Author's response to reviews

Title: Differences between men with screening-detected versus clinically diagnosed prostate cancers

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Author's response to reviews: see over
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Dear BioMed Central:

We are submitting the manuscript entitled “Differences between men with screening-detected versus clinically diagnosed prostate cancers in the USA” by R. M. Hoffman, S. N. Stone, D. Espey and A. L. Potosky. This is original research that was originally submitted to BMC Medicine. We have responded to the reviewer’s comments and now submit the revised paper for consideration by the editorial board of the journal BMC Cancer. A point-by-point description of the reviewer’s comments and author’s responses are attached with this covering letter.

The advent of prostate specific antigen (PSA) testing has led to a dramatic increase in the incidence of prostate cancer in the United States. During the past decade, the number of men undergoing aggressive treatment with radical prostatectomy and radiation therapy also increased substantially. Population-based data on PSA screening are largely unavailable and the association of screening detection with treatment decisions has not been adequately addressed in the medical literature. The purpose of this project was to assess whether PSA screening predicted receiving aggressive treatment for clinically localized cancer. Using data from the American population-based Prostate Cancer Outcomes Study (PCOS) we compared patient characteristics and treatment selection between men with screening-detected versus clinically diagnosed prostate cancers.

All authors of this research paper have directly participated in the planning, execution, or analysis of the study. All authors of this paper have read and approved the final version submitted. None of the authors have any financial interests, direct or indirect, that might affect the conduct or reporting of this manuscript. The contents of this manuscript have not been copyrighted or published previously nor is it now under consideration for publication elsewhere.

We appreciate the editorial board’s efforts to consider our manuscript and are most grateful to the reviewer for providing insightful and constructive comments. We look forward to hearing from you.

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Responses to Reviewer Comments
Differences between men with screening-detected versus clinically diagnosed prostate cancers in the USA
Hoffman, Stone, Espey, Potosky

Major Compulsory Revisions

Reviewer Comment #1
International policy and practice on prostate screening and management varies considerably. For publication in a journal of international scope both the title and the initial background section to the paper should identify that the research is based in the United States.

Author’s Response #1
The title, abstract and background have been updated to reflect that the study was conducted in the United States of America.

Reviewer Comment #2
As the authors acknowledge, the estimates of the proportion of prostate cancer which was detected through screening in the mid 1990's in the USA will have been affected by selection bias within the original sample of 5,672. The authors indicate that this will probably have led to an over estimation of the proportion screen-detected. Some socio-demographic information on non-respondents is available, is it possible to produce a more quantitative sensitivity analysis on this proportion using imputation/modeling? As estimating this proportion is the author's stated primary objective this may be worth exploring, if the data allow.

Author’s Response #2
We appreciate the reviewer’s concerns about estimating the proportion of screen-detected cancers. However, this was not really a primary objective for the analysis; we were more interested in comparing the socioeconomic and tumor characteristics of the men with screening-detected versus clinically-detected cancers. We also wanted to assess the effect of screening-detection on treatment decisions for localized cancers. We acknowledged that the estimates of screening were likely biased by the non-respondents (overestimated) based on differences in demographics, tumor characteristics, and treatment selection. However, we do not have sufficient information on the non-respondents to be able to accurately impute their screening status. We classified screening status based on clinical information available from the patient survey that was not routinely collected by the tumor registry.

Minor Essential Revisions

Reviewer Comment #3
Page 4 para 1, Please identify that incidence data are for the USA.

Author’s Reply #3
We have clarified that the incidence data presented on page 4, paragraph 1 is for the United States of America.

Reviewer Comment #4
Page 4 para 2, It is not appropriate to make general statements about participants in ongoing screening trials grouping North American and European trials together. The
statement that most were “non-Hispanic whites” means very different things in the
different populations involved.

*Author’s response #4*

We have changed the wording of paragraph 2 on page four in order to clarify that the
screening trials mentioned have taken place in both the United States and Europe. We
have also removed the statement referring to “non-Hispanic whites” and specified the age
groups and ethnic population served in these two studies.

*Reviewer comment #5*

Page 13 para 2 sentence 5 typographic error-“Classifying PSA as *a* screening test…”

*Author’s response #5*

We have corrected this error in sentence 5 of paragraph 2 on page 14.

**Discretionary revisions**

*Reviewer comment #6*

The findings of the paper relate to the mid 1990’s, it would be helpful to set them in the
context of current clinical practice and policy. Do the authors think these estimates are
likely to continue to reflect US practice, are they consistent with current incidence, stage
distribution? This probably merits a short comment in the discussion.

*Author’s response #6*

In paragraph 2 on page 12 we have added a statement in the discussion noting the time
period of the study and contemporary incidence and stage information. We have also
added two references reflecting current estimates of PSA test utilization from the
Behavioral Risk Factor Surveillance System (BRFSS). The new references are listed in
the bibliography as numbers 19 and 20.