

## **Author's response to reviews**

**Title:** Disparities in Lipid Management for African Americans and Caucasians with Coronary Artery Disease: A National Cross-Sectional Study

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**Author's response to reviews:** see over

## Response to Reviewers

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### **Response to Reviewer #1:**

**Major Compulsory Revisions: None**

**Minor Essential Revisions: None**

**Discretionary Revisions:**

**General Comment: There should be a section in limitations that describes potential pitfalls in the data.**

Response: Agreed. We have enhanced the discussion section to address limitations where appropriate. This includes the following text:

“There are a number of limitations in the QAP study design and its population that potentially pose a threat to the internal and external validity. These limitations suggest that our findings may not reflect the experiences of the general population. The medical practices included in the QAP were restricted to those writing large numbers of prescriptions for cardiovascular disease drugs. It is difficult to evaluate the impact of this selection bias, but we suspect that medical practices included in the QAP represent the larger and more sophisticated providers of care. Thus, lipid management among QAP participants may be better than that found in the general population. Another limitation to our study is the lack of information characterizing medical practices, physicians, and patients with respect to factors related to race and lipid management. Because of the unavailability of these data, we could not evaluate the extent to which these factors explain our findings. Lipid management data for QAP patients seeing multiple physicians were unavailable from physicians not participating in the QAP and this may have influenced results in an unpredictable manner.”

**Comment A - Less than 12 percent African Americans means sample may be underpowered to comment in general vs US pop.**

Response:

Our study has detected statistically significant differences between African Americans and Caucasians with respect to lipid management. We believe that the reviewer’s comment was related more to the question of generalizability (or external validity) than to statistical power. That is, how well do results from the QAP population reflect what is occurring in the general population with CAD. We agree that this issue should be discussed in more detail. To address this we have inserted the following text into the discussion section:

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“How well African Americans and Caucasians in the QAP represent their national populations of CAD patients is not known. Differences by race in access to QAP medical practices may produce disparity results not generalizable to the national population. We speculate that African Americans in the QAP were likely receiving better care on average than their counterparts in the general population, especially those with little or no access to outpatient care. If this is true, then racial disparities in lipid management in the general population may be even greater than those suggested by our findings”.

### **Comment B – Needs clear and specific definition of coronary artery disease.**

Response: The following text was added to the methods section.

“The presence of CAD was ascertained during analysis from abstracted medical record data based on medical history, *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes (410-414), and cardiac procedures consistent with CAD (i.e., coronary artery bypass graft, angioplasty, and stent).”

### **Comment C – Must clearly define how charts selected to insure randomness**

Response: The following revision was added to the methods section.

#### **“QAP Participant Selection**

Physicians and medical practices throughout the United States with high numbers of prescriptions for medications used in the treatment of cardiovascular disease were invited to participate in the QAP. The specialty of participating physicians included cardiology, internal medicine, family medicine, and endocrinology. Patients with cardiovascular disease were selected using simple random sampling within each participating medical practice.”

### **Comment D – Clearly define the clinician’s offices, i.e., private, academic, public health centers, urban, rural, so that this data may be replicated.**

Response:

Unfortunately, little is available from QAP to characterize participating medical practices. This is a necessary limitation of the study. To acknowledge this, the following was added to the discussion section:

“Another limitation to our study is the lack of information characterizing medical practices, physicians, and patients with respect to factors related to race and lipid management. Because of the unavailability of these data, we could not evaluate the extent to which these factors explain our findings.”

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### **Response to Reviewer #2:**

**Major Compulsory Revisions: None**

**Minor Essential Revisions: None**

#### **Discretionary Revisions:**

**Comment 1 – Authors may need to discuss limitations of the study in the Discussion section. For example, the study patients, physicians and practices were highly selective in participation in the QAP. In addition, the models did not adjust for the patients' SES, which might be due to lack of data in database. Therefore, their findings should be interpreted cautiously, and should not be generalized to general populations.**

Response: The following was added to the discussion section.

“Reports that African Americans are more likely to be of low income have greater implications than simply the inability to afford medications. Income is one of several indicators of socioeconomic status correlated with factors related to health such as education.[30] Low education has been identified as a factor limiting a patient's personal involvement in lipid management.[31] There is evidence that African Americans are less knowledgeable about cholesterol compared to Caucasians.[24] Thus African Americans may be less likely to be aware of the need for lipid management and less likely to pursue it with their physician. The impact of socioeconomic status on disparities in lipid management could not be evaluated in the QAP due to the lack of socioeconomic status data.”

“There are a number of limitations in the QAP study design and its population that potentially pose a threat to the internal and external validity. These limitations suggest that our findings may not reflect the experiences of the general population. The medical practices included in the QAP were restricted to those writing large numbers of prescriptions for cardiovascular disease drugs. It is difficult to evaluate the impact of this selection bias, but we suspect that medical practices included in the QAP represent the larger and more sophisticated providers of care. Thus, lipid management among QAP participants may be better than that found in the general population.”

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**Comment 2 – Clarify the source of diagnosis codes (ICD-9-CM diagnosis codes?) in the last sentence of the third paragraph within the Methods section.**

Response: The following text was added to the methods section.

“The presence of CAD was ascertained during analysis from abstracted medical record data based on medical history, *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes (410-414), and cardiac procedures consistent with CAD (i.e., coronary artery bypass graft, angioplasty, and stent).”

### **Response to Reviewer #3**

#### **General:**

.... **Table 2, it is not clear what the reference group was for the logistic regression analyses and since this is the key result of the paper, this is an important issue to clear up.**

Response: Table 2 was modified to clearly indicate that Caucasian men are the reference group.

#### **Major Compulsory Revisions:**

**A more careful and complete addressing of the available literature is critical**

Response: The discussion section was completely revised and enhanced to include a thorough review of the literature. Enhancements include the following text:

“Consistent with previous reports, our findings demonstrate that outpatient lipid management for CAD patients in the late 1990’s had much room for improvement and that substantial race-sex disparities existed.[8,12,16,21-26] African Americans experienced markedly lower levels of LDL-C testing than Caucasians and, as a result, they may benefit more than Caucasians from interventions to improve testing. Marked lipid testing disparities by sex suggest a need for more aggressive testing in women. Among those tested, African Americans were less likely to be treated and, if treated, they were less likely to be at goal compared to Caucasians.

Much of the information needed to assess lipid management can be found only in the medical record. This information is generally not available to national and local public health programs attempting to implement policies promoting quality improvement in the many and diverse medical practices treating large patient populations. The most readily available data for patients seen in the fee-for-service setting is derived from administrative insurance claims for the reimbursement of costs associated with drugs and services. Insurance coverage for lipid lowering drugs varies across plans. In contrast, lipid testing for CAD patients is a widely covered service that can be identified using

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electronic billing data without the need to review patient records in medical practices. For this reason, lipid testing is a focus of national efforts in the Medicare population to improve outpatient lipid management in the fee-for-service setting.[17] Our findings demonstrate that substantial disparities in treatment and goal attainment exist among CAD patients with lipid tests. This implies that public health programs and policies designed to increase lipid testing alone will have limited impact on lipid management disparities. Substantial disparities in lipid treatment and control will likely persist in the absence of disparities in testing.

Underlying causes of inadequate lipid management among CAD patients are multiple and likely vary by race and aspect of care (i.e., detection, treatment, and control). Factors that limit patient-physician encounters and continuity of care may partially account for racial disparities in lipid management. For example, African-American Medicare consumers with diabetes were more likely to receive outpatient care from emergency departments and had fewer physician visits per year than their Caucasian counterparts.[12,27] The QAP data provide insufficient information to evaluate whether health care access and continuity explain lipid management disparities.

A report regarding racial disparities in the use of prescription drugs from the Center for Studying Health System Change provides evidence of other factors explaining racial disparities in lipid management.[11] In this report, Medicare consumers 65 years of age and older were surveyed regarding their ability to obtain prescription drugs. African Americans were more than twice as likely as Caucasians to have not filled a prescription because they could not afford it. More than 16% of Medicare insured African Americans reported that they could not afford to fill at least one prescription in 2001. One fifth of African Americans and 13% of Caucasians with low income could not afford to fill at least one prescription. Medicare does not cover the cost of lipid lowering drugs and many Medicare consumers have supplemental insurance that assists with these costs. In the Medicare population African Americans were less likely than Caucasians to have supplemental insurance and more likely to be of low income.[11]

Barriers to lipid management due to affordability may result in racial disparities if affordability differs by race. Patients who cannot afford treatment may be less likely to aggressively pursue it with their physicians and may be less likely to comply with physician recommendations for testing and treatment. Secondary prevention of cardiovascular diseases among CAD patients with pharmacologic agents such as statins has been shown to be cost effective.[28] But drug costs that may exceed \$2,000 annually can be beyond the reach of low income and underinsured patients.[29] These costs are more likely a barrier for African Americans than for Caucasians and may contribute to lipid management disparities.

Reports that African Americans are more likely to be of low income have greater implications than simply the inability to afford medications. Income is one of several indicators of socioeconomic status correlated with factors related to health such as education.[30] Low education has been identified as a factor limiting a patient's personal involvement in lipid management.[31] There is evidence that African Americans are less knowledgeable about cholesterol compared to Caucasians.[24] Thus African Americans may be less likely to be aware of the need for lipid management and less likely to pursue it with their physician. The impact of socioeconomic status on disparities in lipid

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management could not be evaluated in the QAP due to the lack of socioeconomic status data.

Achieving LDL-C goal is challenging for all races, but African Americans may require especially aggressive lipid management accompanied by an enhanced understanding of reasons for failure to achieve goal. A recent report concerning patients with CAD and/or diabetes seen at a Veterans Affairs Medical Center found that African Americans were less likely to achieve lipid goal than Caucasians when prescribed identical doses of the same lipid-lowering drug even though African Americans had more clinic visits and lipid profiles.[10] The authors speculate that racial disparities in goal attainment may have occurred due to differences in compliance, lifestyle, and baseline LDL-C (higher for African Americans). In a study of LDL-C lowering and pravastatin in an African-American population, only 13% of patients with an LDL-C goal of 100 mg/dL actually achieved it. Factors associated with not achieving targeted LDL-C levels included incorrect drug regimen, inadequate lipid monitoring, and compliance.[32] Additional studies are needed to investigate the underlying causes of lower goal attainment rates for African Americans receiving treatment for dyslipidemia.

Physicians have indicated that oversight is a common reason for failure to adhere to lipid testing guidelines.[33] Whether oversight contributes to racial disparities in lipid management is not known, but oversight can be alleviated by system changes in the medical practice.[34] Awareness is growing that implementation of electronic health records is a necessary component of efforts to improve healthcare quality and prevent medical errors.[35,36] The impact of electronic systems on disparities is an interesting area for future. Lipid management is also influenced by physician attitudes about guidelines and drug effectiveness.[37] A better understanding is needed of physician attitudes and their relations with healthcare disparities.

Physician-patient interactions are influenced by race and cultural factors related to race. African-American and Caucasian patients may differ with respect to cultural perceptions of health and disease and their ability to influence health outcomes.[38] African Americans may be less likely than Caucasians to trust their physicians and race groups may view their relationship with physicians differently.[39] A survey of adults seen in a managed care setting revealed that African Americans viewed their visits with physicians as less participatory than did Caucasians, but they felt more participatory when seeing a physician of their own race.[40]

The relatively poorer lipid management for African Americans compared to Caucasians may be partially explained by racial differences in the prevalence of co-morbid conditions. African Americans in the QAP were more likely than Caucasians to suffer from multiple chronic conditions including diabetes and heart failure. It has been shown that patients with diabetes compared to those without diabetes receive poorer lipid management and are less likely to be at goal.[41] An earlier report from the QAP has shown that patients with CAD and heart failure are less likely to receive lipid testing and cholesterol-lowering drugs than those without heart failure.[42] Patients with multiple chronic conditions may be more likely to find medications unaffordable than those with one or fewer chronic conditions.[11] But even after controlling for several such conditions in logistic regression analyses, we find that lipid management disparities by race persist.”

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**.. a descriptor of the QAP-II database and the implications of the inclusion and exclusion criteria... and a clearer description of the analyses.**

Response:

The methods section was enhanced and reorganized as follows:

### **The Quality Assurance Program**

The Quality Assurance Program (QAP) is a national program sponsored by Merck & Company conducted during the late 1990's to identify physician practice patterns and to promote evidence-based best practices for the medical management of patients seen in the outpatient setting with cardiovascular disease.[18] The QAP database provides abstracted medical record data collected during two distinct time periods and study populations nationwide. In order to examine the most recent data possible, our analyses were limited to the study population identified in the most recent period of data collection (QAP-II). Patients from QAP-II included in these analyses were seen at participating medical practices from January, 1995 through March, 1998.

Medical records were reviewed by Access Medical Ltd (Arlington, VA) using a standardized electronic abstraction tool developed specifically for QAP-II. The QAP database contains data obtained from the medical record including race, sex, date of birth, medical history, and medical procedures. The most recent serum lipid testing results and the most recently recorded prescriptions for lipid-lowering drugs were also determined from the medical record. The medical record of each patient was reviewed only once. Patients were not followed over time. Patient and physician identifying information were not included in the QAP-II database to ensure confidentiality.

### **QAP Participant Selection**

Physicians and medical practices throughout the United States with high numbers of prescriptions for medications used in the treatment of cardiovascular disease were invited to participate in the QAP. The specialty of participating physicians included cardiology, internal medicine, family medicine, and endocrinology. Patients with cardiovascular disease were selected using simple random sampling within each participating medical practice.

### **Inclusion and Exclusion Criteria**

Patients included in the QAP study were at least 21 years of age with CAD and/or heart failure and were seen at least twice in two years by the participating physician. Patients were excluded if the medical record indicated a terminal illness, history of a transplant or awaiting transplant, or deceased.

Patients without medical record documentation of CAD were excluded from analysis. The presence of CAD was ascertained during analysis from abstracted medical record data based on medical history, *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes (410-414), and cardiac procedures consistent with CAD (i.e., coronary artery bypass graft, angioplasty, and stent).

Patients without medical record documentation of race were excluded from analysis and, when race was specified, only African-American and Caucasian patients were included. Medical practices were excluded if they were located in states with fewer than 10 African-American patients in QAP-II to reduce the influence of between-state

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variation in lipid management from states that contribute little information about African American populations.

### Indicators of Lipid Management

Measures of detection (lipid testing), treatment (lipid-lowering drug prescription), and control (goal attainment) were the indicators of lipid management considered in this study. Low density lipoprotein cholesterol (LDL-C) testing was measured as the percentage of patients with at least one serum LDL-C value documented in the medical record. The use of lipid-lowering drugs (i.e., “treated” patients) was measured as the percentage of patients with medical record documentation of at least one prescription for a statin (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor) or non-statin lipid drug (e.g., gemfibrozil). Goal attainment among those with documented LDL-C values was based on recommended guidelines for patients with coronary artery disease (LDL-C < 100 mg/dL).[5]

### Analysis

We conducted a cross-sectional analysis of abstracted medical record data obtained from QAP-II. Indicators of lipid management (i.e., LDL-C testing, lipid-lowering drug prescription, and LDL-C goal attainment rates) and potential confounding or explanatory variables were examined within strata of race and sex. Co-morbid conditions including diabetes mellitus, myocardial infarction, heart failure, and hypertension were identified from medical history and diagnosis codes.

Logistic regression analyses were performed to evaluate the associations of race and sex with dichotomous lipid management indicators while simultaneously controlling multiple confounding and explanatory variables. We accounted for correlations within medical practices using the generalized estimation equation (GEE) method.[19] This method was implemented in generalized linear models with PROC GENMOD of SAS Version 9 (SAS, Inc, Cary, North Carolina) for logistic regression with correlated data.[20] Separate models were run for each indicator of lipid management as the dependent variable. The entire study population was included for logistic regression analyses of LDL-C testing as the dependent variable. Regression analyses with lipid-lowering drug prescription as the dependent variable included only patients with LDL-C tests. Regression analyses for LDL-C goal attainment were limited to patients who received at least one LDL-C test and had a documented prescription for a lipid-lowering drug.

The independent variables included in the regression models in addition to race and sex were age, medical history (diabetes mellitus, myocardial infarction, heart failure, hypertension), and geographic region of medical practice. Logistic models predicting lipid-lowering drug prescriptions included a term for serum LDL-C concentration in addition to the above variables. LDL-C concentration was included to control for the severity of hyperlipidemia as a consideration in the physician’s decision to treat with lipid-lowering drugs.

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### **.. addressing of the possible nesting of patients within physicians for the analyses**

Response: A very good point. We felt that nesting of patients at the level of practices rather than physicians was more relevant to lipid management because disease management systems are implemented at the practice level. To account for correlations within medical practices, we repeated the logistic regression analyses using SAS PROC GENMOD and the GEE method for correlated data. The methods section (above) was revised to describe this and Table 2 was updated with GEE results. Point estimates and confidence intervals changed little after GEE and this approach did not alter our conclusions.

### **Minor Essential Revisions:**

**Specify the time period to which the results apply. It is not clear when the QAP-II dataset was created, early or late 1990s, and 10 years can make a substantial difference. If it relates to the early 1990's, the data are over 10 years old and may now be irrelevant.**

Response: Revised the methods section

“Patients from QAP-II included in these analyses were seen at participating medical practices from January, 1995 through March, 1998.”

### **Discretionary Revisions:**

**Comment 1 – Something seems amiss in the typing of references 4 and 5.**

Response: Thank you. This is corrected.