Author's response to reviews

Title: The Trends in Prostate Specific Antigen Usage Amongst United Kingdom Urologists, a Questionnaire Based Study.

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Author's response to reviews: see over
Re: The Trends in Prostate Specific Antigen Usage Amongst United Kingdom Urologists – a Questionnaire Based Study.
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Dear Editor,

Please find a detailed response to the reviewers’ comments attached on the pages below this covering letter. The manuscript has been changed accordingly and changes have been highlighted in green. We have answered the reviewers’ comments as fully as possible.

The main comments from reviewer 1 were based upon why we thought it was important to have surveyed urologists regarding the PSA cut offs as suggested by the Department of Health (DoH) in it’s guidelines for General Practitioners (GPs). The reasons for this are multiple:
Firstly, to provide safe and efficient urological patient care, in the transition of patient care between referral to secondary care from primary care, it is important for any secondary care practitioner to be aware of the referral guidelines. As the DoH PSA guidelines for GPs suggest onward referral to a urologist with PSA results outside the suggested cut-offs, urologists should be aware of the guidelines.
Secondly, whilst the DoH guidelines are not intended for urologists, many hospital laboratories provide age-related reference ranges for PSA based upon these guidelines. Therefore when a urologist is making a decision of whether to perform a TRUS biopsy, whilst other factors are taken into account, the PSA result heavily influences this decision. Thus urologists should be aware that hospital reference ranges are based upon the guidelines and the basis for these guidelines.
Thirdly, many studies have shown that the PSA test does not rule out prostate cancer at any level. Therefore whilst several large prostate cancer screening studies are awaited, not only GPs, but also urologists need guidance as to the PSA cut-off levels to guide further practice.

Hopefully this has explained the reasons behind our paper fully. Please see below for our other responses. We very much look forward to hearing from you in the near future regarding taking the manuscript further.

Best wishes,
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Responses to reviewer 1

1. The response rate has improved from 19% to 47%. However it is still low thereby introducing the possibility of bias. This needs to be discussed in more detail as it still affects any comparisons e.g. the regional comparisons.

We have expanded this point in the discussion.

2. An important point to take into consideration is the fact that the PSA guidelines are intended as referral guidelines for GPs to be used with asymptomatic men. They were not intended for use by urologists and were therefore not sent to urologists (a copy was sent to each GP in the country). The authors need to discuss how urologists are using the guidelines e.g. to guide whether a man should have a biopsy or not. Also it is not necessarily the case that the same PSA level as was used for referral should be used to guide further investigation. A recent publication has looked at GP use of the guidelines: Melia J et al. Urological referral of asymptomatic men in general practice in England. British Journal of Cancer 2008 (available on-line).

We acknowledge this important issue and thank the reviewer for raising it. To address this point we have added the following sections to the discussion:

‘Whilst these guidelines were intended for GPs, they have also been sent to many urologists within the United Kingdom. The PSA guidelines were formed because of the dilemma faced by all medical staff dealing with asymptomatic men who request or have a PSA test, in that there are many pitfalls associated with the sensitivity and specificity of the PSA test. Because of this there is no screening programme within the UK. However opportunistic testing occurs both in general practice and within secondary care by urologists and other physicians. Whilst further research is awaited the government has attempted to guide practice in a practical manner via these PSA guidelines. It is important to raise awareness of how the PSA test should be correctly utilised not just amongst GPs, but amongst all of the medical profession.

The transition of patients between primary care and secondary care via referral pathways is much more efficient if both Urologists and GPs are aware of the referral guidelines. Therefore for this point alone it is important for urologists to be aware of the DoH PSA guidelines.

Once a patient arrives in the secondary care setting after being referred with an abnormal PSA result a decision must be made as to whether the patient needs to undergo a prostate biopsy. When making this decision, the urologist takes not only the PSA result into account, but also urological symptoms, family history and digital rectal examination. This is a complex decision, involving discussion with the patient regarding the sensitivity and specificity of a PSA test, together with morbidity involved in a prostate biopsy. However, when making the final decision of when to biopsy – whether the PSA is within
the “normal” levels, and what these levels are perceived to be plays a large role. Many laboratories within the UK are using the DoH referral guidelines as PSA cut-off values, which will in turn be used by urologists as a guide to normality levels, and thus will aid in the decision making process of whether to biopsy a man.’


Apologies, this has been changed.

4. This should also be corrected on page 4 - the guidelines are for GPs not 'physicians'.

Corrected.

5. I can not see why the regional information is anonymised. As such it is not informative.

The regions details have now been included.

6. In the conclusions it states that a significant proportion of urologists appear to be unaware of the guidelines. As the guidelines were not intended for urologists is this surprising?

See our response to point 2.
**Responses to reviewer 2**

**General**

1. **This paper is not only for the UK medical staff. The foreign people do not know the different social insurances for the UK patients. Could you explain these differences?**

   The following sentence has been added to the background section: ‘This was investigated in Consultants working in both the National Health Service (the free UK Government led service) and/or the private sector.’

2. **With 47% response rate, this paper is representative of the urologist population. More could be better, but the data was interesting. The authors could discuss about this 47% in the discussion and limit the conclusion.**

   The discussion section has been expanded to include discussion around this point.

3. **In the table 1: are sure for the “% of responders”? 174% seem to be a lot?**

   I have amended the y axis for Figure 1 accordingly.

4. **The authors must present the statistical analysis in “material and method”.**

   A statistical analysis section has been added to the material and methods.

5. **In the conclusion, the authors write that differences create “an inequality in the healthcare”. In the results and in the table 1, the authors write that private patients were detected with a lower PSA. What is this difference using the PCPT data?**

   The median PSA cut-off values for ages 60-69 and 70-79 were higher in NHS (4.5 and 6.0 ng/ml respectively) compared to private practice (4.0 and 5.5, respectively). The PCPT data was analysed in PSA groupings of – 0-1ng/ml, 1.1-2.0ng/ml, 2.1-3.0ng/ml, 3.1-4.0ng/ml, 4.1-6.0ng/ml and >6.0ng/ml. As such all the NHS and private practice PSA-cut offs, whilst different, fall into the same PCPT category and therefore it is not possible to comment upon this difference using the PCPT data.

   **The authors must change the discussion and the conclusion with the result of the active surveillance.**

   I’m unfortunately not sure which active surveillance data the reviewer is referring to, but would be pleased to include it if he could elaborate.
Are the authors sure that the difference could change the cancer prognosis for the NHS patients (see the results of the last AUA congress)?

I am not aware as to which data the reviewer is referring to. The AUA is a large congress with hundreds of abstracts, the data from which may not have been published yet. We would be grateful if the reviewer could expand on the results he is referring to, so that we can decide whether reference to this would be relevant to our paper - otherwise it is difficult to refer to unpublished data.

The prognosis for NHS patients is based upon the wide PSA cut-offs used within the NHS. Therefore the likelihood of detecting high-grade prostate cancer changes dependent upon which PSA cut-off is used. Extrapolation of prognosis is therefore based upon the fact that high-grade prostate cancer carries a higher risk of mortality than low-grade prostate cancer (Albertsen nomograms).

Minor Essential Revisions and Discretionary Revisions

1. In the abstract, you must explain DoH (or DOH the 2 orthographies were used).

   Thank you for pointing this out - we have corrected this.

2. In the introduction and in the discussion, the authors must write about the Tyrol and Malmo experiences. Are the authors sure that all the USA had a “national screening program”?

   The Tyrol and ERSPC data have been added to the introduction. As far as we are aware the USA has an FDA – approved national screening programme.