CHOLESTEROL-LOWERING THERAPHY

TRIALS

NUMBER OF PARTICIPANTS	NUMBER OF WOMEN	PERCENTAGE OF WOMEN	MEAN AGE	MEAN FOLLOW-UP (YEARS)	TRIALS WITH ANALYSIS BY GENDER N, (%)
50,194	15,036	30.0%	60.8	3.2	1/ 6 (16.7%)

TRIAL	YEAR	POPULATION	AGE	N° OF SUBJECTS	FOLLOW UP	TREATMENT	DESCRIPTION OF END-POINT	PRIMARY END-POINT	PRIMARY END-POINT HR	NOTES
		(Country)	**mean ± sd, range**	**TOTAL (WOMEN n,%)**	**DURATION**			**TOTAL (WOMEN n,%) (MEN n,%)**	**(CI) P (WOMEN (MEN)**	
SPARCL (Amarenco et al [77])	AUG 2006	International trial with significant European component in patients who had had a stroke or TIA within one to six months before study entry, had low-density lipoprotein (LDL) cholesterol levels of 100 to 190 mg per deciliter (2.6 to 4.9 mmol per liter), and had no known coronary heart disease	PLACEBO 62.5 ± 0.2 ATORVA STATIN 63.0 ± 0.2	TOTAL: 4731 **(WOMEN: 1908, 40.3%)** (MEN: 2823)	Median of 4.9 years	PLACEBO vs. ATORVASTATIN (80 mg per day)	A first nonfatal or fatal stroke	PLACEBO 311 (13.1 %) vs. ATORVASTAT IN 265 (11.2 %)	5-year absolute reduction in risk: 2.2 % $HR_{ADJUSTED}$ = 0.84 [95% CI: 0.71 - 0.99] P = 0.03 $P_{UNADJUSTED}$ = 0.05	**Results by gender not reported**

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TNT (Waters et al [78])	NOV 2006	International trial with significant European component in patients with documented coronary disease with low-density lipoprotein cholesterol (LDL-C) levels substantially below 100 mg/dl.	60.9 ± 8.8 ATORVASTATIN (10 mg/day) vs. 61.2 ± 8.8 ATORVASTATIN (80 mg/day) (RANGE: 35-75)	TOTAL: 10001 **(WOMEN : 1902, 19%)** (MEN: 8099)	Median of 4.9 years	ATORVASTATIN (10 mg/day) vs. ATORVASTATIN (80 mg/day)	Cerebrovascular events	Cerebrovascular event: ATORVASTATIN (10 mg/day): 252 (5.0%) vs. ATORVASTATIN (80 mg/day): 196 (3.9%)	Cerebrovascular event: HR = .77 [95% CI: 0.64–0.93] P = 0.007	**Results by gender not reported**
ILLUMINATE (Barter et al [79])	NOV 2007	International trial with significant European component in patients at high cardiovascular risk	61.3 ± 7.6	TOTAL: 15067 **(WOMEN: 3352, 22.2%)** (MEN: 11715)	Median of 550 days	ATORVASTATIN ALONE vs. TORCETRAPIB PLUS ATORVASTATIN	Time to the first major cardiovascular event (defined as death from coronary heart disease, nonfatal myocardial infarction, stroke, or hospitalization for unstable angina)	ATORVASTATIN-ONLY: 373 vs. TORCETRAPIB PLUS ATORVASTATIN: 464	HR = 1.25 [95% CI: 1.09 - 1.44] P = 0.001	Trial terminated prematurely because of an increased risk of death and cardiac events in patients receiving torcetrapib. **Results by gender not reported**

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ENHANCE (Kastelein et al [80])	APRIL 2008	International trial conducted at 18 ambulatory care centers in the United States, Canada, South Africa, Spain, Denmark, Norway, Sweden, and the Netherlands in patients with familial hypercholesterolemia	45.7 ± 10.0 SIMVASTATIN MONOTHERAPY vs. 46.1 ± 9.0 SIMVASTATIN PLUS EZETIMIBE	TOTAL: 720 **(WOMEN: 350, 48.6%)** (MEN: 370)	24 months	Daily therapy with SIMVASTATIN (80 mg of daily) WITH PLACEBO vs. SIMVASTATIN with EZETIMIBE (10 mg)	Change in the mean carotid-artery intima – media thickness, which was defined as the average of the means of the far-wall intima – media thickness of the right and left common carotid arteries, carotid bulbs, and internal carotid arteries	SIMVASTATIN-ONLY: 0.0058 ± 0.0037 mm vs. SIMVASTATIN-PLUS-EZETIMIBE: combined-therapy) 0.0111 ± 0.0038 mm	Difference between mean (±SE) in he simvastatin-only group and in the combined-therapy group = 0.0053 mm P = 0.29	**Results by gender not reported**
SEAS (Rossebø et al [81])	SEPT 2008	International trial conducted at 173 study sites in seven European countries in patients with mild-tomoderate, asymptomatic aortic stenosis	PLACEBO 67.4 ± 9.7 SIMVASTATIN–EZETIMIBE 67.7 ± 9.4 (RANGE: 45 - 85)	TOTAL: 1873 **(WOMEN: 723, 38.6%)** (MEN: 1150)	Median of 52.2 months	PLACEBO vs. SIMVASTATIN (40 mg daily) plus EZETIMIBE (10 mg daily)	Major cardiovascular events (including death from cardiovascular causes, aortic-valve replacement, nonfatal myocardial infarction, hospitalization for unstable angina pectoris, heart failure, coronary-artery bypass grafting, percutaneous coronary intervention, and nonhemorrhagic stroke)	PLACEBO : 355 (38.2%) vs. SIMVASTATIN – EZETIMIBE : 333 (35.3%)	HR= 0.96 [95% CI: 0.83 - 1.12] P = 0.59	In the simvastatin–ezetimibe group, incident cancer was diagnosed in 105 patients (11.1%), as compared with 70 patients (7.5%) in the placebo group (P = 0.01) **Results by gender not reported**

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JUPITER (Ridker et al [82])	NOV 2008	International trial conducted at 1315 sites in 26 countries in apparently healthy men and women with low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter (3.4 mmol per liter) and high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher **Inclusion criteria: Men age ≥ 50 years Women ≥ 60 years**	Median 66.0 (nterquartile range 60.0–71.0)	TOTAL: 17802 **(WOMEN: 6801, 38.2%)** (MEN: 11001)	Median of 1.9 years (maximal: 5.0 years)	PLACEBO vs. ROSUVASTATIN (20 mg daily)	Myocardial infarction or stroke or arterial revascularization or hospitalization for unstable angina or death from cardiovascular causes	PLACEBO: 251 ROSUVASTATIN: 142	HR = 0.56 [95% CI: 0.46 - 0.69] P<0.00001 **HR_{WOMEN} = 0.54** HR_{MEN} = 0.58 $P_{INTERACTION}$ = 0.80	Prematurely stopped for an excess of events in the placebo group **Similar effect in men and women**

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JUPITER (Glynn et al [83])	APRIL 2009	International trial conducted at 1315 sites in 26 countries apparently healthy men and women with low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter (3.4 mmol per liter) and high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher. **Inclusion criteria: Men age ≥ 50 years Women ≥ 60 years**	Median 66.0 Interquartile range 60.0–71.0	TOTAL: 17802 **(WOMEN: 6801, 38.2%)** (MEN: 11001)	Median of 1.9 years (maximum, 5.0)	PLACEBO vs. ROSUVASTATIN (20 mg/day)	First occurrence of pulmonary embolism or deep-vein thrombosis	Symptomatic venous thromboembolism : TOTAL: 94 PLACEBO: 60 vs. ROSUVASTATIN: 34 **WOMEN: 28/6801 (0.4%)** MEN: 66/11001 (0.6%) *Pulmonary embolism:* PLACEBO: 22 vs. ROSUVASTATIN: 17 *Deep-vein thrombosis only:* PLACEBO: 38 vs. ROSUVASTATIN: 17	Symptomatic venous thromboembolism HR_{TOTAL} = 0.57 [95%CI: 0.37 - 0.86] P = 0.007 Incidence Rate in Subgroup Placebo: **IR_{WOMEN} = 0.24** IR_{MEN} = 0.37 **$P_{INTERACTION}$ > 0.10** *Pulmonary embolism:* HR =0.77 [95%CI: 0.41–1.45] P = 0.42 *Deep-vein thrombosis only:* HR =0.45 [95%CI: 0.25–0.79] P = 0.004	**Consistent effects were observed in all the subgroups examined (sex included).** No significant differences were seen between treatment groups in the rates of bleeding episodes

META-ANALYSIS

TRIAL	YEAR	POPULATION	AGE	N° OF SUBJECTS	FOLLOW UP	TREATMENT	DESCRIPTION OF END-POINT	PRIMARY END-POINT	PRIMARY END-POINT HR	NOTES
		(Country)	**mean ± sd, range**	**TOTAL (WOMEN n,%)**	**DURATION**			**TOTAL (WOMEN n,%) (MEN n,%)**	**(CI) P (WOMEN (MEN)**	
Statins and gender meta-analysis (Peretta et al [86])	[epub ahead of print] SEPT 2008	Meta-analysis including 8 randomized controlled trials of patients without known cardiovascular disease		TOTAL: 49246 **(WOMEN: 19052, (63%))** (MEN: 30194)	Mean of 3.9 years (2.8- to 5.3 year)	STATINS vs. PLACEBO OR USUAL CARE OR DIET	At least 1 clinical outcome: total mortality, coronary heart disease (CHD) mortality, nonfatal myocardial infarction,CHD events (defined as CHD mortality, nonfatal MI, unstable angina, or sudden cardiac death) revascularization procedures	NOT REPORTED	Total mortality: **RR_{WOMEN} = 0.96 [95%CI: 0.81–1.13]** RR_{MEN} = 0.93 [95%CI: 0.83–1.04] Coronary heart disease (CHD): **RR_{WOMEN} = 0.89 [95%CI: 0.79–1.00]** RR_{MEN} = 0.59; [95%CI: 0.48–0.74]	**Effects on total mortality non significant in both women and men** **Effects of CHD significant in men, weakly significant in women**

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Meta-Analysis on Statins and Reduction in Risk of Cardiovascular Outcomes (Delahoy et al [85])	FEB 2009	Meta-regression analysis of twenty-five randomized Trials of statins	> 18	TOTAL: 155613	Median of 4.2 years	Statins : placebo controlled, active controlled, or usual care	Cardiovascular end points: vascular mortality, major coronary events [defined as nonfatal myocardial infarction or coronary heart disease death], major vascular events [defined as major coronary event, fatal or nonfatal stroke, or coronary revascularization], fatal and nonfatal stroke	Primary analysis: (25 trials) 6321 vascular deaths 23791 major vascular events 11357 major coronary events 4717 fatal and nonfatal strokes.	For every 25-mg/dL reduction in LDL-C: Primary analysis: Vascular mortality: RR = 0.89 [95% CI: 0.87-0.92] $r^2 = 0.75$ Major coronary events RR = 0.84 [95% CI: 0.82-0.86] $r^2 = 0.87$ Major vascular events RR = 0.86 [95% CI: 0.84-0.88] $r^2 = 0.84$ Fatal and nonfatal stroke: RR = 0.90 [95% CI: 0.86-0.94] $r^2 = 0.47$	**Percentage of woman enrolled not reported** **Results by gender not reported**

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Benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors (Brugts et al [87])	JUN 2009	Meta-analysis of 10 randomised trials in people without established cardiovascular disease but with cardiovascular risk factors	63 years (range: 55.3 to 75.0)	TOTAL: 70388 **(WOMEN: 23681 (34%))** (MEN: 46707)	Mean of 4.1 years (range: 1.9 to 5.3).	Statins compared with controls (placebo, active control, or usual care)	Mortality and major cardiovascular disease events *Secondary end points* the composite of major coronary events (defined as death from coronary heart disease and non-fatal myocardial infarction), and the composite of major cerebrovascular events (defined as fatal and non-fatal stroke)	*All cause mortality (based* on mean follow-up of 4.1 years, with data from nine trials, and 67476 patients free of cardiovascular disease) TOTAL CONTROL: 1925/33793 (5.7%) STATIN: 1725/33683 (5.1%)	OR_{TOTAL} = 0.88 [95% CI: 0.81 - 0.96] **OR_{WOMEN} = 0.91 [95% CI: 0.76 - 1.08]** OR_{MEN} = 0.95 [95% CI: 0.86 - 1.06] **$P_{HETEROGENEITY}$ = 0.62**	**No significant gender differences in the outcomes** The association between statin therapy and risk of cancer was not significant (OR_{TOTAL} = 0.97, [95% CI: 0.89 - 1.05])

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Benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors								*SECONDARY END POINTS: major coronary events* TOTAL: CONTROL: 1266/23946 (5.4%) STATIN: 966/23823 (4.1%) *major cerebrovascular events* TOTAL: CONTROL: *767/33 793 (*2.3%) STATIN: 627/33 683 (1.9%)	OR_{TOTAL} = 0.70 [95% CI: 0.61 - 0.81] **OR_{WOMEN} = 0.79 [95% CI: 0.56 - 1.13]** OR_{MEN} = 0.72 [95% CI: 0.61 - 0.86] **$P_{HETEROGENEITY}$ = 0.65** OR_{TOTAL} = 0.81 [95% CI: 0.71 - 0.93] **OR_{WOMEN} = 0.74 [95% CI: 0.54 - 1.00**] OR_{MEN} = 0.77 [95% CI: 0.44 - 1.36] **$P_{HETEROGENEITY}$ = 0.90**	

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