THE LANCET Diabetes & Endocrinology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1·2 million participants. *Lancet Diabetes Endocrinol* 2015; published online May 8. http://dx.doi.org/10.1016/S2213-8587(15)00086-8.

The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants

SUPPLEMENTARY APPENDIX

Supplemental Methods S1. Full search criteria for Pubmed/Medline and EMBASE

Medline/Pubmed search:
((("Coronary Disease"[Mesh] OR "Coronary Artery Disease"[Mesh]) OR "Myocardial Ischemia"[Mesh] OR "coronary artery disease"[All Fields] OR "ischaemic heart disease"[All Fields] OR "coronary heart disease"[All Fields]) AND (("Overweight"[Mesh] OR ("Obesity"[Mesh] OR "Obesity, Morbid"[Mesh])) OR "Body Mass Index"[Mesh] OR "overweight"[All Fields] OR "obesity"[All Fields] OR "obese"[All Fields] OR "body mass index"[All Fields] OR "BMI"[All Fields] OR "over weight"[All Fields]) AND ("men"[MeSH Terms] OR "men"[All Fields] OR "male"[MeSH Terms] OR "male"[All Fields]) AND ("women"[MeSH Terms] OR "women"[All Fields] OR "female"[MeSH Terms] OR "female"[All Fields])) AND (("Cohort Studies"[Mesh] OR "Prospective Studies"[Mesh]) OR "Longitudinal Studies"[Mesh] OR "cohort"[All Fields] OR "prospective"[All Fields] OR "longitudinal"[All Fields])

EMBASE search:
((('Coronary Disease'/exp OR 'Coronary Artery Disease'/exp) OR 'Myocardial Ischemia'/exp OR 'coronary artery disease' OR 'ischemic heart disease' OR 'coronary heart disease') AND (('Overweight'/exp OR ('Obesity'/exp OR 'Obesity, Morbid'/exp)) OR 'Body Mass'/exp OR 'overweight' OR 'obesity' OR 'obese' OR 'body mass index' OR 'BMI' OR 'bmi' OR 'over weight') AND ('men'/exp OR 'men' OR 'male'/exp OR 'male') AND ('women'/exp OR 'women' OR 'female'/exp OR 'female')) AND (('cohort analysis'/exp OR 'cohort studies' OR 'cohort studies' OR 'prospective study'/exp) OR 'longitudinal study'/exp OR 'cohort' OR 'prospective' OR 'longitudinal')

Supplementary Method S2. Inclusion and exclusion criteria

Inclusion criteria
- Study population consists of women and men from the same source population - General population cohort - Body mass index (BMI) used as study exposure - Incident coronary heart disease used as study outcome - Estimates for the association between BMI and CHD provided separately for women and men - Estimates had be adjusted for age
Exclusion criteria
- Duplicate for the same study - Estimates reported only for z-scores or percentiles of BMI - No report of the variability around the relative risk estimate - Studies conducted in cohorts which recruited predominantly from individuals with a prior history of cardiovascular disease or from selected populations, such as those with kidney disease, diabetes, or hypertension - Articles where the full text was not available in English

Supplemental Methods S3. Reconciling body mass index categories

Studies reporting estimates for a per unit difference in BMI chose different units including one unit, five units, standard deviation, and sex-specific standard deviations. In order to compare the different estimates across the studies, all per unit estimates were transformed into estimates for a one unit difference in BMI(kg/m^2). Similarly, studies reporting estimates for categories of BMI chose different cut-points for their categories, including standard WHO categories (underweight: BMI<18.5kg/m^2, normal weight: 18.5≤BMI<25.0, overweight: 25.0≤BMI<30.0, obese: 30.0≤BMI), quartiles, quintiles, and sex-specific percentiles. To reconcile estimates based on different cut-points, all groupings based on percentiles were coded to the nearest WHO category. For example, a group that ranged from 24.5-29.8kg/m^2 was coded as "overweight" and grouped with the WHO category ranging from 25.0-30.0 kg/m^2. Estimates for groups that overlapped the WHO overweight and obesity categories were coded as obese. The group that contained the range most comparable to the WHO category for "normal weight", 18.5-25.0 kg/m^2, was coded as the reference group for our analyses. When percentile cut-points created multiple groups that fit roughly within a single WHO category, we combined the groups to form a single group for each WHO category. For example, one study included two "overweight" groups, 24.5-27.0kg/m^2 and 27.0-29.9kg/m^2. In most cases, percentile based cut-points were similar to the WHO categories.

Supplementary methods S4. Modified Newcastle-Ottawa Quality Assessment Scale
Modified from reference 20

Selection

S1) Representativeness of the exposed cohort
- a) truly representative of the general population*****
- b) somewhat representative of the general population
- c) selected group of users e.g. nurses, volunteers
- d) no description of the derivation of the cohort

S2) Selection of the non exposed cohort
- a) drawn from the same community as the exposed cohort *****
- b) drawn from a different source
- c) no description of the derivation of the non exposed cohort

S3) Ascertainment of exposure
- a) secure record (measured BMI only) *****
- b) secure record or written self report
- c) written self report
- d) no description

S4) Demonstration that outcome of interest was not present at start of study
- a) yes *****
- b) no

Comparability

C1) Comparability of cohorts on the basis of the design or analysis
- a) study controls for age*****
- b) study controls for additional cardiovascular risk factors including smoking*****

Outcome

O1) Assessment of outcome
- a) independent blind assessment or record linkage of fatal and non-fatal events*****
- b) independent blind assessment or record linkage of fatal events
- c) self report
- d) no description

O2) Was follow-up long enough for outcomes to occur
- a) yes (at least 10 years) *****
- b) no

O3) Adequacy of follow up of cohorts
- a) complete follow up - all subjects accounted for *****
- b) subjects lost to follow up unlikely to introduce bias - > 10% follow up, or description provided of those lost *****
- c) follow up rate < 90% and no description of those lost
- d) no statement

***Studies get a point for each**

Supplemental Methods S5. Articles excluded for not having sex-specific estimates

1. Bradshaw PJ, Alfonso HS, Finn JC, Owen J, Thompson PL. Coronary heart disease events in Aboriginal Australians: Incidence in an urban population. Medical Journal of Australia. 2009;190(10):583-6.

2. Braekkan SK, Hald EM, Mathiesen EB, Njolstad I, Wilsgaard T, Rosendaal FR, et al. Competing risk of atherosclerotic risk factors for arterial and venous thrombosis in a general population: the Tromso study. Arterioscler Thromb Vasc Biol. 2012;32(2):487-91.

3. Chien KL, Hsu HC, Sung FC, Su TC, Chen MF, Lee YT. Metabolic syndrome as a risk factor for coronary heart disease and stroke: An 11-year prospective cohort in Taiwan community. Atherosclerosis. 2007;194(1):214-21.

4. Haapanen-Niemi N, Miilunpalo S, Pasanen M, Vuori I, Oja P, Malmberg J. Body mass index, physical inactivity and low level of physical fitness as determinants of all-cause and cardiovascular disease mortality - 16 y follow-up of middle-aged and elderly men and women. International Journal of Obesity. 2000;24(11):1465-74.

5. Hamer M, Batty GD, Stamatakis E, Kivimaki M. Comparison of risk factors for fatal stroke and ischemic heart disease: A prospective follow up of the health survey for England. Atherosclerosis. 2011;219(2):807-10.

6. Hopkins PN, Williams RR, Kuida H, Stults BM, Hunt SC, Barlow GK, et al. Family history as an independent risk factor for incident coronary artery disease in a high-risk cohort in Utah. American Journal of Cardiology. 1988;62(10 PART I):703-7.

7. Huerta JM, Tormo MJ, Gavrila D, Navarro C. Cardiovascular risk estimated after 13 years of follow-up in a low-incidence Mediterranean region with high-prevalence of cardiovascular risk factors. BMC public health. 2010;10:640.

8. Kizer JR, Biggs ML, Ix JH, Mukamal KJ, Zieman SJ, de Boer IH, et al. Measures of adiposity and future risk of ischemic stroke and coronary heart disease in older men and women. Am J Epidemiol. 2011;173(1):10-25.

9. Mann JI, Appleby PN, Key TJ, Thorogood M. Dietary determinants of ischaemic heart disease in health conscious individuals. Heart. 1997;78(5):450-5.

10. Merry AHH, Erkens PMG, Boer JMA, Schouten LJ, Feskens EJM, Verschuren WMM, et al. Co-occurrence of metabolic factors and the risk of coronary heart disease: A prospective cohort study in the Netherlands. International Journal of Cardiology. 2012;155(2):223-9.

11. Mora S, Yanek LR, Moy TF, Fallin MD, Becker LC, Becker DM. Interaction of body mass index and framingham risk score in predicting incident coronary disease in families. Circulation. 2005;111(15):1871-6.

12. Morkedal B, Romundstad PR, Vatten LJ. Mortality from ischaemic heart disease: Age-specific effects of blood pressure stratified by body-mass index: The HUNT cohort study in Norway. Journal of Epidemiology and Community Health. 2011;65(9):814-9.

13. Shimozato M, Nakayama T, Yokoyama T, Yoshi-ike N, Yamaguchi M, Date C. A 15.5-year cohort study on risk factors for possible myocardial infarction and sudden death within 24 hours in a rural Japanese community. Journal of epidemiology / Japan Epidemiological Association. 1996;6(1):15-22.

14. Tsai SP, Donnelly RP, Wendt JK. Obesity and mortality in a prospective study of a middle-aged industrial population. Journal of Occupational and Environmental Medicine. 2006;48(1):22-7.

15. Woo J, Ho SC, Yuen YK, Yu LM, Lau J. Cardiovascular risk factors and 18-month mortality and morbidity in an elderly Chinese population aged 70 years and over. Gerontology. 1998;44(1):51-5.

16. Xu J, Lee ET, Peterson LE, Devereux RB, Rhoades ER, Umans JG, et al. Differences in risk factors for coronary heart disease among diabetic and nondiabetic individuals from a population with high rates of diabetes: the Strong Heart Study. The Journal of clinical endocrinology and metabolism. 2012;97(10):3766-74.

17. Yan LL, Daviglus ML, Liu K, Stamler J, Wang R, Pirzada A, et al. Midlife body mass index and hospitalization and mortality in older age. Journal of the American Medical Association. 2006;295(2):190-8.

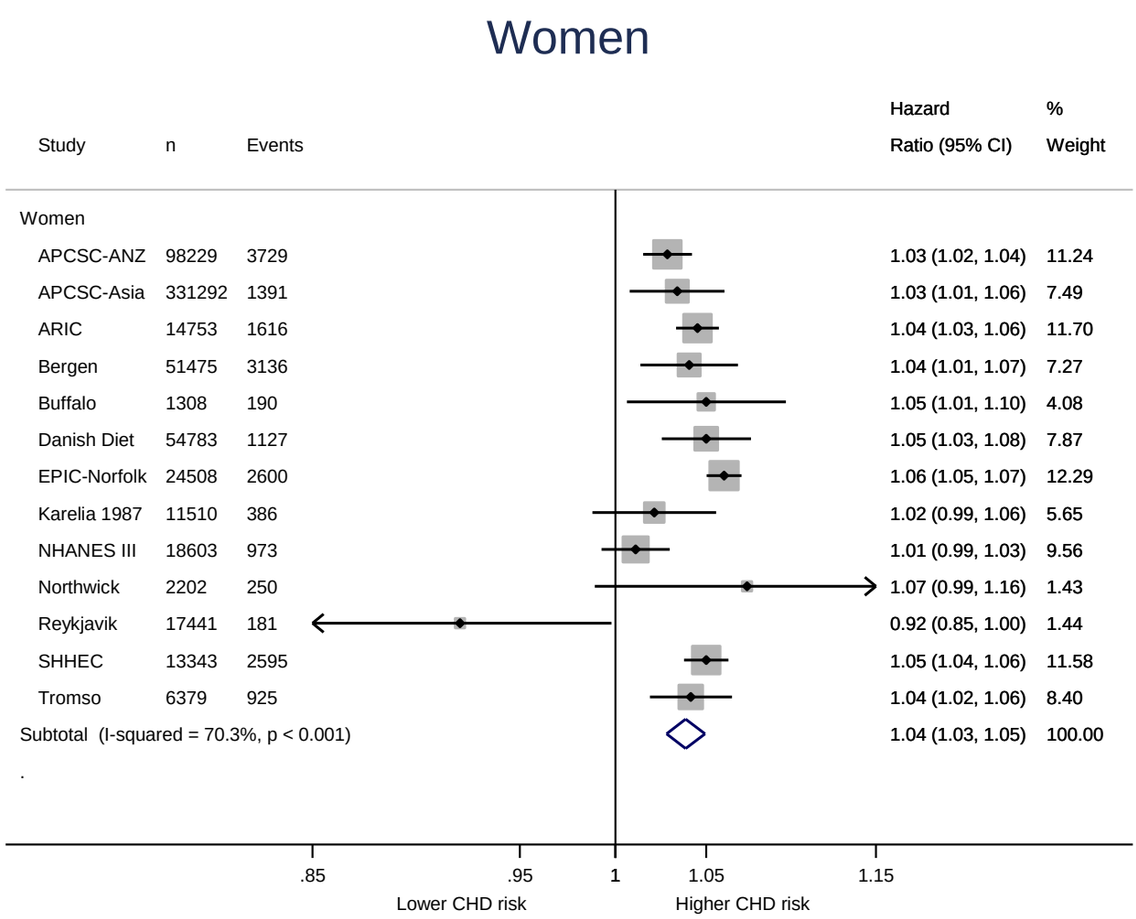
18. Zhou B, Wu Y, Yang J, Li Y, Zhang H, Zhao L. Overweight is an independent risk factor for cardiovascular disease in Chinese populations. Obesity Reviews. 2002;3(3):147-56.

Supplemental Methods S6. PRISMA Checklist

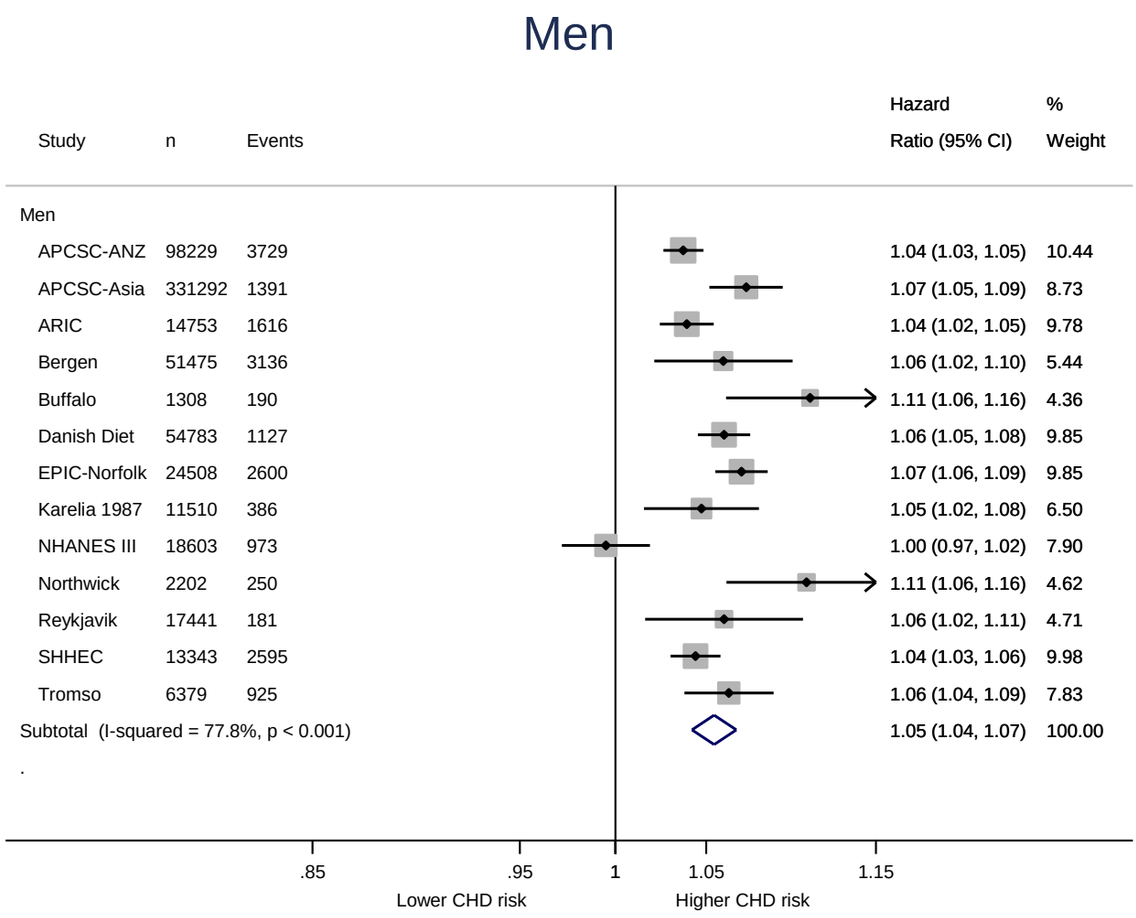
Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4, Methods S2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4, 7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Methods S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4-7, Figure 1
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7, Methods S3
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this	6, Methods

		was done at the study or outcome level), and how this information is to be used in any data synthesis.	S4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5-6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Supplemental Figure S1. Age-adjusted coronary heart disease hazard ratios and 95% confidence intervals for a one unit (kg/m^2) increase in body mass index

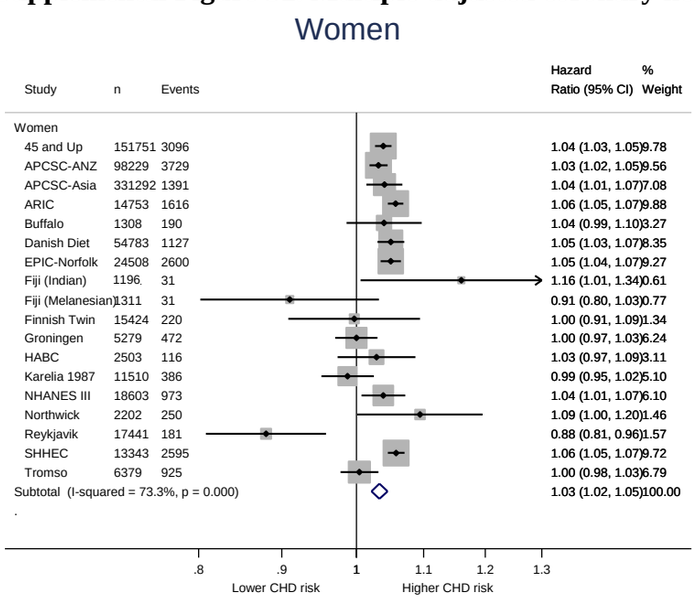


P-value for pooled results: p<0.001

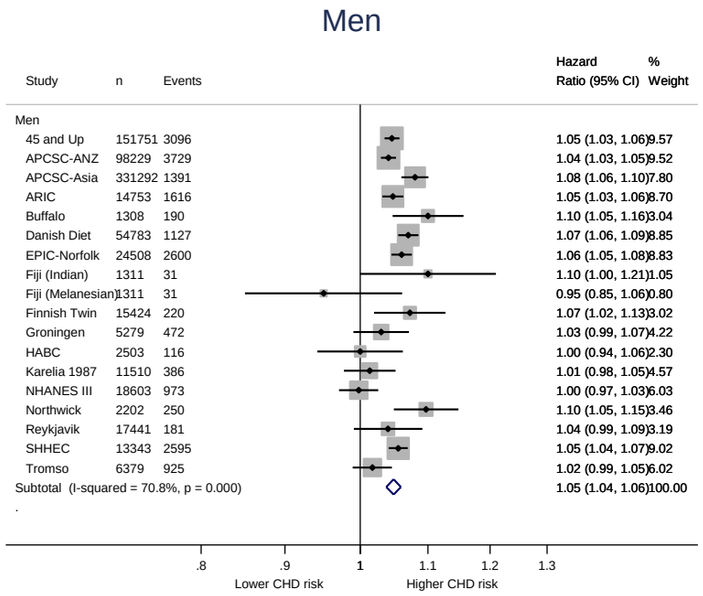


P-value for pooled results: p<0.001

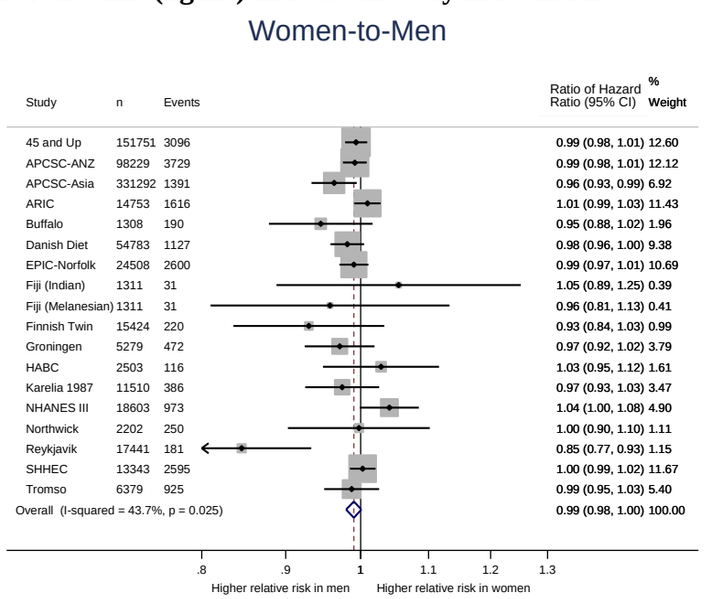
Supplemental Figure S2. Multiple-adjusted coronary heart disease hazard ratios and 95% confidence intervals for a one unit (kg/m^2) increase in body mass index



P-value for pooled results: p<0.001



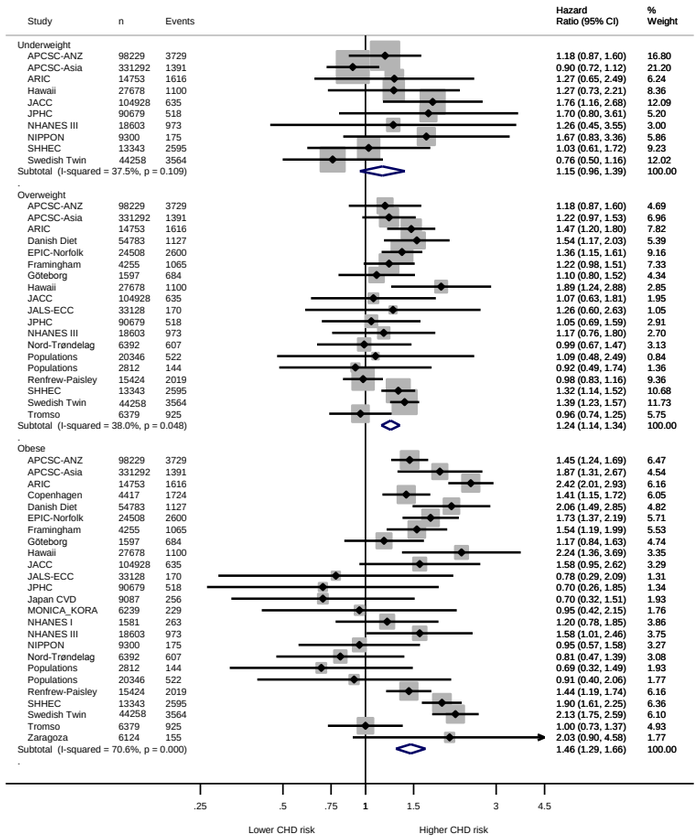
P-value for pooled results: p<0.001



P-value for pooled results: p = 0.077

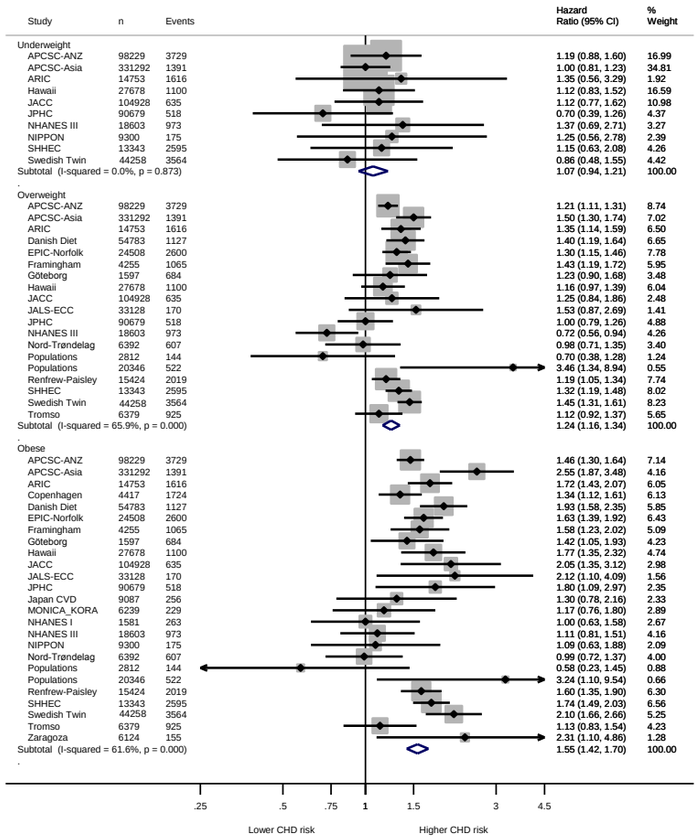
Supplemental Figure S3. Multiple-adjusted coronary heart disease hazard ratios and 95% confidence intervals for body mass index categories relative to normal weight

Women



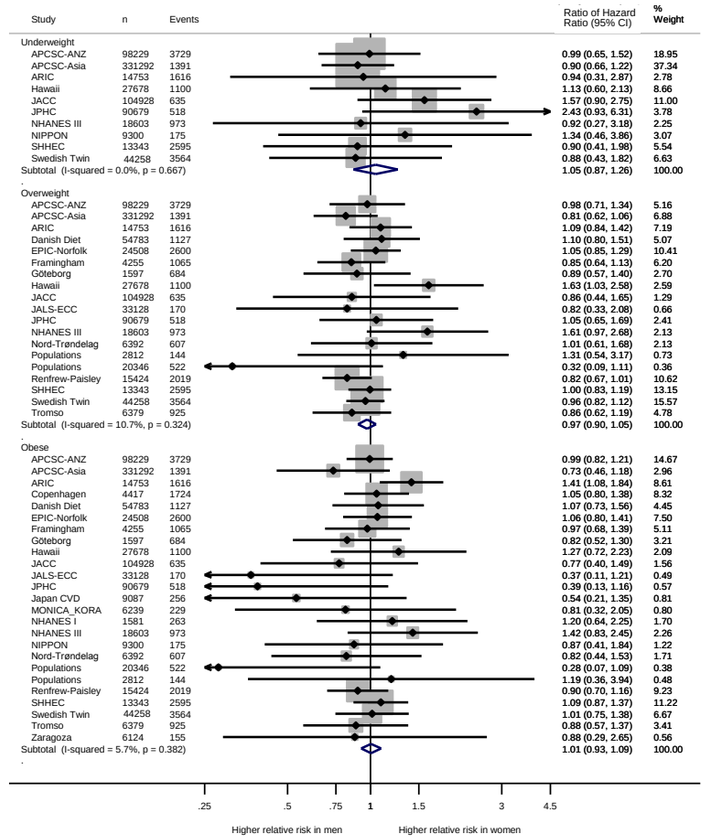
P-value for pooled results:
Underweight p = 0.14
Overweight p<0.001
Obese p<0.001

Men



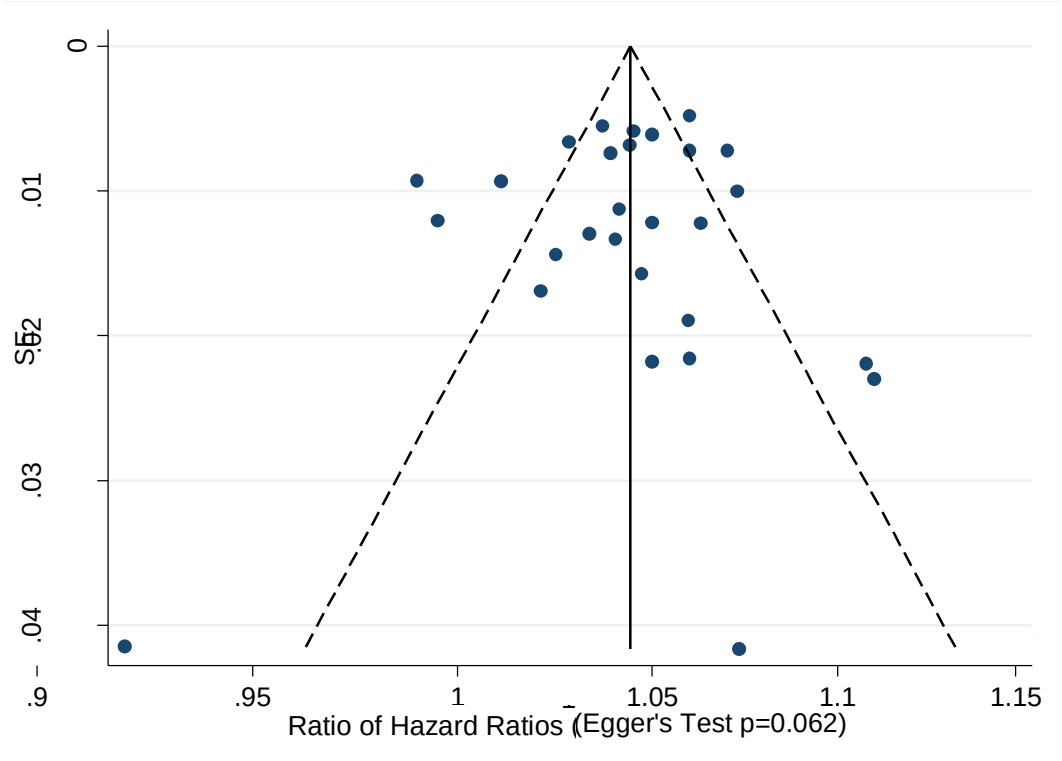
P-value for pooled results:
Underweight p = 0.30
Overweight p<0.001
Obese p<0.001

Women-to-Men

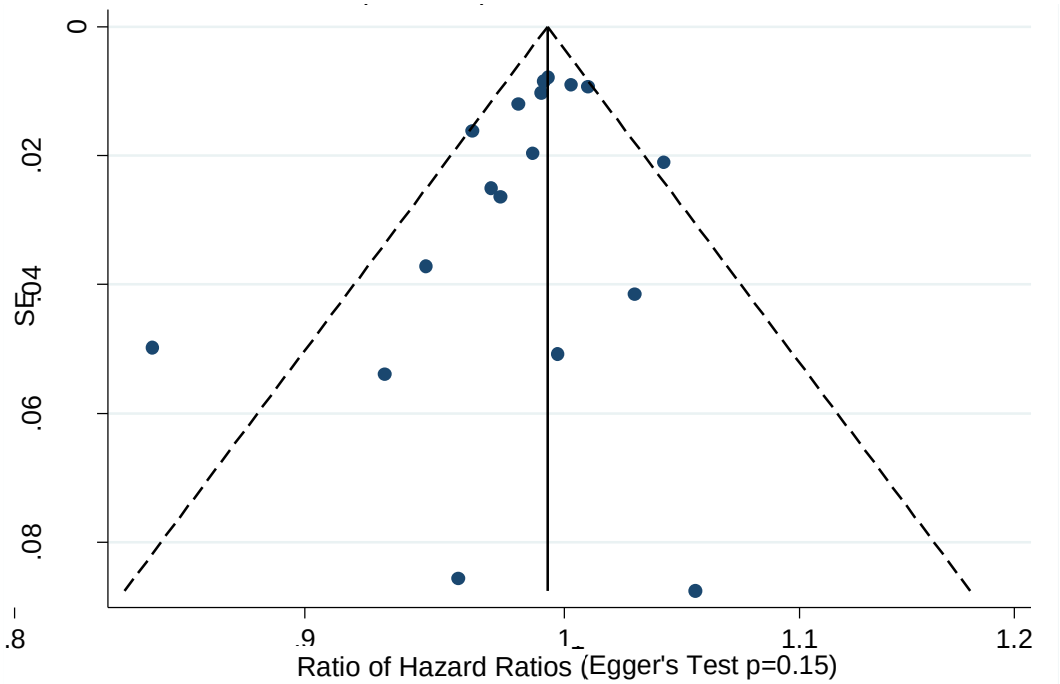


P-value for pooled results:
Underweight p = 0.64
Overweight p = 0.45
Obese p = 0.90

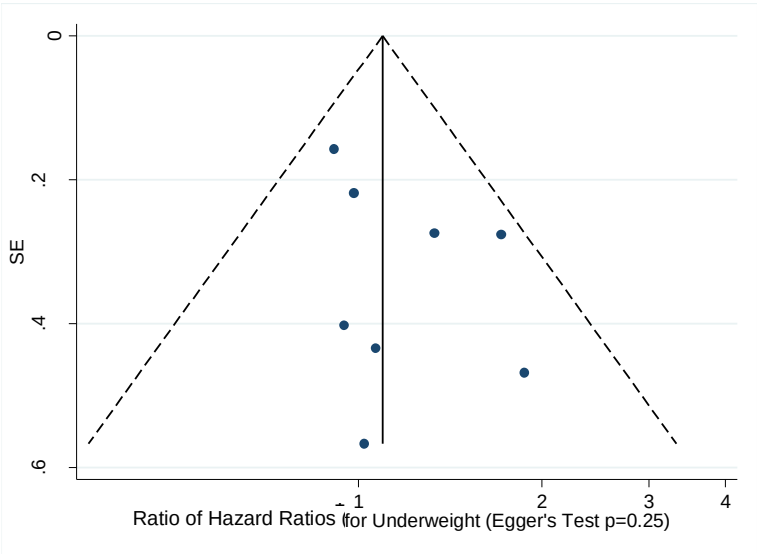
Supplemental Figure S4. Funnel plot with pseudo 95% confidence limits for age-adjusted coronary heart disease ratio of relative risks and 95% confidence intervals for a one unit (kg/m^2) increase in body mass index

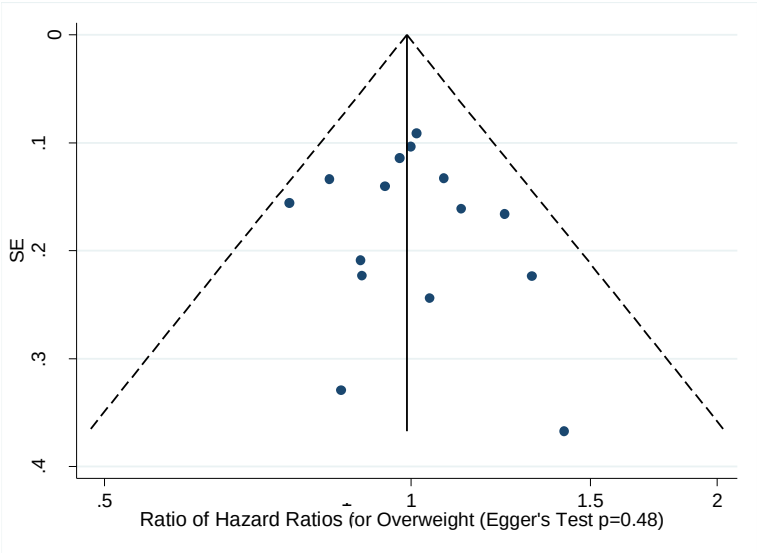


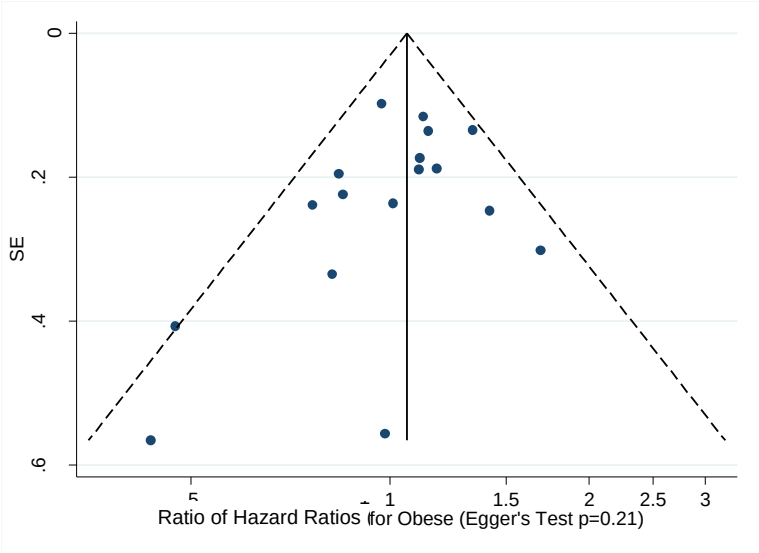
Supplemental Figure S5. Funnel plot with pseudo 95% confidence limits for multiple-adjusted coronary heart disease ratio of relative risks and 95% confidence intervals for a one unit (kg/m^2) increase in body mass index



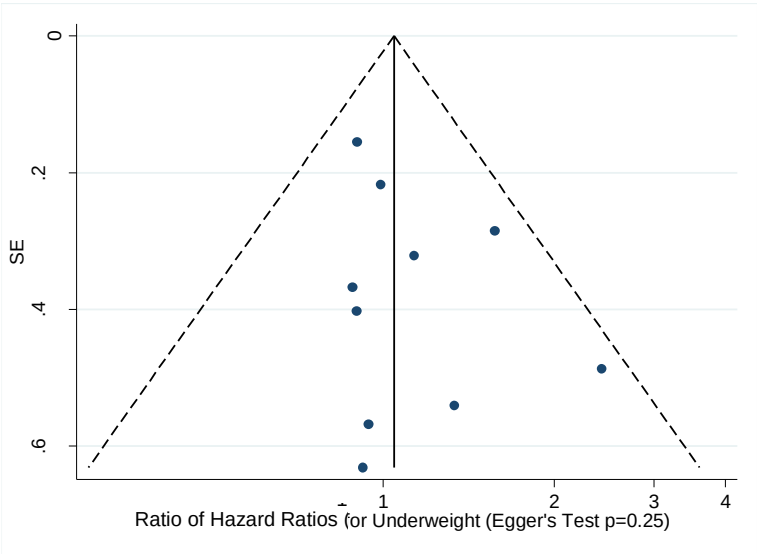
Supplemental Figure S6. Funnel plot with pseudo 95% confidence limits for age-adjusted coronary heart disease ratio of relative risks and 95% confidence intervals for body mass index categories relative to normal weight

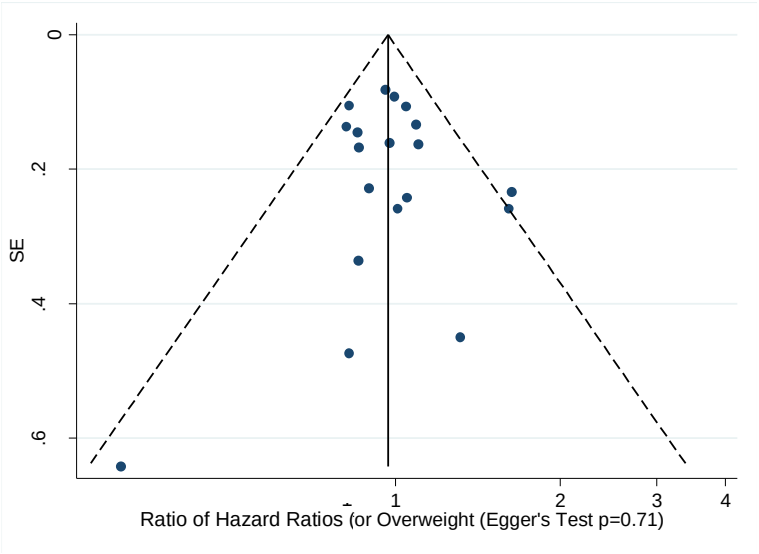


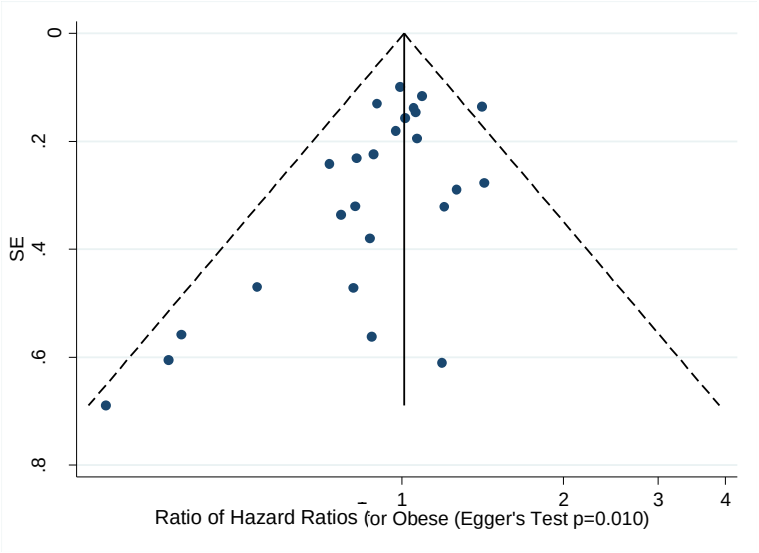




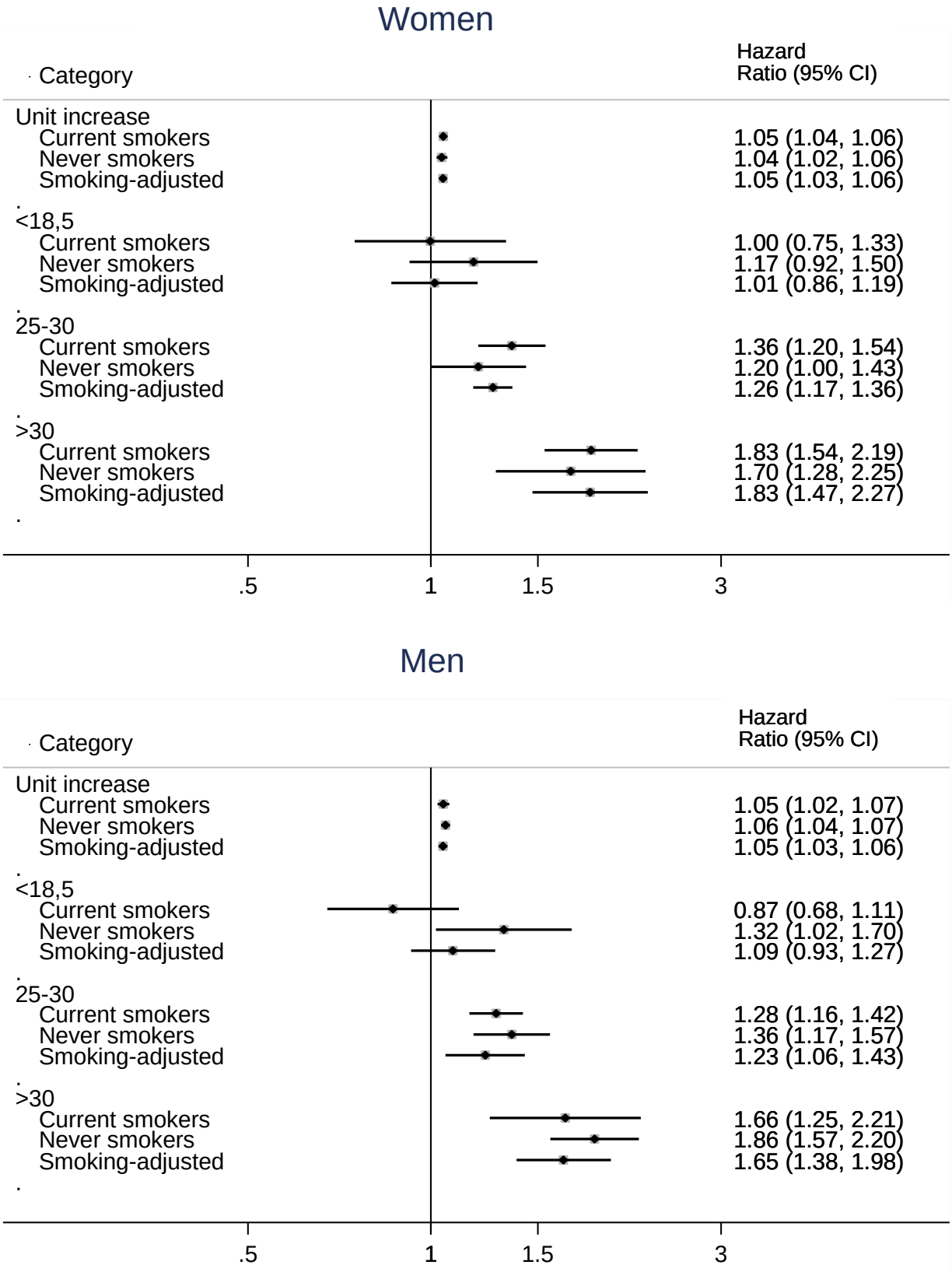
Supplemental Figure S7. Funnel plot with pseudo 95% confidence limits for multiple-adjusted coronary heart disease ratio of relative risks and 95% confidence intervals for body mass index categories relative to normal weight



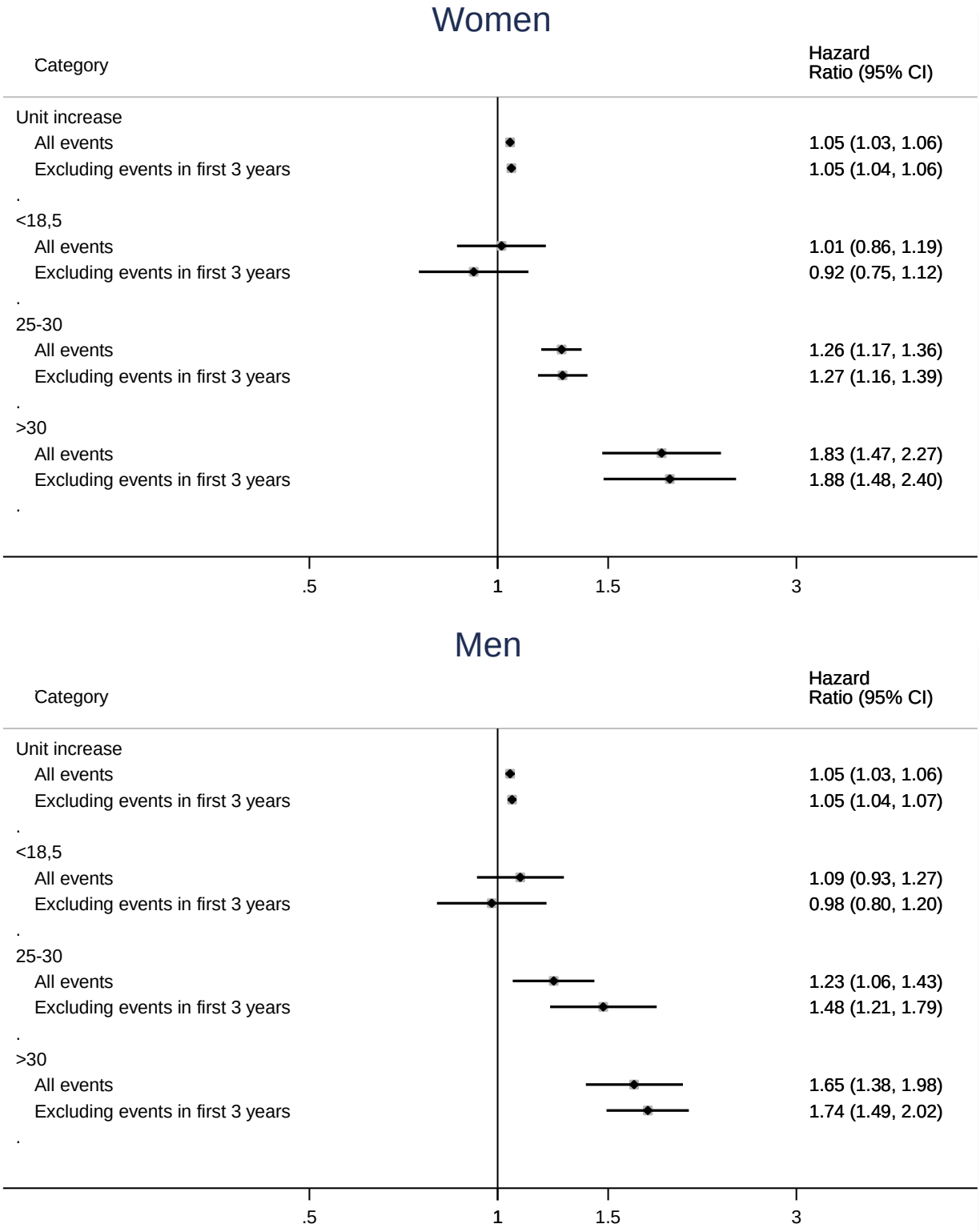




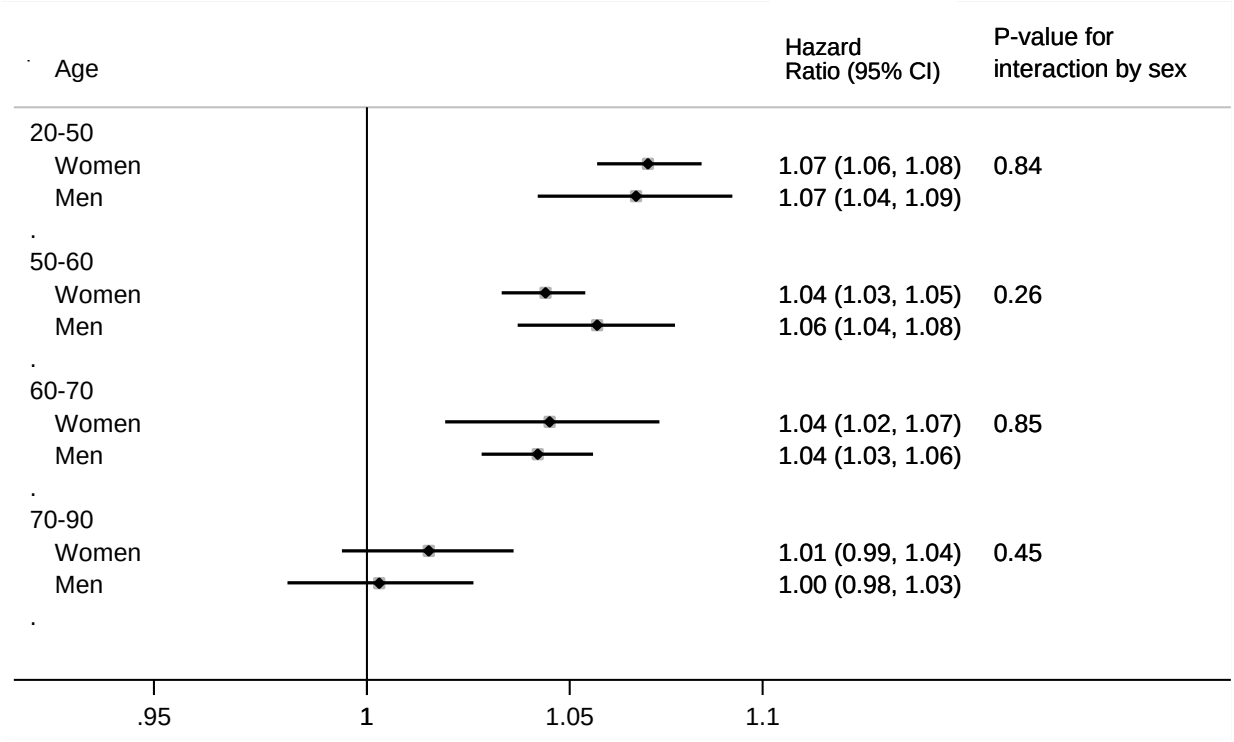
Supplemental Figure S8. Individual participant data sensitivity analysis by smoking adjustment for age-adjusted coronary heart disease hazard ratios and 95% confidence intervals for body mass index categories relative to normal weight in women and men



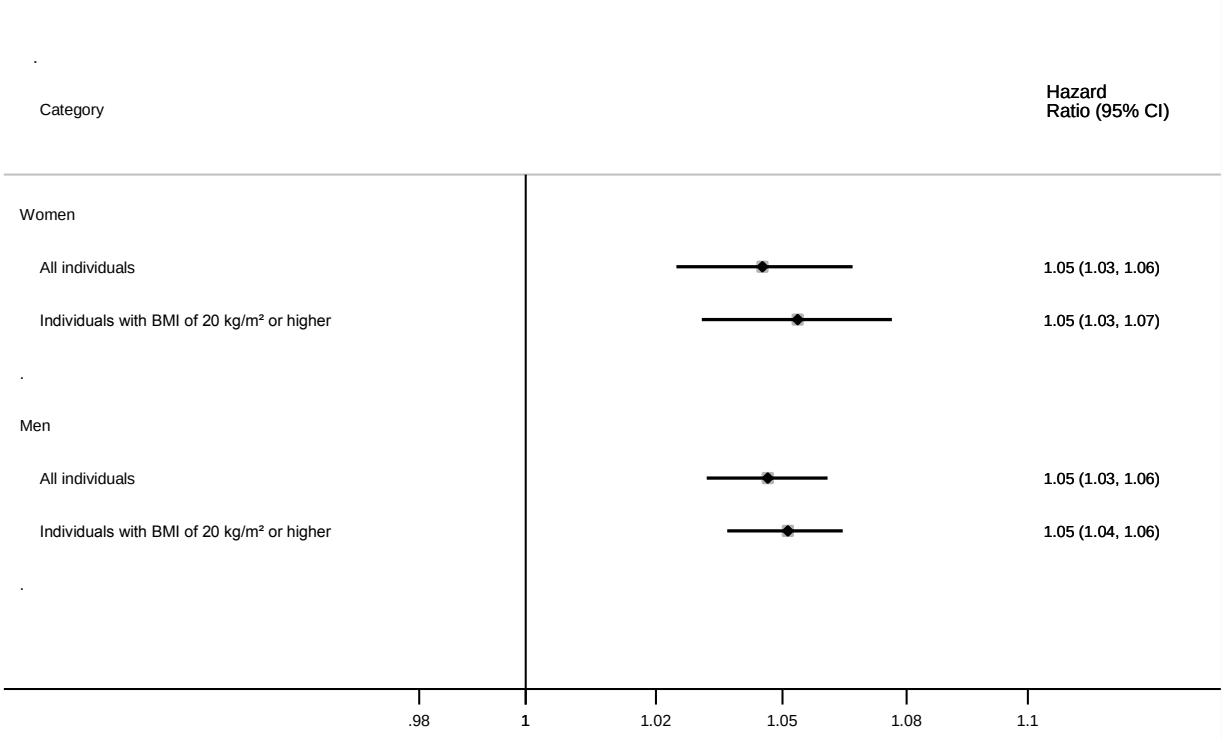
Supplemental Figure S9. Individual participant data sensitivity analysis for reverse causality for age- and smoking-adjusted coronary heart disease hazard ratios and 95% confidence intervals for body mass index categories relative to normal weight in women and men



Supplemental Figure S10. Individual participant data sensitivity analysis by age category for coronary heart disease hazard ratios and 95% confidence intervals for a one unit (kg/m^2) increase in body mass index



Supplemental Figure S11. Individual participant data sensitivity analysis for underestimate of continuous association due to non-linearity for age- and smoking-adjusted coronary heart disease hazard ratios and 95% confidence intervals for a one unit (kg/m^2) increase in body mass index



Supplemental Table S1. Abbreviations for included studies

Abbreviation	Study
Adventist	The Adventist Health Study
APCSC-ANZ	Asia Pacific Cohort Studies Collaboration-Australia and New Zealand
APCSC-Asia	Asia Pacific Cohort Studies Collaboration-Asia
ARIC	Atherosclerosis Risk in Communities study
Bergen	Bergen study
Buffalo	Buffalo Health Study
Consultation	Consultation Bureau Project on Cardiovascular Diseases
Copenhagen	The Copenhagen City Heart Study
Danish Diet	Danish Diet, Cancer and Health study
EPIC-Norfolk	European Prospective Investigation into Cancer-Norfolk
Fiji (Indian)	Risk Factors in Indian and Melanesian Fijians (Indian)
Fiji (Melanesian)	Risk Factors in Indian and Melanesian Fijians (Melanesian)
Finnish Twin	Finnish Twin Cohort
Framingham	Framingham Heart Study
Göteborg	Göteborg (3 cohorts)
Groningen	Groningen Longitudinal Aging Study
HABC	The Health, Aging and Body Composition Study
Hawaii	Hawaii Multiethnic Prospective Cohort
JACC	Japan Collaborative Cohort Study
JALS-ECC	Japan Arteriosclerosis Longitudinal Study-Existing Cohorts Combine
Japan CVD	Japanese Cardiovascular Risk Surveys
JPHC	Japan Public Health Center–based prospective study
Karelia 1987	North Karelia, Kuopio, and Turku-Loimaa provinces Finland 1987
MONICA-Kora	MONICA_KORA Augsburg
NHANES I	National Health and Nutrition Examination Survey I
NHANES III	National Health and Nutrition Examination Survey III
Nippon	Nippon data 80 study
Nord-Trøndelag	Nord-Trøndelag Health Study
Northwick	Northwick Park heart study
Populations	Populations for Epidemiologic Studies of the Elderly
Post Office	General Post Office study
Renfrew-Paisley	Renfrew-Paisley study
Reykjavik	Reykjavik study
SHHEC	Scottish Heart Health Extended Cohort study
Swedish Twin	Swedish Twin Registry
Tromsø	Tromsø Study, Fourth Survey
Zaragoza	Province of Zaragoza
45 and Up	The Sax Institute's 45 and Up Study

Supplemental Table S2. I^2 and Cochran's Q test to assess heterogeneity in the association between body mass index and coronary heart disease

Model for BMI	**I^2** (%)	**Cochran's Q test** (p-value)
Age-adjusted one unit	74.3	<0.001
Multiple-adjusted one unit	72.2	<0.001
Age-adjusted underweight	27.6	0.014
Age-adjusted overweight	53.7	0.012
Age-adjusted obese	68.9	0.035
Multiple-adjusted underweight	0.0	<0.001
Multiple-adjusted overweight	54.8	0.012
Multiple-adjusted obese	66.1	0.037

Supplemental Table S3. Sensitivity analysis for coronary heart disease hazard ratios (HR) and 95% confidence intervals (CI) for a one unit (kg/m^2) increase in body mass index

Model (#cohorts/#events)	Women HR	Women CI	Men HR	Men CI	Women-to- Men RHR	Women-to- Men CI	p-value for ratio
Age-adjusted							
Age-adjusted (55/19,099)	**1.04**	**1.03-1.05**	**1.05**	**1.04-1.07**	0.992	0.980-1.003	0.059
By Region							
Asia (35/1,391)	1.03	1.01-1.06	1.07	1.05-1.09	0.964	0.933-0.995	0.024
Other (20/17,708)	1.04	1.03-1.05	1.05	1.04-1.07	0.992	0.981-1.003	0.15
Outcome							
Fatal Only (4/4,549)	1.03	1.01-1.06	1.07	1.01-1.13	0.987	0.955-1.020	0.45
All Incidence (51/14,550)	1.04	1.03-1.05	1.05	1.0341.06	0.989	0.977-1.001	0.076
Data Source							
Individual Participant Data (47/10,304)	1.04	1.02-1.05	1.04	1.02-1.06	0.998	0.985-1.012	0.79
Abstracted (8/8,795	1.04	1.03-1.06	1.07	1.06-1.08	0.979	0.963-0.995	0.011
Multiple-Adjusted							
Multiple-adjusted (60/19,929)	**1.03**	**1.02-1.05**	**1.05**	**1.04-1.06**	0.990	0.980-1.001	0.077
By Region							
Asia (37/1,453)	1.03	0.93-1.14	1.05	0.98-1.13	0.966	0.937-0.996	0.027
Other (23/18,476)	1.03	1.02-1.05	1.05	1.04-1.06	0.992	0.981-1.003	0.17
Outcome							
Fatal Only (6/1,695)	1.04	1.00-1.08	1.06	1.01-1.11	0.991	0.945-1.040	0.72
All Incidence (54/18,234)	1.03	1.02-1.05	1.05	1.04-1.06	0.989	0.979-1.000	0.072
BMI Measurement							
Self Report (2/3,668)	1.02	0.99-1.06	1.05	1.03-1.06	0.991	0.977-1.006	0.26
Measured (58/16,261)	1.04	1.23-1.05	1.05	1.04-1.06	0.990	0.977-1.003	0.13
Data Source							
Individual Participant Data (47/10,304)	1.05	1.04-1.06	1.05	1.03-1.06	1.000	0.983-1.017	0.97
Abstracted (13/9,625)	1.02	1.00-1.04	1.05	1.04-1.06	0.983	0.970-0.996	0.014

Bold values for pooled estimate indicates estimate significantly different from 1.0 at the $p<0.05$ level.
Bold values for subgroup estimate indicates estimate significantly different from pooled estimate at the $p<0.05$ level.
All age-adjusted estimates were from measured BMI.

Supplemental Table S4. Sensitivity analysis for age-adjusted coronary heart disease hazard ratios (HR) and 95% confidence intervals (CI) for body mass index categories

		Women		Men		Women-to- Men		P for ratio between women
Model (#cohorts/#events)		**HR**	**CI**	**HR**	**CI**	**RHR**	**CI**	**and men**
Age-adjusted								
(59/19,836)	*Underweight*	**1.25**	**1.05-1.49**	1.09	0.91-1.23	1.10	0.91-1.32	0.42
	Normal (REF)	1.0		1.0				
	Overweight	**1.20**	**1.12-1.29**	**1.22**	**1.12-1.32**	0.99	0.92-1.07	0.91
	Obese	**1.61**	**1.42-1.82**	**1.60**	**1.43-1.79**	1.06	0.95-1.17	0.37
By region								
Asia	*Underweight*	1.13	0.83-1.50	1.01	0.85-1.21	1.08	0.77-1.52	0.67
(38/2,805)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.23	1.03-1.47	1.32	1.14-1.52	0.91	0.74-1.13	0.40
	Obese	1.41	1.03-1.95	2.18	1.79-2.64	**0.67**	**0.49-0.92**	**0.013**
Other	*Underweight*	1.26	1.05-1.50	1.14	0.86-1.52	1.15	0.87-1.52	0.33
(21/17,031)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.20	1.11-1.31	1.20	1.09-1.32	1.01	0.93-1.90	0.84
	Obese	1.63	1.43-1.86	1.50	1.33-1.69	**1.10**	**1.00-1.20**	**0.045**
Outcome								
Fatal Only	*Underweight*	1.29	1.03-1.62	1.02	0.68-1.53	1.39	0.97-2.00	0.072
(6/3,330)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.13	0.88-1.44	1.04	0.80-1.33	1.16	0.95-1.41	0.14
	Obese	1.48	1.11-1.97	1.39	0.99-1.94	1.16	0.94-1.42	0.18
All Incidence	*Underweight*	1.12	0.92-1.35	1.08	0.92-1.26	0.98	0.78-1.23	0.87
(53/16,506)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.23	1.16-1.31	1.30	1.24-1.37	0.97	0.89-1.05	0.45
	Obese	1.67	1.48-1.90	1.68	1.54-1.83	1.02	0.90-1.15	0.78
Reference Group								
Includes Underweight (5/6,199)	*Underweight and Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.23	1.08-1.40	1.25	1.10-1.42	1.00	0.91-1.09	0.85
	Obese	1.40	1.05-1.86	1.54	1.23-1.94	0.97	0.81-1.16	0.75
Does Not Include Underweight	*Underweight*	1.16	1.01-1.32	1.06	0.91-1.23	1.08	0.89-1.31	0.47
(54/13,637)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.20	1.10-1.31	1.20	1.07-1.35	1.00	0.91-1.10	0.97
	Obese	1.68	1.49-1.91	1.62	1.41-1.86	1.09	0.96-1.25	0.20
Overweight and Obesity								
Combined	*Underweight*	1.25	0.98-1.59	0.89	0.57-1.39	1.48	0.99-2.20	0.055
(4/1,418)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight and Obese	1.46	1.06-1.97	1.65	1.20-2.28	0.84	0.45-1.56	0.58
Separate	*Underweight*	1.17	0.96-1.42	1.10	0.95-1.28	0.99	0.79-1.23	0.90
(55/18,418)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.20	1.12-1.30	1.21	1.11-1.33	0.99	0.92-1.07	0.85
	Obese	1.62	1.42-1.86	1.59	1.40-1.80	1.07	0.97-1.17	0.19
BMI Measurement								
Self-Report	*Underweight*	1.27	1.01-1.59	0.88	0.66-1.16	1.53	1.06-2.21	0.022

(3/1,680)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.31	0.97-1.76	1.18	0.97-1.43	1.09	0.76-1.56	0.65
	Obese	1.60	1.28-1.99	1.74	1.19-2.54	0.87	0.47-1.63	0.67
Measured	*Underweight*	1.16	0.94-1.44	1.13	0.97-1.33	0.95	0.76-1.19	0.65
(56/18,156)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.20	1.11-1.30	1.22	1.10-1.34	0.99	0.92-1.07	0.83
	Obese	1.61	1.40-1.84	1.58	1.40-1.78	1.06	0.96-1.17	0.27
BMI Cutpoints								
Sex-Specific	*Underweight*	1.20	0.90-1.60	0.70	0.44-1.11	1.71	1.00-2.95	0.051
(4/4,413)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.26	1.10-1.44	1.15	0.88-1.50	1.03	0.86-1.21	0.78
	Obese	1.40	0.99-1.99	1.28	0.90-1.81	1.10	0.91-1.32	0.34
Not Sex-Specific	*Underweight*	1.18	0.99-1.40	1.10	0.96-1.27	1.01	0.83-1.24	0.90
(55/15,423)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.20	1.10-1.31	1.23	1.12-1.35	0.99	0.91-1.08	0.79
	Obese	1.66	1.46-1.88	1.69	1.50-1.90	1.03	0.90-1.18	0.66
Data Source								
Individual Participant Data	*Underweight*	1.16	0.94-1.44	1.13	0.97-1.33	0.95	0.76-1.19	0.65
(47/10,301)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.18	1.06-1.30	1.16	0.97-1.38	1.00	0.90-1.12	0.95
	Obese	1.64	1.36-1.97	1.53	1.29-1.81	1.08	0.93-1.26	0.30
Abstracted	*Underweight*	1.27	1.01-1.59	0.88	0.66-1.16	1.53	1.06-2.21	0.022
(12/9,532)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.24	1.12-1.38	1.25	1.14-1.37	0.99	0.89-1.10	0.81
	Obese	1.56	1.31-1.86	1.64	1.40-1.92	1.01	0.87-1.19	0.86

Bold values for pooled estimate indicates estimate significantly different from 1.0 at the $p<0.05$ level.
Bold values for subgroup estimate indicates that subgroups are significantly different at the $p<0.05$ level.
Results were available for 50 cohorts in the underweight category and all 59 in the overweight and obese categories.

Supplemental Table S5. Sensitivity analysis for multiple-adjusted coronary heart disease hazard ratios (HR) and 95% confidence intervals (CI) for body mass index categories

Model (#cohorts/#events)		Women HR	Women CI	Men HR	Men CI	Women-to-Men RHR	Women-to-Men CI	P for diff
Multiple-adjusted								
(81/28,269)	Underweight	1.15	0.96-1.39	1.07	0.94-1.21	1.05	0.87-1.26	0.64
	Normal (REF)	1.0		1.0		1.0		
	Overweight	**1.24**	**1.14-1.34**	**1.24**	**1.16-1.34**	0.97	0.90-1.05	0.45
	Obese	**1.46**	**1.29-1.66**	**1.55**	**1.42-1.70**	1.01	0.93-1.09	0.90
By region								
Asia	*Underweight*	1.20	0.86-1.67	1.02	0.88-1.19	1.12	0.79-1.59	0.51
(47/3,150	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.23	1.04-1.48	1.26	0.99-1.61	0.91	0.74-1.13	0.41
	Obese	1.09	0.76-1.57	1.81	1.38-2.36	**0.64**	**0.48-0.86**	**0.003**
Other	*Underweight*	1.07	0.88-1.30	1.14	0.96-1.37	0.98	0.74-1.30	0.90
(34/25,119)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.27	1.16-1.40	1.23	1.14-1.33	0.99	0.91-1.07	0.81
	Obese	1.54	1.35-1.76	1.50	1.37-1.65	**1.05**	**0.96-1.13**	**0.29**
Outcome								
Fatal Only (8/9,222)	*Underweight*	1.14	0.85-1.51	1.11	0.93-1.33	1.09	0.79-1.50	0.61
	Normal (REF)	1.0		1.0		1.0		
	Overweight	1.24	1.02-1.50	1.08	0.90-1.29	1.10	0.90-1.35	0.37
	Obese	1.37	1.06-1.79	1.44	1.15-1.80	0.97	0.82-1.13	0.66
All Incidence (43/19,047)	*Underweight*	1.04	0.88-1.24	1.04	0.89-1.22	0.98	0.78-1.23	0.85
	Normal (REF)	1.0		1.0		1.0		
	Overweight	1.27	1.18-1.37	1.30	1.22-1.38	0.97	0.89-1.06	0.50
	Obese	1.50	1.29-1.74	1.58	1.41-1.74	1.01	0.91-1.13	0.81
Reference Group								
Includes Underweight	*Underweight and Normal (REF)*	1.0		1.0		1.0		
(21/10,903)	*Overweight*	1.14	0.98-1.32	1.22	1.12-1.34	0.94	0.84-1.06	0.40
	Obese	**1.28**	**1.08-1.51**	1.40	1.22-1.60	0.96	0.85-1.08	0.47
Does Not Include Underweight	*Underweight*	1.07	0.93-1.24	1.07	0.95-1.21	1.01	0.84-1.22	0.89
(60/17,366)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.34	1.25-1.43	1.24	1.12-1.37	1.02	0.91-1.14	0.79
	Obese	**1.70**	**1.45-2.00**	1.69	1.50-1.91	1.03	0.90-1.19	0.66
Overweight and Obesity								
Combined (6/1,489)	*Underweight*	1.39	0.96-2.01	1.13	0.88-1.46	1.18	0.75-1.88	0.47
	Normal (REF)	1.0		1.0		1.0		
	Overweight and Obese	1.14	0.88-1.47	1.44	1.03-2.00	0.81	0.58-1.13	0.22
Separate (75/26,780)	*Underweight*	1.01	0.88-1.17	1.06	0.93-1.21	0.98	0.81-1.20	0.87
	Normal (REF)	1.0		1.0		1.0		
	Overweight	1.24	1.14-1.35	1.24	1.15-1.33	0.98	0.91-1.05	0.50
	Obese	1.53	1.34-1.75	1.56	1.42-1.72	1.02	0.94-1.11	0.63

BMI Measurement								
Self-Report	*Underweight*	1.13	0.81-1.59	1.05	0.88-1.25	1.19	0.85-1.65	0.31
(5/5,966)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.38	1.15-1.65	1.15	0.94-1.41	1.13	0.91-1.41	0.28
	Obese	1.40	0.90-2.18	1.81	1.44-2.29	0.90	0.65-1.26	0.55
Measured	*Underweight*	1.04	0.89-1.22	1.09	0.94-1.28	0.94	0.76-1.18	0.60
(76/22,303)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.22	1.11-1.33	1.25	1.16-1.35	0.96	0.89-1.04	0.29
	Obese	1.46	1.28-1.66	1.50	1.36-1.65	1.02	0.94-1.11	0.68
BMI Cutpoints								
Sex-Specific	*Underweight*	1.27	0.73-2.21	1.12	0.83-1.52	1.13	0.60-2.13	0.70
(5/5,254)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.29	1.03-1.61	1.22	1.11-1.35	1.09	0.89-1.35	0.41
	Obese	1.37	1.02-1.85	1.38	1.11-1.72	1.02	0.83-1.24	0.86
Not Sex-Specific	*Underweight*	1.07	0.91-1.35	1.06	0.94-1.21	1.00	0.83-1.22	0.89
(76/23,015)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.24	1.13-1.35	1.24	1.14-1.35	0.96	0.89-1.03	0.27
	Obese	1.49	1.29-1.72	1.59	1.44-1.77	1.00	0.90-1.11	0.95
Data Source								
Individual Participant Data	*Underweight*	1.01	0.86-1.19	1.09	0.93-1.27	0.93	0.74-1.16	0.52
(47/10,301)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.31	1.19-1.44	1.22	1.05-1.43	1.01	0.86-1.17	0.93
	Obese	1.83	1.48-2.27	1.64	1.37-1.98	1.10	0.93-1.33	0.31
Abstracted	*Underweight*	1.20	0.88-1.62	1.05	0.88-1.26	1.20	0.88-1.64	0.26
(34/17,968)	*Normal (REF)*	1.0		1.0		1.0		
	Overweight	1.23	1.09-1.37	1.24	1.15-1.34	0.97	0.89-1.05	0.45
	Obese	1.34	1.16-1.56	1.51	1.35-1.68	0.95	0.86-1.06	0.35

Bold values for pooled estimate indicates estimate significantly different from 1.0 at the $p<0.05$ level.
Bold values for subgroup estimate indicates that subgroups are significantly different at the $p<0.05$ level.
Results were available for 53 cohorts in the underweight category, 75 in the overweight category, and 81 in the obese category.

Supplemental Table 6. Meta-regression for one unit body mass index and coronary heart disease: Difference in hazard ratios and 95% confidence intervals (CI) for a one unit difference in study characteristics

	Women		Men		Women-to-Men		
Study Characteristic	**Difference**	**CI**	**Difference**	**CI**	**Difference**	**CI**	**P-value**
Age-adjusted*							
Start year (year)	1.0001	0.9991-1.0012	0.9992	0.9977-1.0008	1.0006	0.9993-1.0019	0.35
Follow-up (years)	1.0007	0.9989-1.0026	1.0017	0.9992-1.0041	1.0000	0.9974-1.0025	0.99
Sample size (n)	1.0	0.9999-1.0	1.0	0.9999-1.0	0.9999	0.9999-1.0	0.15
Events (#)	1.0000	0.9999-1.0000	0.9999	0.9999-1.0000	1.0000	0.9999-1.0000	0.57
Percent Women (%)	1.0000	0.9991-1.0010	1.0002	0.9987-1.0017	1.1306	0.9985-1.0009	0.63
Quality Score	1.003	0.98201.-23	0.989	0.960-1.019	1.007	0.981-1.035	0.56
Multiple-adjusted**							
Start year (year)	0.9997	0.9982-1.0012	0.9991	0.9981-1.0002	1.0004	0.9994-1.0014	0.44
Follow-up (years)	1.0012	0.9985-1.0038	1.0013	0.9994-1.0033	1.0008	0.9993-1.0024	0.26
Sample size (n)	1.0	0.9999-1.0	1.0	0.9999-1.0	0.9999	0.9999-1.0	0.20
Events (#)	1.0000	0.9999-1.0000	1.0000	0.9999-1.0000	1.0000	0.9999-1.0000	0.36
Percent Women (%)	0.9997	0.9990-1.0004	0.9997	0.9989-1.0004	1.0000	0.9993-1.0007	0.99
Quality Score	1.003	0.987-1.020	0.999	0.985-1.014	1.003	0.992-1.015	0.55

*All age-adjusted models contain 14 observations, except Percent Women which contains 13 estimates.
** All multiple-adjusted models contain 18 observations, except Percent Women which contains 16 observations.
Bold values indicates estimate significantly different from 0.0 at the $p<0.05$ level.

Supplemental Table 7. Meta-regression for body mass index categories and coronary heart disease: Difference in hazard ratios and 95% confidence intervals (CI) for a one unit difference in study characteristics

		Women		Men		Women-to-Men		
Study Characteristic	**BMI Category**	**Difference**	**CI**	**Difference**	**CI**	**Difference**	**CI**	**P-Value**
Age-adjusted*								
Start year (year)	*Underweight vs. Normal*	1.015	1.000-1.031	1.001	0.984-1.019	1.013	0.991-1.035	0.19
	Overweight vs. Normal	1.001	0.995-1.007	0.997	0.989-1.005	1.003	0.997-1.009	0.31
	Obese vs. Normal	0.999	0.987-1.012	0.999	0.987-1.011	1.002	0.993-1.010	0.63
Follow-up (years)	*Underweight vs. Normal*	1.030	0.993-1.067	1.011	0.971-1.054	1.017	0.966-1.071	0.46
	Overweight vs. Normal	1.000	0.992-1.007	1.000	0.990-1.010	0.998	0.990-1.006	0.67
	Obese vs. Normal	1.007	0.992-1.021	0.998	0.983-1.013	1.006	0.995-1.017	0.28
Sample size (n)	*Underweight vs. Normal*	1.000	0.999-1.0	1.000	0.999-1.000	0.999	0.999-1.000	0.19
	Overweight vs. Normal	1.0	0.999-1.000	1.000	0.999-1.000	0.999	0.999-1.0	0.26
	Obese vs. Normal	1.0	0.999-1.0	1.000	1.0-1.000	0.999	0.999-1.0	0.096
Events (#)	*Underweight vs. Normal*	0.999	0.999-1.000	1.000	0.999-1.000	0.999	0.999-1.000	0.26
	Overweight vs. Normal	1.000	0.999-1.000	1.000	0.999-1.000	0.999	0.999-1.000	0.90
	Obese vs. Normal	1.000	0.999-1.000	0.999	0.999-1.000	0.999	0.999-1.000	0.86
Percent Women (%)	*Underweight vs. Normal*	3.326	0.617-17.926	0.523	0.499-5.481	0.993	0.980-0.999	0.075
	Overweight vs. Normal	0.997	0.991-1.003	1.003	0.994-1.011	0.994	0.988-1.001	0.097
	Obese vs. Normal	0.998	0.987-1.010	1.002	0.990-1.015	0.995	0.986-1.004	0.30
Quality Score (#)	*Underweight vs. Normal*	1.011	0.808-1.265	1.197	0.941-1.523	0.801	0.591-1.084	0.12
	Overweight vs. Normal	1.020	0.889-1.171	1.046	0.896-1.221	0.954	0.830-1.096	0.48
	Obese vs. Normal	1.048	0.958-1.146	0.983	0.902-1.071	1.057	0.964-1.159	0.22
Multiple-adjusted**								
Start year (year)	*Underweight vs. Normal*	1.014	0.999-1.029	1.002	0.988-1.014	1.011	0.991-1.032	0.23
	Overweight vs. Normal	1.001	0.994-1.008	0.995	0.988-1.002	1.006	1.000-1.012	0.059
	Obese vs. Normal	0.997	0.984-1.001	0.996	0.987-1.006	1.004	0.996-1.011	0.31
Follow-up (years)	*Underweight vs. Normal*	0.996	0.972-1.020	1.002	0.983-1.022	1.003	0.976-1.031	0.81
	Overweight vs. Normal	1.002	0.993-1.011	1.006	0.996-1.015	0.997	0.990-1.005	0.44
	Obese vs. Normal	1.007	0.992-1.023	1.006	0.993-1.018	1.000	0.992-1.001	0.86
Sample size (n)	*Underweight vs. Normal*	0.999	0.999-1.0	0.999	0.999-1.000	0.999	0.999-1.000	0.36
	Overweight vs. Normal	1.0	0.999-1.000	1.000	0.999-1.000	0.999	0.999-1.000	0.31
	Obese vs. Normal	1.000	0.999-1.000	**1.000**	**1.0-1.000**	0.999	0.999-1.0	0.16
Events (#)	*Underweight vs. Normal*	0.999	0.999-1.000	1.000	0.999-1.000	0.999	0.999-1.000	0.44
	Overweight vs. Normal	1.000	0.999-1.000	1.000	0.999-1.000	0.999	0.999-1.000	0.69
	Obese vs. Normal	**1.000**	**1.000-1.000**	1.000	0.999-1.000	1.000	0.999-1.000	0.36
Percent Women (%)	*Underweight vs. Normal*	11.018	0.824-147.408	1.782	0.217-14.510	5.319	0.172-164,051	0.29
	Overweight vs. Normal	0.995	0.988-1.002	0.998	0.991-1.006	0.997	0.989-1.004	0.44

	Obese vs. Normal	0.993	0.980-1.006	0.994	0.983-1.004	0.998	0.988-1.008	0.62
Quality Score (#)	*Underweight vs. Normal*	0.988	0.924-1.056	0.983	0.936-1.033	1.000	0.931-1.073	0.99
	Overweight vs. Normal	0.954	0.846-1.076	1.050	0.923-1.195	0.947	0.845-1.-62	0.33
	Obese vs. Normal	1.080	0.973-1.197	1.007	0.930-1.089	1.077	0.989-1.173	0.085

*All age-adjusted models contain 16 observations.

** For multiple-adjusted models, the models for study start year and number of events contain 24 estimates, the models for length of follow-up and total sample size contain 23 estimates, and the model for percent women contains 22 estimates.

Bold values in the table indicate estimate significantly different from 0.0 at the $p<0.05$ level.

Supplementary Table S8: Quality assessment of the included studies

	S1	**S2**	**S3**	**S4**	**C1**	**O1**	**O2**	**O3**		Sum
Adventist Health	1	1	0	1	1	0	1	1		6
Asia Pacific Cohort Studies Collaboration-ANZ	1	1	1	1	2	1	0	1		8
Asia Pacific Cohort Studies Collaboration-Asia	1	1	1	1	2	1	0	1		8
Atherosclerosis Risk in Communities	1	1	1	1	2	1	1	1		9
Bergen	1	1	1	1	1	0	1	1		7
Buffalo Health	1	1	1	1	2	0	1	1		8
Consultation Bureau Project	1	1	1	1	1	0	1	1		7
Copenhagen City Heart	1	1	1	1	2	1	1	1		9
Danish Diet, Cancer, and Health	1	1	1	1	2	1	0	1		8
European Prospective Investigation into Cancer Norfolk	1	1	1	1	2	1	0	1		8
Fiji (Indian)	1	1	1	1	2	0	1	1		8
Fiji (Melanesian)	1	1	1	1	2	0	1	1		8
Finnish Twin	1	1	1	1	2	0	1	1		8
Framingham Heart	1	1	1	1	2	1	1	1		9
Göteborg	1	1	1	1	2	1	1	1		9
Groningen Longitudinal Aging15	1	1	0	0	2	1	0	0		5
Hawaii Multiethnic Prospective Cohort16	1	1	0	1	2	0	1	1		7
Health, Aging and Body Composition	1	1	1	1	2	1	0	0		7
Japanese Cardiovascular Risk Surveys	1	1	1	1	2	1	1	1		9
Japan Collaborative Cohort	1	1	0	1	2	0	1	1		7
Japan Arteriosclerosis Longitudinal	1	1	1	1	2	1	0	1		8
Japan Public Health Center	1	1	0	1	2	1	1	1		8
Karelia, Kuopio, and Turku-Loimaa provinces 1987	1	1	1	1	2	1	1	1		9
MONICA-KORA	1	1	1	1	2	1	0	1		8
National Health and Nutrition Examination I	1	1	1	1	2	1	0	1		8
National Health and Nutrition Examination III	1	1	1	1	2	0	1	1		8
Nippon Data 80	1	1	1	0	2	0	1	1		7
Nord-Trøndelag Health	1	1	1	1	2	0	1	1		8
Northwick Park Heart	1	1	1	1	2	0	1	0		7
Populations for Epidemiologic Studies for the Elderly	1	1	0	1	2	0	0	1		6
General Post Office	1	1	1	1	1	0	1	1		7
Renfrew-Paisley	1	1	1	1	2	0	1	1		8
Reykjavik	1	1	1	0	2	1	1	1		8
SHHEC	1	1	1	1	2	1	1	1		9
Swedish Twin	1	1	0	1	2	0	1	1		7
Trømso	1	1	1	1	2	1	1	1		9
Zaragoza	1	1	1	1	1	1	0	1		7
45 and Up Study	1	1	0	1	2	0	0	1		6