Cholesterol Treatment Trialists' (CTT) Collaboration

Slide deck

CTT Collaboration: Background*

History:

- Founded in 1993 (prior to publication of 4S trial in 1994)
- Original protocol published in 1995

Trial eligibility for inclusion in CTT:

- Randomized
- Principal effects of treatment is modification of blood lipids
- Unconfounded (i.e. treatment arms differ only by lipid intervention)
- Recruited at least 1000 participants
- Scheduled study treatment duration of at least 2 years

*American Journal of Cardiology 1995; 75: 1130-4

CTT Collaboration: Analyses*

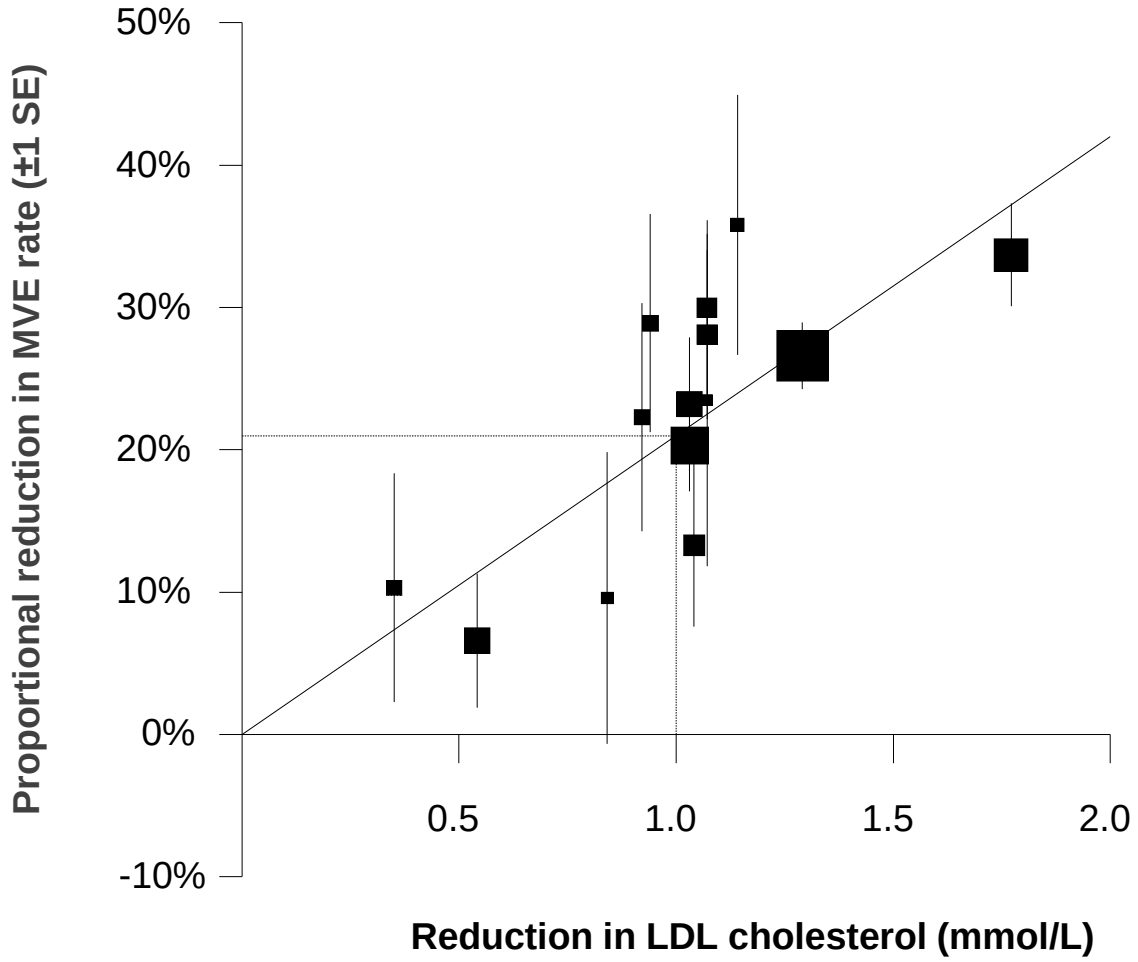
- Based on individual participant data (as opposed to tabular data)
- Intention-to-treat analyses
- Main results standardised per mmol/L LDL-cholesterol reduction

*American Journal of Cardiology 1995; 75: 1130-4

CTT Lancet 2005: included 14 trials of statin vs control

Study	Treatment comparison	N	Target population	Entry lipid criteria
4S	S20-40 vs. placebo	4444	Angina or previous MI	Total cholesterol 5.5-8.0 mmol/L
WOSCOPS	P40 vs. placebo	6595	Primary prevention	LDL-C ≥4.0 mmol/L
CARE	P40 vs. placebo	4159	Previous MI	Total cholesterol <6.2 mmol/L; LDL-C 3.0 to 4.5 mmol/L
Post-CABG	L40–80 vs. L2·5–5	1351	Previous coronary bypass surgery	LDL-C 3.4-4.5 mmol/L
AFCAPS/TexCAPS	L20–40 vs. placebo	6605	Primary prevention	Total cholesterol 4.65-6.82 mmol/L; LDL-C 3.36-4.91 mmol/L
LIPID	P40 vs. placebo	9014	Previous MI or hospitalization for unstable angina	Total cholesterol 4.0-7.0 mmol/L
GISSI-P	P20 vs. no treatment	4271	Recent MI	Total cholesterol ≥ 5.2 mmol/L
LIPS	F80 vs. placebo	1677	Previous PCI	Total cholesterol 3.5-7.0 mmol/L
HPS	S40 vs. placebo	20,536	CHD, other occlusive arterial disease or DM	Non-fasting total cholesterol ≥ 3·5 mmol/L
PROSPER	P40 vs. placebo	5804	History of or risk factors for vascular disease	Total cholesterol 4·0-9·0 mmol/L
ALLHAT-LLT	P40 vs. usual care	10,355	Hypertension + at least 1 additional CHD risk factor	Fasting LDL-C 3.1-4.9 mmol/L (no known CHD); 2.6 to 3.3 mmol/L (known CHD)
ASCOT-LLA	A10 vs. placebo	10,305	Hypertension + CVD risk factors	Non-fasting total cholesterol ≤6·5 mmol/L
ALERT	F40 vs. placebo	2102	Renal transplant patients	Total cholesterol 4·0-9·0 mmol/L.
CARDS	A10 vs. placebo	2838	Type 2 DM with no previous history of CVD	LDL-C ≤ 4.14 mmol/L

Relation between the proportional reduction in MAJOR VASCULAR EVENTS and mean absolute LDL-C reduction in 14 statin trials



Lancet 2005; 366: 1267-78

CTT Collaboration

CTT Lancet 2010*: additional trials of statin vs control

Study	Treatment comparison	N	Target population	Entry lipid criteria
MEGA	P 10-20 + diet vs. diet	8214	Primary prevention	Total cholesterol 5.69-6.98 mmol/L
JUPITER	R 20 vs. placebo	17 802	Primary prevention in people with CRP ≥2 mg/L	LDL-C <3.4 mmol/L
4D	A 20 vs. placebo	1255	Type 2 DM on haemodialysis	LDL-C 2.1-4.9 mmol/L
AURORA	R 10 vs. placebo	2776	Haemodialysis	None
ALLIANCE	A 10-80 (until LDL <2.1 mmol/L) vs. usual care	2442	Known CHD	LDL-C 2.8-5.2 mmol/L if on lipid lowering drugs; LDL-C 3.4-6.5 mmol/L if not
ASPEN	A 10 vs. placebo	2410	Type 2 DM	LDL-C ≤3.6mmol/Lin those with previous MI or intervention; LDL-C ≤ 4.1 mmol/L if not
GISSI-HF	R 10 vs. placebo	4574	Chronic heart failure	None

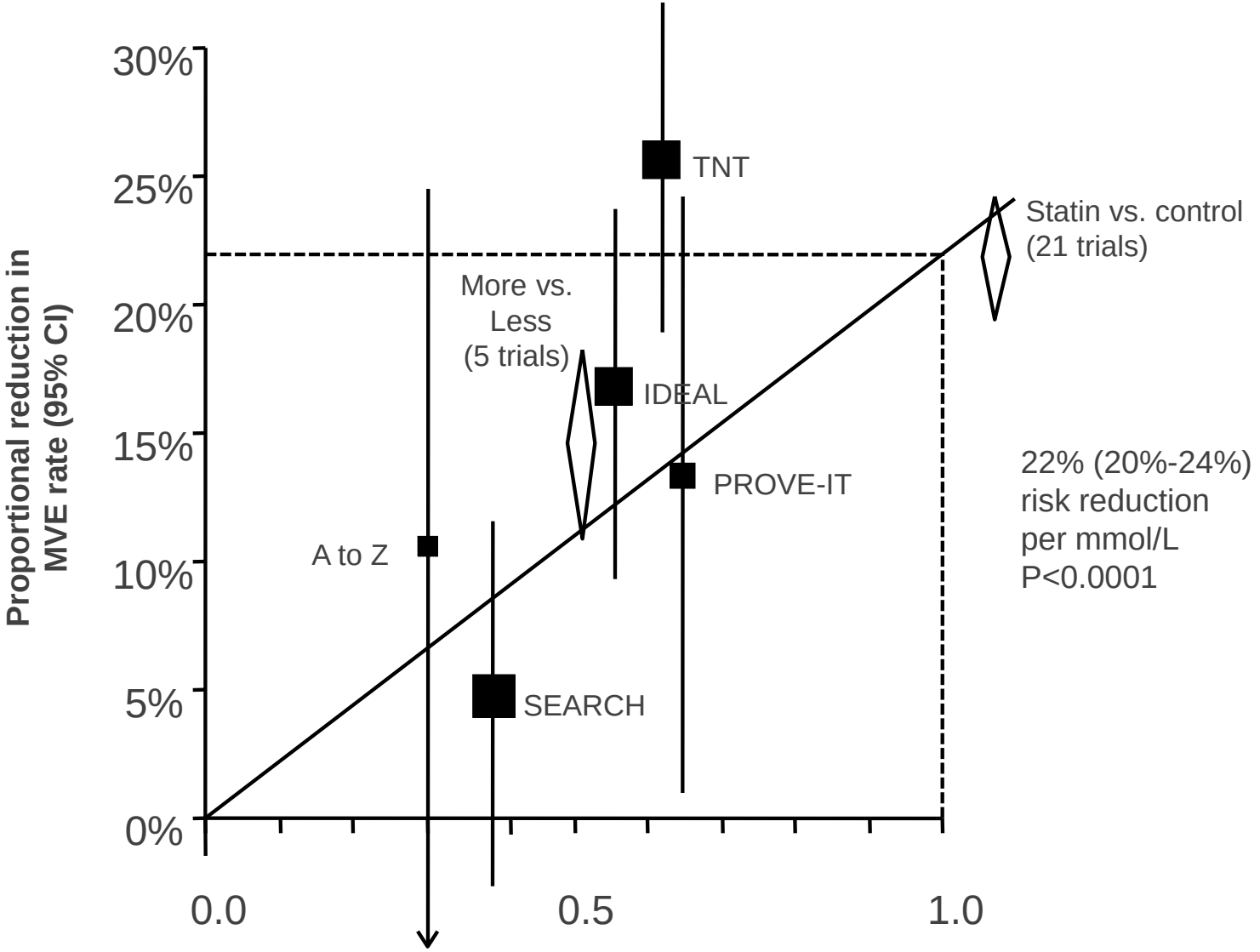
*Lancet 2010; 376: 1670-81

CTT Lancet 2010*: more vs less intensive statin therapy

Study	Treatment comparison	N	Target population	Entry lipid criteria
PROVE-IT	A 80 vs. P 40	4162	Recent ACS	Total cholesterol ≤ 6.21 mmol/L
A to Z	S 40 then S 80 vs. placebo then S 20	4497	ACS	Total cholesterol ≤ 6.48 mmol/L
TNT	A 80 vs. A 10	10,001	Prior CHD	LDL-C <3.4 mmol/L
IDEAL	A 80 vs. S 20-40	8888	Previous MI	Qualified for statin therapy according to guidelines at the time of recruitment
SEARCH	S 80 vs. S 20	12,064	Previous MI	Total cholesterol ≥4.5 mmol/L or ≥3.5 if already on statin

*Lancet 2010; 376: 1670-81

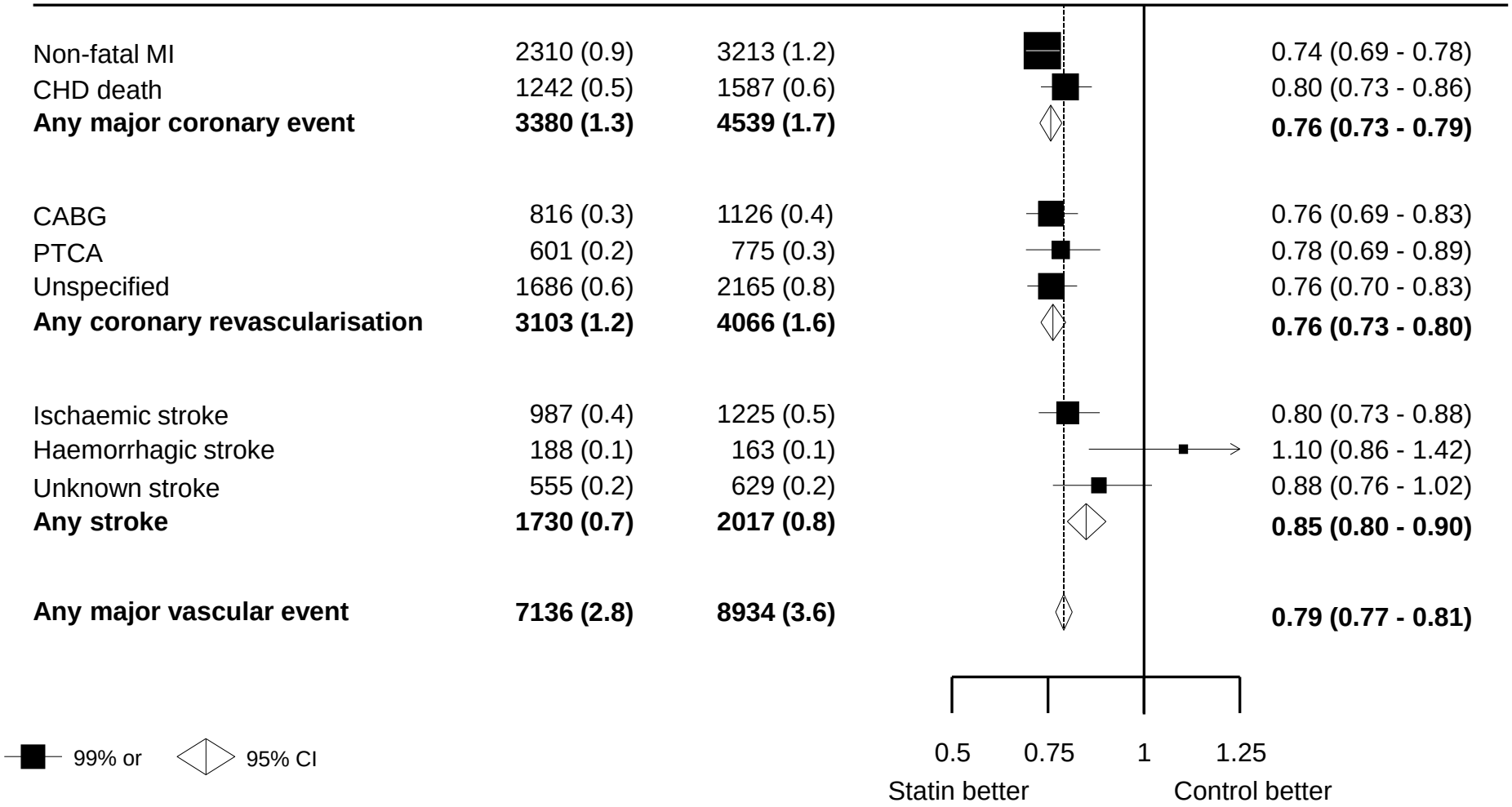
CTT meta analysis: Proportional reduction in MAJOR VASCULAR EVENTS versus absolute LDL-C reduction



CTT Collaboration

Statin vs control trials: Proportional effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction

Outcome	No. of events (% per annum) Statin	Control	RR (CI) per mmol/L LDL-C reduction
Non-fatal MI	2310 (0.9)	3213 (1.2)	0.74 (0.69 - 0.78)
CHD death	1242 (0.5)	1587 (0.6)	0.80 (0.73 - 0.86)
Any major coronary event	**3380 (1.3)**	**4539 (1.7)**	**0.76 (0.73 - 0.79)**
CABG	816 (0.3)	1126 (0.4)	0.76 (0.69 - 0.83)
PTCA	601 (0.2)	775 (0.3)	0.78 (0.69 - 0.89)
Unspecified	1686 (0.6)	2165 (0.8)	0.76 (0.70 - 0.83)
Any coronary revascularisation	**3103 (1.2)**	**4066 (1.6)**	**0.76 (0.73 - 0.80)**
Ischaemic stroke	987 (0.4)	1225 (0.5)	0.80 (0.73 - 0.88)
Haemorrhagic stroke	188 (0.1)	163 (0.1)	1.10 (0.86 - 1.42)
Unknown stroke	555 (0.2)	629 (0.2)	0.88 (0.76 - 1.02)
Any stroke	**1730 (0.7)**	**2017 (0.8)**	**0.85 (0.80 - 0.90)**
Any major vascular event	**7136 (2.8)**	**8934 (3.6)**	**0.79 (0.77 - 0.81)**

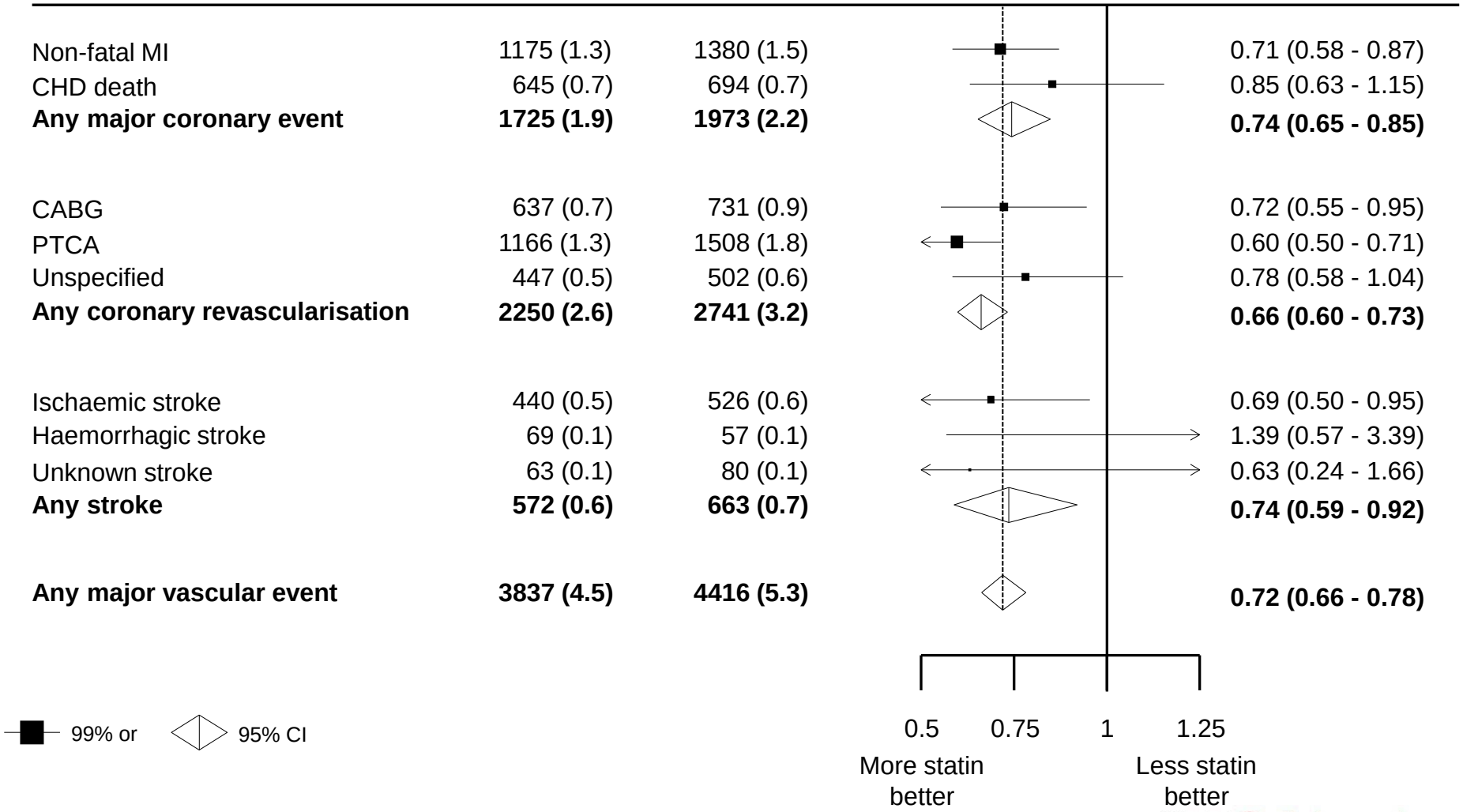


Lancet 2010; 376: 1670-81

CTT Collaboration

More vs less statin: Proportional effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction

Outcome	No. of events (% per annum) More statin	Less statin	RR (CI) per mmol/L LDL-C reduction
Non-fatal MI	1175 (1.3)	1380 (1.5)	0.71 (0.58 - 0.87)
CHD death	645 (0.7)	694 (0.7)	0.85 (0.63 - 1.15)
Any major coronary event	**1725 (1.9)**	**1973 (2.2)**	**0.74 (0.65 - 0.85)**
CABG	637 (0.7)	731 (0.9)	0.72 (0.55 - 0.95)
PTCA	1166 (1.3)	1508 (1.8)	0.60 (0.50 - 0.71)
Unspecified	447 (0.5)	502 (0.6)	0.78 (0.58 - 1.04)
Any coronary revascularisation	**2250 (2.6)**	**2741 (3.2)**	**0.66 (0.60 - 0.73)**
Ischaemic stroke	440 (0.5)	526 (0.6)	0.69 (0.50 - 0.95)
Haemorrhagic stroke	69 (0.1)	57 (0.1)	1.39 (0.57 - 3.39)
Unknown stroke	63 (0.1)	80 (0.1)	0.63 (0.24 - 1.66)
Any stroke	**572 (0.6)**	**663 (0.7)**	**0.74 (0.59 - 0.92)**
Any major vascular event	**3837 (4.5)**	**4416 (5.3)**	**0.72 (0.66 - 0.78)**

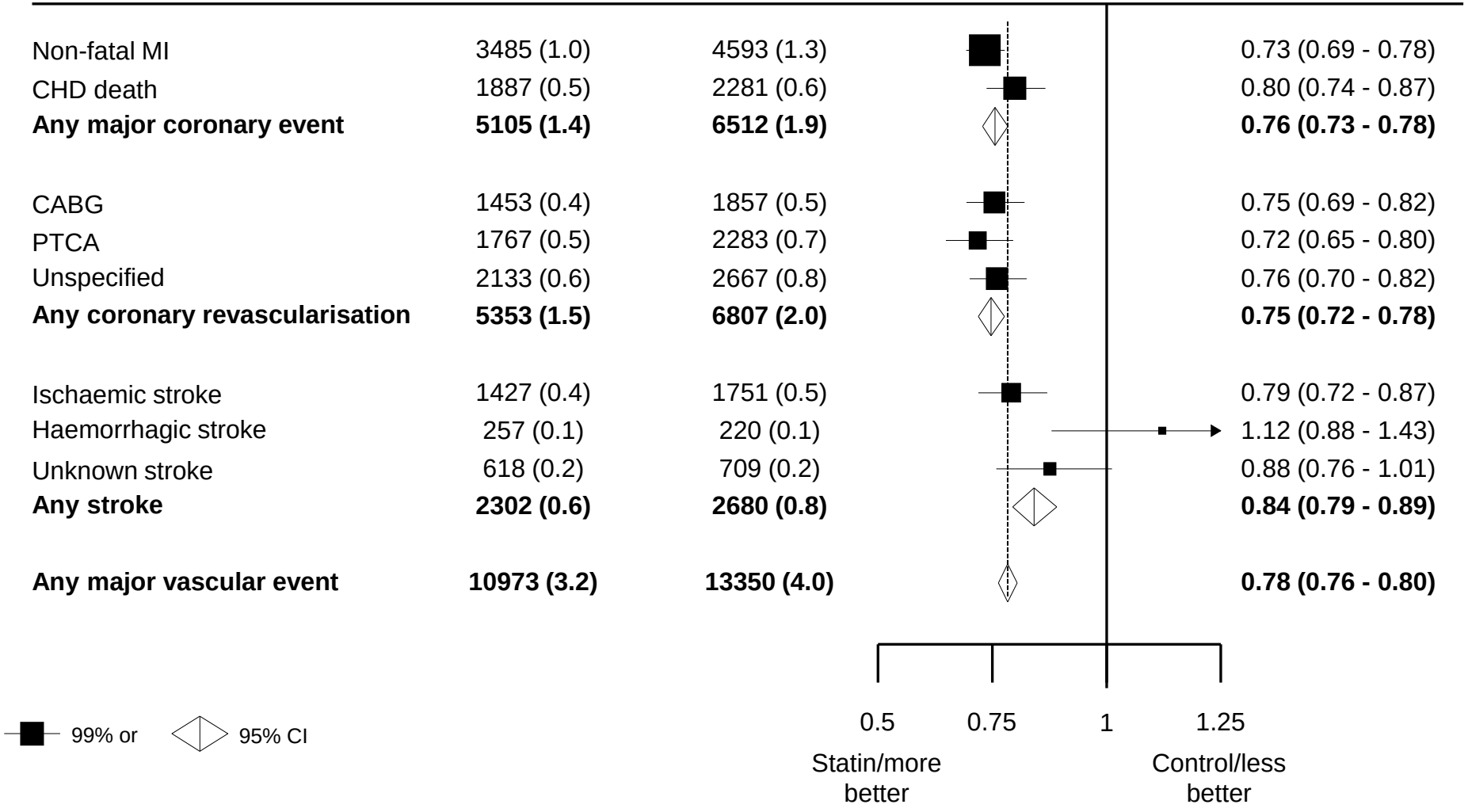


Lancet 2010; 376: 1670-81

CTT Collaboration

All trials (statin vs control OR more vs less statin): Proportional effects on MAJOR VASCULAR EVENTS per mmol/L reduction in LDL-C

Outcome	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
Non-fatal MI	3485 (1.0)	4593 (1.3)	0.73 (0.69 - 0.78)
CHD death	1887 (0.5)	2281 (0.6)	0.80 (0.74 - 0.87)
Any major coronary event	**5105 (1.4)**	**6512 (1.9)**	**0.76 (0.73 - 0.78)**
CABG	1453 (0.4)	1857 (0.5)	0.75 (0.69 - 0.82)
PTCA	1767 (0.5)	2283 (0.7)	0.72 (0.65 - 0.80)
Unspecified	2133 (0.6)	2667 (0.8)	0.76 (0.70 - 0.82)
Any coronary revascularisation	**5353 (1.5)**	**6807 (2.0)**	**0.75 (0.72 - 0.78)**
Ischaemic stroke	1427 (0.4)	1751 (0.5)	0.79 (0.72 - 0.87)
Haemorrhagic stroke	257 (0.1)	220 (0.1)	1.12 (0.88 - 1.43)
Unknown stroke	618 (0.2)	709 (0.2)	0.88 (0.76 - 1.01)
Any stroke	**2302 (0.6)**	**2680 (0.8)**	**0.84 (0.79 - 0.89)**
Any major vascular event	**10973 (3.2)**	**13350 (4.0)**	**0.78 (0.76 - 0.80)**



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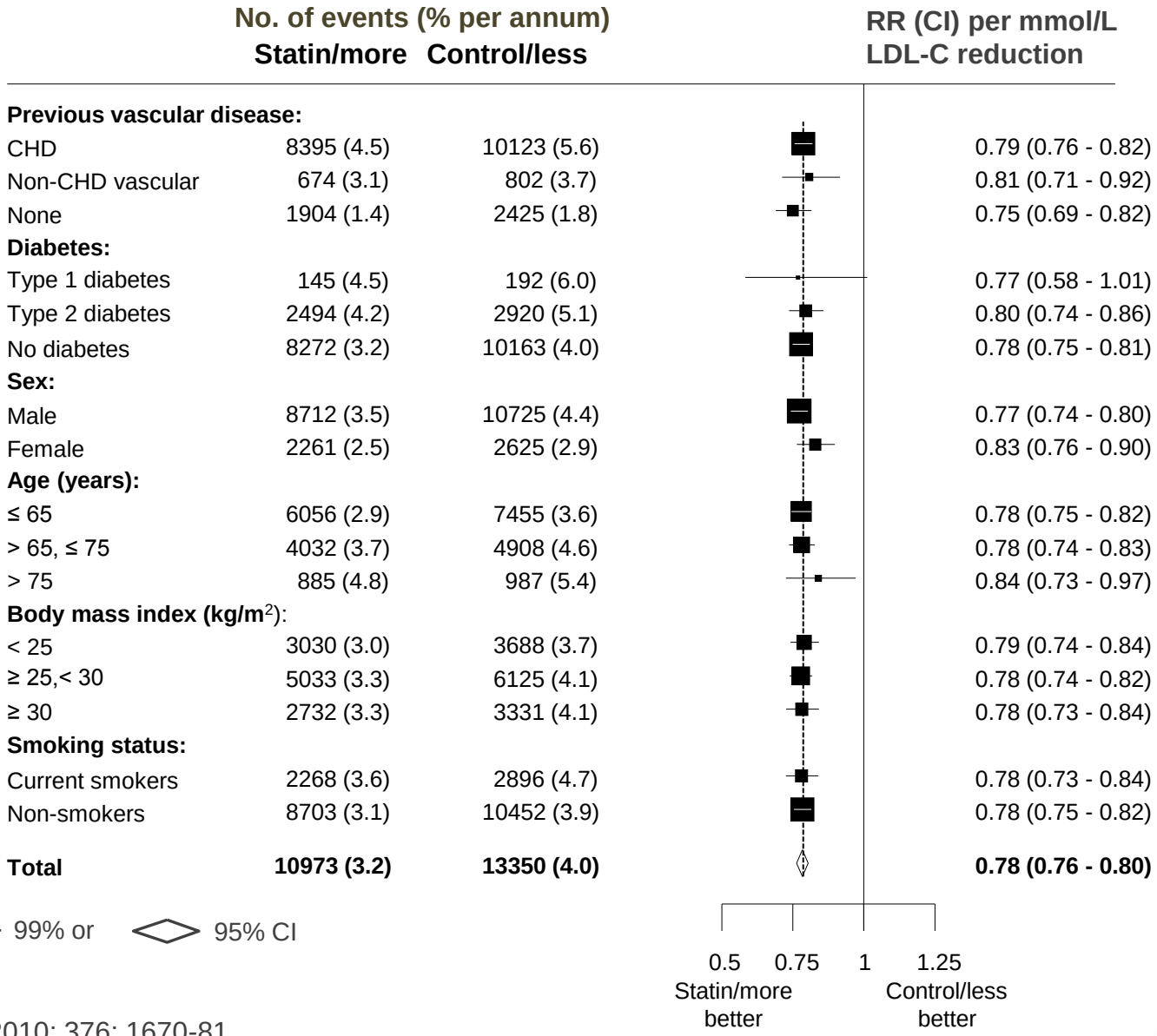
Proportional effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction, by baseline prognostic factors

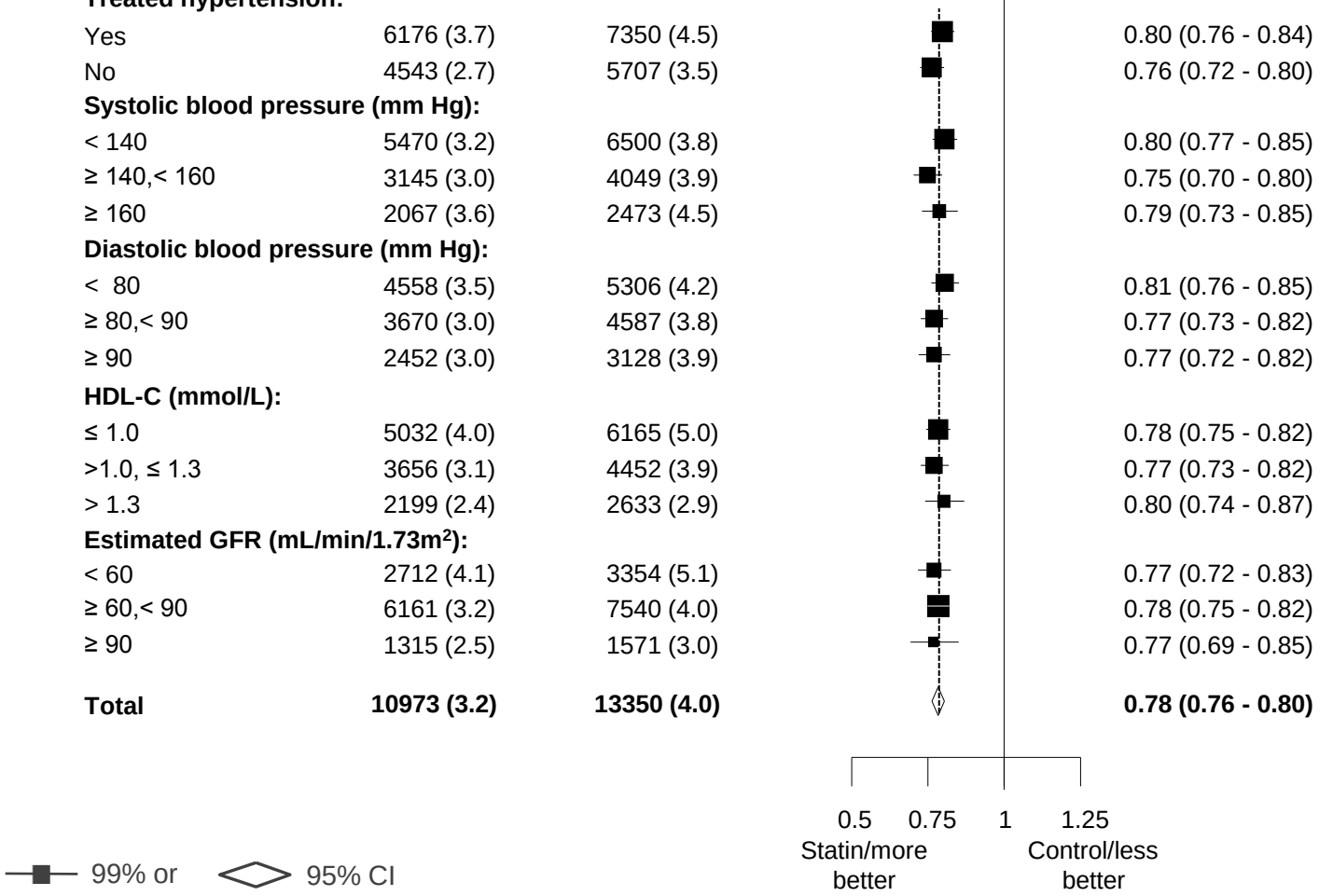


Lancet 2010; 376: 1670-81

CTT Collaboration

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

	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
Treated hypertension:			
Yes	6176 (3.7)	7350 (4.5)	0.80 (0.76 - 0.84)
No	4543 (2.7)	5707 (3.5)	0.76 (0.72 - 0.80)
Systolic blood pressure (mm Hg):			
< 140	5470 (3.2)	6500 (3.8)	0.80 (0.77 - 0.85)
≥ 140,< 160	3145 (3.0)	4049 (3.9)	0.75 (0.70 - 0.80)
≥ 160	2067 (3.6)	2473 (4.5)	0.79 (0.73 - 0.85)
Diastolic blood pressure (mm Hg):			
< 80	4558 (3.5)	5306 (4.2)	0.81 (0.76 - 0.85)
≥ 80,< 90	3670 (3.0)	4587 (3.8)	0.77 (0.73 - 0.82)
≥ 90	2452 (3.0)	3128 (3.9)	0.77 (0.72 - 0.82)
HDL-C (mmol/L):			
≤ 1.0	5032 (4.0)	6165 (5.0)	0.78 (0.75 - 0.82)
>1.0, ≤ 1.3	3656 (3.1)	4452 (3.9)	0.77 (0.73 - 0.82)
> 1.3	2199 (2.4)	2633 (2.9)	0.80 (0.74 - 0.87)
Estimated GFR (mL/min/1.73m²):			
< 60	2712 (4.1)	3354 (5.1)	0.77 (0.72 - 0.83)
≥ 60,< 90	6161 (3.2)	7540 (4.0)	0.78 (0.75 - 0.82)
≥ 90	1315 (2.5)	1571 (3.0)	0.77 (0.69 - 0.85)
Total	**10973 (3.2)**	**13350 (4.0)**	**0.78 (0.76 - 0.80)**

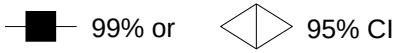


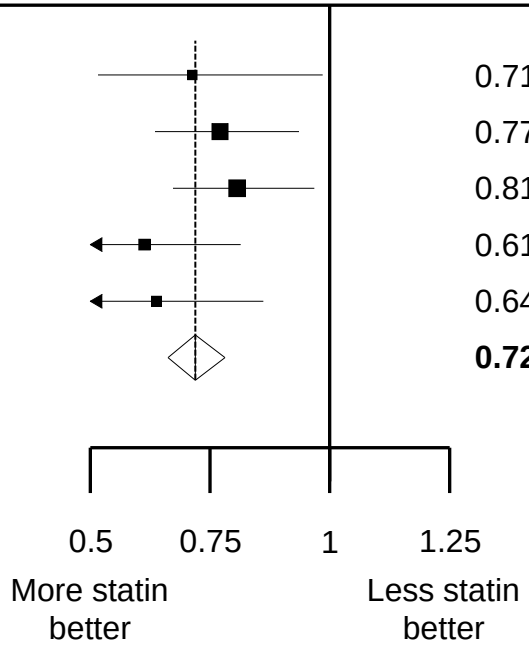
Lancet 2010; 376: 1670-81

CTT Collaboration

More vs less trials: Proportional effects on MAJOR VASCULAR EVENTS per mmol/L reduction in LDL-C, by baseline LDL-C

Baseline LDL-C (mmol/L)	No. of events (% per annum)		RR (CI) per mmol/L LDL-C reduction
	More statin	Less statin	
< 2.0	704 (4.6)	795 (5.2)	0.71 (0.52 - 0.98)
≥ 2.0 ,<2.5	1189 (4.2)	1317 (4.8)	0.77 (0.64 - 0.94)
≥ 2.5, <3.0	1065 (4.5)	1203 (5.0)	0.81 (0.67 - 0.97)
≥ 3.0, <3.5	517 (4.5)	633 (5.8)	0.61 (0.46 - 0.81)
≥ 3.0	303 (5.7)	398 (7.8)	0.64 (0.47 - 0.86)
Total	**3837 (4.5)**	**4416 (5.3)**	**0.72 (0.66 - 0.78)**





Lancet 2010; 376: 1670-81

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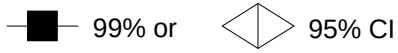
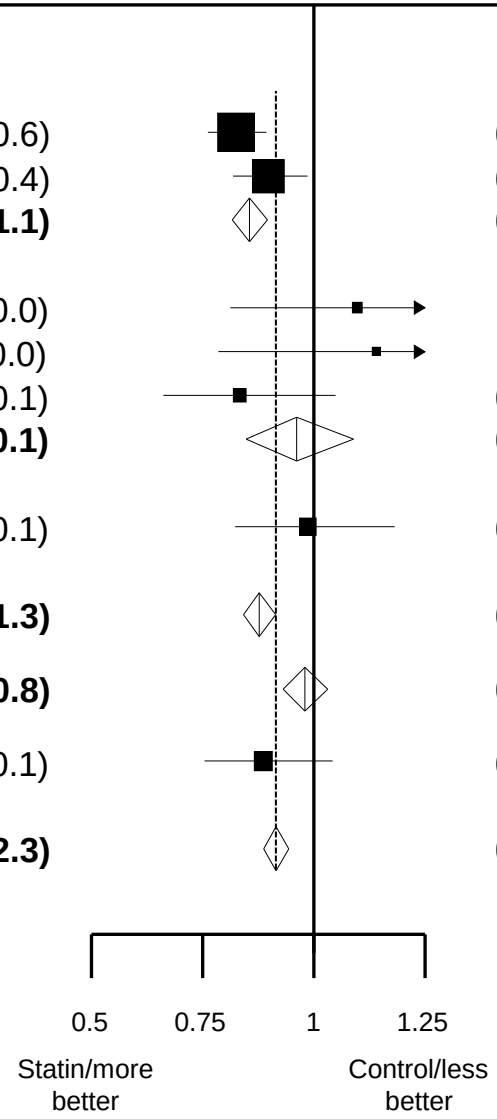
Proportional effects on CAUSE-SPECIFIC MORTALITY per mmol/L LDL-C reduction

Cause of death	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
Vascular causes:			
CHD	1887 (0.5)	2281 (0.6)	0.82 (0.76 - 0.89)
Other cardiac	1446 (0.4)	1603 (0.4)	0.90 (0.82 - 0.99)
All cardiac	**3333 (0.9)**	**3884 (1.1)**	**0.85 (0.82 - 0.90)**
Ischaemic stroke	153 (0.0)	139 (0.0)	1.10 (0.81 - 1.48)
Haemorrhagic stroke	102 (0.0)	89 (0.0)	1.14 (0.79 - 1.66)
Unknown stroke	228 (0.1)	273 (0.1)	0.83 (0.66 - 1.05)
Stroke	**483 (0.1)**	**501 (0.1)**	**0.96 (0.85 - 1.09)**
Other vascular	404 (0.1)	409 (0.1)	0.99 (0.82 - 1.18)
Any vascular	**4220 (1.2)**	**4794 (1.3)**	**0.88 (0.84 - 0.91)**
Any non-vascular	**2943 (0.8)**	**2994 (0.8)**	**0.98 (0.93 - 1.03)**
Unknown	479 (0.1)	539 (0.1)	0.89 (0.75 - 1.04)
Any death	**7642 (2.1)**	**8327 (2.3)**	**0.91 (0.89 - 0.94)**





Lancet 2010; 376: 1670-81

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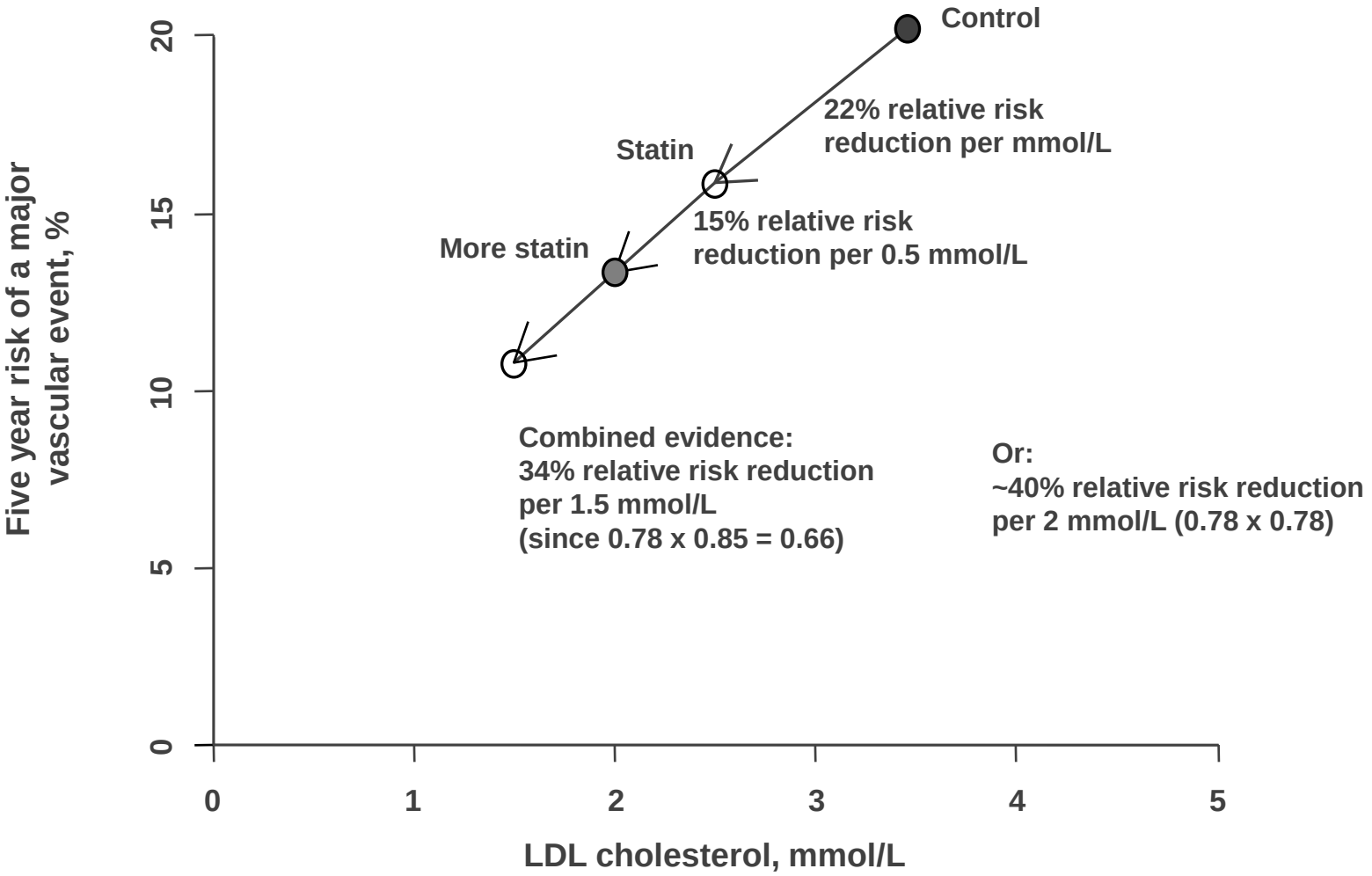
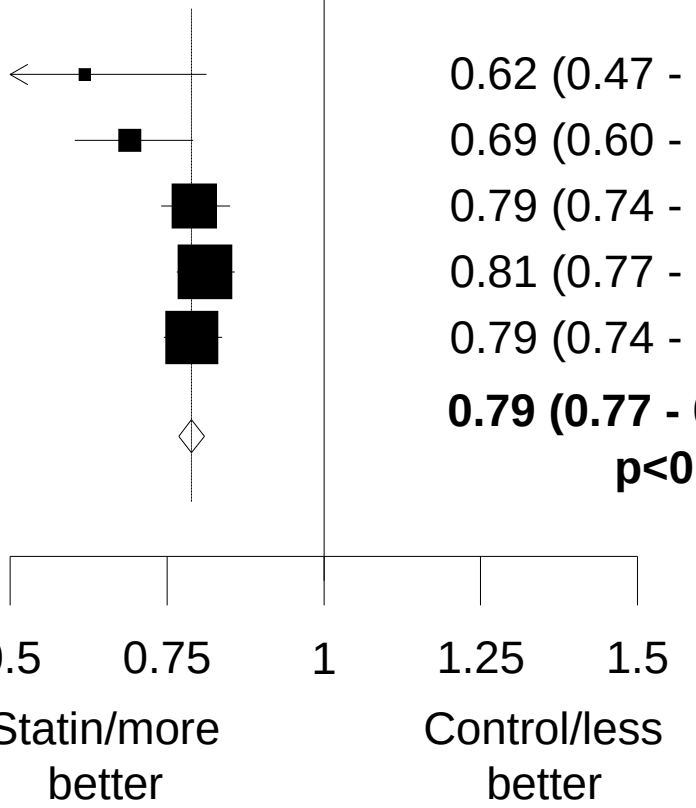
Expected reduction in MAJOR VASCULAR EVENT risk from lowering LDL-C with STATIN therapy



CTT Collaboration

Effects on MAJOR VASCULAR EVENTS per mmol/L reduction in LDL-C at different levels of risk

5-year MVE risk at baseline	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
< 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)
≥ 20%,<30%	4108 (4.74)	4919 (5.80)	0.81 (0.77 - 0.86)
≥ 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**



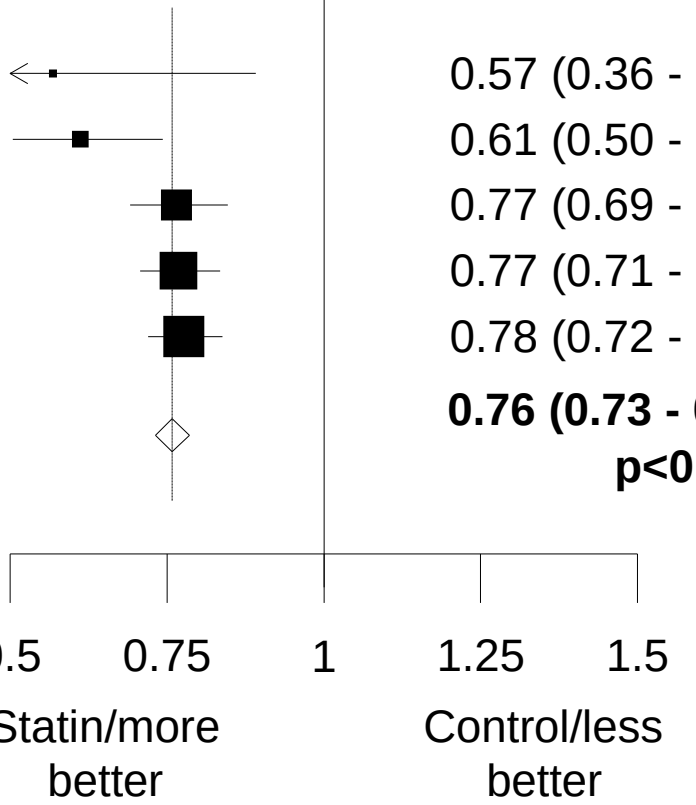
99% or 95% CI

Lancet 2012; 380: 581-90

CTT Collaboration

Effects on MAJOR CORONARY EVENTS per mmol/L reduction in LDL-C at different levels of risk

5-year MVE risk at baseline	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
< 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)
≥ 20%,<30%	1789 (1.93)	2282 (2.49)	0.77 (0.71 - 0.83)
≥ 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**



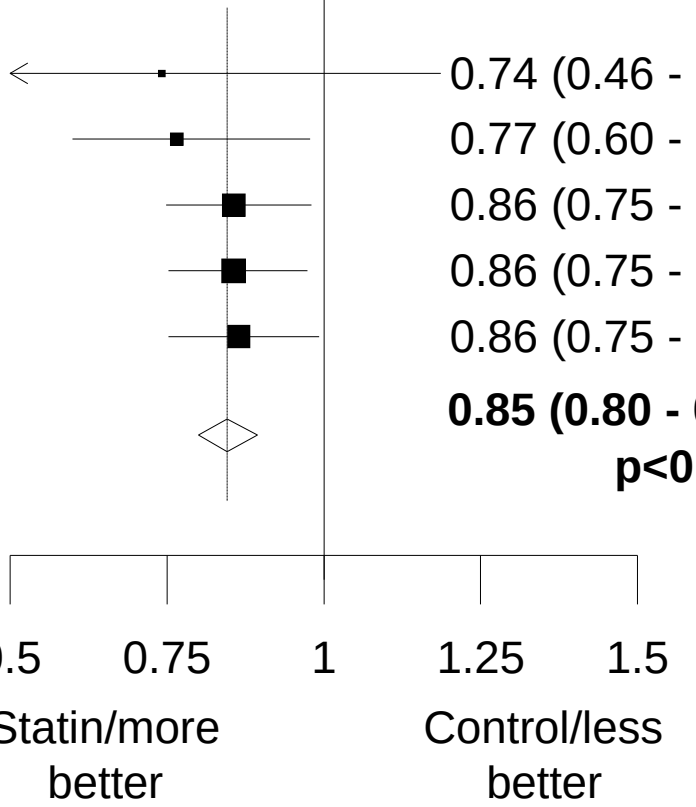
99% or 95% CI

Lancet 2012; 380: 581-90

CTT Collaboration

Effects on ANY STROKE
per mmol/L reduction in LDL-C at different levels of risk

5-year MVE risk at baseline	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
< 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)
≥ 20%,<30%	781 (0.84)	900 (0.97)	0.86 (0.75 - 0.97)
≥ 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**



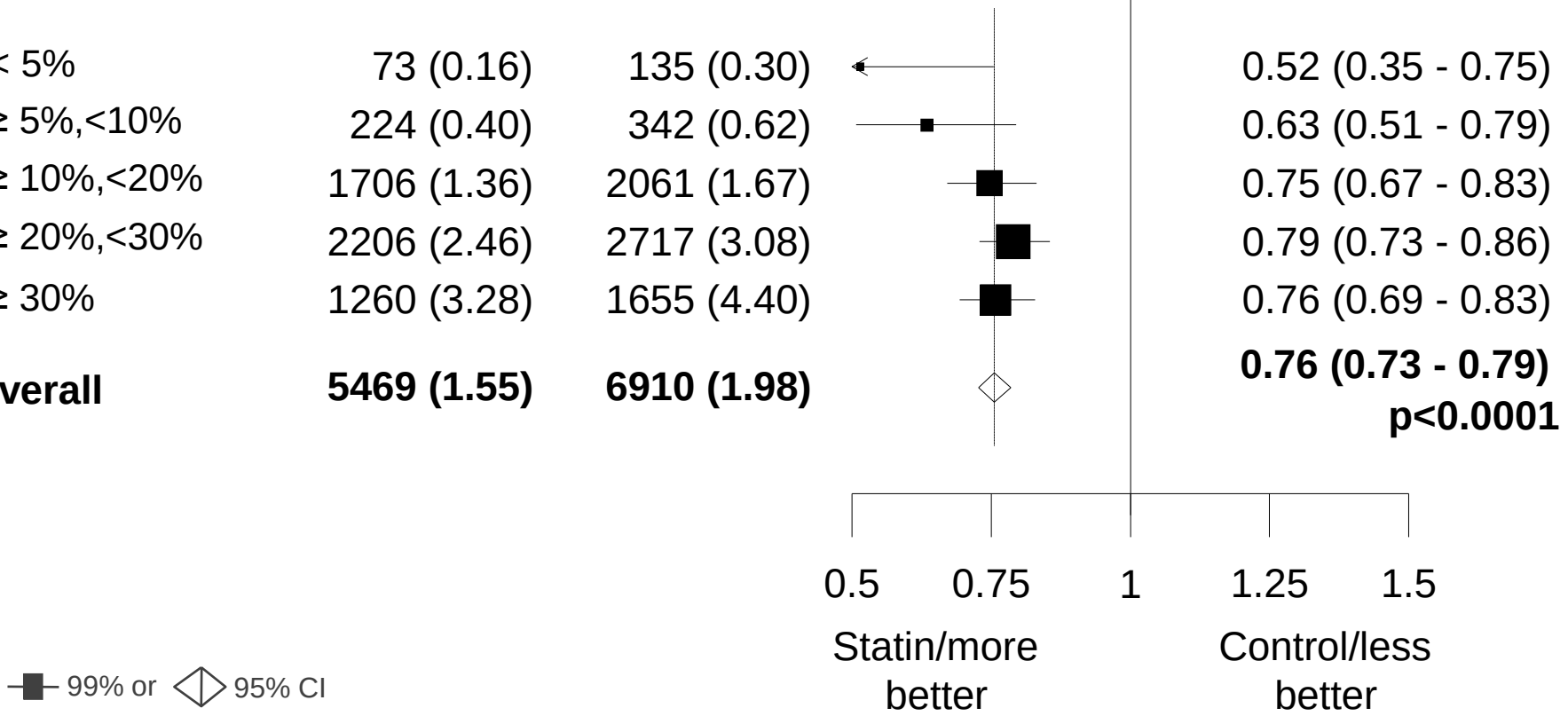
99% or 95% CI

Lancet 2012; 380: 581-90

CTT Collaboration

Effects on ANY CORONARY REVASCULARISATION per mmol/L reduction in LDL-C at different levels of risk

5-year MVE risk at baseline	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
< 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)
≥ 20%,<30%	2206 (2.46)	2717 (3.08)	0.79 (0.73 - 0.86)
≥ 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**

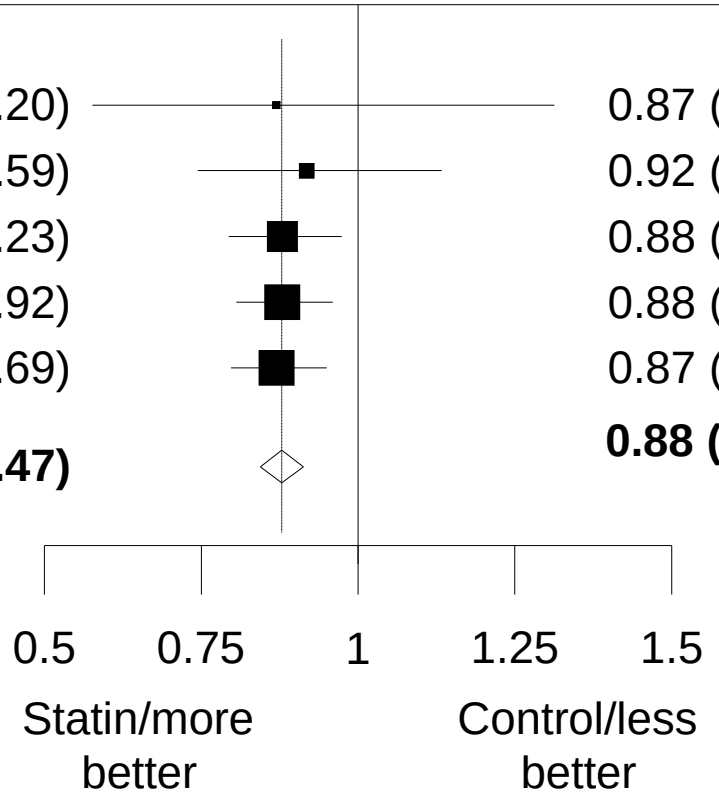


Lancet 2012; 380: 581-90

CTT Collaboration

Effects on VASCULAR MORTALITY per mmol/L LDL-C reduction at different levels of risk

5-year MVE risk at baseline	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
< 5%	79 (0.18)	92 (0.20)	0.87 (0.58 - 1.31)
≥ 5%,<10%	310 (0.55)	330 (0.59)	0.92 (0.74 - 1.13)
≥ 10%,<20%	1473 (1.14)	1591 (1.23)	0.88 (0.79 - 0.97)
≥ 20%,<30%	1596 (1.67)	1833 (1.92)	0.88 (0.81 - 0.96)
≥ 30%	1340 (3.23)	1533 (3.69)	0.87 (0.80 - 0.95)
Overall	**4798 (1.30)**	**5379 (1.47)**	**0.88 (0.84 - 0.91)** **p<0.0001**



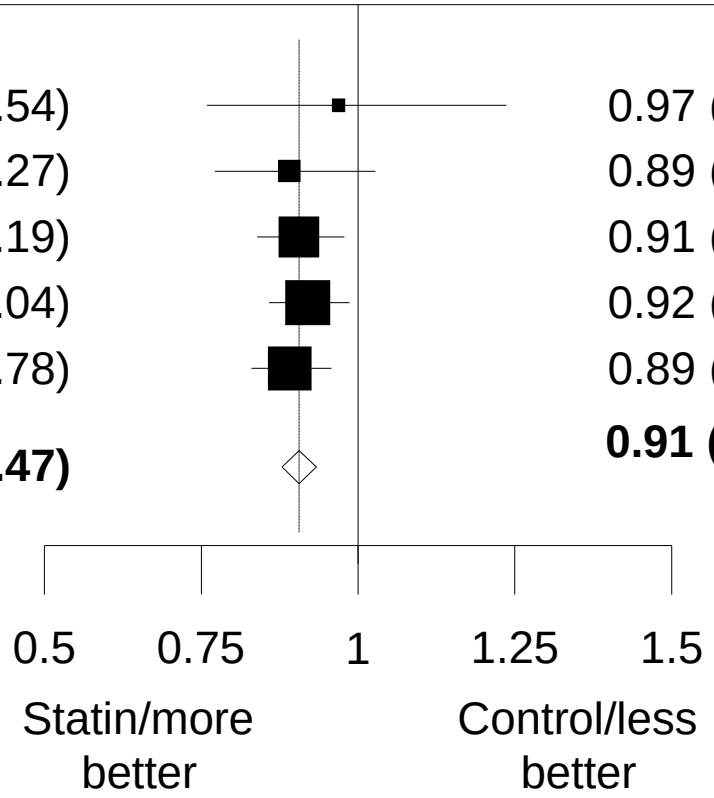
99% or 95% CI

Lancet 2012; 380: 581-90

CTT Collaboration

Effects on ALL CAUSE MORTALITY per mmol/L LDL-C reduction at different levels of risk

5-year MVE risk at baseline	No. of events (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
< 5%	232 (0.52)	244 (0.54)	0.97 (0.76 - 1.24)
≥ 5%,<10%	639 (1.14)	710 (1.27)	0.89 (0.77 - 1.03)
≥ 10%,<20%	2651 (2.04)	2827 (2.19)	0.91 (0.84 - 0.98)
≥ 20%,<30%	2683 (2.80)	2903 (3.04)	0.92 (0.86 - 0.99)
≥ 30%	2165 (5.22)	2403 (5.78)	0.89 (0.83 - 0.96)
Overall	**8370 (2.27)**	**9087 (2.47)**	**0.91 (0.88 - 0.93)** **p<0.0001**



99% or 95% CI

Lancet 2012; 380: 581-90

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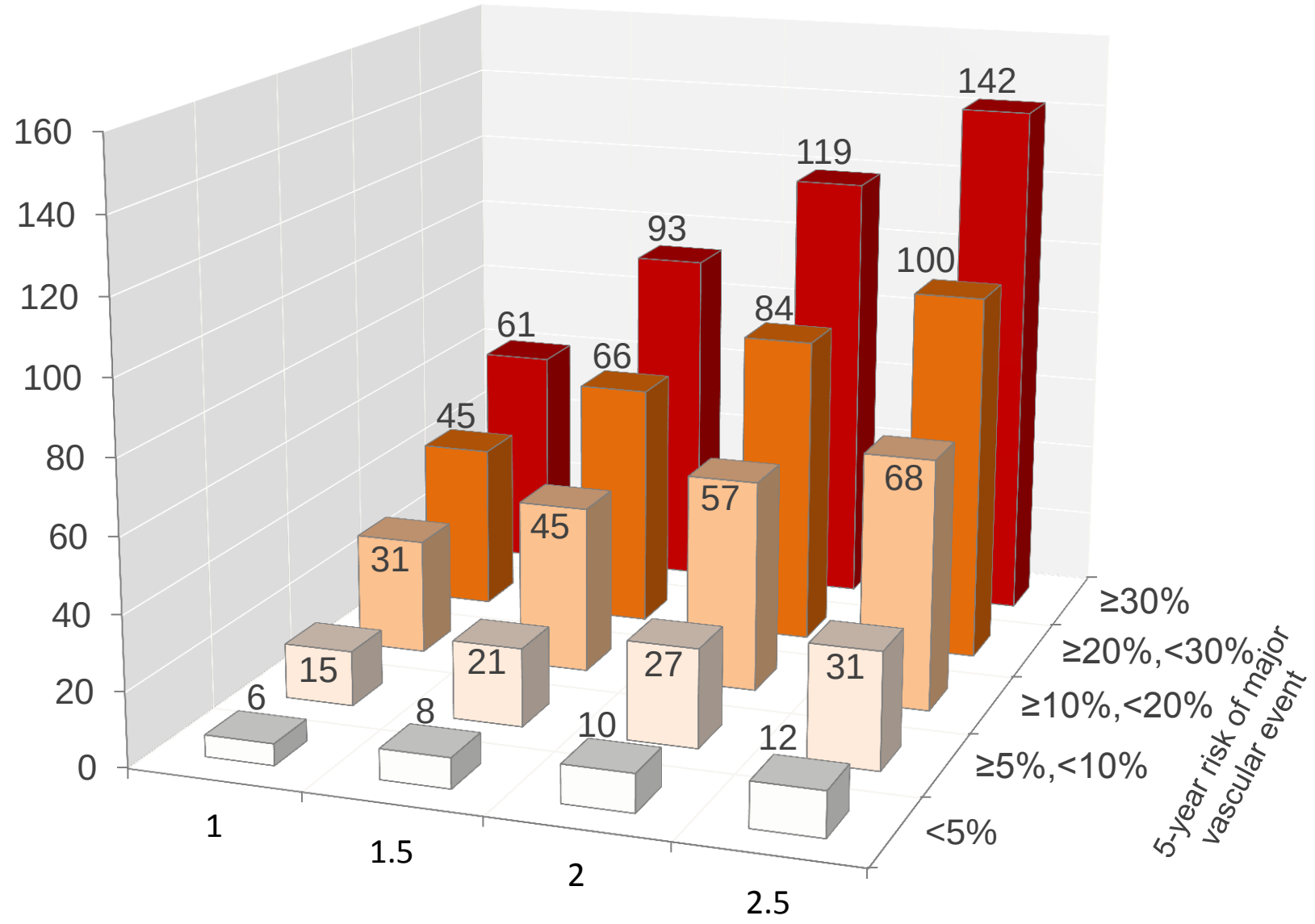
MAJOR VASCULAR EVENTS avoided per 1,000 treated over 5 years



Lancet 2012; 380: 581-90

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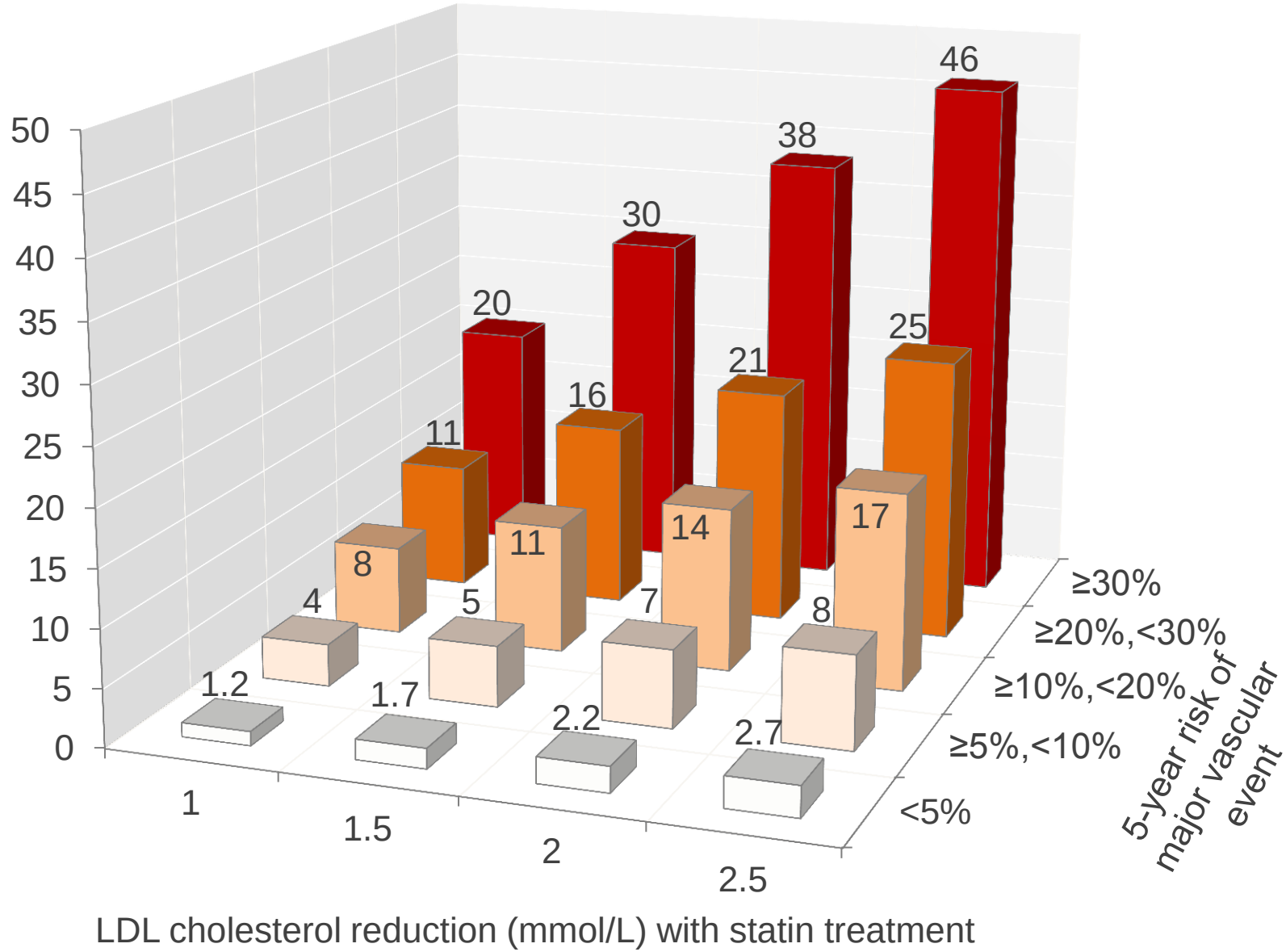
VASCULAR DEATHS avoided per 1,000 treated over 5 years



Lancet 2012; 380: 581-90

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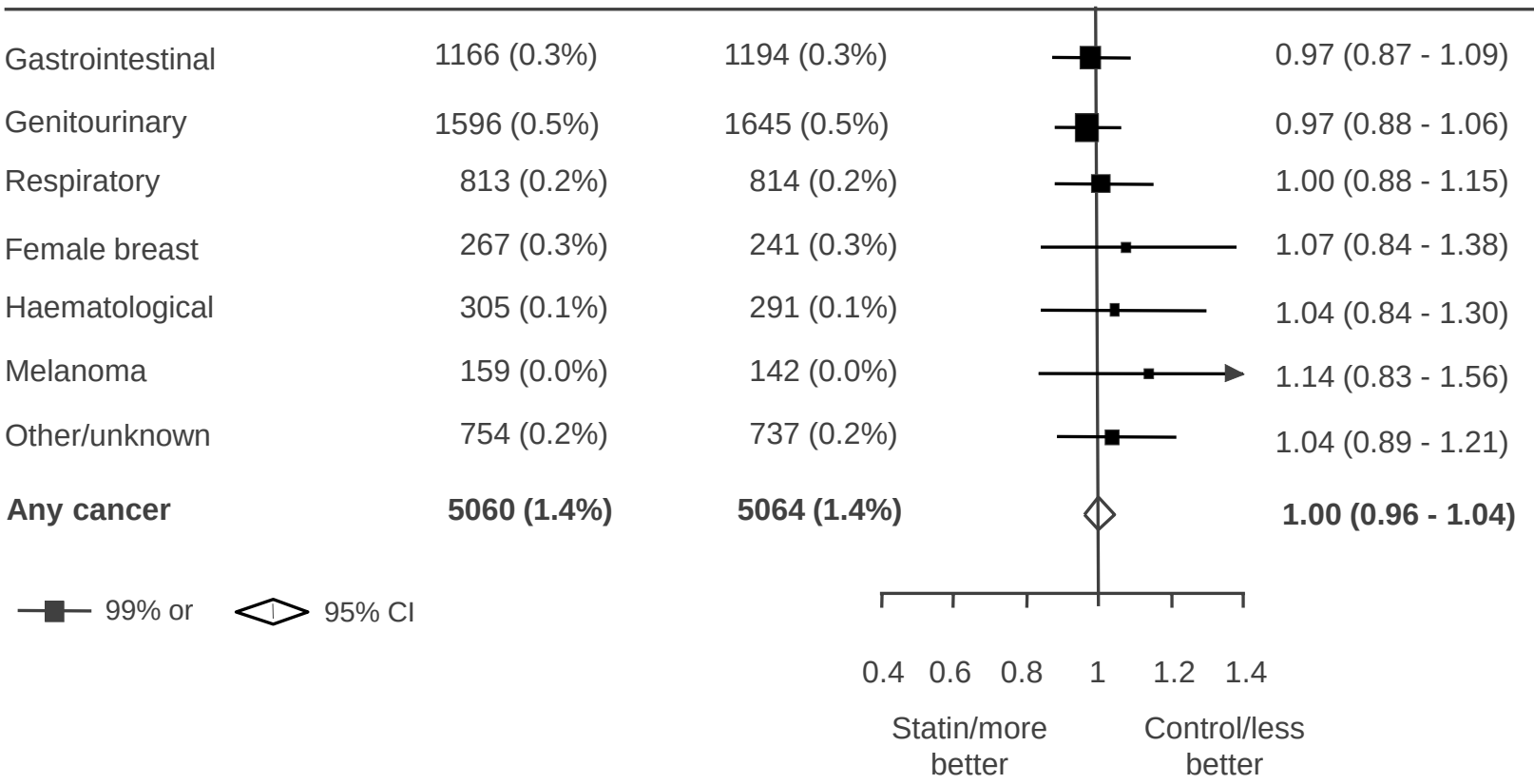
Proportional effects on SITE SPECIFIC CANCER per mmol/L LDL-C reduction

Primary site	No. of first cancers (% per annum) Statin/more	Control/less	RR (CI) per mmol/L LDL-C reduction
Gastrointestinal	1166 (0.3%)	1194 (0.3%)	0.97 (0.87 - 1.09)
Genitourinary	1596 (0.5%)	1645 (0.5%)	0.97 (0.88 - 1.06)
Respiratory	813 (0.2%)	814 (0.2%)	1.00 (0.88 - 1.15)
Female breast	267 (0.3%)	241 (0.3%)	1.07 (0.84 - 1.38)
Haematological	305 (0.1%)	291 (0.1%)	1.04 (0.84 - 1.30)
Melanoma	159 (0.0%)	142 (0.0%)	1.14 (0.83 - 1.56)
Other/unknown	754 (0.2%)	737 (0.2%)	1.04 (0.89 - 1.21)
Any cancer	**5060 (1.4%)**	**5064 (1.4%)**	**1.00 (0.96 - 1.04)**



Lancet 2010; 376: 1670-81

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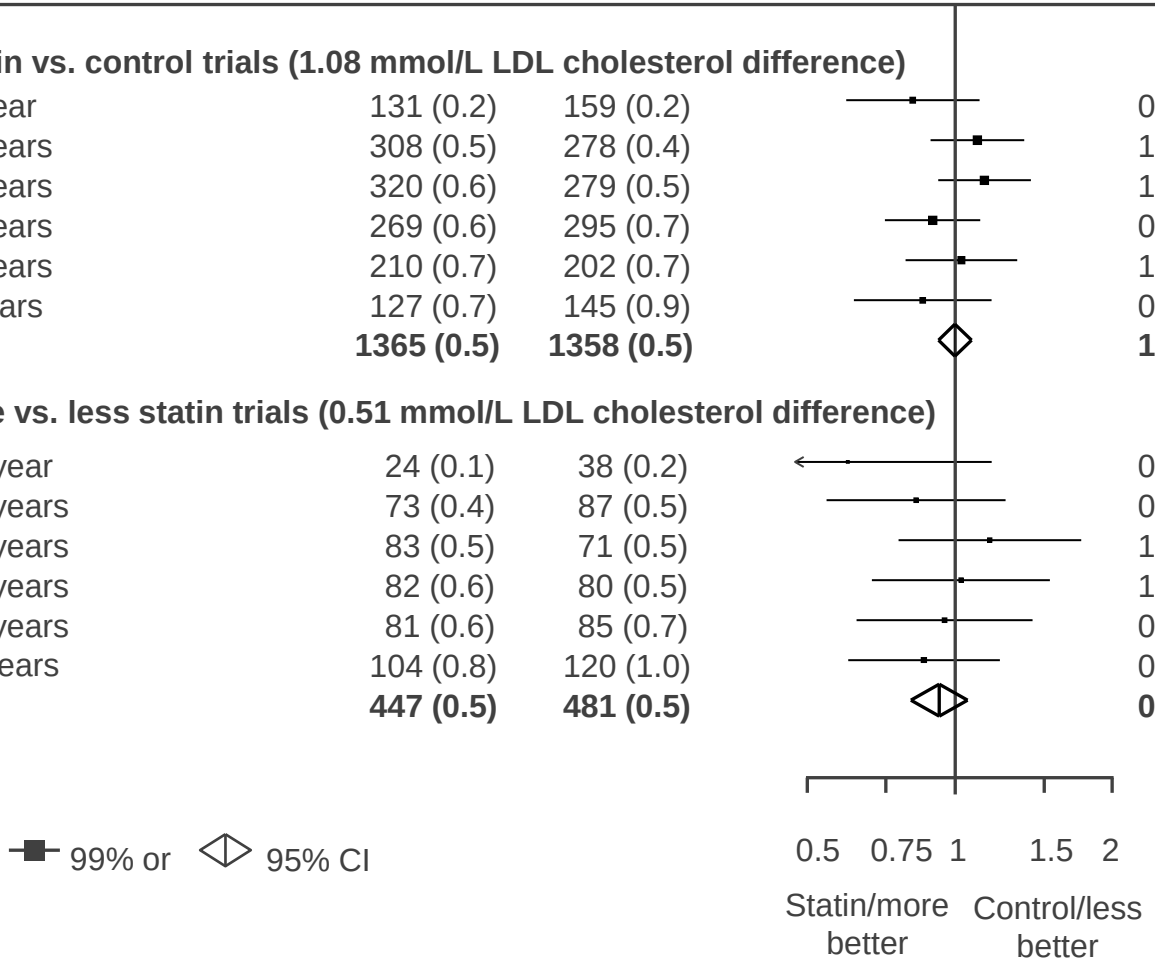
Effects of statin therapy on CANCER MORTALITY by duration of treatment

Year	No. of events (% per annum) Statin/more	Control/less	RR (CI)	Trend test
22 Statin vs. control trials (1.08 mmol/L LDL cholesterol difference)				
0-1 year	131 (0.2)	159 (0.2)	0.82 (0.61 - 1.12)	χ^2_1=0.43 (p=0.51)
1-2 years	308 (0.5)	278 (0.4)	1.11 (0.89 - 1.37)	
2-3 years	320 (0.6)	279 (0.5)	1.14 (0.93 - 1.41)	
3-4 years	269 (0.6)	295 (0.7)	0.90 (0.73 - 1.12)	
4-5 years	210 (0.7)	202 (0.7)	1.03 (0.80 - 1.33)	
>5 years	127 (0.7)	145 (0.9)	0.86 (0.63 - 1.18)	
Total	**1365 (0.5)**	**1358 (0.5)**	**1.00 (0.93 - 1.08)**	
5 More vs. less statin trials (0.51 mmol/L LDL cholesterol difference)				
0-1 year	24 (0.1)	38 (0.2)	0.64 (0.33 - 1.22)	
1-2 years	73 (0.4)	87 (0.5)	0.84 (0.56 - 1.26)	χ^2_1=0.18 (p=0.67)
2-3 years	83 (0.5)	71 (0.5)	1.17 (0.77 - 1.77)	
3-4 years	82 (0.6)	80 (0.5)	1.03 (0.69 - 1.54)	
4-5 years	81 (0.6)	85 (0.7)	0.95 (0.64 - 1.42)	
>5 years	104 (0.8)	120 (1.0)	0.87 (0.62 - 1.22)	
Total	**447 (0.5)**	**481 (0.5)**	**0.93 (0.82 - 1.06)**	



PLoS ONE 7(1): e29849.doi:10.1371/journal.pone.002849

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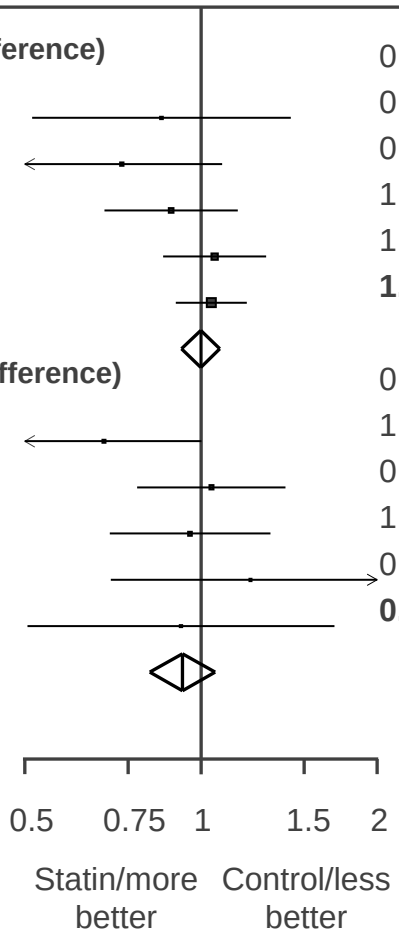
Effects of statin therapy on CANCER MORTALITY by baseline LDL cholesterol

Baseline LDL-C, mmol/L	No. of events (% per annum) Statin/more	Control/less	RR (CI)	Trend test
22 Statin vs. control trials (1.08 mmol/L LDL cholesterol difference)				
< 2	49 (0.7)	54 (0.7)	0.86 (0.51 - 1.42)	$\chi^2_1 = 5.02$
≥ 2,<2.5	72 (0.5)	99 (0.6)	0.73 (0.49 - 1.09)	(p=0.03)
≥ 2.5,<3.0	183 (0.5)	203 (0.6)	0.89 (0.68 - 1.16)	
≥ 3.0,<3.5	334 (0.6)	313 (0.6)	1.06 (0.86 - 1.29)	
≥ 3.5	701 (0.4)	670 (0.4)	1.04 (0.91 - 1.20)	
Total	**1365 (0.5)**	**1358 (0.5)**	**1.00 (0.93 - 1.08)**	
5 More vs. less statin trials (0.51 mmol/L LDL cholesterol difference)				
< 2	73 (0.4)	107 (0.6)	0.68 (0.46 - 1.00)	$\chi^2_1 = 2.23$
≥ 2,<2.5	160 (0.5)	151 (0.5)	1.04 (0.78 - 1.40)	(p=0.14)
≥ 2.5,<3.0	127 (0.5)	139 (0.5)	0.96 (0.70 - 1.31)	
≥ 3.0,<3.5	49 (0.4)	39 (0.3)	1.22 (0.70 - 2.10)	
≥ 3.5	35 (0.6)	38 (0.6)	0.92 (0.51 - 1.69)	
Total	**447 (0.5)**	**481 (0.5)**	**0.93 (0.82 - 1.06)**	



PLoS ONE 7(1): e29849.doi:10.1371/journal.pone.002849

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Cholesterol Treatment Trialists' Collaboration