.0)	34,867 (10.6)
Prefer not to answer	612 (0.3)	417 (0.3)	358 (0.3)	1,387 (0.3)	159 (0.4)	136 (0.4)	113 (0.4)	408 (0.4)	354 (0.3)	281 (0.3)	245 (0.3)	979 (0.3)
Alcohol drinker status (%)												
Never	9,951 (5.3)	4,741 (3.7)	3,656 (3.3)	18,348 (4.3)	2,640 (7.1)	1,494 (4.7)	1,204 (3.8)	5,338 (5.3)	7,311 (4.9)	3,247 (3.3)	2,452 (3.1)	13,010 (4.0)
Previous	7,366 (3.9)	3,756 (2.9)	3,139 (2.8)	14,261 (3.3)	1,976 (5.3)	1,177 (3.7)	1,100 (3.5)	4,253 (4.2)	5,390 (3.6)	2,579 (2.7)	2,039 (2.5)	10,008 (3.1)
Current	170,259 (90.7)	120,164 (93.3)	104,741 (93.8)	395,164 (92.3)	32,619 (87.5)	28,916 (91.5)	28,974 (92.6)	90,509 (90.3)	137,640 (91.5)	91,248 (93.9)	75,767 (94.3)	304,655 (92.9)
Prefer not to answer	135 (0.1)	79 (0.1)	83 (0.1)	297 (0.1)	28 (0.1)	22 (0.1)	25 (0.1)	75 (0.1)	107 (0.1)	57 (0.1)	58 (0.1)	222 (0.1)
Activity (Duration of moderate activity)	40 (20-60)	40 (20-60)	40 (20-70)	40 (20-60)	30 (20-60)	30 (20-60)	30 (20-60)	30 (20-60)	40 (20-60)	40 (20-60)	40 (20-75)	40 (20-60)
Overall health rating												
Excellent	151,736 (80.8)	104,679 (81.3)	89,385 (80.1)	345,800 (80.8)	28,075 (75.3)	24,338 (77.0)	23,896 (76.3)	76,310 (76.2)	123,661 (82.2)	80,340 (82.7)	65,489 (81.5)	269,490 (82.2)
Good	24,643 (13.1)	16,373 (12.7)	14,491 (13.0)	55,507 (13.0)	5,778 (15.5)	4,603 (14.6)	4,528 (14.5)	14,909 (14.9)	18,865 (12.5)	11,770 (12.1)	9,963 (12.40)	40,598 (12.4)
Fair	10,854(5.8)	7,375 (5.7)	7,384 (6.6)	25,613 (6.0)	3,292 (8.8)	2,568 (8.1)	2,788 (8.9)	8,648 (8.6)	7,562 (5.0)	4,807 (4.9)	4,596 (5.7)	16,965 (5.2)
Prefer not to answer	470 (0.3)	308 (0.2)	353 (0.3)	1,131 (0.3)	118 (0.3)	98 (0.3)	91 (0.3)	307 (0.3)	352 (0.2)	210 (0.2)	262 (0.3)	824 (0.2)

Table 2

HR (95%CI) of red and processed meat consumption frequency for all participants, participants with and without obesity.[1]

Events	HR (95%CI)		
	All adults (n=428,070)	Obese (n=100,175)	Non-obese (n=327,895)
Cardiovascular death			
Model 1	1.12 (1.10-1.14)***	1.09 (1.07-1.13)***	1.12 (1.09-1.14)***
Model 2	1.07 (1.05-1.09)***	1.05 (1.02-1.09)**	1.07 (1.04-1.09)***
Model 3	1.05 (1.03-1.07)***	1.04 (1.01-1.08)*	1.04 (1.02-1.07)***
Cerebrovascular disease			
Model 1	1.03 (0.99-1.07)	1.05 (0.98-1.12)	1.02 (0.98-1.07)
Model 2	1.01 (0.97-1.05)	1.01 (0.96-1.10)	0.99 (0.95-1.04)
Model 3	1.00 (0.96-1.04)	1.02 (0.96-1.10)	0.98 (0.94-1.03)
Ischemic heart disease			
Model 1	1.07 (1.05-1.09)***	1.03 (0.99-1.07)	1.08 (1.05-1.10)***
Model 2	1.02 (1.00-1.04)*	0.99 (0.95-1.02)	1.03 (1.00-1.05)*
Model 3	1.01 (0.99-1.03)	0.98 (0.95-1.02)	1.02 (0.99-1.04)

Model 1: unadjusted. Model 2: Model 1+ adjusted for age and sex. Model 3: Model 2+ further adjusted for ethnicity, education, smoking status, alcohol status, and overall health.

Significant of HRs: ***p<0.001; **p<0.01; *p<0.05.

[1]Separate multivariable analyses were performed by adding additional variables. Supplementary Table 8 showed the results obtained from Model 3 by including the intake of poultry, fish, fruit and vegetables as additional variables. The results showed that after adding the additional variables in Model 3, the associations obtained were similar to the results generated from Model 3 excluding these additional variables (shown in the above table). Supplementary Table 9 demonstrated that diabetes variable was added to Model 3 for the multivariable analysis (n= 327,142 participants available) to evaluate the association between red and processed meat consumption frequency and the outcomes. The associations were not altered compared with the results in Model 3 before diabetes variable was considered.

Table 3

HR (95%CI) of terciles of red and processed meat consumption for all participants, participants with and without obesity.

	All participants			Obese			Non-obese		
	Tercile 1 (n=187,711)	Tercile 2 (n=128,740)	Tercile 3 (n=111,619)	Tercile 1 (n=37,263)	Tercile 2 (n=31,609)	Tercile 3 (n=31,303)	Tercile 1 (n=150,448)	Tercile 2 (n=97,131)	Tercile 3 (n=80,316)
Cardiovascular death									
Model 1	Ref.	1.48 (1.32-1.66)***	1.89 (1.69-2.12)***	Ref.	1.74 (1.41-2.15)***	2.02 (1.64-2.48)***	Ref.	1.34 (1.16-1.53)***	1.76 (1.53-2.01)***
Model 2	Ref.	1.25 (1.11-1.40)***	1.42 (1.27-1.60)***	Ref.	1.47 (1.19-1.82)***	1.49 (1.21-1.84)***	Ref.	1.10 (0.96-1.26)	1.22 (1.06-1.40)***
Model 3	Ref.	1.22 (1.09-1.37)**	1.33 (1.19-1.49)***	Ref.	1.47 (1.19-1.82)***	1.46 (1.18-1.79)*	Ref.	1.09 (0.95-1.25)	1.20 (1.05-1.38)**
Cerebrovascular disease									
Model 1	Ref.	1.08 (0.88-1.33)	1.22 (0.99-1.50)	Ref.	1.06 (0.71-1.59)	1.29 (0.88-1.89)	Ref.	1.07 (0.84-1.36)	1.15 (0.90-1.48)
Model 2	Ref.	0.99 (0.81-1.22)	1.06 (0.86-1.31)	Ref.	0.99 (0.66-1.48)	1.12 (0.76-1.66)	Ref.	0.98 (0.77-1.25)	1.00 (0.78-1.29)
Model 3	Ref.	0.99 (0.80-1.22)	1.04 (0.84-1.29)	Ref.	0.98 (0.66-1.48)	1.12 (0.75-1.66)	Ref.	0.97 (0.76-1.24)	0.97 (0.75-1.26)
Ischemic heart disease									
Model 1	Ref.	1.36 (1.19-1.55)***	1.54 (1.35-1.76)***	Ref.	1.03 (0.84-1.26)	1.10 (0.90-1.35)	Ref.	1.36 (1.19-1.55)***	1.54 (1.35-1.76)***
Model 2	Ref.	1.16 (1.01-1.32)*	1.18 (1.03-1.35)*	Ref.	0.89 (0.73-1.10)	0.86 (0.70-1.05)	Ref.	1.16 (1.01-1.32)*	1.18 (1.03-1.35)*
Model 3	Ref.	1.09 (0.97-1.21)*	1.08 (0.96-1.21)	Ref.	0.89 (0.73-1.10)	0.85 (0.69-1.05)	Ref.	1.14 (1.00-1.30)*	1.15 (1.00-1.31)*

Model 1: unadjusted. Model 2: Model 1+ adjusted for age and sex. Model 3: Model 2+ further adjusted for ethnicity, education, smoking status, alcohol status, and overall health.

Significant of HRs: ***p<0.001; **p<0.01; *p<0.05.