THE LANCET

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: The Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects). Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1·8 million participants. *Lancet* 2013; published online Nov 22. http://dx.doi.org/10.1016/S0140-6736(13)61836-X.

Webmaterials

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Webappendix 1. Cohort identification and selection

We identified cohorts through a systematic literature search of the Medline (PubMed) and Embase databases, through the National Heart, Lung, and Blood Institute (NHLBI) in the United States; and through personal communication with researchers.

Medline search

We searched Medline (via PubMed) for articles published up to 23 March 2010, with no restrictions on publication language. PubMed was searched based on a combination of three themes, using both exploded version of Medical Subject Heading (MeSH) terms and text word. The first theme included various measures of adiposity, such as body mass index, waist circumference, waist-to-hip ratio, overweight and obesity. The second theme consisted of different cardiovascular outcomes of interest, in particular CHD and stroke. And the third theme was used to restrict articles to prospective studies.

The query appeared as ("overweight "[Mesh] OR "obesity"[tiab] OR "obese"[tiab] OR "overweight"[tiab] OR "Body Mass Index"[Mesh] OR "body mass index"[tiab] OR "BMI"[tiab] OR "Waist-Hip Ratio"[Mesh] OR "Waist-Hip Ratio"[tiab] OR "Waist-to-hip ratio"[tiab] OR "Waist Circumference"[Mesh] OR "Waist Circumference"[tiab] OR "adiposity"[Mesh] OR "adiposity"[tiab]) AND (("Coronary Disease"[Mesh] OR "Coronary Heart Disease"[tiab] OR "Coronary Disease"[tiab] OR "Coronary Aneurysm"[tiab] OR "Coronary Artery Disease"[tiab] OR "Arteriosclerosis"[tiab] OR "atherosclerotic"[tiab] OR "Coronary Occlusions"[tiab] OR "Coronary Occlusion"[tiab] OR "stenosis"[tiab] OR "coronary thrombosis"[tiab] OR "coronary Thromboses"[tiab] OR "Coronary Artery Vasospasm"[tiab] OR "Coronary Artery Vasospasms"[tiab] OR "Coronary Vasospasm"[tiab] OR "Coronary Vasospasms"[tiab] OR "atherosclerotic"[tiab]) OR ("Stroke"[Mesh] OR

("Cerebrovascular Disorders"[Mesh] AND 1964:1999[pdat]) OR ("Intracranial Arteriosclerosis"[Mesh] AND 1965:1999[pdat]) OR ("Intracranial Embolism and Thrombosis"[Mesh] AND 1965:1999[pdat]) OR "stroke"[tiab] OR "strokes"[tiab] OR "Cerebrovascular Accident"[tiab] OR "Cerebrovascular Accidents"[tiab] OR "vascular accident"[tiab] OR "vascular accidents"[tiab] OR "Apoplexy"[tiab]) OR ("Death, Sudden, Cardiac"[Mesh] OR "Cardiac Sudden Death"[tiab] OR "Sudden Cardiac Death"[tiab] OR "Sudden Cardiac Arrest"[tiab]) OR ("Congestive Heart Failure"[All Fields])) AND ("Cohort Studies"[Mesh] OR "cohort"[tiab] OR "longitudinal study"[tiab] OR "longitudinal studies"[tiab] OR "prospective study"[tiab] OR "prospective studies"[tiab] OR "Nested Case-Control Studies"[tiab] OR "Nested Case-Control Study"[tiab] OR "Incidence Studies"[tiab] OR "Incidence Study"[tiab] OR "Concurrent Studies"[tiab] OR "Concurrent Study"[tiab] OR "Follow Up"[tiab] OR random*)

Embase search

Embase was searched based on a similar strategy using Embase TREE tool (EMTREE) and text word.

The query was ('obesity'/exp OR 'body mass'/exp OR 'waist hip ratio'/exp OR 'waist circumference'/exp OR 'obesity':ab,ti OR 'obese':ab,ti OR 'overweight':ab,ti OR 'body mass index':ab,ti OR 'bmi':ab,ti OR 'waist-hip ratio':ab,ti OR 'waist-to-hip ratio':ab,ti OR 'waist circumference':ab,ti OR 'adiposity':ab,ti) AND (('coronary artery disease'/exp OR 'ischemic heart disease'/exp OR 'coronary disease':ab,ti OR 'coronary artery disease':ab,ti OR 'ischaemic heart disease':ab,ti OR 'ischemia heart disease':ab,ti OR 'ischemic cardiac disease':ab,ti OR 'ischemic cardial disease':ab,ti OR 'coronary artery occlusive disease':ab,ti OR 'coronary heart disease':ab,ti OR 'coronary occlusive disease':ab,ti) OR ('stroke'/exp OR

'brain hemorrhage'/exp OR 'brain ischemia'/exp OR 'cerebrovascular accident'/exp OR "stroke':ab,ti OR 'strokes':ab,ti OR 'ischaemic stroke':ab,ti OR 'ischemic stroke':ab,ti OR 'haemorrhagic stroke':ab,ti OR 'hemorrhagic stroke':ab,ti OR 'Cerebrovascular Accident':ab,ti OR 'Cerebrovascular Accidents':ab,ti OR 'vascular accident':ab,ti OR 'vascular accidents':ab,ti OR 'Apoplexy':ab,ti) OR ('sudden death'/exp OR 'Cardiac Sudden Death':ab,ti OR 'Sudden Cardiac Death':ab,ti OR 'Sudden Cardiac Arrest':ab,ti) OR ('congestive heart failure'/exp OR 'cardiac congestive failure':ab,ti OR 'congestive cardiac failure':ab,ti OR 'heart failure':ab,ti)) AND ('cohort analysis'/exp OR 'follow up'/exp OR 'intervention study'/exp OR 'longitudinal study'/exp OR 'prospective study'/exp OR 'cohort':ab,ti OR 'longitudinal study':ab,ti OR 'longitudinal studies':ab,ti OR 'prospective study':ab,ti OR 'prospective studies':ab,ti OR 'Nested Case-Control Studies':ab,ti OR 'Nested Case-Control Study':ab,ti OR 'Incidence Studies':ab,ti OR 'Incidence Study':ab,ti OR 'Concurrent Studies':ab,ti OR 'Concurrent Study':ab,ti OR 'Follow Up':ab,ti OR random*)

Published articles were evaluated by two reviewers (YL, KH) first at the title and abstract stage, followed by a full text screening. The number of articles identified and retained is summarised in Webfigure 1. Cohort studies were considered eligible if they met the following criteria: (1) prospective design with at least 1 year of follow-up; (2) participants were not selected based on prior history of CHD or stroke; (3) height and weight were measured (not self-reported) at baseline; (4) at least one of the mediators (blood pressure, serum cholesterol, and blood glucose or diabetes) was also measured at baseline; (5) fatal and/or non-fatal CHD or stroke were ascertained during follow-up.

Webappendix 2. Estimating the uncertainty of percentage excess risk mediated (PERM)

As described in the Methods, we estimated the uncertainty of PERM by randomly drawing 5000 pairs of $HR_{(confounder\ adjusted)}$ and $HR_{(confounder\ and\ mediator\ adjusted)}$ from their corresponding uncertainty distributions while accounting for their correlations. To estimate the correlations between $HR_{(confounder\ adjusted)}$ and $HR_{(confounder\ and\ mediator\ adjusted),}$ we applied the bootstrap method. We first randomly drew a bootstrap sample of size N with replacement from a selected cohort of the size N, and then fitted Cox proportional hazard models to obtain bootstrap estimate of $HR_{(confounder\ adjusted)}$ and $HR_{(confounder\ and\ mediator\ adjusted)}$ on log scale. The process was repeated 5000 times. The correlations were calculated using the 5000 bootstrap estimates of $HR_{(confounder\ adjusted)}$ and $HR_{(confounder\ and\ mediator\ adjusted)}$.

The estimated correlations $HR_{(confounder\ adjusted)}$ and $HR_{(confounder\ and\ mediator\ adjusted)}$ on log scale from 7 selected cohorts are summarised in Webtable 1. We used 0.95 as the conservative estimate of this correlation and incorporate it in estimating the uncertainty of percentage excess risks.

Webtable 1: Correlation between $HR_{(confounder\ adjusted)}$ and $HR_{(confounder\ and\ mediator\ adjusted)}$ on log scale from 7 cohorts

Cohort	Model 1 vs. Model 2	Model 1 vs. Model 3	Model 1 vs. Model 4	Model 1 vs. Model 5	Model 1 vs. Model 6	Model 1 vs. Model 7	Model 1 vs. Model 8
Coronary heart disease							
The Cardiovascular Health Study (CHS)	0.984	0.995	0.974	0.981	0.961	0.970	0.959
Honolulu Heart Program (HHP)	0.962	0.981	0.981	0.944	0.950	0.966	0.935
Multi-Ethnic Study of Atherosclerosis (MESA)	0.989	0.996	0.990	0.985	0.981	0.986	0.978
Multiple Risk Factor Intervention Trial (MRFIT)	0.997	0.995	0.982	0.992	0.979	0.976	0.973
Puerto Rico Heart Health Program (PRHHP)	0.968	0.986	0.992	0.957	0.960	0.980	0.950
Framingham Offspring Study	0.943	0.985	0.950	0.936	0.906	0.951	0.916
Framingham Heart Study-Cohort	0.937	0.986	0.987	0.930	0.928	0.971	0.920
Stroke							
The Cardiovascular Health Study (CHS)	0.988	0.997	0.976	0.985	0.964	0.975	0.963
Honolulu Heart Program (HHP)	0.966	0.992	0.989	0.956	0.956	0.983	0.950
Multi-Ethnic Study of Atherosclerosis (MESA)	0.984	0.997	0.988	0.978	0.969	0.981	0.959
Multiple Risk Factor Intervention Trial (MRFIT)	0.996	1.000	0.951	0.995	0.947	0.950	0.946
Puerto Rico Heart Health Program (PRHHP)	0.962	0.994	0.992	0.954	0.960	0.987	0.953
Framingham Offspring Study	0.956	0.998	0.972	0.955	0.931	0.974	0.933
Framingham Heart Study-Cohort	0.935	0.998	0.998	0.931	0.935	0.995	0.931

Model 1: adjusted for confounder only
Model 2: adjusted for confounder and blood pressure
Model 3: adjusted for confounder and cholesterol
Model 4: adjusted for confounder and blood glucose
Model 5: adjusted for confounder and blood pressure and cholesterol
Model 6: adjusted for confounder and blood pressure and blood glucose
Model 7: adjusted for confounder and cholesterol and blood glucose
Model 8: adjusted for confounder and blood pressure, cholesterol and blood glucose

Webtable 2: Characteristics of cohorts included in the pooled analysis

Cohort name	Country	Baseline study date	Mean duration or end year of follow-up	No. of participants	Proportion of female(%)	Age range at baseline	Number of event (n) [1]	Event adjudication	Source of event [4]	Confounders adjusted [2]	Mediators adjusted [3]
Abdominal Aortic Aneurysm Screening Program	Australia	1996-1998	3.2	8212	0	65-84	IHD (327), stroke (126)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, diabetes
Age 40-programme linked with National Cause of Death Register	Norway	1985-1999	End of 2009	389571	52	39-45	IHD (1781) , stroke (572)	Not adjudicated	Death registries	Age, sex, smoking status	All combinations of SBP, TC, diabetes
Aito Town Study	Japan	1980	16.4	835	58	21-73	IHD (6), stroke (10)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, diabetes
Akabane Study	Japan	1985	11.2	1417	57	40-69	IHD (54), stroke (27)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
Anzhen 02 Cohort Study	China	1992	3	3694	50	34-65	Stroke (13)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
Atherosclerosis Risk in Communities Study (ARIC)	United States	1987-1989	17	10981	56	45-64	CHD (1134)	Adjudicated	Medical records, death certificates, autopsy reports	Age, sex, smoking status, race, alcohol intake, physical activity, SES, diet, family history of CHD, baseline menopausal status, baseline hormone therapy use, pack years cigarettes [6]	All combinations of SBP, TC, FPG
Australia Longitudinal Study of Ageing (ALSA)	Australia	1992	5.7	870	50	65-98	IHD (31), stroke (22)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC
Beijing Aging Study	China	1992	4.8	1010	53	55-92	Stroke (27)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
Beijing Anzhen Cohort Study	China	1991	4.3	6858	55	35-92	IHD (29), stroke (104)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	SBP
Beijing Iron and Steel Worker Cohort Study	China	1974, 1979, 1980	13.5	4400	0	35-74	CHD (83) , stroke (124)	Adjudicated	Medical records, death certificates	Age, smoking status	All combinations of SBP, TC
Busselton Health Study	Australia	1966-1981	24.1	3863	51	20-94	IHD (897), stroke (475)	Not adjudicated	Medical records, death registries	Age, sex, smoking status	All combinations of SBP, TC
Busselton Health Study, phase II	Australia	1994-1995	14	4492	56	18-97	CHD (433)	Not adjudicated	Medical records, death registries	Age, sex, smoking status	All combinations of SBP, TC, FPG
Canada Nutrition Database	Canada	1970-1972	22	9575	55	18-99	CHD (764)	Not adjudicated	Death registries	Age, sex, smoking status, race, alcohol intake, SES	All combinations of hypertension, TC, diabetes
Capital Iron and Steel Company Hospital Cohort (CISCH)	China	1992	3.3	1970	51	34-64	IHD (14), stroke (9)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, diabetes
CardioVascular Disease risk FACtors Two-township Study (CVDFACTS)	Taiwan	1991-1993	End of 2002	2917 (CHD analysis), 3453 (ischaemic stroke analysis)	57	≥ 30 (CHD analysis), ≥ 20 (ischaemic stroke analysis)	CHD (203), ischaemic stroke (132)	Adjudicated	Medical records, death registries	Age, age square, sex, smoking status, alcohol intake, education level, physical activity, family history of stroke, residential area	All combinations of SBP, TC, FPG
Cardiovascular Health Study (CHS)	United States	1989-1990, 1992-1993	End of 2002	4805	61	⩾65	CHD (1498), stroke (686)	Adjudicated	Medical records	Age, sex, smoking status, alcohol intake, education, race	All combinations of SBP, TC, PPG
China Prospective Study (CPS)	China	1991-1992	End of 2005	209918	0	40-79	CHD (1953), stroke (6379)	Not adjudicated	Death registries	Age, smoking status, alcohol intake, education level, area	SBP
Chinese Multi-Provincial Cohort Study (CMCS)	China	1992	11	30378	47	35-64	CHD (227), stroke (582)	Adjudicated	Medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG

Cohort name	Country	Baseline study date	Mean duration or end year of follow-up	No. of participants	Proportion of female(%)	Age range at baseline	Number of event (n) [1]	Event adjudication	Source of event [4]	Confounders adjusted [2]	Mediators adjusted [3]
Cohort of Norway (CONOR) (except Tromsø and HUNT studies)	Norway	1997-2003	2009	66530	49	40- 77	CHD (771), stroke (422)	Not adjudicated	Death registries	Age, sex, smoking status	All combinations of SBP, TC, PPG
Cohort study from Porto Alegre, southern Brazil	Brazil	1995-1996	6	1091	55	18-88	CHD (11), stroke (19)	Adjudicated	Self-report, next of kin, medical records, and death certificates	Age, sex, smoking status, alcohol intake, race, SES†	All combinations of SBP, diabetes
Corfu and Crete Cohort, Seven Countries Study	Greece	1960-1961	25	1160	0	39-59	CHD (41), stroke (79)	Adjudicated	Death certificates, death registries, medical records	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
Crevalcore, Montegiorgio and Rome Cohort, Seven Countries Study	Italy	1960-1962	25	2379	0	39-59	CHD (206), stroke (129)	Adjudicated	Medical records, death certificates	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
Dalmatia and Slavonia Cohort, Seven Countries Study	Croatia	1958	25	1309	0	39-59	CHD (94), stroke (136)	Adjudicated	Medical records, death certificates, next of kin	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
Danish Diet, Cancer and Health study	Denmark	1993-1997	End of 2004	57053	53	50-64	ACS (1127)	Adjudicated	Medical records, death registries	Age, sex, smoking status	All combinations of SBP, TC, diabetes
Diabetes Cardiovascular Risk-Evaluation: Targets and Essential Data for Commitment of Treatment (DETECT)	Germany	2003	End of 2008	7519	59	18-95	CHD (93), stroke (69)	Not adjudicated	Medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG
Diabetes Intervention Study	Germany	1977	11	1139	44	28-56	MI (112) , stroke (23)	Adjudicated	Medical records, death certificates, autopsy reports	Age, sex, smoking status	All combinations of SBP, TC, FPG
Dubbo Study of the Elderly	Australia	1988-1989	16	2805	58	60-98	CHD (645) , ischaemic stroke (272)	Adjudicated	Medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG
East and West Finland Cohort, Seven Countries Study, Phase I	Finland	1959	25	1561	0	39-59	CHD (329), stroke (74)	Not adjudicated	Medical records, death registries	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
East and West Finland Cohort, Seven Countries Study, Phase II	Finland	1990	10	469	0	69-89	CHD (55), stroke (18)	Not adjudicated	Medical records, death registries	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC, FPG
Electrical Generating Authority of Thailand Study (EGAT)	Thailand	1985	11.4	2951	22	35-54	IHD (27), stroke (13)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
EURODIAB Prospective Complications Study	16 European countries	1989-1991	7	3250	48	18-60	CHD (147)	Adjudicated	Self-report, medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, HbA1c
EUROSTROKE	Finland, the Netherlands and United Kingdom	1979-1983, 1984-1989, 1990-1993	NR	698	0	42-95	Stroke (219)	Collaborative study with events adjudicated in some cohorts	Self-report, medical records, death certificates and death registries	Age, smoking status, alcohol intake, family history of stroke, family history of MI, previous MI, previous stroke	All combinations of SBP, TC, diabetes
Fangshan Cohort Study	China	1991	2.7	752	68	34-71	Stroke (7)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
Finnish Mobile Clinic Health Examination Survey (FMC)	Finland	1966-1972	End of 1994	29297	47	30- 69	CHD (3118)	Adjudicated	Medical records, death certificates, autopsy reports	Age, sex, smoking status, physical activity	All combinations of SBP, TC, PPG
Fletcher Challenge Heart and Health Study	New Zealand	1992	5.9	7442	20	20-89	IHD (234), stroke (44)	Not adjudicated	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, PPG
Framingham Heart Study-Cohort	United States	1948-1951	End of 2007	2742	51	29-62	CHD (1055), stroke (576)	Adjudicated	Medical records, autopsy reports, death certificates, next of kin	Age, sex, smoking status, education	All combinations of SBP, TC, CBG
Framingham Heart Study-Offspring	United States	1971	End of 2007	4226	49	18-62	CHD (725), stroke (223)	Adjudicated	Medical records, autopsy reports, death certificates, next of kin	Age, sex, smoking status, alcohol intake	All combinations of SBP, TC, FPG
General Post Office Study (GPO)	United Kingdom	1966-1967	End of 2007	1136	36	35-70	CHD (218) , stroke (72)	Adjudicated	Death certificates	Age, sex, smoking status	All combinations of SBP, TC, PPG
Goteborg BEDA study	Sweden	1980	End of 1999	1408	100	38-64	CHD (64), stroke (57)	Not adjudicated	Medical records, death certificates	Age, smoking status	All combinations of SBP, TC, diabetes
Health Risks and Quality of Life in the Hong Kong Elderly	China, Hong Kong	1991-1992	3	2032	51	≥ 70	IHD (72) , stroke (50)	Not adjudicated	Self-report, medical records, death registry	Age, sex, smoking status	All combinations of SBP, diabetes

Cohort name	Country	Baseline study date	Mean duration or end year of follow-up	No. of participants	Proportion of female(%)	Age range at baseline	Number of event (n) [1]	Event adjudication	Source of event [4]	Confounders adjusted [2]	Mediators adjusted [3]
Hisayama Study	Japan	1961	25.1	1055	54	40-91	IHD (64), stroke (207)	Adjudicated	Medical records, death certificates, autopsy reports	Age, sex, smoking status	All combinations of SBP, TC
Hisayama Study, phase II	Japan	1988	14	2632	58	40-96	CHD (135) , stroke (237)	Adjudicated	Medical records, death certificates, autopsy reports	Age, sex, smoking status, alcohol intake	All combinations of SBP, TC, FPG
Honolulu Heart Program (HHP)	United States	1965-1968	End of 1994	6722	0	45-68	CHD (2093), stroke (942)	Adjudicated	Medical records, self-report	Age, smoking status, alcohol intake, education	All combinations of SBP, TC, PPG
Huashan Study	China	1992	2.8	1496	53	35-75	Stroke (11)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
Jichi Medical School-Ambulatory blood pressure monitoring(JMS-ABPM), wave 1	Japan	1992	3.4	821	62	50-97	Stroke (59)	Adjudicated	Medical records	Age, sex, smoking status	All combinations of SBP, TC, FPG
Kaunas Rotterdam Intervention Study (KRIS)	Lithuania	1972-1974	End of 2010	2447	0	45-59	CHD (646) , stroke (168)	Adjudicated	Medical records, death certificates	Age, smoking status	All combinations of SBP, TC, PPG
Kinmen Neurological Disorders Survey (KINDS)	Taiwan	1993	2.9	895	49	50-91	IHD (5)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, diabetes
Konan Health and Nutrition Study	Japan	1987	6.4	799	55	20-91	Stroke (7)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
Korean Medical Insurance Corporation Study (KMIC)	South Korea	1990	4	143312	31	35-59	IHD (259), stroke (939)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
LIFE (Losartan Intervention For Endpoint reduction in hypertension) Study	Sweden	1995-1997	4	9079	54	55-80	MI (380) , stroke (534)	Adjudicated	Medical records, death certificates, autopsy reports	Age, sex, smoking status, race	All combinations of SBP, TC, FPG
ManAgement of Elevated Cholesterol in Primary Prevention Group of Adult Japanese (MEGA)	Japan	1994	5.3	8214	68	40-70	CHD (142), stroke (97)	Adjudicated	Medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG
Melbourne Collaborative Study (MCCS)	Australia	1990-1994	13.3	35975	59	27-76	CHD (335), stroke (74)	Adjudicated	Death registries	Age, sex, smoking status, ethnicity	All combinations of SBP, TC, FPG
Multi-Ethnic Study of Atherosclerosis (MESA)	United States	2000-2002	End of 2008	6558	52	45-84	CHD (271), stroke (102)	Adjudicated	Medical records	Age, sex, smoking status, alcohol intake, education, race	All combinations of SBP, TC, FPG
Multifactor Primary Prevention Study	Sweden	1970-1973	End of 1998	7399	0	47-55	CHD (1698), stroke (837)	Not adjudicated	Medical records, death certificates	Age, smoking status	All combinations of SBP, TC, diabetes
Multiple Risk Factor Intervention Trial for the Prevention of Coronary Heart Disease (MRFIT)	United States	1973-1976	End of 1985	12508	0	35–57	CHD (2137), stroke (101)	Adjudicated	Medical records, next of kin, death registries, autopsy reports	Age, smoking status, alcohol intake, education, race	All combinations of SBP, TC, FPG
National Heart Foundation Risk Factor Prevalence Study	Australia	1989	15	9309	51	20- 69	CHD (140)	Not adjudicated	Death registries	Age, sex, smoking status	All combinations of SBP, TC, diabetes
Newcastle Study	Australia	1983-1984	5.7	2939	51	21-77	IHD (20), stroke (6)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, diabetes
NHANES I Epidemiologic Follow-up Study (NHEFS)	United States	1971-1975	End of 1992	9180	62	25-74	CHD (1394) , stroke (671)	Not adjudicated	Death registries	Age, sex, race, smoking status, alcohol intake, education level	All combinations of SBP, TC, diabetes
NIPPON DATA80	Japan	1980	14	9462	56	30-93	CHD (86) , stroke (226)	Adjudicated	Death certificates	Age, sex, smoking status, alcohol intake	All combinations of SBP, TC, PPG
NIPPON DATA90	Japan	1990	10	7317	58	≥ 30	CHD (39) , stroke (74)	Adjudicated	Death certificates	Age, sex, smoking status, alcohol intake	All combinations of SBP, TC, FBG

Cohort name	Country	Baseline study date	Mean duration or end year of follow-up	No. of participants	Proportion of female(%)	Age range at baseline	Number of event (n) [1]	Event adjudication	Source of event [4]	Confounders adjusted [2]	Mediators adjusted [3]
Nord-Trondelag Health Study 1 (HUNT 1)	Norway	1984-1986	End of 2007	74286	51	19-103	CHD (4248), stroke (2263)	Adjudicated for subarachnoid hemorrhage, not adjudicated for CHD and other stroke types	Medical records, autopsy reports, death registries	Age, sex, smoking status	SBP
Nord-Trondelag Health Study 2 (HUNT 2)	Norway	1995-1997	End of 2008	64382	53	19-94	CHD (1026), stroke (1011)	Adjudicated for subarachnoid hemorrhage, not adjudicated for CHD and other stroke types	Medical records, autopsy reports, death registries	Age, sex, smoking status	All combinations of SBP, TC, FPG
Northern Manhattan Study (NOMAS)	United States	1993-2001	10	2822	64	≥ 40	MI (239) , stroke (282)	Adjudicated	Self-report, medical records, death certificates	Age, sex, smoking status, race, alcohol intake, physical activity, SES	All combinations of SBP, TC, PPG
Norwegian Counties Study (NCS)	Norway	1974-1978	End of 2009	57535	50	20-50	IHD (3397) , stroke (1089)	Not adjudicated	Death registries	Age, sex, smoking status	All combinations of SBP, TC, PPG
Ohasama Study	Japan	1992	4.1	1370	67	35-89	Stroke (24)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, PPG
Perth Risk Factors Survey (Perth MONICA)	Australia	1979-1994	14.4	8725	46	20-90	IHD (145), stroke (48)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, diabetes
Prospective Cardiovascular Munster Study (PROCAM)	Germany	1979-1996	12	26975	32	20-65	CHD (544), stroke (196)	Adjudicated	Medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG
Prospective Study of Women in Gothenburg	Sweden	1968	End of 2008	1462	100	38-60	CHD (228) , stroke (225)	Adjudicated	Medical records, death certificates, self-report	Age, smoking status, alcohol intake, physical activity, education level, SES	All combinations of SBP, TC, FPG
Puerto Rico Heart Health Program (PRHHP)	United States	1965	8.3	8462	0	45-64	CHD (530), stroke (163)	Adjudicated	Medical records, death certificates, next of kin, self-report, autopsy reports	Age, smoking status, alcohol intake, education, race	All combinations of SBP, TC, FPG
Risk of ischaemic heart disease in Zaragoza (ZACARIS)	Spain	1994	5	6262	55	25-99	CHD (127)	Adjudicated	Medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG
Rotterdam Study (RS)	The Netherlands	1990	17	6910	59	55-99	CHD (1192) , stroke (752)	Adjudicated	Medical records, death registries	Age, sex, smoking status	All combinations of SBP, TC, PPG
Saitama Cohort Study	Japan	1986	11	2769	63	20-94	IHD (12), stroke (33)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC
Seven Cities Cohort Study	China	1987	2.7	4152	58	35-90	IHD (30), stroke (138)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, diabetes
Shibata Cohort Study	Japan	1977	20	1728	59	40-89	IHD (46), stroke (121)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC
Singapore Cardiovascular Cohort Study	Singapore	1982-1984, 1992, 1993-1995	8.5	2879	0	18-89	CHD (125)	Not adjudicated	Medical records, death registries	Age, smoking status, race, alcohol intake	All combinations of SBP, HDL cholesterol, FPG
Six Chinese Cohorts Study	China	1982	8.3	9099	47	35-59	IHD (26), stroke (91)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC
Study of Multifactorial Prevention of Ischemic Heart Disease	Lithuania	1977-1980	End of 2010	5678	0	40-59	CHD (1092) , stroke (292)	Adjudicated	Medical records, death certificates	Age, smoking status	All combinations of SBP, TC, PPG

Cohort name	Country	Baseline study date	Mean duration or end year of follow-up	No. of participants	Proportion of female(%)	Age range at baseline	Number of event (n) [1]	Event adjudication	Source of event [4]	Confounders adjusted [2]	Mediators adjusted [3]
Survey in Europe on Nutrition and the Elderly, a Concerted Action (SENECA)	9 European countries	1988-1989	10	1279	50	70-77	CHD (79) , stroke (59)	Adjudicated	Death certificates, death registries	Age, sex, smoking status, alcohol intake, physical activity, diet	All combinations of hypertension, TC, FPG
Tanno - Soubetsu Study	Japan	1977	16.4	1763	54	39-65	IHD (17), stroke (32)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC, FPG
Tanushimaru and Ushibuka Cohort, Seven Countries Study	Japan	1958-1960	25	859	0	39-59	CHD (30), stroke (93)	Adjudicated	Medical records, death certificates	age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
Tehran Lipid and Glucose Study (TLGS)	Iran	1999-2001	7.6	5406	55	40-80	CHD (291), stroke (49)	Adjudicated	Medical records, death certificates, autopsy reports	Age, sex, smoking status, SES, family history of CVD	All combinations of SBP, TC, FPG
Tianjin Study	China	1984	6.1	7527	51	35-95	IHD (79), stroke (277)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	SBP
Tromsø Study (4th cohort)	Norway	1994-1995	2010	27158	53	25- 97	MI (1777), stroke (1277)	Adjudicated	Medical records, death certificates, death registries, autopsy reports	Age, sex, smoking status, physical activity, alcohol, SES	All combinations of SBP, TC, diabetes
Turkish Adult Risk Factor Study (TARF)	Turkey	1998	End of 2010	3687	51	20-80	CHD (460)	Not adjudicated	Medical records	Age, sex, smoking status	All combinations of SBP, TC, PPG
Uppsala Longitudinal Study of Adult Men (ULSAM)	Sweden	1991-1995	End of 2008	1221	0	70	CHD (216) , stroke (156)	Adjudicated	Medical records, death registries	Age, smoking status, physical activity, SES	All combinations of SBP, TC, PPG
US Railroad Cohort, Seven Countries Study	United States	1957-1959	25	2216	0	39-59	CHD (389), stroke (83)	Adjudicated	Medical records, death certificates	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
Ventimiglia di Sicilia Heart Study	Italy	1989	15	685	55	35-75	MI (31), stroke (28)	Adjudicated	Medical records, death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG
Vorarlberg Health Monitoring & Promotion Programme (VHM&PP)	Austria	1985-2005	14.4	185316	54	18-96	CHD (4953), stroke (2275)	Not adjudicated	Death certificates	Age, sex, smoking status	All combinations of SBP, TC, FPG
Western Collaborative Group Study (WCGS)	United States	1960	33	3152	0	39-59	CHD (1153) , stroke (354)	Adjudicated	Self-report, medical records and death registries	Age, smoking status, race, physical activity,SES	All combinations of SBP, TC, PPG
Whitehall I Study	United Kingdom	1967-1970	End of 2010	14283	0	40-69	CHD (3080) , stroke (1072)	Not adjudicated	Death certificates	Age, smoking status, employment grade	All combinations of SBP, TC, PPG
Whitehall II Study	United Kingdom	1991-1993	End of 2010	6687	30	39-63	CHD (71) , stroke (26)	Adjudicated	Self-report, medical records, death certificates	Age, sex, smoking status, employment grade	All combinations of SBP, TC, FPG
Women's Health Initiative Study (WHI-OS)	United States	1993-1998	End of 2005	69351	100	50-79	CHD (2604), stroke (1231)	Adjudicated	Medical records, next of kin, death registries, autopsy reports	Age, smoking status, alcohol intake, education, race	All combinations of SBP, hypercholesterolemia, diabetes
Women's Health Initiative: Clinical Trials (WHI-CT)	United States	1993	7	3836	100	50-79	CHD (197), stroke (71)	Adjudicated	Medical records, next of kin, death registries, autopsy reports	Age, smoking status, alcohol intake, education, race, treatment	All combinations of SBP, TC, FPG
Yunnan Tin Miner Cohort Study	China	1992	4.5	1919	5	39-81	Stroke (20)	Unknown	Most APCSC cohorts used death registries, medical records or self-report [5]	Age, sex, smoking status	All combinations of SBP, TC
Zrenjanin, Belgrade and Velika Krsna Cohort, Seven Countries Study	Serbia	1962-1964	25	1492	0	39-59	CHD (125), stroke (123)	Adjudicated	Medical records, death registries, next of kin	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
Zutphen cohort, Seven Countries Study, Phase I	The Netherlands	1960	25	809	0	39-59	CHD (141), stroke (31)	Adjudicated	Medical records, death certificates	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC
Zutphen cohort, Seven Countries Study, Phase II	The Netherlands	1990	10	556	0	69-89	CHD (39), stroke (26)	Adjudicated	Medical records, death certificates	Age, sex, smoking status, physical activity, SES	All combinations of SBP, TC, FPG

1. SES may be measured by various indicators such as income, education, etc.

2. Abbreviations: ACS, acute coronary syndrome; CHD, coronary heart disease; IHD, ischaemic heart disease; MI, myocardial infarction.

3. Abbreviations: SBP, systolic blood pressure; TC, total cholesterol; HDL, HDL cholesterol; FPG, fasting plasma glucose; PPG, post-prandial plasma glucose; FBG: fasting blood glucose; CBG, casual blood glucose; HbA1c, Hemoglobin A1c .

4. Medical records included hospital records, physical examinations, cardiac enzymes or electrocardiography (ECG).

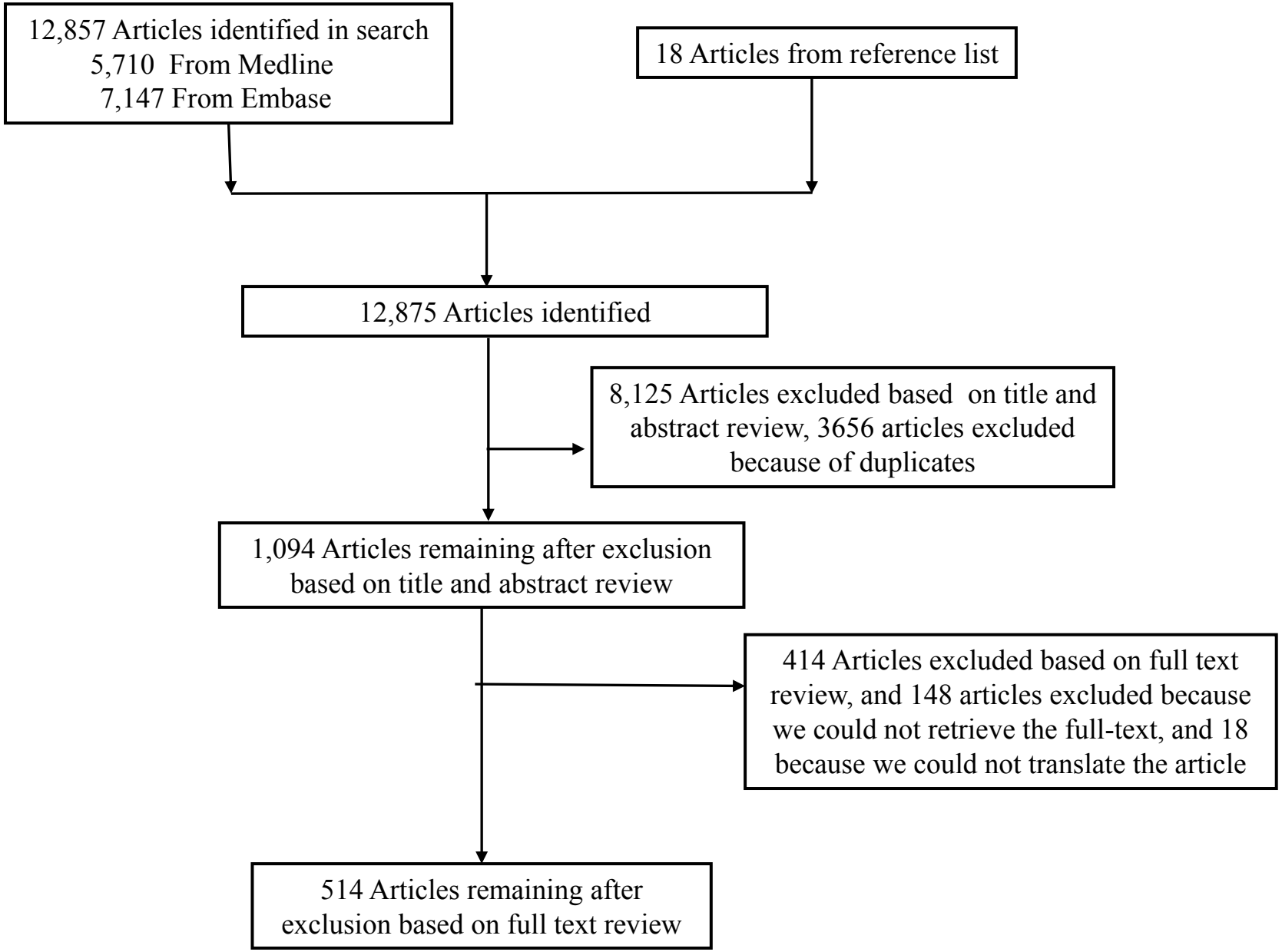
5. Woodward M, Barzi F, Martiniuk A, Fang X, Gu DF, Imai Y, et al. Cohort profile: the Asia Pacific Cohort Studies Collaboration. Int J Epidemiol. 2006; 35(6): 1412-6.

6. In categorical BMI analysis, age, sex, smoking status, race, alcohol intake, physical activity and income were adjusted as confounders in the ARIC Study.

Webtable 3: Stratified analyses of hazard ratios (HRs) for overweight and obesity vs. normal weight. All HRs were also adjusted for confounders as described in Methods and Webtable 2.

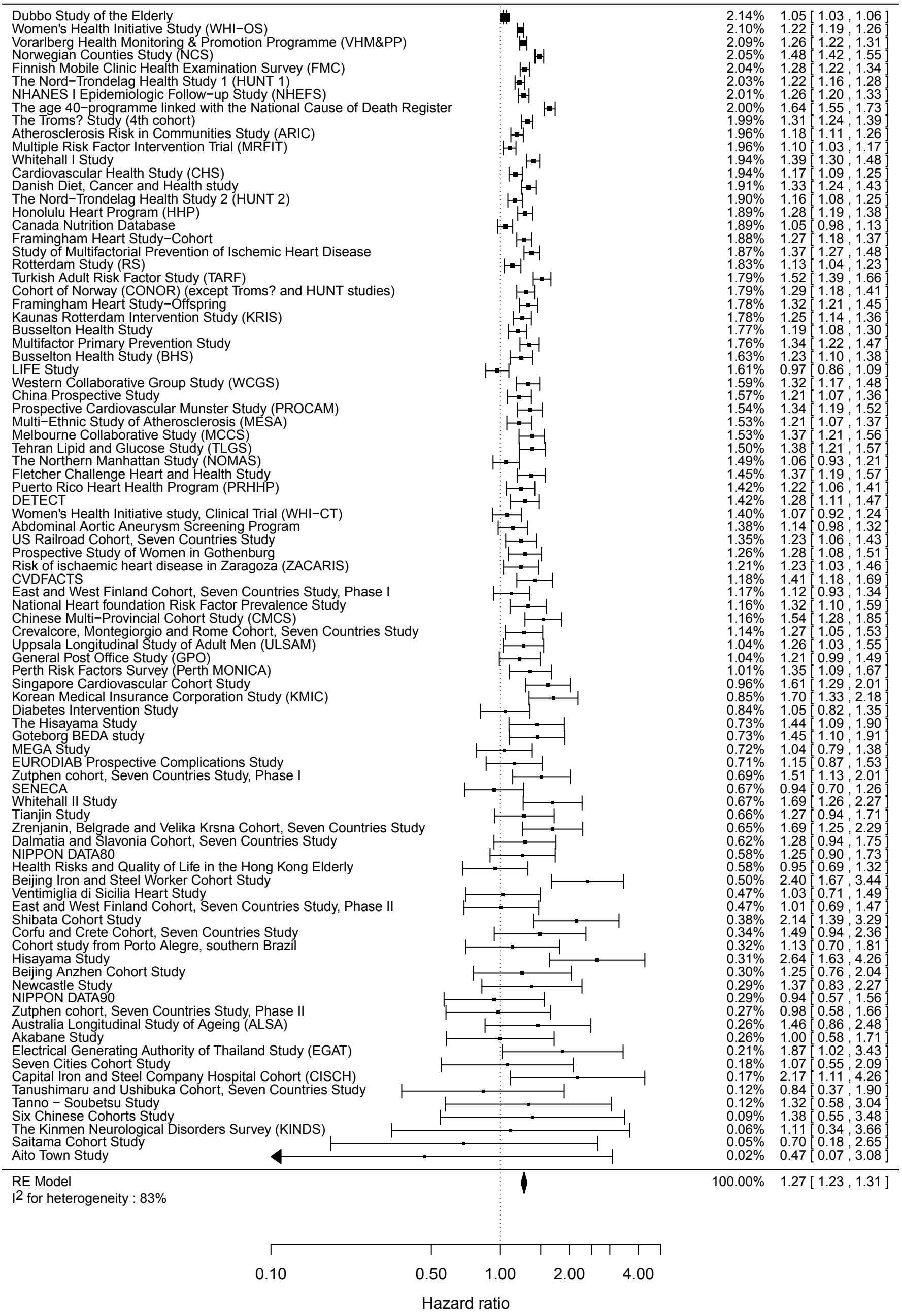
Category	Overweight		Obesity	
	CHD	Stroke	CHD	Stroke
Cohort location				
North America, Western Europe, Australia and New Zealand	1.25 (1.21-1.29)	1.09 (1.04-1.14)	1.63 (1.52-1.75)	1.36 (1.25-1.47)
East and Southeast Asia	1.38 (1.26-1.52)	1.27 (1.19-1.36)	2.26 (1.69-3.02)	2.02 (1.68-2.44)
Baseline year				
< 1990	1.23 (1.18-1.28)	1.14 (1.08-1.20)	1.69 (1.55-1.84)	1.61 (1.45-1.79)
≥ 1990	1.29 (1.23-1.36)	1.11 (1.03-1.19)	1.69 (1.52-1.88)	1.35 (1.20-1.52)

Webfigure 1: Flow diagram for articles identified and retained in Medline and Embase

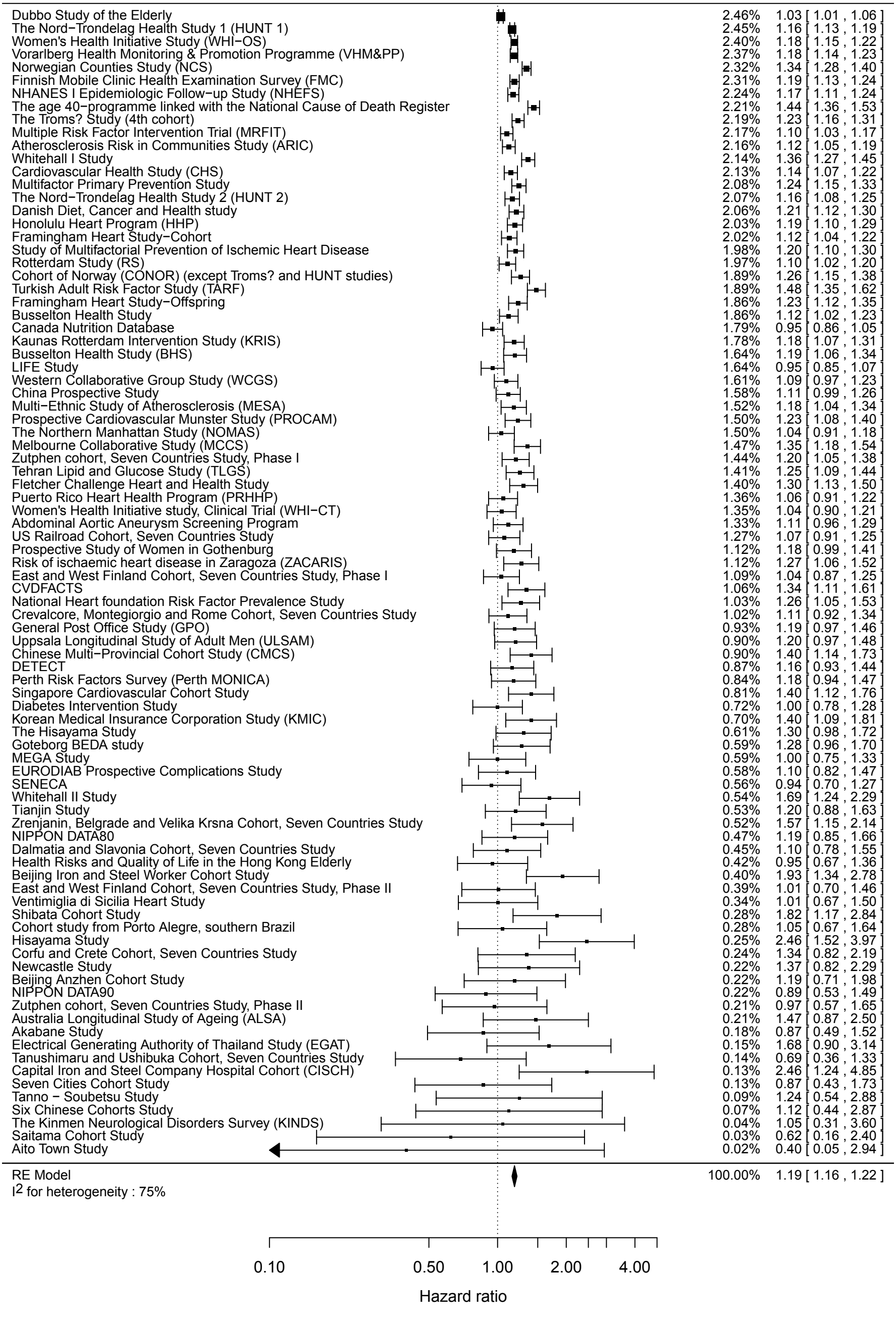

12,857 Articles identified in search
5,710 From Medline
7,147 From Embase
18 Articles from reference list
12,875 Articles identified
8,125 Articles excluded based on title and abstract review, 3656 articles excluded because of duplicates
1,094 Articles remaining after exclusion based on title and abstract review
414 Articles excluded based on full text review, and 148 articles excluded because we could not retrieve the full-text, and 18 because we could not translate the article
514 Articles remaining after exclusion based on full text review

Webfigure 2: Cohort-specific hazard ratios (HRs) of CHD per 5 kg/m^2 higher BMI

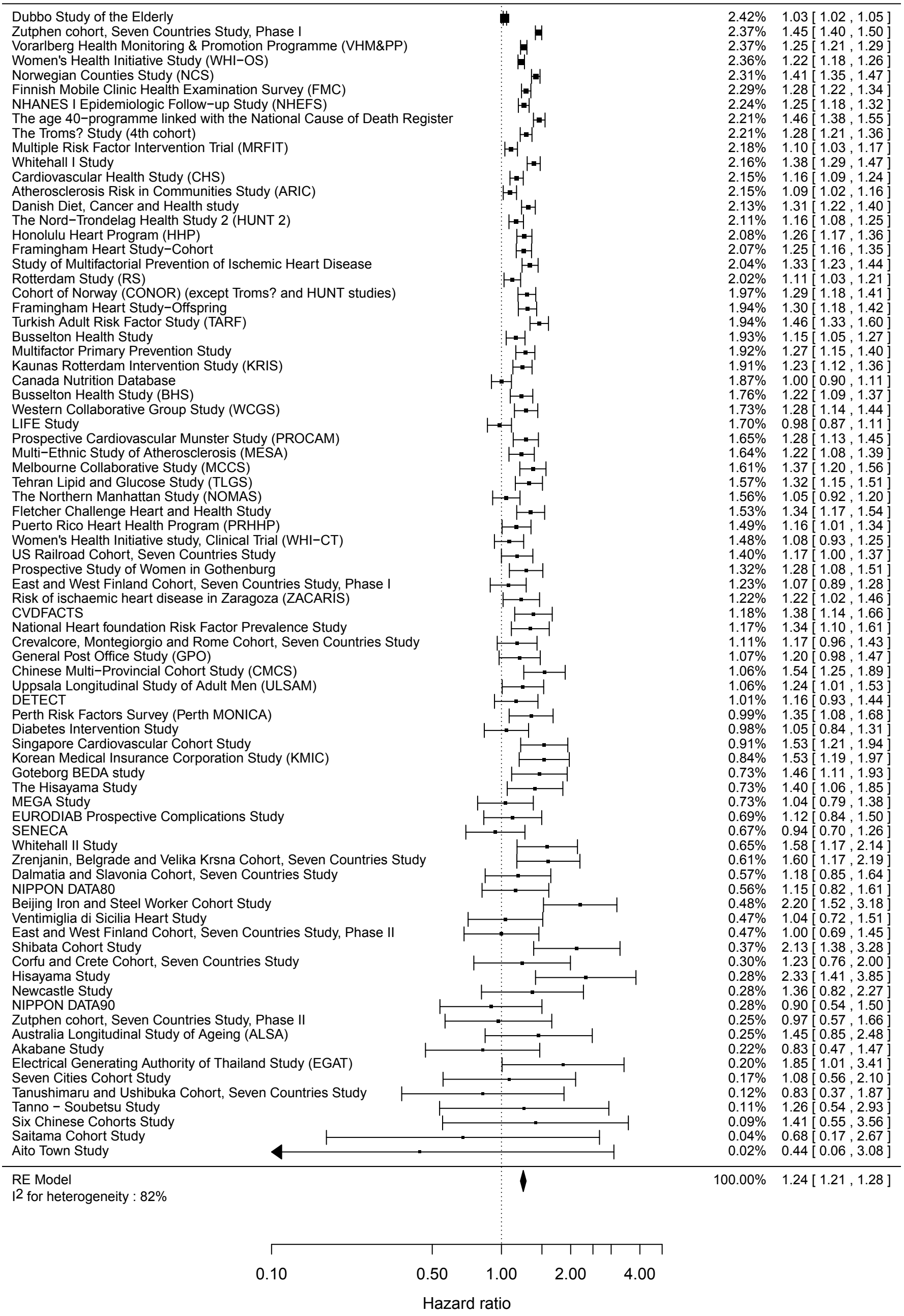
A. Adjusted for confounders



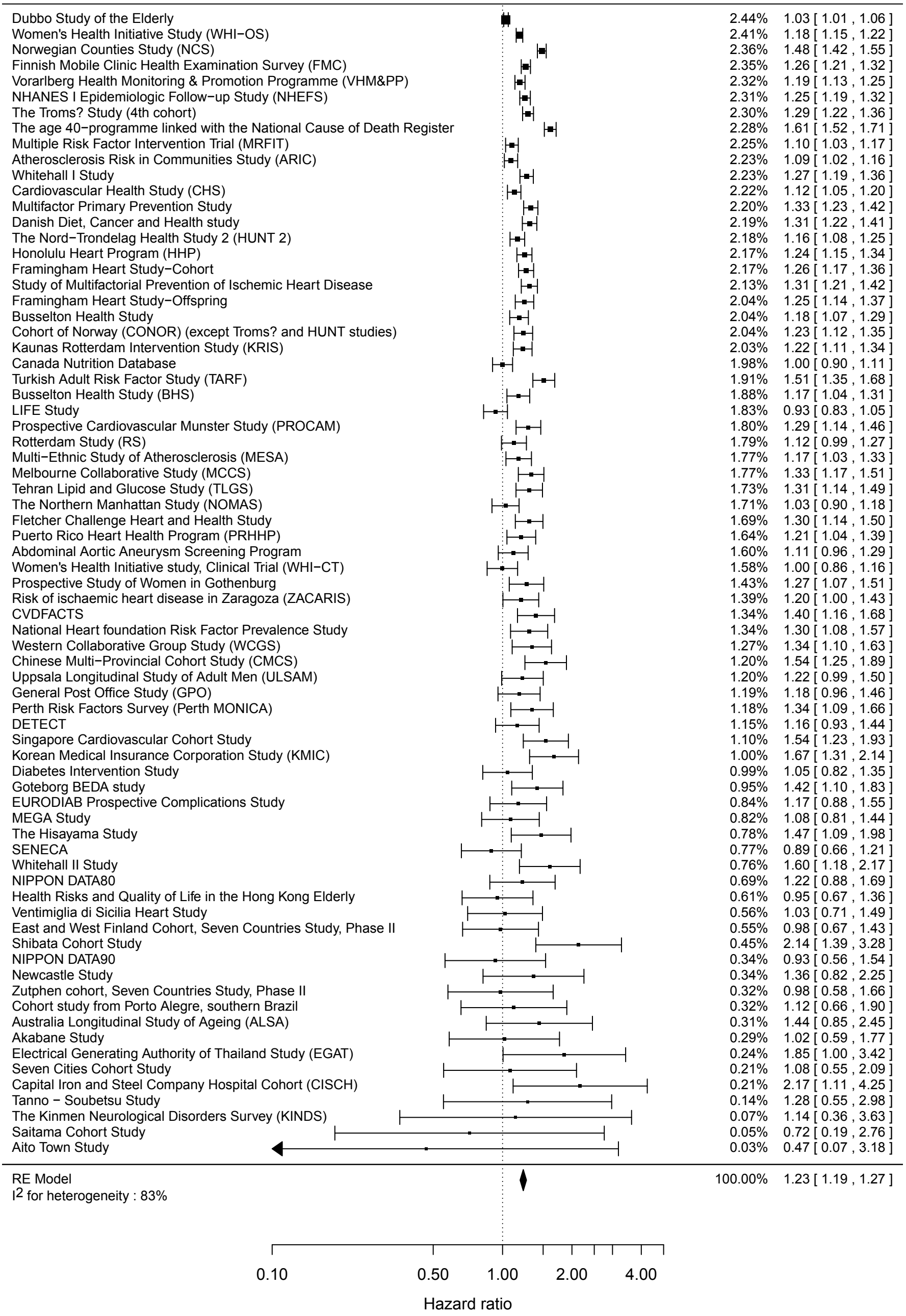
B. Adjusted for confounders and blood pressure



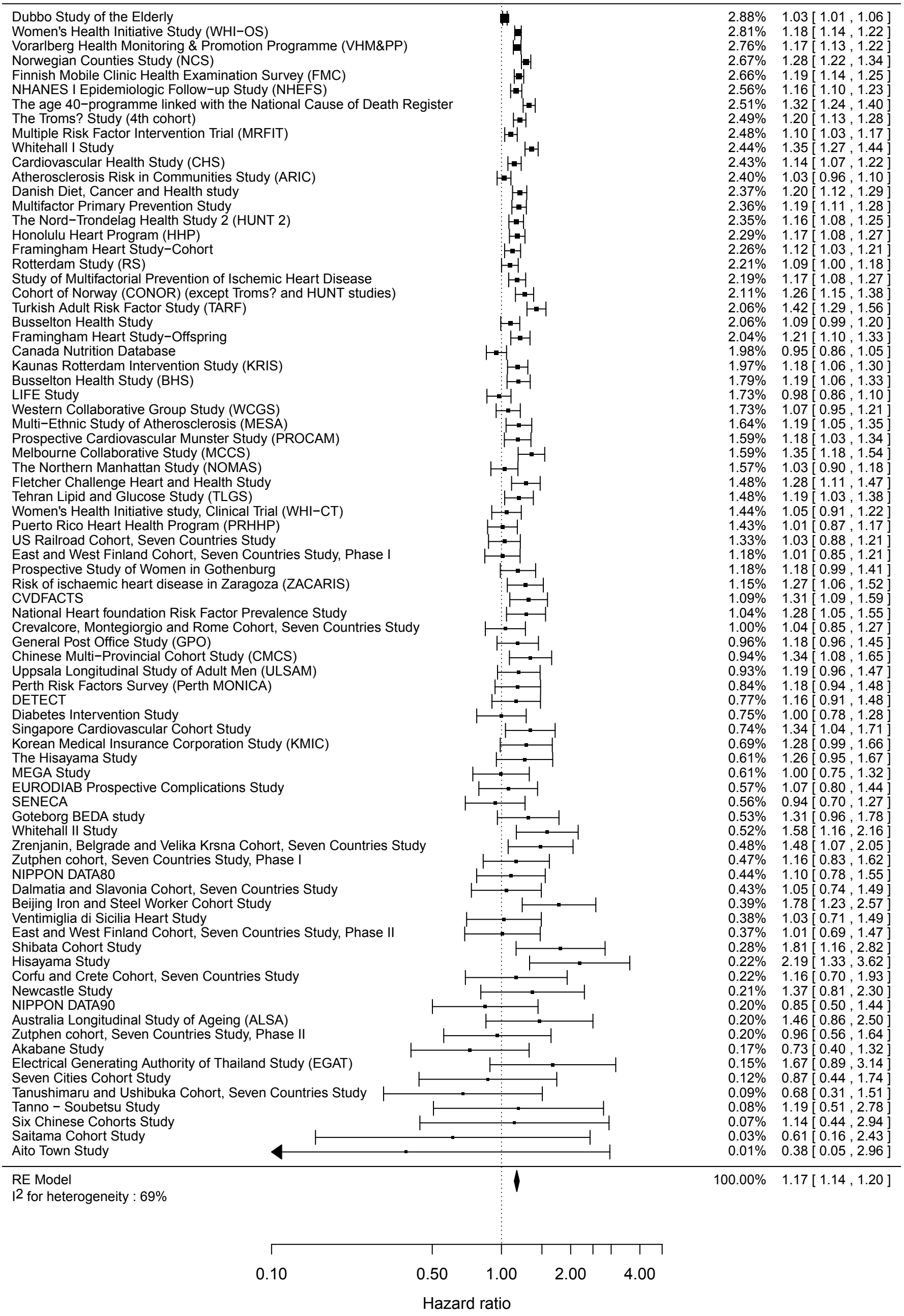
C. Adjusted for confounders and cholesterol



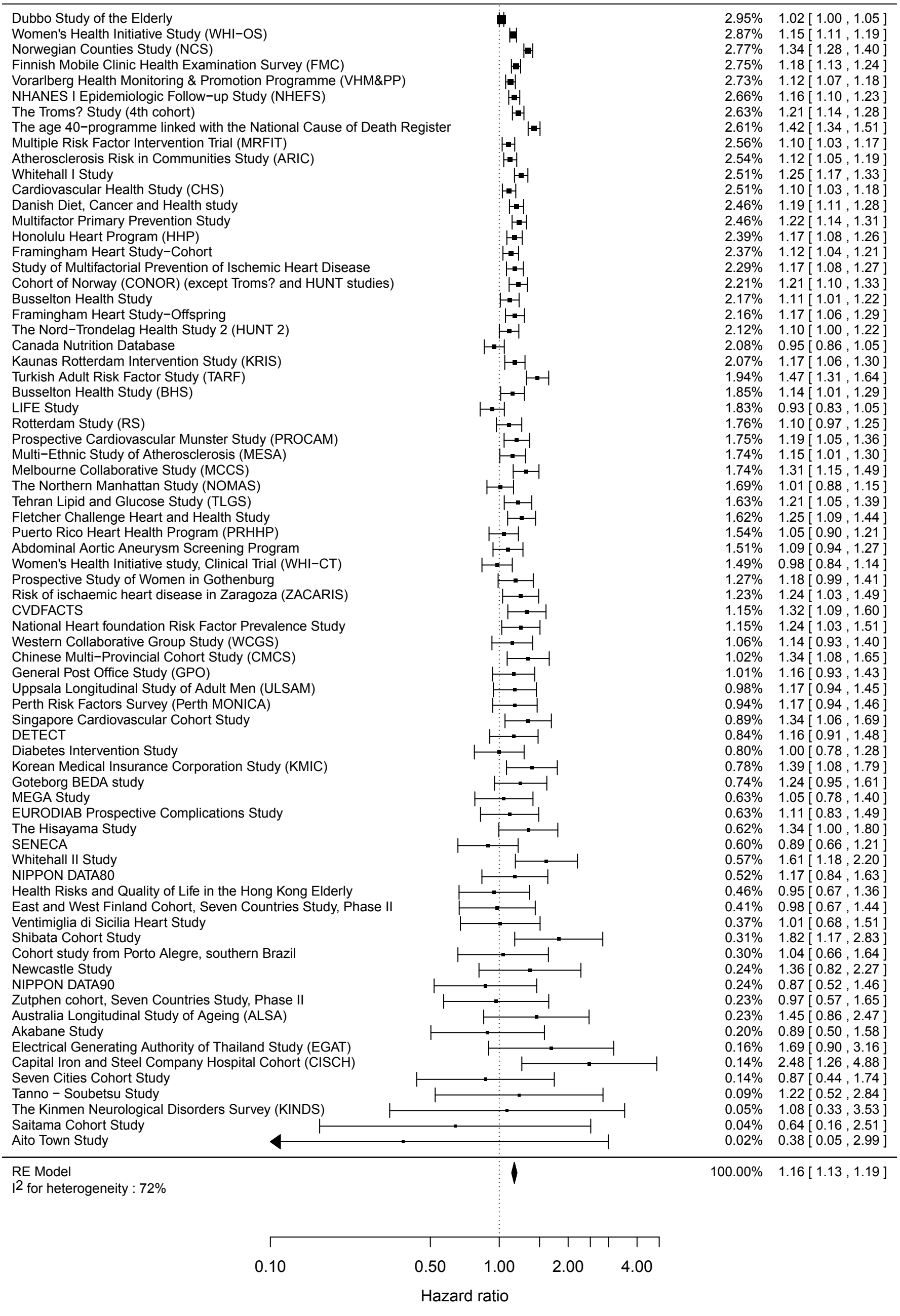
D. Adjusted for confounders and glucose



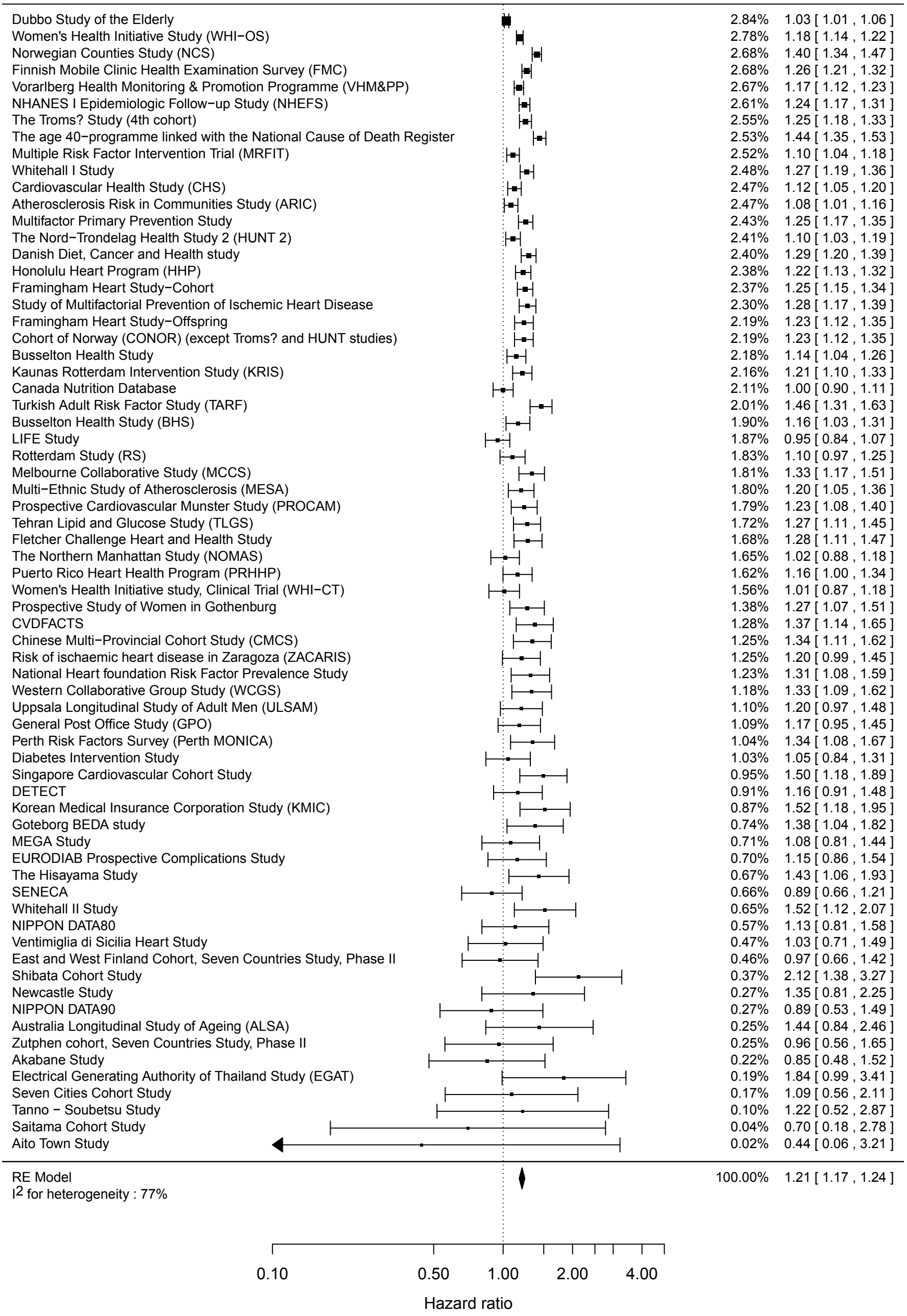
E. Adjusted for confounders and blood pressure, cholesterol



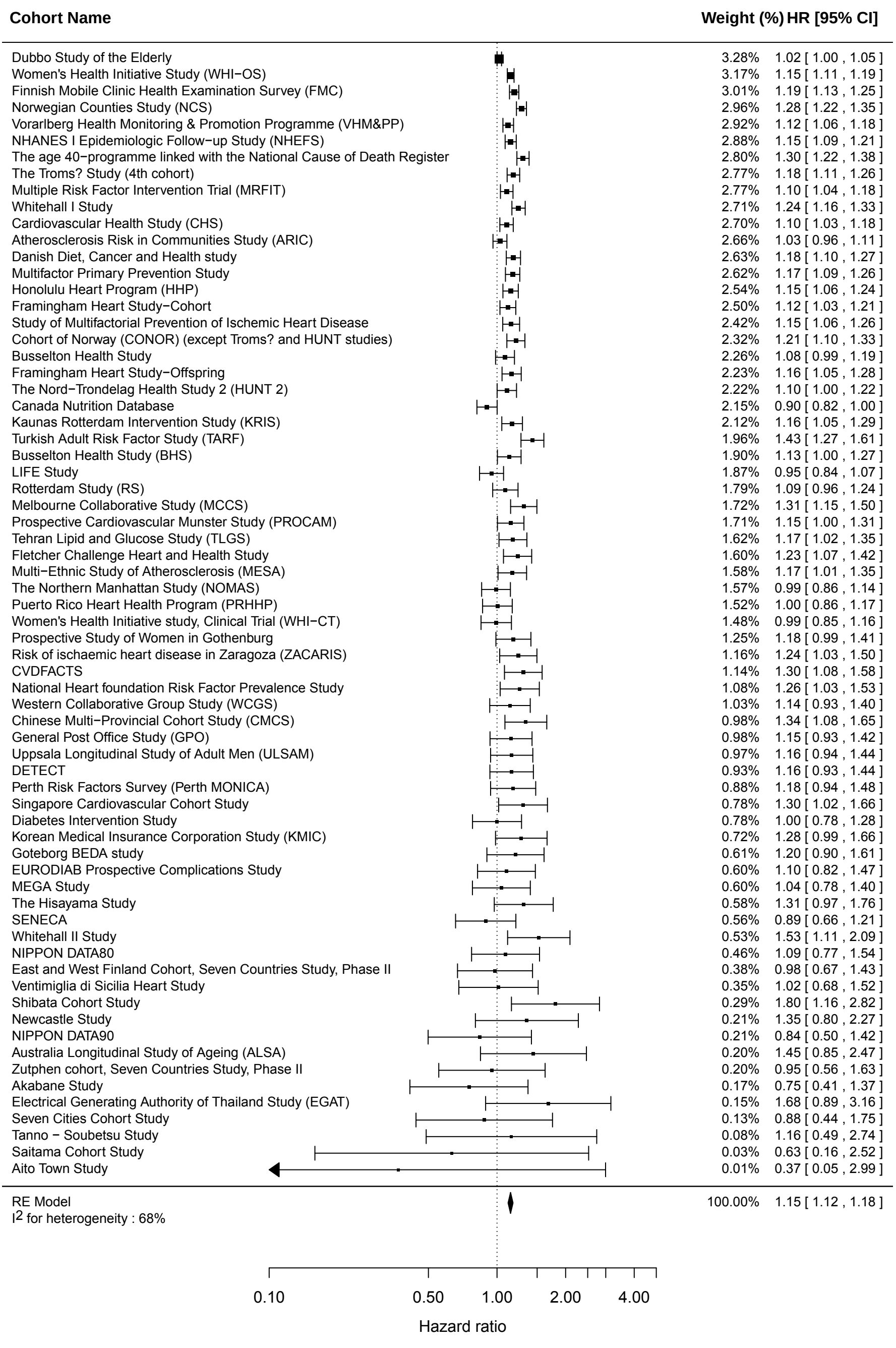
F. Adjusted for confounders and blood pressure, glucose



G. Adjusted for confounders and cholesterol, glucose

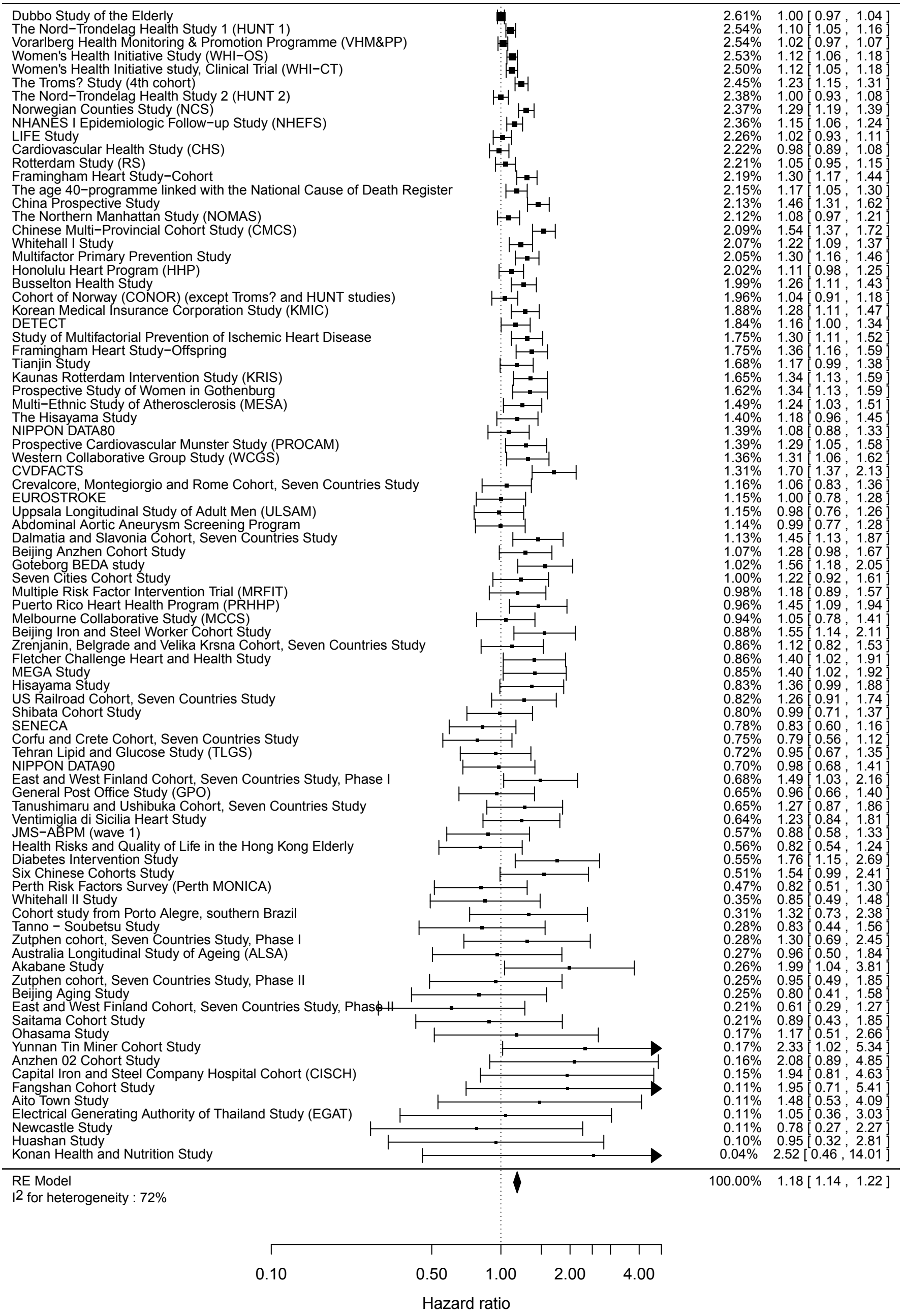


H. Adjusted for confounders and blood pressure, cholesterol, glucose

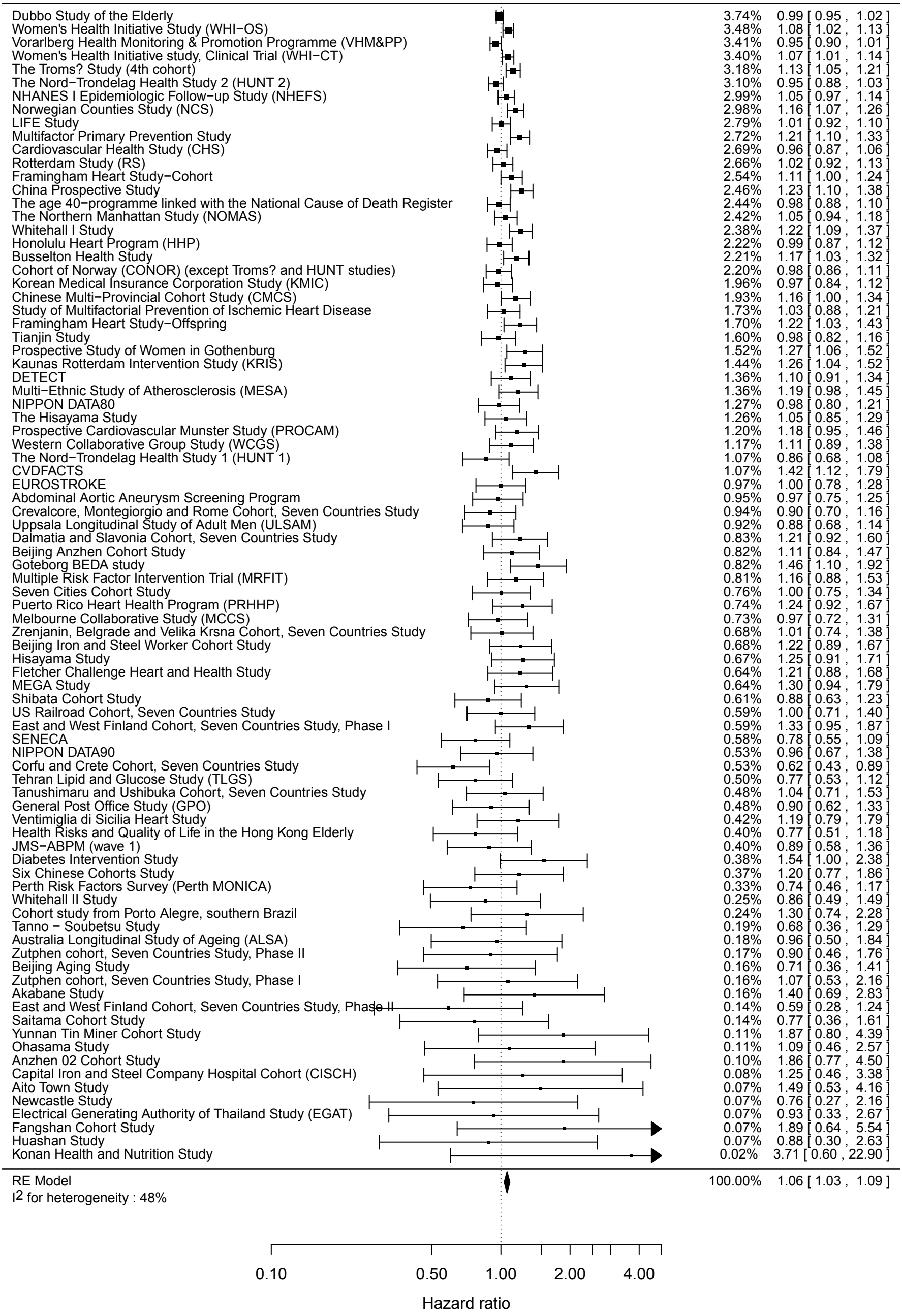


Webfigure 3: Cohort-specific hazard ratios (HRs) of stroke per 5 kg/m^2 higher BMI .

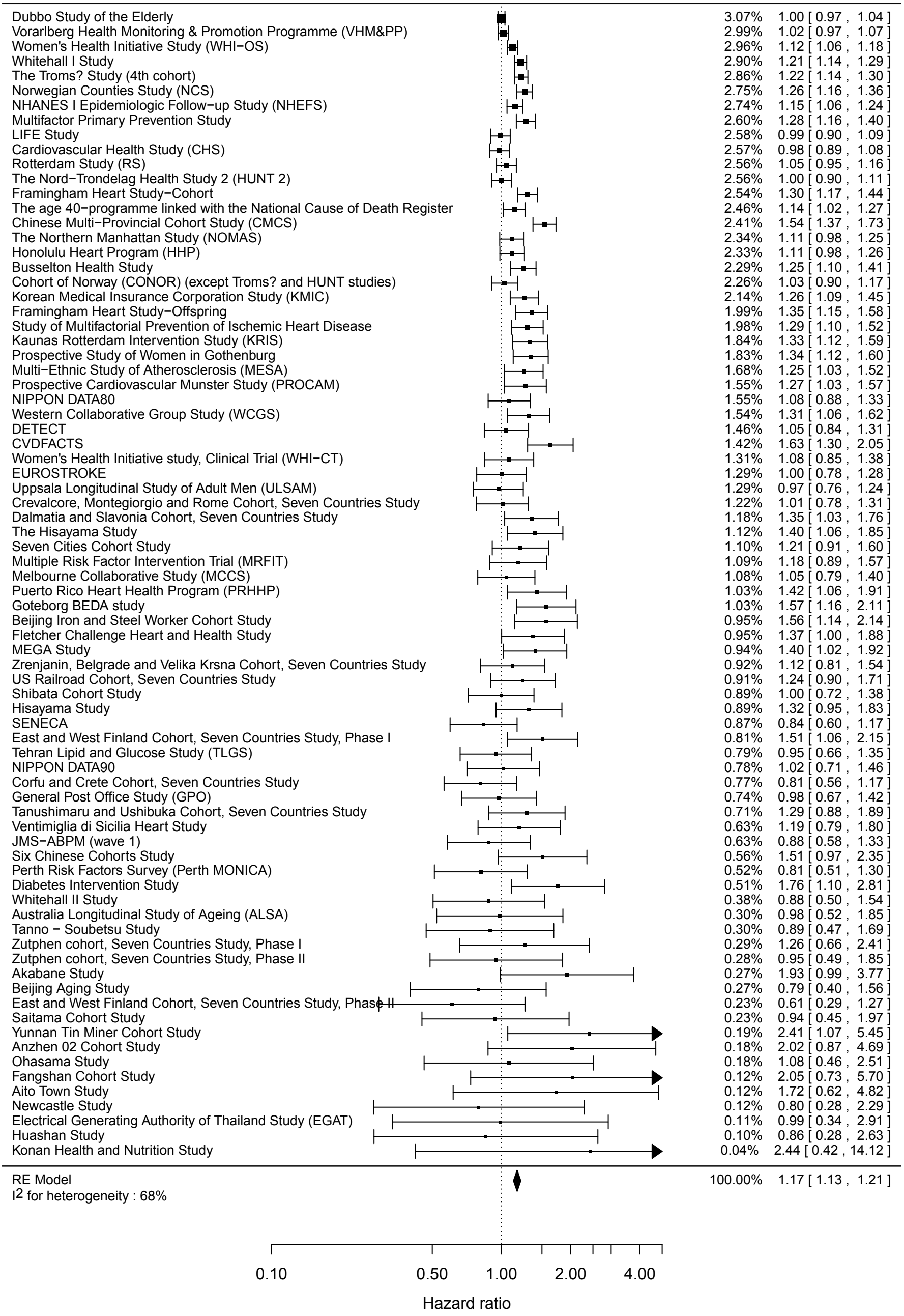
A. Adjusted for confounders



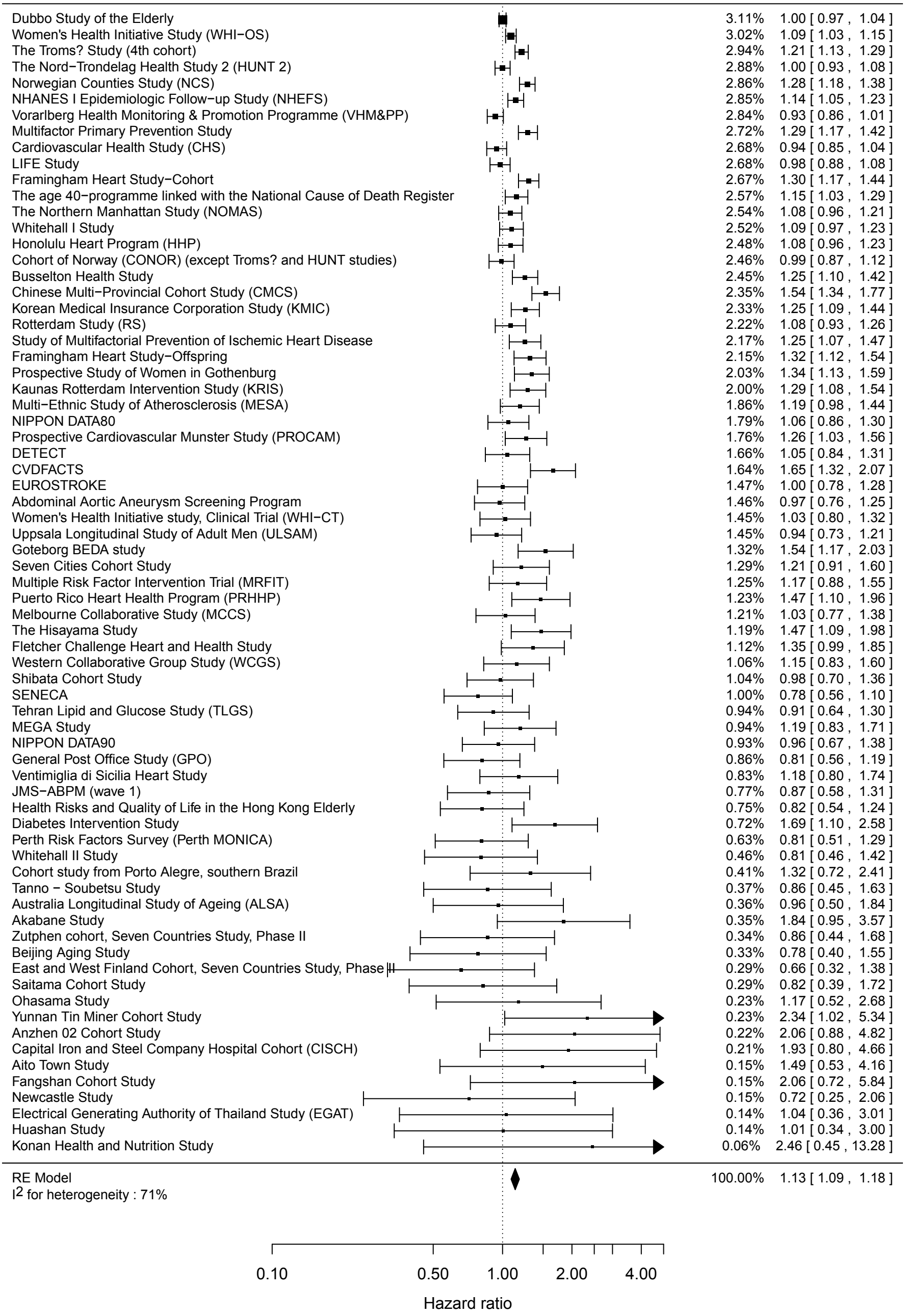
B. Adjusted for confounders and blood pressure



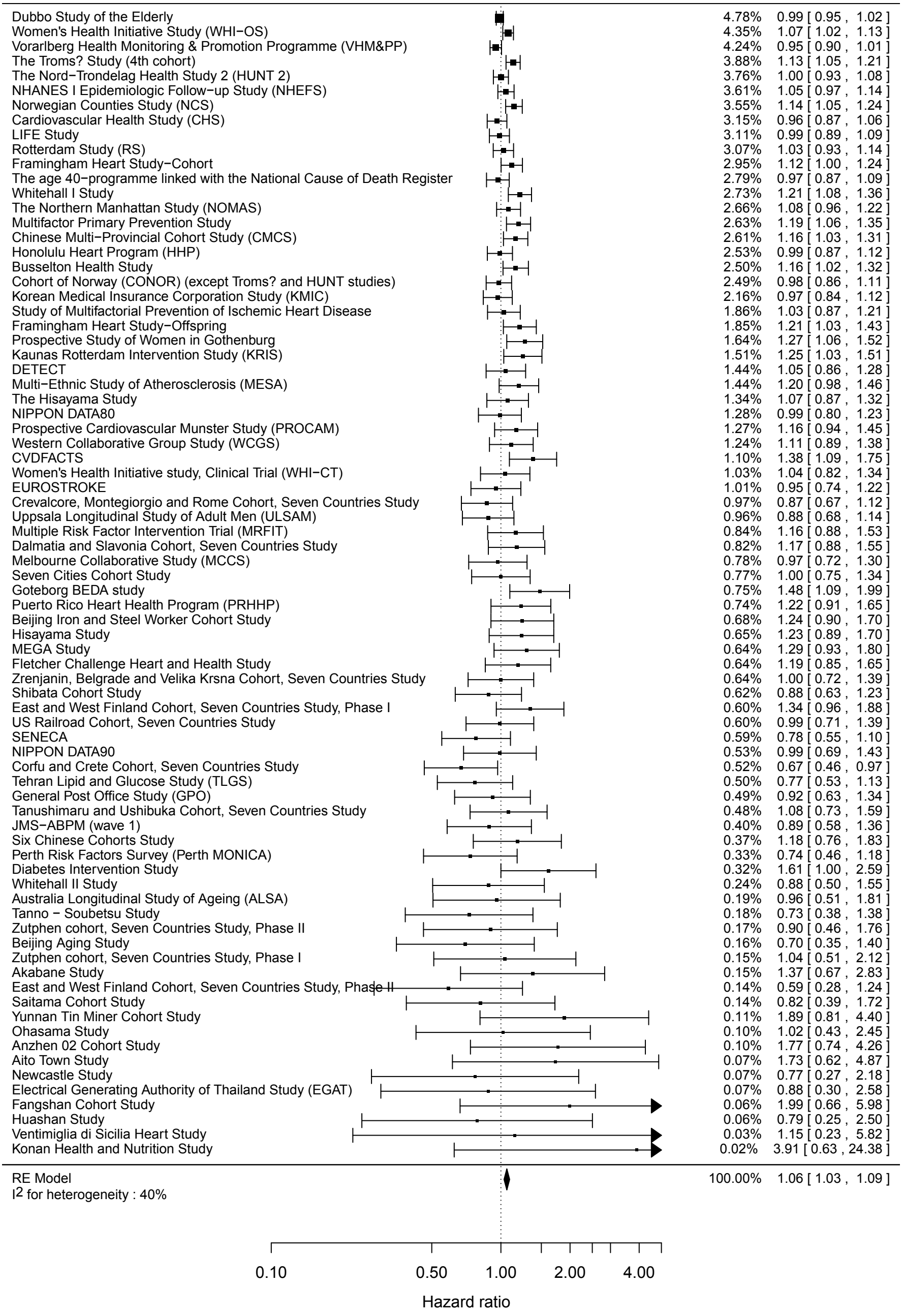
C. Adjusted for confounders and cholesterol



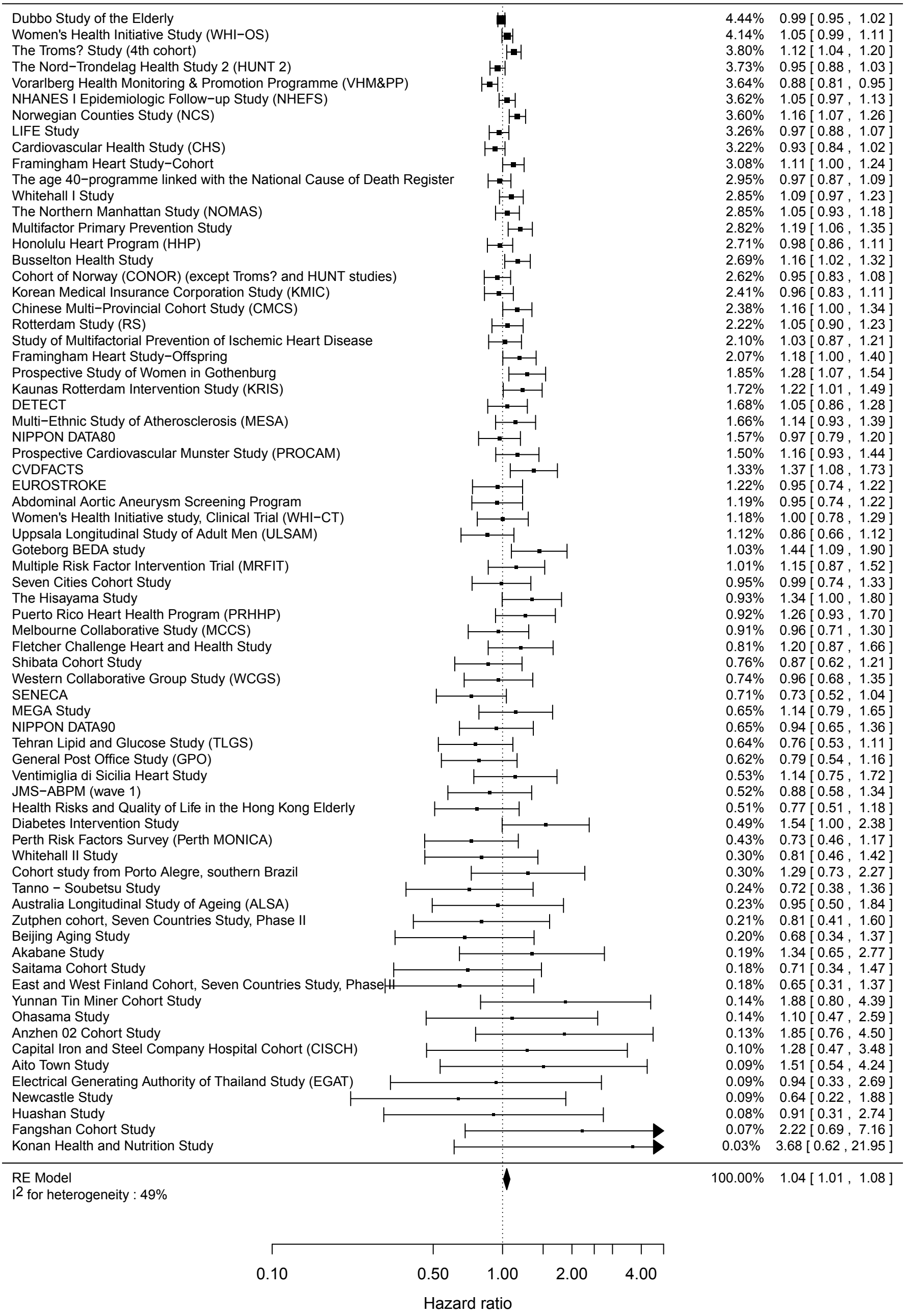
D. Adjusted for confounders and glucose



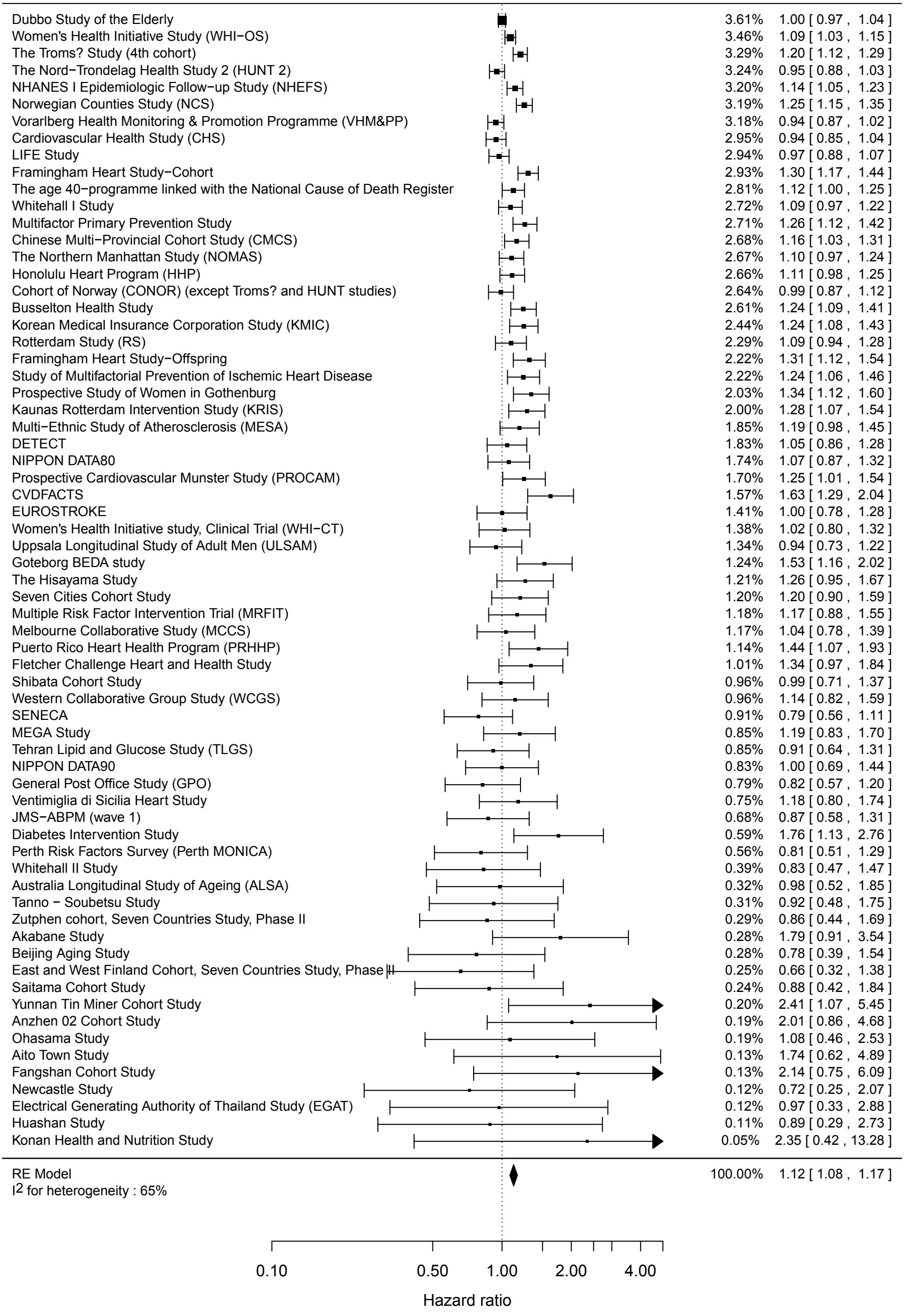
E. Adjusted for confounders and blood pressure, cholesterol



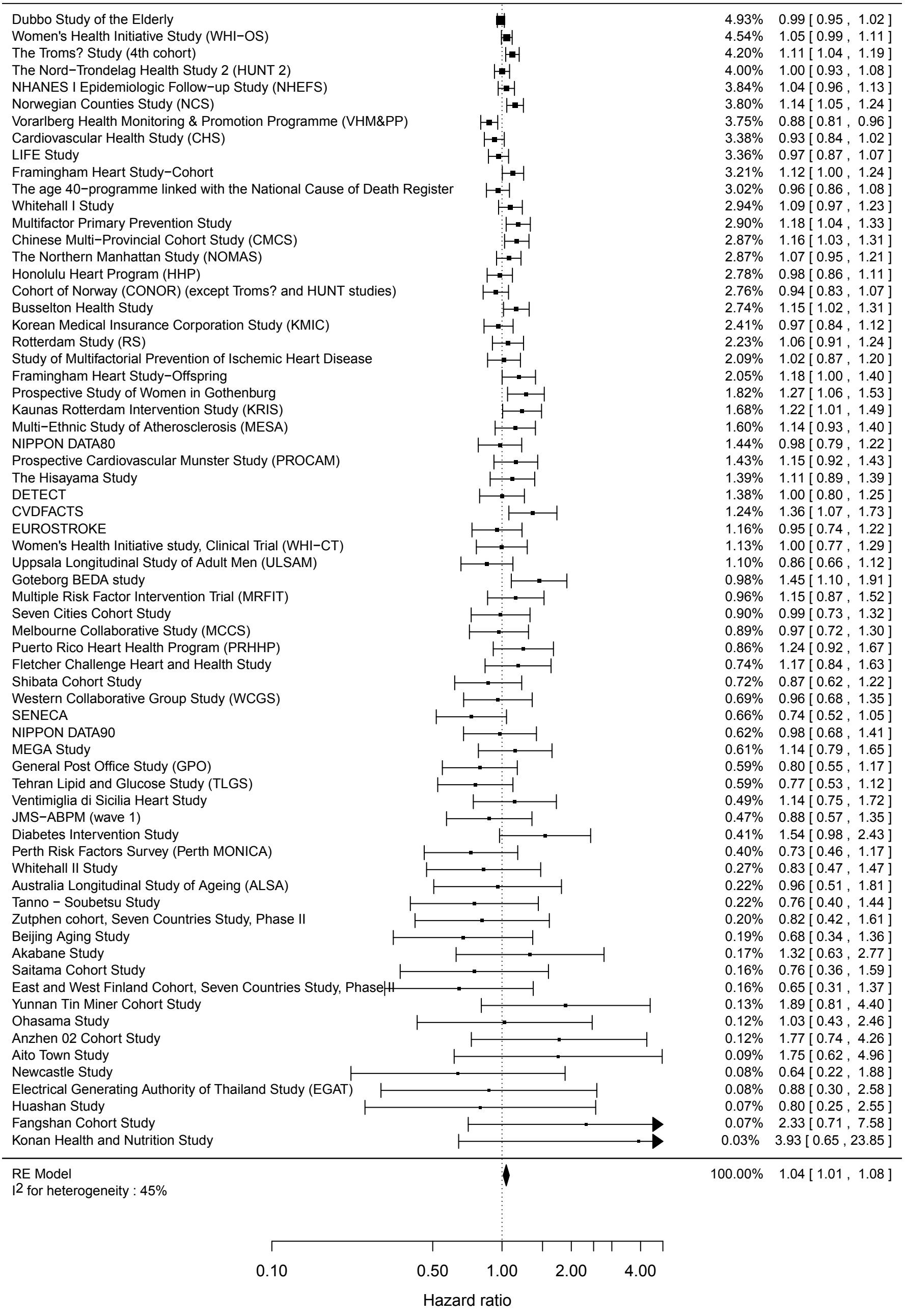
F. Adjusted for confounders and blood pressure, glucose



G. Adjusted for confounders and cholesterol, glucose

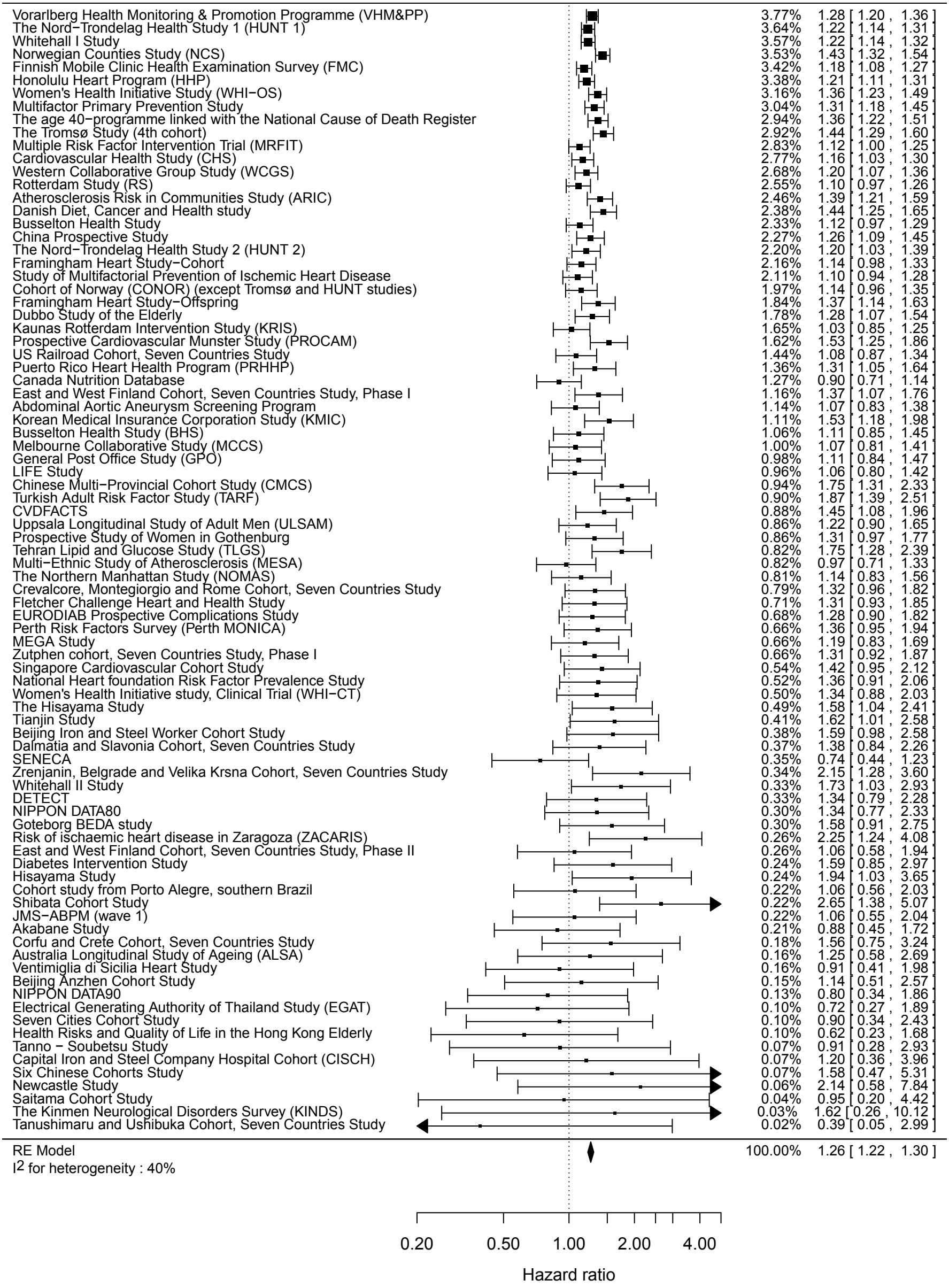


H. Adjusted for confounders and blood pressure, cholesterol, glucose

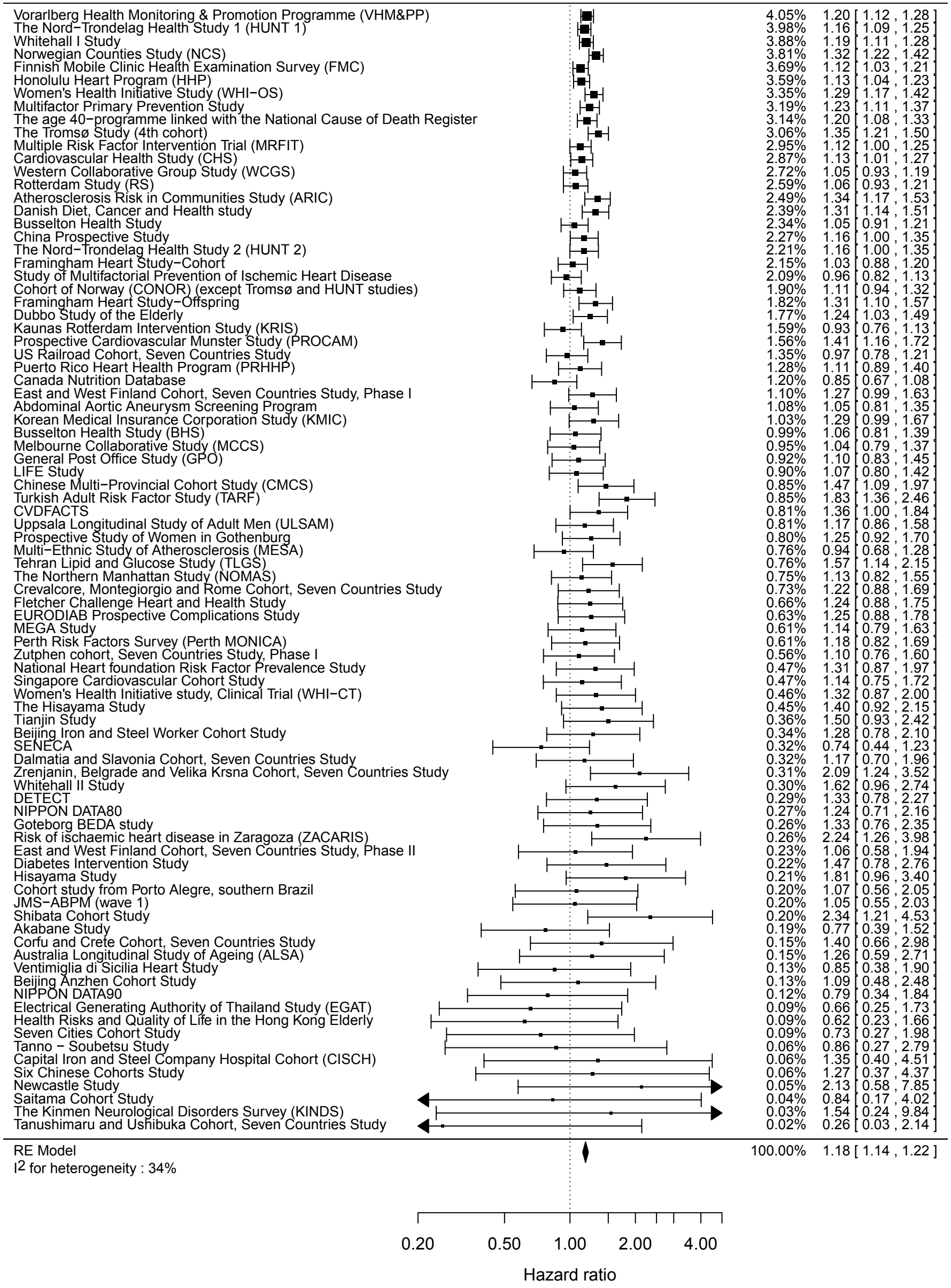


Webfigure 4: Cohort-specific hazard ratios (HRs) of CHD for overweight vs. normal weight. (Some cohorts that had BMI continuously did not have sufficient events in this BMI range for categorical analysis.)

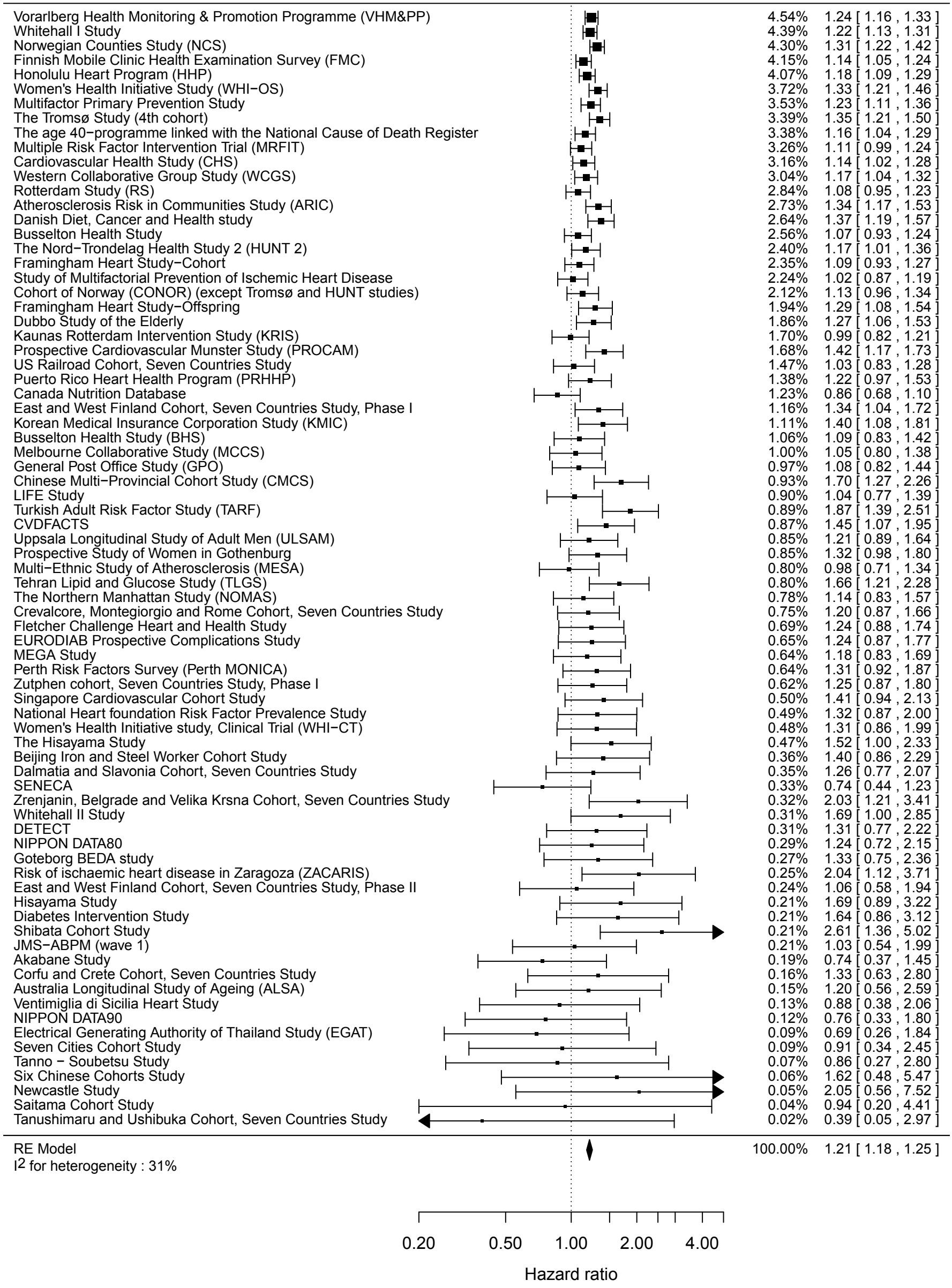
A. Adjusted for confounders



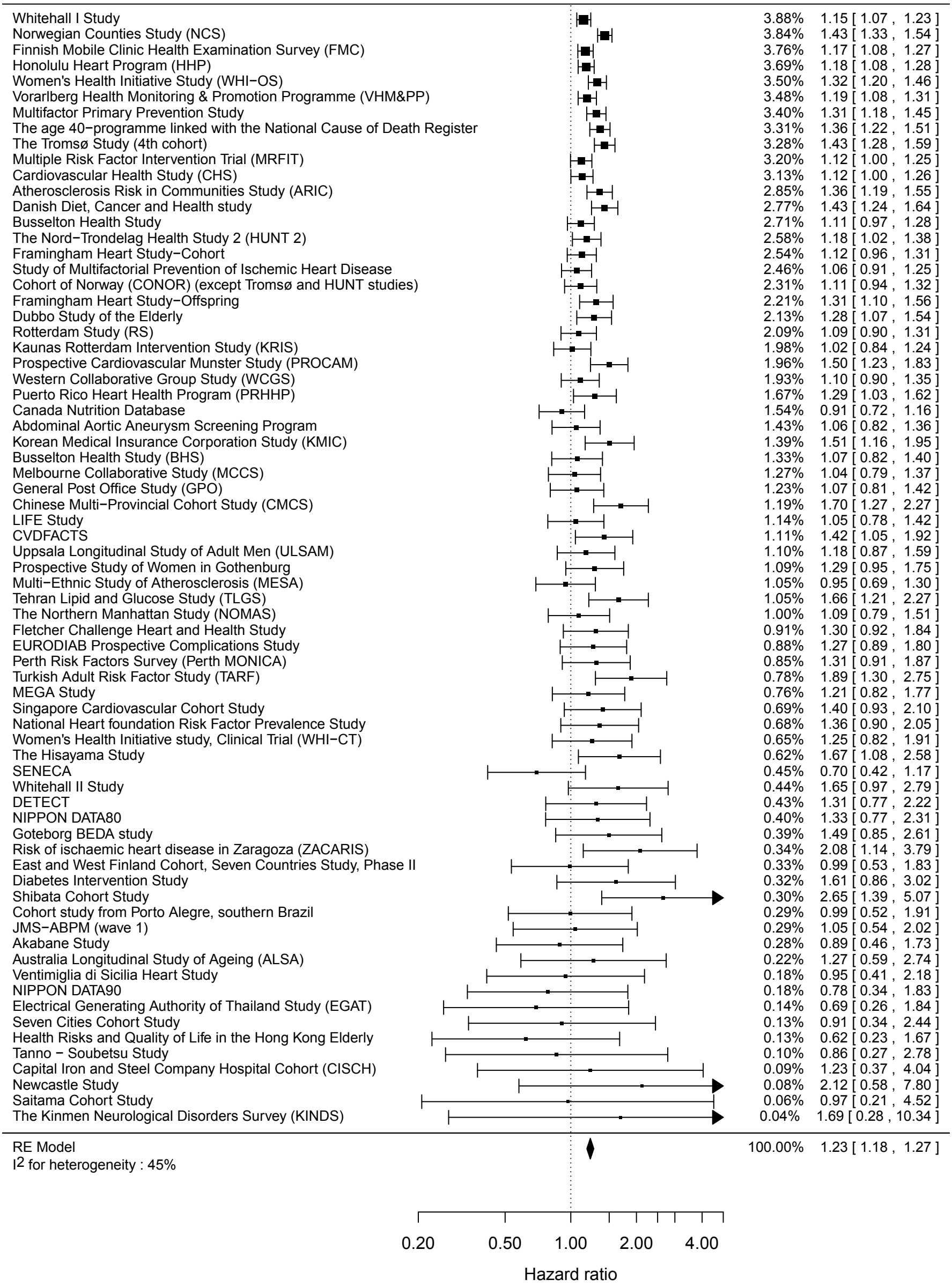
B. Adjusted for confounders and blood pressure



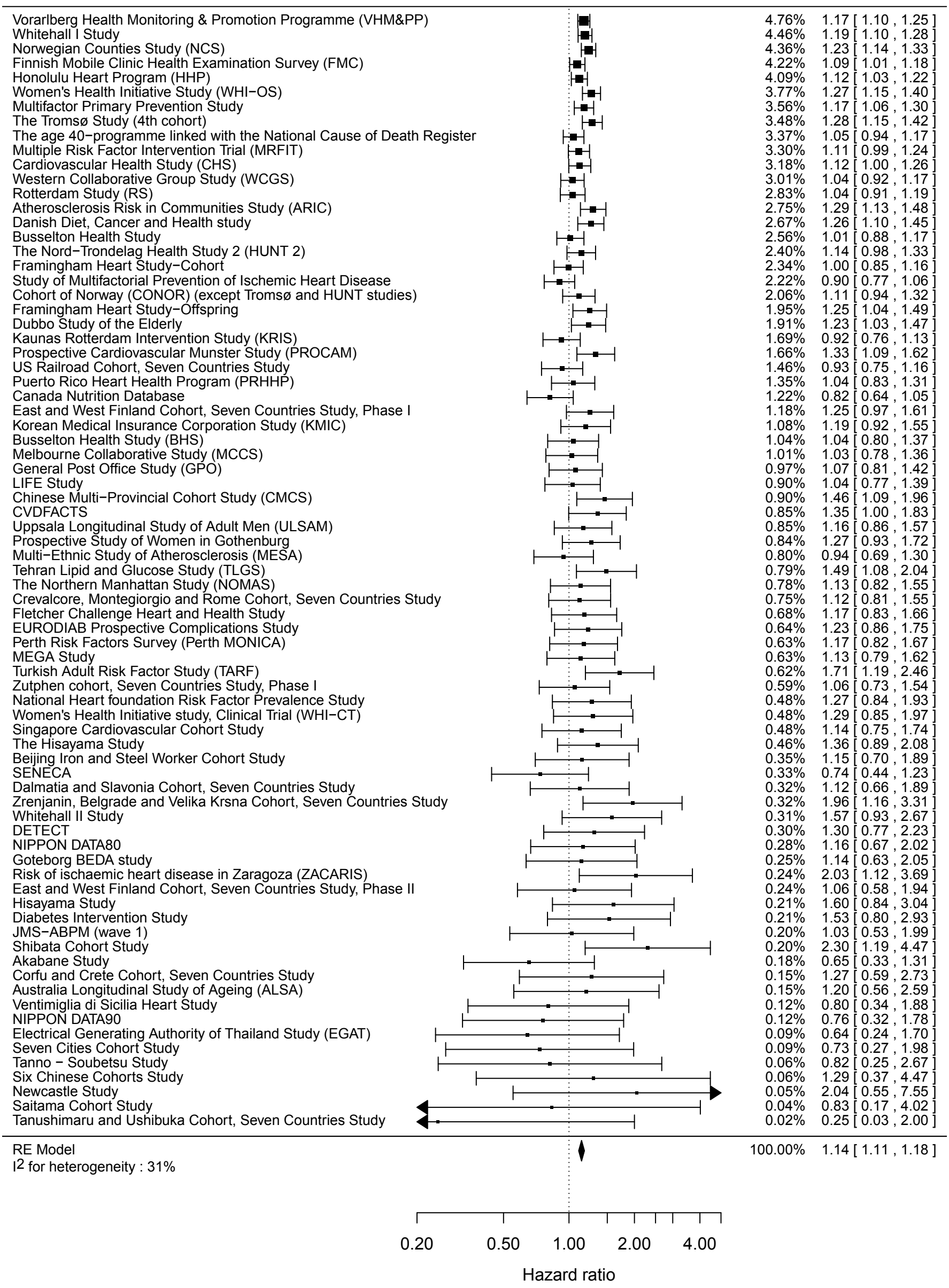
C. Adjusted for confounders and cholesterol



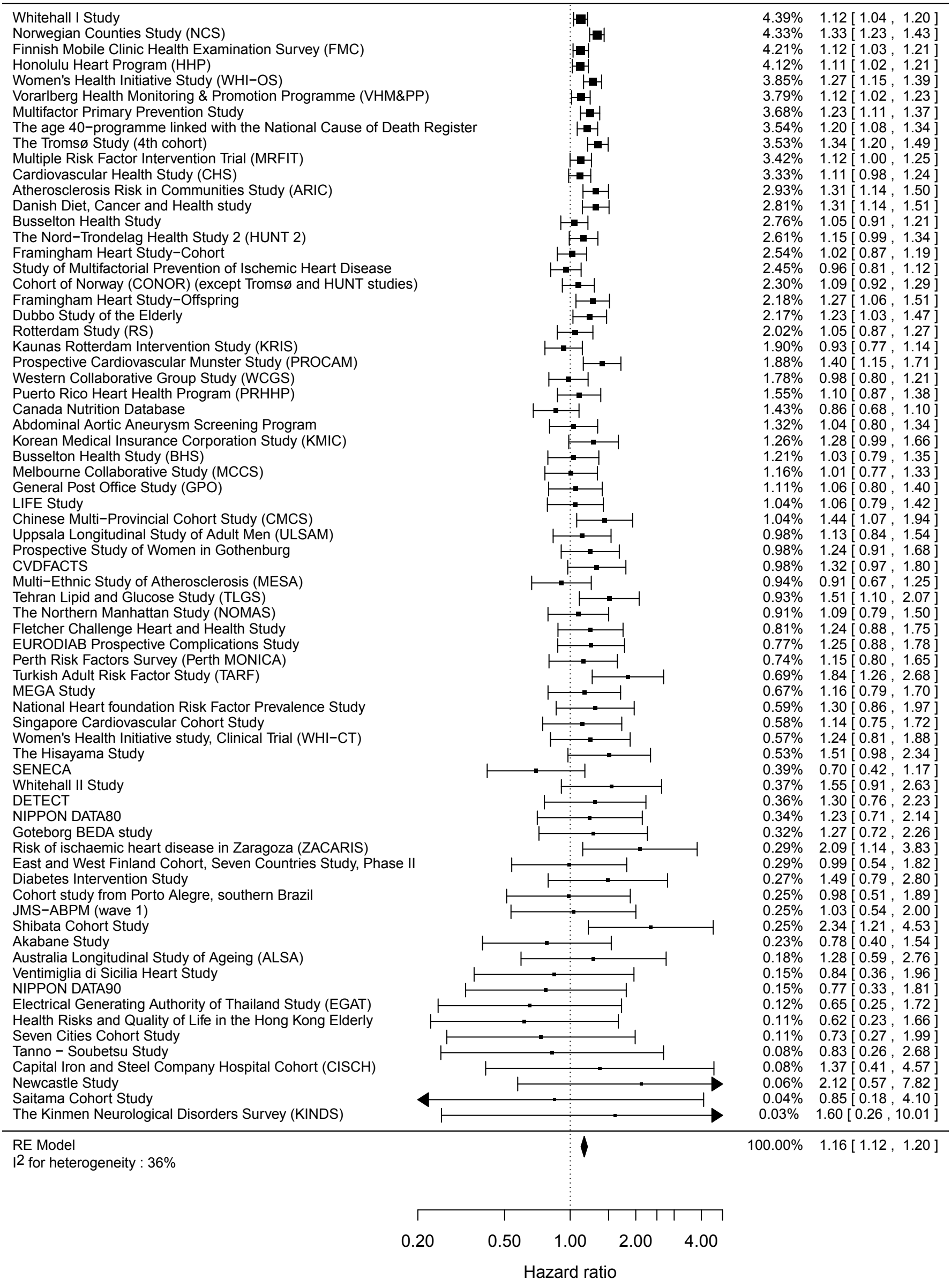
D. Adjusted for confounders and glucose



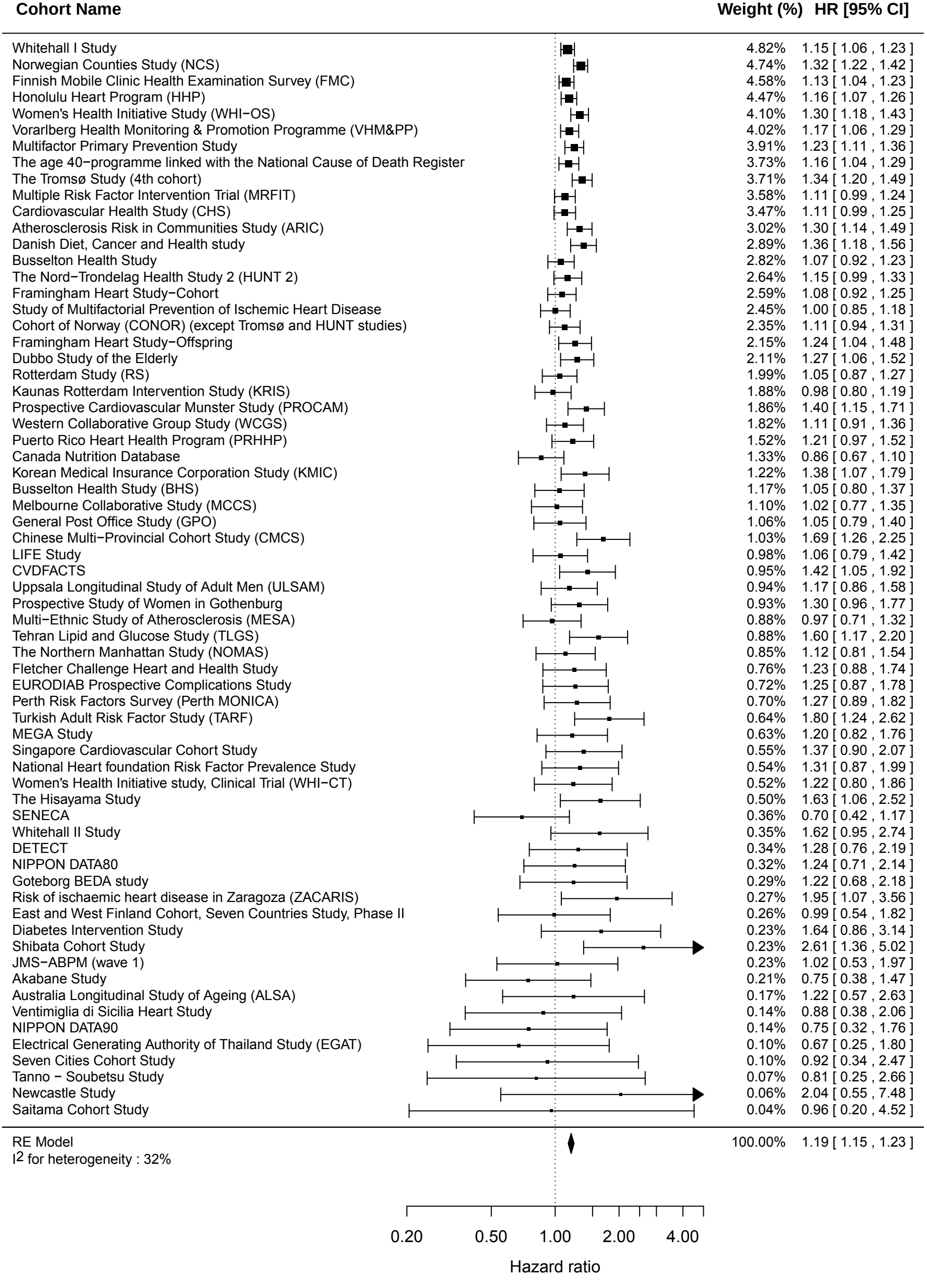
E. Adjusted for confounders and blood pressure, cholesterol



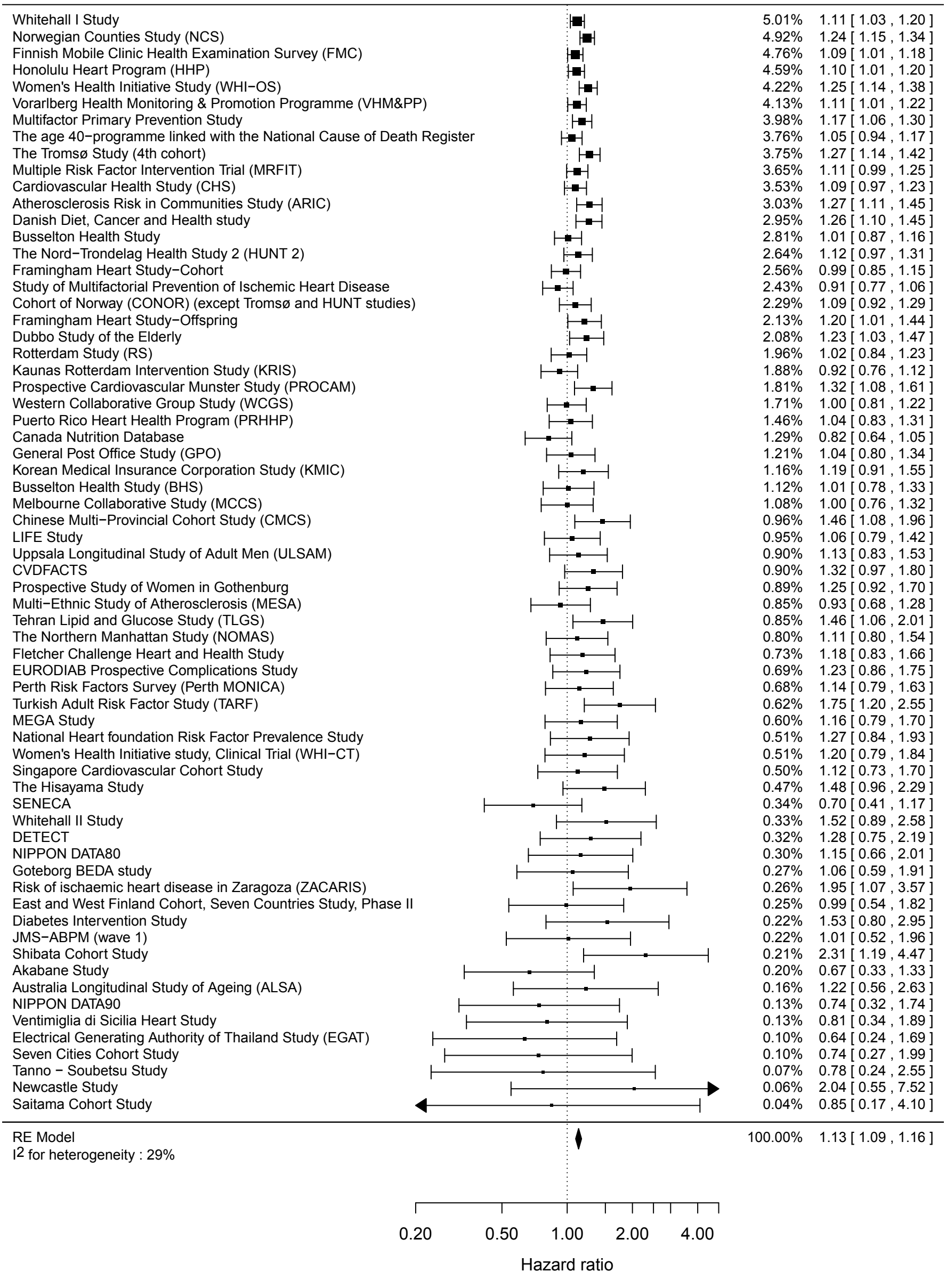
F. Adjusted for confounders and blood pressure, glucose



G. Adjusted for confounders and cholesterol, glucose

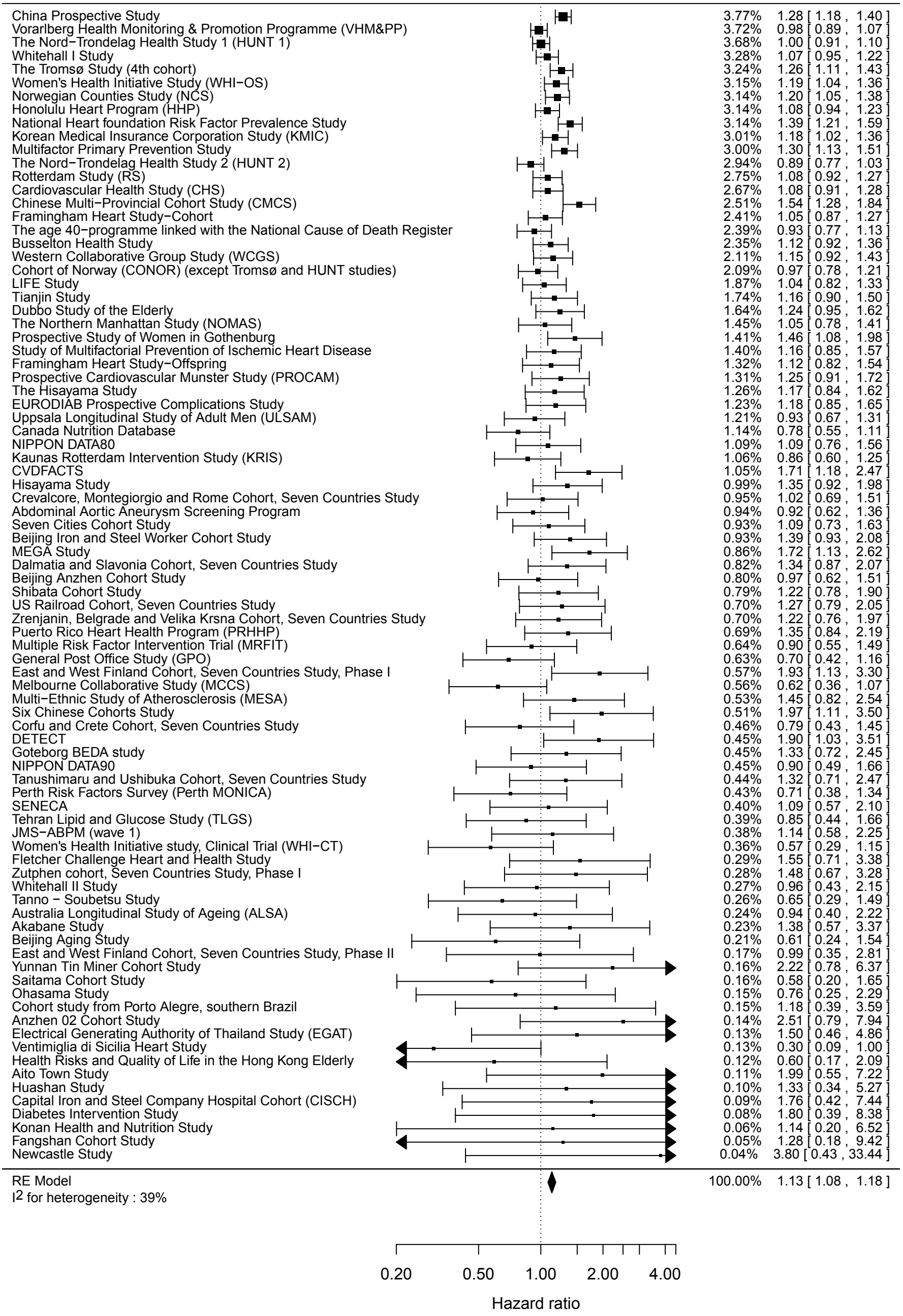


H. Adjusted for confounders and blood pressure, cholesterol, glucose

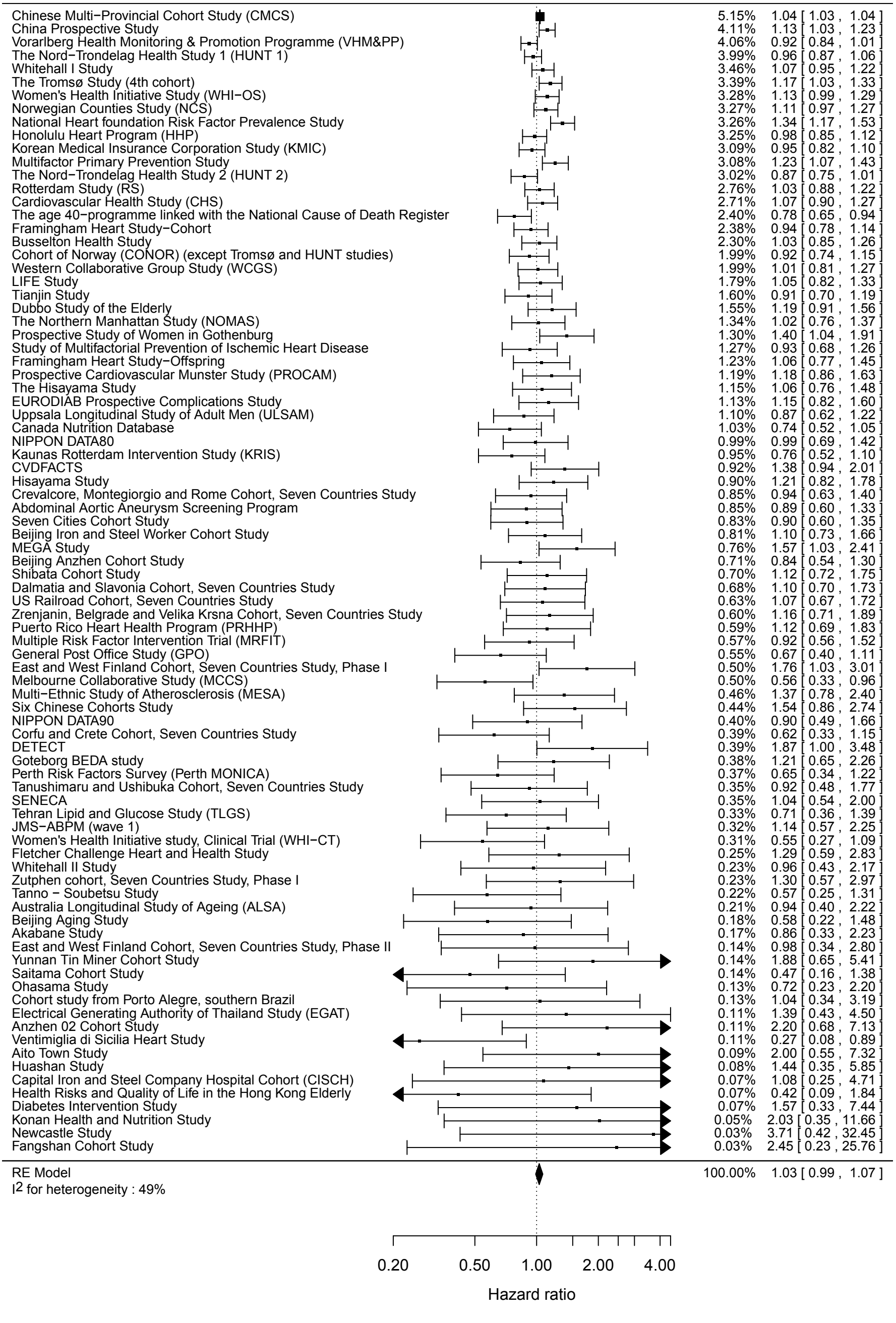


Webfigure 5: Cohort-specific hazard ratios (HRs) of stroke for overweight vs. normal weight. (Some cohorts that had BMI continuously did not have sufficient events in this BMI range for categorical analysis.)

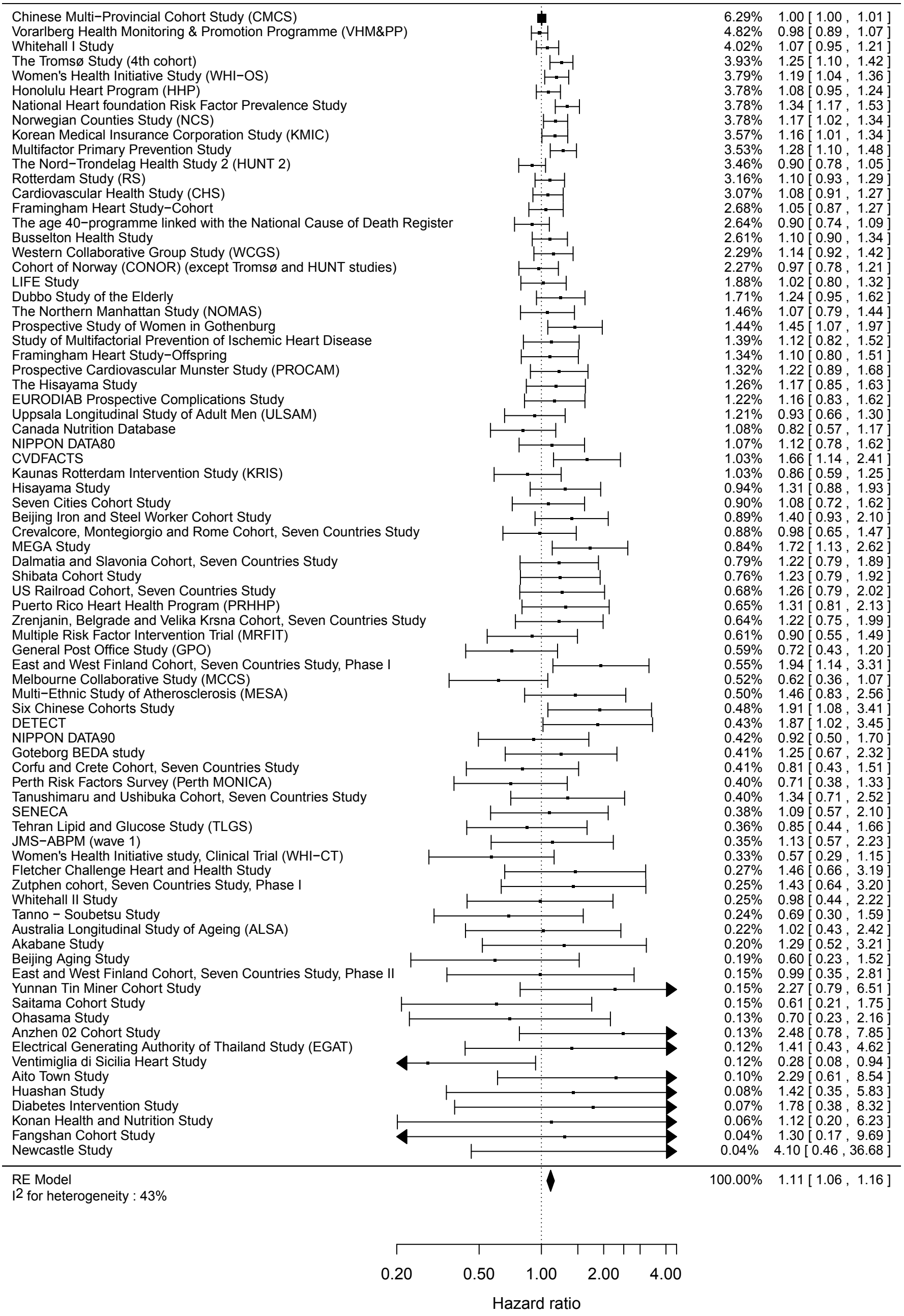
A. Adjusted for confounders



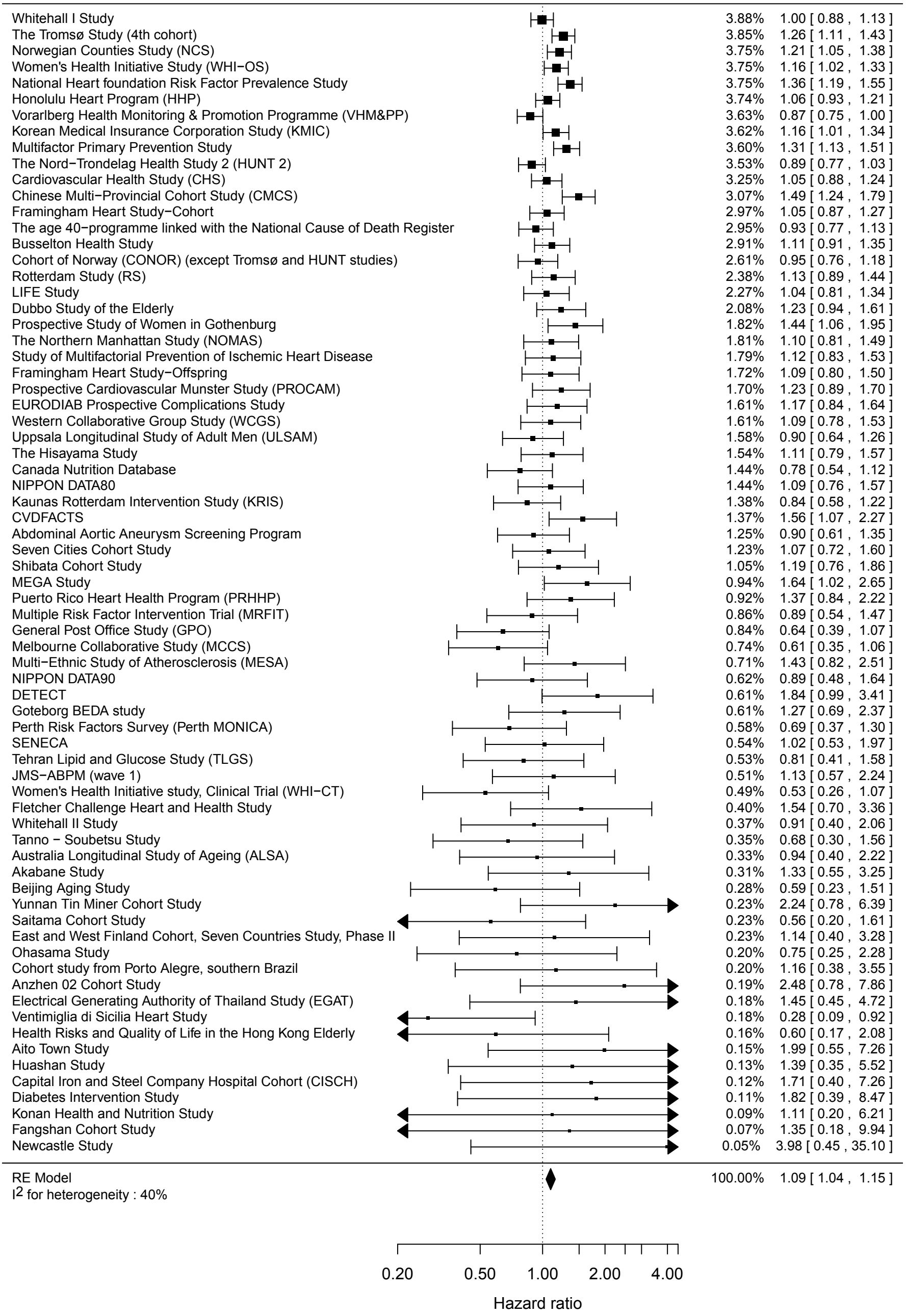
B. Adjusted for confounders and blood pressure



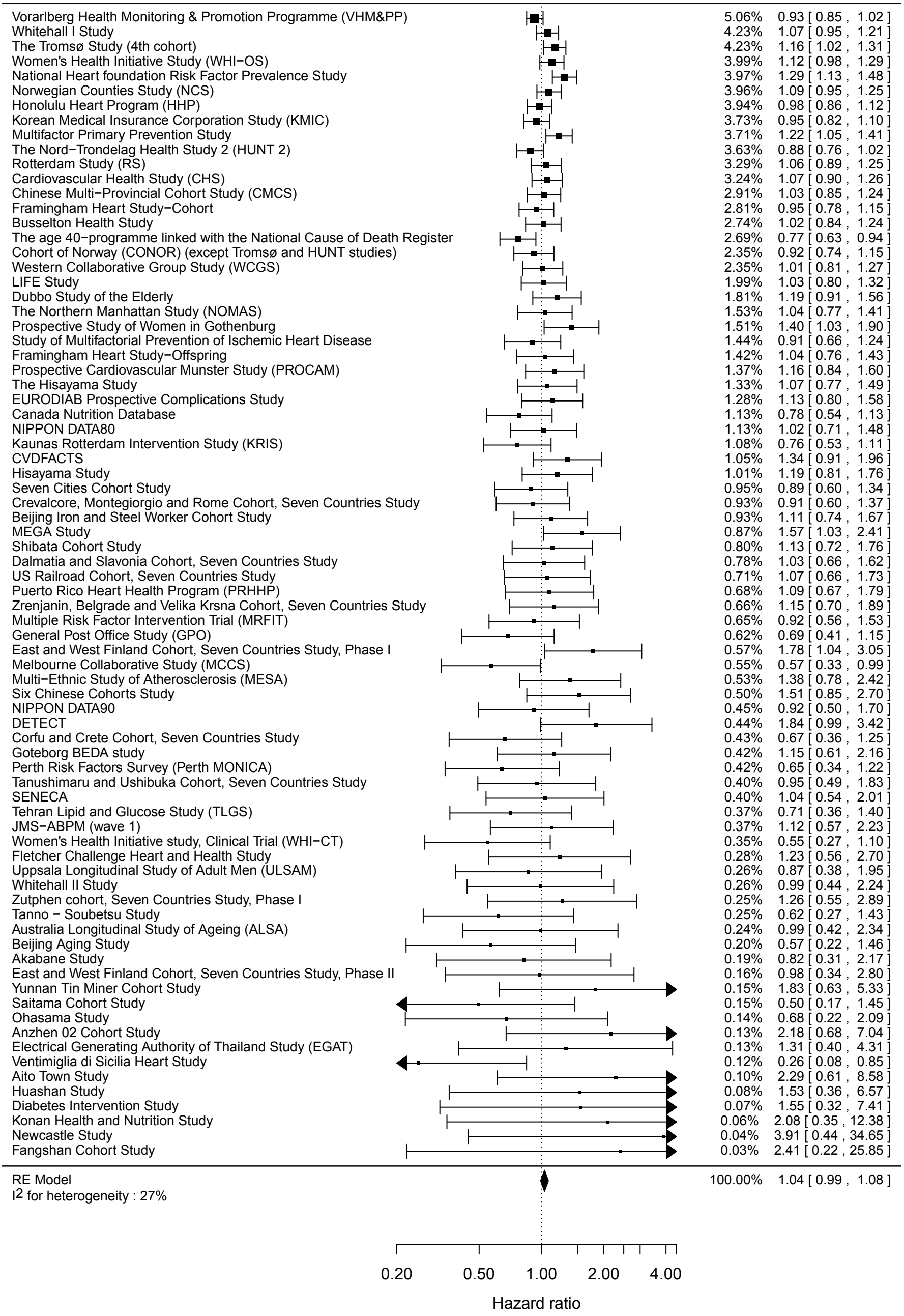
C. Adjusted for confounders and cholesterol



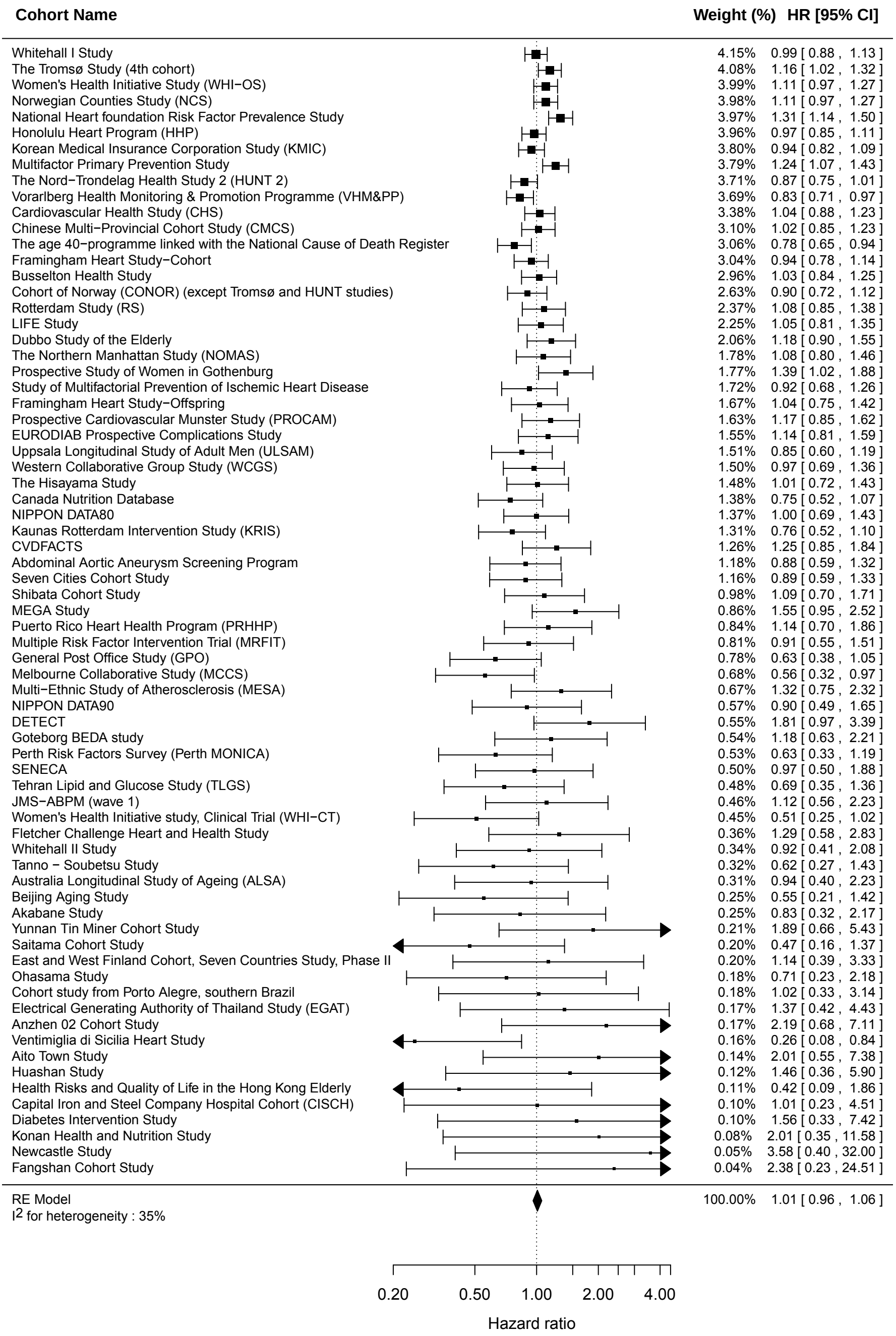
D. Adjusted for confounders and glucose



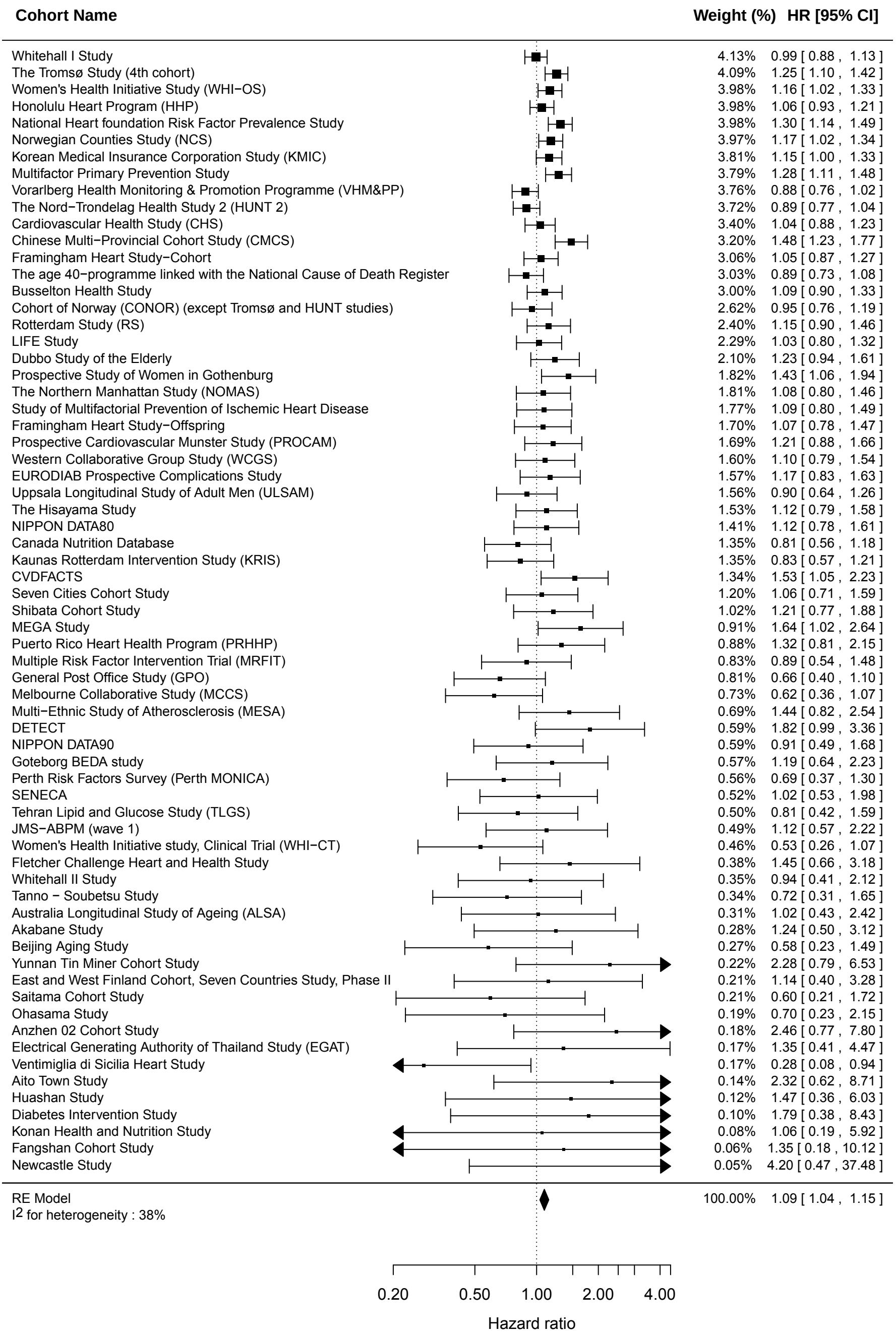
E. Adjusted for confounders and blood pressure, cholesterol



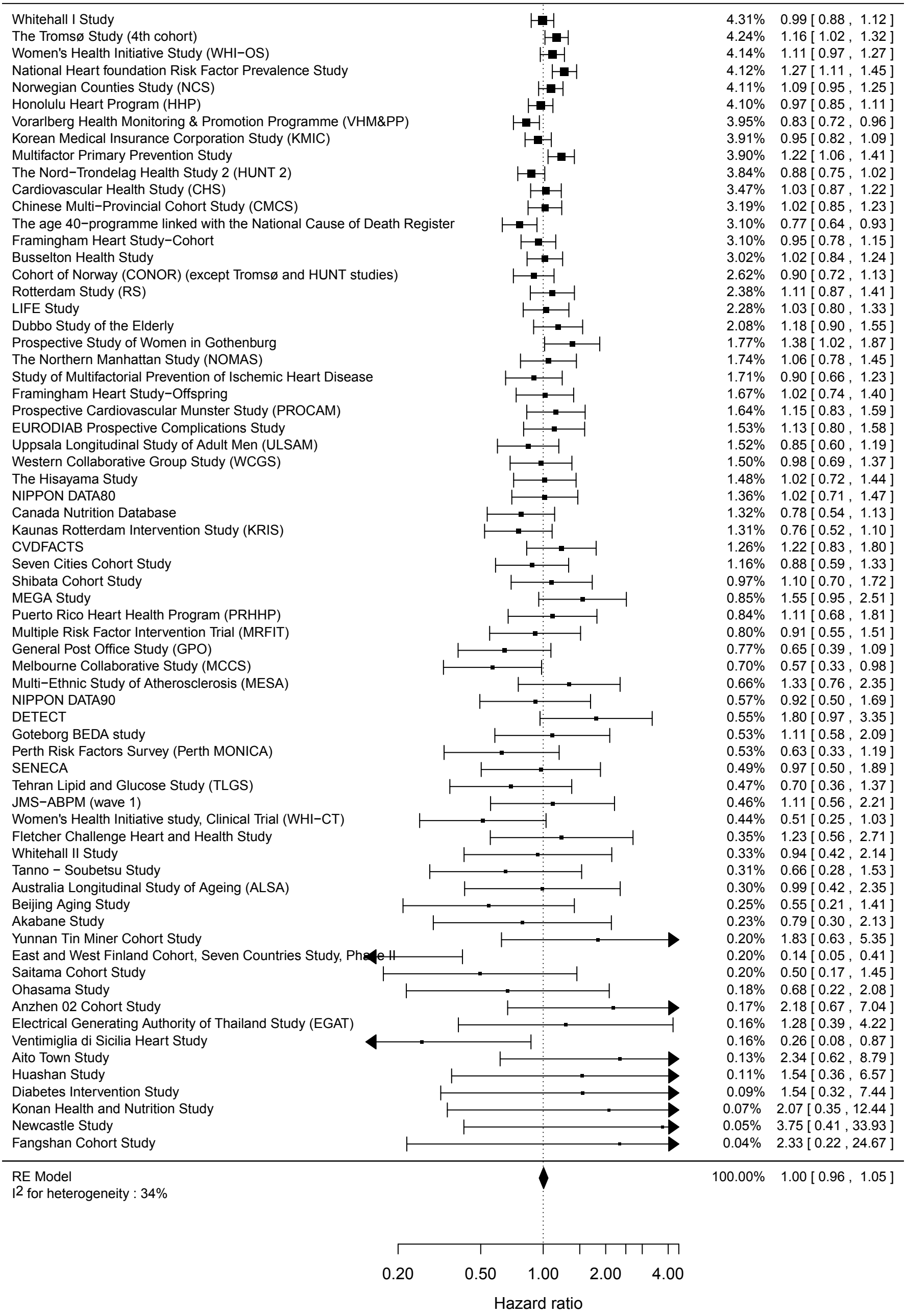
F. Adjusted for confounders and blood pressure, glucose



G. Adjusted for confounders and cholesterol, glucose

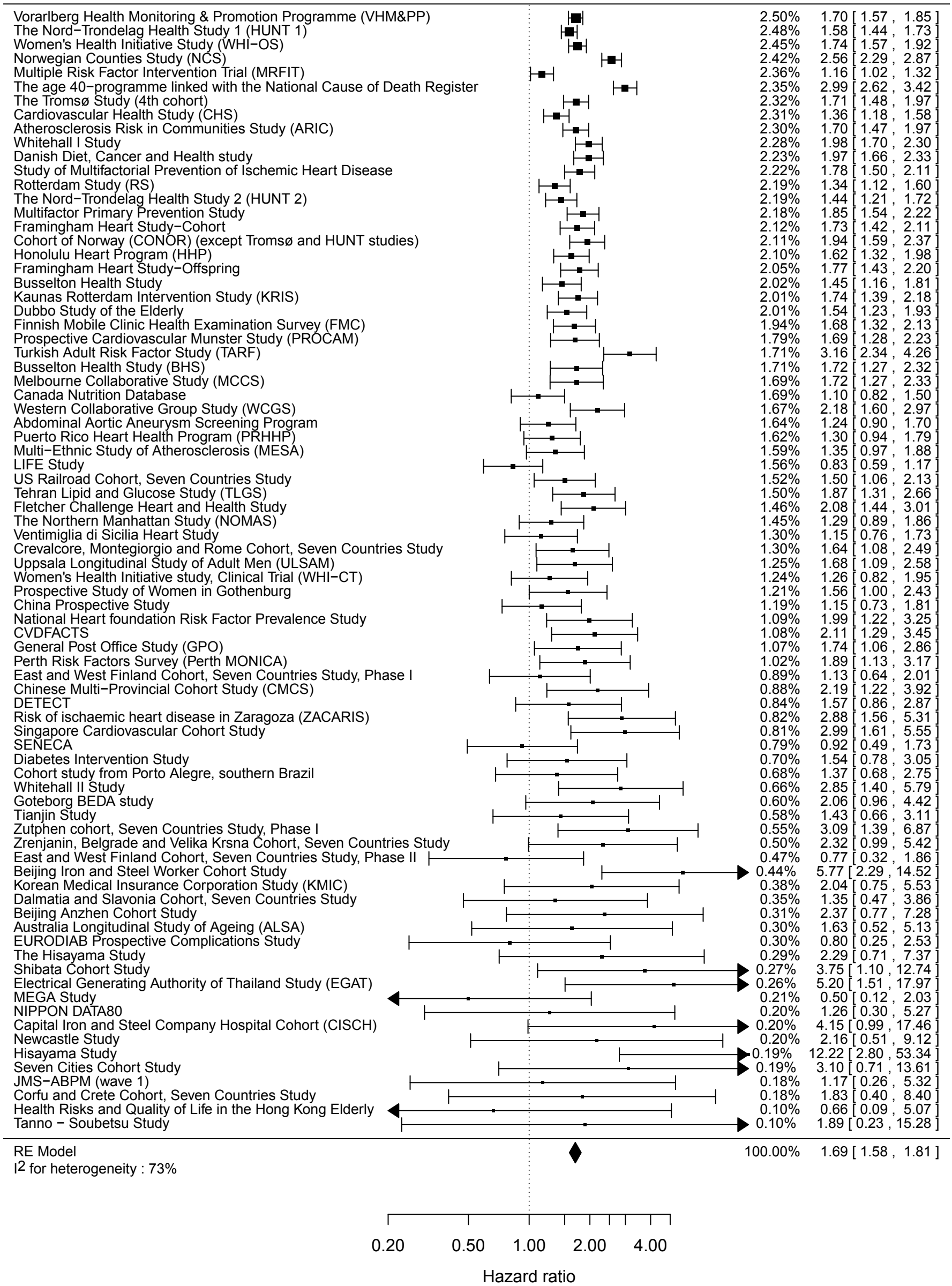


H. Adjusted for confounders and blood pressure, cholesterol, glucose

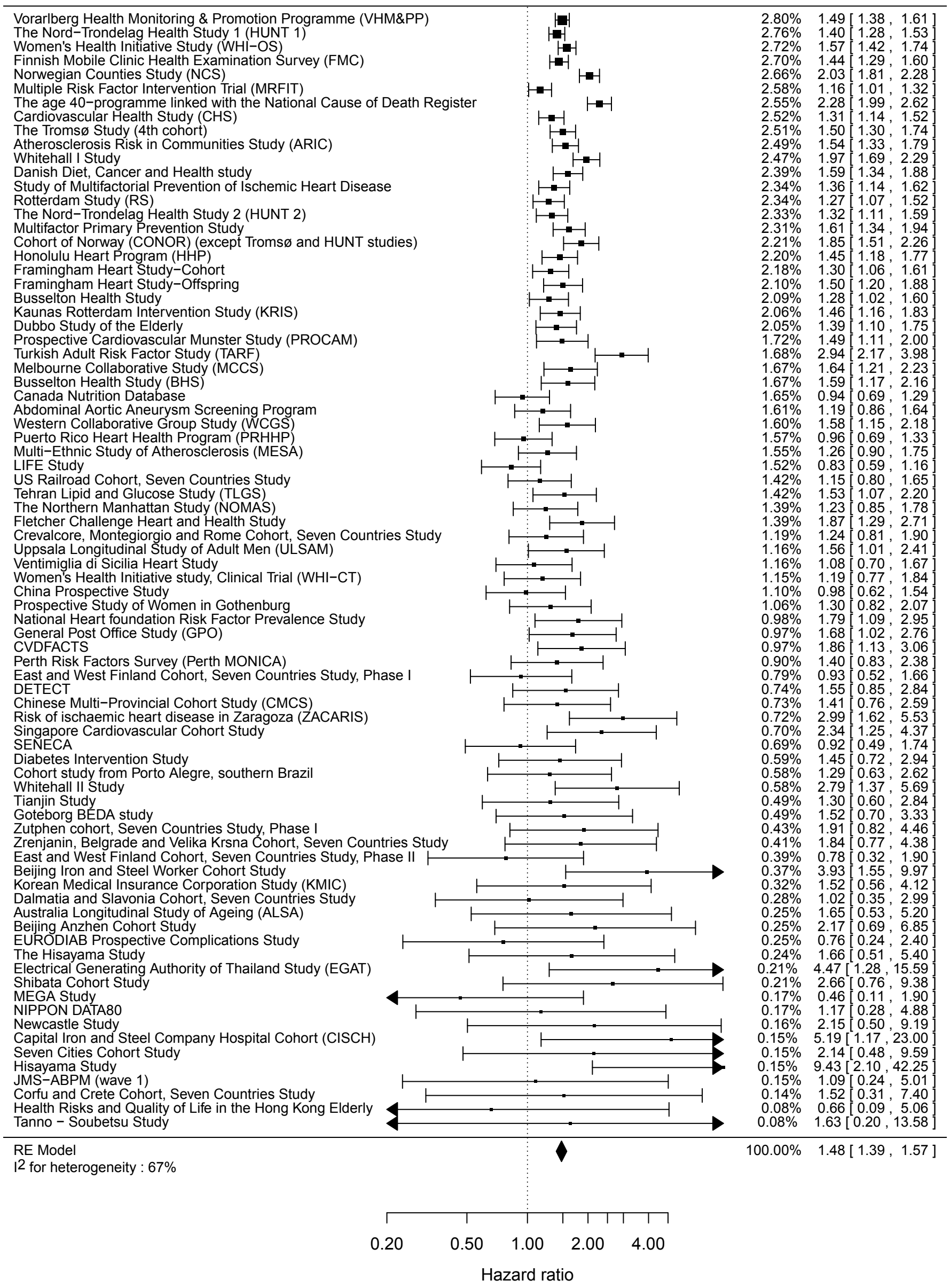


Webfigure 6: Cohort-specific hazard ratios (HRs) of CHD for obesity vs. normal weight. (Some cohorts that had BMI continuously did not have sufficient events in this BMI range for categorical analysis.)

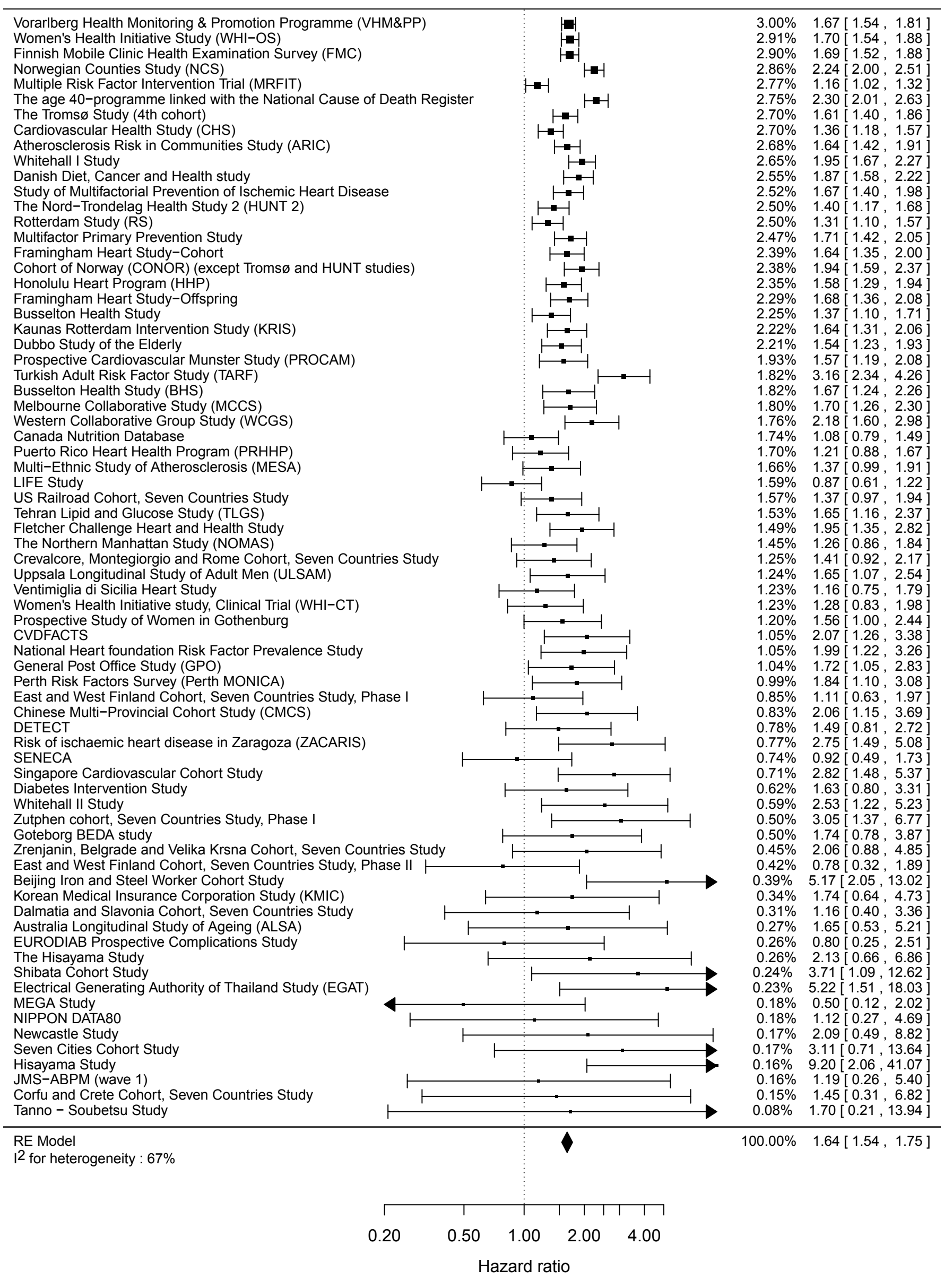
A. Adjusted for confounders



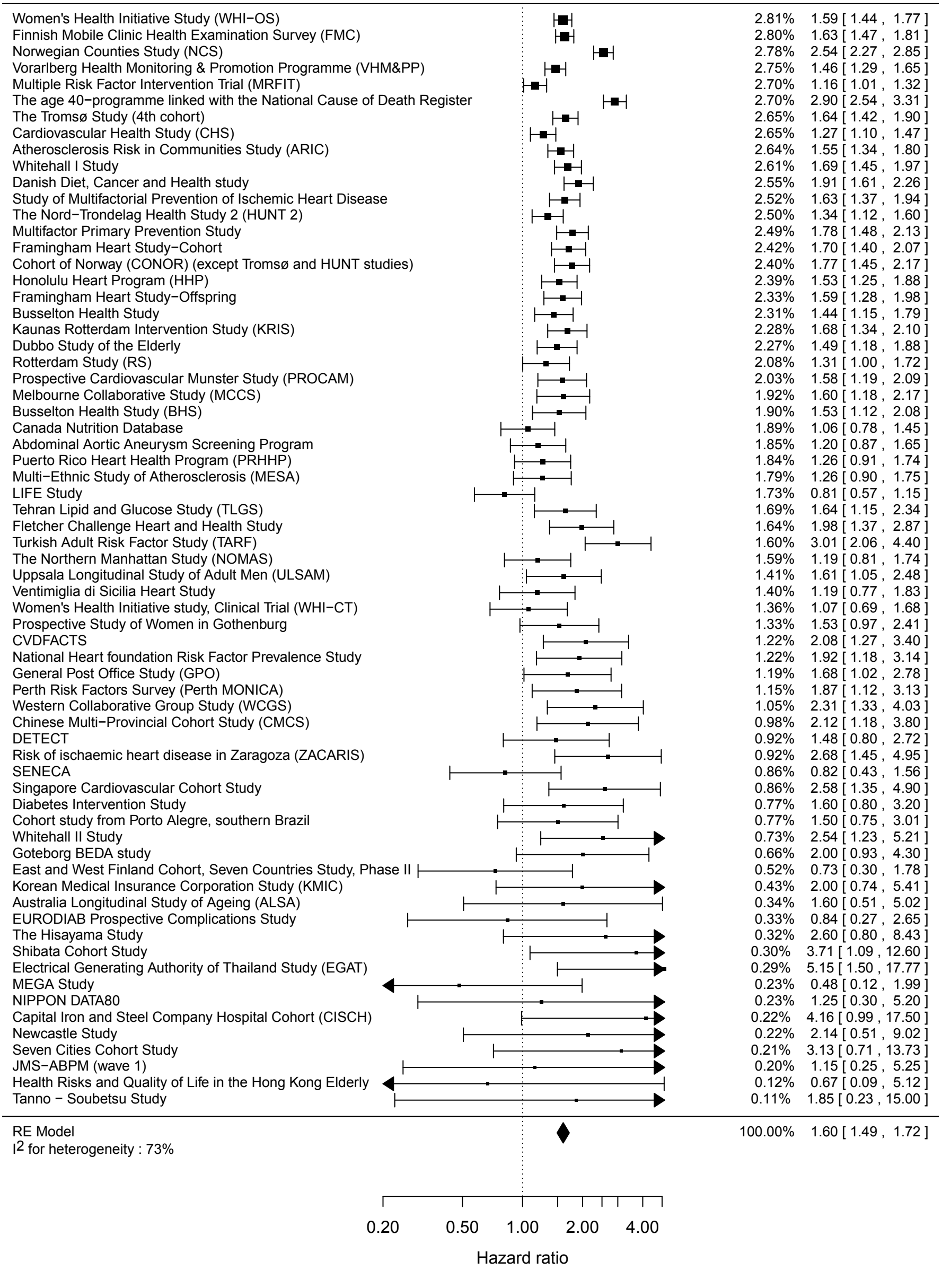
B. Adjusted for confounders and blood pressure



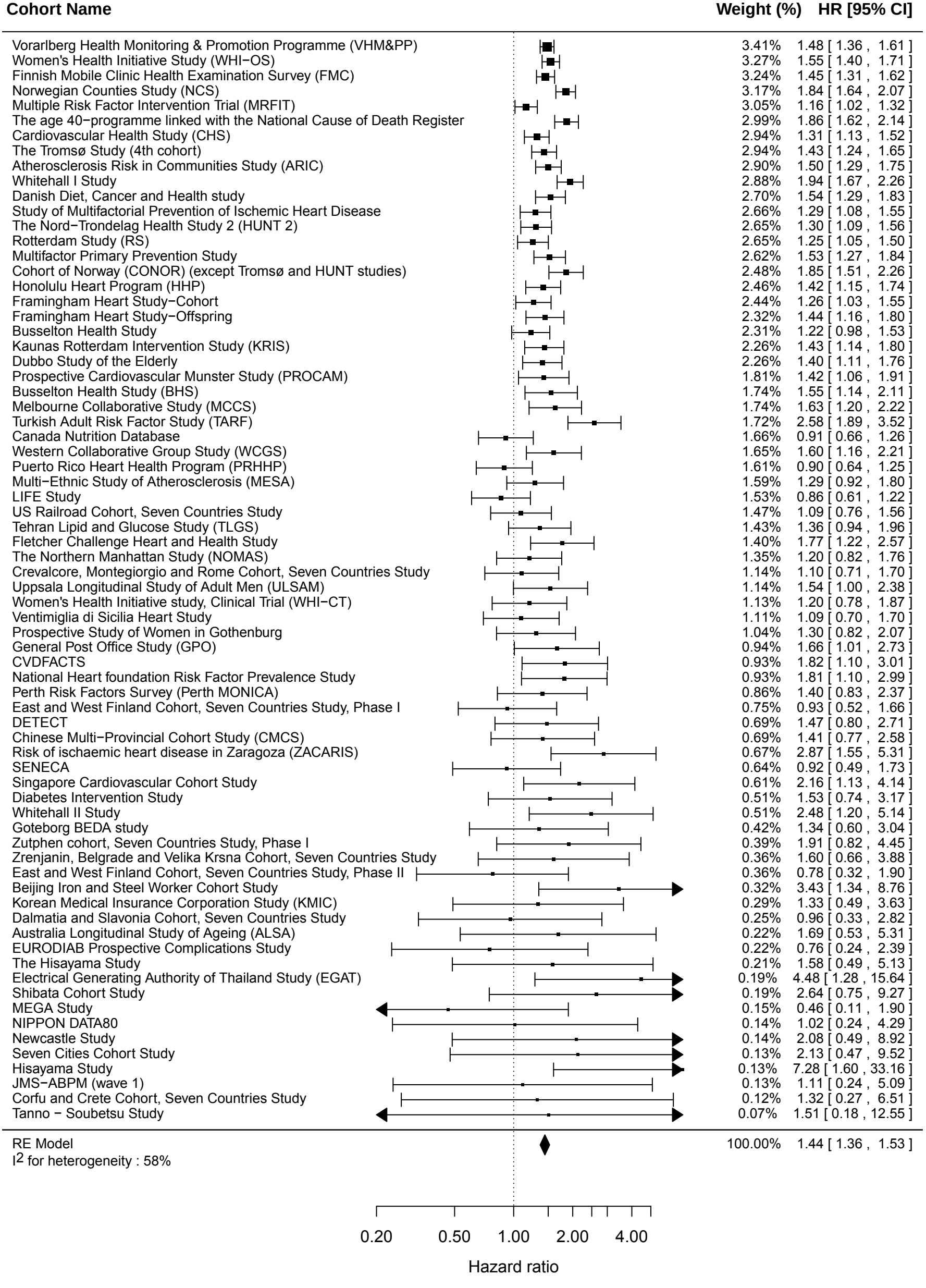
C. Adjusted for confounders and cholesterol



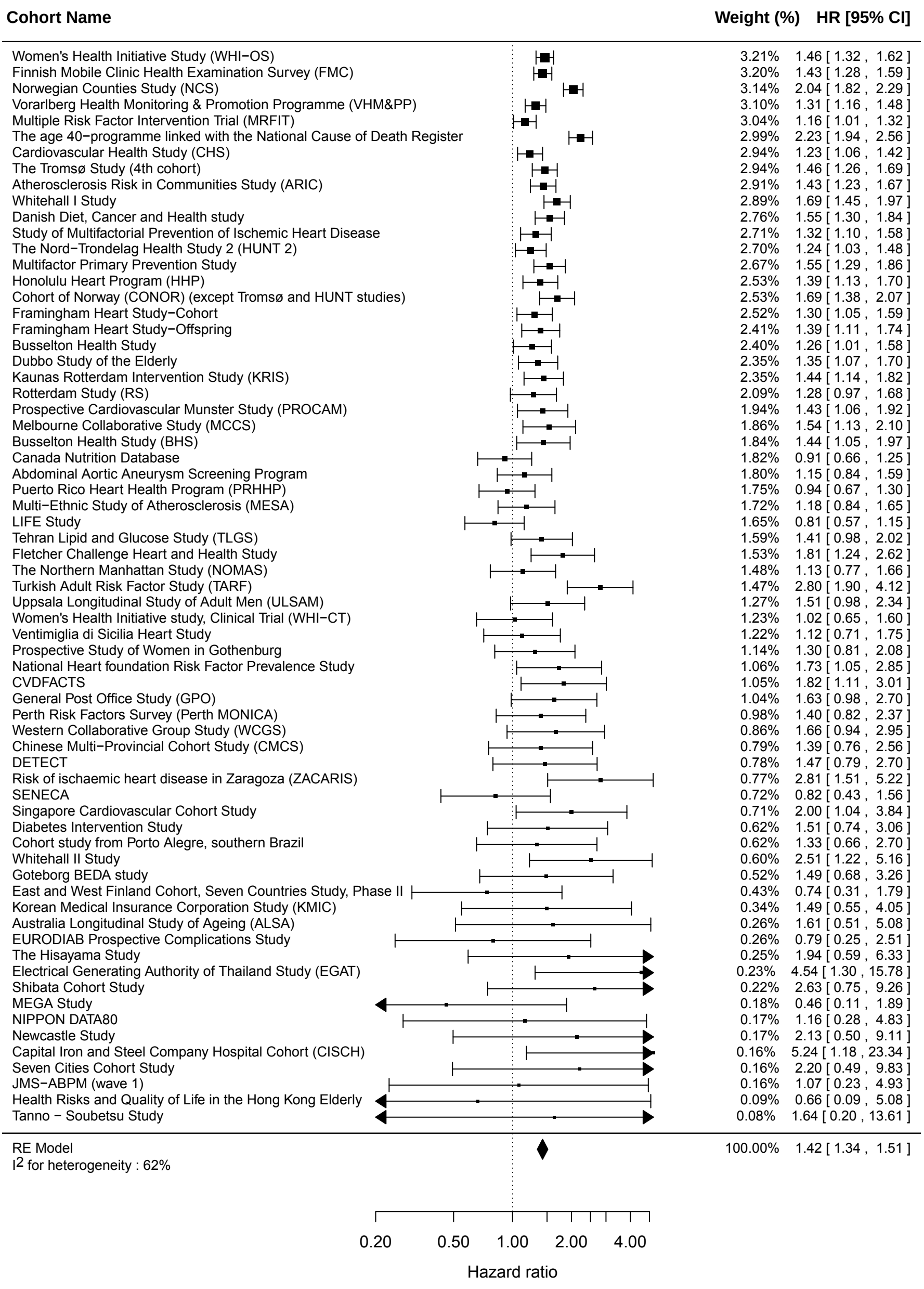
D. Adjusted for confounders and glucose



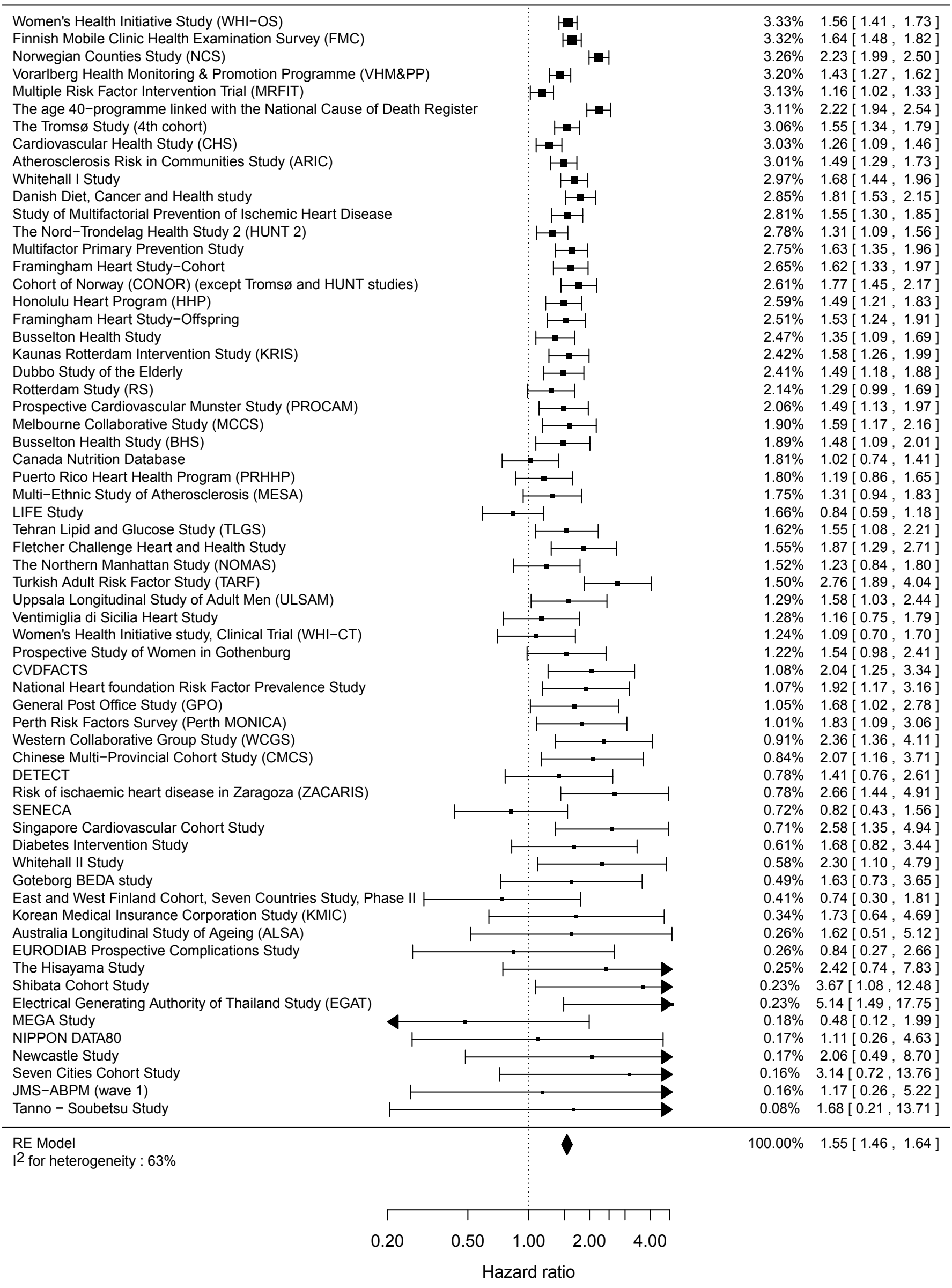
E. Adjusted for confounders and blood pressure, cholesterol



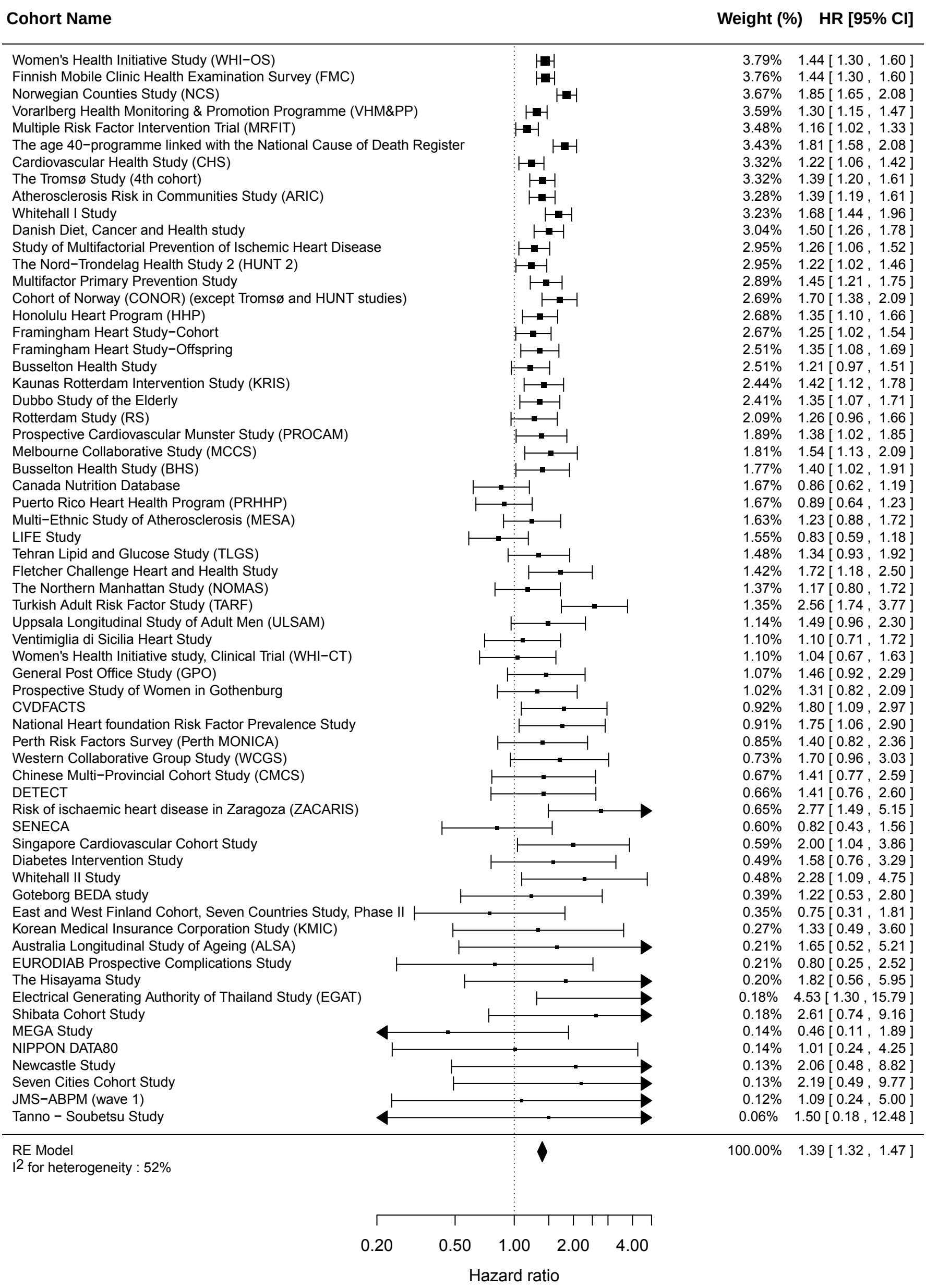
F. Adjusted for confounders and blood pressure, glucose



G. Adjusted for confounders and cholesterol, glucose

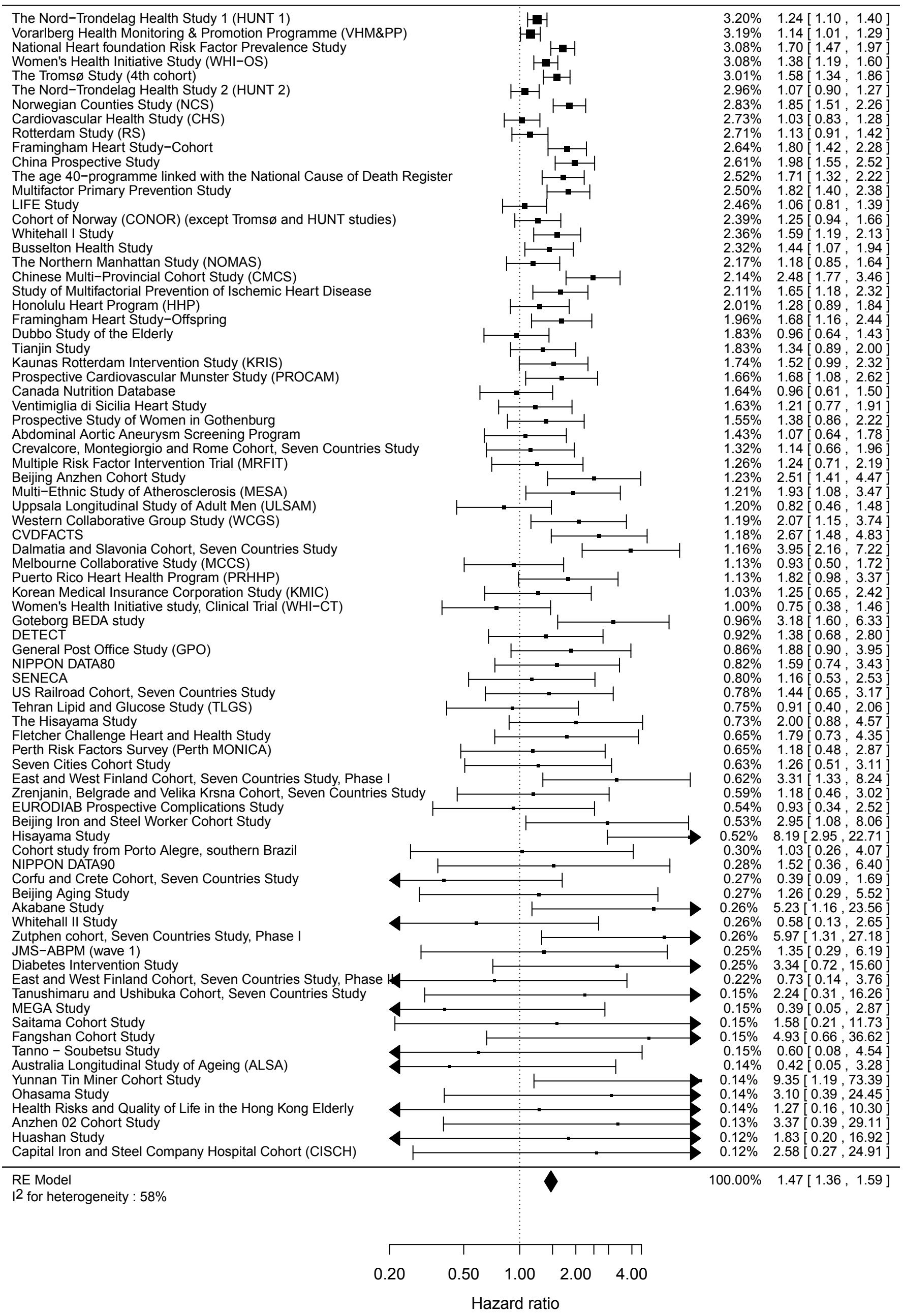


H. Adjusted for confounders and blood pressure, cholesterol, glucose

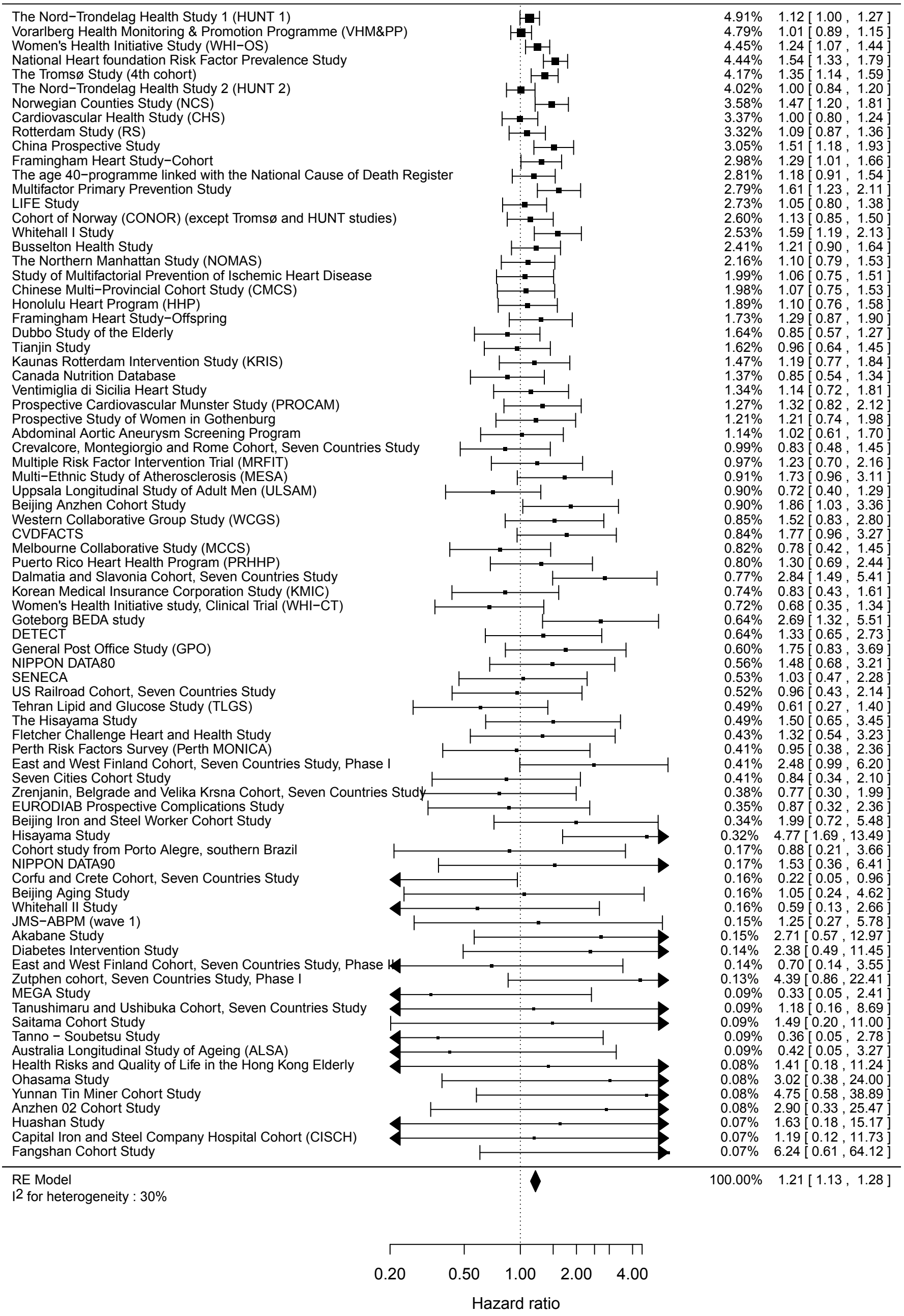


Webfigure 7: Cohort-specific hazard ratios (HRs) of stroke for obesity vs. normal weight. (Some cohorts that had BMI continuously did not have sufficient events in this BMI range for categorical analysis.)

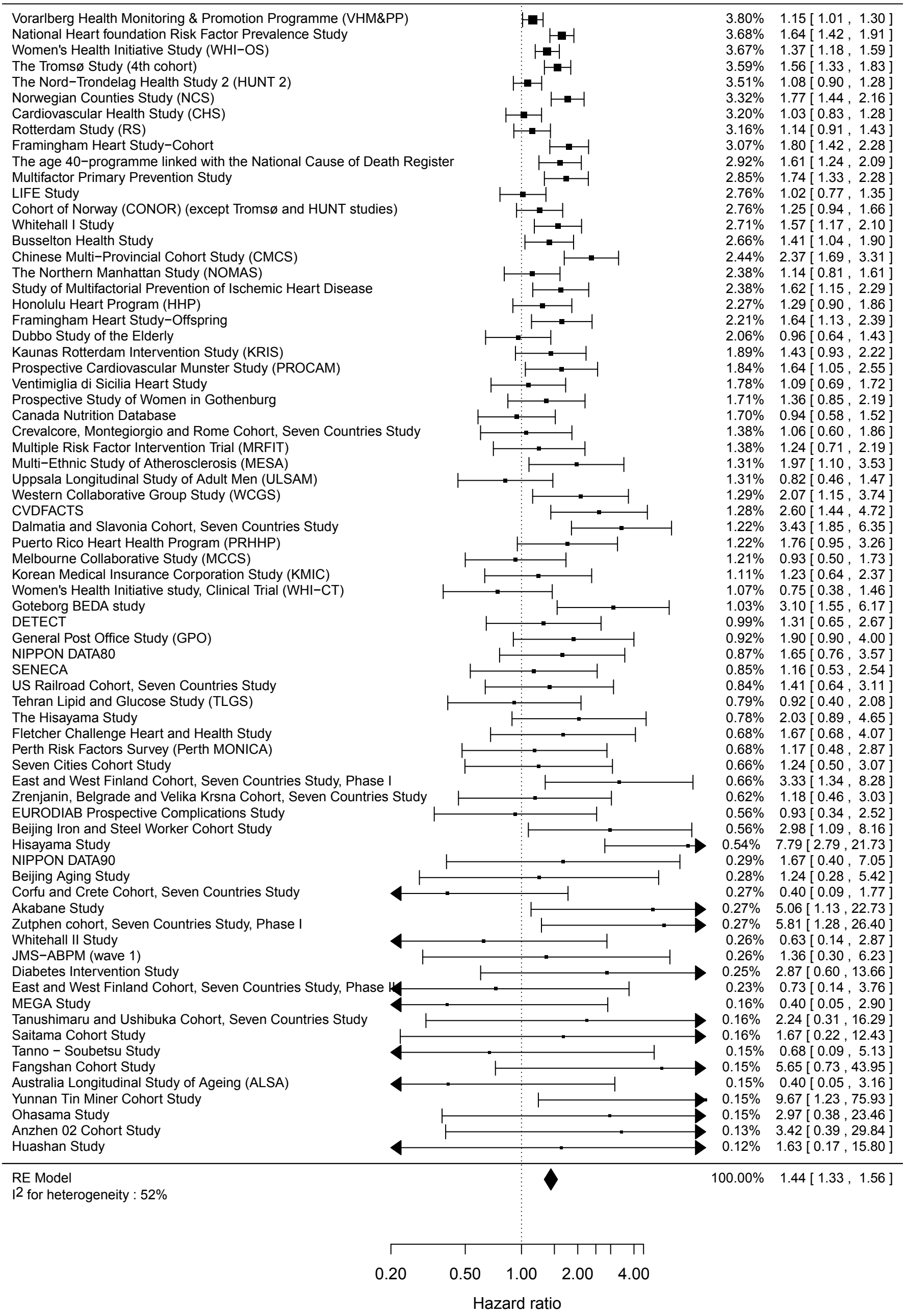
A. Adjusted for confounders



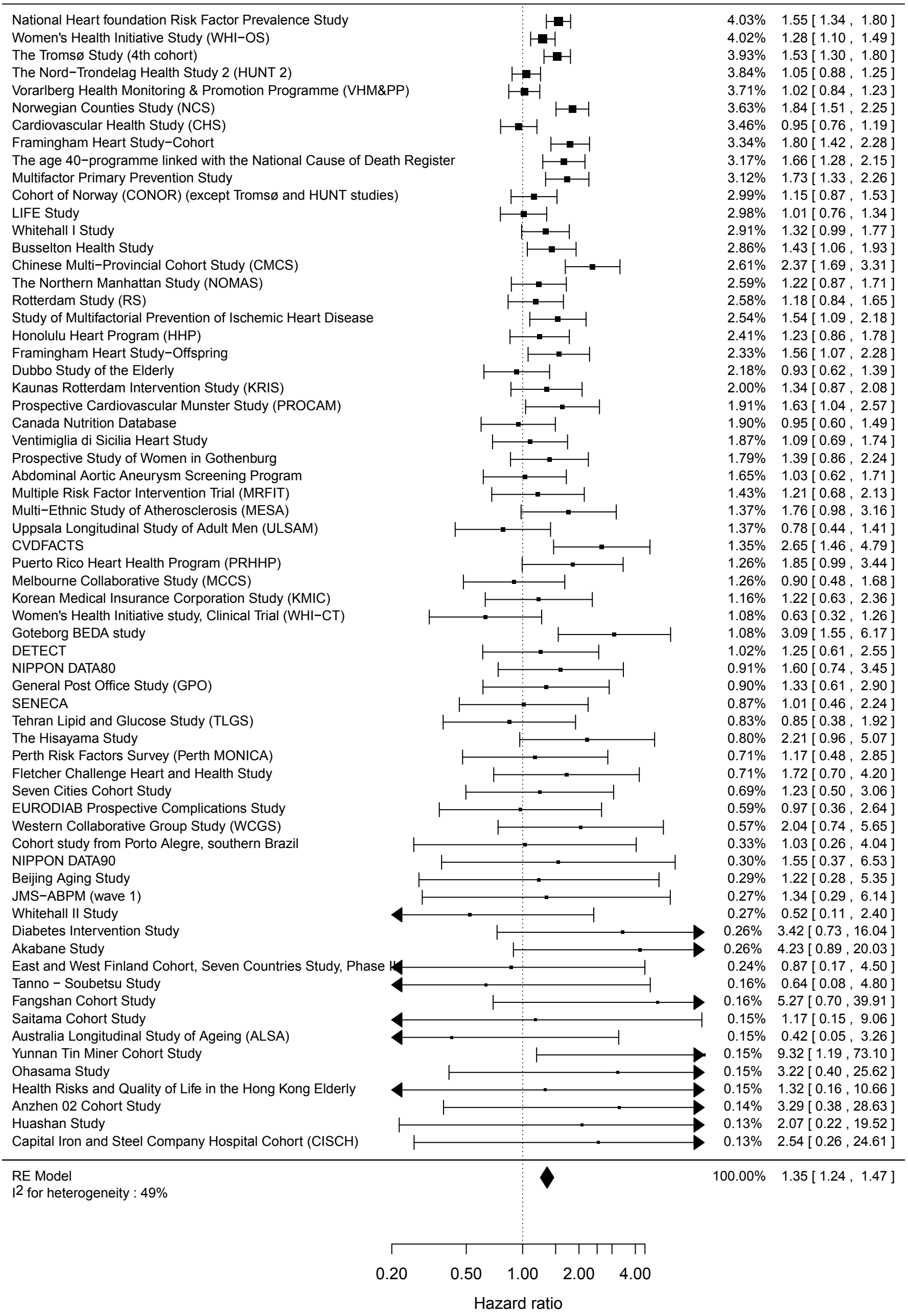
B. Adjusted for confounders and blood pressure



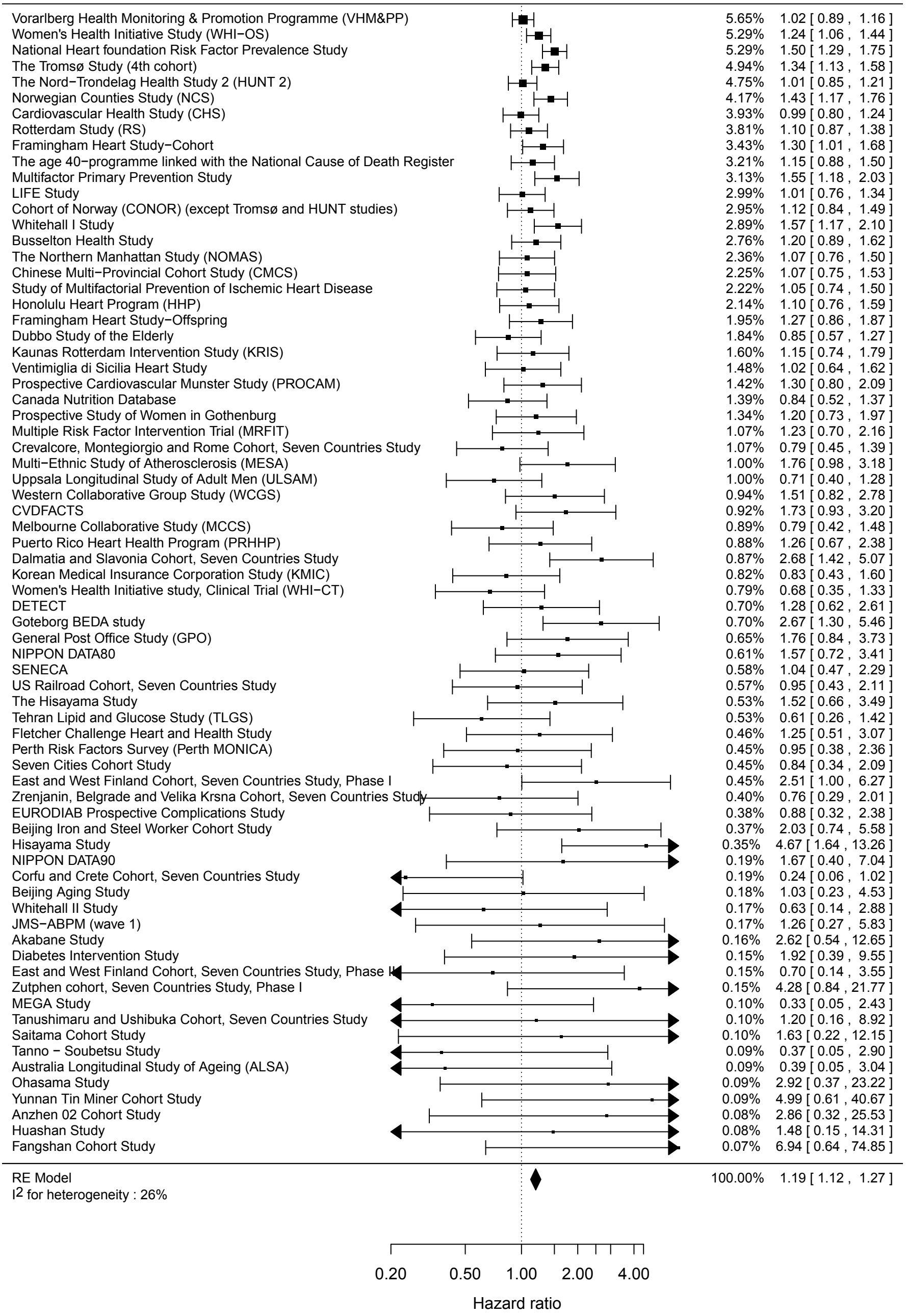
C. Adjusted for confounders and cholesterol



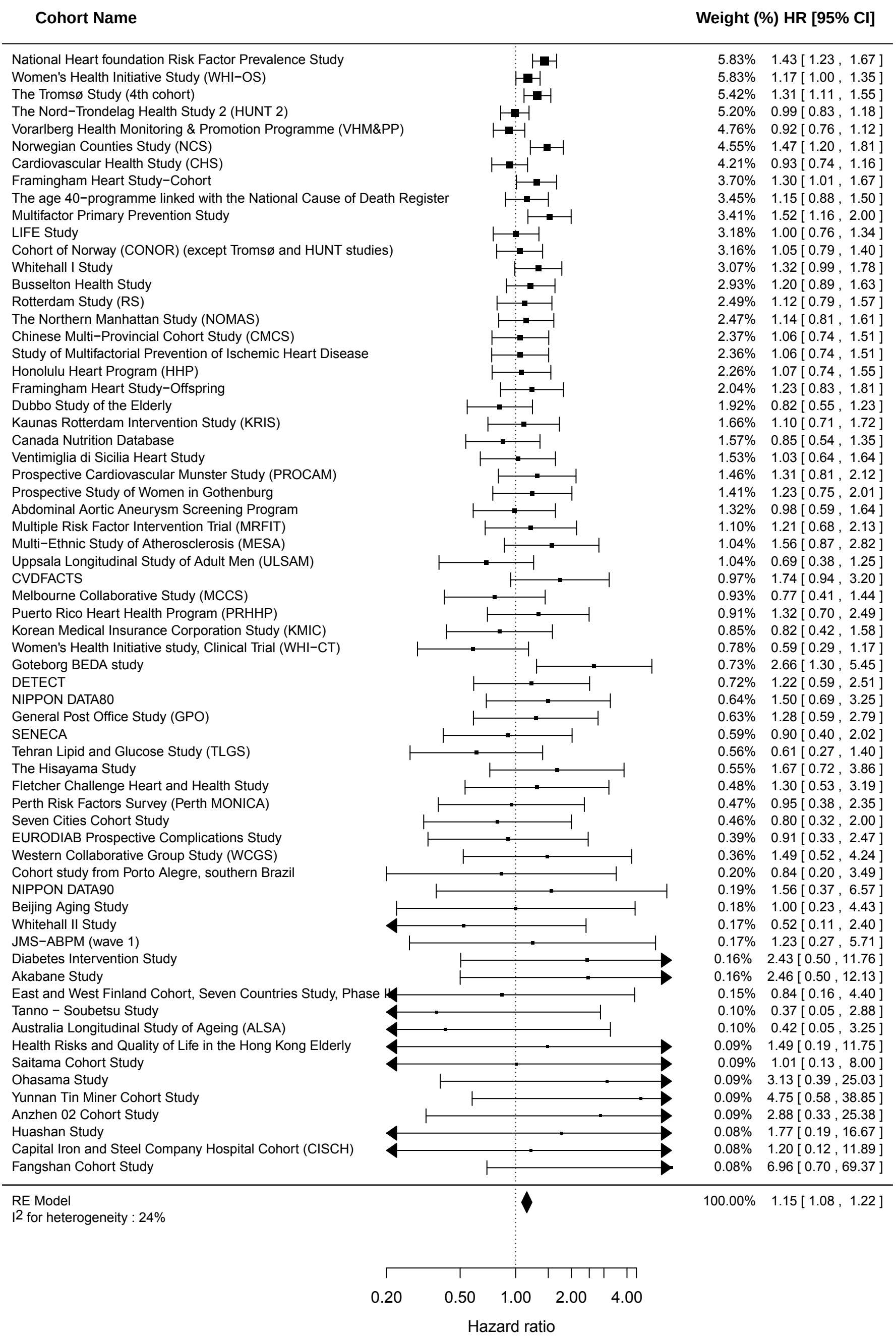
D. Adjusted for confounders and glucose



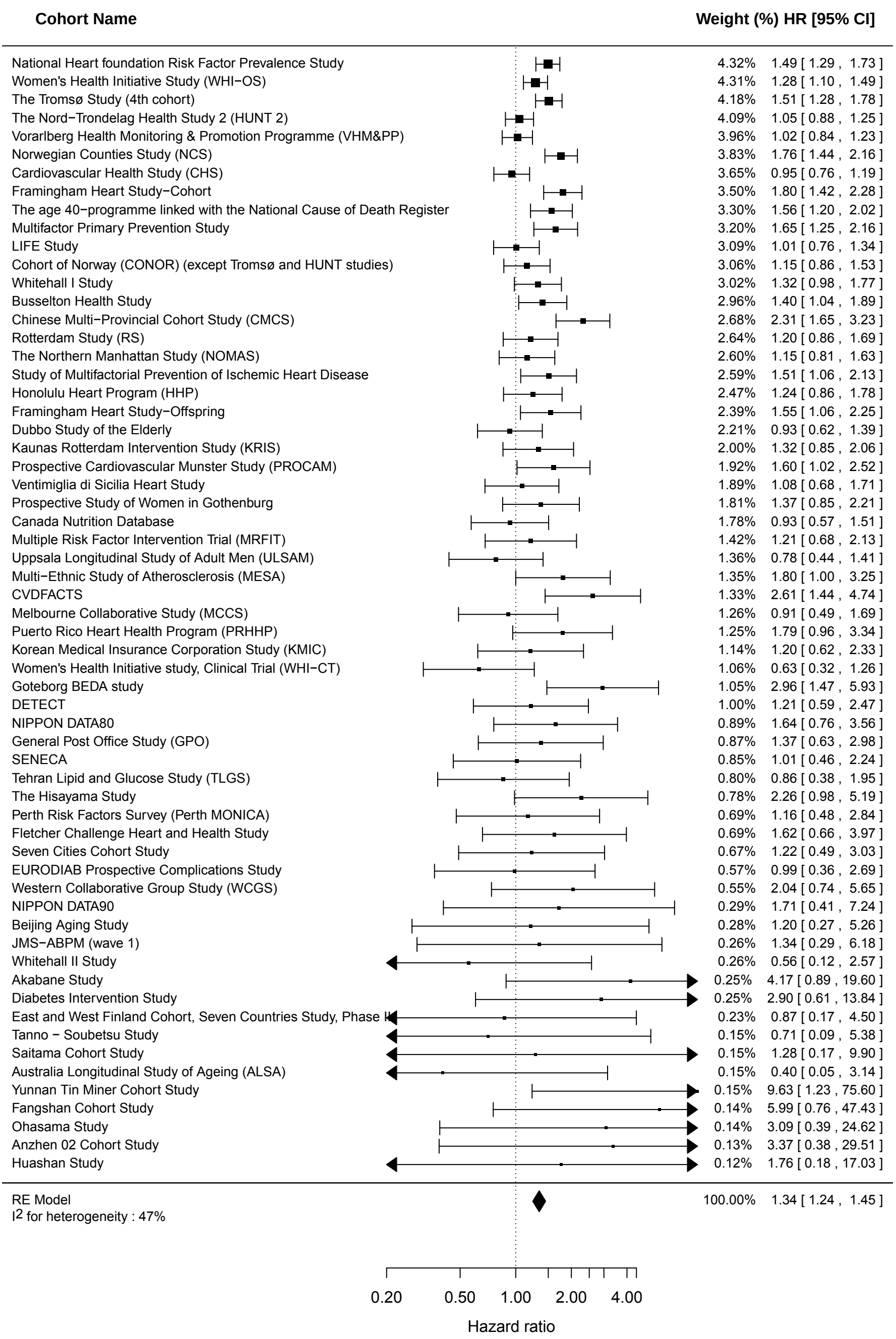
E. Adjusted for confounders and blood pressure, cholesterol



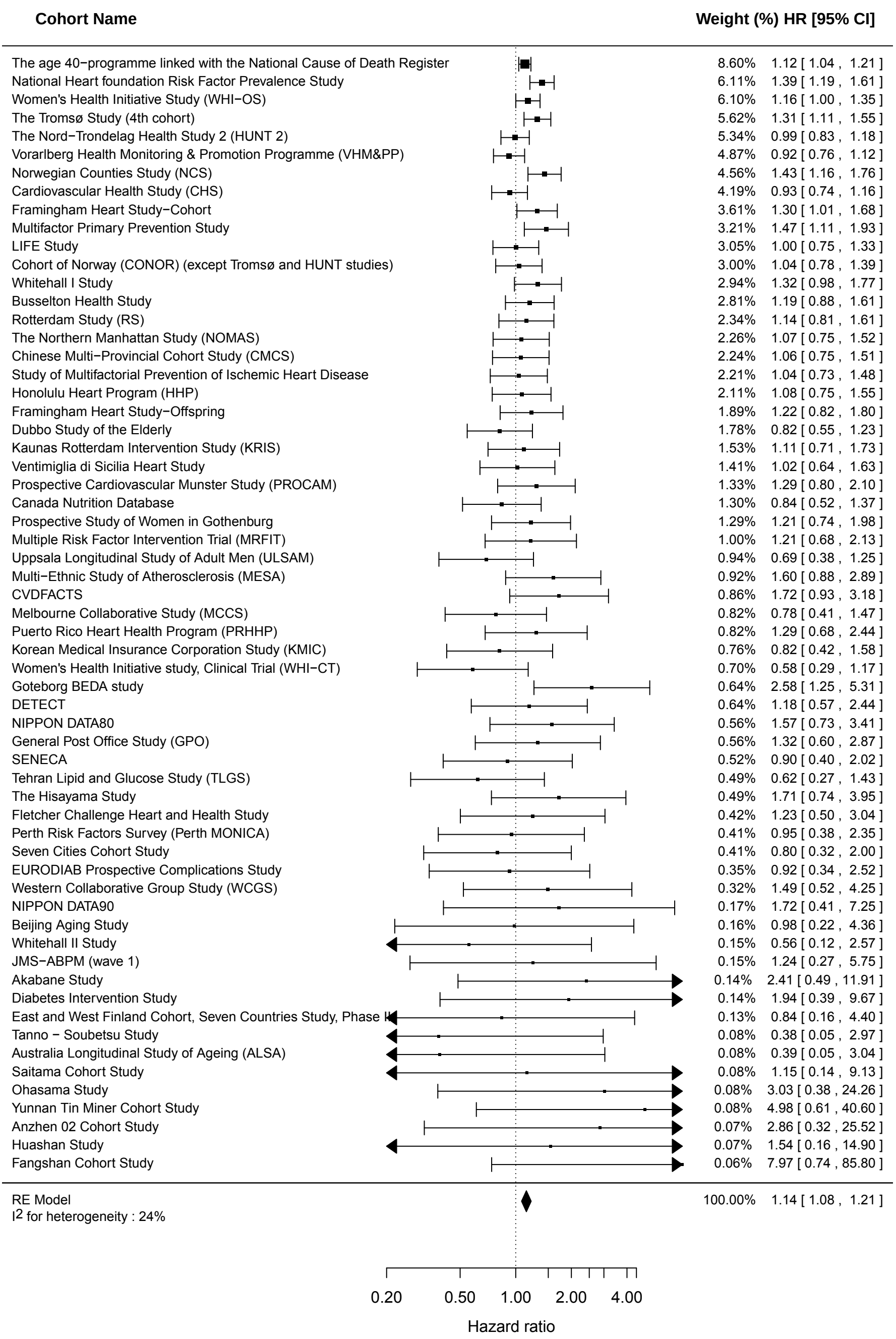
F. Adjusted for confounders and blood pressure, glucose



G. Adjusted for confounders and cholesterol, glucose



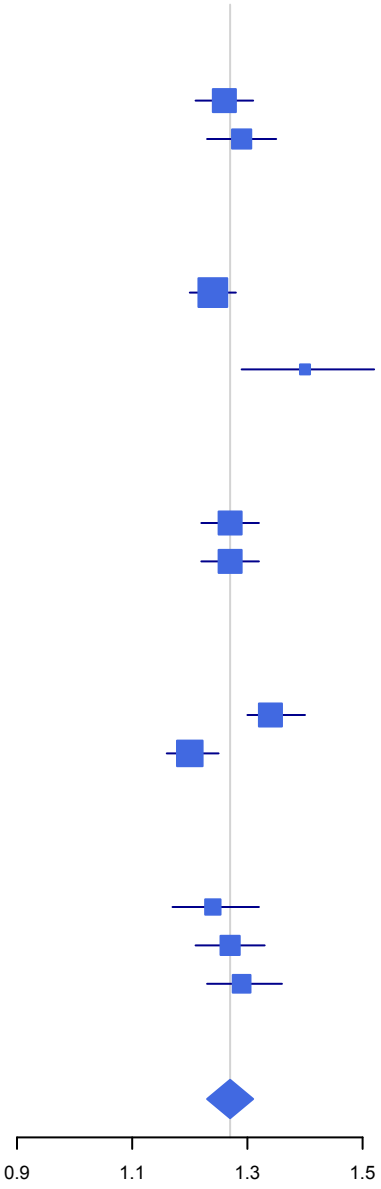
H. Adjusted for confounders and blood pressure, cholesterol, glucose



Webfigure 8: Stratified analyses of hazard ratios (HRs) of CHD per 5 kg/m^2 higher BMI (P values were meta-regression P values between groups)

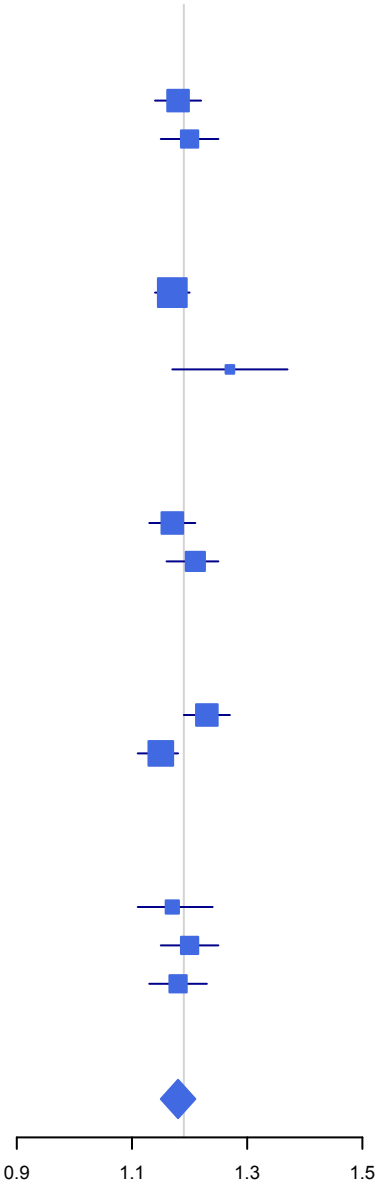
A. Adjusted for confounders

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	44	86	1.26 (1.21−1.31)
Fatal CHD	41	78	1.29 (1.23−1.35)
P value			0.45
Cohort location			
North America, Western Europe, Australia and New Zealand	56	85	1.24 (1.2−1.28)
East and Southeast Asia	25	59	1.4 (1.29−1.52)
P value			0.01
Baseline year			
<1990	47	81	1.27 (1.22−1.32)
≥1990	41	82	1.27 (1.22−1.32)
P value			0.99
Median age at baseline (year)			
< 55	44	72	1.34 (1.3−1.4)
≥ 55	44	78	1.2 (1.16−1.25)
P value			<0.001
Follow−up years			
<10	26	64	1.24 (1.17−1.32)
10 to 20	37	90	1.27 (1.21−1.33)
>20	25	72	1.29 (1.23−1.36)
P value			0.63
All	**88**	**83**	**1.27 (1.23−1.31)**



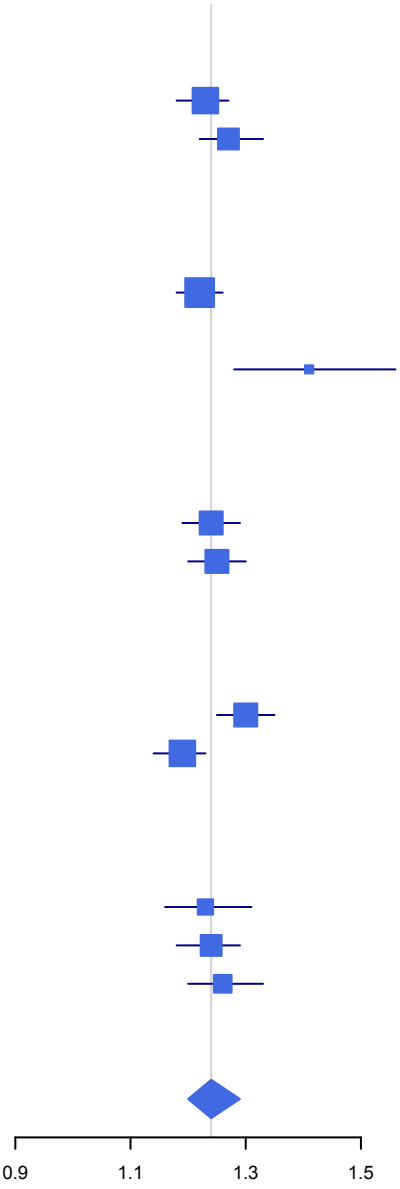
B. Adjusted for confounders and blood pressure

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	44	73	1.18 (1.14−1.22)
Fatal CHD	41	76	1.20 (1.15−1.25)
P value			0.2
Cohort location			
North America, Western Europe, Australia and New Zealand	56	79	1.17 (1.14−1.2)
East and Southeast Asia	25	40	1.27 (1.17−1.37)
P value			0.05
Baseline year			
<1990	47	71	1.17 (1.13−1.21)
≥1990	41	71	1.21 (1.16−1.25)
P value			0.19
Median age at baseline (year)			
< 55	44	68	1.23 (1.19−1.27)
≥ 55	44	67	1.15 (1.11−1.18)
P value			0.002
Follow−up years			
<10	26	46	1.17 (1.11−1.24)
10 to 20	37	81	1.2 (1.15−1.25)
>20	25	75	1.18 (1.13−1.23)
P value			0.78
All	**88**	**75**	**1.19 (1.16−1.22)**



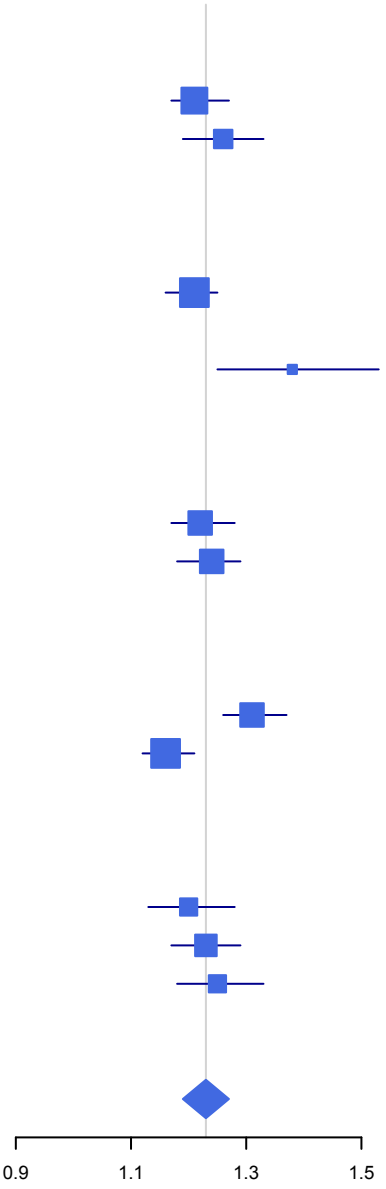
C. Adjusted for confounders and cholesterol

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	40	83	1.23 (1.18−1.27)
Fatal CHD	36	79	1.27 (1.22−1.33)
P value			0.24
Cohort location			
North America, Western Europe, Australia and New Zealand	54	85	1.22 (1.18−1.26)
East and Southeast Asia	19	47	1.41 (1.28−1.56)
P value			0.004
Baseline year			
<1990	45	85	1.24 (1.19−1.29)
≥1990	34	76	1.25 (1.2−1.3)
P value			0.74
Median age at baseline (year)			
< 55	42	73	1.3 (1.25−1.35)
≥ 55	37	80	1.19 (1.14−1.23)
P value			0.001
Follow−up years			
<10	19	59	1.23 (1.16−1.31)
10 to 20	36	87	1.24 (1.18−1.29)
>20	24	77	1.26 (1.2−1.33)
P value			0.72
All	**79**	**82**	**1.24 (1.21−1.28)**



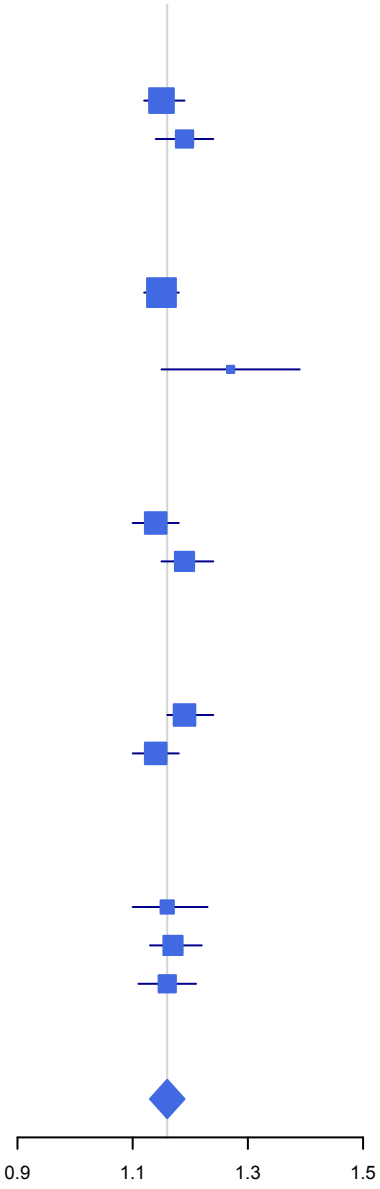
D. Adjusted for confounders and glucose

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	40	83	1.21 (1.17−1.27)
Fatal CHD	30	82	1.26 (1.19−1.33)
P value			0.3
Cohort location			
North America, Western Europe, Australia and New Zealand	50	85	1.21 (1.16−1.25)
East and Southeast Asia	18	33	1.38 (1.25−1.53)
P value			0.01
Baseline year			
<1990	34	82	1.22 (1.17−1.28)
≥1990	39	82	1.24 (1.18−1.29)
P value			0.74
Median age at baseline (year)			
< 55	34	76	1.31 (1.26−1.37)
≥ 55	39	76	1.16 (1.12−1.21)
P value			<0.001
Follow−up years			
<10	23	68	1.2 (1.13−1.28)
10 to 20	35	87	1.23 (1.17−1.29)
>20	15	78	1.25 (1.18−1.33)
P value			0.67
All	**73**	**83**	**1.23 (1.19−1.27)**



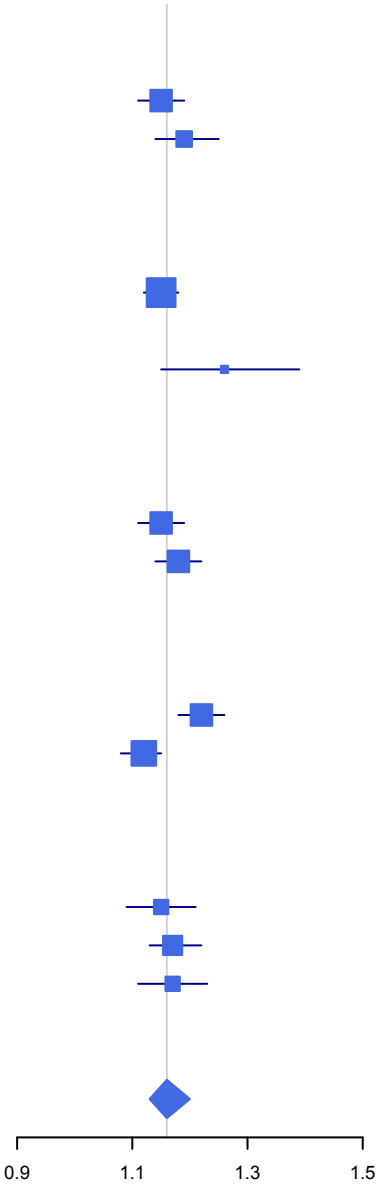
E. Adjusted for confounders and blood pressure, cholesterol

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	40	69	1.15 (1.12−1.19)
Fatal CHD	36	67	1.19 (1.14−1.24)
P value			0.22
Cohort location			
North America, Western Europe, Australia and New Zealand	54	70	1.15 (1.12−1.18)
East and Southeast Asia	19	3	1.27 (1.15−1.39)
P value			0.05
Baseline year			
<1990	45	70	1.14 (1.1−1.18)
≥1990	34	60	1.19 (1.15−1.24)
P value			0.07
Median age at baseline (year)			
< 55	42	65	1.19 (1.16−1.24)
≥ 55	37	63	1.14 (1.1−1.18)
P value			0.05
Follow−up years			
<10	16	43	1.16 (1.1−1.23)
10 to 20	36	80	1.17 (1.13−1.22)
>20	24	67	1.16 (1.11−1.21)
P value			0.87
All	**79**	**69**	**1.17 (1.14−1.20)**



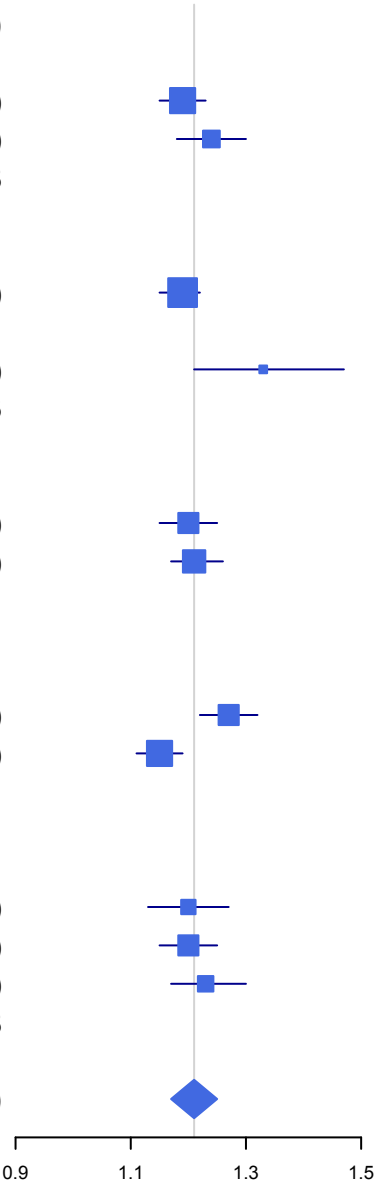
F. Adjusted for confounders and blood pressure, glucose

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	40	67	1.15 (1.11−1.19)
Fatal CHD	30	73	1.19 (1.14−1.25)
P value			0.17
Cohort location			
North America, Western Europe, Australia and New Zealand	50	76	1.15 (1.12−1.18)
East and Southeast Asia	18	0.001	1.26 (1.15−1.39)
P value			0.07
Baseline year			
<1990	34	70	1.15 (1.11−1.19)
≥1990	39	70	1.18 (1.14−1.22)
P value			0.32
Median age at baseline (year)			
< 55	34	64	1.22 (1.18−1.26)
≥ 55	39	60	1.12 (1.08−1.15)
P value			<0.001
Follow−up years			
<10	23	44	1.15 (1.09−1.21)
10 to 20	35	78	1.17 (1.13−1.22)
>20	15	72	1.17 (1.11−1.23)
P value			0.79
All	**73**	**72**	**1.16 (1.13−1.19)**



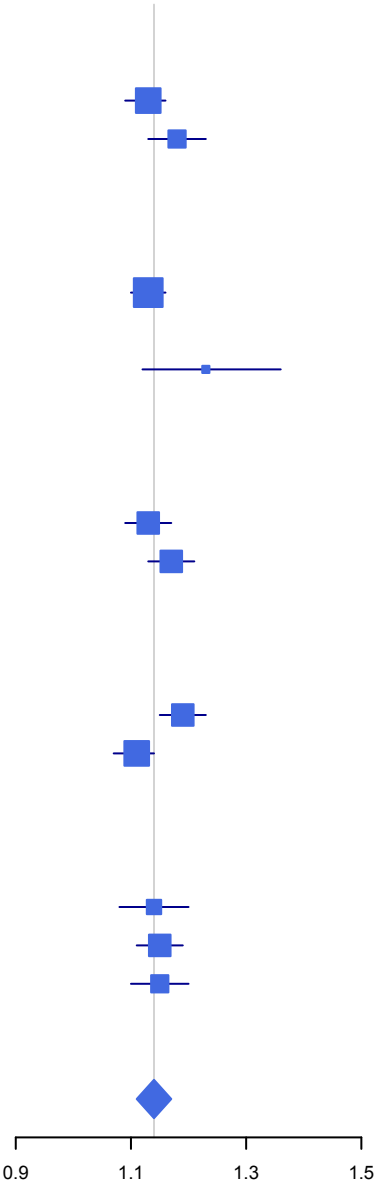
G. Adjusted for confounders and cholesterol, glucose

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	37	77	1.19 (1.15−1.23)
Fatal CHD	28	75	1.24 (1.18−1.3)
P value			0.18
Cohort location			
North America, Western Europe, Australia and New Zealand	49	81	1.19 (1.15−1.22)
East and Southeast Asia	15	0.01	1.33 (1.21−1.47)
P value			0.03
Baseline year			
<1990	34	77	1.2 (1.15−1.25)
≥1990	34	74	1.21 (1.17−1.26)
P value			0.71
Median age at baseline (year)			
< 55	32	64	1.27 (1.22−1.32)
≥ 55	36	73	1.15 (1.11−1.19)
P value			<0.001
Follow−up years			
<10	18	61	1.2 (1.13−1.27)
10 to 20	35	81	1.2 (1.15−1.25)
>20	15	70	1.23 (1.17−1.3)
P value			0.68
All	**68**	**77**	**1.21 (1.17−1.24)**



H. Adjusted for confounders and blood pressure, cholesterol, glucose

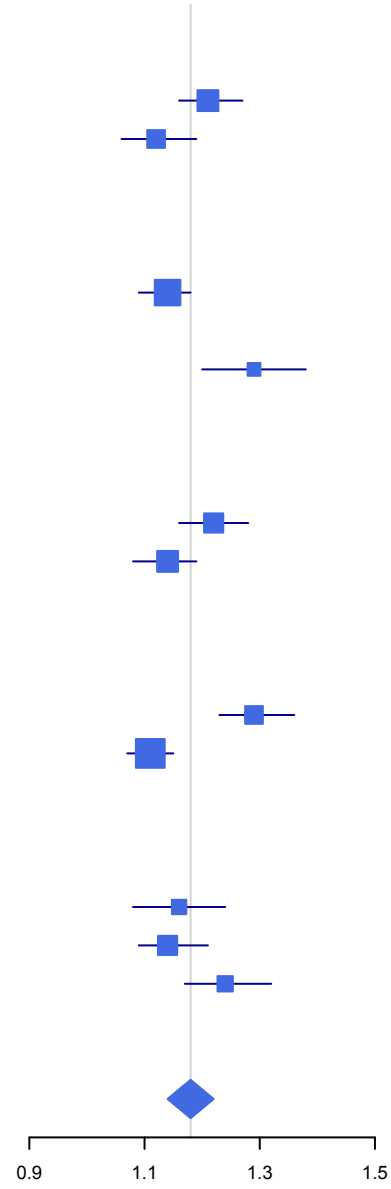
	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal CHD	37	63	1.13 (1.09−1.16)
Fatal CHD	28	68	1.18 (1.13−1.23)
P value			0.11
Cohort location			
North America, Western Europe, Australia and New Zealand	49	71	1.13 (1.1−1.16)
East and Southeast Asia	15	0.004	1.23 (1.12−1.36)
P value			0.1
Baseline year			
<1990	34	70	1.13 (1.09−1.17)
≥1990	34	59	1.17 (1.13−1.21)
P value			0.17
Median age at baseline (year)			
< 55	32	58	1.19 (1.15−1.23)
≥ 55	36	62	1.11 (1.07−1.14)
P value			0.003
Follow−up years			
<10	18	42	1.14 (1.08−1.2)
10 to 20	35	73	1.15 (1.11−1.19)
>20	15	71	1.15 (1.1−1.2)
P value			0.97
All	**68**	**68**	**1.15 (1.12−1.18)**



Webfigure 9: Stratified analyses of hazard ratios (HRs) of stroke per 5 kg/m^2 higher BMI (P values were meta-regression P values between groups)

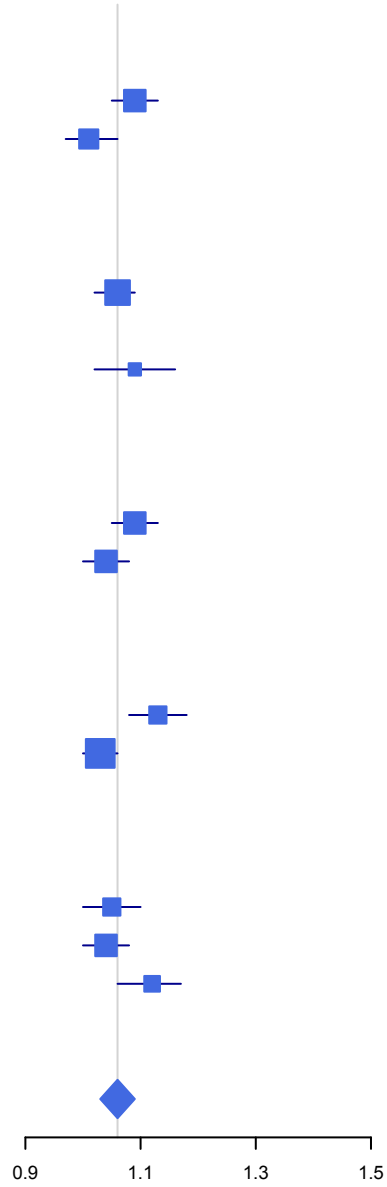
A. Adjusted for confounders

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	45	76	1.21 (1.16−1.27)
Fatal stroke	38	67	1.12 (1.06−1.19)
P value			0.04
Cohort location			
North America, Western Europe, Australia and New Zealand	49	72	1.14 (1.09−1.18)
East and Southeast Asia	31	43	1.29 (1.20−1.38)
P value			0.002
Baseline year			
<1990	44	57	1.22 (1.16−1.28)
≥1990	42	77	1.14 (1.08−1.19)
P value			0.05
Median age at baseline (year)			
< 55	41	15	1.29 (1.23−1.36)
≥ 55	45	72	1.11 (1.07−1.15)
P value			<0.001
Follow−up years			
<10	28	22	1.16 (1.08−1.24)
10 to 20	36	84	1.14 (1.09−1.21)
>20	22	40	1.24 (1.17−1.32)
P value			0.12
All	**86**	**72**	**1.18 (1.14−1.22)**



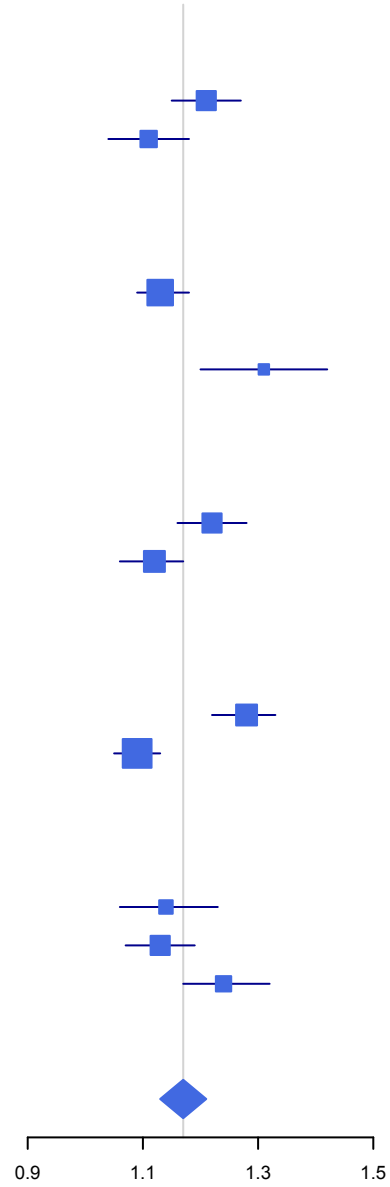
B. Adjusted for confounders and blood pressure

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	45	40	1.09 (1.05−1.13)
Fatal stroke	38	55	1.01 (0.97−1.06)
P value			0.02
Cohort location			
North America, Western Europe, Australia and New Zealand	49	59	1.06 (1.02−1.09)
East and Southeast Asia	31	21	1.09 (1.02−1.16)
P value			0.41
Baseline year			
<1990	44	45	1.09 (1.05−1.13)
≥1990	42	44	1.04 (1−1.08)
P value			0.1
Median age at baseline (year)			
< 55	41	24	1.13 (1.08−1.18)
≥ 55	45	47	1.03 (1−1.06)
P value			0.001
Follow−up years			
<10	28	0.09	1.05 (1−1.1)
10 to 20	36	56	1.04 (1−1.08)
>20	22	39	1.12 (1.06−1.17)
P value			0.06
All	**86**	**48**	**1.06 (1.03−1.09)**



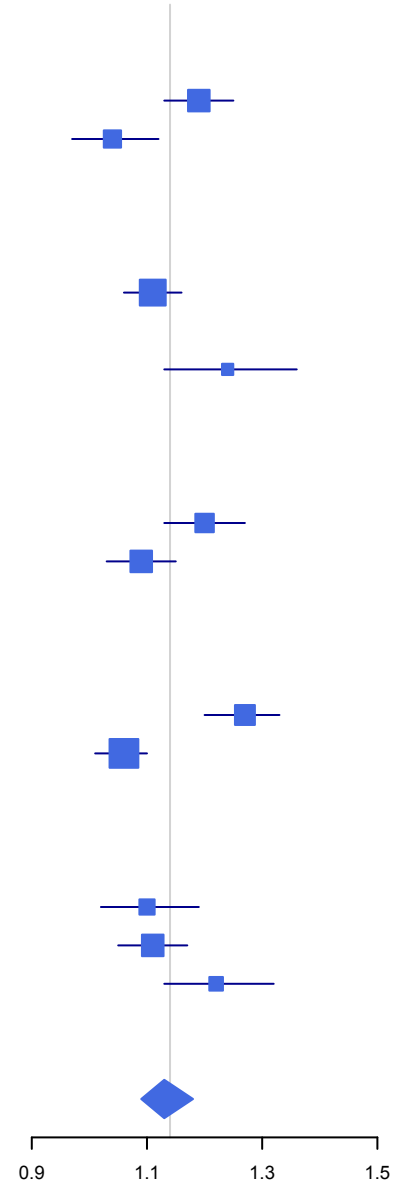
C. Adjusted for confounders and cholesterol

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	40	76	1.21 (1.15−1.27)
Fatal stroke	35	48	1.11 (1.04−1.18)
P value			0.03
Cohort location			
North America, Western Europe, Australia and New Zealand	47	69	1.13 (1.09−1.18)
East and Southeast Asia	26	32	1.31 (1.20−1.42)
P value			0.002
Baseline year			
<1990	42	53	1.22 (1.16−1.28)
≥1990	36	72	1.12 (1.06−1.17)
P value			0.01
Median age at baseline (year)			
< 55	39	22	1.28 (1.22−1.33)
≥ 55	39	58	1.09 (1.05−1.13)
P value			<0.001
Follow−up years			
<10	22	34	1.14 (1.06−1.23)
10 to 20	35	80	1.13 (1.07−1.19)
>20	21	0	1.24 (1.17−1.32)
P value			0.05
All	**78**	**68**	**1.17 (1.13−1.21)**



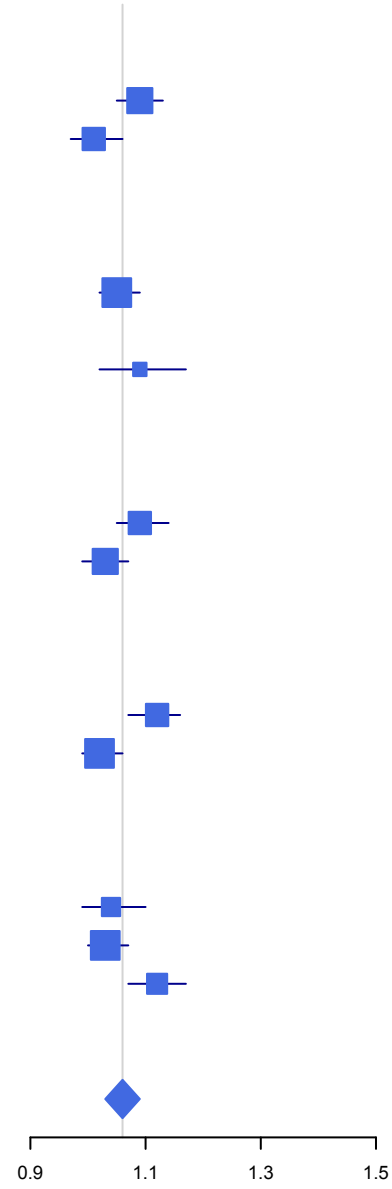
D. Adjusted for confounders and glucose

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	40	76	1.19 (1.13−1.25)
Fatal stroke	28	57	1.04 (0.97−1.12)
P value			0.004
Cohort location			
North America, Western Europe, Australia and New Zealand	43	74	1.11 (1.06−1.16)
East and Southeast Asia	24	47	1.24 (1.13−1.36)
P value			0.04
Baseline year			
<1990	31	61	1.2 (1.13−1.27)
≥1990	40	70	1.09 (1.03−1.15)
P value			0.02
Median age at baseline (year)			
< 55	31	24	1.27 (1.2−1.33)
≥ 55	40	63	1.06 (1.01−1.1)
P value			<0.001
Follow−up years			
<10	25	31	1.1 (1.02−1.19)
10 to 20	34	81	1.11 (1.05−1.17)
>20	12	30	1.22 (1.13−1.32)
P value			0.07
All	**71**	**71**	**1.13 (1.09−1.18)**



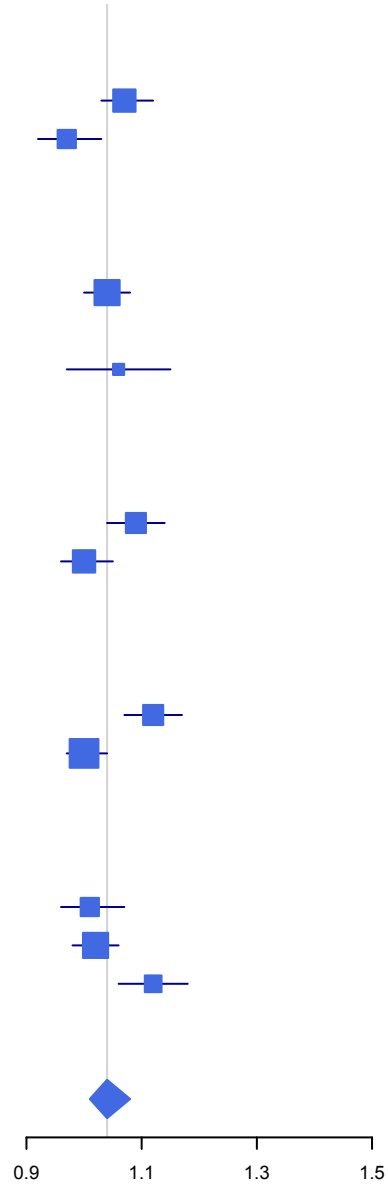
E. Adjusted for confounders and blood pressure, cholesterol

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	40	40	1.09 (1.05−1.13)
Fatal stroke	35	28	1.01 (0.97−1.06)
P value			0.02
Cohort location			
North America, Western Europe, Australia and New Zealand	47	51	1.05 (1.02−1.09)
East and Southeast Asia	26	9	1.09 (1.02−1.17)
P value			0.41
Baseline year			
<1990	42	36	1.09 (1.05−1.14)
>=1990	36	33	1.03 (0.99−1.07)
P value			0.03
Median age at baseline (year)			
< 55	39	20	1.12 (1.07−1.16)
>= 55	39	33	1.02 (0.99−1.06)
P value			0.001
Follow−up years			
<10	22	5	1.04 (0.99−1.1)
10 to 20	35	40	1.03 (1−1.07)
>20	21	11	1.12 (1.07−1.17)
P value			0.01
All	**78**	**40**	**1.06 (1.03−1.09)**



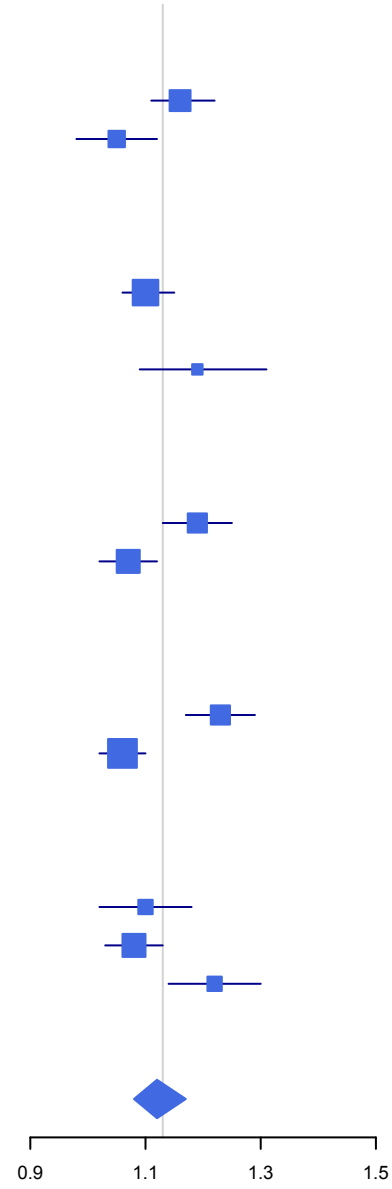
F. Adjusted for confounders and blood pressure, glucose

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	40	44	1.07 (1.03−1.12)
Fatal stroke	28	45	0.97 (0.92−1.03)
P value			0.01
Cohort location			
North America, Western Europe, Australia and New Zealand	43	59	1.04 (1.00−1.08)
East and Southeast Asia	24	21	1.06 (0.97−1.15)
P value			0.72
Baseline year			
<1990	31	43	1.09 (1.04−1.14)
≥1990	40	38	1 (0.96−1.05)
P value			0.01
Median age at baseline (year)			
< 55	31	20	1.12 (1.07−1.17)
≥ 55	40	45	1 (0.97−1.04)
P value			<0.001
Follow−up years			
<10	25	3	1.01 (0.96−1.07)
10 to 20	34	57	1.02 (0.98−1.06)
>20	12	14	1.12 (1.06−1.18)
P value			0.01
All	**71**	**49**	**1.04 (1.01−1.08)**



G. Adjusted for confounders and cholesterol, glucose

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	37	68	1.16 (1.11−1.22)
Fatal stroke	27	58	1.05 (0.98−1.12)
P value			0.01
Cohort location			
North America, Western Europe, Australia and New Zealand	42	72	1.1 (1.06−1.15)
East and Southeast Asia	22	15	1.19 (1.09−1.31)
P value			0.14
Baseline year			
<1990	31	55	1.19 (1.13−1.25)
≥1990	36	58	1.07 (1.02−1.12)
P value			0.004
Median age at baseline (year)			
< 55	29	7	1.23 (1.17−1.29)
≥ 55	38	62	1.06 (1.02−1.1)
P value			<0.001
Follow−up years			
<10	21	32	1.1 (1.02−1.18)
10 to 20	34	68	1.08 (1.03−1.13)
>20	12	15	1.22 (1.14−1.3)
P value			0.01
All	**67**	**65**	**1.12 (1.08−1.17)**



H. Adjusted for confounders and blood pressure, cholesterol, glucose

	Num of cohorts	I^2 (%)	HR (95% CI)
Event type			
Combined fatal and non−fatal stroke	37	42	1.07 (1.03−1.11)
Fatal stroke	27	41	0.99 (0.93−1.04)
P value			0.01
Cohort location			
North America, Western Europe, Australia and New Zealand	42	55	1.04 (1−1.08)
East and Southeast Asia	22	13	1.06 (0.98 − 1.15)
P value			0.6
Baseline year			
<1990	31	37	1.08 (1.04−1.13)
≥1990	36	40	1.01 (0.97−1.05)
P value			0.02
Median age at baseline (year)			
< 55	29	18	1.11 (1.06−1.16)
≥ 55	38	41	1.01 (0.97−1.04)
P value			0.001
Follow−up years			
<10	21	5	1.01 (0.95−1.07)
10 to 20	34	52	1.02 (0.98−1.06)
>20	12	0.03	1.11 (1.06−1.17)
P value			0.02
All	**67**	**45**	**1.04 (1.01 − 1.08)**