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	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	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15	Method of handling abstracts and unpublished studies	5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	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) Assessment of study quality, including blinding of quality assessors, stratification or 	4-6
21	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	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 c	f 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 c	f 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	Country	Disease	Source of	Gene-typing	Sample Size	Genotype	Distribution	P _{HWE}	
/Year	country		Controls	Methods	Cases/Controls	Cases	Controls	THWE	
Hind III						TT/TG/GG	TT/TG/GG		1
Thorn 1990	UK	CAD	PB	PCR	63/108	37/23/3	37/51/20	0.743	
Mattu 1994	Welsh	CAD	PB	PCR-RFLP	90/123	50/34/6	72/45/6	0.760	
Jemaa 1995	France	CAD	PB	PCR	614/733	318/258/38	343/314/76	0.742	
Anderson 1999	America	CAD	НВ	PCR	483/168	259/194/30	94/52/22	>0.05	
Holmer 2000	Germany	MI	PB	PCR	1159/1361	616/456/87	697/564/100	0.332	
Abu-Amero 2003	Saudi Arabia	CAD	НВ	PCR	352/410	189/138/25	206/173/31	0.518	t
Goodarzi 2003	USA	CAD	PB	PCR	77/164	39/33/5	105/52/7	0.861	┢
Whiting 2005	America	CAD	НВ	PCR	713/196	385/269/59	103/77/16	0.763	+
Pasalić 2006	Croatia	CAD	НВ	PCR-RFLP	132/98	78/46/8	47/45/6	0.262	+
AshokKumar 2010	India	CAD	НВ	PCR	414/424	220/168/26	245/158/21	0.486	
Abd 2011	Egypt	MI	НВ	PCR	200/100	120/70/10	50/36/14	0.834	_
Al-Jafari 2012	Saudi Arabia	CAD	НВ	PCR	120/65	61/53/6	29/23/13	0.050	+
Rebhi 2012	Tunisia	CAD	НВ	PCR-RFLP	212/104	114/83/15	47/39/18	0.569	_
Abd-El-Aziz 2013	Egypt	CAD	НВ	PCR-RFLP	156/154	100/53/3	78/54/22	>0.05	
	-972								
Tanguturi 2013	India	MI	PB	PCR	202/210	98/72/32	70/68/72	>0.05	
Daoud 2013	Saudi Arabia	CAD	НВ	PCR-RFLP	226/103	102/81/43	42/35/26	>0.05	
Ahmadi 2015	Iran	CAD	НВ	PCR-RFLP	108/89	61/41/6	53/33/3	0.430	T
Bahrami 2015	Iran	MI	НВ	PCR-RFLP	211/203	116/81/14	101/83/19	0.745	T
S477X						CC/CG/GG	CC/CG/GG		+
Peacock 1992	Sweden	CAD	HB	PCR	86/87	77/9 ^ª	78/9 ^ª	>0.05	t
Mattu 1994	Welsh	CAD	PB	PCR-RFLP	90/123	76/14/0	101/21/1	0.936	╞
Jemaa 1995	France	CAD	PB	PCR	649/730	525/118/6	563/154/13	0.514	╀
Zhang 1995	Germany	CAD	HB	PCR	243/86	195/46/2	68/17/1	0.959	╀
Gagné 1999	America	CAD	PB	PCR-RFLP	120/2138	107/13 ^ª	1772/366 ^ª	>0.05	╀
Arca 2000	Italy	CAD	HB	PCR-RFLP	416/407	329/87 ^a	321/86 ^ª	>0.05	╀
Moennig 2000	Germany	CAD	PB	PCR	229/150	198/28/3	113/37/0	0.085	╀
Sawano 2001	Japan	CAD	PB	PCR	93/96	82/10/1	71/23/2	0.932	╀
VAN 2001	Australia.	CAD	PB	PCR	516/589	438/78 ^a	498/91 ^a	>0.05	╀
Myllykangas 2001	Finland	CAD	НВ	PCR	149/113	138/11 ^a	89/24 ^a	>0.05	╀
Ferencak 2003	Croatia	CAD	НВ	PCR	479/200	378/97/4	167/32/1	0.686	╀

Goodarzi 2003	USA	CAD	PB	PCR	77/164	61/15/1	142/22/0	>0.05	Τ
Martin 2004	UK	MI	НВ	PCR-RFLP	547/505	440/104/3	402/99/4	0.483	
Baum 2006	China	MI	НВ	PCR	231/313	180/51/0	248/64/1	0.137	
Pasalić 2006	Croatia	CAD	НВ	PCR-RFLP	132/98	113/19/0	69/28/1	0.312	
Yamada 2006	Japan	MI	НВ	PCR	1192/2291	949/231/12	1699/547/45	0.900	
Ak 2007	Turkey	CAD	НВ	PCR	40/66	33/7/0	57/8/1	0.275	╞
Katia 2007	Brazil	CAD	PB	PCR-RFLP	313/150	257/47/9	115/34/1	0.110	+
Aydogan 2009	Turkey	CAD	PB	PCR-RFLP	41/23	27/4/10	17/4/2	0.058	
AshokKumar 2010	India	CAD	НВ	PCR	414/424	348/62/4	329/87/8	0.427	+
Bhanushali 2010	India	CAD	НВ	PCR	90/150	78/11/1	127/21/2	0.306	_
Abd 2011	Egypt	MI	НВ	PCR	200/100	164/32/4	70/26/4	0.431	
Agirbasli 2011	Turkey	CAD	НВ	PCR-RFLP	97/81	86/10/1	64/16/1	1.000	_
	Saudi				97/01			1.000	_
Al-Jafari 2012	Arabia	CAD	HB	PCR	120/65	100/20/0	57/8/0	0.597	
Daoud 2013	Saudi Arabia	CAD	НВ	PCR-RFLP	226/103	185/41/0	92/11/0	0.567	T
Ahmadi 2015	Iran	CAD	НВ	PCR-RFLP	115/89	58/23/34	75/7/7	>0.05	T
Abdel 2015	Sudan	CAD	НВ	PCR-RFLP	54/59	46/8 ^a	51/8ª	>0.05	T
N291S						AA/AG/GG	AA/AG/GG		
Wittrup 1997	Danish	IHD	PB	PCR	1715/9214	1614/101 ^b	8762/452 ^b	>0.05	
Arca 2000	Italy	CAD	HB	PCR-RFLP	416/407	398/18/0	391/16/0	0.686	╈
Moennig 2000	Germany	CAD	PB	PCR	229/150	219/10/0	140/10/0	0.673	┢
VAN 2001	Australia.	CAD	PB	PCR	599/664	579/20 ^b	642/22 ^b	>0.05	┢
Myllykangas 2001	Finland	CAD	НВ	PCR	149/113	140/9 ^b	110/3 ^b	>0.05	╉
Ferencak 2003	Croatia	CAD	НВ	PCR	479/200	472/7/0	192/8/0	0.773	╞
Martin 2004	UK	MI	НВ	PCR-RFLP	547/505	527/20/0	490/15/0	0.242	╞
Keavney 2004	UK	MI	PB	PCR	4524/3332	4359/162/3	3216/112/4	>0.05	╞
Tripathi 2010	India	CAD	НВ	PCR	329/331	295/34/0	308/23/0	0.513	╞
Rebhi 2012	Tunisia	CAD	НВ	PCR-RFLP	212/104	211/1/0	103/1/0	>0.05	+
Abdel 2015	Sudan	CAD	НВ	PCR-RFLP	73/54	51/22 ^b	37/17 ^b	>0.05	+
D9N						GG/GA/AA	GG/GA/AA		+
Zhang 1995	Germany	CAD	НВ	PCR	243/86	233/10/0	84/2/0	0.913	╞
Arca 2000	Italy	CAD	НВ	PCR-RFLP	416/407	382/17/0	373/17/0	0.660	╞
	-								╞
VAN 2001	Australia.		PB		631/606	597/34 °	592/14 [°]	>0.05	╞
Martin 2004	UK	MI	HB	PCR-RFLP	547/505	534/13/0	493/12/0	0.787	╞
Izar 2009	Brazil	MI	PB	PCR-RFLP	379/583	305/71/3	507/73/3	0.832	╞
Bhanushali 2010	India	CAD	HB	PCR	90/150	89/1/0	146/4/0	0.869	
Rebhi 2012	Tunisia	CAD	HB	PCR-RFLP	212/104	9/47/156	3/17/84	0.848	
Abdel 2015	Sudan	CAD	HB	PCR-RFLP	65/78	62/3 ^c	75/3 °	>0.05	
Pvull						CC/CT/TT	CC/CT/TT		T
Thorn 1990	UK	CAD	PB	PCR	60/93	15/39/6	30/43/20	0.534	T

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
Mallu 1994	VVEISIT	CAD	ГD	FGK-KFLF	90/123	20/42/20	30/04/23	0.501	0
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	НВ	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	РВ	PCR	4569/3377	957/2266/134 6	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	НВ	PCR	120/65	50/52/18	25/28/12	0.408	7
Rebhi 2012	Tunisia	CAD	НВ	PCR-RFLP	212/104	60/90/62	20/55/29	0.503	7
Daoud 2013	Saudi Arabia	CAD	НВ	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	Representative ness 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.

	Case	nts Total Events Total Weigh 26 63 71 108 3.19			Odds Ratio		Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	Year	M-H, Random, 95% Cl
Caucasians								
Thorn 1990	26	63	71	108	3.1%	0.37 [0.19, 0.69]	1990	
Mattu 1994	40	90	51	123	3.9%	1.13 [0.65, 1.96]	1994	
Jemaa 1995	296	614	390	733	10.4%	0.82 [0.66, 1.01]	1995	
Anderson 1999	224	483	74	168	6.9%	1.10 [0.77, 1.56]	1999	
Holmer 2000	543	1159	664	1361	12.1%	0.93 [0.79, 1.08]	2000	+
Whiting 2005	328	713	93	196	7.7%	0.94 [0.69, 1.30]	2005	-
Pasalić 2006	54	132	51	98	4.2%	0.64 [0.38, 1.08]	2006	
Abd 2011	80	200	50	100	4.7%	0.67 [0.41, 1.08]	2011	
Abd-El-Aziz 2013	56	156	76	154	5.1%	0.57 [0.36, 0.91]	2013	
Subtotal (95% CI)		3610		3041	58.3%	0.81 [0.69, 0.96]		•
Fotal events	1647		1520					
-leterogeneity: Tau ² =	0.03; Chi ²	² = 16.3	1, df = 8 ((P = 0.0))4); l² = 51%	0		
Test for overall effect:	Z = 2.44 (P = 0.0	1)					
					P = 0.04); l ² = 51% 410 8.5% 0.87 [0.65, 1.16] 2003 424 8.8% 1.21 [0.92, 1.59] 2010			
Asians						8.5% 0.87 [0.65, 1.16] 2003 8.8% 1.21 [0.92, 1.59] 2010		
Abu-Amero 2003	163	352	204	410	8.5%	0.87 [0.65, 1.16]	2003	
AshokKumar 2010	194	414	179	424	8.8%	1.21 [0.92, 1.59]	2010	
Al-Jafari 2012	59	120	36	410 8.5% C 424 8.8% 1		0.78 [0.43, 1.43]	2012	
Daoud 2013	124	226	61	103	4.9%	0.84 [0.52, 1.34]	2013	
Fanguturi 2013	104	202	140	210	6.1%	0.53 [0.36, 0.79]	2013	
Ahmadi 2015	47	108	36	89	3.7%	1.13 [0.64, 2.00]	2015	
Bahrami 2015	95	211	102	203	6.3%	0.81 [0.55, 1.19]	2015	
Subtotal (95% CI)		1633		1504	41.7%	0.86 [0.70, 1.07]		\bullet
Total events	786		758					
Heterogeneity: Tau ² =	0.04; Chi ²	² = 12.4	7, df = 6 ((P = 0.0)5); l² = 52%	, 0		
Test for overall effect:	Z = 1.32 (P = 0.1	9)					
Fotal (95% Cl)		5243		4545	100.0%	0.84 [0.74, 0.95]		♦
Total events	2433		2278					
Heterogeneity: Tau ² =	0.03; Chi ²	² = 28.9	8, df = 15	6 (P = 0	.02); l² = 48	%		
Test for overall effect:			•					0.01 0.1 1 10 100
Test for subaroup diffe	•			(D - 0)	66) 12 - 00/	,		Favours [experimental] Favours [control]

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).

	Case	s	Contro	ols		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight I	<u>/I-H, Random, 95% CI Ye</u>	ear M-H, Random, 95% Cl
large simple siz	zes						
Jemaa 1995	296	614	390	733	9.1%	0.82 [0.66, 1.01] 19	95 -
Anderson 1999	224	483	74	168	6.4%	1.10 [0.77, 1.56] 19	999
Holmer 2000	543	1159	664	1361	10.3%	0.93 [0.79, 1.08] 20	000 +
Abu-Amero 2003	163	352	204	410	7.6%	0.87 [0.65, 1.16] 20	03
Whiting 2005	328	713	93	196	7.0%	0.94 [0.69, 1.30] 20	05
AshokKumar 2010	194	414	179	424	7.9%	1.21 [0.92, 1.59] 20	10
Subtotal (95% CI)		3735		3292	48.4%	0.94 [0.85, 1.05]	•
Total events	1748		1604				
Heterogeneity: Tau ² =	0.00; Chi ²	= 5.88	, df = 5 (F	P = 0.32	2); I² = 15%		
Test for overall effect:	Z = 1.03 (P = 0.3	0)				
small simple si	zes						
Thorn 1990	26	63	71	108	3.0%	0.37 [0.19, 0.69] 19	90
Mattu 1994	40	90	51	123	3.8%	1.13 [0.65, 1.96] 19	
Goodarzi 2003	38	77	59	164	3.8%	1.73 [1.00, 3.00] 20	
Pasalić 2006	54	132	51	98	4.0%	0.64 [0.38, 1.08] 20	
Abd 2011	80	200	50	100	4.5%	0.67 [0.41, 1.08] 20	
Rebhi 2012	98	212	57	104	4.6%	0.71 [0.44, 1.14] 20	
Al-Jafari 2012	59	120	36	65	3.3%	0.78 [0.43, 1.43] 20	
Abd-El-Aziz 2013	56	156	76	154	4.8%	0.57 [0.36, 0.91] 20	
Daoud 2013	124	226	61	103	4.6%	0.84 [0.52, 1.34] 20	
Tanguturi 2013	104	202	140	210	5.6%	0.53 [0.36, 0.79] 20	
Ahmadi 2015	47	108	36	89	3.6%	1.13 [0.64, 2.00] 20	
Bahrami 2015	95	211	102	203	5.8%	0.81 [0.55, 1.19] 20	
Subtotal (95% CI)	50	1797	102	1521	51.6%	0.76 [0.62, 0.94]	▲
Total events	821		790	-			
Heterogeneity: Tau ² =	0.07; Chi ²	= 23.1	9, df = 11	(P = 0	.02); l² = 53%	6	
Test for overall effect:					<i>,,</i>		
Total (95% CI)		5532		4813	100.0%	0.85 [0.75, 0.97]	•
Total events	2569		2394				
Heterogeneity: Tau ² =		= 35.7		(P = 0	.005): ² = 52	2%	
Test for overall effect:				0			0.02 0.1 1 10 50
Test for subaroup diffe	· ·		,	(D - 0	07) 12 - 00	70/	Favours [Cases] Favours [Controls]

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).

	Case	S	Contro	ols		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Caucasians								
Peacock 1992	9	86	9	87	2.4%	1.01 [0.38, 2.69]	1992	
Mattu 1994	14	90	22	123	3.4%	0.85 [0.41, 1.76]	1994	
Jemaa 1995	124	649	167	730	6.3%	0.80 [0.61, 1.03]	1995	
Zhang 1995	48	243	18	86	4.0%	0.93 [0.51, 1.71]	1995	
Gagné 1999	13	120	366	2138	4.2%	0.59 [0.33, 1.06]	1999	
Moennig 2000	31	229	37	150	4.5%	0.48 [0.28, 0.81]	2000	
Arca 2000	87	416	86	407	5.8%	0.99 [0.71, 1.38]	2000	+
VAN 2001	78	516	91	589	5.9%	0.97 [0.70, 1.35]	2001	+
Myllykangas 2001	11	149	24	113	3.2%	0.30 [0.14, 0.63]	2001	
Ferencak 2003	101	479	33	200	5.2%	1.35 [0.88, 2.09]	2003	
Martin 2004	107	547	103	505	6.1%	0.95 [0.70, 1.28]	2004	+
Pasalić 2006	19	132	29	98	3.8%	0.40 [0.21, 0.77]		
Ak 2007	7	40	9	66	2.1%		2007	
Aydogan 2009	14	41	6	23	1.9%	1.47 [0.47, 4.56]	2009	
Abd 2011	36	200	30	100	4.3%	0.51 [0.29, 0.90]		
Agirbasli 2011	11	97	17	81	2.9%	0.48 [0.21, 1.10]	2011	
Subtotal (95% CI)		4034		5496	65.9%	0.77 [0.64, 0.93]		\bullet
Total events	710		1047					
Test for overall effect:	: Z = 2.65 (P = 0.00	J8)					
Asians								
	11	93	25	96	3.1%	0.38 [0.18, 0.83]	2001	
Sawano 2001	11 243	93 1192	25 592		3.1% 6.8%	0.38 [0.18, 0.83] 0.73 [0.62, 0.87]		
Sawano 2001 Yamada 2006					6.8%	0.73 [0.62, 0.87]	2006	
Sawano 2001 Yamada 2006 Baum 2006	243	1192	592	2291	6.8% 5.3%		2006 2006	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010	243 51	1192 231	592 65	2291 313	6.8%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80]	2006 2006 2010	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010	243 51 12	1192 231 90	592 65 23	2291 313 150	6.8% 5.3% 3.3%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93]	2006 2006 2010 2010	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012	243 51 12 66	1192 231 90 414	592 65 23 95	2291 313 150 424	6.8% 5.3% 3.3% 5.8%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80]	2006 2006 2010 2010 2012	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013	243 51 12 66 20	1192 231 90 414 120	592 65 23 95 8	2291 313 150 424 65	6.8% 5.3% 3.3% 5.8% 2.7% 3.5%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77]	2006 2006 2010 2010 2012 2012 2013	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015	243 51 12 66 20 41	1192 231 90 414 120 226	592 65 23 95 8 11	2291 313 150 424 65 103	6.8% 5.3% 3.3% 5.8% 2.7%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44]	2006 2006 2010 2010 2012 2012 2013	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015 Subtotal (95% CI)	243 51 12 66 20 41	1192 231 90 414 120 226 115	592 65 23 95 8 11	2291 313 150 424 65 103 89	6.8% 5.3% 3.3% 5.8% 2.7% 3.5% 3.6%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77] 5.26 [2.67, 10.37]	2006 2006 2010 2010 2012 2012 2013	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015 Subtotal (95% CI) Total events	243 51 12 66 20 41 57 501	1192 231 90 414 120 226 115 2481	592 65 23 95 8 11 14 833	2291 313 150 424 65 103 89 3531	6.8% 5.3% 3.3% 5.8% 2.7% 3.5% 3.6% 34.1%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77] 5.26 [2.67, 10.37] 1.08 [0.71, 1.65]	2006 2006 2010 2010 2012 2012 2013	
Asians Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect:	243 51 12 66 20 41 57 501 = 0.28; Chi ²	1192 231 90 414 120 226 115 2481 * = 44.10	592 65 23 95 8 11 14 833 0, df = 7 (2291 313 150 424 65 103 89 3531	6.8% 5.3% 3.3% 5.8% 2.7% 3.5% 3.6% 34.1%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77] 5.26 [2.67, 10.37] 1.08 [0.71, 1.65]	2006 2006 2010 2010 2012 2012 2013	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect:	243 51 12 66 20 41 57 501 = 0.28; Chi ²	1192 231 90 414 120 226 115 2481 * = 44.10	592 65 23 95 8 11 14 833 0, df = 7 (2291 313 150 424 65 103 89 3531 P < 0.0	6.8% 5.3% 3.3% 5.8% 2.7% 3.5% 3.6% 34.1%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77] 5.26 [2.67, 10.37] 1.08 [0.71, 1.65]	2006 2006 2010 2010 2012 2012 2013	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015 Subtotal (95% CI) Total events Heterogeneity: Tau ² =	243 51 12 66 20 41 57 501 = 0.28; Chi ²	1192 231 90 414 120 226 115 2481 * = 44.10 P = 0.73	592 65 23 95 8 11 14 833 0, df = 7 (2291 313 150 424 65 103 89 3531 P < 0.0	6.8% 5.3% 3.3% 5.8% 2.7% 3.5% 3.6% 34.1%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77] 5.26 [2.67, 10.37] 1.08 [0.71, 1.65]	2006 2006 2010 2010 2012 2012 2013	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: Total (95% CI)	243 51 12 66 20 41 57 501 = 0.28; Chi ² : Z = 0.35 (1211	1192 231 90 414 120 226 115 2481 * = 44.10 P = 0.73 6515	592 65 23 95 8 11 14 833 0, df = 7 (3)	2291 313 150 424 65 103 89 3531 P < 0.0 9027	6.8% 5.3% 3.3% 5.8% 2.7% 3.5% 3.6% 34.1%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77] 5.26 [2.67, 10.37] 1.08 [0.71, 1.65] = 84%	2006 2010 2010 2012 2013 2015	
Sawano 2001 Yamada 2006 Baum 2006 Bhanushali 2010 AshokKumar 2010 Al-Jafari 2012 Daoud 2013 Ahmadi 2015 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: Total (95% CI) Total events	243 51 12 66 20 41 57 501 = 0.28; Chi ² ; Z = 0.35 (1211 = 0.12; Chi ²	1192 231 90 414 120 226 115 2481 $= 44.10$ P = 0.73 6515 $= 75.6^{2}$	592 65 23 95 8 11 14 833 0, df = 7 (3) 1880 7, df = 23	2291 313 150 424 65 103 89 3531 P < 0.0 9027	6.8% 5.3% 3.3% 5.8% 2.7% 3.5% 3.6% 34.1%	0.73 [0.62, 0.87] 1.08 [0.71, 1.64] 0.85 [0.40, 1.80] 0.66 [0.46, 0.93] 1.43 [0.59, 3.44] 1.85 [0.91, 3.77] 5.26 [2.67, 10.37] 1.08 [0.71, 1.65] = 84%	2006 2006 2010 2010 2012 2012 2013	

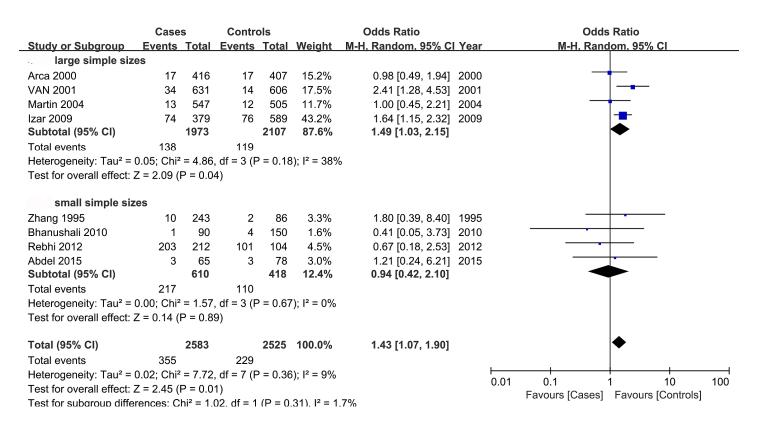
Supplementary Figure 3. Stratified analysis based on ethnicity for the association between the LPL S447X polymorphism and

CAD risk using dominant genetic model (GG+GC vs. CC).

	Case		Contro			Odds Ratio		Odds Ratio
Study or Subgroup		Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
large simple siz								
Jemaa 1995	124	649	167	730	5.8%	0.80 [0.61, 1.03]		-
Gagné 1999	13	120	366	2138	3.8%	0.59 [0.33, 1.06]		
Arca 2000	87	416	86	407	5.3%	0.99 [0.71, 1.38]	2000	
VAN 2001	78	516	91	589	5.4%	0.97 [0.70, 1.35]	2001	+
Ferencak 2003	101	479	33	200	4.7%	1.35 [0.88, 2.09]	2003	
Martin 2004	107	547	103	505	5.5%	0.95 [0.70, 1.28]	2004	+
Yamada 2006	243	1192	592	2291	6.3%	0.73 [0.62, 0.87]	2006	-
Baum 2006	51	231	65	313	4.8%	1.08 [0.71, 1.64]	2006	+-
AshokKumar 2010	66	414	95	424	5.2%	0.66 [0.46, 0.93]	2010	
Subtotal (95% CI)		4564		7597	46.8%	0.87 [0.75, 1.00]		•
Total events	870		1598					
Heterogeneity: Tau ² =	0.02; Chi ²	= 14.2	6, df = 8 ((P = 0.0))8); I ² = 44	%		
Test for overall effect:	Z = 1.97 (I	P = 0.0	5)					
small simple siz								
Peacock 1992	9	86	9	87	2.1%	1.01 [0.38, 2.69]	1992	
Mattu 1994	14	90	22	123	3.0%	0.85 [0.41, 1.76]	1994	
Zhang 1995	48	243	18	86	3.6%	0.93 [0.51, 1.71]	1995	
Moennig 2000	31	229	37	150	4.1%	0.48 [0.28, 0.81]	2000	
Sawano 2001	11	93	25	96	2.8%	0.38 [0.18, 0.83]		
Myllykangas 2001	11	149	24	113	2.9%	0.30 [0.14, 0.63]		
Goodarzi 2003	16	77	22	164	3.1%	1.69 [0.83, 3.45]		+
Pasalić 2006	19	132	29	98	3.4%	0.40 [0.21, 0.77]		
Katia 2007	56	313	35	150	4.4%	0.72 [0.44, 1.15]		+
Ak 2007	7	40	9	66	1.8%	1.34 [0.46, 3.94]		
Aydogan 2009	14	41	6	23	1.7%	1.47 [0.47, 4.56]		
Bhanushali 2010	12	90	23	150	2.9%	0.85 [0.40, 1.80]		
Abd 2011	36	200	30	100	3.9%	0.51 [0.29, 0.90]		_
Agirbasli 2011	11	200 97	17	81	2.6%	0.48 [0.21, 1.10]		
Al-Jafari 2012	20	120	8	65	2.0%	1.43 [0.59, 3.44]		
Daoud 2013	20 41	226		103	2.4 % 3.1%			<u> </u>
	41	226 54	11	59		1.85 [0.91, 3.77]		
Abdel 2015	-		8		1.9%	1.11 [0.38, 3.19]		
Ahmadi 2015 Subtotal (95% CI)	57	115 2395	14	89 1803	3.3% 53.2%	5.26 [2.67, 10.37]	2015	A
Subtotal (95% CI)	404	2393	247	1005	JJ.Z /0	0.87 [0.62, 1.22]		
Total events	421	- 65 0	347 0 df = 17	/	00004)- 12	- 740/		
Heterogeneity: Tau ² =				(P < 0	.00001); 12	- 14%		
Test for overall effect: 2	∠ = 0.79 (I	P = 0.43	3)					
Total (95% Cl)		6959		9400	100.0%	0.87 [0.73, 1.03]		•
Total events	1291		1945					
Heterogeneity: Tau ² =	0.12; Chi²	= 80.1	9, df = 26	(P < 0	.00001): l²	= 68%		
Test for overall effect: 2			•		.,,.			0.01 0.1 1 10 10
	•		,	-	.96). I² = 0	a.		Favours [Cases] Favours [Controls]

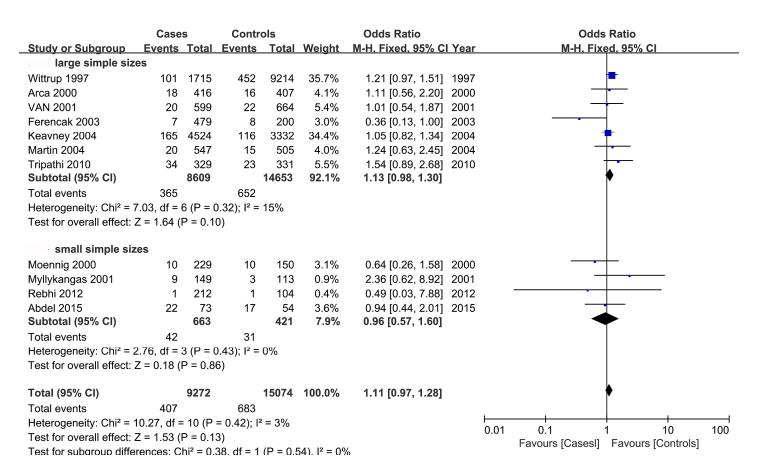
Supplementary Figure 4. Stratified analysis based on sample size for the association between the LPL S447X polymorphism

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).

	Case		Contro			Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	l Year	M-H, Fixed, 95% Cl
Caucasians								
Thorn 1990	45	60	63	93	1.0%	1.43 [0.69, 2.96]	1990	
Peacock 1992	56	85	61	90	1.7%	0.92 [0.49, 1.72]	1992	
Mattu 1994	62	90	87	123	1.9%	0.92 [0.51, 1.66]	1994	
Jemaa 1995	430	614	544	732	12.4%	0.81 [0.64, 1.03]	1995	
Wang 1996	247	350	87	125	3.2%	1.05 [0.67, 1.63]	1996	
Stepanov 1998	67	93	90	119	1.8%	0.83 [0.45, 1.54]	1998	
Anderson 1999	341	483	108	168	3.9%	1.33 [0.92, 1.93]	1999	
Isbir 2003	63	100	52	72	1.9%	0.65 [0.34, 1.26]	2003	
Keavney 2004	3612	4569	2656	3377	53.5%	1.02 [0.92, 1.14]	2004	
Duman 2004	53	78	35	49	1.2%	0.85 [0.39, 1.85]	2004	
Georgiev 2008	84	109	27	32	0.8%	0.62 [0.22, 1.78]	2008	
Subtotal (95% CI)		6631		4980	83.4%	0.99 [0.91, 1.08]		•
Total events	5060		3810					
Heterogeneity: Chi ² =	,	`		= 0%				
Test for overall effect:	,	`		= 0%				
Test for overall effect: Asians	: Z = 0.24 (P = 0.8	1)		8.1%	1.17 [0.90, 1.54]	2003	
Test for overall effect: Asians Abu-Amero 2003	: Z = 0.24 (293	P = 0.8 431	1) 329	511	8.1% 1.8%	1.17 [0.90, 1.54] 0.88 [0.47, 1.62]		
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012	293 70	P = 0.8 431 120	1) 329 40	511 65	1.8%	0.88 [0.47, 1.62]	2012	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013	293 70 137	P = 0.8 431 120 226	1) 329 40 57	511 65 103	1.8% 2.6%	0.88 [0.47, 1.62] 1.24 [0.78, 1.99]	2012 2013	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013 Bahrami 2015	293 70	P = 0.8 431 120	1) 329 40	511 65	1.8%	0.88 [0.47, 1.62]	2012 2013	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013	293 70 137	P = 0.8 431 120 226 211	1) 329 40 57	511 65 103 203	1.8% 2.6% 4.1%	0.88 [0.47, 1.62] 1.24 [0.78, 1.99] 0.94 [0.63, 1.40]	2012 2013	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013 Bahrami 2015 Subtotal (95% CI)	293 70 137 133 633	P = 0.8 431 120 226 211 988	1) 329 40 57 131 557	511 65 103 203 882	1.8% 2.6% 4.1%	0.88 [0.47, 1.62] 1.24 [0.78, 1.99] 0.94 [0.63, 1.40]	2012 2013	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013 Bahrami 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² =	Z = 0.24 (293 70 137 133 633 1.62, df =	P = 0.8 431 120 226 211 988 3 (P = 0	1) 329 40 57 131 557 0.66); l ² =	511 65 103 203 882	1.8% 2.6% 4.1%	0.88 [0.47, 1.62] 1.24 [0.78, 1.99] 0.94 [0.63, 1.40]	2012 2013	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013 Bahrami 2015 Subtotal (95% CI) Total events	Z = 0.24 (293 70 137 133 633 1.62, df =	P = 0.8 431 120 226 211 988 3 (P = 0	1) 329 40 57 131 557 0.66); l ² =	511 65 103 203 882 0%	1.8% 2.6% 4.1%	0.88 [0.47, 1.62] 1.24 [0.78, 1.99] 0.94 [0.63, 1.40]	2012 2013	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013 Bahrami 2015 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect:	Z = 0.24 (293 70 137 133 633 1.62, df =	P = 0.8 431 120 226 211 988 3 (P = 0 P = 0.3	1) 329 40 57 131 557 0.66); l ² =	511 65 103 203 882 0%	1.8% 2.6% 4.1% 16.6%	0.88 [0.47, 1.62] 1.24 [0.78, 1.99] 0.94 [0.63, 1.40] 1.09 [0.90, 1.33]	2012 2013	
Test for overall effect: Asians Abu-Amero 2003 Al-Jafari 2012 Daoud 2013 Bahrami 2015 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Total (95% Cl)	Z = 0.24 (293 70 137 133 633 1.62, df = Z = 0.91 (5693	P = 0.8 431 120 226 211 988 3 (P = 0 P = 0.3 7619	1) 329 40 57 131 557 0.66); l ² = 6) 4367	511 65 103 203 882 0% 5862	1.8% 2.6% 4.1% 16.6%	0.88 [0.47, 1.62] 1.24 [0.78, 1.99] 0.94 [0.63, 1.40] 1.09 [0.90, 1.33]	2012 2013	

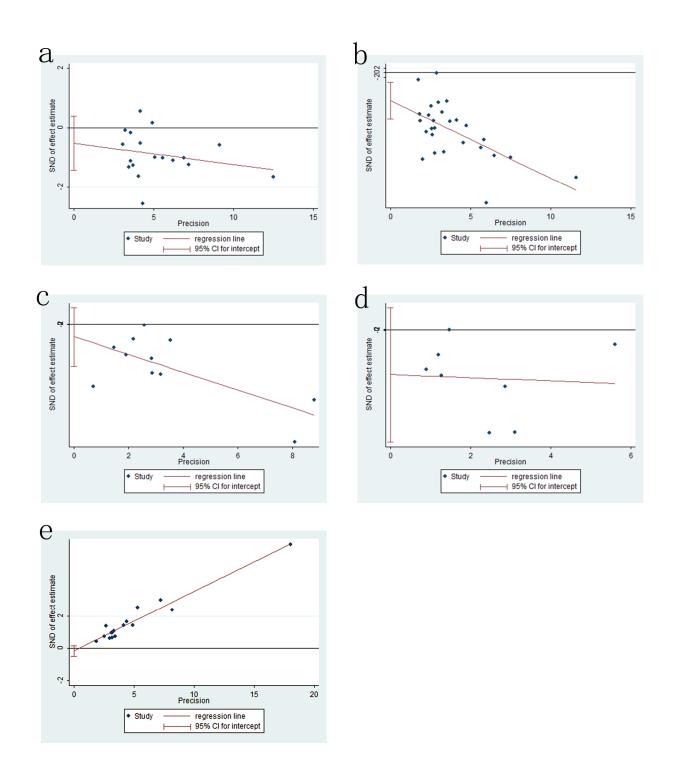
Supplementary Figure 7. Stratified analysis based on ethnicity for the association between the LPL Pvull polymorphism and

CAD risk using dominant genetic model (TT+CT vs. CC).

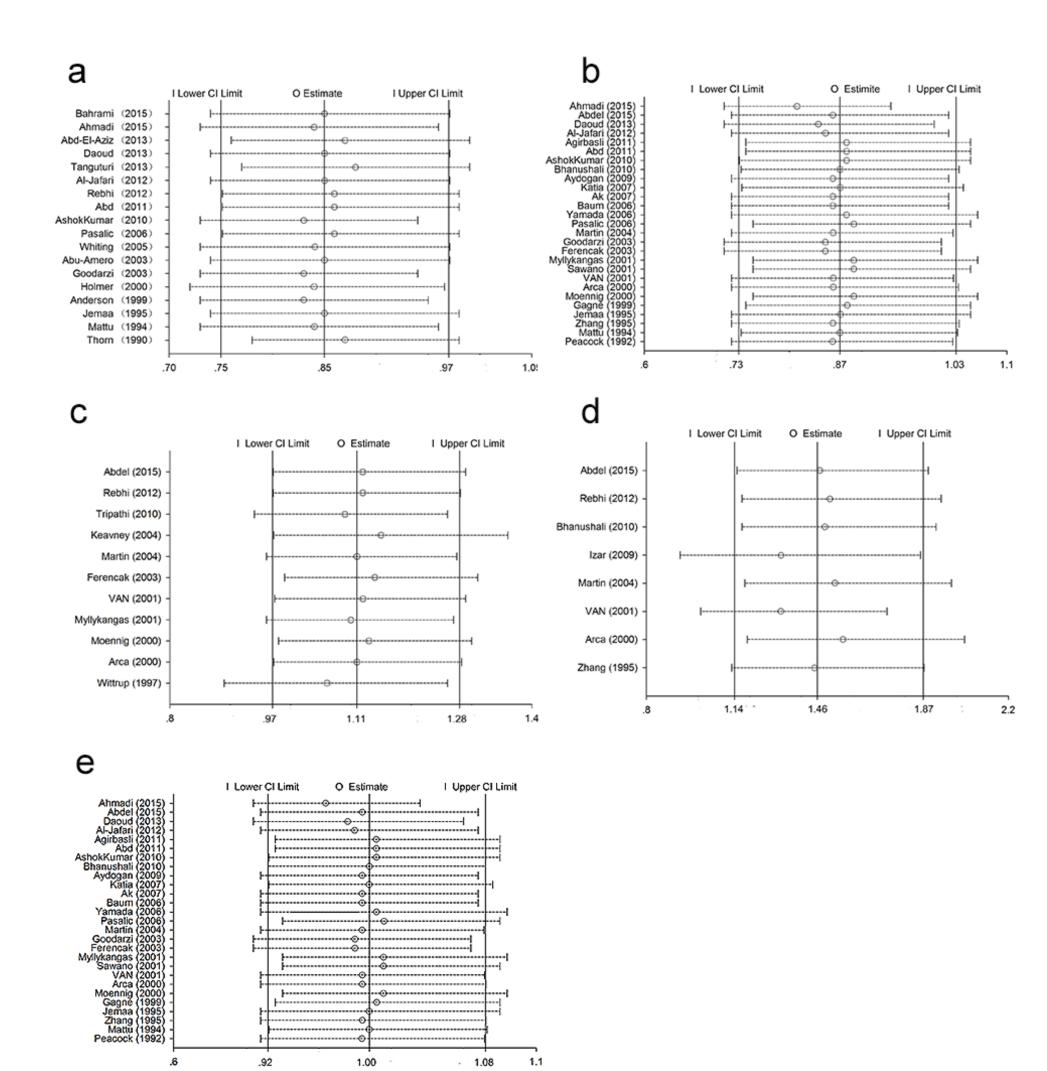
	Case	s	Contro	ols		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% Cl
large simple siz	zes							
Jemaa 1995	430	614	544	732	11.0%	0.81 [0.64, 1.03]	1995	-
Anderson 1999	341	483	108	168	4.6%	1.33 [0.92, 1.93]	1999	
Abu-Amero 2003	293	431	329	511	8.6%	1.17 [0.90, 1.54]	2003	
Keavney 2004	3612	4569	2656	3377	52.8%	1.02 [0.92, 1.14]	2004	•
Subtotal (95% Cl)		6097		4788	77.0%	1.03 [0.87, 1.23]		•
Total events	4676		3637					
Heterogeneity: Tau ² =	0.02; Chi ²	= 6.70	, df = 3 (F	P = 0.08	8); l² = 55%			
Test for overall effect:	Z = 0.39 (P = 0.7	0)					
small simple size								
Thorn 1990	45	60	63	93	1.2%	1.43 [0.69, 2.96]		
Peacock 1992	56	85	61	90	1.6%	0.92 [0.49, 1.72]	1992	
Mattu 1994	62	90	87	123	1.8%	0.92 [0.51, 1.66]		
Wang 1996	247	350	87	125	3.2%	1.05 [0.67, 1.63]		
Stepanov 1998	67	93	90	119	1.7%	0.83 [0.45, 1.54]	1998	
Isbir 2003	63	100	52	72	1.5%		2003	
Duman 2004	53	78	35	49	1.0%		2004	
Georgiev 2008	84	109	27	32	0.6%	0.62 [0.22, 1.78]	2008	
Rebhi 2012	152	212	84	104	1.9%	0.60 [0.34, 1.07]	2012	
Al-Jafari 2012	70	120	40	65	1.7%	0.88 [0.47, 1.62]	2012	
Daoud 2013	137	226	57	103	2.9%	1.24 [0.78, 1.99]	2013	
Bahrami 2015	133	211	131	203	3.9%	0.94 [0.63, 1.40]	2015	
Subtotal (95% CI)		1734		1178	23.0%	0.92 [0.78, 1.09]		•
Total events	1169		814					
Heterogeneity: Tau ² =	-			(P = 0.7	'9); l² = 0%			
Test for overall effect:	Z = 0.99 (P = 0.3	2)					
Total (95% CI)		7831		5966	100.0%	1.00 [0.92, 1.08]		•
Total events	5845		4451					
Heterogeneity: Tau ² =	0.00; Chi ²	= 15.0	2, df = 15	(P = 0	.45); l² = 0%	6	I	
Test for overall effect:								0.01 0.1 1 10 10
Test for subaroup diffe	•		,	(P = 0)	.33). I ² = 0%	6		Favours [Cases] Favours [Controls]

Supplementary Figure 8. Stratified analysis based on sample size for the association between the LPL Pvull 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). Pvull 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 Pvull and CAD risk;