Associations between *LPL* gene polymorphisms and coronary artery disease: evidence based on an updated and cumulative meta-analysis

Short title: *LPL* gene polymorphisms and coronary artery disease

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Supplementary Table 1. MOOSE checklist for meta-analysis of observational studies.

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	2-3
2	Hypothesis statement	2-3
3	Description of study outcome(s)	2-3
4	Type of exposure or intervention used	2-3
5	Type of study designs used	2-3
6	Study population	2-3
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	4
8	Search strategy, including time period included in the synthesis and key words	4
9	Effort to include all available studies, including contact with authors	4
10	Databases and registries searched	4
11	Search software used, name and version, including special features used (eg, explosion)	5
12	Use of hand searching (eg, reference lists of obtained articles)	4
13	List of citations located and those excluded, including justification	4-5
14	Method of addressing articles published in languages other than English	4
15	Method of handling abstracts and unpublished studies	5
16	Description of any contact with authors	No
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	4-5
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	4-5
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	4-6
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	4-6
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	4-6
22	Assessment of heterogeneity	5-6
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	5-6
24	Provision of appropriate tables and graphics	5-6
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	6-9
26	Table giving descriptive information for each study included	Table1
27	Results of sensitivity testing (eg, subgroup analysis)	6-14
28	Indication of statistical uncertainty of findings	6-9
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	10-11
30	Justification for exclusion (eg, exclusion of non-English language citations)	10-11
31	Assessment of quality of included studies	14-16
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	10-11
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	10-11
34	Guidelines for future research	11
35	Disclosure of funding source	11

Supplementary Table 2. Characteristics of the individual studies included in the meta-analysis.

First Author /Year	Country	Disease	Source of Controls	Gene-typing Methods	Sample Size	Genotype Distribution		P_{HWE}	NOS
					Cases/Controls	Cases	Controls		
Hind III						**TT/TG/GG**	**TT/TG/GG**		
Thorn 1990	UK	CAD	PB	PCR	63/108	37/23/3	37/51/20	0.743	7
Mattu 1994	Welsh	CAD	PB	PCR-RFLP	90/123	50/34/6	72/45/6	0.760	8
Jemaa 1995	France	CAD	PB	PCR	614/733	318/258/38	343/314/76	0.742	7
Anderson 1999	America	CAD	HB	PCR	483/168	259/194/30	94/52/22	>0.05	7
Holmer 2000	Germany	MI	PB	PCR	1159/1361	616/456/87	697/564/100	0.332	8
Abu-Amero 2003	Saudi Arabia	CAD	HB	PCR	352/410	189/138/25	206/173/31	0.518	6
Goodarzi 2003	USA	CAD	PB	PCR	77/164	39/33/5	105/52/7	0.861	7
Whiting 2005	America	CAD	HB	PCR	713/196	385/269/59	103/77/16	0.763	7
Pasalić 2006	Croatia	CAD	HB	PCR-RFLP	132/98	78/46/8	47/45/6	0.262	7
AshokKumar 2010	India	CAD	HB	PCR	414/424	220/168/26	245/158/21	0.486	7
Abd 2011	Egypt	MI	HB	PCR	200/100	120/70/10	50/36/14	0.834	7
Al-Jafari 2012	Saudi Arabia	CAD	HB	PCR	120/65	61/53/6	29/23/13	0.050	7
Rebhi 2012	Tunisia	CAD	HB	PCR–RFLP	212/104	114/83/15	47/39/18	0.569	7
Abd-El-Aziz 2013	Egypt	CAD	HB	PCR-RFLP	156/154	100/53/3	78/54/22	>0.05	7
Tanguturi 2013	India	MI	PB	PCR	202/210	98/72/32	70/68/72	>0.05	7
Daoud 2013	Saudi Arabia	CAD	HB	PCR-RFLP	226/103	102/81/43	42/35/26	>0.05	7
Ahmadi 2015	Iran	CAD	HB	PCR-RFLP	108/89	61/41/6	53/33/3	0.430	6
Bahrami 2015	Iran	MI	HB	PCR-RFLP	211/203	116/81/14	101/83/19	0.745	7
S477X						**CC/CG/GG**	**CC/CG/GG**		
Peacock 1992	Sweden	CAD	HB	PCR	86/87	77/9 [a]	78/9 [a]	>0.05	7
Mattu 1994	Welsh	CAD	PB	PCR-RFLP	90/123	76/14/0	101/21/1	0.936	8
Jemaa 1995	France	CAD	PB	PCR	649/730	525/118/6	563/154/13	0.514	7
Zhang 1995	Germany	CAD	HB	PCR	243/86	195/46/2	68/17/1	0.959	7
Gagné 1999	America	CAD	PB	PCR-RFLP	120/2138	107/13 [a]	1772/366 [a]	>0.05	7
Arca 2000	Italy	CAD	HB	PCR-RFLP	416/407	329/87 [a]	321/86 [a]	>0.05	6
Moennig 2000	Germany	CAD	PB	PCR	229/150	198/28/3	113/37/0	0.085	8
Sawano 2001	Japan	CAD	PB	PCR	93/96	82/10/1	71/23/2	0.932	8
VAN 2001	Australia.	CAD	PB	PCR	516/589	438/78 [a]	498/91 [a]	>0.05	7
Myllykangas 2001	Finland	CAD	HB	PCR	149/113	138/11 [a]	89/24 [a]	>0.05	7
Ferencak 2003	Croatia	CAD	HB	PCR	479/200	378/97/4	167/32/1	0.686	7

Goodarzi 2003	USA	CAD	PB	PCR	77/164	61/15/1	142/22/0	>0.05	7
Martin 2004	UK	MI	HB	PCR-RFLP	547/505	440/104/3	402/99/4	0.483	7
Baum 2006	China	MI	HB	PCR	231/313	180/51/0	248/64/1	0.137	6
Pasalić 2006	Croatia	CAD	HB	PCR-RFLP	132/98	113/19/0	69/28/1	0.312	7
Yamada 2006	Japan	MI	HB	PCR	1192/2291	949/231/12	1699/547/45	0.900	7
Ak 2007	Turkey	CAD	HB	PCR	40/66	33/7/0	57/8/1	0.275	6
Katia 2007	Brazil	CAD	PB	PCR-RFLP	313/150	257/47/9	115/34/1	0.110	7
Aydogan 2009	Turkey	CAD	PB	PCR-RFLP	41/23	27/4/10	17/4/2	0.058	8
AshokKumar 2010	India	CAD	HB	PCR	414/424	348/62/4	329/87/8	0.427	7
Bhanushali 2010	India	CAD	HB	PCR	90/150	78/11/1	127/21/2	0.306	7
Abd 2011	Egypt	MI	HB	PCR	200/100	164/32/4	70/26/4	0.431	7
Agirbasli 2011	Turkey	CAD	HB	PCR-RFLP	97/81	86/10/1	64/16/1	1.000	7
Al-Jafari 2012	Saudi Arabia	CAD	HB	PCR	120/65	100/20/0	57/8/0	0.597	7
Daoud 2013	Saudi Arabia	CAD	HB	PCR-RFLP	226/103	185/41/0	92/11/0	0.567	7
Ahmadi 2015	Iran	CAD	HB	PCR-RFLP	115/89	58/23/34	75/7/7	>0.05	6
Abdel 2015	Sudan	CAD	HB	PCR-RFLP	54/59	46/8 [a]	51/8 [a]	>0.05	5
N291S						**AA/AG/GG**	**AA/AG/GG**		
Wittrup 1997	Danish	IHD	PB	PCR	1715/9214	1614/101[b]	8762/452[b]	>0.05	8
Arca 2000	Italy	CAD	HB	PCR-RFLP	416/407	398/18/0	391/16/0	0.686	6
Moennig 2000	Germany	CAD	PB	PCR	229/150	219/10/0	140/10/0	0.673	8
VAN 2001	Australia.	CAD	PB	PCR	599/664	579/20 [b]	642/22 [b]	>0.05	7
Myllykangas 2001	Finland	CAD	HB	PCR	149/113	140/9 [b]	110/3 [b]	>0.05	7
Ferencak 2003	Croatia	CAD	HB	PCR	479/200	472/7/0	192/8/0	0.773	7
Martin 2004	UK	MI	HB	PCR-RFLP	547/505	527/20/0	490/15/0	0.242	7
Keavney 2004	UK	MI	PB	PCR	4524/3332	4359/162/3	3216/112/4	>0.05	7
Tripathi 2010	India	CAD	HB	PCR	329/331	295/34/0	308/23/0	0.513	6
Rebhi 2012	Tunisia	CAD	HB	PCR–RFLP	212/104	211/1/0	103/1/0	>0.05	7
Abdel 2015	Sudan	CAD	HB	PCR-RFLP	73/54	51/22 [b]	37/17 [b]	>0.05	5
D9N						**GG/GA/AA**	**GG/GA/AA**		
Zhang 1995	Germany	CAD	HB	PCR	243/86	233/10/0	84/2/0	0.913	7
Arca 2000	Italy	CAD	HB	PCR-RFLP	416/407	382/17/0	373/17/0	0.660	6
VAN 2001	Australia.	CAD	PB	PCR	631/606	597/34 [c]	592/14 [c]	>0.05	7
Martin 2004	UK	MI	HB	PCR-RFLP	547/505	534/13/0	493/12/0	0.787	7
Izar 2009	Brazil	MI	PB	PCR-RFLP	379/583	305/71/3	507/73/3	0.832	8
Bhanushali 2010	India	CAD	HB	PCR	90/150	89/1/0	146/4/0	0.869	7
Rebhi 2012	Tunisia	CAD	HB	PCR–RFLP	212/104	9/47/156	3/17/84	0.848	7
Abdel 2015	Sudan	CAD	HB	PCR-RFLP	65/78	62/3 [c]	75/3 [c]	>0.05	5
Pvull						**CC/CT/TT**	**CC/CT/TT**		
Thorn 1990	UK	CAD	PB	PCR	60/93	15/39/6	30/43/20	0.534	7

Peacock 1992	Sweden	CAD	HB	PCR	85/90	29/38/18	29/42/19	0.602	7
Mattu 1994	Welsh	CAD	PB	PCR-RFLP	90/123	28/42/20	36/64/23	0.561	8
Jemaa 1995	France	CAD	PB	PCR	614/732	184/302/128	188/357/187	0.506	7
Wang 1996	Australia	CAD	HB	PCR-RFLP	350/125	103/180/67	38/59/28	0.577	7
Stepanov 1998	Russia	CAD	PB	PCR-RFLP	93/119	26/52/15	29/57/33	0.655	7
Anderson 1999	America	CAD	HB	PCR	483/168	142/236/105	60/76/32	0.368	7
Abu-Amero 2003	Saudi Arabia	CAD	HB	PCR	431/511	138/225/68	182/248/81	0.819	6
Isbir 2003	Turkey	CAD	PB	PCR	100/72	37/49/14	20/40/12	0.289	7
Duman 2004	Turkey	CAD	HB	PCR	78/49	25/39/14	14/16/19	0.017	6
Keavney 2004	UK	MI	PB	PCR	4569/3377	957/2266/1346	721/1694/962	0.626	7
Georgiev 2008	Macedon	CAD	HB	PCR-RFLP	109/32	25/58/26	5/20/7	0.149	7
Al-Jafari 2012	Saudi Arabia	CAD	HB	PCR	120/65	50/52/18	25/28/12	0.408	7
Rebhi 2012	Tunisia	CAD	HB	PCR–RFLP	212/104	60/90/62	20/55/29	0.503	7
Daoud 2013	Saudi Arabia	CAD	HB	PCR-RFLP	226/103	89/102/35	46/44/13	0.627	7
Bahrami 2015	Iran	MI	HB	PCR-RFLP	211/203	78/101/32	72/93/38	0.414	7

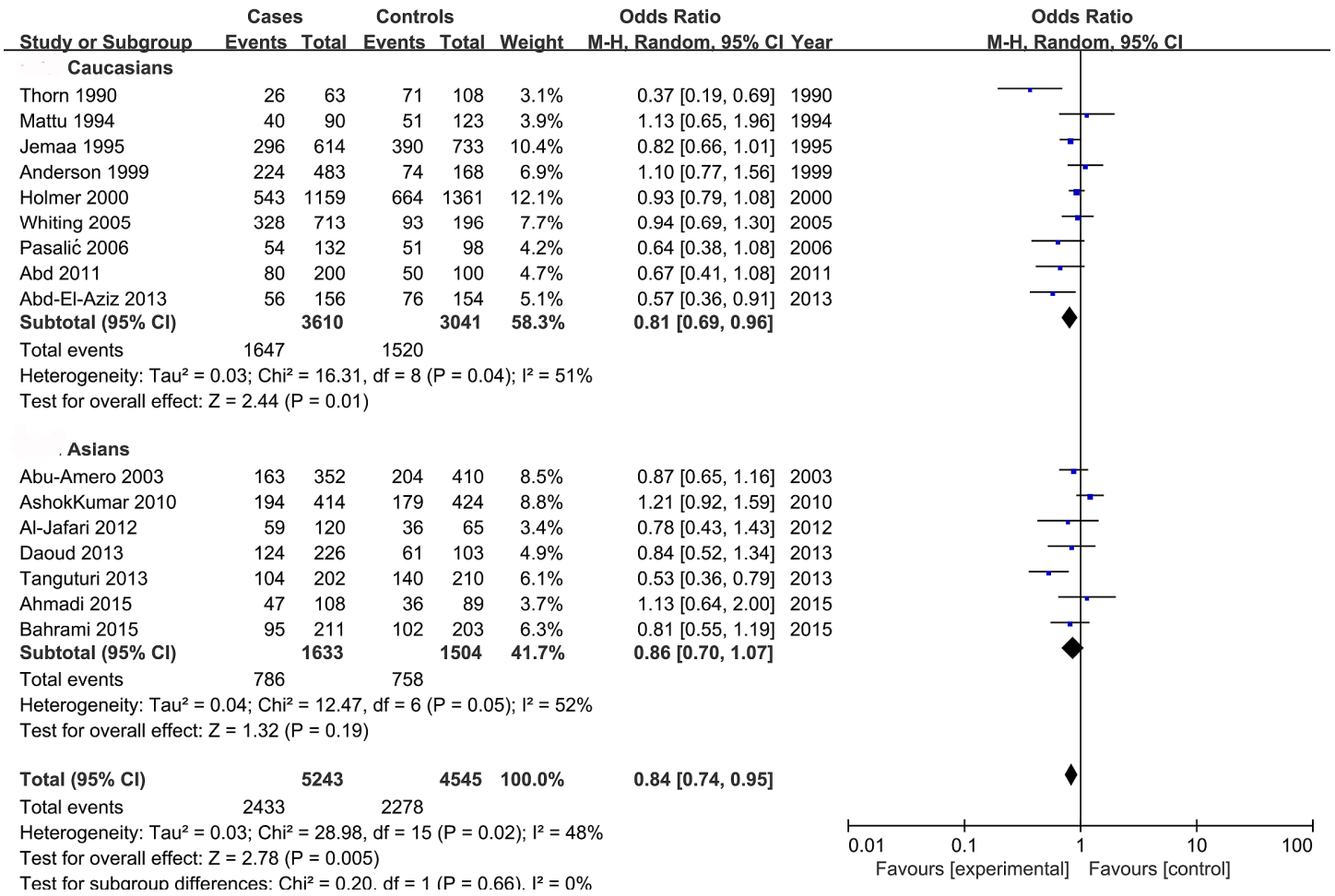
Abbreviations: CAD, coronary artery disease; MI, myocardial infarction; PCR, polymerase chain reaction; PCR-RFLP, polymerase chain reaction-restriction fragment length polymorphism; HWE, Hardy–Weinberg equilibrium for controls; NOS, Newcastle–Ottawa quality scale; IHD, ischemic heart disease; PB, population-based control; HB, hospital-based control. Note: a, CC vs. GC+GG; b, AA vs. AG+GG; c, GG vs. AG+AA.

Supplementary Table 3. Methodological quality of the selected studies according to the Newcastle-Ottawa Scale.

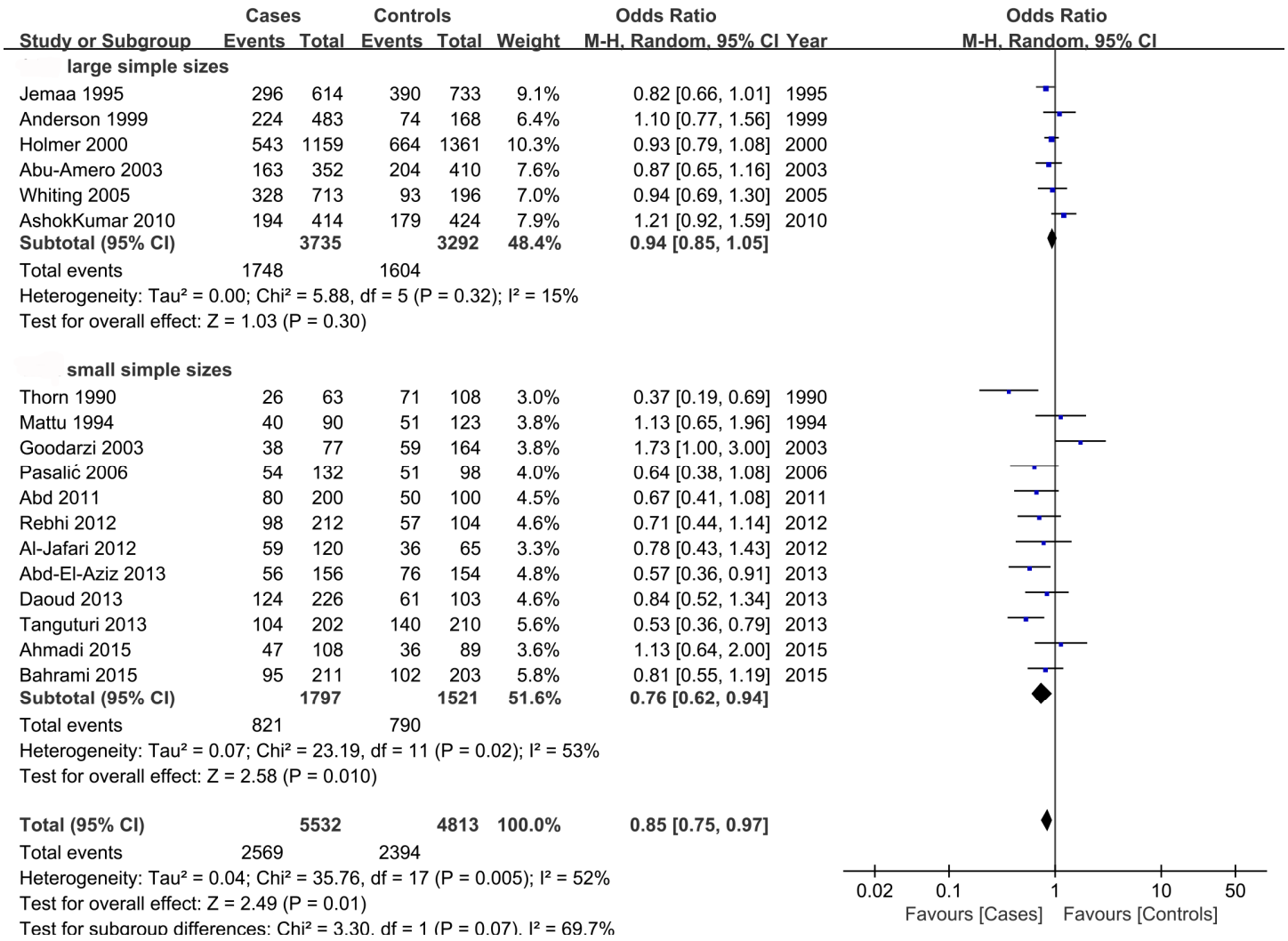
Study	Adequacy of Case Definition	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cases/controls	Ascertainment of exposure	Same method of ascertainment	Non-Response rate
Thorn 1990	★	★	★	★	★	★	★	N/A
Peacock 1992	★	★	N/A	★	★★	★	★	N/A
Mattu 1994	★	★	★	★	★★	★	★	N/A
Jemaa 1995	★	★	★	★	★	★	★	N/A
Zhang 1995	★	★	N/A	★	★★	★	★	N/A
Wang 1996	★	★	N/A	★	★★	★	★	N/A
Wittrup 1997	★	★	★	★	★★	★	★	N/A
Stepanov 1998	★	★	★	★	★	★	★	N/A
Anderson 1999	★	★	N/A	★	★★	★	★	N/A
Gagné 1999	★	★	★	★	★	★	★	N/A
Holmer 2000	★	★	★	★	★★	★	★	N/A
Arca 2000	★	★	N/A	★	★	★	★	N/A
Moennig 2000	★	★	★	★	★★	★	★	N/A
VAN 2001	★	★	★	★	★	★	★	N/A
Myllykangas 2001	★	★	N/A	★	★★	★	★	N/A
Sawano 2001	★	★	★	★	★★	★	★	N/A
Abu-Amero 2003	★	★	N/A	★	★	★	★	N/A
Goodarzi 2003	★	★	★	★	★	★	★	N/A
Ferencak 2003	★	★	N/A	★	★★	★	★	N/A
Isbir 2003	★	★	★	★	★	★	★	N/A
Martin 2004	★	★	N/A	★	★★	★	★	N/A
Keavney 2004	★	★	★	★	★	★	★	N/A
Duman 2004	★	★	N/A	★	★	★	★	N/A
Whiting 2005	★	★	N/A	★	★★	★	★	N/A
Baum 2006	★	★	N/A	★	★	★	★	N/A
Pasalić 2006	★	★	N/A	★	★★	★	★	N/A
Yamada 2006	★	★	N/A	★	★★	★	★	N/A
Ak 2007	★	★	N/A	★	★	★	★	N/A
Katia 2007	★	★	★	★	★	★	★	N/A
Georgiev 2008	★	★	N/A	★	★★	★	★	N/A
Izar 2009	★	★	★	★	★★	★	★	N/A
Aydogan 2009	★	★	★	★	★★	★	★	N/A
AshokKumar 2010	★	★	N/A	★	★★	★	★	N/A
Bhanushali 2010	★	★	N/A	★	★★	★	★	N/A
Tripathi 2010	★	★	N/A	★	★	★	★	N/A
Abd 2011	★	★	N/A	★	★★	★	★	N/A

Agirbasli 2011	★	★	N/A	★	★★	★	★	N/A
Al-Jafari 2012	★	★	N/A	★	★★	★	★	N/A
Rebhi 2012	★	★	N/A	★	★★	★	★	N/A
Abd-El-Aziz 2013	★	★	N/A	★	★★	★	★	N/A
Tanguturi 2013	★	★	★	★	★	★	★	N/A
Daoud 2013	★	★	N/A	★	★★	★	★	N/A
Ahmadi 2015	★	★	N/A	★	★	★	★	N/A
Abdel 2015	★	★	N/A	★	★	N/A	★	N/A
Bahrami 2015	★	★	N/A	★	★★	★	★	N/A

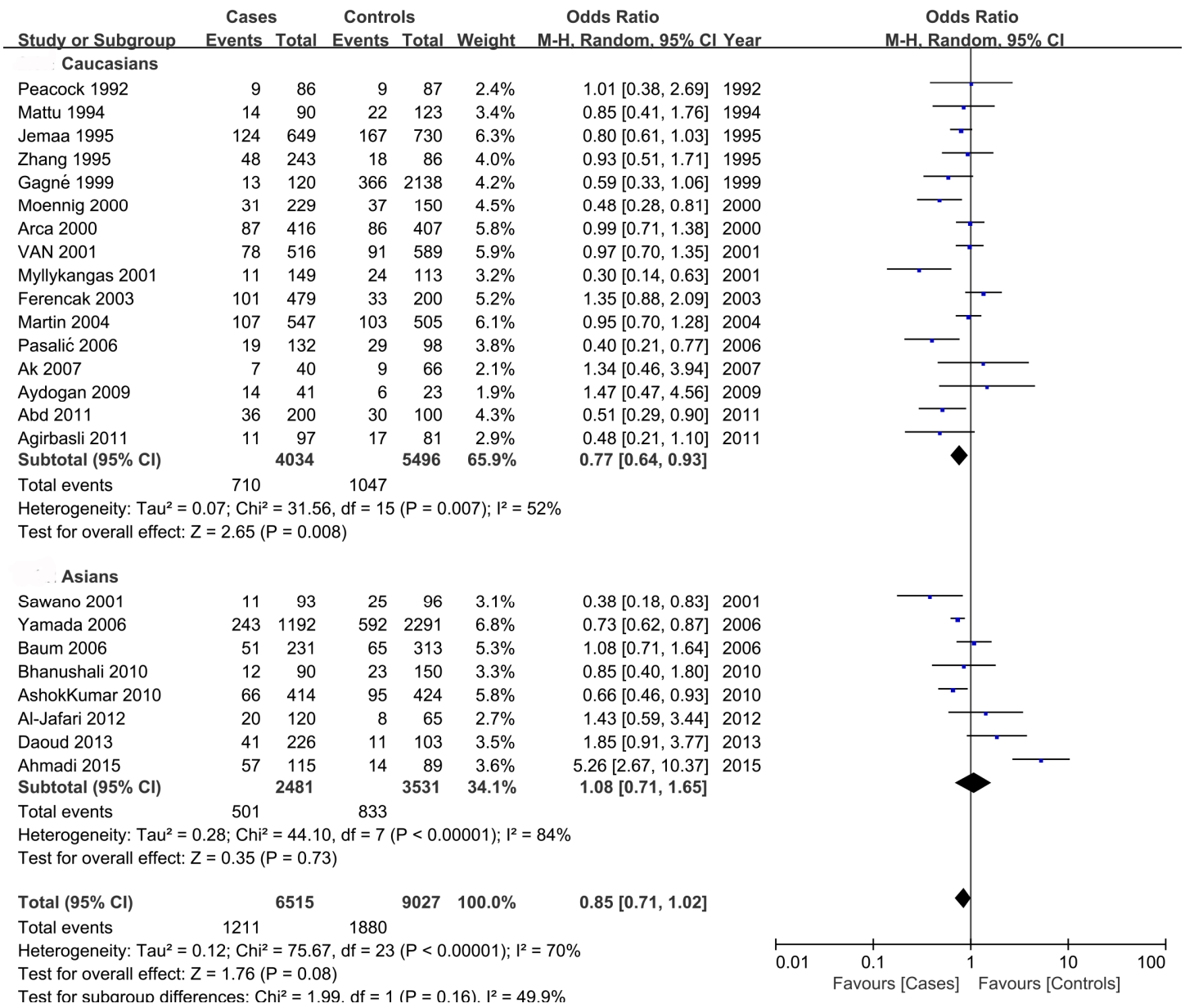
This table identifies ‘high’ quality choices with a ‘star’. A study can be awarded a maximum of 1 star for each numbered item within the Selection and Exposure categories. A maximum of 2 stars can be given for Comparability. ★, Yes; N/A, not applicable.



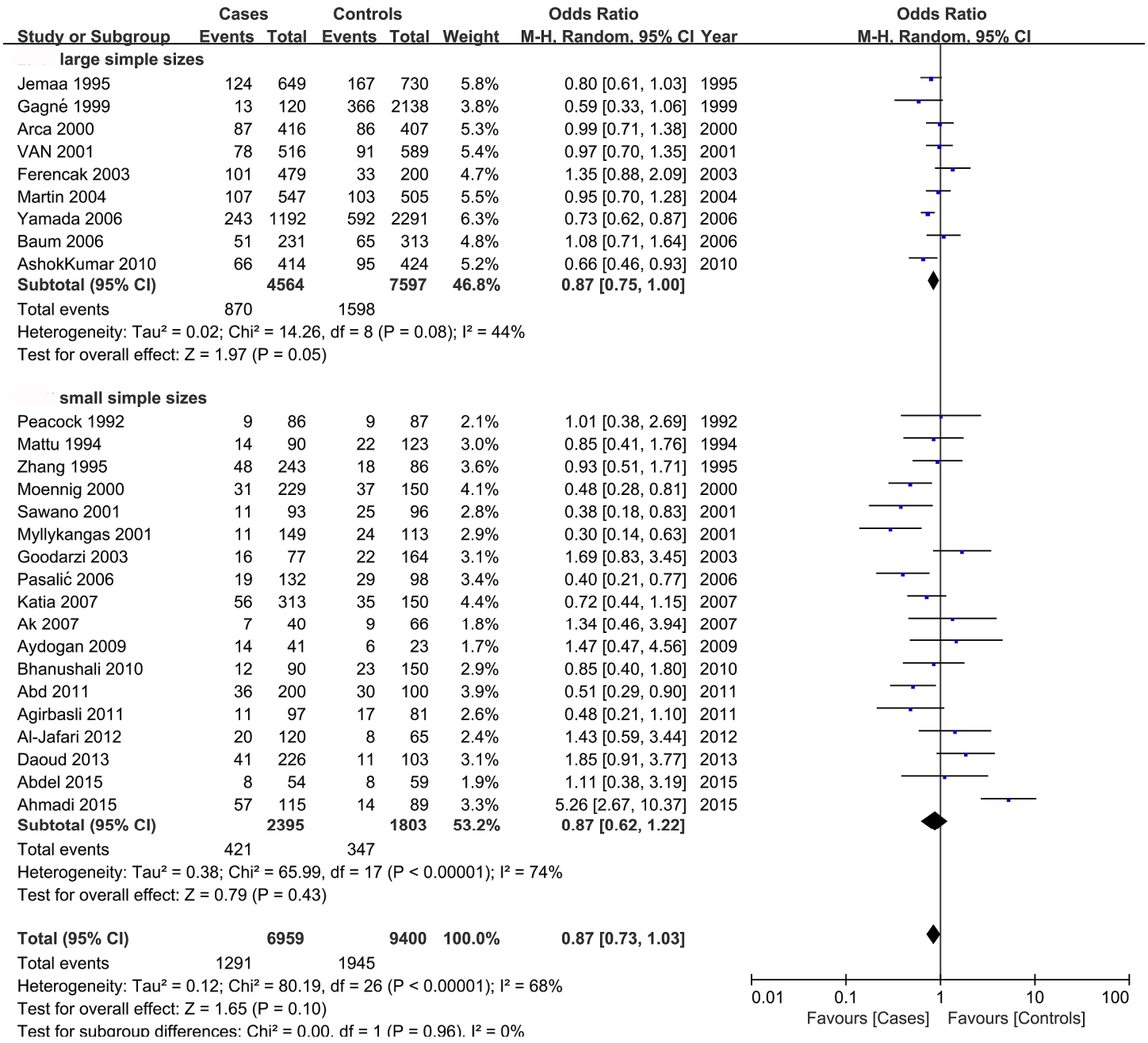
Supplementary Figure 1. Stratified analysis based on ethnicity for the association between the *LPL* HindIII polymorphism and CAD risk using dominant genetic model (GG+GT vs. TT).



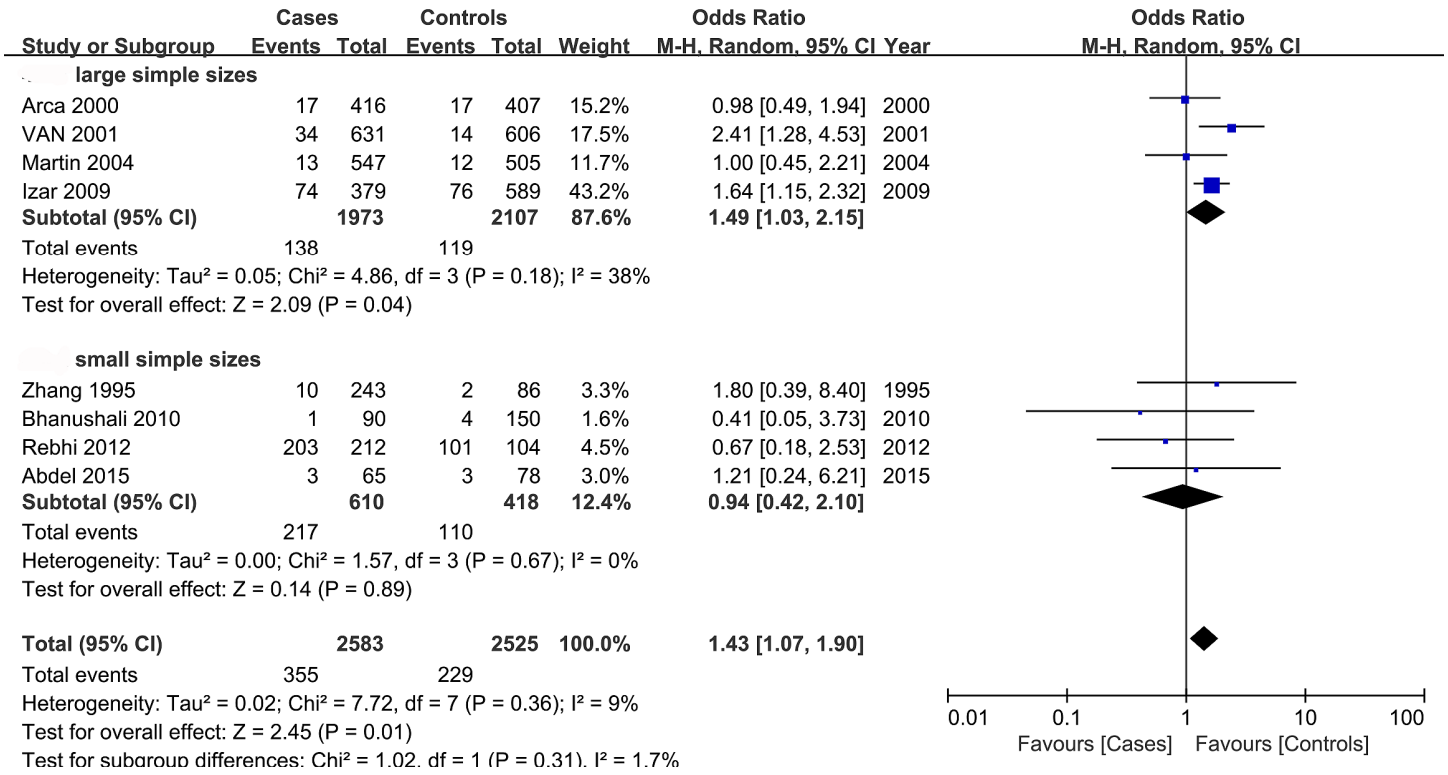
Supplementary Figure 2. Stratified analysis based on sample size for the association between the *LPL* HindIII polymorphism and CAD risk using dominant genetic model (GG+GT vs. TT).



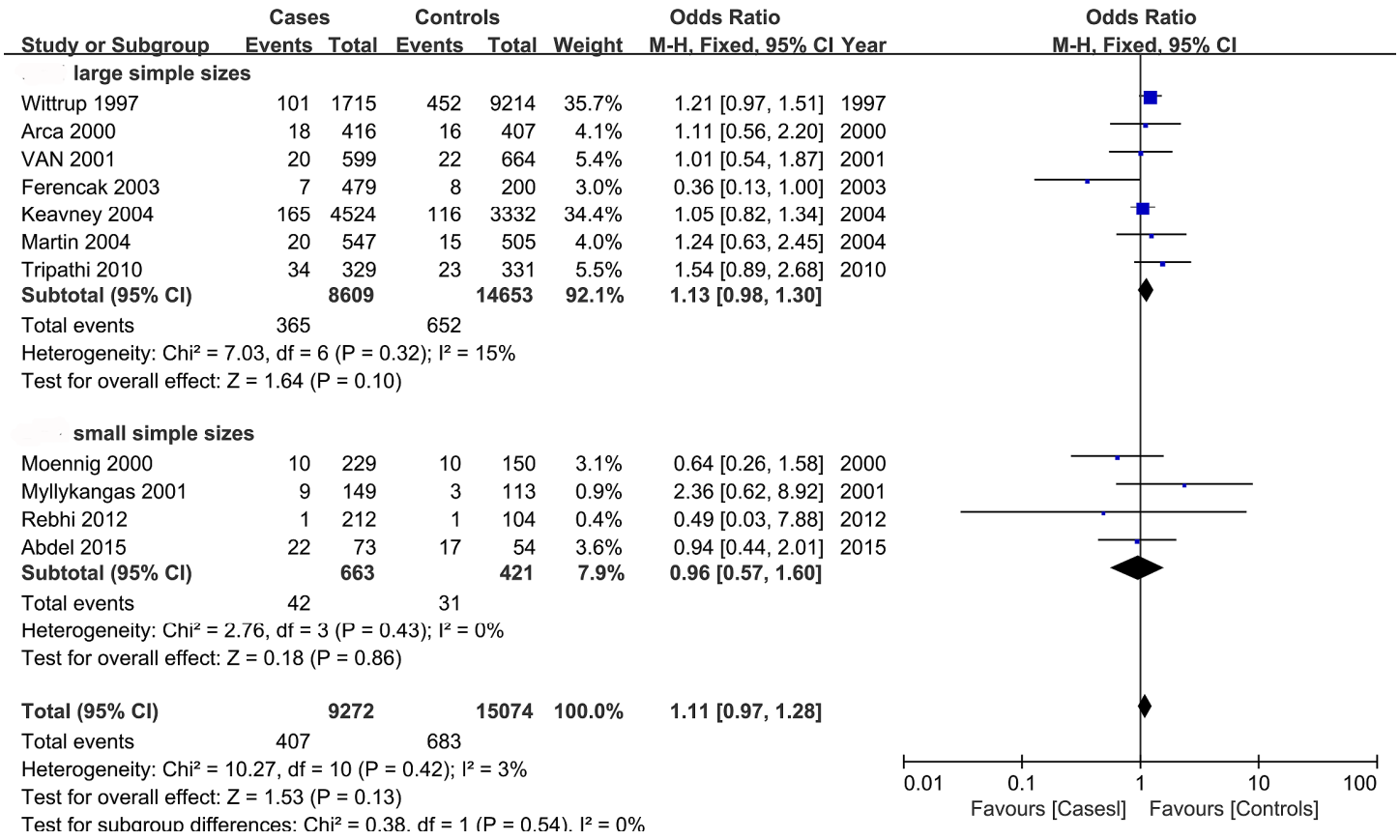
Supplementary Figure 3. Stratified analysis based on ethnicity for the association between the *LPL* S447X polymorphism and CAD risk using dominant genetic model (GG+GC vs. CC).



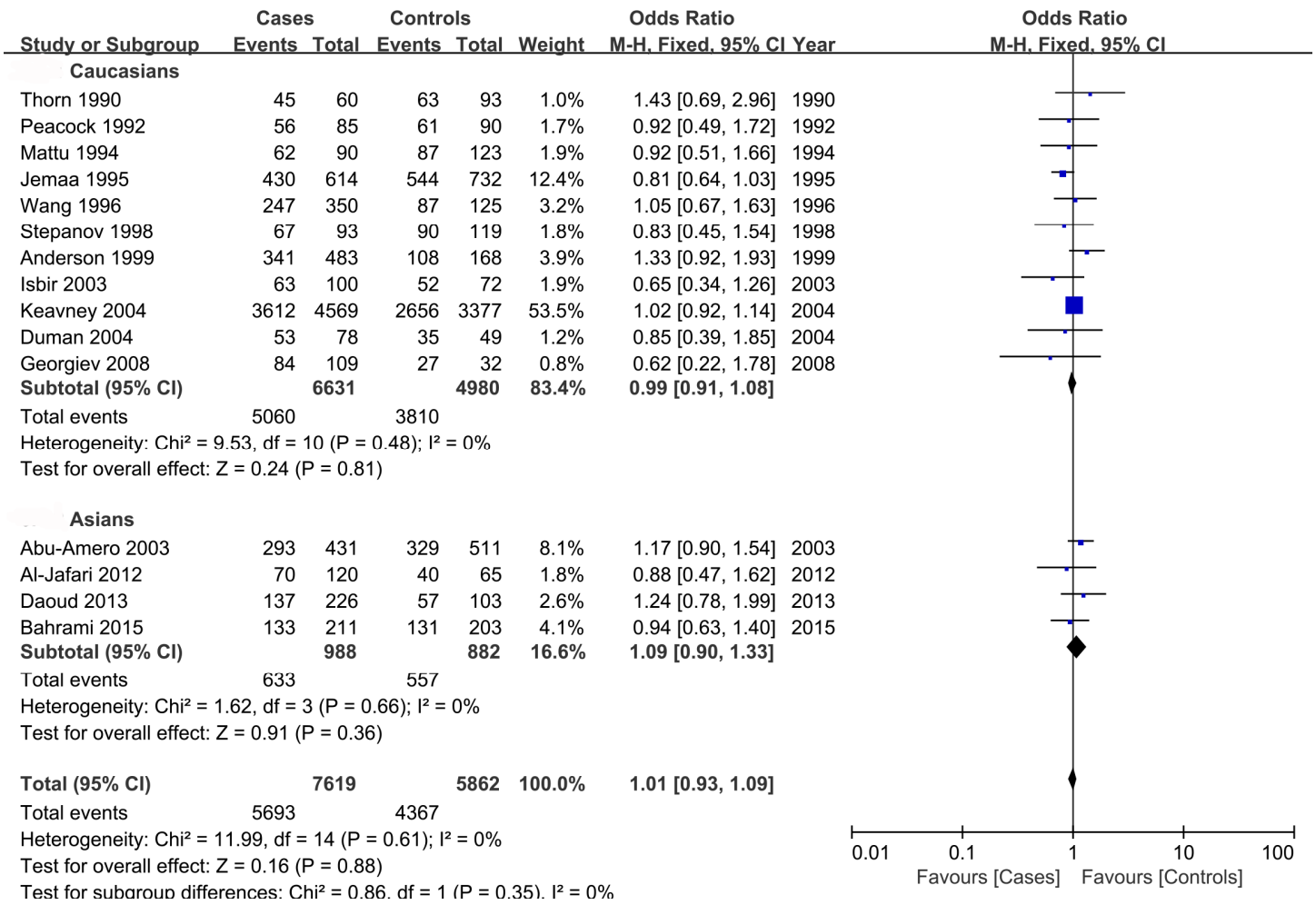
Supplementary Figure 4. Stratified analysis based on sample size for the association between the *LPL* S447X polymorphism and CAD risk using dominant genetic model (GG+GC vs. CC).



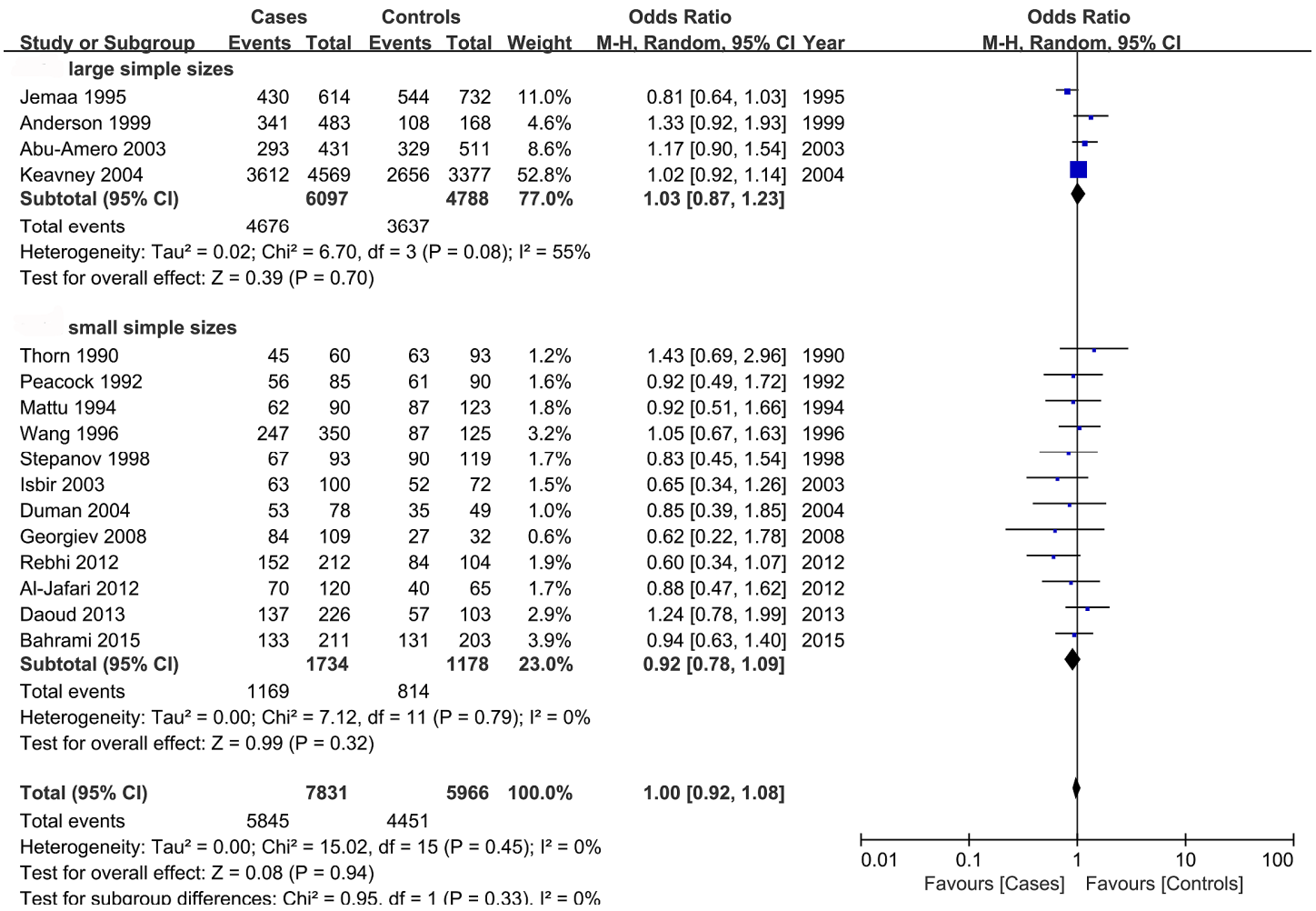
Supplementary Figure 5. Stratified analysis based on sample size for the association between the *LPL* D9N polymorphism and CAD risk using dominant genetic model (AA+GA vs. GG).



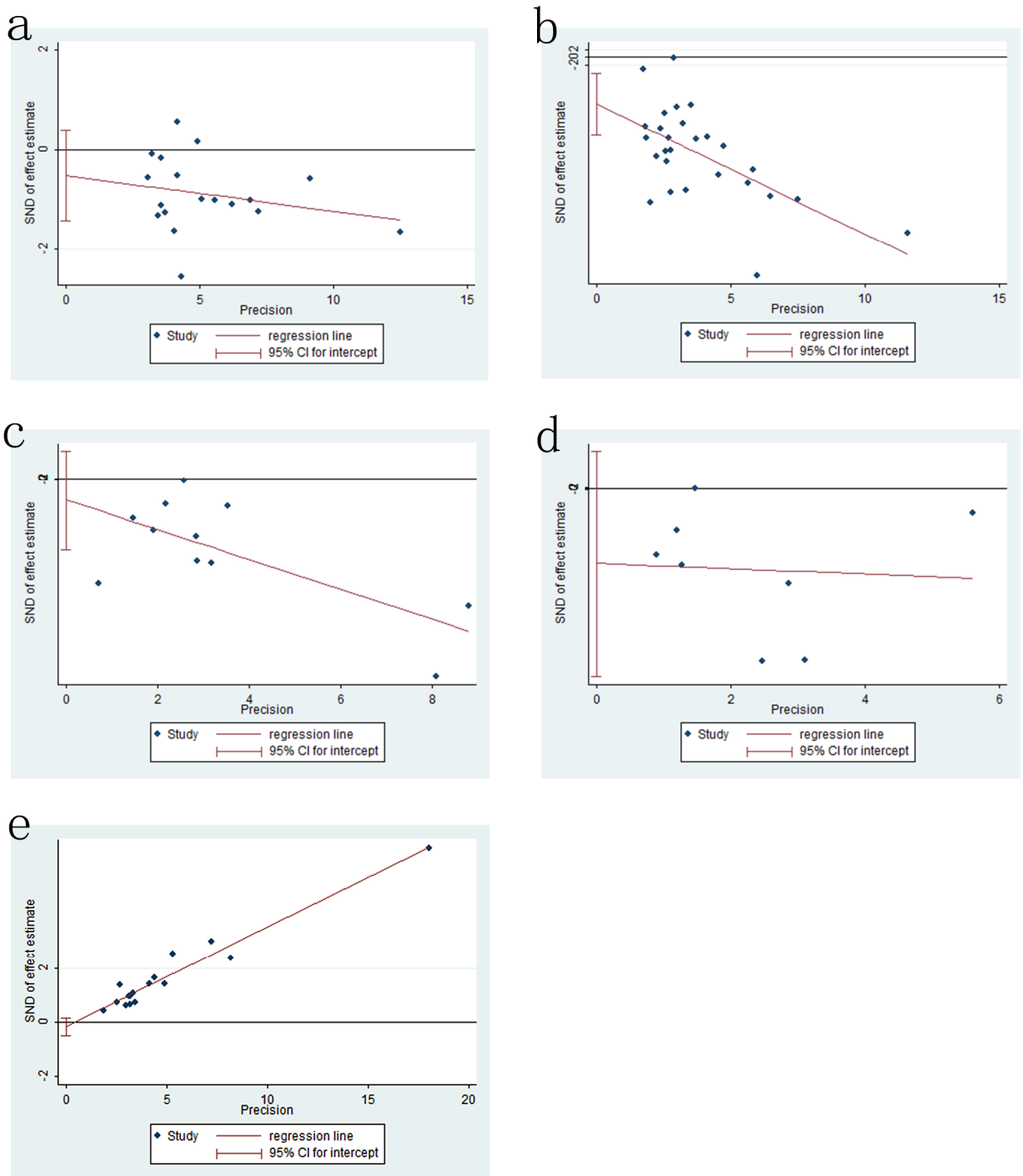
Supplementary Figure 6. Stratified analysis based on sample size for the association between the *LPL* N291S polymorphism and CAD risk using dominant genetic model (GG+GA vs. AA).



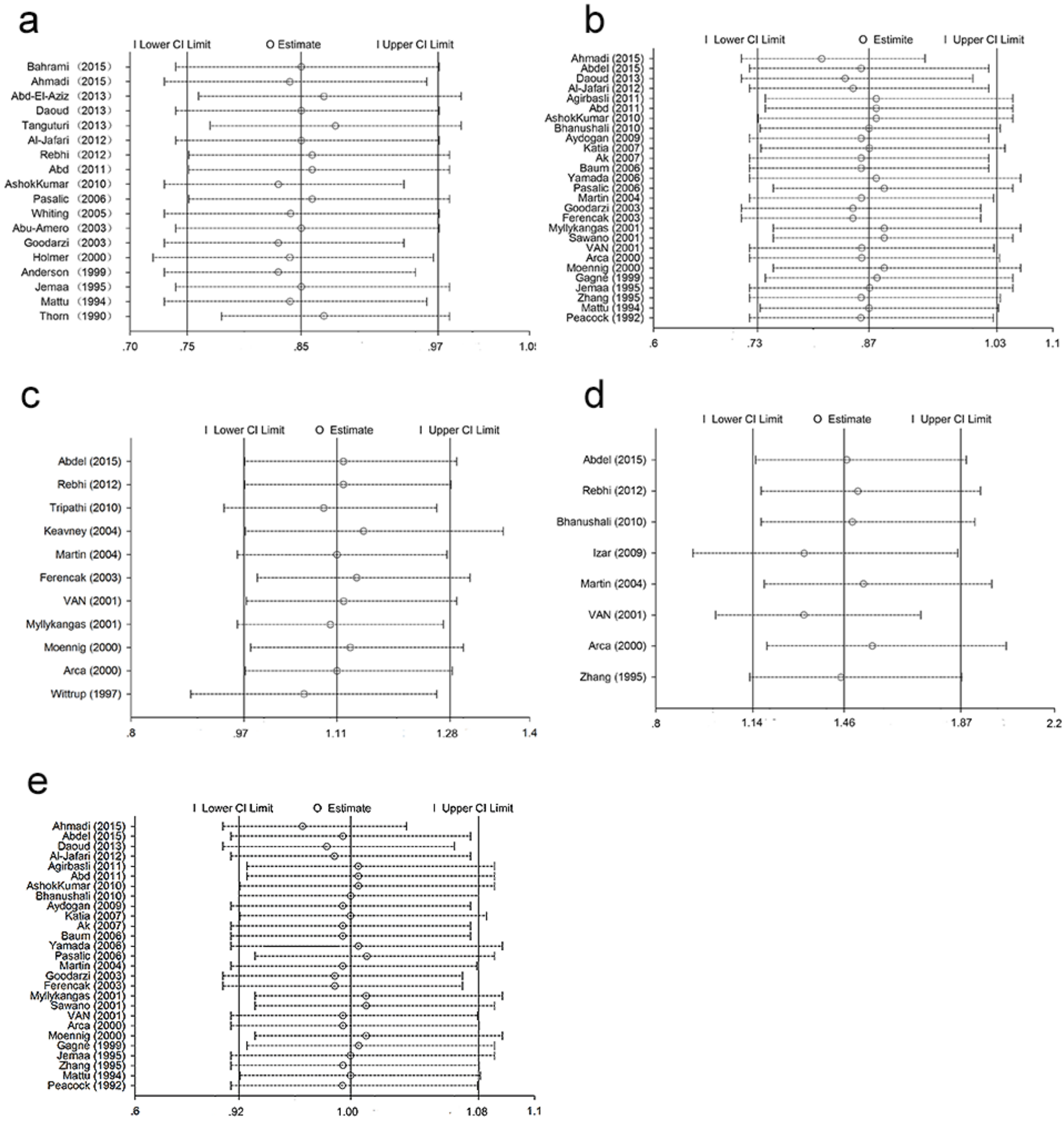
Supplementary Figure 7. Stratified analysis based on ethnicity for the association between the *LPL* PvuII polymorphism and CAD risk using dominant genetic model (TT+CT vs. CC).



Supplementary Figure 8. Stratified analysis based on sample size for the association between the *LPL* PvuII polymorphism and CAD risk using dominant genetic model (TT+CT vs. CC).



Supplementary Figure 9. Egger's regression test of publication bias for the association between the *LPL* gene polymorphisms and susceptibility to CAD. (a). HindIII polymorphism; (b). S447X polymorphism; (c). N291S polymorphism; (d). D9N polymorphism; (e). PvuII polymorphism.



Supplementary Figure 10. Sensitivity analysis on the correlation between *LPL* gene polymorphisms and susceptibility to CAD.

(a). sensitivity analysis for HindIII and CAD risk; (b). sensitivity analysis for S447X and CAD risk; (c). sensitivity analysis for N291S and CAD risk; (d). Sensitivity analysis for D9N and CAD risk; (e). sensitivity analysis for PvuII and CAD risk;