CVS-23 The Heart Protection Study findings with simvastatin reanalysed by number needed to treat

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Introduction: *Number Needed to Treat* (NNT) is superior to *Relative Risk Reduction* (RRR) as a means of assessing clinical trial results. We therefore opted to compare relevant RRRs and NNTs in the *MRC/BHF Heart Protection Study (HPS) with Simvastatin* the largest randomized trial of coronary heart disease (CHD) prevention to date, which recruited patients with prior CHD, diabetes or hypertension [HPS Collaborative Group 2002 Lancet 360:7-22].
Methods: Using an Excel spreadsheet to enter event rates, NNTs and respective 95% CIs were calculated and compared with corresponding published (or derived) RRRs.
Results: Respective event rates, 5 year NNTs & CIs are shown in the table.
Conclusions: NNTs are more discriminating than RRRs. They confirm that the benefits of statins: are clinically significant in terms of all-cause mortality and stroke, and that for major vascular events they are similar in persons with CHD only or diabetes only and in all cholesterol level and age categories.

Outcome of Interest		Event Rate (%)		%RRR	NNT
		Simvastatin	Placebo	(95% CIs)	(95% CIs)
All Cause Mortality		12.9	14.7	12 (5 to 18.)	57 (37 to 128)
Vascular Mortality		7.6	9.1	17 (8 to 24)	66 (44 to 134)
Non-vascular Mortality		5.3	5.6	4 (* to 15)	444 (* to 117)
1st Major CHD Event		8.7	11.8	26 (19 to 32)	32.7 (26 to 45)
1st Stroke		4.3	5.7	24 (14 to 33)	73 (50 to 131)
Revascularisaton		9.1	11.7	22 (15 to 29)	39 (29 to 58)
1st Major Vascular Event					
Total Cholesterol (mmol/L)	<5.0	17.7	23.1	23 (12 to 33)	19 (13 to 35)
	≥5.0 <6.0	16.9	24.5	23 (15 to 30)	18 (13 to 27)
	≥6.0	21.6	26.8	19 (12 to 26)	19 (14 to 30)
Age (years)	<65	16.9	22.1	23 (16 to 30)	19 (15 to 28)
	≥65 <70	20.9	27.2	23 (14 to 32)	16 (11 to 26)
	≥70	23.6	28.7	18 (9 to 26)	20 (14 to 36)
Prior CHD only		16.8	22.5	25 (17 to 33)	18 (13 to 26)
Prior Diabetes only		13.8	18.6	26 (13 to 37)	21 (14 to 40)
Prior CHD + Diabetes		33.4	37.8	11 (* to 24)	23 (12 to *)

* Denotes a negative value indicating an increased event rate in the treated group, renderng further analysis inappropriate; 1st major coronary event = non-fatal MI or CHD death; Revascularisation = coronary and non-coronary bypass and angioplasty; 1st major vascular event = 1st major coronary event, stroke or revascularisation

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CVS-24 Endotoxin increases adrenomedullin expression in heart, lung and mesenteric artery

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Introduction: Previous studies have shown that the circulating levels of adrenomedullin (AM) are elevated during inflammation. The levels of AM and its messenger RNA (mRNA) in various tissues during the time course of inflammation remain to be determined.

Method: Inflammation was induced in rats by intraperitoneal injection of lipopolysaccharide (LPS, 10mg/kg). The tissues were harvested at 0, 1, 3 and 6 hours after LPS administration. Tissue levels of AM were determined by radioimmunoassay. The gene expression levels of AM were determined by solution hybridization-RNase protection assay of preproAM mRNA levels.

Results: PreproAM mRNA levels were increased in mesenteric artery and right atrium at 1 hour, in the left ventricle and the lung at 3 and 6 hours and in the right ventricle at 6 hours, after LPS injection. AM levels in the mesenteric artery were increased at 1, 3 and 6 hours and at 3 and 6 hours in the lung after LPS injection.

Conclusions: There is an increase in AM release in the lung, so it may be an important organ for AM secretion in the septic state. However, the response of the lung and the mesenteric artery to LPS in terms of AM secretion appears to be different.