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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	Post-trial	Clinical outcome	Post-tr	Post-trial events by original allocation						
	statin comparison	follow-up		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 Non-fatal or fatal stroke	268 (8.6%) 161 (5.1%)	310 (10.3%) 176 (5.6%)	0.82 (0.69-0.96) 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	In-trial +	Clinical outcome	In-trial and post-trial events by original allocation						
	statin comparison	post-trial follow-up		Statin	Placebo	OR (95% CI)				
4S	20-40mg S daily vs placebo for 5 y	5 + 5 y	Non-vascular mortality All cancer incidence	123 (6.3%) 227 (11.7%)	133 (6.7%) 248 (13.9%)	0.89 (0.70-1.14) 0.88 (0.73-1.05)				
LIPID	40mg P daily vs placebo for 5 y	5 + 2 y	Non-vascular mortality All cancer incidence	256 (5.7%) 499 (11.1%)	292 (6.5%) 526 (11.7%)	0.87 (0.73-1.03) 0.91 (0.81-1.03)				
WOSCOPS	40mg P daily vs placebo for 6 y	6 + 10 y	Non-vascular mortality All cancer incidence	367 (11.1%) 431 (13.1%)	377 (11.4%) 404 (12.3%)	0.94 (0.82-1.09) 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 All cancer incidence	1523 (14.8%) 1749 (17.0%)	1555 (15.1%) 1744 (17.0%)	0.96 (0.89-1.03) 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

	e:-	nvastatin a	Uoootio		•	Risk ratio	8 0E9/ CI	
Baseline characteristic	Simvas		Place		Simvastatiı		Placebo better	
	(n=75	43)	(n=69	67)				
In-trial						į		
Age (years)					_	<u> </u>		
<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)						<u> </u>		
<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)						느 ㅣ		
<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
						1		
Post-trial						i		
Age (years)						<u> </u>		
<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)						1		
<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)						il		
<3.0	510	(20.1%)	485	(20.2%)		_	<u> </u>	
>=3.0 <3.5	412	(21.7%)	383	(22.6%)			<u> </u>	
>=3.5	714	(23.0%)	698	(24.3%)		-	_	
All patients	1636	(21.7%)	1566	(22.5%)			•	0.95 (0.89-1.02)
All patietits	1030	(21.1/0)	1300	(22.3/0)				p=0.17
								p-0
					0.4 0.6	0.8 1.	0 1.2 1.4	

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

	Sir	nvastatin a	llocatio	n	Risk ratio & 95% CI				
Cause of death	Simvastatin (n=8863)		Placebo (n=8656)		Simvastatin better F	Placebo better			
In-trial									
Coronary Other vascular	620 206	(6.0%) (2.0%)	751 247	(7.3%) (2.4%)	- -				
		, ,		, ,					
Any vascular	826	(8.0%)	998	(9.7%)	→ L	0.82 (0.75-0.90)			
Neoplastic	380	(3.7%)	371	(3.6%)	_ i				
Respiratory	95	(0.9%)	124	(1.2%)					
Other medical	88	(0.9%)	96	(0.9%)					
Non-medical	17	(0.2%)	22	(0.2%)	- 1				
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					1				
Coronary	741	(8.4%)	695	(8.0%)	<u> </u>				
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)			
		•		•	0.4 0.6 0.8 1.0	1.2 1.4			

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

•	Simvastatin allocation					Risk ratio & 95% CI					
Baseline characteristic	Simva: (n=8	statin	Place (n=86	ebo	Sim	Simvastatin better			Placebo	better	
In-trial											
Age (years) <65 >=65 <70 >=70	235 232 359	(4.8%) (9.5%) (12.3%)	293 266 439	(5.9%) (10.9%) (15.2%)		_		_			
Total cholesterol (mmol/L) <5.0 >=5.0 <6.0 >=6.0	154 293 379	(7.6%) (7.4%) (8.8%)	184 372 442	(9.0%) (9.4%) (10.3%)		_ _	 	-			
LDL cholesterol (mmol/L) <3.0 >=3.0 <3.5 >=3.5	259 192 375	(7.6%) (7.5%) (8.7%)	307 243 448	(9.0%) (9.7%) (10.3%)		_	-	_			
All patients	826	(8.0%)	998	(9.7%)				-			0.82 (0.75-0.90)
Post-trial											
Age (years) <65 >=65 <70 >=70	301 254 464	(6.7%) (12.3%) (20.3%)	311 279 417	(6.9%) (13.9%) (19.3%)			_		_ ├─		
Total cholesterol (mmol/L) <5.0 >=5.0 <6.0 >=6.0	172 397 450	(9.9%) (11.6%) (12.2%)	187 380 440	(10.9%) (11.4%) (12.2%)			——————————————————————————————————————				
LDL cholesterol (mmol/L) <3.0 >=3.0 <3.5 >=3.5	293 261 465	(10.0%) (11.7%) (12.5%)	323 231 453	(11.2%) (10.9%) (12.4%)			-		<u> </u>		
All patients	1019	(11.5%)	1007	(11.6%)							0.98 (0.90-1.07)
					0.4	0.6	0.8	1.0	1.2	1.4	

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

	Simvastatin allocation					Risk ratio & 95% CI					
Baseline characteristic	aracteristic Simvastatin Placebo Simvastatin bet (n=8863) (n=8656)		in bette	er 	Placeb	o better					
In-trial											
Age (years)								i			
<65	151	(3.1%)	158	(3.2%)				-			
>=65 <70	154	(6.3%)	167	(6.8%)				-			
>=70	275	(9.4%)	288	(10.0%)				7	_		
Total cholesterol (mmol/L)								!			
<5.0	143	(7.0%)	142	(7.0%)				┼╞		-	
>=5.0 <6.0	217	(5.5%)	227	(5.8%)				+			
>=6.0	220	(5.1%)	244	(5.7%)				₽ ` †	_		
LDL cholesterol (mmol/L)								i l			
<3.0	213	(6.3%)	216	(6.3%)							
>=3.0 <3.5	135	(5.3%)	149	(5.9%)							
>=3.5	232	(5.4%)	248	(5.7%)				+			
All patients	580	(5.6%)	613	(6.0%)			<		-		0.94 (0.83-1.05)
Post-trial								<u>'</u>			
								i			
Age (years)											
<65	271	(6.0%)	265	(5.9%)			-				
>=65 <70	259	(12.6%)	248	(12.3%)			_	- 			
>=70	413	(18.1%)	429	(19.9%)			-	■┼	-		
Total cholesterol (mmol/L)								i			
<5.0	210	(12.1%)	195	(11.4%)			-		-	_	
>=5.0 <6.0	348	(10.1%)	334	(10.0%)			-				
>=6.0	385	(10.4%)	413	(11.5%)				■⊹	-		
LDL cholesterol (mmol/L)								- il			
<3.0	348	(11.9%)	330	(11.5%)				_4			
>=3.0 <3.5	218	(9.8%)	221	(10.4%)							
>=3.5	377	(10.1%)	391	(10.7%)			_	╼┼	_		
All patients	943	(10.6%)	942	(10.9%)					>		0.97 (0.89-1.06)
					0.4	0.6	0.8	1.0) 1.2	 1.4	

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

	Sin	nvastatin a	allocatio	n	Risk ratio		
Baseline characteristic	Simvas (n=102		Placebo (n=10267)		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%)	<u></u>		
>=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%)	<u>- </u> 		
All patients	1749	(17.0%)	1744	(17.0%)			0.98 (0.92-1.05)
					0.4 0.6 0.8 1	.0 1.2 1.4	