PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Determinants for choosing and adhering to active surveillance for localized prostate cancer: a nationwide population-based study
AUTHORS	Bergengren, Oskar; Garmo, Hans; Bratt, Ola; Holmberg, Lars; Johansson, Eva; Bill-Axelson, Anna

VERSION 1 - REVIEW

REVIEWER	Jeremy Millar Alfred Health and Monash University, Melbourne, Victoria, Australia.
REVIEW RETURNED	27-Sep-2019

GENERAL COMMENTS	This is an interesting and important question, and the Swedish Registry provides a good tool to allow exploration of the issues. It was clearly written, and easy to understand. The work seems reasonably well-designed apart from the definition of active surveillance (see below) and the statistics appropriate. The authors recognise the problem of patient recall: the reasons provided might not have actually been the reasons, but the ones the men recalled, which may be different. To the extent they are different would make measures aimed at addressing the expressed reason rather than the real reason will be ineffective. How was "watchful waiting" dealt with? Or "refused treatment" or "prevaricated" or some other non-treatment option that was not surgery, or radiotherapy, or programatic active surveillance? Did *any* have focal treatment? The subset of men who do do not have surgery or radiotherapy do not all have active surveillance. This seems problematic in that it creates inhomogeneity in the active surveillance group, and if for example a large proportion of men in the Registry were not actually on active surveillance but actually were in the "couldn't make up their mind" category, then one might expect that if they progressed to treatment then it would be largely because doctors recommended it. In your Figure 2, in the Legend at the bottom of the Forest Plot, you should indicate that Odds above 1 favour AS. The same general observation applies for the expiration of the direction of OR in your Figure 4.

	"The vast majority of men primarily consulted either a urologist or a medical oncologist" Your questionnaire does not, I believe, ask about Medical Oncologist but "Oncologist (doctor that gives radiotherapy treatment)". It sounds as if this would be a Radiation Oncologist (to use the Canadian, Australian, or American terminology, or Clinical Oncologist in the UK terminology. "Interestingly, men whose PC was detected during the investigation of LUTS rather than through screening was more likely to adhere to AS."as this because a significant proportion of men presenting with LUTS were diagnosed by TURP and had cT1a disease? Or were more elderly and managed with "watchful waiting" with no intention of radical treatment in the future, but conflated in your study with AS?

REVIEWER	Simon Kim University of Colorado Denver CO USE
REVIEW RETURNED	27-Oct-2019

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. This is a well done survey study with a nice response rate looking at reasons for patient elect to chose active surveillance for prostate cancer. The results have an important implications about why men elect for active surveillance. I do have several questions. First, can the authors clarify why they mean about "the questionnaire was further validated in an unpublished pilot study among men not included in the present study"? Why not simply put the validation data in the results section. Second, how did the authors identify the themes for item response in picking active surveillance in the survey? More specifically, the ideal situation would be for the patient focus groups to identify themes for "My doctor recommended AS" rather than for the researchers or surgeons to solely develop the survey item. This is crucial because patient focus group developed themes for the survey items would limit bias. The study would also greatly benefit to assess whether the patent perceptions were associated with the initial treatment choice as well as for those patients who came off active surveillance. I would suggest that the authors perform these analyses. Thank you.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Jeremy Millar

Institution and Country: Alfred Health and Monash University, Melbourne, Victoria, Australia.

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

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The work seems reasonably well-designed apart from the definition of active surveillance (see below) and the statistics appropriate. The authors recognise the problem of patient recall: the reasons provided might not have actually been the reasons, but the ones the men recalled, which may be different. To the extent they are different would make measures aimed at addressing the expressed reason rather than the real reason will be ineffective.

1. How was "watchful waiting" dealt with? Or "refused treatment" or "prevaricated" or some other non-treatment option that was not surgery, or radiotherapy, or programatic active surveillance? Did *any* have focal treatment? The subset of men who do do not have surgery or radiotherapy do not all have active surveillance. This seems problematic in that it creates inhomogeneity in the active surveillance group, and if for example a large proportion of men in the Registry were not actually on active surveillance but actually were in the "couldn't make up their mind" category, then one might expect that if they progressed to treatment then it would be largely because doctors recommended it.

Answer: Our population was all stated in the National Prostate Cancer Register of Sweden as having received radical prostatectomy, radiotherapy or programmatic active surveillance as their primary treatment strategy, all other options were excluded from this study. Further, we actively chose men, younger than 70 years with low-risk disease because we didn´t want men on watchful waiting in our active surveillance group. Additionally, the Swedish guidelines clearly advocates active surveillance for all low-risk tumors which isn´t the case for all intermediate-risk tumors why we didn´t include intermediate risk men.

2. In your Figure 2, in the Legend at the bottom of the Forest Plot, you should indicate that Odds above 1 favour AS. The same general observation applies for the expiration of the direction of OR in your Figure 4.

Answer: The figure legends has been changed accordingly.

3. "The vast majority of men primarily consulted either a urologist or a medical oncologist" Your questionnaire does not, I believe, ask about Medical Oncologist but "Oncologist (doctor that gives radiotherapy treatment)". It sounds as if this would be a Radiation Oncologist (to use the Canadian, Australian, or American terminology, or Clinical Oncologist in the UK terminology.

Answer: The text has been changed to “Clinical Oncologist”.

4. "Interestingly, men whose PC was detected during the investigation of LUTS rather than through screening was more likely to adhere to AS "as this because a significant proportion of men presenting with LUTS were diagnosed by TUR-P and had cT1a disease? Or were more elderly and managed with "watchful waiting" with no intention of radical treatment in the future, but conflated in your study with AS?

Answer: In our material 3.5% where T1a, 0.6% T1b, 74.0% T1c and 21.9% T2. Thus, the vast majority of T1 tumors where detected through biopsies and not through TUR-P. This has now been added to our results section. The analysis showing that the men whose prostate cancer was detected during the investigation of LUTS was more likely to adhere to AS was adjusted for age, retirement, education and Charlson comorbidity index.

Reviewer: 2

Reviewer Name: Simon Kim

Institution and Country: University of Colorado, Denver CO USE

Please state any competing interests or state ‘None declared’: None

Please leave your comments for the authors below

Thank you for the opportunity to review this manuscript. This is a well done survey study with a nice response rate looking at reasons for patient elect to chose active surveillance for prostate cancer. The results have an important implication about why men elect for active surveillance. I do have several questions.

1. First, can the authors clarify why they mean about "the questionnaire was further validated in an unpublished pilot study among men not included in the present study"? Why not simply put the validation data in the results section?

Answer: The pilot study was constructed simply to test the logistics of the questionnaire and to test that the questionnaire worked as intended. It was performed among a smaller number of men why we don´t think that these results would add any additional value to the manuscript.

2. Second, how did the authors identify the themes for item response in picking active surveillance in the survey? More specifically, the ideal situation would be for the patient focus groups to identify

themes for "My doctor recommended AS" rather than for the researchers or surgeons to solely develop the survey item. This is crucial because patient focus group developed themes for the survey items would limit bias.

Answer: For men with prostate cancer to be involved in developing the survey items would be ideal. Unfortunately, as this questionnaire was created several years ago, this survey item was created by us as researchers. We will try to develop our patient involvement in the future.

3. The study would also greatly benefit to assess whether the patent perceptions were associated with the initial treatment choice as well as for those patients who came off active surveillance. I would suggest that the authors perform these analyses.

Answer: The men´s perceptions of their care is of great interest. We have already published an article on the men's perceptions in terms of their overall satisfaction with care. However, we don´t think that it would fit in the context of this article.

VERSION 2 – REVIEW

REVIEWER	Simon Kim University of Colorado
REVIEW RETURNED	24-Nov-2019

GENERAL COMMENTS	This is a nice study worthy of publication.