Supplementary Material

Supplemental Tables

Supplemental Figures

Table 1 **PICOS criteria for inclusion of studies.**

Parameter	Study selection criteria
Population	Caucasian, Asian, American, and Other ethnicities individuals
Intervention or exposure	Carriers of D allele in angiotensin-converting enzyme
Comparison	Carriers of I allele in angiotensin-converting enzyme
Outcomes	Triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, body mass index
Study design	Observational study design, published in English only

Table S2 **Checklist of items to include when reporting a systematic review or meta-analysis.**

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3,4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	8
Study characteristics	17	Cite each included study and present its characteristics.	8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	9
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	8,9
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	8,9
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	8,9
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	8,9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	8,9

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	10
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	10
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10
	23b	Discuss any limitations of the evidence included in the review.	12
	23c	Discuss any limitations of the review processes used.	12
	23d	Discuss implications of the results for practice, policy, and future research.	12
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	1
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	1
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	1
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	13
Competing interests	26	Declare any competing interests of review authors.	13
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	13

Table S3 **Characteristics of the included studies.**

First author, reference	Year	Country	Race	Sex	Health status	Outcomes
Temel SG [S1]	2019	Turkey	Other	M/F	Patients with CAD	TG/TC/LDL-C/HDL-C/FPG
Temel SG [S1]	2019	Turkey	Other	M/F	Healthy individuals	TG/TC/LDL-C/HDL-C/FPG
Tkác I [S2]	2003	Slovakia	Caucasian	M/F	Patients witht T2DM	TG/TC/LDL-C/HDL-C/SBP
Meyer T [S3]	2020	Germany	Caucasian	M/F	Patients with CAD	TG/TC/LDL-C/HDL-C
Luptáková L [S4]	2013	Slovakia	Caucasian	F	Healthy individuals	TG/TC/LDL-C/HDL-C/FPG/SBP/DBP/BMI
Khamlaoui W [S5]	2020	Tunisia	Other	M/F	Patients with obesity	TG/TC/LDL-C/HDL-C/WC
Liu A [S6]	2019	China	Asian	M/F	Patients with sudden cardiac arrest and	TC/LDL-C/HDL-C/SBP/DBP/BMI
Tsukada K [S7]	1997	Japan	Asian	M/F	Patients with CAD and control subjects	TG/TC/HDL-C/DBP/BMI/Genotype count for case-control
Hubacek JA [S8]	2000	Czech Republic	Caucasian	M	Healthy individuals	TG/TC/LDL-C/HDL-C
Akin F [S9]	2010	Turkey	Other	M/F	Patients with obesity	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI/WC
Alsaeid M [S10]	2004	Kuwait	Other	M/F	Patients witht T1DM	TC/LDL-C/HDL-C/DBP
Alsaeid M [S10]	2004	Kuwait	Other	M/F	Healthy individuals	TC/LDL-C/HDL-C/DBP
Araz M [S11]	2001	Turkey	Other	M/F	Patients witht T2DM	TG/TC/LDL-C/HDL-C/SBP
Arnett DK [S12]	2005	USA	American	M/F	Patients witht CVD	TG/TC/LDL-C/HDL-C/SBP/DBP
Bednarska-Makaruk M [S13]	2005	Poland	Caucasian	M	Patients witht alcohol-dependent	TG/TC/LDL-C/HDL-C
Bhatti GK [S14]	2017	India	Other	M/F	Patients with CAD	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI
Bhatti GK [S14]	2017	India	Other	M/F	Healthy individuals	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI
Eichner JE [S15]	2001	USA	American	M	Patients with CVD	TG/TC/HDL-C
Eichner JE [S15]	2001	USA	American	F	Patients with CVD	TG/TC/HDL-C
El-Kabbany ZA [S16]	2019	Egypt	Other	M/F	Patients with obesity	TG/TC/LDL-C/HDL-C
Felehgari V [S17]	2011	Iran	Other	M/F	Patients with T2DM	TG/TC/LDL-C/HDL-C
Felehgari V [S17]	2011	Iran	Other	M/F	Patients with T2DM	TG/TC/LDL-C/HDL-C
Fossum E [S18]	2001	Norway	Other	M	Healthy individuals	TG/TC
Friedl W [S19]	1995	Austria	Caucasian	M/F	Patients with CAD	TG/TC/HDL-C
Friedl W [S19]	1995	Austria	Caucasian	M/F	Healthy individuals	TG/TC/HDL-C
Guneri S [S20]	2005	Turkey	Other	M/F	Patients with CAD	LDL-C/BMI
Ha SK [S21]	2003	Korea	Asian	M/F	Patients with T2DM	TG/TC/HDL-C
Hadjadj S [S22]	2008	France	Caucasian	M/F	Patients with T2DM	TC/LDL-C/HDL-C/SBP/DBP
Hamelin BA [S23]	2011	Canada	Caucasian	M	Patients with PCAD	TG/TC/LDL-C/HDL-C/FPG/DBP/Genotype count for
Huang XH [S24]	1998	Finland	Caucasian	M/F	Patients with T2DM	TG/TC/HDL-C/FPG/SBP/DBP
Huang XH [S24]	1998	Finland	Caucasian	M/F	Healthy individuals	TG/TC/HDL-C/FPG/SBP/DBP
Huang XH [S25]	1999	Finland	Caucasian	M	Healthy individuals	TG/TC/LDL-C/HDL-C/FPG/SBP/DBP
Islam MS [S26]	2006	Finland	Caucasian	M/F	Healthy individuals	TG/TC/LDL-C/HDL-C
Jacobson AM [S27]	2010	USA/Canada	Caucasian	M/F	Patients with T1DM	TG/TC/LDL-C/HDL-C
Katsuya T [S28]	1995	USA	American	M/F	Patients with T2DM	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI
Kim K [S29]	2009	Korea	Asian	F	Patients with CVD	TC/LDL-C/HDL-C/SBP/DBP/WC
Kim K [S30]	2009	Korea	Asian	M/F	Healthy individuals	TG/TC/LDL-C/HDL-C/SBP/DBP/WC
Kobayashi K [S31]	1999	Japan	Asian	M/F	Patients with T2DM	TG/TC/LDL-C/HDL-C
Kogawa K [S32]	1997	Japan	Asian	M/F	Patients with T2DM	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI
Kogawa K [S32]	1997	Japan	Asian	M/F	Healthy individuals	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI
Kondo H [S33]	2015	Japan	Asian	M/F	Healthy individuals	TC/SBP/DBP
Moorthy N [S34]	2007	India	Other	M/F	Patients with CAD	TC/LDL-C/HDL-C/Genotype count for case-control subjects
Maitland-van der Zee AH[S35]	2008	USA	American	M/F	Patients with hypertension	TC/LDL-C/HDL-C
Maitland-van der Zee AH[S35]	2008	USA	American	M/F	Patients with hypertension	TC/LDL-C/HDL-C
Makris TK [S36]	2000	Greece	Caucasian	M/F	Patients with hypertension	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI
Mannami T [S37]	2001	Japan	Asian	M	Healthy individuals	TG/TC/HDL-C/FPG/SBP/DBP/BMI
Mannami T [S37]	2001	Japan	Asian	F	Healthy individuals	TG/TC/HDL-C/FPG/SBP/DBP/BMI
Marian AJ [S38]	2000	USA	American	M/F	Patients with CAD	TG/TC/LDL-C/HDL-C
Marian AJ [S38]	2000	USA	American	M/F	Patients with CAD	TG/TC/LDL-C/HDL-C
Nagi DK [S39]	1998	UK	Other	M/F	Patients with T2DM	TC/LDL-C/HDL-C
Nagi DK [S39]	1998	UK	Other	M/F	Healthy individuals	TC/LDL-C/HDL-C
Nakai K [S40]	1994	Japan	Asian	M/F	Patients with CAD	TC/HDL-C/Genotype count for case-control subjects
Nordestgaard BG [S41]	2010	Denmark/Finlan	Caucasian	M/F	Patients with hypertension	TC
Okuno S [S42]	1992	Japan	Asian	M/F	Patients with T2DM	TG/TC/HDL-C
Okura Y [S43]	2003	Japan	Asian	M/F	Patients with CAD	TG/TC/LDL-C/HDL-C
Oren I [S44]	1999	Israel	Other	M	Healthy individuals	TG/TC/LDL-C/HDL-C/SBP/DBP/BMI
Passaro A [S45]	2011	Italy	Caucasian	M/F	Patients with MetS	TC/LDL-C/HDL-C/SBP/DBP/BMI
Pedrinelli R [S46]	2006	Italy	Caucasian	M	Patients with hypertension	TG/TC/LDL-C/HDL-C/FPG/SBP/DBP/BMI
Prasad A [S47]	2000	USA	American	M/F	Patients with coronary atherosclerosis	TC/HDL-C/DBP
Sayed-Tabatabaei FA [S48]	2005	The Netherlands	Caucasian	M/F	Healthy individuals	TC/HDL-C/SBP/DBP
Tseng CH [S49]	2012	China	Asian	M/F	Patients with T2DM	TC/LDL-C/HDL-C
Uemura K [S50]	2000	Japan	Asian	M	Healthy individuals	TG/TC/LDL-C/HDL-C/FPG/SBP/DBP/BMI
Mittal G [S51]	2011	India	Other	M/F	Patients with MetS	WC
Herrera CL [S52]	2016	Chile	Other	M/F	Patients with MetS	WC
Herrera CL [S52]	2016	Chile	Other	M/F	Healthy individuals	WC
Das M [S53]	2008	India	Other	M/F	Healthy individuals	WC
Montes-de-Oca-García A [S54]	2021	Spain	Caucasian	M/F	Healthy individuals	WC
Lemes VA [S55]	2013	Brazil	Other	M	Patients with obesity	WC
Lemes VA [S55]	2013	Brazil	Other	F	Patients with obesity	WC
Jhawat V [S56]	2019	India	Other	M/F	Patients with hypertension	WC
Alvarez R [S57]	2001	M	Spain	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Alvarez R [S58]	1998	M/F	Spain	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Bøhn M [S59]	1993	M	Norway	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Bøhn M [S59]	1993	F	Norway	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Mohammad AM [S60]	2020	M/F	Iraq	Other	Patients with PCAD	Genotype count for case-control subjects
Yý Lmaz Ciftdoð An D [S61]	2014	M/F	Turkey	Other	Patients with PCAD	Genotype count for case-control subjects
Abd El-Aziz TA [S62]	2012	M/F	Egypt	Other	Patients with PCAD	Genotype count for case-control subjects
Agirbasli M [S63]	2011	M/F	Turkey	Other	Patients with PCAD	Genotype count for case-control subjects
Batalla A [S64]	2000	M	Spain	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Berdeli A [S65]	2005	M/F	Turkey	Other	Patients with PCAD	Genotype count for case-control subjects
Biggart S [S66]	1998	M/F	UK	Caucasi	Patients with PCAD	Genotype count for case-control subjects
van Bockxmeer FM [S67]	2000	M/F	Australia	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Ermis C [S68]	2002	M/F	Turkey	Other	Patients with PCAD	Genotype count for case-control subjects
McCarthy JJ [S69]	2004	M/F	USA	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Miettinen HE [S70]	1994	M/F	Finland	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Rallidis LS [S71]	2009	M/F	Greece	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Ramasawmy R [S72]	1996	M	France	Caucasi	Patients with PCAD	Genotype count for case-control subjects
Sekuri C [S73]	2005	M/F	Turkey	Other	Patients with PCAD	Genotype count for case-control subjects
Vaisi-Raygani A [S74]	2010	M/F	Iran	Other	Patients with PCAD	Genotype count for case-control subjects

Poorzand H [S75]	2023	M/F	Iran	Other	Patients with PCAD	Genotype count for case-control subjects
Park HY [S76]	1997	M/F	Korea	Asian	Patients with CAD	Genotype count for case-control subjects
Tran DC [S77]	2023	M/F	Vietnam	Asian	Patients with CAD	Genotype count for case-control subjects
Ferrari M [S78]	2002	M/F	Germany/Swe	Caucasi	Patients with CAD	Genotype count for case-control subjects
Gardemann A [S79]	1998	M/F	Germany	Caucasi	Patients with CAD	Genotype count for case-control subjects
Karavannis G [S80]	2010	M/F	Greece	Caucasi	Patients with CAD	Genotype count for case-control subjects
Koch W [S81]	2000	M/F	Germany/Swe	Caucasi	Patients with CAD	Genotype count for case-control subjects
Nakauchi Y [S82]	1996	M/F	Japan	Asian	Patients with CAD	Genotype count for case-control subjects
Narne P [S83]	2012	M/F	India	Other	Patients with CAD	Genotype count for case-control subjects
Niemiec P [S84]	2008	M/F	Poland	Caucasi	Patients with CAD	Genotype count for case-control subjects
Qiu C [S85]	2007	M/F	China	Asian	Patients with CAD	Genotype count for case-control subjects
Vaisi-Raygani A [S86]	2012	M/F	Iran	Other	Patients with CAD	Genotype count for case-control subjects
Vaisi-Raygani A [S86]	2012	M/F	Iran	Other	Patients with CAD	Genotype count for case-control subjects
Sigusch HH [S87]	1997	M/F	Germany/Swe	Caucasi	Patients with CAD	Genotype count for case-control subjects
Wang XL [S88]	1996	M	Australia	Caucasi	Patients with CAD	Genotype count for case-control subjects
Wang XL [S88]	1996	F	Australia	Caucasi	Patients with CAD	Genotype count for case-control subjects
Pfohl M [S89]	1998	M/F	Germany/Swe	Caucasi	Patients with CAD	Genotype count for case-control subjects
Dzimiri N [S90]	2000	M	Saudi Arabia	Other	Patients with CAD	Genotype count for case-control subjects
Pfohl M [S91]	1999	M	Germany	Caucasi	Patients with CAD	Genotype count for case-control subjects
Pfohl M [S91]	1999	F	Germany	Caucasi	Patients with CAD	Genotype count for case-control subjects

M: male; F: female; PCAD: premature coronary artery disease; CAD: coronary artery disease; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus; CVD: cardiovascular disease; Mets: Metabolic Syndrome; OSAHS: obstructive sleep apnea hypopnea syndrome patients; TG: triglycerides; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; WC: waist circumference.

Table S4 **Plasma lipid levels by the genotypes of the *ACE* rs4646994 polymorphism.**

First author, reference	Number		TG, mmol/L		TC, mmol/L		LDL-C, mmol/L		HDL-C, mmol/L	
	II	ID+DD	II	ID+DD	II	ID+DD	II	ID+DD	II	ID+DD
Temel SG [S1]	21	66	1.09±0.48	1.14±0.43	5.51±1.06	5.11±1.07	3.48±0.72	3.28±0.78	1.33±0.37	1.3±0.27
Temel SG [S1]	54	132	1.26±0.64	1.47±1.22	4.99±1.02	5.1±1.37	3.17±0.86	3.39±1.06	1.38±0.3	1.39±0.33
Tkác I [S2]	18	91	2.81±1.69	2.63 ±1.43	5.39 ± 1.42	5.42± 1.29	3.19 ± 1.55	3.22 ± 1.14	0.89 ± 0.28	1.02 ± 0.3
Meyer T [S3]	115	392	1.54±1.14	1.8±1.41	4.41±1.86	4.24±2.01	2.5±1.51	2.68±1.33	0.99±0.54	1.05±0.46
Luptáková L [S4]	73	241	1.43±0.89	1.41±0.87	5.23 ± 0.97	5.50± 1.05	3.03 ± 0.83	3.3 ± 0.97	1.54 ± 0.38	1.59 ± 0.44
Khamlaoui W [S5]	48	211	-	-	-	-	-	-	-	-
Liu A [S6]	53	179	-	-	4.75±0.73	4.99±0.85	2.85±0.4	2.96±0.31	1.41±0.17	1.47±0.23
Tsukada K [S7]	68	81	1.57±0.75	1.61±0.65	4.99±1.07	4.89±0.87	-	-	1.09±0.43	0.99±0.21
Hubacek JA [S8]	65	237	2.4 ± 2.0	2.2 ± 1.83	5.7 ± 1.1	5.74± 1.16	3.5 ± 1.0	3.54 ± 0.96	1.2 ± 0.3	1.2 ± 0.3
Akin F [S9]	1	61	1.43 ± 0	1.66± 0.92	3.03± 0	4.74±1.17	1.55	2.88±0.91	0.83	1.12±0.3
Alsaeid M [S10]	12	113	-	-	4.24 ±0.83	4.62 ±0.88	2.85 ± 0.67	3.14 ± 0.78	1.29 ± 0.33	1.31±0.38
Alsaeid M [S10]	11	114	-	-	4.04 ± 0.90	4.21±0.60	2.71 ± 0.73	2.9 ±0.56	1.21 ± 0.36	1.17±0.34
Araz M [S11]	41	198	2.43±1.11	2.67±2.04	5.64± 1.16	5.8±1.23	3.44±1.03	3.54± 0.98	1.14±0.39	1.19±0.39
Arnett DK [S12]	7484	30455	2.01±1.6	1.93±1.46	5.57±1.11	5.59±1.11	3.49±0.94	3.52±0.96	1.19±0.37	1.21±0.38
Bednarska-Makaruk M [S13]	38	92	1.31±0.7	1.55±0.93	5.2±1.24	5.2±1.07	2.89±0.97	2.8±0.94	1.78±0.7	1.69±0.72
Bhatti GK [S14]	84	246	1.73±0.72	1.61±0.60	3.73±1.1	4.27±1.49	1.82±1.12	2.42±1.44	1.11±0.14	1.1±0.19
Bhatti GK [S14]	108	224	1.92±0.99	1.98±1.06	4.49±1.3	5.12±1.23	2.47±1.13	3.08±1.16	1.14±0.21	1.12±0.19
Eichner JE [S15]	123	453	2.11±1.69	2.1±1.47	5.51±1.45	5.65±1.39	-	-	0.83±0.23	0.83±0.24
Eichner JE [S15]	29	95	2.3±1.93	2.58±2.16	6.13±1.45	6.11±1.56	-	-	0.88±0.28	0.94±0.29
El-Kabbany ZA [S16]	19	51	1.60±1.16	1.66±0.87	4.11±0.93	4.33±1.74	2.12±1.07	2.15±1.37	1.27±0.42	1.4±0.74
Felehgari V [S17]	6	62	1.48±0.28	1.8±0.66	4.84±0.64	4.13±0.87	2.64±0.39	2.65±0.76	1.16±0.38	1±0.22
Felehgari V [S17]	14	58	1.78±0.71	1.84±0.62	4.44±0.68	4.70±0.77	2.69±0.82	2.57±0.64	1.03±0.26	1.15±0.27
Fossum E [S18]	24	61	0.8 ± 0.4	1.1 ± 0.6	3.8 ±0.9	4.2±0.7	-	-	-	-
Friedl W [S19]	62	188	2.17±1.03	1.95±1.02	5.85±1.34	5.96±1.19	-	-	1.1±0.33	1.08±0.31
Friedl W [S19]	31	118	1.29±0.58	1.48±0.86	5.53±0.9	5.44±1	-	-	1.43±0.52	1.26±0.35
Guneri S [S20]	11	83	-	-	-	-	2.69±0.84	2.98±0.85	-	-
Ha SK [S21]	68	171	1.87±0.83	1.96±1.32	5.12±1.43	5.24±1.67	-	-	1 ± 0.3	0.96 ± 0.28
Hadiadi S [S22]	549	2577	-	-	5.9 ±1.1	5.8 ±1.1	3.6±0.9	3.5±0.9	1.3 ±0.3	1.3± 0.4
Hamelin BA [S23]	17	18	2.4 ± 1.0	2.08± 1.09	5.8 ± 0.9	5.9 ± 0.9	4.2 ± 0.7	4.06 ± 0.79	0.8 ± 0.2	0.9 ± 0.2
Huang XH [S24]	12	72	1.60 ± 0.66	1.95 ± 1.13	5.4 ± 1.1	5.45± 1.15	-	-	1.18 ± 0.27	1.22 ± 0.35
Huang XH [S24]	14	101	1.41 ± 0.43	1.56 ± 0.81	6.6 ± 1.5	6.19± 1.21	-	-	1.3 ± 0.51	1.49± 0.45
Huang XH [S25]	42	177	1.69±0.91	1.52±0.86	5.41±0.93	5.51±0.9	3.44±0.78	3.6±0.83	1.18±0.23	1.24±0.28
Islam MS [S26]	39	185	1.03±1.48	1.2±1.68	5.04 ± 0.85	5.2 ± 1.02	3.39± 0.77	3.33±0.91	1.16 ± 0.32	1.25± 0.32
Jacobson AM [S27]	252	841	-	-	-	-	2.8 ± 0.8	2.8±0.74	-	-
Katsuya T [S28]	10	47	1.91±0.23	2.29±0.39	4.68±0.31	5.02±0.28	2.43±0.26	2.64+0.24	1.14±0.1	1.06+0.08
Kim K [S29]	40	65	-	-	4.76 ± 0.13	4.93 ± 0.41	3.07 ± 0.12	3.22 ± 0.39	1.48 ± 0.05	1.51 ± 0.06
Kim K [S30]	286	502	0.91 ±0.44	0.9± 0.46	4.3 ±0.66	4.33±0.69	2.35±0.65	2.38±0.62	1.44±0.31	1.47±0.31
Kobayashi K [S31]	25	38	0.63±0.28	0.68±0.29	4.45±0.83	4.64±0.86	-	-	1.74±0.32	1.8±0.4
Kogawa K [S32]	147	209	1.56 ± 1.50	1.55±1	5.31 ± 1.28	5.48 ± 1.04	3.30 ± 1.22	3.49 ± 0.9	1.31 ± 0.40	1.28 ± 0.38
Kogawa K [S32]	87	148	1.33 ± 0.70	1.28 ± 0.74	5.17 ±0.86	5.26 ± 0.77	3.04 ± 0.78	3.12 ±0.76	1.57 ± 0.49	1.58 ± 0.43
Kondo H [S33]	918	1207	-	-	5.33 ± 1.09	5.37± 1.06	-	-	-	-
Moorthy N [S34]	221	713	-	-	4.63±1.05	4.83±1.71	3.11±0.96	3.3±1.82	0.88±0.27	0.88±0.26
Maitland-van der Zee AH [S35]	922	3804	-	-	5.77±0.68	5.78±0.68	3.75±0.54	3.76±0.55	1.21±0.35	1.22±0.35
Maitland-van der Zee AH [S35]	951	3790	-	-	5.81±0.68	5.77±0.71	3.76±0.53	3.75±0.56	1.22±0.35	1.23±0.35
Makris TK [S36]	32	72	1.16±0.36	1.11±0.33	6±0.65	6.01±0.62	4.06±0.7	4.12±0.7	1.08±0.1	1.08±0.14
Mannami T [S37]	694	1006	1.45± 0.96	1.58± 1.24	5.24± 0.80	5.24±0.84	-	-	1.42±0.36	1.41±0.38
Mannami T [S37]	846	1111	1.16± 0.67	1.19± 0.8	5.59±0.86	5.57±0.85	-	-	1.67±0.39	1.65±0.39
Marian AJ [S38]	35	142	1.84±0.61	1.76±0.63	5.66±0.66	5.7±0.64	3.71±0.53	3.74±0.52	1.12±0.24	1.16±0.3
Marian AJ [S38]	40	143	1.99±0.71	1.81±0.66	5.63±0.5	5.75±0.65	3.67±0.49	3.79±0.52	1.03±0.24	1.14±0.31
Nagi DK [S39]	83	86	-	-	4.63±0.94	4.68± 1.09	2.72±0.83	2.7±0.87	1±0.22	1.05±0.27
Nagi DK [S39]	72	60	-	-	4.45±0.75	4.36±0.86	2.67±0.61	2.6±0.7	1.08±0.24	1.06±0.23
Nakai K [S40]	44	134	-	-	4.97±1.09	5.03±0.97	-	-	1.06±0.36	1.02±0.3
Nordestgaard BG [S41]	737	2766	-	-	6.1	6.17±0.05	-	-	-	-
Okuno S [S42]	22	28	1.19 ± 0.68	1.27 ± 0.54	5.07 ± 0.83	5.28 ± 0.8	-	-	1.51 ± 0.45	1.41± 0.36
Okura Y [S43]	67	105	1.52±0.96	1.73±1.05	4.99±1.11	5.2±1.15	3.23±1.11	3.33±1.07	1.09±0.41	1.09±0.38
Oren I [S44]	30	167	1.7±0.91	1.65±0.79	5.2±0.75	5.43±0.79	3.36±0.69	3.62±1.4	1.09±0.29	1.06±0.31
Passaro A [S45]	55	309	-	-	5.3 ± 1.2	5.74 ± 1.4	3.2 ± 1.1	3.6 ± 1.25	1.4 ± 0.3	1.3 ± 0.4
Pedrinelli R [S46]	20	218	1.83±1.46	1.51±1.03	5.56±1.34	5.55±1.06	3.49±1.19	3.58±1.1	1.06±0.49	1.17±0.31
Prasad A [S47]	13	43	-	-	5.43±0.65	6.01±1.27	-	-	0.98±0.28	1.06±0.42
Sayed-Tabatabaei FA [S48]	1473	5241	-	-	6.58±1.26	6.61±1.21	-	-	1.34±0.36	1.35±0.36
Tseng CH [S49]	465	480	-	-	5.28±1.11	5.35±1.12	2.95±0.9	2.96±0.85	1.23±0.35	1.25±0.35
Uemura K [S50]	132	168	1.31±0.81	1.5±0.76	4.99±0.69	5.01±0.76	3.28±0.8	3.25±0.84	1.11±0.37	1.07±0.35

ACE: Angiotensin converting enzyme gene; TG: triglycerides; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol.

Table S5 **Plasma fasting glucose levels by the genotypes of the *ACE* rs4646994 polymorphism.**

First author, reference	Number		FPG, mmol/L	
	II	ID+DD	II	ID+DD
Temel SG [S1]	21	66	5.52±0.6	5.81±1.47
Temel SG [S1]	54	132	5.14±0.45	5.28±1.51
Luptáková L [S4]	73	241	5.01 ± 1.00	5 ± 1.48
Hamelin BA [S23]	17	18	5.9 ± 2.8	6.0 ± 1.81
Huang XH [S24]	12	72	7.1 ± 1.4	7.97 ± 2.57
Huang XH [S24]	14	101	4.9 ± 0.4	4.8 ± 0.55
Mannami T [S37]	694	1006	5.71±1.36	5.64±1.15
Mannami T [S37]	846	1111	5.27±0.77	5.31±0.83
Pedrinelli R [S46]	20	218	5.38±0.5	5.44±0.67
Uemura K [S50]	132	168	5.7±1.04	5.73±1.19

ACE: Angiotensin converting enzyme gene; FPG: fasting plasma glucose.

Table S6 **Systolic blood pressure levels by the genotypes of the *ACE* rs4646994 polymorphism.**

First author, reference	Number		SBP, mmHg	
	II	ID+DD	II	ID+DD
Tkác I [S2]	18	91	137 ± 13	145.68 ± 22.29
Luptáková L [S4]	73	241	121.03 ± 13.65	123 ± 18.25
Liu A [S6]	53	179	131.26 ± 23.13	135.41 ± 21.64
Akin F [S9]	1	61	120	134.24± 22.11
Araz M [S11]	41	198	139± 28	142.56± 26.06
Arnett DK [S12]	7484	30455	156 ±12	156.62 ±12.01
Bhatti GK [S14]	84	246	135.29±22.16	140.75±20.73
Bhatti GK [S14]	108	224	138.27±25.45	141.94±20.78
Hadiadi S [S22]	549	2577	131 ± 16	135 ±18.44
Huang XH [S24]	12	72	152.4 ± 22.1	156.46± 22.98
Huang XH [S24]	14	101	138.6 ± 16.9	145.09± 22.46
Huang XH [S25]	42	177	130.4±16.3	131.98±17.14
Katsuya T [S28]	10	47	140+25.3	142±32.08
Kim K [S29]	40	65	114.69 ± 13.03	114.92 ±36.84
Kim K [S30]	286	502	100.38 ±21.98	100±48.84
Kogawa K [S32]	147	209	137.0 ± 22.5	138.19±21.54
Kondo H [S33]	918	1207	133±21	134.23±21.77
Makris TK [S36]	32	72	141.1 ± 8.6	140.33 ± 8.7
Mannami T [S37]	694	1006	127.0±19.4	128.9±19.14
Mannami T [S37]	846	1111	126.2±20.5	126.69±20.11
Oren I [S44]	30	167	123.39±17.22	130.4±17.69
Passaro A [S45]	55	309	132.6± 16.3	133.64± 17.68
Pedrinelli R [S46]	20	218	147 ± 11	150.54± 15.67
Saved-Tabatabaei FA [S48]	1473	5241	138.33±22.08	139.63±22.48
Uemura K [S50]	132	168	118.5±14.7	121.37±14.99

ACE: Angiotensin converting enzyme gene; SBP: systolic blood pressure.

Table S7 **Diastolic blood pressure levels by the genotypes of the *ACE* rs4646994 polymorphism.**

First author, reference	Number		DBP, mmHg	
	II	ID+DD	II	ID+DD
Luptáková L [S4]	73	241	78.04 ± 14.56	79 ± 10.39
Liu A [S6]	53	179	82.13 ± 14.23	80.92 ± 10.68
Tsukada K [S7]	68	81	71±1	72.35±2.13
Akin F [S9]	1	61	80	85.92 ±14.54
Araz M [S11]	41	198	85± 13	85.94± 13.01
Arnett DK [S12]	7484	30455	89±9	89.38±9.01
Bhatti GK [S14]	84	246	84.49±10.09	84.07±11.75
Bhatti GK [S14]	108	224	84.79±11.69	85.2±11.98
Hadiadi S [S22]	549	2577	72 ± 10	73 ± 11
Hamelin BA [S23]	17	18	76 ± 14	77.28± 8.9
Huang XH [S24]	12	72	87.5 ± 12.1	88.7±9.98
Huang XH [S24]	14	101	83.1 ± 10.3	83 ±9.96
Huang XH [S25]	42	177	82.5±8.8	84.49±10.7
Katsuya T [S28]	10	47	77+4	83.62±5.2
Kim K [S29]	40	65	75.19 ± 1.29	75.39±3.58
Kim K [S30]	286	502	63.52 ± 0.98	63.57±1.16
Kogawa K [S32]	147	209	74.7 ± 10.9	75.71±11.28
Kondo H [S33]	918	1207	78±12	77.23±11
Makris TK [S36]	32	72	94.9 ± 4.0	95.85 ± 4.31
Mannami T [S37]	694	1006	79.3±10.8	80.01±10.99
Mannami T [S37]	846	1111	76.8±10.5	77.34±11.27
Oren I [S44]	30	167	79.39±9.48	83.14±10.05
Passaro A [S45]	55	309	81.2 ± 8.5	82.51 ± 8.7
Pedrinelli R [S46]	20	218	96 ± 8	96 ± 9.53
Sayed-Tabatabaei FA [S48]	1473	5241	73.60±11.78	73.79 ±11.55
Uemura K [S50]	132	168	76.3±11.9	79.76±11.34

ACE: Angiotensin converting enzyme gene; DBP: diastolic blood pressure.

Table S8 **Body mass index levels by the genotypes of the *ACE* rs4646994 polymorphism.**

First author, reference	Number		BMI, kg/m^2	
	II	ID+DD	II	ID+DD
Luptáková L [S4]	73	241	27.56 ± 5.34	27.33 ± 5.68
Liu A [S6]	53	179	25.42 ± 3.63	27.59 ±8.03
Tsukada K [S7]	68	81	23±0.4	23.51±0.62
Akin F [S9]	1	61	29	36.11±6.2
Bhatti GK [S14]	84	246	23.4±4.75	24.26±4.67
Bhatti GK [S14]	108	224	25.85±5.1	27.52±4.73
Guneri S [S20]	11	83	26.9 ± 2.0	27.47 ± 3.1
Katsuya T [S28]	10	47	27.0+9	28.62+0.58
Kogawa K [S32]	147	209	22.9 ± 3.0	23.29± 3.78
Makris TK [S36]	32	72	24.5 ± 2.0	24.96±1.82
Mannami T [S37]	694	1006	23.0±2.8	23.04±2.82
Mannami T [S37]	846	1111	22.3± 3.1	22.32± 3.38
Oren I [S44]	30	167	26.45±2.4	27.17±3.2
Passaro A [S45]	55	309	30.9 ± 5.5	30.8± 5.82
Pedrinelli R [S46]	20	218	26.2 ± 2.2	27.12 ±3.11
Uemura K [S50]	132	168	22.8± 2.3	23.32± 2.8

ACE: Angiotensin converting enzyme gene; BMI: body mass index.

Table S9 **Waist circumference levels by the genotypes of the *ACE* rs4646994 polymorphism.**

First author, reference	Number		WC, cm	
	II	ID+DD	II	ID+DD
Khamlaoui W [S5]	48	211	115.8±12.4	120.3±12.26
Akin F [S9]	1	61	94	100.37±12.43
Kim K [S29]	40	65	79.01±13.66	79.68±9.3
Mittal G [S51]	6	24	92±11	100.75±12.28
Herrera CL [S52]	32	51	97.9 ± 11.3	98.79 ± 13.41
Herrera CL [S52]	27	42	86.0 ± 8.8	96.95 ± 9.1
Das M [S53]	46	93	86.65±12.40	89.21±9.71
Montes-de-Oca-García A [S54]	18	56	78.26 ± 9.77	85.15 ± 15.61
Lemes VA [S55]	19	97	93 ± 8.72	100.65 ±9.36
Lemes VA [S55]	43	161	92 ± 13.11	95 ± 9.29
Jhawat V [S56]	64	206	93.75±7.56	94.25±6.94

ACE: Angiotensin converting enzyme gene; WC: waist circumference.

Table S10 **PubMed search strategy.**

Search	Search terms
#1	[“ACE” OR “angiotensin-converting enzyme” OR “RAS” OR “renin-angiotensin system”]
#2	[“rs4646994” OR “variant” OR “polymorphism” OR “mutation” OR “variation” OR “mutant” OR “SNP” OR “single nucleotide polymorphism”]
#3	[“lipids” OR “circulating lipids” OR “blood lipids” OR “plasma lipids” OR “serum lipids” OR “lipid profile” OR “triglycerides” OR “total cholesterol” OR “low-density lipoprotein cholesterol” OR “high-density lipoprotein cholesterol” OR “TG” OR “TC” OR “LDL-C” OR “HDL-C” OR “blood pressure” OR “systolic blood pressure” OR “diastolic blood pressure” OR “FPG” OR “fasting plasma glucose” OR “FBG” OR “fasting blood glucose” OR “BMI” OR “body mass index” OR “PCAD” OR “premature coronary artery disease” OR “PCAD” OR “early-onset coronary artery disease” OR “coronary artery disease severity” OR “triple-vessel lesions” OR “multiple-vessel lesions”]
#4	**#1** AND **#2** AND **#3**

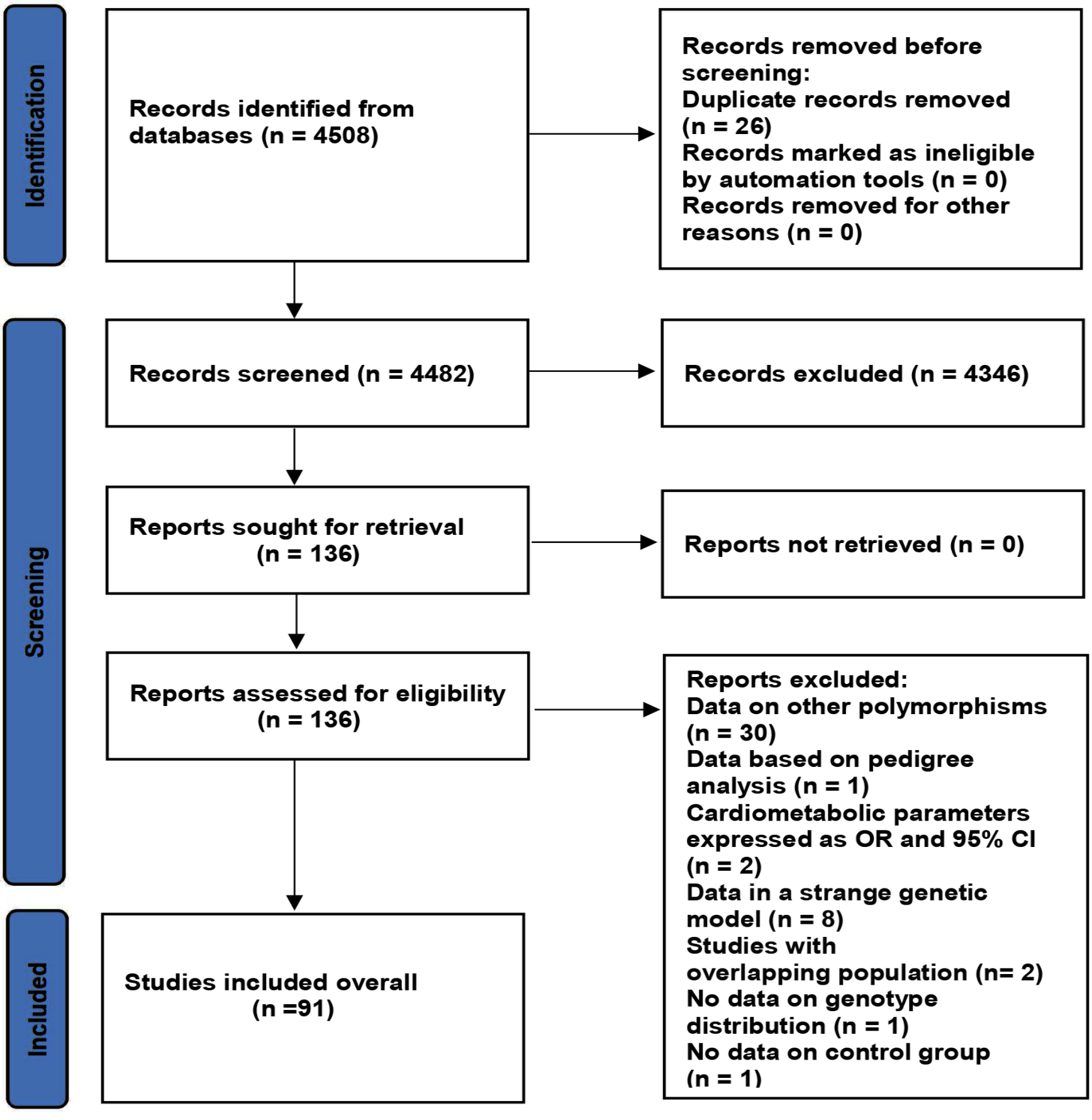

Figure S1 **Flow diagram of the studies selection process.**

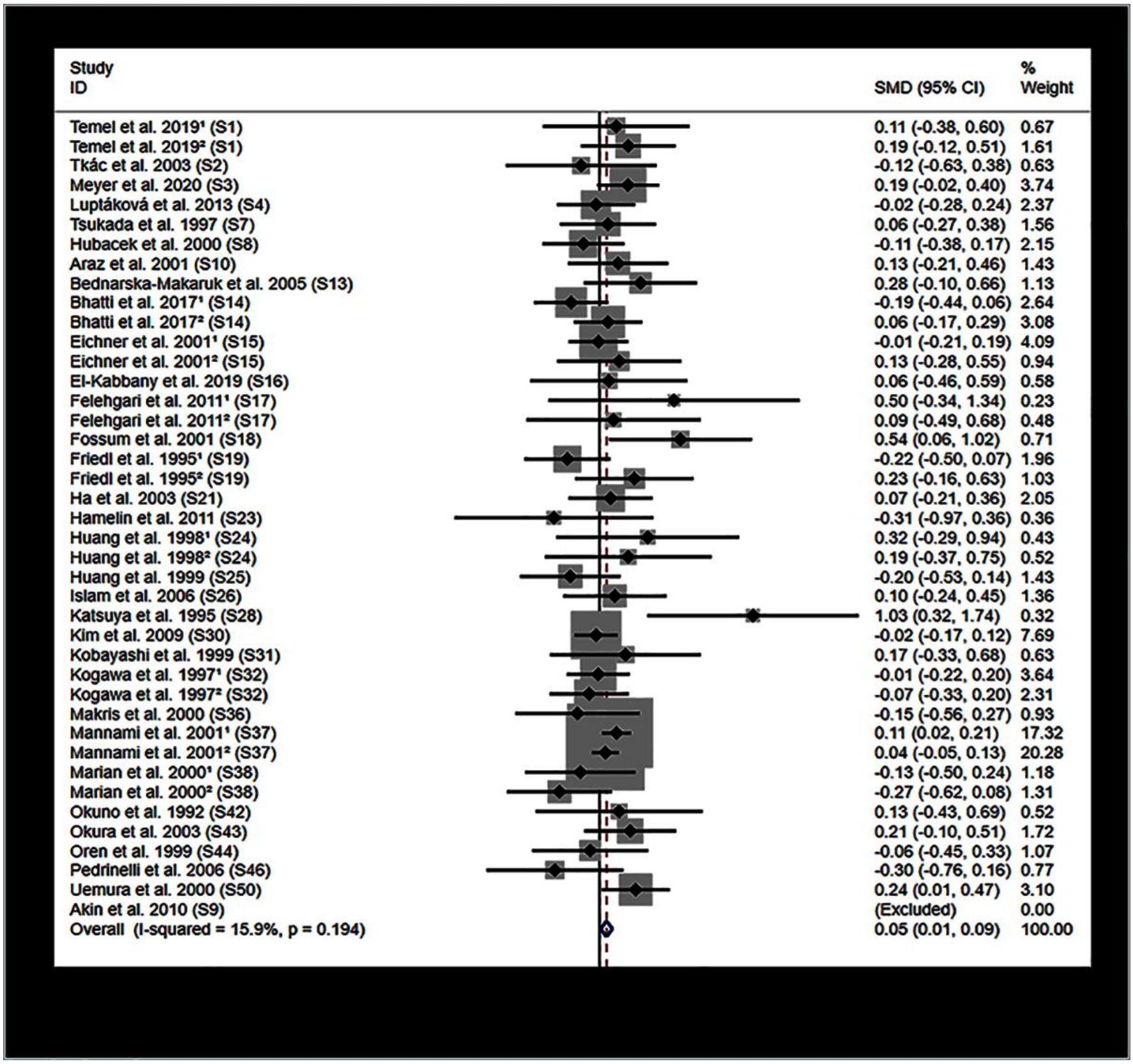

Figure S2 **Forest plot of the meta-analysis between rs4646994 and triglycerides levels.**

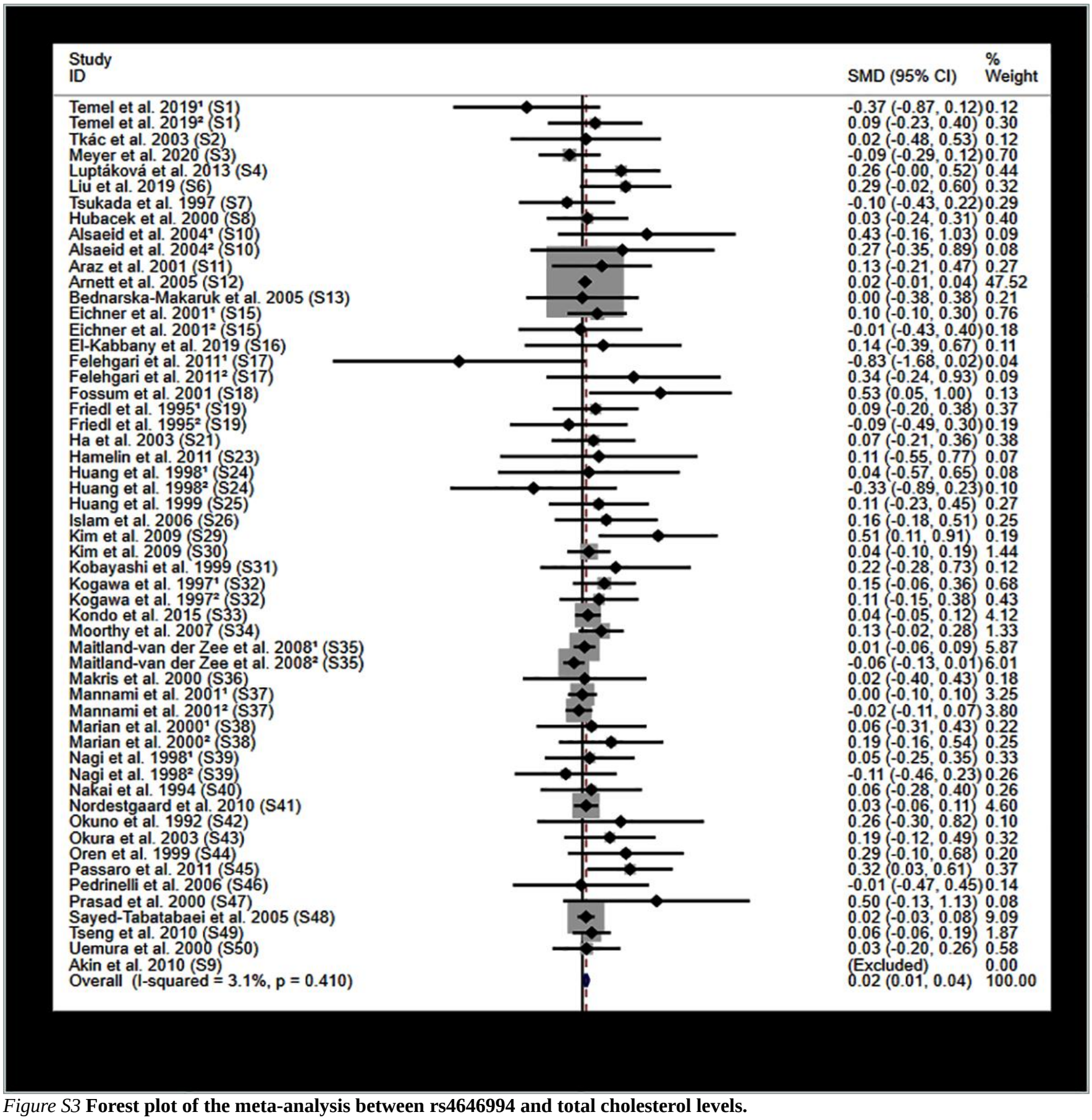

Figure S3 **Forest plot of the meta-analysis between rs4646994 and total cholesterol levels.**

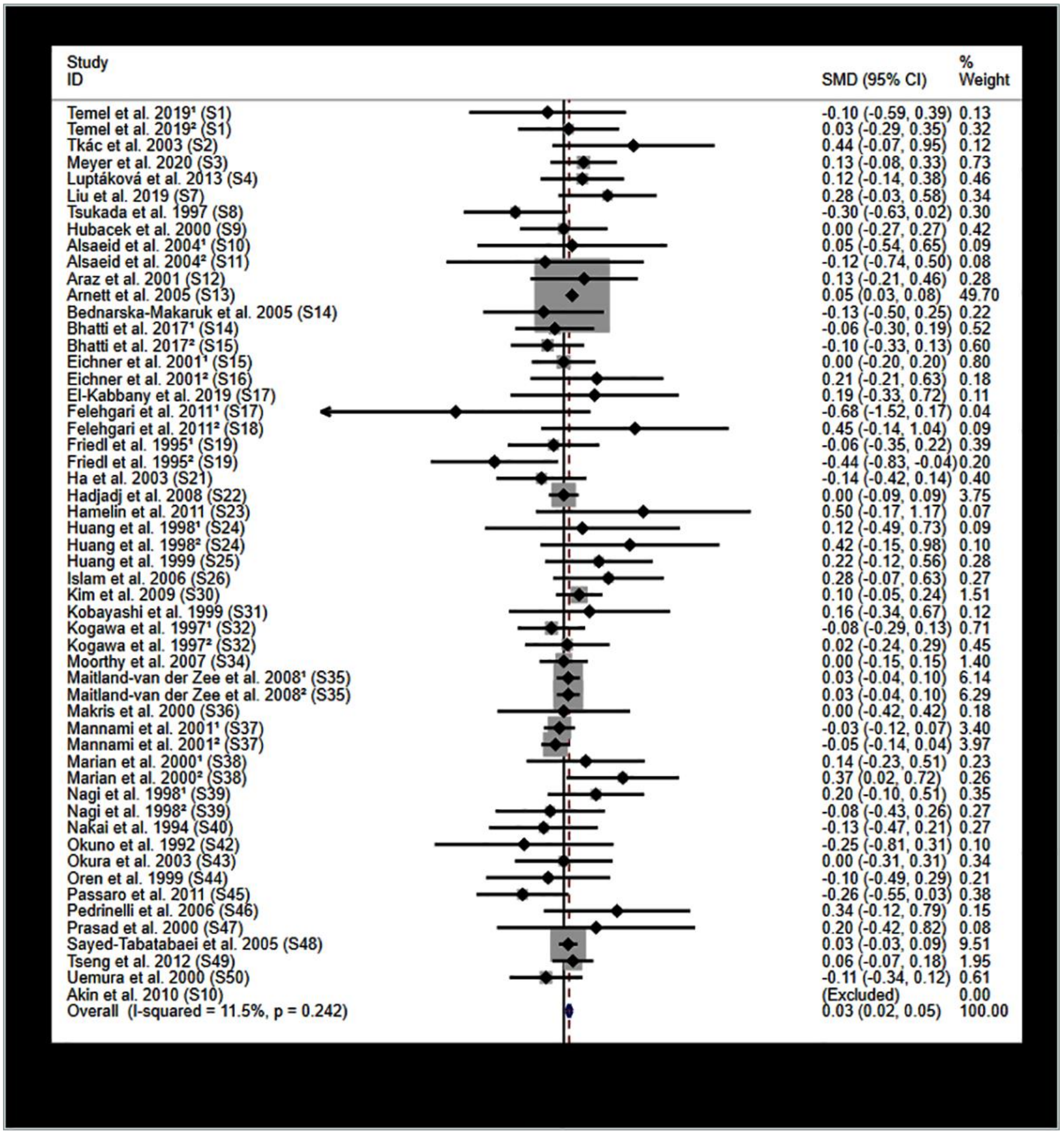

Figure S4 **Forest plot of the meta-analysis between rs4646994 and high-density lipoprotein cholesterol levels.**

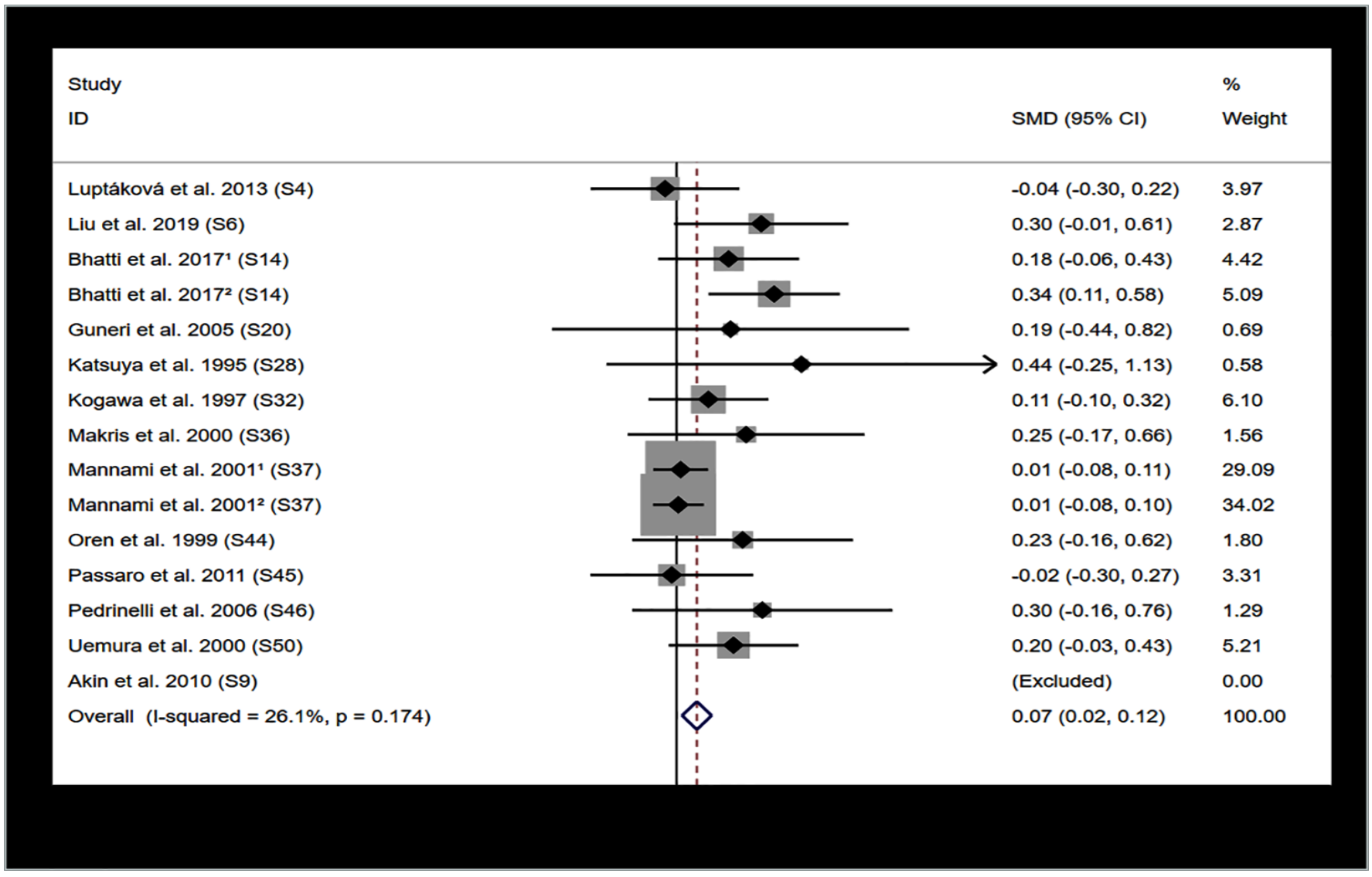

Figure S5 **Forest plot of the meta-analysis between rs4646994 and body mass index levels.**

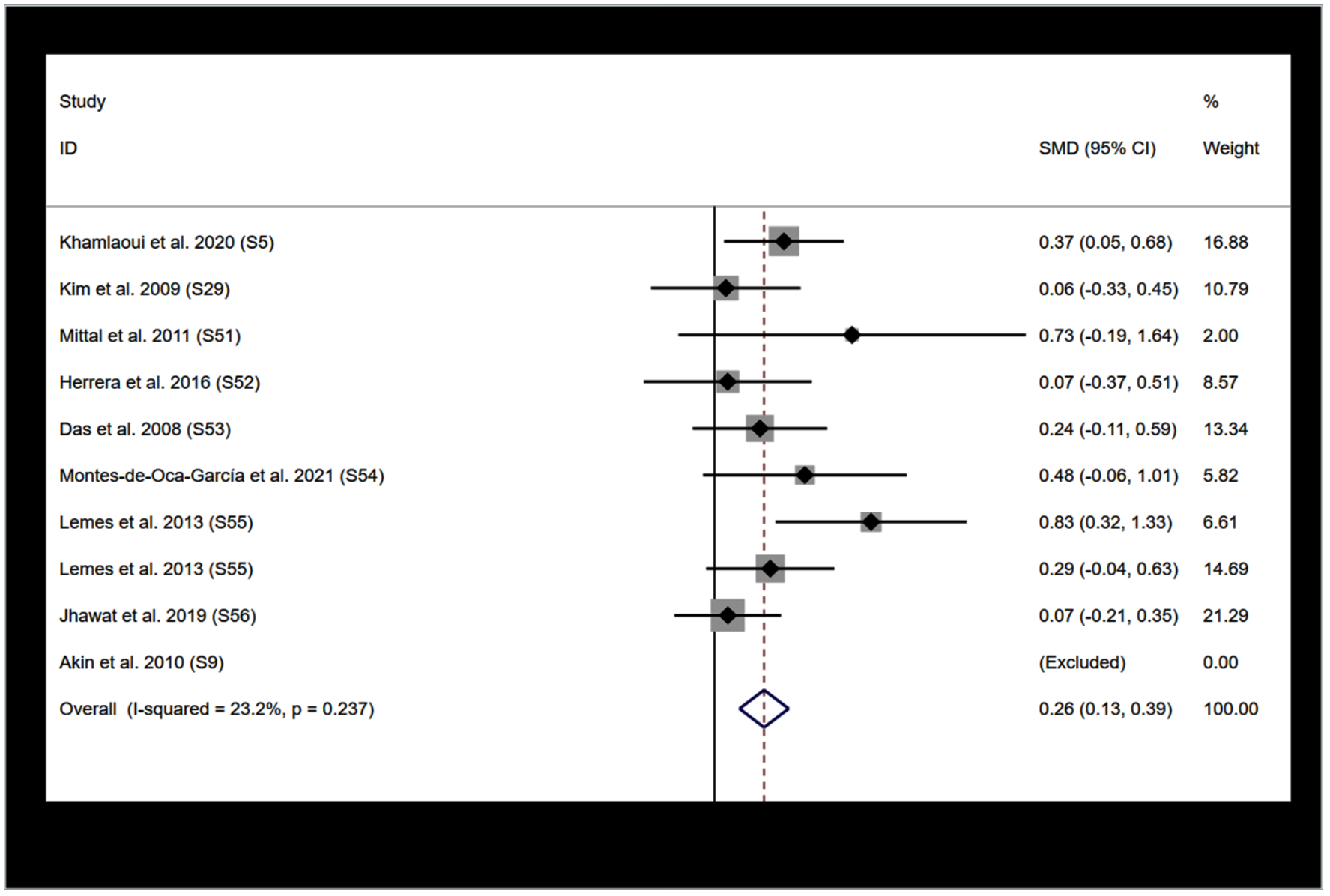

Figure S6 **Forest plot of the meta-analysis between rs4646994 and waist circumference levels.**

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