THE LANCET

Supplementary webappendix

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

Supplement to: Heart Protection Study Collaborative Group. Effects on 11-year mortality and morbidity of lowering LDL cholesterol with simvastatin for about 5 years in 20 536 high-risk individuals: randomised controlled trial. *Lancet* 2011; published online Nov 23. DOI:10.1016/S0140-6736(11)61125-2.

Webappendix for "Effects on 11 year mortality and morbidity of lowering LDL cholesterol with simvastatin for about 5 years in 20,536 high-risk individuals"

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Webtable 1: Previously reported post-trial follow-up of vascular outcomes in randomised statin trials

Trial	In-trial randomised statin comparison	Post-trial follow-up	Clinical outcome	Post-trial events by original allocation		
				Statin	Placebo	OR (95% CI)
4S	20-40 mg S daily vs placebo for 5 y	5 y	Vascular mortality	155 (7.7%)	128 (6.6%)	1.14 (0.90-1.44)
LIPID	40 mg P daily vs placebo for 5 y	2 y	Vascular mortality	130 (3.3%)	163 (4.3%)	0.76 (0.60-0.96)
WOSCOPS	40 mg P daily vs placebo for 6 y	10 y	Non-fatal MI or CHD death	268 (8.6%)	310 (10.3%)	0.82 (0.69-0.96)
			Non-fatal or fatal stroke	161 (5.1%)	176 (5.6%)	0.88 (0.71-1.08)
ASCOT-LLA	10 mg A daily vs placebo for 3 y	2 y	Non-fatal MI or CHD death	59 (1.2%)	91 (1.9%)	0.63 (0.45-0.87)
HPS	40 mg S daily vs placebo for 5 y	6 y	Major Vascular Event	1636 (21.7%)	1566 (22.5%)	0.95 (0.89-1.02)

S=simvastatin; P=pravastatin; A=atorvastatin; MI=myocardial infarction; CHD=coronary heart disease

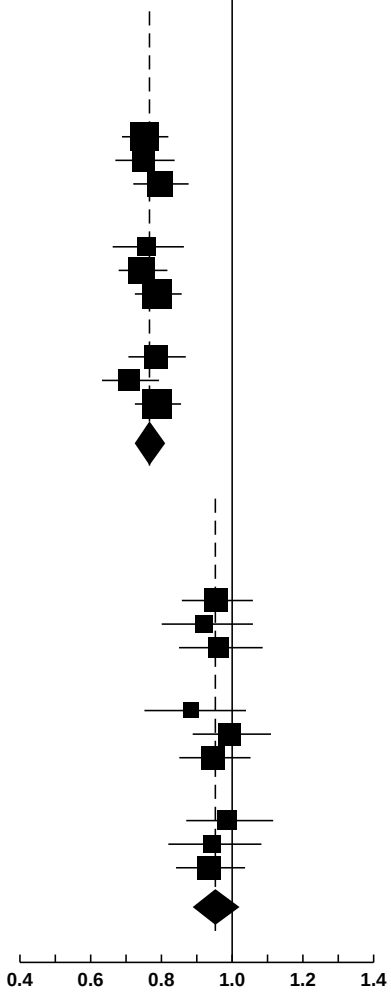
Webtable 2: Previously reported post-trial and in-trial follow-up of combined non-vascular outcomes in randomised statin trials

Trial	In-trial randomised statin comparison	In-trial + post-trial follow-up	Clinical outcome	In-trial and post-trial events by original allocation		
				Statin	Placebo	OR (95% CI)
4S	20-40mg S daily vs placebo for 5 y	5 + 5 y	Non-vascular mortality	123 (6.3%)	133 (6.7%)	0.89 (0.70-1.14)
			All cancer incidence	227 (11.7%)	248 (13.9%)	0.88 (0.73-1.05)
LIPID	40mg P daily vs placebo for 5 y	5 + 2 y	Non-vascular mortality	256 (5.7%)	292 (6.5%)	0.87 (0.73-1.03)
			All cancer incidence	499 (11.1%)	526 (11.7%)	0.91 (0.81-1.03)
WOSCOPS	40mg P daily vs placebo for 6 y	6 + 10 y	Non-vascular mortality	367 (11.1%)	377 (11.4%)	0.94 (0.82-1.09)
			All cancer incidence	431 (13.1%)	404 (12.3%)	1.05 (0.92-1.20)
ASCOT-LLA	10mg A daily vs placebo for 3 y	3 + 2 y	Non-vascular mortality	247 (4.8%)	284 (5.5%)	0.86 (0.72-1.02)
HPS	40 mg S daily vs placebo for 5 y	5 + 6 y	Non-vascular mortality	1523 (14.8%)	1555 (15.1%)	0.96 (0.89-1.03)
			All cancer incidence	1749 (17.0%)	1744 (17.0%)	0.98 (0.92-1.05)

S=simvastatin; P=pravastatin; A=atorvastatin; MI=myocardial infarction; CHD=coronary heart disease

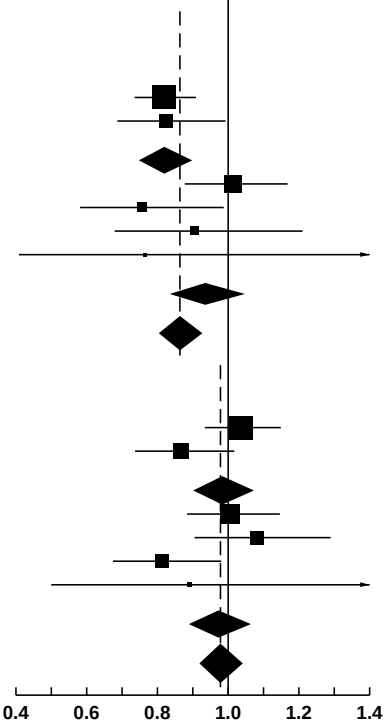
Webfigure 1: Major vascular events during in-trial and post-trial follow-up subdivided by baseline characteristics

Baseline characteristic	Simvastatin allocation: Simvastatin (n=7543)		Simvastatin allocation: Placebo (n=6967)		Risk ratio & 95% CI
In-trial					
Age (years)					
<65	884	(18.0%)	1148	(23.3%)	
>=65 <70	541	(22.1%)	695	(28.4%)	
>=70	728	(24.9%)	869	(30.1%)	
Total cholesterol (mmol/L)					
<5.0	380	(18.7%)	493	(24.1%)	
>=5.0 <6.0	791	(20.1%)	1018	(25.8%)	
>=6.0	982	(22.9%)	1201	(28.0%)	
LDL cholesterol (mmol/L)					
<3.0	640	(18.9%)	799	(23.5%)	
>=3.0 <3.5	512	(20.1%)	678	(27.0%)	
>=3.5	1001	(23.1%)	1235	(28.4%)	
All patients	**2153**	**(21.0%)**	**2712**	**(26.4%)**	**0.77 (0.72-0.81) p<0.0001**
Post-trial					
Age (years)					
<65	703	(18.2%)	686	(18.9%)	
>=65 <70	401	(22.9%)	390	(24.5%)	
>=70	532	(27.5%)	490	(28.2%)	
Total cholesterol (mmol/L)					
<5.0	290	(19.2%)	300	(21.2%)	
>=5.0 <6.0	646	(22.0%)	599	(22.2%)	
>=6.0	700	(22.6%)	667	(23.4%)	
LDL cholesterol (mmol/L)					
<3.0	510	(20.1%)	485	(20.2%)	
>=3.0 <3.5	412	(21.7%)	383	(22.6%)	
>=3.5	714	(23.0%)	698	(24.3%)	
All patients	**1636**	**(21.7%)**	**1566**	**(22.5%)**	**0.95 (0.89-1.02) p=0.17**

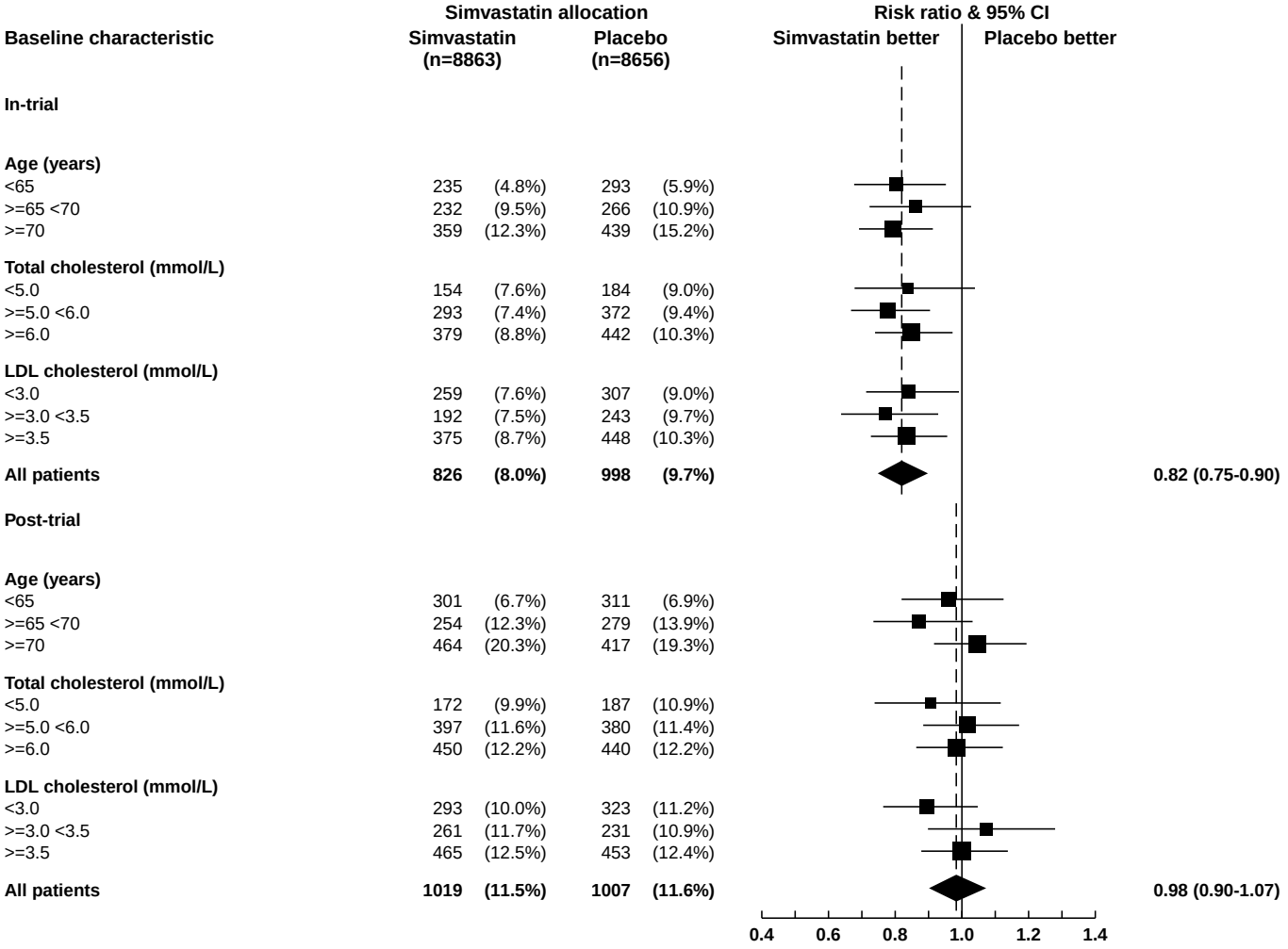


Webfigure 2: Cause-specific mortality during in-trial and post-trial follow-up

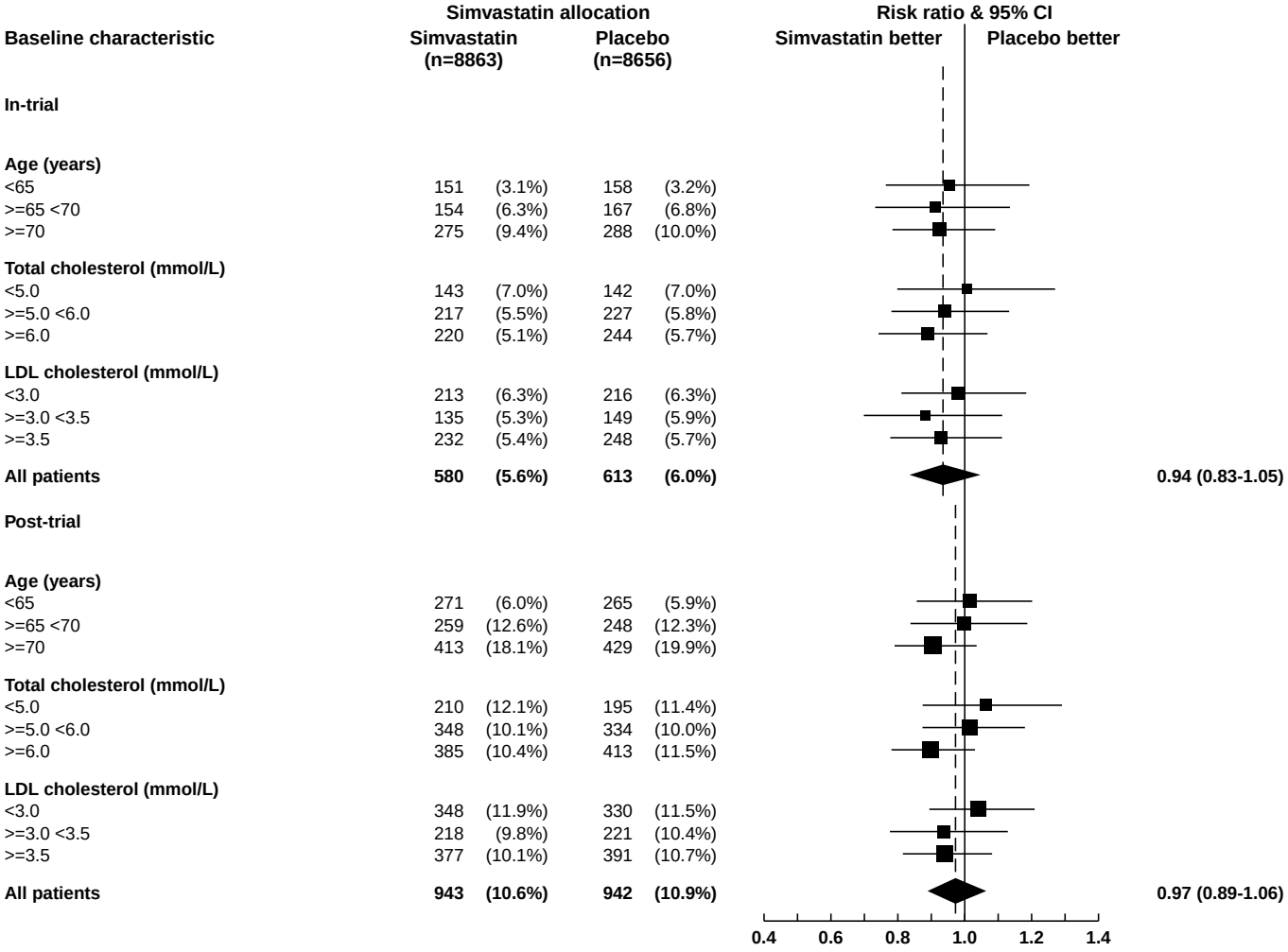
Cause of death	Simvastatin allocation: Simvastatin (n=8863)		Simvastatin allocation: Placebo (n=8656)		Risk ratio & 95% CI
In-trial					
Coronary	620	(6.0%)	751	(7.3%)	
Other vascular	206	(2.0%)	247	(2.4%)	
Any vascular	**826**	**(8.0%)**	**998**	**(9.7%)**	**0.82 (0.75-0.90)**
Neoplastic	380	(3.7%)	371	(3.6%)	
Respiratory	95	(0.9%)	124	(1.2%)	
Other medical	88	(0.9%)	96	(0.9%)	
Non-medical	17	(0.2%)	22	(0.2%)	
Non-vascular	**580**	**(5.6%)**	**613**	**(6.0%)**	**0.94 (0.83-1.05)**
All causes	**1406**	**(13.7%)**	**1611**	**(15.7%)**	**0.86 (0.80-0.93)**
Post-trial					
Coronary	741	(8.4%)	695	(8.0%)	
Other vascular	278	(3.1%)	312	(3.6%)	
Any vascular	**1019**	**(11.5%)**	**1007**	**(11.6%)**	**0.98 (0.90-1.07)**
Neoplastic	463	(5.2%)	447	(5.2%)	
Respiratory	258	(2.9%)	232	(2.7%)	
Other medical	200	(2.3%)	239	(2.8%)	
Non-medical	22	(0.2%)	24	(0.3%)	
Non-vascular	**943**	**(10.6%)**	**942**	**(10.9%)**	**0.97 (0.89-1.06)**
All causes	**1962**	**(22.1%)**	**1949**	**(22.5%)**	**0.98 (0.92-1.04)**

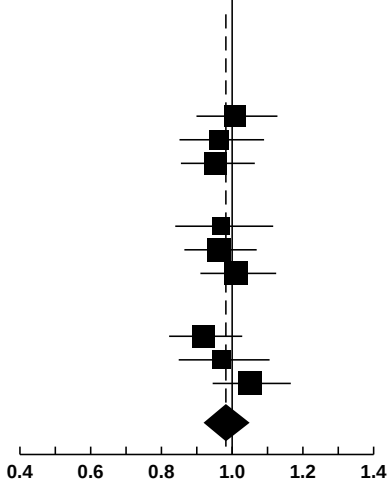


Webfigure 3: Vascular mortality during in-trial and post-trial follow-up subdivided by baseline characteristics



Webfigure 4: Non-vascular mortality during in-trial and post-trial follow-up subdivided by baseline characteristics



Webfigure 5: Cancer incidence during total follow-up period subdivided by baseline characteristics

Baseline characteristic	Simvastatin allocation: Simvastatin (n=10269)		Simvastatin allocation: Placebo (n=10267)		Risk ratio & 95% CI
					Simvastatin better / Placebo better
Age (years)					
<65	602	(12.3%)	596	(12.1%)	
>=65 <70	502	(20.5%)	504	(20.6%)	
>=70	645	(22.1%)	644	(22.3%)	
Total cholesterol (mmol/L)					
<5.0	374	(18.4%)	382	(18.7%)	
>=5.0 <6.0	675	(17.1%)	686	(17.4%)	
>=6.0	700	(16.3%)	676	(15.8%)	
LDL cholesterol (mmol/L)					
<3.0	589	(17.4%)	631	(18.5%)	
>=3.0 <3.5	441	(17.3%)	437	(17.4%)	
>=3.5	719	(16.6%)	676	(15.5%)	
All patients	**1749**	**(17.0%)**	**1744**	**(17.0%)**	**0.98 (0.92-1.05)**