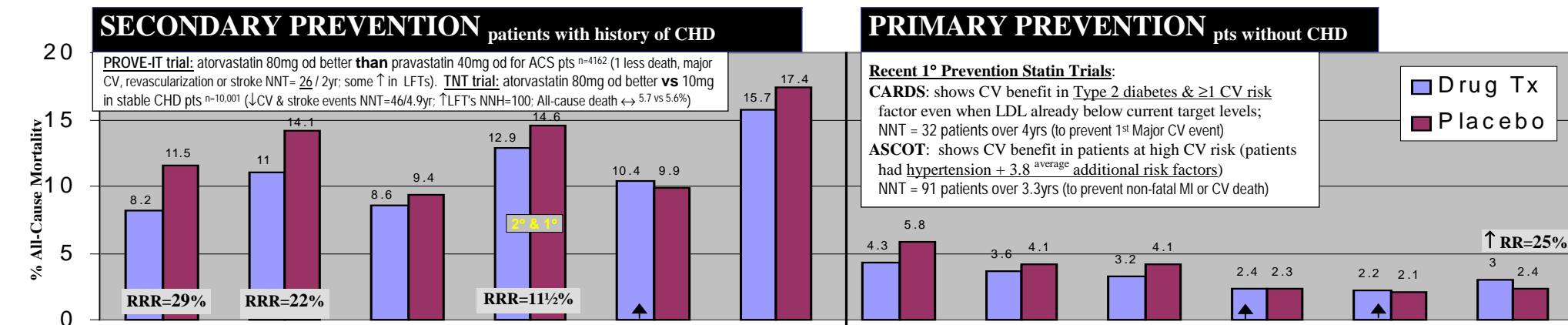


Figure 3. ALL-CAUSE MORTALITY OUTCOMES from MAJOR LIPID TRIALS



	4S	LIPID	CARE	HPS	BIP	VA-HIT	CARDS	ASCOT	WOSCOPS	AFCAPS	HHS	WHO-CLOF
Drug & dose used	Simvastatin 20-40mg/day ^{1,2}	Pravastatin 40mg/day ^{3,4}	Pravastatin 40mg/day ⁵	Simvastatin 40mg/d ^{6,7,8,9,10}	Bezafibrate 400mg/day ¹¹	Gemfibrozil 600mg BID ¹²	Atorvastatin 10mg/day ¹³	Atorvastatin 10mg/day ¹⁴	Pravastatin 40mg/day ¹⁵	Lovastatin 20-40mg/day ¹⁶	Gemfibrozil 600mg BID ¹⁷	Clofibrate 1.6g/day ¹⁸
ARR all death	3.3% $p=0.0003$	3.1% $p<0.001$	NS	1.7% $p<0.001$	NS	NS	NS	NS	0.9% $p=0.051$	NS	NS	(-0.6%) _p <0.05
NNT	30	32	NS	57	NS	NS	NS	NS	111 ($p=0.051$)	NS	NS	NNH=167
Duration	5.4 yrs	6.1 yrs	5 yrs	5 yrs	6.2 yrs	5.1 yrs	4 yrs	3.3 yrs	4.9 yrs	5.2 yrs	5 yrs	5.3 yrs
All-cause mortality in English based on NNT	Treat 30 patients for 5.4 yrs to prevent 1 death	Treat 32 patients for 6.1 yrs to prevent 1 death	No statistical difference in all-cause mortality	Treat 57 patients for 5 yrs to prevent 1 death	No statistical difference in all-cause mortality	No statistical difference in all-cause mortality	No statistical difference in all-cause mortality; trial halted early	No statistical difference in all-cause mortality; trial halted early	Trend: 1 death prevented per 111 patients over 4.9yrs	No statistical difference in all-cause mortality	No statistical difference in all-cause mortality	Treating 167 patients for 5.3yrs caused 1 extra death
n= (♂+♀) publication yr	3617+827 1994	7498+1516 1998	3583+576 1996	15454♂+5082♀ 2002	2825♂ + 265♀ 2000	2531♂ 1998	1929 ♂ + 909 ♀ Aug 2004	8363♂+1942♀ 2003	6595♂ 1995	5608+997 1998	4081♂ 1987	15745♂ 1978
Patients studied	pts with angina or previous MI & TC >5.5 age 35-70	recent hx of acute MI or unstable angina; age 31-75	recent hx of acute MI & average LDL; age 21-75	High risk patients: MI, CHD, PVD, PVD, DM, HTN; TC ≥3.5; age 40-80	recent hx of MI or stable angina; age 45-74	♂ with CHD, low HDL & normal LDL; age <74	Type 2 Diabetes ≥1 risk factor; no CHD/CVD, LDL ≤4.14; age 40-75	≥3 risk factors ^{CHD} TC ≤6.5 & HTN (24% diabetes) age 40-79	♂ with cholesterol ≥7; (44% smokers) age 45-64	↓HDL but normal LDL & TC; ♂ 45-73yr & ♀ 55-73yrs	♂ with high levels of non-HDL cholesterol age 40-55	♂ with normal or high TC; age 30-59
LDL (ave) initial⇒end	4.9⇒3.2	3.9⇒2.9	3.6⇒2.5	3.3⇒2.3 (Adjusted - 3.9) ¹⁹	3.9⇒3.6	2.9;↔LDL	3.0⇒2.1	3.4⇒2.3	5⇒4.1	3.9⇒3.0	4.9⇒4.5	not available
1° Endpoint Placebo/Drug	↓ total mortality 11.5%/8.2% NNT=31	↓ death ^{CHD} 8.3%/6.4% NNT=53	↓ MI / death ^{CHD} 13.2%/10.2% NNT=34	↓Vascular ^{fatal & non} 25.2%/19.8% NNT=19	MI or death ^{sudden} NS 15% / 13.6%	↓ MI / death ^{CHD} 21.7%/17.3% NNT=23	↓1st CHD Event 9.0%/5.8% NNT=32	↓MI / death ^{CHD} 3%/1.9% NNT=91	↓MI / death ^{CHD} 7.9%/5.5% NNT=42	↓ 1st CV event 10.9%/6.8% NNT=25	↓ MI / death ^{CHD} 41.4%/27.3% NNT=8	↓ heart disease
Comment	impact after ~1 yr 10yr data NNT=42		benefit most in ♀ & high LDL _{baseline}	benefits similar in low & high LDL	benefit only in pts with TG >2.3	some benefit in ↑HDL & ↓TGs	benefit even in LDL ⇒ <2	benefit only in ♂; especially >60yrs	higher risk ♂ pts	Serious adverse outcome events 34% in both groups	↑ in non-CHD mortality?	↑ death; ↑ liver/GI risk
	STATINS			FIBRATES			STATINS			FIBRATES		

ACS=acute coronary syndrome ARR=% absolute risk reduction CHD=coronary heart disease CV=cardiovascular CVD= cardiovascular death DM=diabetes GI=gastrointestinal hx=history LFTs=liver function tests MI=myocardial infarction MI^{NF}=nonfatal MI NNH= # needed to harm one NNT= # needed to treat to benefit one (e.g. in 4S trial, treating 30patients for 5.4yr would prevent 1 death) NS= not statistically significant pts=patients RRR= relative risk reduction Tx= treatment

⚡ in the CARE trial pts with initial LDL < 3.2 did not receive CV benefit from pravastatin; Lipid values in mmol/L (HDL= high density lipoprotein LDL= low density lipoprotein TC= total cholesterol TG= triglycerides)

NOTE: This collection of data is from different studies of varying patient groups and with varying methodology; it presents data and demonstrates overall trends but can not be used for direct quantitative comparison.

Summary of All-Cause Mortality Evidence { many studies not powered to evaluate this endpoint ; of published trials, only the 4S & HPS "overall" had this as the primary (1°) endpoint }

- ♦ **Statins**^{20,21}: strong evidence for 2° prevention (including high-dose atorvastatin 80mg in ACS²²); some evidence for 1° prevention in diabetes & male pts at ↑d risk of CHD.
- ♦ **Fibrates**: no evidence yet for reductions in 1° or 2° all-cause mortality²³; possible benefit in subset of patients with low HDL, TG's >2.3 &/or pts with diabetes
- ♦ **Lack data** to assess risk vs benefit in: 1) age ≥80 2) combination therapy 3) 1° prevention in low risk pts 4) aggressive pursuit of targets

Trials support statins for high risk rather than just high TC or LDL; few treat to target trials e.g.TNT.

TNT: CV benefit in 2° prevention with achieved LDL of 2.0^{80mg ator} vs 2.6^{10mg ator} mmol/L, however a non significant ↑ in non-CV death 3.2 vs 2.5% & ↑LFTs 1.2 vs 0.2%

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