MEDICAL FACULTY ASSOCIATES

THE GEORGE WASHINGTON UNIVERSITY

June 23, 2014

Dear Editor,
Please find enclosed the edited manuscript in Word format (file name: PSA Screening Revision 1 Track Final.doc).

Title: Effects of USPSTF guidelines on patterns of screening and treatment outcomes for Prostate Cancer

Authors: Vindya Gunawardena and Jeanny B. Aragon-Ching

Name of Journal: World Journal of Translational Medicine

ESPS Manuscript NO: 10798; Invitation ID (00106354)

The manuscript has been improved according to the suggestions of reviewers outlining each Reviewer's comments and responses:

1. Reviewer 1 comments:
In this study, the authors provided an excellent review on the role of PSA-based screening for prostate cancer and focused on the many controversies around it, pointing out the discrepancy between recent U.S. guidelines that recommends against it as weak (grade D) recommendation and both patients and physicians, who seem to be rather reluctant to change their minds owing to personal beliefs, cultural differences, as well as time and legal ethical issues. This well written manuscript is of high interest for the uro-oncological community and deserve to be publicated on World Journal of Translational Medicine. In my opinion, a brief insight on new promising biomarkers (Pro-PSA, pHi, and TMPRSS2-ERG) available on the market could be acknowledged too, to improve the quality of the discussion. At pag. 9 (line 3) the term "retroprospective" is misleading and need to be clarified

Response: We thank the Reviewer for this insight and have added a whole section on promising biomarkers and discussed the differences of these biomarkers in the interest of the readership of World Journal of Translational Medicine.

2. Reviewer 2: The article "Effects of USPSTF guidelines on screening and treatment outcomes for Prostate Cancer" submitted by Gunawardena and Aragon-Ching is a timely review and appropriate for an open discussion on why the PSA test should or should not be done. PSA value "> 4 ng/mL" elevated by a number of reasons lights up an orange signal in the life style of patients that confusing the physicians and patients. Authors conclusion that younger patients prefer aggressive treatment and older patients opted for

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“wait and see” based on evidence-based information from randomized control trial provided by the physician. The mention of probability of having early stage of prostate cancer to patients creates psychological ripples through the minds of younger patients for the preference on aggressive treatments. Asymptomatic or dormant prostate cancer does no harm no doubt but offers no guarantee. The recommendations from RCT on patients are based analysis of data using strict statistical parameters excluding psychological dilemma. “Over- diagnosis” or “over-treatment” is rests in the hands of decisions by the physicians. Moreover, racial factors play a critical role in prostate cancer and should be handled in a separate RCT. The article should include these facts into consideration.

Response: We appreciate the Reviewer’s comments and added these sections accordingly to address these concerns.

3. Reviewer 3: This is a well written review on a topic which has been poorly analyzed before. My suggestion regards the consideration and the discussion of a recentlt published article on a similar topic : Decision making and prostate cancer, Urol Clin North Am, 2014 by Knight.

Response: We appreciate the Reviewer’s comment and added the Knight paper accordingly.

4. Reviewer 4: The title implies a discussion on how the USPSTF guidelines has affected screening and treatment outcome - there is no conclusive cause-effect relationship on the basis of these guidelines. The title should better reflect the intent of the article being to examine what has happened post release of USPSTF guidelines. The key randomised controlled trials used to justify a given stance on prostate cancer testing are prone to what aspects are emphasised and presented. For example, in the PIVOT study, it was hugely underpowered and the major of the men were older than usual cohorts and had low risk disease - for many of these patients, we would be much less likely to offer surgery in today’s practice environment. Another is the SPCG-4 study where it is criticised for being less relevant as it was carried out in the pre-PSA era but the cohorts now are more representative of who we treat today since we are less likely to treat clinically significant disease. In the table outlining differences between PLCO and EPSPC, a more detailed table would be useful. It could include a line on ‘contamination’ in the control arm and the frequency of re-testing

Response: We greatly appreciate the Reviewer’s comments and have revised accordingly the table as well as added those counterpoints to both the PIVOT and ERSPC trials. We agree with the Reviewer regarding the observation that no conclusive cause-effect relationship between the USPSTF guidelines and treatment outcomes for prostate cancer can be made. Therefore, we changed the title to hopefully reflect this more appropriately.

Thank you again for continued working with us in reviewing our manuscript in the World Journal of Translational Medicine.

Sincerely yours,

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