SUPPLEMENTAL MATERIAL

**Supplementary Table.** Multivariable determinants of post year 1 major cardiovascular events (MCVE) excluding baseline medications

| Risk factors | Major cardiovascular events: Hazard Ratio (95% CI)* | χ2 Statistics* | P-value* |
|---|---|---|---|
| **Basic model** | | | |
| Treatment (Atorvastatin 80 mg) | 0.82 (0.71, 0.95) | 7.02 | 0.008 |
| Age (years): per 1SD | 1.149 (1.06, 1.25) | 10.38 | 0.001 |
| Men | 1.34 (1.08, 1.66) | 6.91 | 0.009 |
| Smoking | | | |
| Current | 1.68 (1.31, 2.16) | 16.59 | <0.001 |
| Previous | 1.01 (0.83, 1.22) | 0.01 | 0.94 |
| Never | 1.00 | ------ | ------- |
| Hypertension | 1.45 (1.23, 1.70) | 19.97 | <0.001 |
| Diabetes | 1.36 (1.13, 1.63) | 10.68 | 0.001 |
| **Variables selected by forward stepwise elimination** | | | |
| Body mass index (kg/m$^2$): per 1SD | 1.09 (1.02, 1.17) | 6.55 | 0.01 |
| Myocardial infarction | 1.58 (1.34, 1.85) | 31.13 | <0.001 |
| Angina | 1.37 (1.11, 1.69) | 8.52 | 0.004 |
| Cerebrovascular disease | 1.79 (1.41, 2.28) | 22.77 | <0.001 |
| Peripheral vascular disease | 1.37 (1.13, 1.67) | 10.11 | 0.002 |
| Congestive heart failure | 1.57 (1.27, 1.94) | 17.09 | <0.001 |
| Coronary revascularization: Bypass | 1.24 (1.06, 1.45) | 7.50 | 0.006 |
| Baseline apolipoprotein A-I (mg/dL) : per 1SD | 0.91 (0.84, 0.99) | 4.44 | 0.04 |
| Baseline apolipoprotein B (mg/dL) : per 1SD | 1.19 (1.11, 1.28) | 22.29 | <0.001 |
| Baseline blood urea nitrogen (mg/dL): per 1SD | 1.09 (1.03, 1.16) | 8.49 | 0.004 |

***** Hazard ratio, and 95% confidence intervals (CIs) are based on multivariable Cox proportional hazard analysis forcing age, gender, smoking, systemic hypertension, and diabetes in the model; and the remaining significant (p< 0.10) variables identified from the univariable analyses (but excluding baseline concomitant medications) were entered into the model by forward stepwise elimination process with a critical value of 0.05.

Cardiovascular risk among statin-treated individuals remains high and has been termed "residual risk", but the mechanisms underlying this residual risk are uncertain. Hence, we aimed to identify determinants of this risk above and beyond lipid-related risk factors in a secondary prevention population that achieved low LDL cholesterol targets. The study population comprised 9,251 coronary patients with LDL cholesterol<130 mg/dL randomized to double-blind atorvastatin 10 or 80 mg/day in the Treating to New Targets (TNT) study who had complete on-treatment 1-year lipid data. Median follow-up was 4.9 years. The primary endpoint was major cardiovascular events (n=729): coronary death, non-fatal myocardial infarction, resuscitation after cardiac arrest, or fatal or non-fatal stroke. Multivariable determinants of increased risk were older age, increased BMI, male gender, hypertension, diabetes, baseline apolipoprotein B and blood urea nitrogen, current smoking, prior cardiovascular disease, and calcium channel blocker use. Determinants of decreased risk were high-dose statin, aspirin use, and baseline apolipoprotein A-I. These known baseline clinical and lipid-related variables performed moderately well in discriminating future cases from non-cases. On-treatment 1-year levels of lipids and apolipoproteins were not selected into the multivariable model because they were not associated with risk after taking into account baseline apolipoproteins and clinical risk factors. In sum, residual risk among statin-allocated coronary patients was related to baseline lipid-related and non-lipid risk factors. Thus, a multi-faceted secondary prevention approach targeting modifiable risk factors should be underscored as the cornerstone of optimal residual risk assessment and prevention.