Author's response to reviews

Title: Is There a Clinically Significant Gender Bias in Post-Myocardial Infarction Pharmacological Management in the Older (>60) Population of a Primary Care Practice?

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Dr. Fiona Godlee
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Dear Dr. Godlee:

We are writing to respond to the peer-review comments on our paper entitled “Is there a clinically significant gender bias in post-myocardial infarction pharmacological management in the older (>60) population of a primary care practice?” Thank you for the opportunity to revise and review this manuscript. Essentially, we had two conflicting peer reviews. Peer reviewer no. 1, Dr. Todd Miller, regarded this as a paper of limited interest and advised it be rejected because it was scientifically unsound. We find these comments unfortunate and would like to rebut them.

Dr. Miller has three major criticisms:

His first criticism is that the study is not a significant contribution to the existing medical literature, and that numerous such studies have examined gender bias differences in health care utilization of patients with coronary artery disease, and furthermore, that it was a small study and the results were of borderline statistical significance. We state quite clearly in the introduction to our paper that most of these studies have come from the tertiary care specialist literature, that is, they are done by cardiologists or internists. To the best of our knowledge, the only paper that examines this in a primary care setting is the Hippisley-Cox paper that we reference, and, of interest, our results replicate theirs quite closely. As is stated in the article’s feature box (BMJ 2001;322:832) entitled “What is known on the topic”: “Substantial evidence of sex inequality for this disease exists for access to secondary care less but less is known about equity for its management in general practice.” We commenced our study prior to this publication and had hoped to be one of the first primary care studies on this issue. Therefore, I would disagree with the claim that this is not a significant contribution to the literature. We have submitted our paper to the Family Practice section of BioMed Central, as this is directed at family practitioners, where the literature is not as extensive as it is for cardiologists and general internal medicine specialists.

The results are significant at the customary level of significance. We argue in the paper that this is of clinical relevance. We recognize that the sample size is small, and acknowledge the ongoing controversy concerning statistical significance and clinical relevance, but the 0.05 standard, though arbitrary, is almost universally recognized.

Secondly, Dr. Miller points out the need to adjust for confounding variables. There are essentially two ways in which one can adjust for the effect of age. One can do a stratified
categorical analysis (Mantel-Haenszel), or one can do a multi-variate analysis. As we point out in the paper, there are no baseline differences between groups except in age. We have done the age adjusted analysis and the results are as follows: Mantel-Haenszel age adjusted Odds Ratio 1.2918, 95% C.I. 1.0348 - 1.6126, p=0.0319. Thus the effect holds, and the level of significance is more robust so we regard the claim that adjusting for age will make the effect disappear to be rebutted.

Finally, the third major comment is that the reviewer argues that we have incorrectly classified the proportions of those who are receiving medication for hyperlipidemia. The current guidelines that are disseminated to primary care providers indicate that almost everybody in the post-MI situation should be on some form of lipid-lowering medication. So we believe that Dr Miller’s claim that “logically clinicians are going to prescribe these medications only to those patients with a diagnosis of hyperlipidemia” to be questionable, as the trend has been downward on the acceptable level, particularly of LDL, which means that lipid-lowering agents are recommended to virtually everyone post-MI. (see for example: Statins are the new aspirin, Oxford researchers say BMJ 2001; 323: 1145.) Dr. Miller asks us to analyse whether there is a significant difference between the 28/35 women and 68/70 men on lipid lowering medication with a diagnosis of hyperlipidemia. A comparison of proportions performed in Epicalc, confirms a statistically significant difference:

Difference : 17.14 % [1.19, 33.10]
Z : 2.59
One-sided p-value : 0.004823
Two-sided p-value : 0.009646

With respect to the minor comments, we did not use any established guidelines but simply took the diagnosis from of hyperlipidemia from the chart. I agree it would have been an additional strength to have the actual cholesterol values reported in this study, but we do not have that in our database. Similarly, we do not have the information regarding which medications patients were taking. We know from other audits that statins predominate in our practice, with fibrates a distant second and Niacin rarely used in our practice.

The time frame of the study is now described. We did not examine the use of HRT. We have the data on time from MI to the study and can add it if necessary. We do not think it adds to the analysis. We would be happy to provide our complete data set to Dr Miller if requested.

For minor point 4, we did not perform an adjustment on the basis of PTCA and bypass surgery because, as we noted, these procedures are out of the control of the primary care provider, and this is mentioned explicitly in the discussion section. As noted in the introductory section, our main outcomes are medical management. We are focusing on primary care practice; angiography, bypass and angioplasty are not within the purview of the care we provide. Our interest is in the medical management of these patients which family physicians can influence. Furthermore, it is of interest to note that the point estimates that we arrived at are fairly close to those that are in the published literature.

We have added p values etc for table 1.
The second peer reviewer also points out that adjustment for age could result in the vanishing of the difference, but as we have noted and appended, once we have adjusted the effect remains. With respect to his specific comments, we thank him for his close reading. We have changed the Results section, page 5, paragraph 1 to read “0.005”. We have corrected the typographical errors kindly pointed out.

There is some difference in view on how to best present statistical matters between ourselves and the second peer reviewer. The peer reviewer says that we don’t need to add the 95% confidence interval of the difference as well as its p value. In fact, most journals now are requesting both the 95% confidence interval and the exact p value. That is why in the Results section, page 5, paragraph 3, we have chosen to retain the exact p value. We thank him for his clarification and have altered the tables as needed.

In summary, then, the chief criticism of this paper is that a multi-variate analysis or some form of age adjustment would make the effect that we discovered disappear. This, in fact, is not the case as you will see by the supplementary statistical evidence that we provide. Also, our target audience is largely primary care, family practice providers, not the specialists where the literature is well established. Consequently, we feel that Dr. Miller’s comments about the scientific unsoundness and limited interest are not substantiated, and we have met all of the comments that the second peer reviewer has provided.

We hope that this is satisfactory for you. We believe we have done everything within our power to make this a publishable paper. We stand by the results and believe that this is a paper of interest to the broad primary care field represented by the BioMed Central Family Practice readership. We look forward to your correspondence and decision.

Sincerely,

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