





THE EPIDEMIC OF CORONARY ARTERY DISEASE HAS ARRIVED IN AFRICA.

ARE YOU READY FOR IT?



# Five Myths About Statins (Cholesterol Lowering)

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Nairobi, Kenya



• None







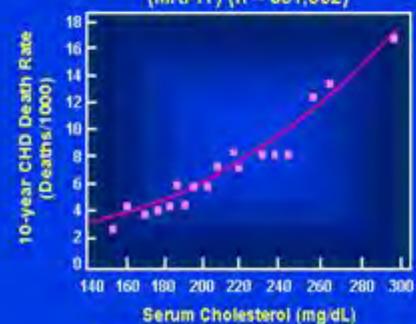
- Does high cholesterol cause heart disease?
- Does lowering LDL cholesterol lower heart disease?
- Is cholesterol lowering useful in primary prevention (low risk)?
- Does the risk of diabetes outweigh benefits of cholesterol lowering?
- Does cholesterol lowering cause neuro-cognitive decline?
- Does cholesterol lowering increase cancer risk?



### Relationship Between Cholesterol and CHD Risk

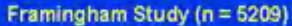
**Epidemiologic Trials** 

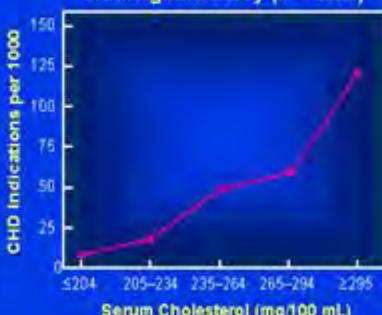
Multiple Risk Factor Intervention Trial (MRFIT) (n = 361,662)



Each 1% increase in total cholesterol level is associated with a 2% increase in CHD risk

Gotto AM Jr. et al. Circulation, 1990;81:1721-1733 Castell VVP. Am J Med 1984;76:4-12.





Serum Cholesterol (mg/100 mL)

1% reduction in total cholesterol resulted in a 2% decrease in CHD risk



## 4S: Cardiovascular Endpoints Post-MI or Angina Patients with Raised Cholesterol

	Number of events					
Outcomes	placebo (n=2223)	simvastatin Relative risk (n=2221) reduction (%)				
Total mortality*	256	182	30	<0.001		
Coronary death	189	111	42	<0.001		
Major coronary event	s 622	431	34	<0.001		
PCTA/CABG	383	252	37	<0.001		

<sup>\*</sup> primary endpoint

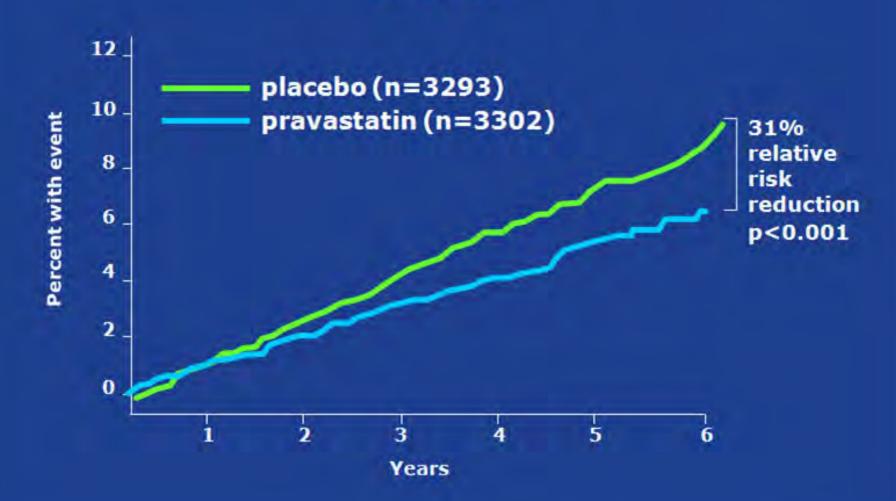
4S Group. Lancet 1994;344:1383-1389.





# WOSCOPS: Nonfatal MI and CHD Death

ca



#### Figure 1

Presenting characteristics	Total number of MVEs	Annual event rate in control arm (% per year)	RR (CI) per 1 mmol/L reduction in LDL cholesterol	p value for heterogeneity or trend	
Pre-treatment LDL cholesterol (mm	nol/L)			p=0-22	
¢2·5	5256	4-3	0.78 (0.69-0.89)		
≥2·5 to <3·0	4182	4.0	0.77 (0.70-0.85)		
≥3·0 to <3.5	4604	4-1	0.76 (0.70-0.82)		
<u>3</u> ·5	10563	3.9	0-80 (0-77-0-84)		
Age (years)				p=0·14	
s65	13623	3.6	0.78 (0.75-0.82)		
-65 to ≤75	9211	4.6	0.79 (0.74-0.83)		
>75	2123	5.5	0.87 (0.76-0.99)		
Sex				p=0.02	
Viale	19922	4.4	0.78 (0.75-0.81)		
emale	5035	3.0	0.84 (0.78-0.91)		
History of vascular disease				p=0·18	
CHD	19097	5.6	0.79 (0.76-0.82)		
Non-CHD vascular	1529	3-7	0.83 (0.73-0.94)		
None	4331	18	0.75 (0.69-0.82)		
Diabetes				p=0.78	
Type 1 diabetes	337	6.0	0.77 (0.58-1.01)	1000	
Type 2 diabetes	5621	5-1	0.80 (0.74-0.86)		
No diabetes	18862	4.0	0.78 (0.76-0.82)		
Freated hypertension				p=0·11	
Yes	13939	4-5	0.80 (0.77-0.84)		
No	10471	3.5	0-77 (0-73-0-81)		
imoking status				p=0.88	
Eurrent smokers	5225	4-7	0.79 (0.73-0.85)		
Non-smokers	19728	3.9	0.79 (0.76-0.82)		
5-year MVE risk				p=0-04	
<5%	421	0.6	0.62 (0.47-0.81)	1,273	
≥5 to <10%	1453	16	0.69 (0.60-0.79)		
≥10 to <20%	7810	3.5	0.79 (0.74-0.85)		
≥20 to <30%	9028	5.8	0.81 (0.77-0.86)		
≥30%	6245	9.8	0.79 (0.74-0.84)		
All patients	24957	4.0	0.79 (0.77-0.81)		
-					
<b></b> 99% CI ⟨ > 95% CI		05 075 1	1.25		
		LDL cholesterol lowering better	LDL cholesterol lowering worse		



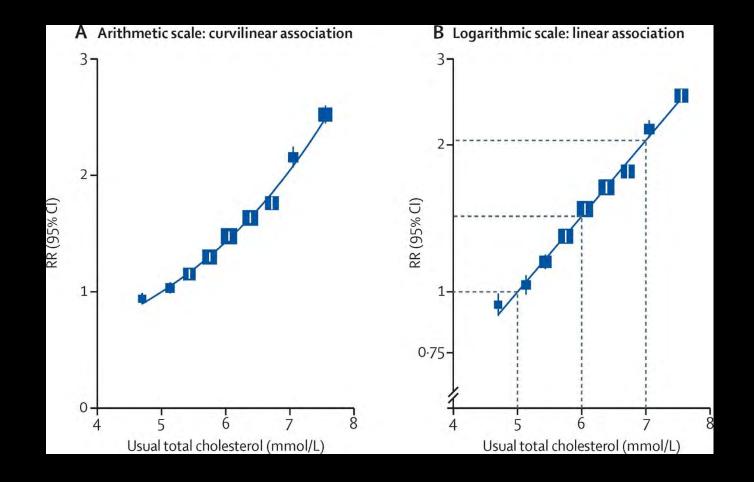




Figure 6

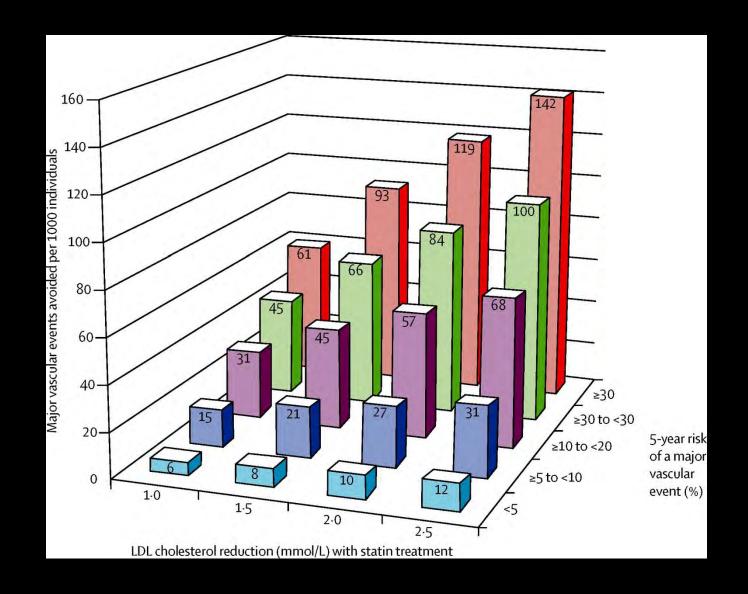




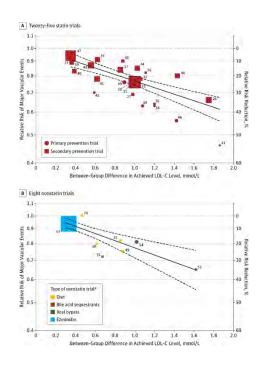
Figure 6

	Total number of deaths	Annual death rate in control arm (% per year)	RR (CI) per 1 mmol/L reductior in LDL cholesterol
Coronary	4192	0.6	0.80 (0.74-0.87)
Other cardiac	4076	0.6	0.92 (0.85-0.99)
Stroke	1054	0.1	0.98 (0.83–1.15)
Other vascular	855	0.1	0.95 (0.80-1.14)
Any vascular	10177	1.5	0.88 (0.84-0.91)
Cancer	3683	0.5	0.99 (0.91–1.09)
Respiratory	538	0.1	0.86 (0.70-1.06)
Trauma	275	0.0	0.97 (0.70–1.34)
Other non-vascular	1748	0.2	0.94 (0.82-1.07)
Any non-vascular	6244	0.9	0.96 (0.92-1.01)
Unknown	1036	0.1	0.87 (0.74–1.04)
Any death	17457	2.5	0.91 (0.88-0.93)
- <b>■</b> - 99% CI ◆	>95% CI	0.5 0.75 1 1.25	1.5
		LDL cholesterol LDL choles lowering better lowering w	



From: Association Between Lowering LDL-C and Cardiovascular Risk Reduction Among Different Therapeutic Interventions A Systematic Review and Meta-analysis

JAMA. 2016;316(12):1289-1297. doi:10.1001/jama.2016.13985



#### Figure Legend:

Association of Between-Group Difference in Achieved Low-Density Lipoprotein Cholesterol (LDL-C) Levels and Risk of Major Vascular EventsThe LDL-C differences are either mean or median depending on what was presented for each trial. Major vascular events include cardiovascular death, acute myocardial infarction or other acute coronary syndrome, coronary revascularization, and stroke (eTables 1-5 in the Supplement provide additional details). The size of the data marker is proportional to the weight in the meta-regression. The meta-regression slope (predicted relative risk for degree of LDL-C reduction) is represented by the solid line and the 95% CIs by the dashed lines. To convert LDL-C from mmol/L to mg/dL, divide by 0.0259.

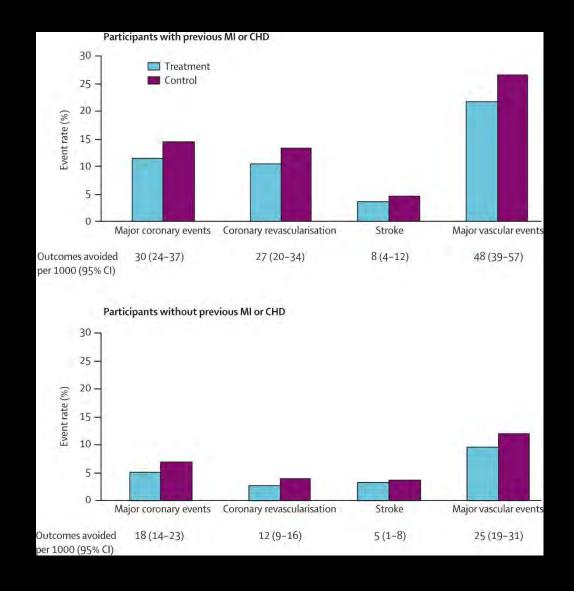
<sup>a</sup>The square data markers indicate secondary prevention trials. There was 1 primary prevention trial and 1 secondary prevention trial

Figure 1

	Events (% per annum)						RR (CI) per 1 mmol/L reduction in LDL cholestero
	Statin or more intensive	Control or less intensive			-2		reduction in LDL cholestero
No known	history of vascul	ar disease†					
Men	1313 (1.5%)	1756 (2-1%)		-			0-72 (0-66-0-80)
Women	593 (1.3%)	669 (1-4%)		+			0-85 (0-72-1-00)
Subtotal	1906 (1.4%)	2425 (1.8%)		$\Diamond$			0.75 (0.71-0.80)
Adjusted he	terogeneity test*	$\chi_1^2 = 5.31 (p=0.02)$		f A			
History of v	ascular disease			100			
Men	7630 (4.5%)	9223 (5.6%)					0.79 (0.76-0.82)
Nomen	1748 (4.0%)	2025 (4.7%)					0.84 (0.77-0.91)
Subtotal	9378 (4.4%)	11248 (5.4%)		•			0.79 (0.77-0.82)
Adjusted he	terogeneity test*	$\chi_1^2 = 0.62 \text{ (p=0.43)}$					
Overall							
Men	8943 (3.5%)	10979 (4-4%)			- 1		0.78 (0.75-0.81)
Nomen	2341 (2.6%)	2694 (3.0%)		1	<u> </u>		0.84 (0.78-0.91)
Total	11284 (3.3%)	13 673 (4.0%)		•	11		0.79 (0.77-0.81)
Adjusted he	terogeneity test*	$\chi_1^2 = 0.95 (p = 0.33)$		.,			
<b>■</b> - 99% CI	<b>♦</b> 95% CI		0.50	0.75	1.00	1.25	
				in or more sive better		ntrol or less	



#### Figure 6





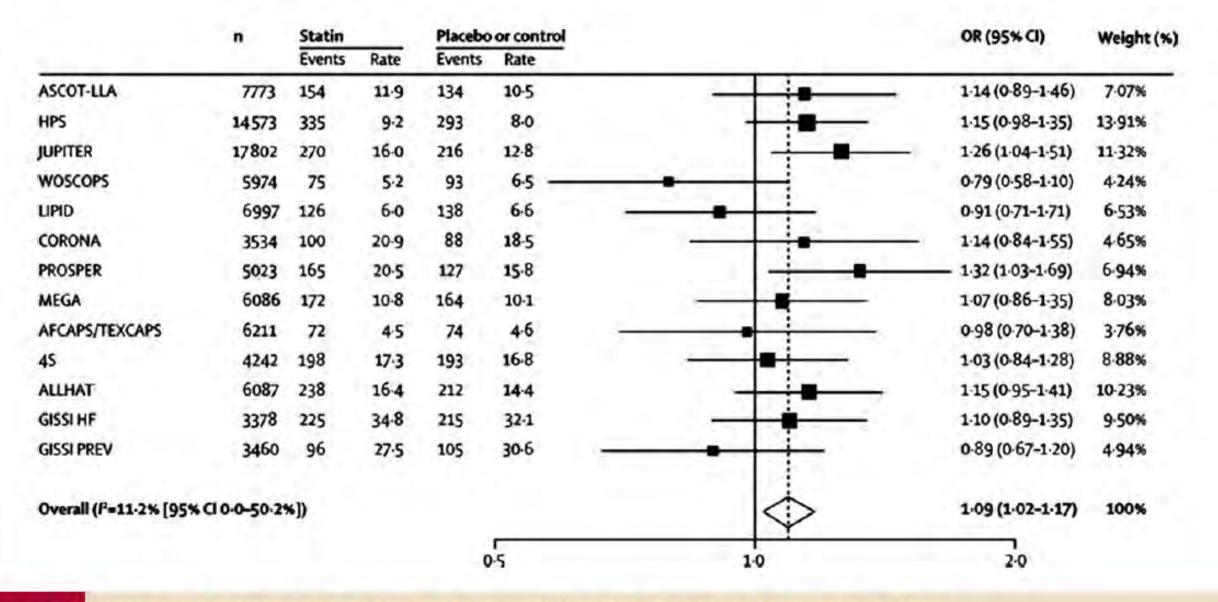


Figure 3 Association Between Statin Therapy and Incident Diabetes in 13 Major Cardiovascular Trials

Events per 1,000 patient-years. Weights are from random-effects analysis. Figure was originally published in Sattar et al. (66); permission for its use granted by the publisher. CI = confidence interval; OR = odds ratio.

## Effects on major vascular events of 1 mmol/L reduction in LDL-C: Patients with and without diabetes from 14 RCTs

Major vascular event	Even	ts (%)		
and prior diabetes	Treatment	Control		RR (CI)
Major coronary event				
Diabetes	776 (8.3%)	979 (10.5%)		0.78 (0.69-0.87)
No diabetes	2561 (7.2%)	3441 (9.6%)		0.77 (0.73-0.81)
Any major coronary event	3337 (7.4%)	4420 (9.8%)	<u> </u>	0.77 (0.74-0.80)
Test for heterogeneity within subgroup: $x_1^2$ =	= 0.1; p=0.8			
Coronary revascularisation				
Diabetes	491 (5.2%)	627 (6.7%)	<del>-</del>	0.75 (0.64-0.88)
No diabetes	2129 (6.0%)	2807 (7.9%)		0.76 (0.72-0.81)
Any Coronary revascularisation	2620 (5.8%)	3434 (7.6%)	<u> </u>	0.76 (0.73-0.80)
Test for heterogeneity within subgroup: $x_1^2$		•	i	
Stroke			1	
Diabetes	407 (4.4%)	501 (5.4%)	<del>-</del>	0.79 (0.67-0.93)
No diabetes	933 (2.7%)	1116 (3.2%)	-	0.84 (0.76-0.93)
Any stroke	1340 (3.0%)	1617 (3.7%)	<b>*</b>	0.83 (0.77-0.88)
Test for heterogeneity within subgroup: $x_1^2$	= 0.8; p=0.4		1	
Major vascular event			<u> </u>	
Diabetes	1465 (15.6%)	1782 (19.2%)	<u> </u>	0.79 (0.72-0.86)
No diabetes	4889 (13.7%)	6212 (17.4%)		0.79 (0.76-0.82)
Any major vascular event	6354 (14.1%)	7994 (17.8%)		0.79 (0.77-0.81)
Test for heterogeneity within subgroup: $x_1^2$	= 0.0; p=0.9	· · · · · · · · · · · · · · · · · · ·	<b>Y</b>	•
DD (00%/ CI)		·	<del>.  </del>	<del></del>
		0.5	0.0	1.5
◆ RR (95% CI)		Treatment bette	r	Control better

Figure 7

	Total number of cancers	Annual cancer rate in control arm (% per year)	RR (CI) per 1 mmol/L reduction in LDL cholesterol
arge bowel or intestine	1116	0.2	0.95 (0.82-1.11)
Other GI	1343	0.2	0.99 (0.86-1.15)
Prostate	1877	0.4	0.97 (0.85-1.10)
Bladder	646	0.1	0.94 (0.76-1.16)
Other GU	797	0.1	1.05 (0.86-1.27)
Respiratory	1692	0.2	1.00 (0.88-1.14)
emale breast	517	0.3	1.09 (0.85-1.39)
Haematological	614	0.1	1.03 (0.83-1.28)
Other/unspecified	1829	0.2	1.05 (0.92-1.21)
Any cancer	10431	1-5	1.00 (0.96-1.04)
	5% CI		





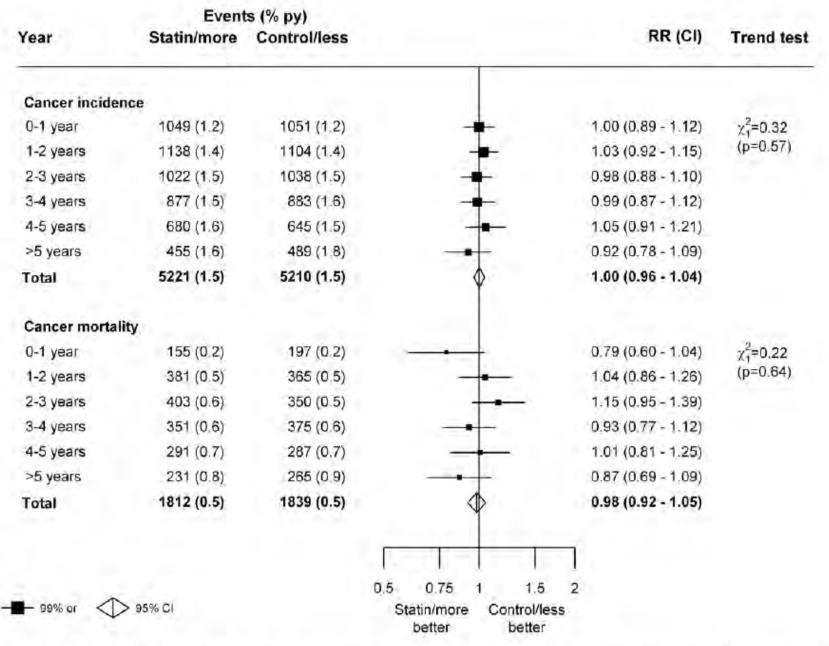


Figure 3. Effects of statin therapy on cancer incidence and mortality, by duration of treatment. Symbols and conventions as in Figure 1. doi:10.1371/journal.pone.0029849.g003

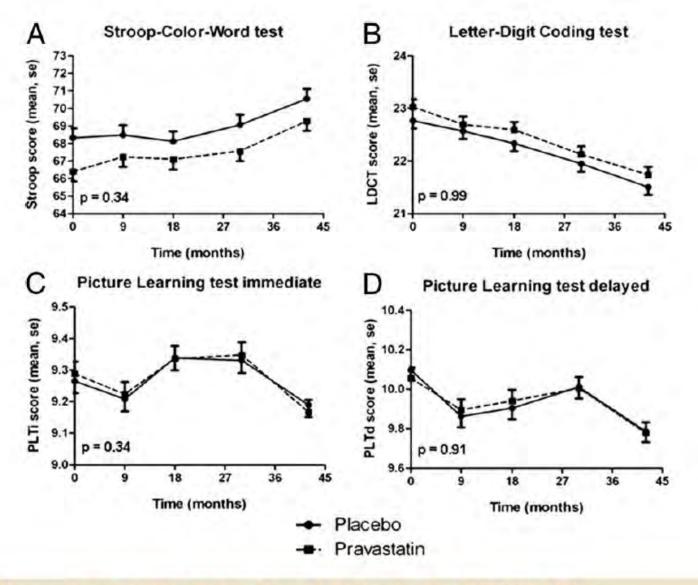


Figure 1 Effect of Pravastatin on Cognitive Function Among Participants of the PROSPER Study

The p values represent the statistical significance of the difference in test score changes over time between statin users (squares) and nonusers (circles) in the PROSPER study. Means were assessed using linear mixed models adjusted for sex, age, educational status, country, and version of test where appropriate. (A) Stroop-color-word test; (B) letter-digit coding test (LDCT); (C) picture learning test immediate (PLTi); (D) picture learning test delayed (PLTd). Figure was originally published in Trompet et al. (42); permission for its use granted by the publisher.



Thank You