Reviewer's report

Title: A Retrospective Cohort Study of the Potency of Lipid-lowering Therapy and Race-gender Differences in LDL Cholesterol Control

Version: 1 Date: 4 January 2011

Reviewer: Stephen D Persell

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The authors analyzed gender and race differences in achievement of LDL control using a cohort assembled from the electronic health record of 6 academically affiliated primary care practices. Accounting for multiple covariates including the intensity of prescribed drug therapy, black women were least likely and white men most likely to achieve LDL targets.

Whether or not racial and gender differences in cholesterol control are due to differences in offered treatment is of interest.

The methods for classifying treatment intensity raise some conceptual challenges here. Time to LDL control is a function of behaviors, drug therapy used, and the frequency with which LDL is tested. LDL is likely to be tested more often in drug treated individuals and in individuals with high risk due to multiple risk factors or due to comorbidities like coronary heart disease or stroke. If women are at lower global cardiovascular risk due to lower overall risk factor burdens, physicians may opt to treat them with lifestyle advice for a longer period of time before initiating drug therapy. A woman patient with a high LDL treated for 3 months with lifestyle change followed by moderate to high potency statin for 9 months might not have any real chance of achieving the LDL target in the first 3 months but have a high chance of doing so in the subsequent 9 months. A male patient with a less severely elevated LDL treated with a low potency statin initially due to higher perceived risk would have a chance to have a statin response right away. These 2 people could be classified the same way with the method used here. It is not completely clear that time to event is the best choice when the outcome is neither routinely assessed at fixed time intervals or able to occur at any time (like clinical events).

Since women has higher mean LDL levels, outcomes that focus exclusively on the arbitrary threshold of <130 mg/dl will make similarly treated groups appear different if their LDLS do not start in the same place. This obscures the fact that a woman whose LDL goes from 175 mg/dl to 135 mg/dl achieves similar benefits to a man whose LDL falls from 150 to 110.

The authors should make more clear what the limitations are of their chosen methods for: 1) classifying drug treatment, 2) the use of time to event, 3) the use of LDL thresholds rather than the amount of the decline in LDL.

Minor comments:
Figure 3. Is the group marked “low” the group that received no treatment or low potency treatment? Are these results from the Cox or the logistic models? Legend says hazards ratios, figure say odds ratios.
Page 5: Cited LDL goal is <130 rather than <129.
Multiple tables and figures are difficult to read in their current format and portions are cut off. Supplemental figures are not labeled.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.