

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

## ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Are There Gender Differences in Acute Management and Secondary Prevention of Acute Coronary Syndromes in Barbados? A Cohort Study
<b>AUTHORS</b>	Sobers, Natasha; Rose, Angela; Samuels, TA; Critchley, Julia; Abed, Melissa; Hambleton, Ian; Harvey, Arianne; Unwin, Nigel

## VERSION 1 – REVIEW

<b>REVIEWER</b>	DE SERVI STEFANO IRCCS MULTIMEDICA , SESTO SAN GIOVANNI , MILAN ITALY
<b>REVIEW RETURNED</b>	10-Sep-2018

<b>GENERAL COMMENTS</b>	<p>The main aim of this paper was to explore gender differences in prescribing practices for acute coronary syndromes (ACS) and to evaluate whether ACS patients in Barbados were treated with optimal medical therapy in both the hospital and community settings. The authors state that in Barbados, unpublished data indicates that in-hospital acute MI case-fatality rate (2013) was 40.8% with higher rates in women after age-adjustment (risk ratio=1.18; 95% CI 1.02–1.37) .</p> <p>The authors however do not give any data concerning death rates in their study population . From Figure 1 we can argue that among 1589 patients admitted for MI ( STEMI or NSTEMI ) 1295 had data abstracted from hospital notes (with 114 having a diagnosis confirmed by autopsy ) and 294 had a diagnosis from a death certificate . The mortality rate for patients arriving alive to hospitals for MI is arguably ( 294+114)/1589 = 31.5% . Unfortunately the authors do not mention the mortality rates for men and women .</p> <p>The data presented concern physicians prescriptions during hospitalization and at discharge . An analysis of factors related to non adherence to guidelines recommendations ( beyond gender ) should be performed .</p> <p>No patients were apparently treated invasively , even though in Table 1 about 10 per cent of patients had undergone coronary angiography in their medical history . This is likely the greatest failure in the health system in Barbados . The authors should comment on this and should specify if organization has changed in the latest years.</p> <p>The clinical variables associated with MI patients look interesting : obesity was present in a range between 70% and 89% of patients , diabetes from 55% to 82% and atrial fibrillation rate was rather high ( from 26% to 35% of all patients ) considering that mean age was globally below 70 years . In this regard , there is a lot of preventive work to do in Barbados.</p> <p>Data concerning unstable angina and chronic angina do not add useful information to the manuscript</p>
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<b>REVIEWER</b>	Dr. Muhammad Aziz Rahman La Trobe University, Australia
<b>REVIEW RETURNED</b>	21-Sep-2018

<b>GENERAL COMMENTS</b>	<p>The authors need to be congratulated for focusing on an important topic of gender disparity. Findings are significant providing further evidence on the gender difference in treatment and outcomes. Having less fibrinolytics within first 24 hours explain more mortality amongst women in Barbados.</p> <p>Few suggestions to consider:</p> <ol style="list-style-type: none"> <li>1. Please, consider references such as Worrall-Carter et al. and Kuhn et al. regarding similar evidence from elsewhere.</li> <li>2. Data analyses section did not explain how adjustment was done. Only age was adjusted as confounders, whereas there were other potential confounders which need to be adjusted to get an unbiased estimate. That's my only concern and would recommend doing the analyses again considering all the potential confounders.</li> <li>3. There should be analyses for younger and older women to examine difference in outcomes and discussion should explain the effects of hormones in this relation.</li> </ol>
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### VERSION 1 – AUTHOR RESPONSE

Article Title: Are There Gender Differences in Acute Management and Secondary Prevention of Acute Coronary Syndromes in Barbados? A Cohort Study

List of revisions as recommended by reviewers and manner in which they have been addressed

Description	Completion status
<p>Reviewer stated: The authors however do not give any data concerning death rates in their study population. From Figure 1 we can argue that among 1589 patients admitted for MI (STEMI or NSTEMI ) 1295 had data abstracted from hospital notes (with 114 having a diagnosis confirmed by autopsy ) and 294 had a diagnosis from a death certificate . The mortality rate for patients arriving alive to hospitals for MI is arguably <math>(294+114)/1589 = 31.5\%</math>. Unfortunately, the authors do not mention the mortality rates for men and women.</p>	<p>I assumed that the reviewer was referring to the ischaemic heart disease cause-specific mortality for men and women. At line 80 I have inserted the age-standardised mortality rate due to MI for both sexes according to the Barbados National Registry but no sex differential given. This data was also not available in the Ministry of Health's last published annual report which was 2012.</p>
<p>An analysis of factors related to non-adherence to guidelines recommendations (beyond gender) should be performed.</p>	<p>In response to this suggestion, we performed univariate analyses of co-morbidities available in the dataset on adherence to fibrinolysis only. We also included the results of the logistic regression model that best described the factors affecting adherence to fibrinolysis. These are</p>

	described at lines 182-187 and reported at lines 193 to 197.
No patients were apparently treated invasively, even though in Table 1 about 10 per cent of patients had undergone coronary angiography in their medical history. This is likely the greatest failure in the health system in Barbados. The authors should comment on this and should specify if organization has changed in the latest years.	Patients are not treated invasively in their acute management. Patients do undergo coronary angiography as part of chronic management of ischaemic heart disease and some undergo procedures out of island. At lines 290-292 we have made mention of this weakness in the Bdos health care system. The more recent change to the system has been added at lines 293-294.
The clinical variables associated with MI patients look interesting: obesity was present in a range between 70% and 89% of patients , diabetes from 55% to 82% and atrial fibrillation rate was rather high ( from 26% to 35% of all patients ) considering that mean age was globally below 70 years . In this regard, there is a lot of preventive work to do in Barbados.	The authors agree with the comments made by the reviewer and was added at lines 217-218.
Please, consider references such as Worrall-Carter et al. and Kuhn et al. regarding similar evidence from elsewhere.	These references have been added to line 278.
Data analyses section did not explain how adjustment was done. Only age was adjusted as confounders, whereas there were other potential confounders which need to be adjusted to get an unbiased estimate. That's my only concern and would recommend doing the analyses again considering all the potential confounders.	Adjustment of age was described at lines 182 – 183 in the first manuscript. We didn't initially adjust for co-morbidities since, of the factors listed in the hospital protocol as absolute contraindications for fibrinolysis only one was adequately collected by the registry – systolic blood pressure on admission.  Since reviewer one appeared to be asking for other factors related to non-adherence to fibrinolytics we conducted univariate and multivariable analyses exploring the associations between several available co-morbidities (hypertension, diabetes, previous ischaemic heart disease, obesity, smoking, history of coronary angiography, atrial fibrillation, congestive cardiac failure and systolic blood pressure on presentation). Additional analyses are described at lines 186-192.
There should be analyses for younger and older women to examine difference in outcomes and discussion should explain the effects of hormones in this relation.	This analysis was attempted and numbers within groups were too small in this population to yield meaningful logistic regression results when adjustments were made for potential confounders as suggested above.

<p>Please provide another copy of your figures with better qualities and please ensure that Figures are of better quality or not pix-elated when zoom in. NOTE: They can be in TIFF or JPG format and make sure that they have a resolution of at least 300 dpi and 90mm x 90mm of width. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable.</p>	<p>The figures have now been saved as Tiff files</p>
<p>2. Please include Figure legends at the end of your main manuscript.</p>	<p>Figure legends have been added at lines 454-457 at end of document</p>
<p>3. Patient and Public Involvement: We have implemented an additional requirement to all articles to include 'Patient and Public Involvement' statement within the main text of your main document. Please refer below for more information regarding this new instruction:</p> <p>Authors must include a statement in the methods section of the manuscript under the sub-heading 'Patient and Public Involvement'.</p> <p>This should provide a brief response to the following questions:</p> <p>How was the development of the research question and outcome measures informed by patients' priorities, experience, and preferences?</p> <p>How did you involve patients in the design of this study?</p> <p>Were patients involved in the recruitment to and conduct of the study?</p> <p>How will the results be disseminated to study participants?</p> <p>For randomised controlled trials, was the burden of the intervention assessed by patients themselves?</p> <p>Patient advisers should also be thanked in the contributorship statement/acknowledgements.</p> <p>If patients and or public were not involved please state this.</p>	<p>Patients and the public were not actively involved in this study. Data from these findings have been disseminated to the health care providers and key stakeholders to facilitate policy and planning around care of myocardial infarction patients in Barbados. Dissemination targeted at the general public will be released at a 70<sup>th</sup> Anniversary Celebration open day of the University of the West Indies in November 2018. This information has been added to lines 193 to 197.</p>

## VERSION 2 – REVIEW

<b>REVIEWER</b>	De Servi Stefano IRCCS Multimedica , Sesto San Giovanni ( Milan ) Italy
<b>REVIEW RETURNED</b>	24-Nov-2018

<b>GENERAL COMMENTS</b>	The manuscript has improved after revision
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<b>REVIEWER</b>	Dr. Muhammad Aziz Rahman La Trobe University, Australia
<b>REVIEW RETURNED</b>	28-Nov-2018

<b>GENERAL COMMENTS</b>	The authors have addressed the comments from reviewers. The only minor issue to be noted that 'univariate' should be replaced with 'multivariate' in line 182 and 230
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## VERSION 2 – AUTHOR RESPONSE

December 4, 2018

**OUR REFERENCE:** Are There Gender Differences in Acute Management and Secondary Prevention of Acute Coronary Syndromes in Barbados? A Cohort Study

Dear BMJ Editorial Team,

I thank you very much for your decision to publish the paper 2018-025977.R1 pending minor revisions. Reviewer two has asked that the word univariate be replaced with multivariate at lines 182 and 230. This line was not describing multivariate analyses so this change was not made.

Given the analyses conducted, line 182 has now been changed to, "We conducted bivariate analyses to explore the effects of documented each of the following co-morbidities ....." and similarly, line 230 was changed to, "After bivariate analysis, smoking was.....". As a result of the apparent confusion I have also inserted the terms crude and adjusted before the various odds ratios reported from lines 230 to 237.

In response to the editorial comments I have completed and included the STROBE checklist and added a line at 108 to state that STROBE guidelines on reporting was followed.

I look forward to further communications.