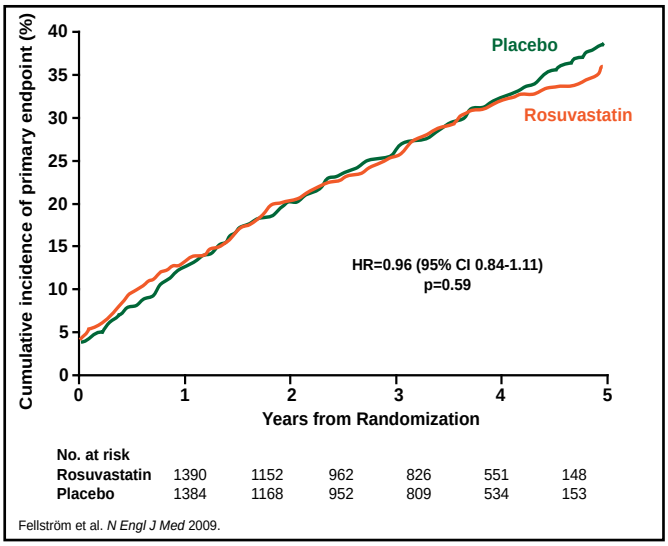
triglyceride levels were reduced by 16.2% from baseline in the rosuvastatin group, compared with an increase of 0.9% in the placebo group (p<0.001). Adverse event rates were similar between the 2 groups. In the rosuvastatin group, 1140 (82.1%) subjects suffered a serious adverse event versus 1159 (84.1%) in the placebo group (p=0.80; Table 1). Drug-related adverse events occurred in 16 (1.2%) subjects in the rosuvastatin group and 11 (0.8%) subjects in the placebo group (p=0.35; Table 1). The baseline characteristics between the 2 groups were balanced. Mean duration of treatment was 2.4 years, and mean duration of follow-up was 3.2 years.

Figure 1. AURORA Primary Study Endpoint of Major Cardiovascular Event.



Fellström et al. *N Engl J Med* 2009.

The AURORA study was an international, multicenter, randomized, double-blind, prospective trial and was the largest and longest trial ever conducted on the efficacy of statins on cardiovascular events in persons with ESRD on hemodialysis. Patients with ESRD have advanced calcification of the arteries, and the lack of benefit on CV outcomes that was observed with statin therapy in 4D and AURORA suggests that cardiovascular disease in patients who receive chronic hemodialysis differs from that in other clinical settings. Inclusion criteria were men and women aged 50 to 80 years who had ESRD and were on hemodialysis for at least 3 months. Major exclusion criteria were taking a statin within the previous 6 months and needing a kidney transplant within the following year. The study design required 2750 subjects, and the study continued until 620 subjects had a major cardiovascular event. Assessment was every 3 months for the first year and every 6 months thereafter until the study's conclusion.

Table 1. Adverse Events for Rosuvastatin 10 mg vs Placebo.

	Rosuvastatin No. of patients (%)	Placebo No. of patients (%)	p Value
Any adverse event	1338 (96.3)	1332 (96.7)	0.56
Serious adverse events			
Any†	1140 (82.1)	1159 (84.1)	0.80
Requiring study drug discontinuation	438 (31.5)	443 (32.1)	0.78
Study drug-related	16 (1.2)	11 (0.8)	0.35
Leading to death **From CV causes** **From non-CV causes** **From unspecified causes**	640 (46.1) 324 (23.3) 248 (17.9) 68 (4.9)	662 (48.0) 324 (23.5) 267 (19.4) 71 (5.2)	0.49 0.92 0.34 0.77
Others			
Infection	976 (70.3)	956 (69.4)	0.16
Gastrointestinal disorder	814 (58.6)	788 (57.2)	0.26
Hepatic disorder	66 (4.8)	54 (3.9)	0.28
Musculoskeletal disorder	310 (22.3)	343 (24.9)	0.21
Newly diagnosed cancer	107 (7.7)	118 (8.6)	0.41

†Some patients suffered more than 1 serious adverse event; CV=cardiovascular; Source: Fellström B et al. *New Engl J Med* 2009.

During the question and answer session after the presentation, an audience member asked if the lack of efficacy resulted from the trial dose only being 10 mg. Dr. Fellström replied, "I wouldn't be surprised if it was a matter of dose."

Polypill May Offer Increased Protection Against Cardiovascular Disease in Patients With Average Risk Factors

Results of the Indian Polycap Study (TIPS; NCT00443794) indicate that it may be possible for individuals who have average risk factors for cardiovascular disease to significantly reduce their risk for heart disease and stroke through the use of a single pill—the Polycap™—which combines low doses of thiazide (12.5 mg), atenolol (50 mg), ramipril (5 mg), simvastatin (20 mg), and aspirin (100 mg). The results of TIPS were presented by the joint principal investigator of the study, Salim Yusuf, PhD, McMaster University, Hamilton, ON, Canada, at the

American College of Cardiology 58th Annual Scientific Session in Orlando, FL.

The primary objective of TIPS was to determine whether the Polycap™ is equivalent to its individual components in reducing blood pressure (BP) and heart rate (HR), modifying lipids, and suppressing urine thromboxane B2 and whether it has a similar adverse event profile. The secondary objective of TIPS was to determine whether the Polycap™ is superior in reducing BP compared with its components.

The study population comprised 2053 subjects aged 45 to 80 years (mean age 54 years; 44% women) without cardiovascular disease but with at least 1 risk factor. One-third (33.9%) of the subjects had diabetes, mean baseline BP was 134/85 mm Hg, and mean cholesterol was 180 mg/dl (HDL 44 mg/dL and LDL 117 mg/dL).

Subjects were randomly assigned to receive either the Polycap™ (n=412) or 1 of 8 other formulations (n≈200 each) for 12 weeks. The 8 other formulations, which used the same doses of agents as Polycap™, were: aspirin alone, thiazide alone, thiazide + either ramipril or atenolol or both, thiazide + ramipril + atenolol + aspirin, ramipril + atenenol, and simvastatin alone.

In the Polycap group, BP reductions (7.4 mm Hg systolic and 5.6 mm Hg diastolic) were comparable with those that were seen in the group that received 3 BP medications (6.9 mm Hg systolic and 5.0 mm Hg diastolic). Aspirin did not interfere with the BP-lowering effects of the Polycap™.

LDL reductions in the group that was randomized to Polycap™ (0.70 mmol/L [23.3%]), however, were significantly lower than those that were seen in the group that received simvastatin alone (0.83 mmol/L [27.7%]; p<0.04), leading the investigators to speculate that the 40 mg dose should be tried instead of the 20 mg dose of simvastatin in order to enhance the benefits. Reductions in LDL for both groups of individuals who received the polycap, however, were significantly (p<0.0001) better than for subjects who did not receive simvastatin.

The reductions in HR with Polycap™ (7.0 beats/min) and other arms using atenolol (7.0 beats/min) were similar, and both were significantly greater than those in subjects who did not receive atenolol (p<0.001). The reduction in thromboxane B2 that was seen with Polycap™ (-322.3) was similar to that seen with aspirin alone (-388.0) or the combination of thiazide, atenolol, and ramipril + aspirin (-389.3; all p<0.001 vs baseline).

Polycap™ was well tolerated, and there was no evidence of increasing rates of adverse effects or discontinuation of study drugs with increasing numbers of active components in the pill.

Based on the results of this study, the investigators estimate that in individuals who are at average risk of cardiovascular disease, the use of Polycap™ could potentially result in a 62% reduction in the relative risk for coronary heart disease and a 48% reduction in the relative risk for stroke. However, they emphasized the need for large, prospective randomized trials to evaluate this hypothesis.

The study was sponsored by Cadila Pharmaceuticals, India, which played no role in data collection, analysis, or interpretation.

Results of the TIPS study were simultaneously published in *The Lancet* (Online Publication, 30 March 2009).

No Benefit from Omega-3 Supplements in Addition to Optimal Medical Therapy

Results from the OMEGA (NCT00251134) trial, presented by Jochen Senges, MD, Heart Center Ludwigshafen, University of Heidelberg, Germany, show that dietary supplementation with omega-3 fatty acids offers no additional benefits when added to optimal medical therapy (OMT) in patients who have suffered a heart attack.

The OMEGA trial primarily evaluated the effect of 1g daily of highly purified omega-3 acid ethylesters for 1 year in addition to OMT on the rate of sudden cardiac death (SCD) in patients with recent acute myocardial infarction (AMI). Secondary endpoints were total mortality, arrhythmic events, and the rates of reinfarction, stroke, and revascularization.

The study involved 3851 subjects with AMI (74.4% males; mean age 64 years), 59% of whom were diagnosed with ST elevated myocardial infarction (STEMI). Approximately 24% of the subjects had an ejection fraction <45%; 66% had hypertension, 50% had hypercholesterolemia, and 27% had diabetes. Coronary angiography was performed in 94% of patients, 78% of subjects underwent percutaneous coronary intervention, and 8% received fibrinolytic therapy.

Three to 14 days after AMI, patients were randomly assigned to 1 year of treatment with highly purified omega-3 fatty acids along with OMT (n=1937) or placebo (1 g olive oil; n=1909) and OMT. At the time of discharge from the hospital, 95% of patients were prescribed