The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials

Lancet 2012; **379**

Study participants [MVEs] by predicted MVE risk

Statin vs. Control

Trial	<5%	≥5%, <10%	≥10%, <20%	≥20%, <30%	≥30%	Total
MEGA	7247 [147]	925 [91]	42 [4]	0 [0]	0 [0]	8214 [242]
JUPITER	11212 [118]	6117 [162]	472 [19]	1 [0]	0 [0]	17802 [299]
AFCAPS/TexCAPS	2944 [72]	3329 [225]	331 [47]	1 [0]	0 [0]	6605 [344]
ASCOT-LLA	1505 [25]	5383 [229]	3168 [245]	234 [22]	15 [3]	10305 [524]
WOSCOPS	34 [0]	3848 [219]	2576 [293]	134 [36]	3 [2]	6595 [550]
GISSI-HF	875 [34]	1523 [78]	1789 [171]	357 [52]	30 [11]	4574 [346]
ALERT	286 [8]	740 [54]	705 [105]	237 [59]	134 [49]	2102 [275]
CARDS	156 [0]	1043 [43]	1524 [144]	109 [16]	6 [1]	2838 [204]
ASPEN	108 [0]	648 [13]	980 [99]	517 [90]	157 [48]	2410 [250]
ALLHAT-LLT	92 [2]	2331 [144]	5468 [803]	1871 [438]	593 [183]	10355 [1570]
Post-CABG	0 [0]	24 [2]	1022 [128]	279 [44]	26 [5]	1351 [179]
GISSI-P	0 [0]	14 [1]	2816 [272]	1268 [140]	173 [26]	4271 [439]
HPS	320 [14]	2041 [134]	9424 [1267]	6722 [1488]	2029 [651]	20536 [3554]
LIPID	0 [0]	27 [3]	2946 [484]	5144 [1278]	897 [324]	9014 [2089]
PROSPER	0 [0]	108 [13]	2208 [224]	1858 [293]	1630 [396]	5804 [926]
CORONA	11 [1]	194 [16]	1463 [144]	2151 [292]	1192 [177]	5011 [630]
CARE	0 [0]	0 [0]	362 [58]	2776 [615]	1021 [313]	4159 [986]
ALLIANCE	0 [0]	0 [0]	288 [46]	1419 [298]	735 [203]	2442 [547]
LIPS	0 [0]	0 [0]	118 [28]	770 [158]	789 [173]	1677 [359]
AURORA	0 [0]	61 [8]	546 [85]	676 [136]	1490 [501]	2773 [730]
SSSS	0 [0]	0 [0]	139 [13]	1159 [275]	3146 [1063]	4444 [1351]
4D	0 [0]	6 [1]	117 [20]	273 [52]	859 [233]	1255 [306]
Subtotal:	**24790 [421]**	**28362 [1436]**	**38504 [4699]**	**27956 [5782]**	**14925 [4362]**	**134537 [16700]**

Study participants [MVEs] by predicted vascular disease risk: More vs. Less statin

Trial	≥10%, <20%†	≥20%, <30%	≥30%	Total
SEARCH	9665 [1969]	2157 [680]	242 [104]	12064 [2753]
A to Z	3097 [307]	1191 [180]	209 [52]	4497 [539]
TNT	3507 [520]	5078 [1075]	1416 [458]	10001 [2053]
IDEAL	1754 [326]	5257 [1125]	1877 [593]	8888 [2044]
PROVE-IT	27 [3]	1125 [185]	3010 [676]	4162 [864]
Subtotal:	**18050 [3125]**	**14808 [3245]**	**6754 [1883]**	**39612 [8253]**

MVE = Major Vascular Event

† includes 141 participants (48 [4MVEs] from A to Z and 93 [11MVEs] from SEARCH) with an estimated 5-year risk of MVE less between 5% and 10%.

Baseline characteristics of participants by vascular disease risk

Predicted 5-year MVE risk	MVE p.a.	MCE p.a.	Follow-up (years)	Women (%)	Age (years)	Baseline LDL-C (mmol/L)	Diabetes (%)	Disease history (%)		
								CHD	Other vascular	None
Statin vs. Control										
<5%	0.6%	0.2%	4.0	54%	59	3.43	7%	0%	4%	96%
≥5%, <10%	1.6%	0.8%	4.3	27%	61	3.68	18%	2%	11%	87%
≥10%, <20%	3.4%	1.5%	4.7	29%	64	3.61	24%	43%	22%	44%
≥20%, <30%	5.7%	2.6%	5.0	16%	65	3.72	19%	80%	28%	13%
≥30%	9.5%	5.1%	4.9	14%	66	3.92	44%	86%	39%	7%
Subtotal	3.6%	1.8%	**4.8**	**29%**	**63**	**3.70**	**21%**	**39%**	**20%**	**52%**
More vs. less statin										
≥10%,<20%	3.7%	1.6%	5.9	22%	60	2.37	4%	100%	1%	0%
≥20%, <30%	5.9%	2.4%	5.2	17%	62	2.59	17%	100%	12%	0%
≥30%	10.7%	4.2%	2.4	18%	64	2.81	35%	100%	35%	0%
Subtotal	5.3%	2.2%	**5.1**	**19%**	**62**	**2.53**	**14%**	**100%**	**11%**	**0%**

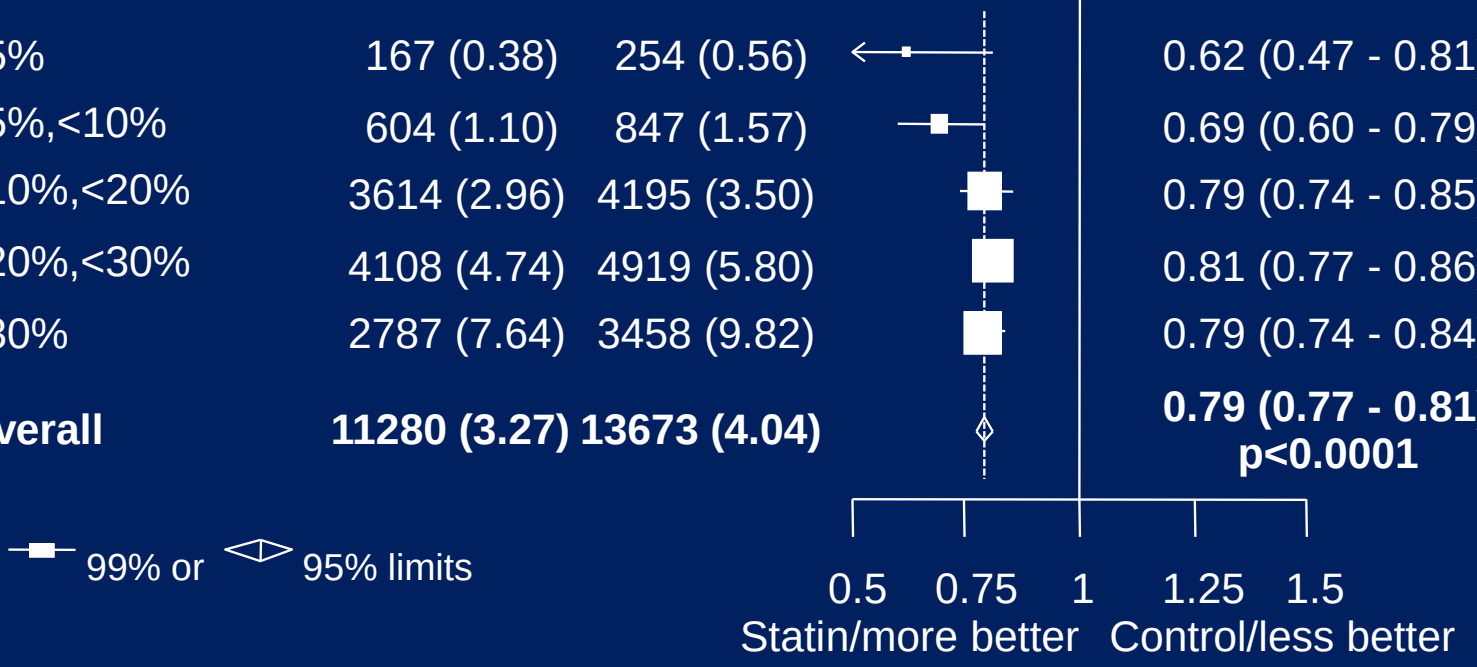
MVE = Major Vascular Event. MCE = Major Coronary Event. CHD = Coronary Heart Disease.

Mean (SE) difference in plasma lipid concentrations at 1 year by vascular disease risk

5-year MVE risk at baseline	Total cholesterol (mmol/L)	LDL cholesterol (mmol/L)	HDL cholesterol (mmol/L)	Triglycerides (mmol/L)
Statin vs. Control				
<5%	-0.94	-0.88	0.034	-0.19
≥5%, <10%	-1.08	-0.96	0.031	-0.25
≥10%, <20%	-1.14	-0.99	0.045	-0.27
≥20%, <30%	-1.26	-1.10	0.032	-0.24
≥30%	-1.31	-1.21	0.034	-0.23
Subtotal	**-1.22**	**-1.08**	**0.038**	**-0.26**
More vs. Less statin				
≥10%, <20%	-0.52	-0.44	0.006	-0.19
≥20%, <30%	-0.65	-0.53	-0.011	-0.24
≥30%	-0.70	-0.58	-0.013	-0.30
Subtotal	**-0.61**	**-0.51**	**-0.005**	**-0.23**

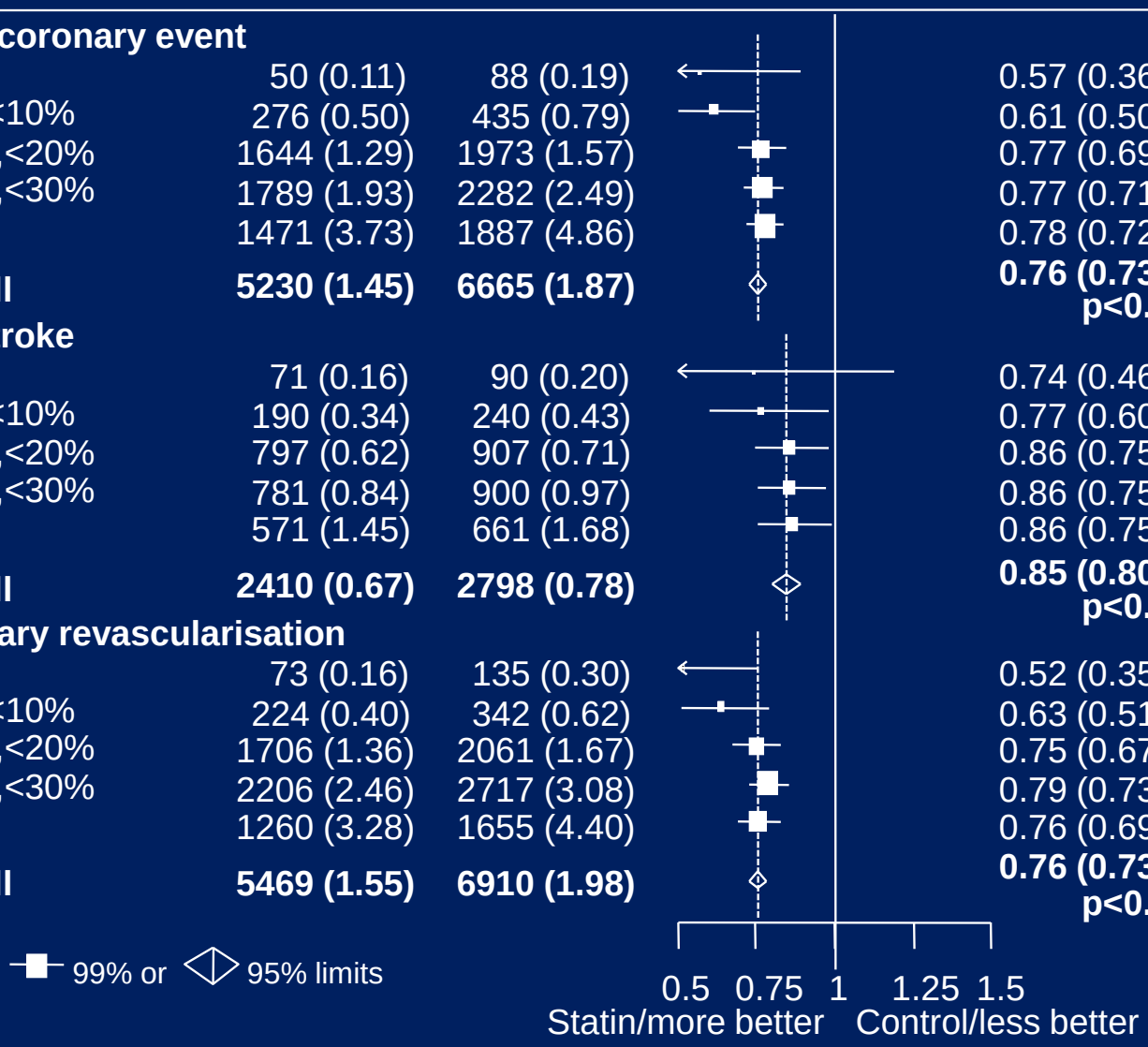
Effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction

5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
<5%	167 (0.38)	254 (0.56)	0.62 (0.47 - 0.81)	
≥5%,<10%	604 (1.10)	847 (1.57)	0.69 (0.60 - 0.79)	
≥10%,<20%	3614 (2.96)	4195 (3.50)	0.79 (0.74 - 0.85)	χ^2_1=4.29
≥20%,<30%	4108 (4.74)	4919 (5.80)	0.81 (0.77 - 0.86)	(p=0.04)
≥30%	2787 (7.64)	3458 (9.82)	0.79 (0.74 - 0.84)	
Overall	**11280 (3.27)**	**13673 (4.04)**	**0.79 (0.77 - 0.81) p<0.0001**	



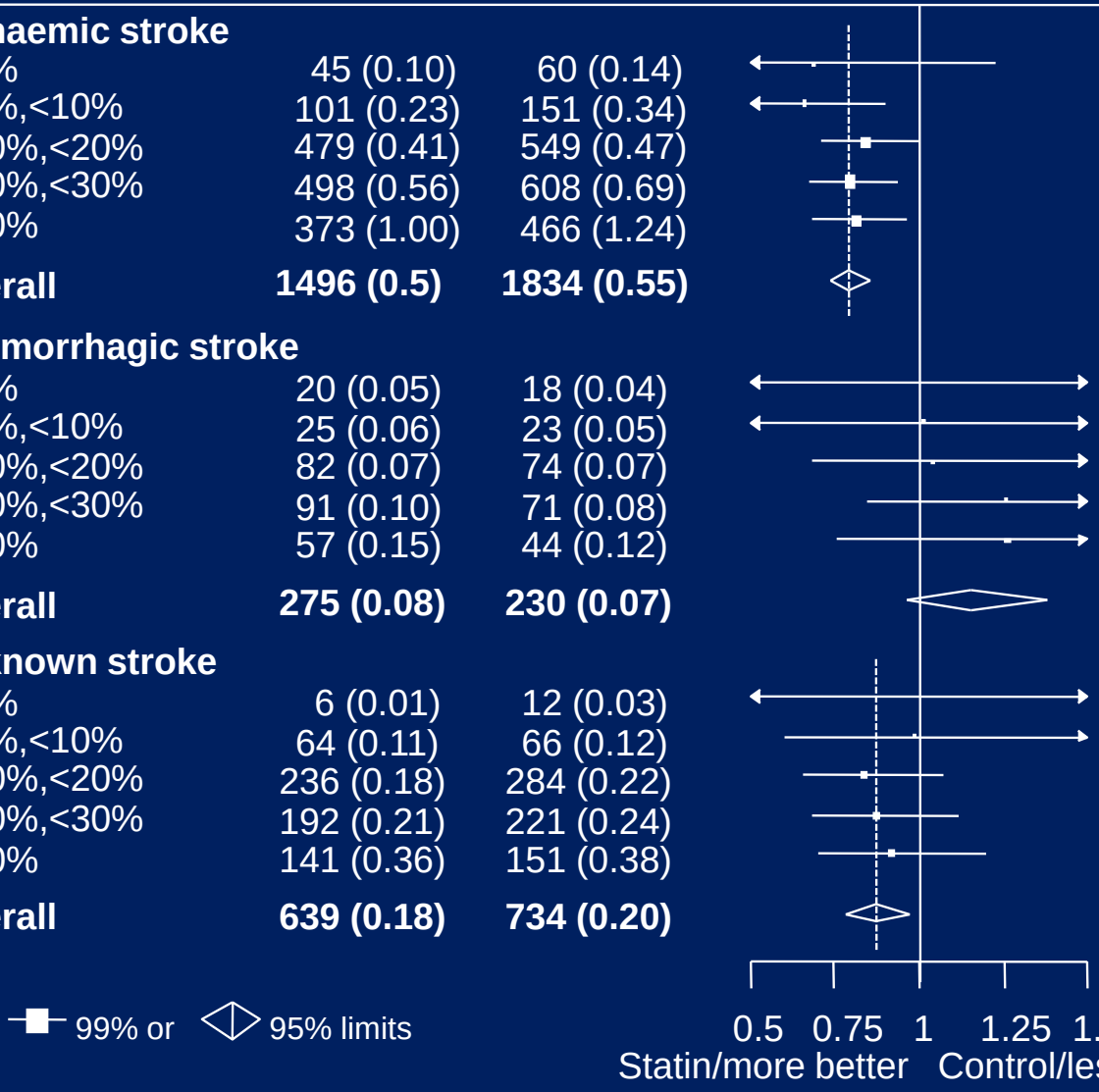
Effects on components of MAJOR VASCULAR EVENT per mmol/L LDL-C reduction

5-year MVE risk at baseline	Events (% per annum) Statin/more	Events (% per annum) Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Major coronary event				
<5%	50 (0.11)	88 (0.19)	0.57 (0.36 - 0.89)	
≥5%,<10%	276 (0.50)	435 (0.79)	0.61 (0.50 - 0.74)	
≥10%,<20%	1644 (1.29)	1973 (1.57)	0.77 (0.69 - 0.85)	χ^2_1=5.66
≥20%,<30%	1789 (1.93)	2282 (2.49)	0.77 (0.71 - 0.83)	(p=0.02)
≥30%	1471 (3.73)	1887 (4.86)	0.78 (0.72 - 0.84)	
Overall	**5230 (1.45)**	**6665 (1.87)**	**0.76 (0.73 - 0.79) p<0.0001**	
Any stroke				
<5%	71 (0.16)	90 (0.20)	0.74 (0.46 - 1.19)	
≥5%,<10%	190 (0.34)	240 (0.43)	0.77 (0.60 - 0.98)	
≥10%,<20%	797 (0.62)	907 (0.71)	0.86 (0.75 - 0.98)	χ^2_1=1.03
≥20%,<30%	781 (0.84)	900 (0.97)	0.86 (0.75 - 0.97)	(p=0.3)
≥30%	571 (1.45)	661 (1.68)	0.86 (0.75 - 0.99)	
Overall	**2410 (0.67)**	**2798 (0.78)**	**0.85 (0.80 - 0.89) p<0.0001**	
Coronary revascularisation				
<5%	73 (0.16)	135 (0.30)	0.52 (0.35 - 0.75)	
≥5%,<10%	224 (0.40)	342 (0.62)	0.63 (0.51 - 0.79)	
≥10%,<20%	1706 (1.36)	2061 (1.67)	0.75 (0.67 - 0.83)	χ^2_1=4.93
≥20%,<30%	2206 (2.46)	2717 (3.08)	0.79 (0.73 - 0.86)	(p=0.03)
≥30%	1260 (3.28)	1655 (4.40)	0.76 (0.69 - 0.83)	
Overall	**5469 (1.55)**	**6910 (1.98)**	**0.76 (0.73 - 0.79) p<0.0001**	



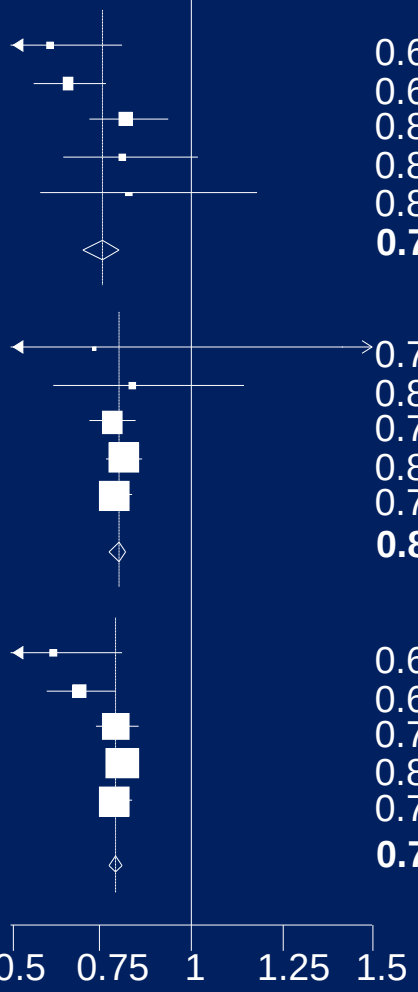
Effects on STROKE SUBTYPES per mmol/L LDL-C reduction

5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Ischaemic stroke				
<5%	45 (0.10)	60 (0.14)	0.69 (0.39 - 1.23)	
≥5%,<10%	101 (0.23)	151 (0.34)	0.66 (0.49 - 0.90)	
≥10%,<20%	479 (0.41)	549 (0.47)	0.84 (0.71 - 1.00)	χ^2_1=0.86
≥20%,<30%	498 (0.56)	608 (0.69)	0.80 (0.68 - 0.94)	(p=0.4)
≥30%	373 (1.00)	466 (1.24)	0.81 (0.68 - 0.96)	
Overall	**1496 (0.5)**	**1834 (0.55)**	**0.79 (0.74 - 0.85) p<0.0001**	
Haemorrhagic stroke				
<5%	20 (0.05)	18 (0.04)	1.19 (0.42 - 3.36)	
≥5%,<10%	25 (0.06)	23 (0.05)	1.01 (0.49 - 2.08)	
≥10%,<20%	82 (0.07)	74 (0.07)	1.04 (0.68 - 1.59)	χ^2_1=0.60
≥20%,<30%	91 (0.10)	71 (0.08)	1.26 (0.84 - 1.88)	(p=0.4)
≥30%	57 (0.15)	44 (0.12)	1.26 (0.75 - 2.12)	
Overall	**275 (0.08)**	**230 (0.07)**	**1.15 (0.97 - 1.38) p= 0.11**	
Unknown stroke				
<5%	6 (0.01)	12 (0.03)	0.53 (0.15 - 1.85)	
≥5%,<10%	64 (0.11)	66 (0.12)	0.99 (0.60 - 1.61)	
≥10%,<20%	236 (0.18)	284 (0.22)	0.84 (0.65 - 1.07)	χ^2_1=0.25
≥20%,<30%	192 (0.21)	221 (0.24)	0.87 (0.68 - 1.12)	(p=0.6)
≥30%	141 (0.36)	151 (0.38)	0.92 (0.70 - 1.20)	
Overall	**639 (0.18)**	**734 (0.20)**	**0.87 (0.79 - 0.97) p= 0.01**	



Effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction, by history of vascular disease

5-year MVE risk at baseline	Events (% per annum) Statin/more	Events (% per annum) Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Participants without vascular disease				
<5%	148 (0.35)	229 (0.53)	0.61 (0.45 - 0.81)	
≥5%,<10%	487 (1.02)	716 (1.53)	0.66 (0.57 - 0.77)	
≥10%,<20%	854 (2.52)	1003 (2.98)	0.82 (0.72 - 0.93)	χ^2_1=9.10
≥20%,<30%	294 (4.40)	351 (5.28)	0.81 (0.65 - 1.01)	(p=0.003)
≥30%	121 (7.29)	126 (8.16)	0.83 (0.58 - 1.18)	
Subtotal	**1904 (1.44)**	**2425 (1.84)**	**0.75 (0.70 - 0.80)**	
			p<0.0001	
Participants with vascular disease				
<5%	19 (0.87)	25 (1.18)	0.73 (0.33 - 1.61)	
≥5%,<10%	117 (1.56)	131 (1.80)	0.84 (0.62 - 1.14)	
≥10%,<20%	2760 (3.13)	3192 (3.71)	0.78 (0.72 - 0.85)	χ^2_1=0.01
≥20%,<30%	3814 (4.77)	4568 (5.85)	0.81 (0.76 - 0.86)	(p=0.9)
≥30%	2666 (7.66)	3332 (9.90)	0.79 (0.74 - 0.84)	
Subtotal	**9376 (4.41)**	**11248 (5.43)**	**0.80 (0.77 - 0.82)**	
			p<0.0001	
All participants				
<5%	167 (0.38)	254 (0.56)	0.62 (0.47 - 0.81)	
≥5%,<10%	604 (1.10)	847 (1.57)	0.69 (0.60 - 0.79)	
≥10%,<20%	3614 (2.96)	4195 (3.50)	0.79 (0.74 - 0.85)	χ^2_1=4.29
≥20%,<30%	4108 (4.74)	4919 (5.80)	0.81 (0.77 - 0.86)	(p=0.04)
≥30%	2787 (7.64)	3458 (9.82)	0.79 (0.74 - 0.84)	
Overall	**11280 (3.27)**	**13673 (4.04)**	**0.79 (0.77 - 0.81)**	
			p<0.0001	

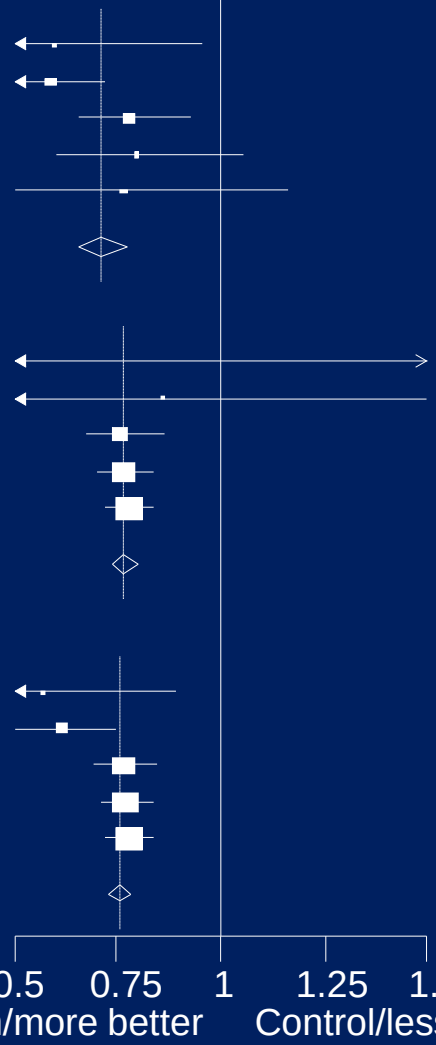


99% or 95% limits

Heterogeneity between participants without and with vascular disease: χ^2_1=2.74(p=0.10)

Effects on MAJOR CORONARY EVENTS per mmol/L LDL-C reduction, by history of vascular disease

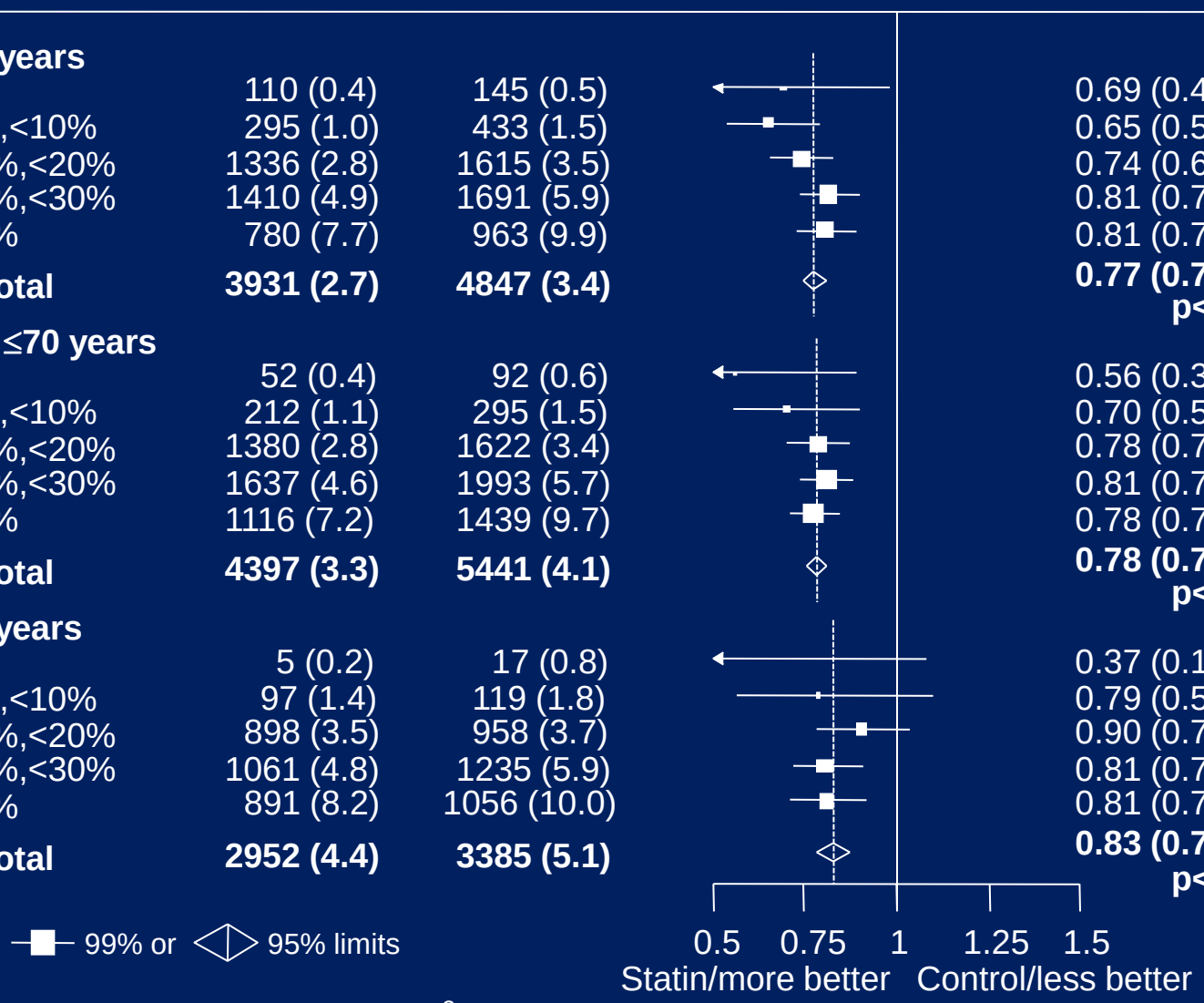
5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Participants without vascular disease				
<5%	47 (0.11)	80 (0.19)	0.59 (0.37 - 0.96)	
≥5%,<10%	238 (0.50)	394 (0.83)	0.58 (0.48 - 0.72)	
≥10%,<20%	447 (1.29)	557 (1.61)	0.78 (0.65 - 0.93)	χ^2_1=6.08
≥20%,<30%	173 (2.51)	217 (3.15)	0.80 (0.60 - 1.06)	(p=0.01)
≥30%	79 (4.52)	91 (5.64)	0.76 (0.50 - 1.17)	
Subtotal	**984 (0.73)**	**1339 (1.00)**	**0.71 (0.65 - 0.77) p<0.0001**	
Participants with vascular disease				
<5%	3 (0.14)	8 (0.37)	0.41 (0.09 - 1.76)	
≥5%,<10%	38 (0.50)	41 (0.55)	0.86 (0.49 - 1.50)	
≥10%,<20%	1197 (1.30)	1416 (1.56)	0.76 (0.67 - 0.86)	χ^2_1 =0.23
≥20%,<30%	1616 (1.88)	2065 (2.44)	0.77 (0.70 - 0.83)	(p=0.6)
≥30%	1392 (3.69)	1796 (4.82)	0.78 (0.72 - 0.84)	
Subtotal	**4246 (1.88)**	**5326 (2.39)**	**0.77 (0.74 - 0.80) p<0.0001**	
All participants				
<5%	50 (0.11)	88 (0.19)	0.57 (0.36 - 0.89)	
≥5%,<10%	276 (0.50)	435 (0.79)	0.61 (0.50 - 0.74)	
≥10%,<20%	1644 (1.29)	1973 (1.57)	0.77 (0.69 - 0.85)	χ^2_1 =5.66
≥20%,<30%	1789 (1.93)	2282 (2.49)	0.77 (0.71 - 0.83)	(p=0.02)
≥30%	1471 (3.73)	1887 (4.86)	0.78 (0.72 - 0.84)	
Overall	**5230 (1.45)**	**6665 (1.87)**	**0.76 (0.73 - 0.79) p<0.0001**	



Heterogeneity between participants without and with vascular disease: χ^2_1=2.80(p=0.09)

Effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction, by age at baseline

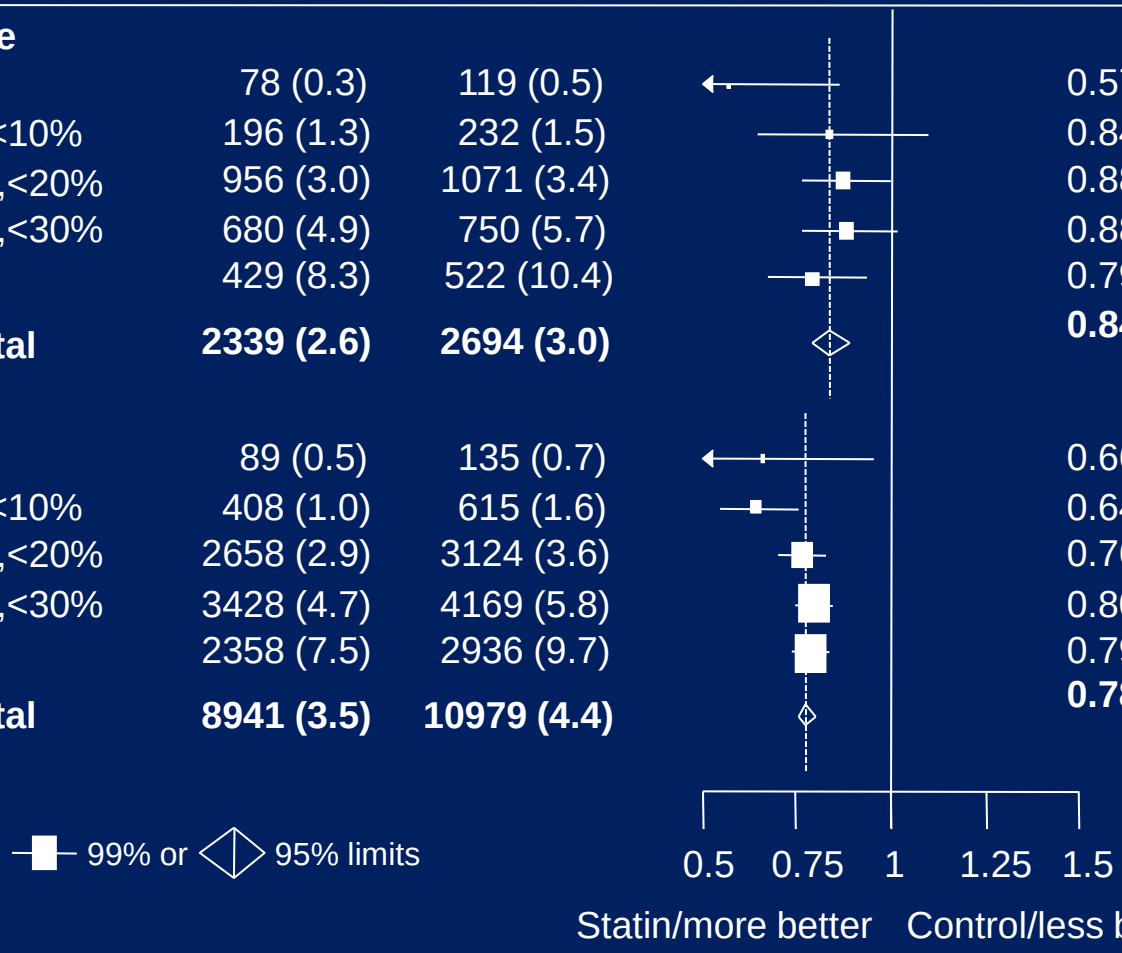
5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
≤60 years				
<5%	110 (0.4)	145 (0.5)	0.69 (0.49 - 0.98)	
≥5%,<10%	295 (1.0)	433 (1.5)	0.65 (0.54 - 0.79)	
≥10%,<20%	1336 (2.8)	1615 (3.5)	0.74 (0.66 - 0.83)	χ^2_1=7.37
≥20%,<30%	1410 (4.9)	1691 (5.9)	0.81 (0.74 - 0.90)	(p=0.007)
≥30%	780 (7.7)	963 (9.9)	0.81 (0.73 - 0.89)	
Subtotal	**3931 (2.7)**	**4847 (3.4)**	**0.77 (0.74 - 0.81) p<0.0001**	
>60, ≤70 years				
<5%	52 (0.4)	92 (0.6)	0.56 (0.35 - 0.89)	
≥5%,<10%	212 (1.1)	295 (1.5)	0.70 (0.55 - 0.90)	
≥10%,<20%	1380 (2.8)	1622 (3.4)	0.78 (0.70 - 0.87)	χ^2_1=0.96
≥20%,<30%	1637 (4.6)	1993 (5.7)	0.81 (0.74 - 0.89)	(p=0.3)
≥30%	1116 (7.2)	1439 (9.7)	0.78 (0.71 - 0.85)	
Subtotal	**4397 (3.3)**	**5441 (4.1)**	**0.78 (0.75 - 0.81) p<0.0001**	
>70 years				
<5%	5 (0.2)	17 (0.8)	0.37 (0.13 - 1.08)	
≥5%,<10%	97 (1.4)	119 (1.8)	0.79 (0.56 - 1.10)	
≥10%,<20%	898 (3.5)	958 (3.7)	0.90 (0.79 - 1.04)	χ^2_1=0.42
≥20%,<30%	1061 (4.8)	1235 (5.9)	0.81 (0.72 - 0.91)	(p=0.5)
≥30%	891 (8.2)	1056 (10.0)	0.81 (0.71 - 0.91)	
Subtotal	**2952 (4.4)**	**3385 (5.1)**	**0.83 (0.78 - 0.87) p<0.0001**	



Test for trend across age groups: χ^2_1=3.29 (p=0.1)

Effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction, by gender

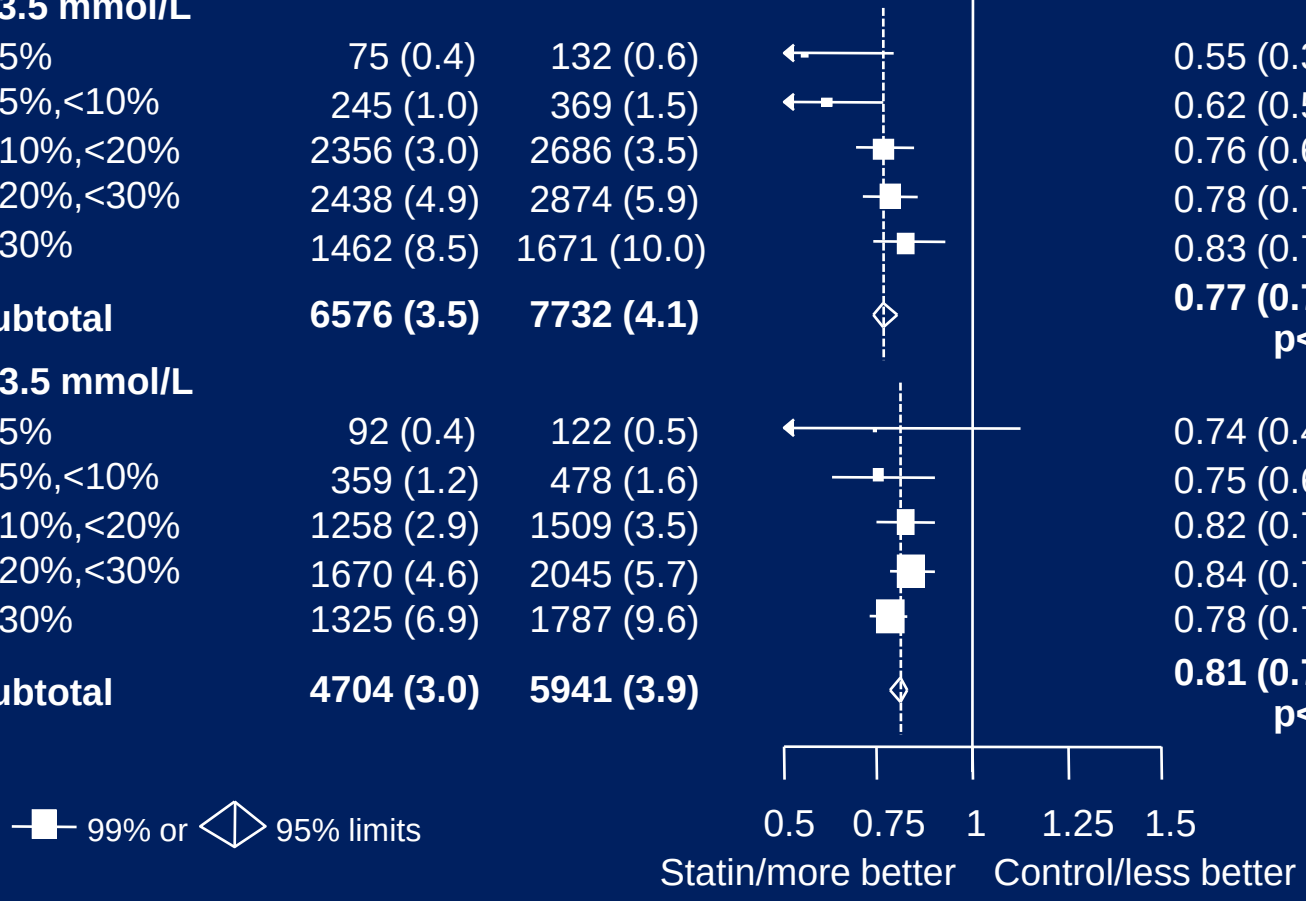
5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Female				
<5%	78 (0.3)	119 (0.5)	0.57 (0.38 - 0.86)	
≥5%,<10%	196 (1.3)	232 (1.5)	0.84 (0.64 - 1.10)	
≥10%,<20%	956 (3.0)	1071 (3.4)	0.88 (0.77 - 1.00)	χ^2_1=0.23
≥20%,<30%	680 (4.9)	750 (5.7)	0.88 (0.76 - 1.02)	(p=0.6)
≥30%	429 (8.3)	522 (10.4)	0.79 (0.67 - 0.94)	
Subtotal	**2339 (2.6)**	**2694 (3.0)**	**0.84 (0.79 - 0.89) p<0.0001**	
Male				
<5%	89 (0.5)	135 (0.7)	0.66 (0.46 - 0.95)	
≥5%,<10%	408 (1.0)	615 (1.6)	0.64 (0.55 - 0.75)	
≥10%,<20%	2658 (2.9)	3124 (3.6)	0.76 (0.70 - 0.83)	χ^2_1=6.73
≥20%,<30%	3428 (4.7)	4169 (5.8)	0.80 (0.75 - 0.85)	(p=0.009)
≥30%	2358 (7.5)	2936 (9.7)	0.79 (0.74 - 0.84)	
Subtotal	**8941 (3.5)**	**10979 (4.4)**	**0.78 (0.76 - 0.80) p<0.0001**	



Heterogeneity between men and women: χ^2_1=5.23 (p=0.02)

Proportional effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction, by baseline LDL cholesterol

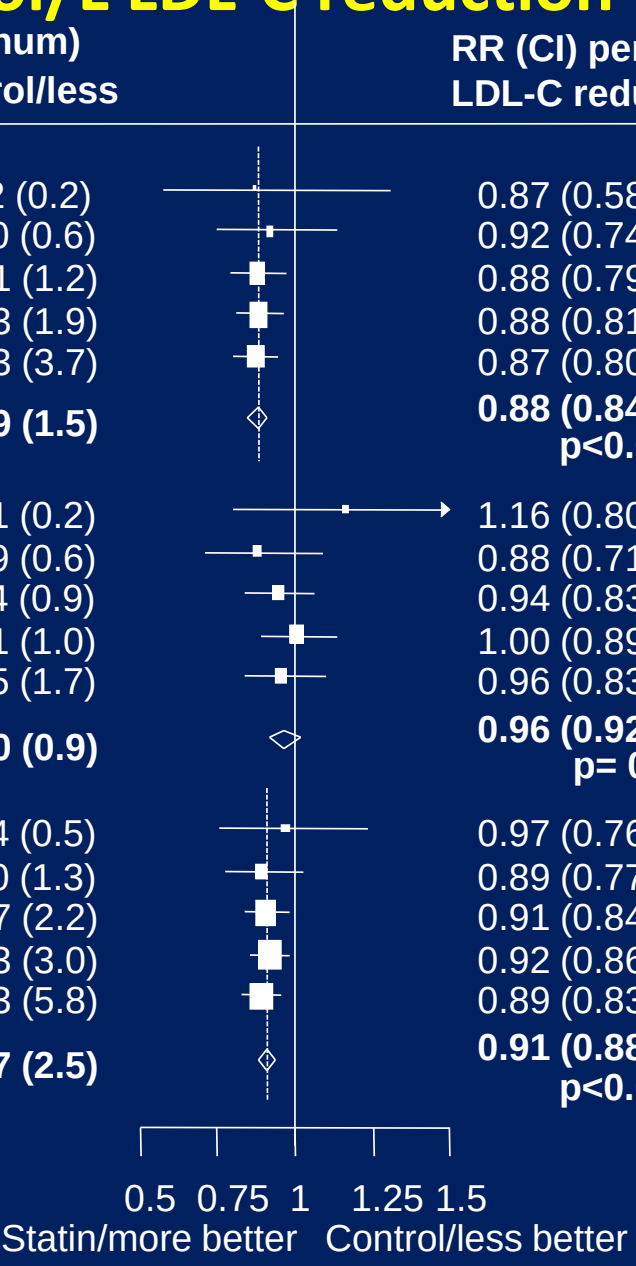
5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
<3.5 mmol/L				
<5%	75 (0.4)	132 (0.6)	0.55 (0.39 - 0.79)	
≥5%,<10%	245 (1.0)	369 (1.5)	0.62 (0.50 - 0.76)	
≥10%,<20%	2356 (3.0)	2686 (3.5)	0.76 (0.69 - 0.85)	χ^2_1 =11.52
≥20%,<30%	2438 (4.9)	2874 (5.9)	0.78 (0.71 - 0.86)	(p=0.0007)
≥30%	1462 (8.5)	1671 (10.0)	0.83 (0.73 - 0.93)	
Subtotal	**6576 (3.5)**	**7732 (4.1)**	**0.77 (0.73 - 0.80) p<0.0001**	
≥3.5 mmol/L				
<5%	92 (0.4)	122 (0.5)	0.74 (0.48 - 1.13)	
≥5%,<10%	359 (1.2)	478 (1.6)	0.75 (0.63 - 0.90)	
≥10%,<20%	1258 (2.9)	1509 (3.5)	0.82 (0.75 - 0.90)	χ^2_1 =0.21
≥20%,<30%	1670 (4.6)	2045 (5.7)	0.84 (0.78 - 0.90)	(p=0.6)
≥30%	1325 (6.9)	1787 (9.6)	0.78 (0.73 - 0.83)	
Subtotal	**4704 (3.0)**	**5941 (3.9)**	**0.81 (0.78 - 0.83) p<0.0001**	



Heterogeneity between participants at different levels of LDL-C at baseline: χ^2_1 =3.26 (p=0.07)

Trial- and LDL-C subgroup-specific LDL weights used in these subgroup analyses.

Effects on CAUSE-SPECIFIC MORTALITY per mmol/L LDL-C reduction

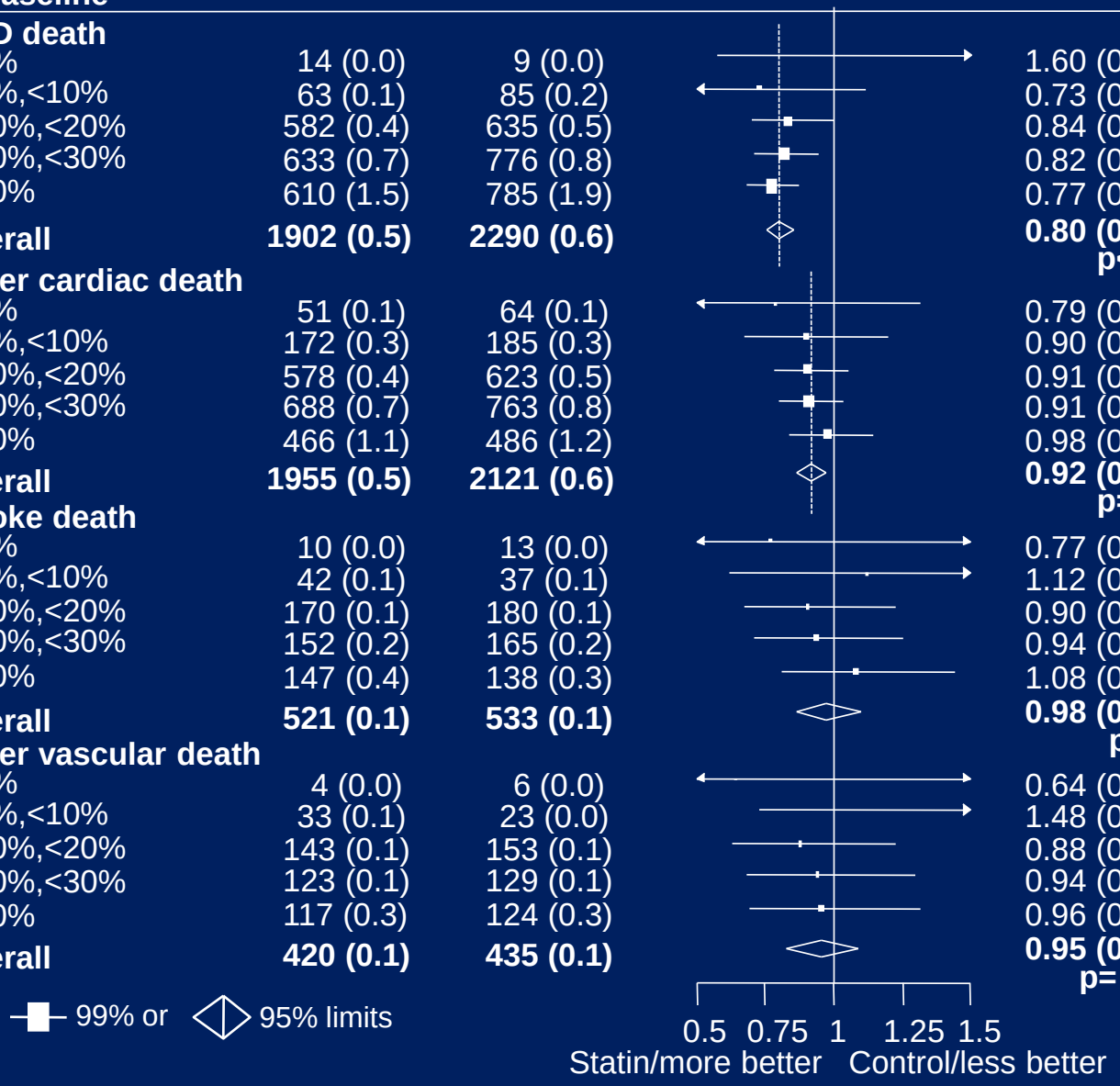


5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Any vascular death				
<5%	79 (0.2)	92 (0.2)	0.87 (0.58 - 1.31)	
≥5%,<10%	310 (0.6)	330 (0.6)	0.92 (0.74 - 1.13)	
≥10%,<20%	1473 (1.1)	1591 (1.2)	0.88 (0.79 - 0.97)	χ^2_1=0.18
≥20%,<30%	1596 (1.7)	1833 (1.9)	0.88 (0.81 - 0.96)	(p=0.7)
≥30%	1340 (3.2)	1533 (3.7)	0.87 (0.80 - 0.95)	
Overall	**4798 (1.3)**	**5379 (1.5)**	**0.88 (0.84 - 0.91) p<0.0001**	
Non-vascular death				
<5%	116 (0.3)	101 (0.2)	1.16 (0.80 - 1.68)	
≥5%,<10%	270 (0.5)	309 (0.6)	0.88 (0.71 - 1.09)	
≥10%,<20%	1054 (0.8)	1104 (0.9)	0.94 (0.83 - 1.07)	χ^2_1=0.02
≥20%,<30%	963 (1.0)	941 (1.0)	1.00 (0.89 - 1.13)	(p=0.9)
≥30%	681 (1.6)	705 (1.7)	0.96 (0.83 - 1.10)	
Overall	**3084 (0.8)**	**3160 (0.9)**	**0.96 (0.92 - 1.01) p= 0.16**	
Any death				
<5%	232 (0.5)	244 (0.5)	0.97 (0.76 - 1.24)	
≥5%,<10%	639 (1.1)	710 (1.3)	0.89 (0.77 - 1.03)	
≥10%,<20%	2651 (2.0)	2827 (2.2)	0.91 (0.84 - 0.98)	χ^2_1=0.22
≥20%,<30%	2683 (2.8)	2903 (3.0)	0.92 (0.86 - 0.99)	(p=0.6)
≥30%	2165 (5.2)	2403 (5.8)	0.89 (0.83 - 0.96)	
Overall	**8370 (2.3)**	**9087 (2.5)**	**0.91 (0.88 - 0.93) p<0.0001**	

99% or 95% limits

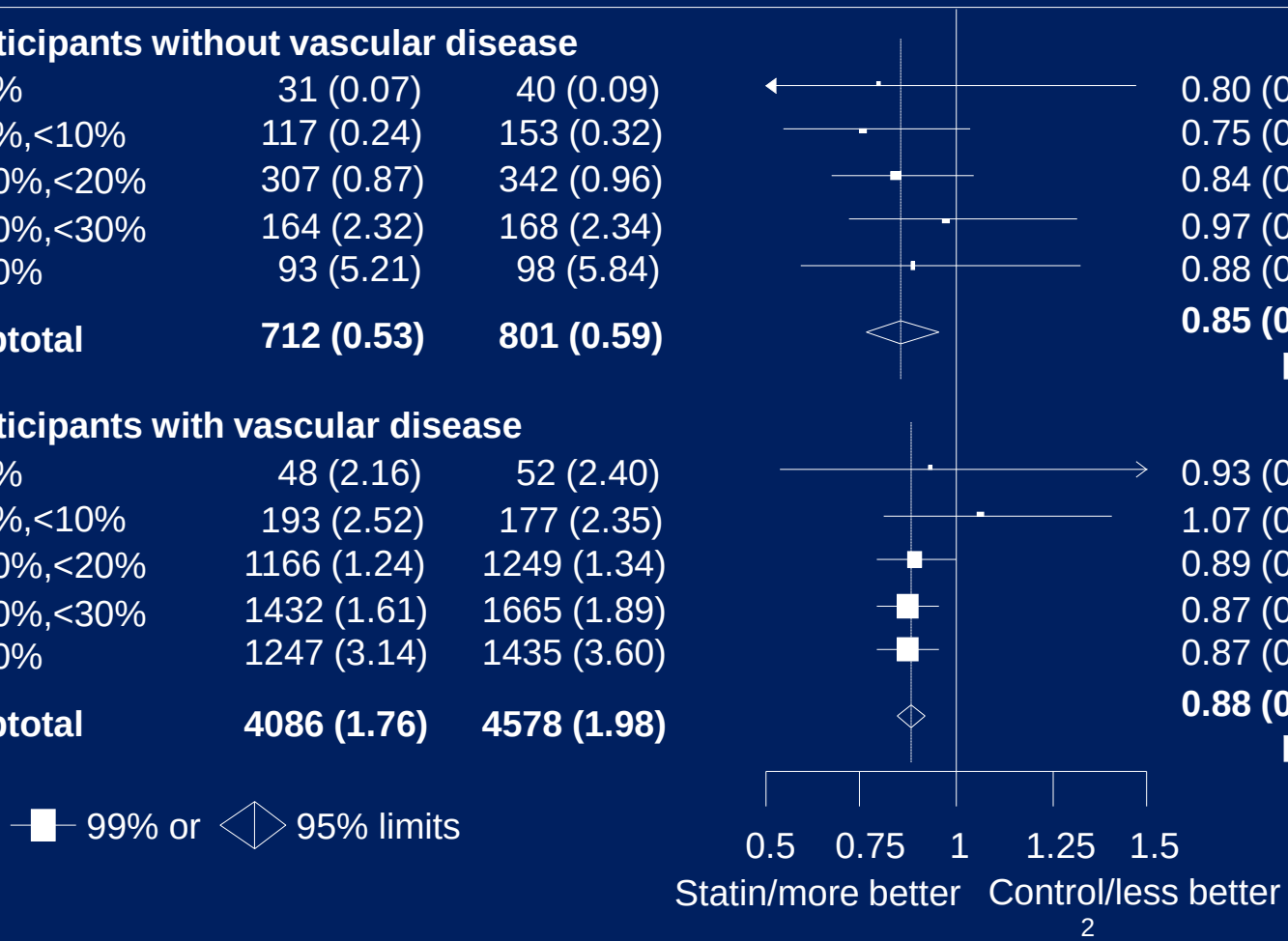
Effects on components of VASCULAR MORTALITY per mmol/L LDL-C reduction

5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
CHD death				
<5%	14 (0.0)	9 (0.0)	1.60 (0.57 - 4.47)	
≥5%,<10%	63 (0.1)	85 (0.2)	0.73 (0.47 - 1.11)	
≥10%,<20%	582 (0.4)	635 (0.5)	0.84 (0.70 - 1.00)	χ^2_1=1.13
≥20%,<30%	633 (0.7)	776 (0.8)	0.82 (0.71 - 0.95)	(p=0.3)
≥30%	610 (1.5)	785 (1.9)	0.77 (0.69 - 0.87)	
Overall	**1902 (0.5)**	**2290 (0.6)**	**0.80 (0.76 - 0.85) p<0.0001**	
Other cardiac death				
<5%	51 (0.1)	64 (0.1)	0.79 (0.47 - 1.32)	
≥5%,<10%	172 (0.3)	185 (0.3)	0.90 (0.68 - 1.20)	
≥10%,<20%	578 (0.4)	623 (0.5)	0.91 (0.78 - 1.05)	χ^2_1=1.25
≥20%,<30%	688 (0.7)	763 (0.8)	0.91 (0.80 - 1.03)	(p=0.3)
≥30%	466 (1.1)	486 (1.2)	0.98 (0.83 - 1.14)	
Overall	**1955 (0.5)**	**2121 (0.6)**	**0.92 (0.87 - 0.98) p= 0.006**	
Stroke death				
<5%	10 (0.0)	13 (0.0)	0.77 (0.25 - 2.35)	
≥5%,<10%	42 (0.1)	37 (0.1)	1.12 (0.62 - 2.03)	
≥10%,<20%	170 (0.1)	180 (0.1)	0.90 (0.67 - 1.22)	χ^2_1=0.54
≥20%,<30%	152 (0.2)	165 (0.2)	0.94 (0.71 - 1.25)	(p=0.5)
≥30%	147 (0.4)	138 (0.3)	1.08 (0.81 - 1.45)	
Overall	**521 (0.1)**	**533 (0.1)**	**0.98 (0.86 - 1.10) p= 0.69**	
Other vascular death				
<5%	4 (0.0)	6 (0.0)	0.64 (0.12 - 3.45)	
≥5%,<10%	33 (0.1)	23 (0.0)	1.48 (0.73 - 3.00)	
≥10%,<20%	143 (0.1)	153 (0.1)	0.88 (0.63 - 1.22)	χ^2_1=0.08
≥20%,<30%	123 (0.1)	129 (0.1)	0.94 (0.68 - 1.30)	(p=0.8)
≥30%	117 (0.3)	124 (0.3)	0.96 (0.69 - 1.32)	
Overall	**420 (0.1)**	**435 (0.1)**	**0.95 (0.83 - 1.09) p= 0.48**	



Effects on ANY VASCULAR DEATH per mmol/L LDL-C reduction, by history of vascular disease

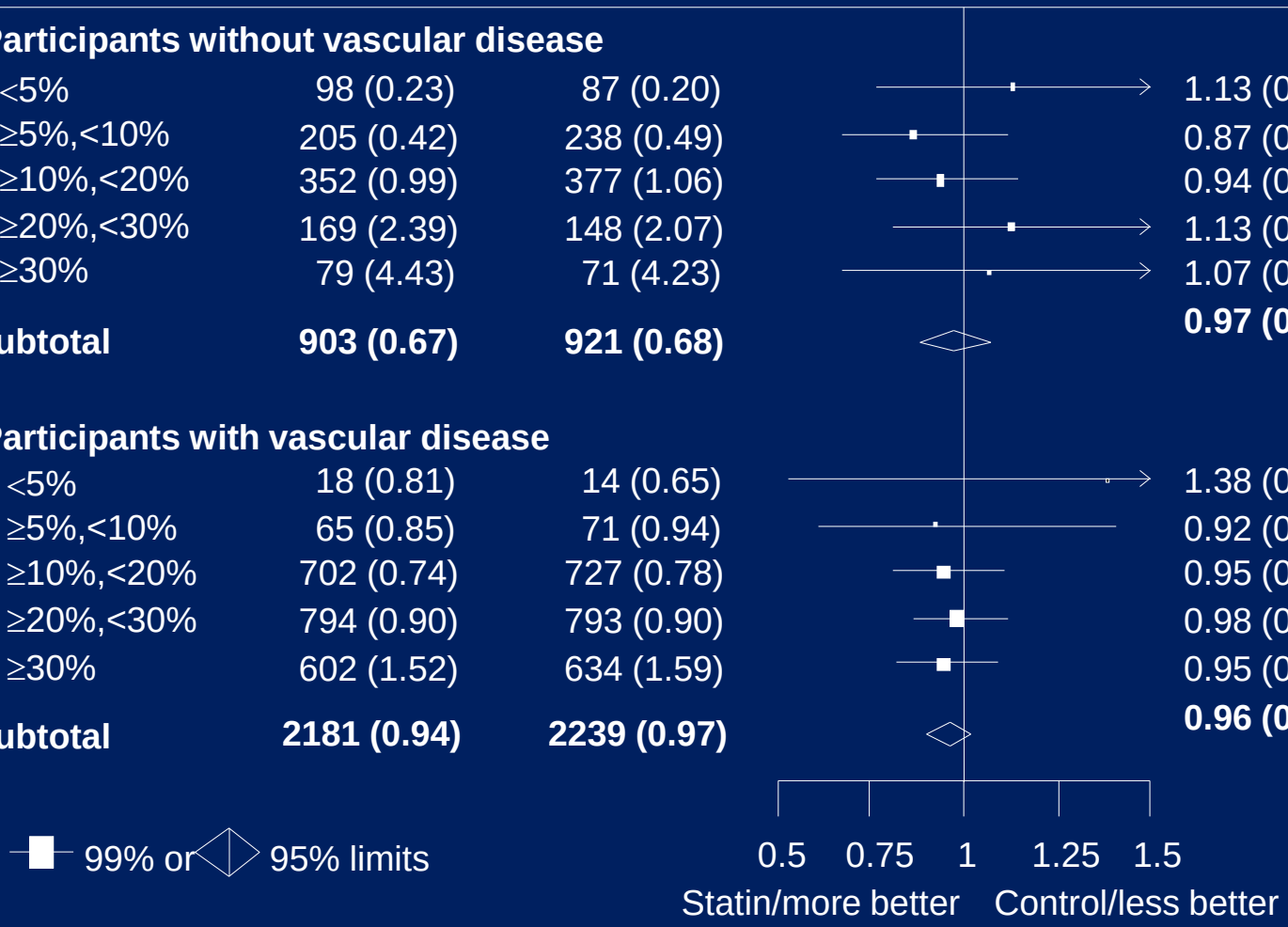
5-year MVE risk at baseline	Events (% per annum) Statin/more	Events (% per annum) Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Participants without vascular disease				
<5%	31 (0.07)	40 (0.09)	0.80 (0.43 - 1.47)	
≥5%,<10%	117 (0.24)	153 (0.32)	0.75 (0.55 - 1.04)	
≥10%,<20%	307 (0.87)	342 (0.96)	0.84 (0.67 - 1.05)	χ^2_1=1.46
≥20%,<30%	164 (2.32)	168 (2.34)	0.97 (0.72 - 1.32)	(p=0.2)
≥30%	93 (5.21)	98 (5.84)	0.88 (0.59 - 1.33)	
Subtotal	**712 (0.53)**	**801 (0.59)**	**0.85 (0.77 - 0.95) p= 0.004**	
Participants with vascular disease				
<5%	48 (2.16)	52 (2.40)	0.93 (0.53 - 1.62)	
≥5%,<10%	193 (2.52)	177 (2.35)	1.07 (0.81 - 1.41)	
≥10%,<20%	1166 (1.24)	1249 (1.34)	0.89 (0.79 - 1.00)	χ^2_1=1.49
≥20%,<30%	1432 (1.61)	1665 (1.89)	0.87 (0.80 - 0.95)	(p=0.2)
≥30%	1247 (3.14)	1435 (3.60)	0.87 (0.79 - 0.95)	
Subtotal	**4086 (1.76)**	**4578 (1.98)**	**0.88 (0.84 - 0.92) p<0.0001**	



Heterogeneity between participants without and with vascular disease: χ^2_1 =0.28 (p=0.6)

Effects on NON-VASCULAR DEATH per mmol/L LDL-C reduction, by history of vascular disease

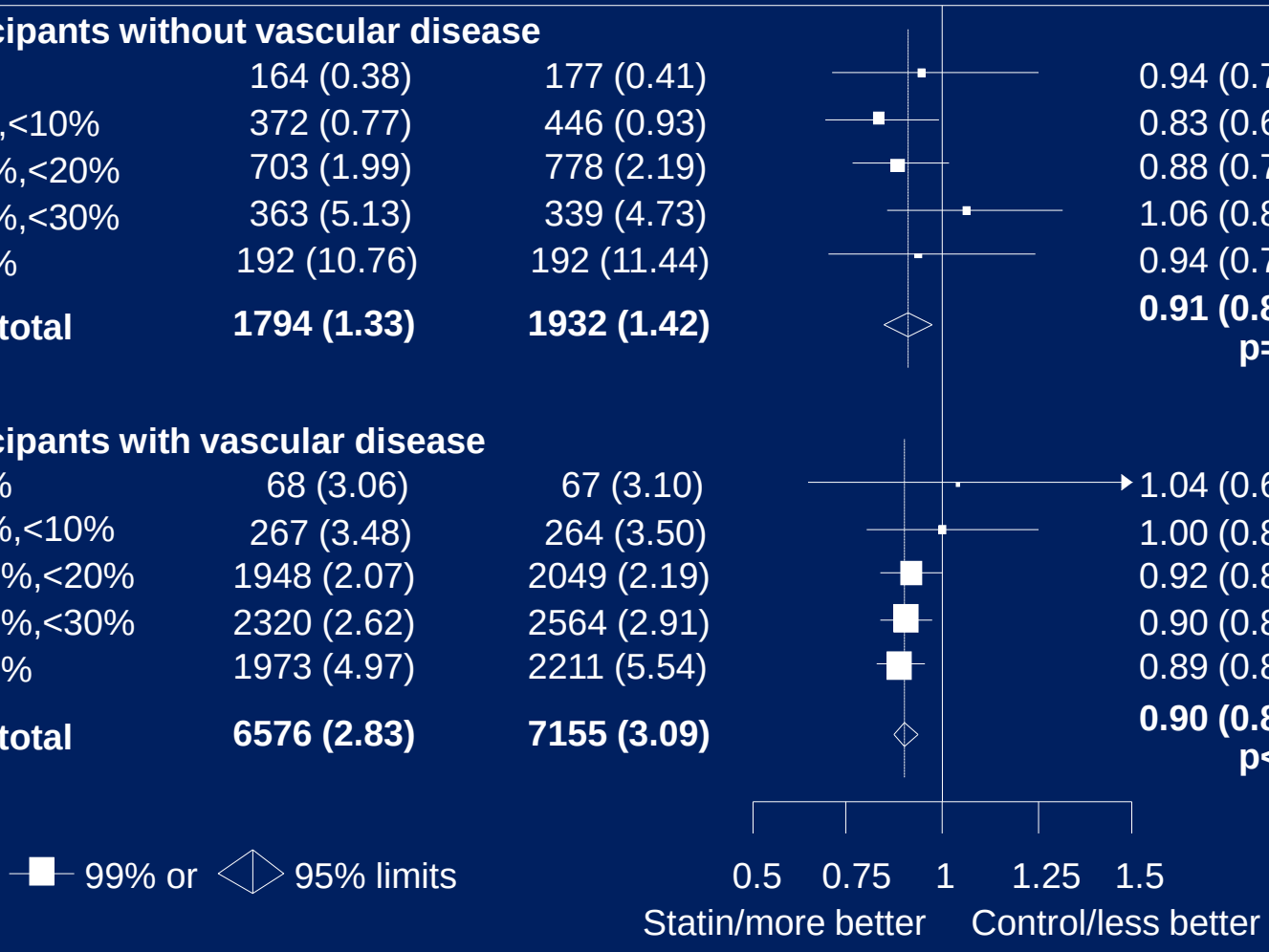
5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Participants without vascular disease				
<5%	98 (0.23)	87 (0.20)	1.13 (0.76 - 1.69)	
≥5%,<10%	205 (0.42)	238 (0.49)	0.87 (0.67 - 1.11)	
≥10%,<20%	352 (0.99)	377 (1.06)	0.94 (0.76 - 1.15)	χ^2_1 =0.47
≥20%,<30%	169 (2.39)	148 (2.07)	1.13 (0.81 - 1.57)	(p=0.5)
≥30%	79 (4.43)	71 (4.23)	1.07 (0.68 - 1.69)	
Subtotal	**903 (0.67)**	**921 (0.68)**	**0.97 (0.88 - 1.07) p= 0.60**	
Participants with vascular disease				
<5%	18 (0.81)	14 (0.65)	1.38 (0.53 - 3.63)	
≥5%,<10%	65 (0.85)	71 (0.94)	0.92 (0.61 - 1.41)	
≥10%,<20%	702 (0.74)	727 (0.78)	0.95 (0.81 - 1.11)	χ^2_1 =0.04
≥20%,<30%	794 (0.90)	793 (0.90)	0.98 (0.86 - 1.12)	(p=0.8)
≥30%	602 (1.52)	634 (1.59)	0.95 (0.82 - 1.09)	
Subtotal	**2181 (0.94)**	**2239 (0.97)**	**0.96 (0.90 - 1.02) p= 0.18**	



Heterogeneity between participants without and with vascular disease: χ^2_1 =0.07 (p=0.8)

Effects on ANY DEATH per mmol/L LDL-C reduction, by history of vascular disease

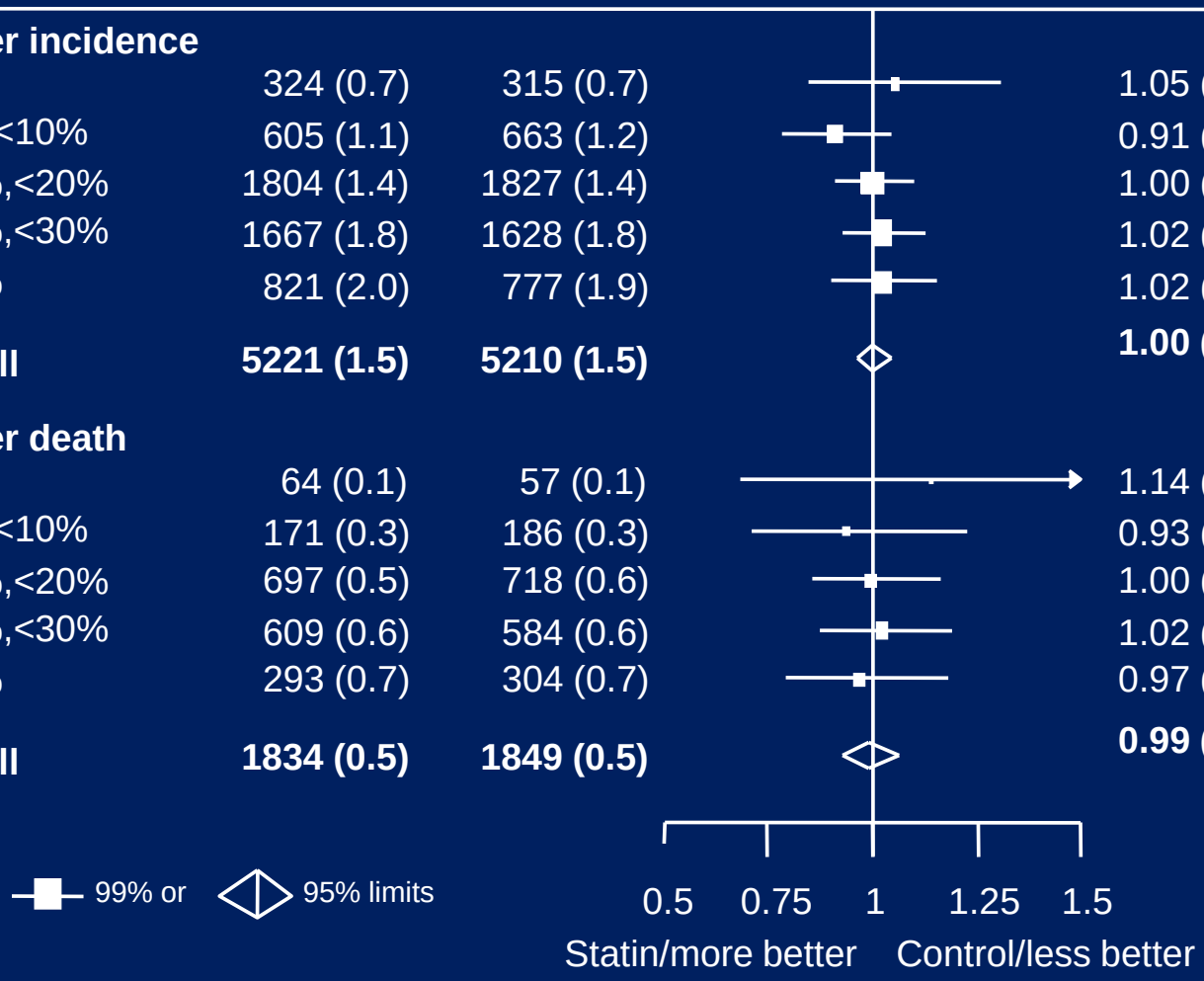
5-year MVE risk at baseline	Events (% per annum) Statin/more	Events (% per annum) Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Participants without vascular disease				
<5%	164 (0.38)	177 (0.41)	0.94 (0.71 - 1.26)	
≥5%,<10%	372 (0.77)	446 (0.93)	0.83 (0.69 - 0.99)	
≥10%,<20%	703 (1.99)	778 (2.19)	0.88 (0.76 - 1.02)	χ^2_1=1.57
≥20%,<30%	363 (5.13)	339 (4.73)	1.06 (0.86 - 1.32)	(p=0.2)
≥30%	192 (10.76)	192 (11.44)	0.94 (0.70 - 1.25)	
Subtotal	**1794 (1.33)**	**1932 (1.42)**	**0.91 (0.85 - 0.97) p= 0.007**	
Participants with vascular disease				
<5%	68 (3.06)	67 (3.10)	1.04 (0.65 - 1.68)	
≥5%,<10%	267 (3.48)	264 (3.50)	1.00 (0.80 - 1.26)	
≥10%,<20%	1948 (2.07)	2049 (2.19)	0.92 (0.84 - 1.00)	χ^2_1=1.82
≥20%,<30%	2320 (2.62)	2564 (2.91)	0.90 (0.84 - 0.97)	(p=0.2)
≥30%	1973 (4.97)	2211 (5.54)	0.89 (0.83 - 0.96)	
Subtotal	**6576 (2.83)**	**7155 (3.09)**	**0.90 (0.87 - 0.93) p<0.0001**	



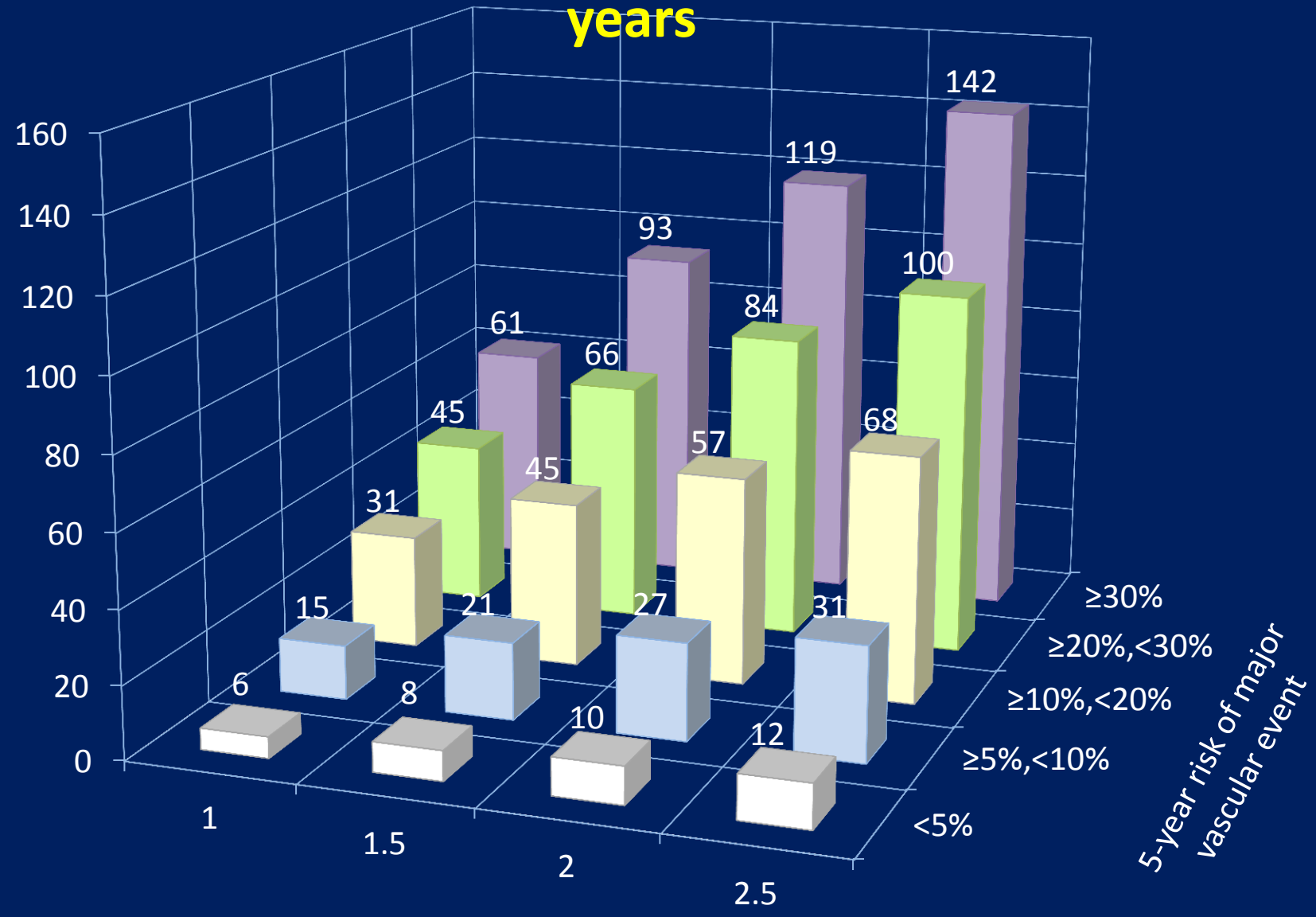
Heterogeneity between participants without and with vascular disease: χ^2_1=0.03 (p=0.9)

Effects on CANCER INCIDENCE and CANCER MORTALITY per mmol/L LDL-C reduction

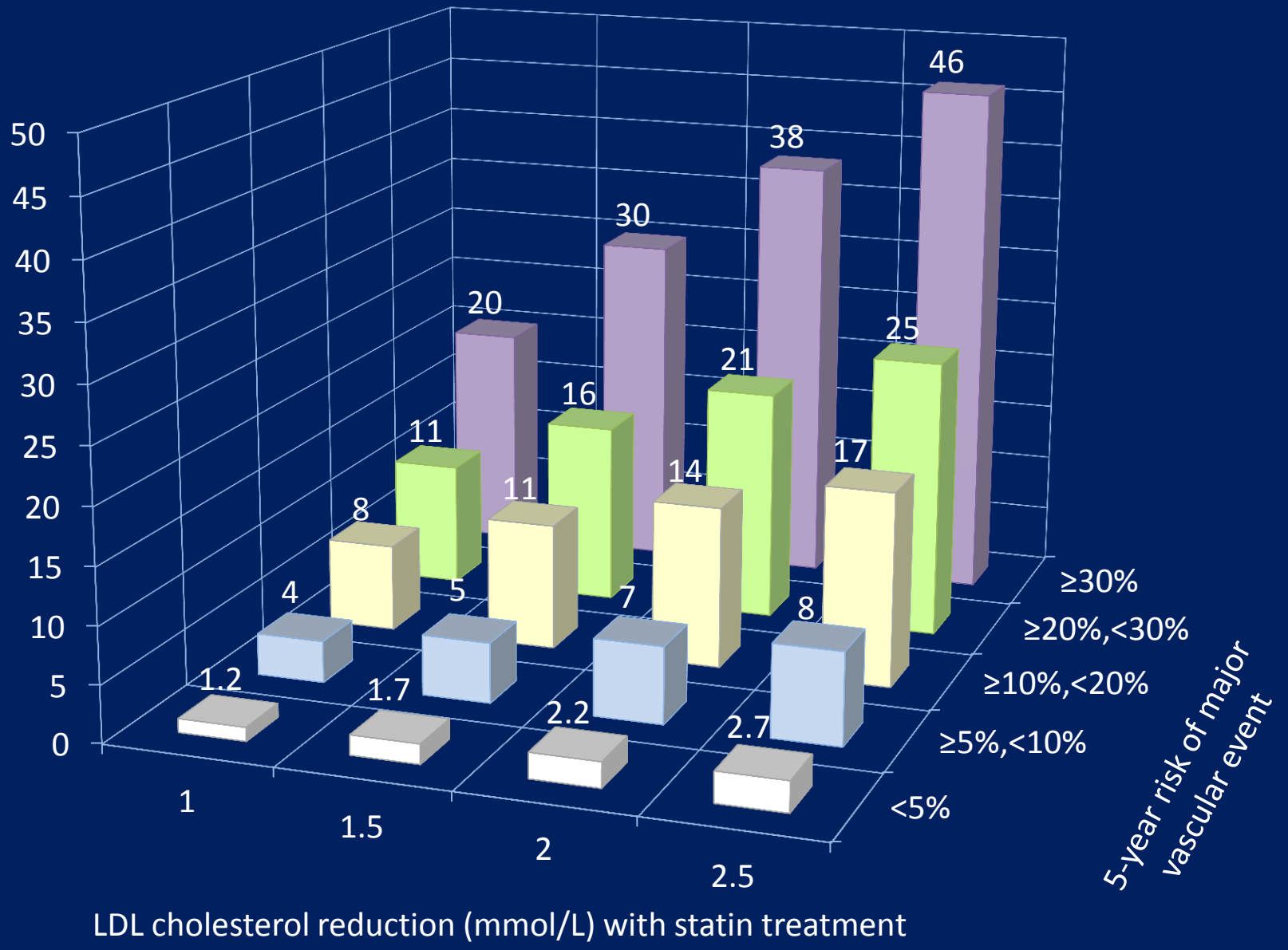
5-year MVE risk at baseline	Events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction	Trend test
Cancer incidence				
<5%	324 (0.7)	315 (0.7)	1.05 (0.85 - 1.31)	
≥5%,<10%	605 (1.1)	663 (1.2)	0.91 (0.78 - 1.05)	
≥10%,<20%	1804 (1.4)	1827 (1.4)	1.00 (0.91 - 1.10)	$\chi^2_1 = 0.83$
≥20%,<30%	1667 (1.8)	1628 (1.8)	1.02 (0.93 - 1.12)	(p=0.4)
≥30%	821 (2.0)	777 (1.9)	1.02 (0.90 - 1.16)	
Overall	**5221 (1.5)**	**5210 (1.5)**	**1.00 (0.96 - 1.04) p= 0.99**	
Cancer death				
<5%	64 (0.1)	57 (0.1)	1.14 (0.69 - 1.89)	
≥5%,<10%	171 (0.3)	186 (0.3)	0.93 (0.71 - 1.23)	
≥10%,<20%	697 (0.5)	718 (0.6)	1.00 (0.86 - 1.16)	$\chi^2_1 = 0.01$
≥20%,<30%	609 (0.6)	584 (0.6)	1.02 (0.88 - 1.19)	(p=0.9)
≥30%	293 (0.7)	304 (0.7)	0.97 (0.80 - 1.19)	
Overall	**1834 (0.5)**	**1849 (0.5)**	**0.99 (0.93 - 1.06) p= 0.86**	



Major Vascular Events avoided per 1,000 treated over 5 years



Vascular Deaths avoided per 1,000 treated over 5 years



Eligibility of CTT participants without a history of vascular disease for statin therapy under existing major guidelines (April 2012)

CTT risk category and event rates			Broad eligibility under current guidelines		
Estimated 5-year MVE risk	Observed MCE event rate (% per annum)*	Observed vascular death rate (% per annum)*	ATP-III[1]	ESC task force[2]	NICE[3]
<5%	0.2	0.1	×	×	×
≥5% to <10%	0.8	0.3	×	×	×
≥10% to <20%	1.6	1.0	✓	✓	✓
≥20% to <30%	3.2	2.3	✓	✓	✓
≥30%	5.6	5.8	✓	✓	✓

✓ Treatment with statin recommended. × Treatment with statin not recommended.

CTT= Cholesterol Treatment Collaboration'. MVE= major vascular event. MCE= major coronary event.

* Among control-allocated participants without a history of vascular disease.

[1] The Adult Treatment Panel III (ATP III) of the National Cholesterol Education program in the US.

[2] The Fourth Joint Task Force of the European Society of Cardiology (ESC) and Other Societies on Cardiovascular Disease Prevention in Clinical Practice and the ESC/EAS Guidelines for the management of dyslipidaemias.

[3] The National Institute for Health and Clinical Excellence (NICE) in the National Health Service (NHS) in England and Wales.