Author's response to reviews

Title: Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: A national survey of general practitioners

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Version: 2 Date: 26 September 2008

Author's response to reviews: see over
Dear Editor

Thank you for considering our manuscript ‘Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: A national survey of general practitioners. Frances J Drummond, Anne Elie Carsin, Linda Sharp and Harry Comber (MS: 1062348605210018) for consideration for publication in BMC Family Practice.

The reviewer’s comments were very useful and insightful. We hope that we have addressed them to your satisfaction (please see below).

We have included a copy of the survey instrument used in this study and we are happy that any interested parties can access a copy of the survey upon request to the authors.

I look forward to hearing from you.

Sincerely,

Dr. Frances Drummond, PhD
Reviewers report
Title: Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: A national survey of general practitioners
Version: 1 Date: 6 August 2008
Reviewer: Jane Melia

Reviewers report:
This is an important topic and original research which could inform understanding of the reasons why GPs frequently test for PSA in Ireland which in turn must contribute to the high detection rate of prostate cancer.

There are several areas where the authors could improve and strengthen this paper.

Major compulsory revisions
1. The paper lacks references to related research in England and Wales, notably papers by Joan Austoker’s team. This research is relevant given the fact that 49% of the GPs in Ireland were found to have worked abroad mostly in the UK. Considerable emphasis is placed on references from Australia and one reference (37), not clearly described, is on factors related to breast examination.

Papers describing the PSA testing practices in the UK have been included (references 33, 48-51).

2. There are many factors besides those of GPs alone which will influence frequency of GP PSA testing: attitudes of local urologists and pathologists, local guidelines, patient demand etc. This should be mentioned in the Background.

We agree with the reviewer and have revised the second paragraph of the background section to acknowledge that other factors are likely to influence the frequency of PSA testing in the population.

3. Although the authors state that guidelines will have influenced use of PSA in other countries, the level of influence varies greatly. For example after the introduction of the Prostate Risk Management Programme in England two studies showed that only about 54% of GPs were actually aware of the programme. Thus other factors are likely to have led to England having overall a more conservative approach to use of the PSA test in asymptomatic men compared with Ireland or the USA.

In paragraph 3 of the background we have acknowledged the fact that guidelines do not appear to have not influenced the PSA testing behaviour of GPs in the UK.

4. The reasons for appropriate or inappropriate testing will differ for men aged <50 and men aged >75 years (possible error in title of Table 2 as states men >80 – if not why was the cut off changed?) so it seems unwise to group these outcomes together. The test of men <50 should take into account whether or not there is a family history, and it would be possible to analyse this separately in
relation to knowledge/awareness of family history collected in the questionnaire.

*The Table title should have read ≥75 years and not ≥80 years, and we have corrected this.*

We chose to base our primary analysis on the combination of these two age groups (<50 and ≥75) because the majority of guidelines state that PSA testing, if done at all, is most appropriate for men ≥50 and those with more than 10 years life expectancy. By implication therefore, the test would be less appropriate amongst men under 50 and men with a life expectancy of less than 10 years. We chose a limit of 75 years to define the older group in whom testing would be less appropriate, to reflect increasing life expectancy.

We would also note that what we asked GPs was: "Do you usually use PSA to test asymptomatic men for prostate cancer?" If they responded yes, we then asked them to indicated in which of the following age groups this applied to (30-39, 40-49, 50-59, 60-64, 65-79, 70-74, 75-79 or ≥80 years). Thus we did not ask specifically about the issue of testing men under 50 who had a positive family history.

It is possible, as the reviewer suggests, that the reasons for inappropriate testing men in these age groups may differ. We re-ran our models to investigate, separately, the factors influencing whether GPs would routinely test asymptomatic men younger than 50 years and 75 and older. The results did not differ to any great extent. Therefore, we feel that the analysis presented is appropriate. We have added a comment to the results that when these two groups were analysed separately the results did not differ notably.

5. The Abstract needs a little more sharpening and clarity: ‘intensive PSA testing’ could mean a high prevalence of testing in the male population or the frequency with which an individual is tested, inappropriate testing of men <50 should not be mentioned without reference to family history, clarify what the meanings or significance of ‘having a PSA testing policy’ or ‘favouring regular PSA testing’ are in relation to inappropriate testing, ‘despite scientific evidence to the contrary’ is wrong – there is no conclusive evidence either for or against PSA screening, and last sentence is rather vague given some of the interesting data collected.

*We have revised the abstract and trust that it is now sharper and clearer. In addition, we have removed from the abstract reference to GPs having a policy on PSA testing, because we do not have any details about what the polices are, when they were implemented or what informed these policies. We have included this as a limitation of the study in the discussion.*

6. In the Methods more information is needed on the questionnaire either in an appendix or table particularly to assess the validity of right and wrong answers to PPV (the cut off is only given in Table 1) and knowledge of prostate cancer and PSA testing.
Two new tables have been included detailing the n’s and % of responders to the questions on knowledge of prostate cancer risk factors (Table 1) and the PPV of PSA and DRE (Table 2). We have also provided more details about the questionnaire in the methods section. In addition, we have made the full questionnaire available to the editor and are willing to make it available to any interested parties on request; we have inserted a comment in the methods section to this effect.

7. Useful descriptive information could include how many pathology laboratories measure PSA in Ireland or the number of urology departments to which men would be referred, and the distribution of number of GP per practice.

Information has been added to the text on the number of laboratories measuring PSA in Ireland; we have a paper in press on this topic and a reference has been made to it. We have also added information on the number of practicing urologists (38 in a population of 2.1 million males). The number of GPs working in solo and multidoctor practices is presented in Table 1.

8. The section on Statistical Analyses should include a statement on the power of the analyses to analyse this large number of variables in multivariate regression with a sample size of 1497. There is also no mention of confounding between variables – were all these factors truly independent and were there no interactions?

We do not report an a priori sample size or power calculation mainly because, from the start, we intended to invite the entire population of GPs working in Ireland to take part in the survey, rather than a sample of them. Therefore, we had no way to increase the population size beyond what was available.

The issue of post-hoc power calculations is controversial. This is simply a function of the observed p value and does not tell us anything that we do not already know from having done the study. Many statisticians strongly suggest that such post-hoc calculations are inappropriate (see, for example, Hoening & Heisey, 2001; Levine & Ensom, 2001; Walters, 2008). Instead they advocate that a confidence interval should be provided for the effect estimate (as we have done).

Since the reviewer raised this issue, we provide below a post-hoc power calculation. However, we would strongly prefer not to include this in the paper.

Post-hoc power calculation: Given the large sample size, the power to detect significant effects remained high even after adjustment. Using the powerlog command from Stata v9, we found that this study had >90% power to detect a 20% increase in the multivariate OR at a level of 5%.

In building our model we checked quite carefully for inter-relationships between variables. In any situations where there was a close relationship between two variables, we did not include both variables in the model, as this might lead to unstable estimates.
Thus we are confident that the variables in the final model are "independent". In addition, we have investigated whether there were any important and meaningful interactions between the variables in the model. However to ease the interpretation given the large number of variables, we felt that none of them were meaningful enough or would add anything to the interpretation of the results. Therefore none of them were included. We added a mention of this in the statistical analysis section.

9. In the Results it would help to have a table summarising the frequency of characteristics, levels of knowledge etc and thus reduce the descriptive text. Under Information needs, what were ‘the topics’ – again a table may have helped.

Tables detailing the demographics of the respondents (Table 1), answers to the questions investigating knowledge of risk factors (Table 2) and the efficacy of PSA and DRE (Table 3) and a table listing the information needs (Table 4) have been added to the manuscript.

10. Was the inclusion of all variables in the regression analysis of Table 1 (dependent variable ‘propensity of GPs to testing asymptomatic men’) hypothesis driven? If so, it is unclear why Frequency of PSA testing and Inform patient prior to testing were included. These are more related to characteristics of clinical practice for PSA testing than factors influencing the decision whether or not to test. Table 1 has a lot of information and may benefit from being split into two parts with the regression results presented separated.

Before starting the analysis we drew up a list of factors that we wanted to investigated in the regression analyses. These were selected on the basis that they fulfilled one of three criteria: (1) they had been found to be important predictors of GP testing practice in previous studies; (2) they were more novel factors which we specifically wanted to explore the effect of; or (3) they were possible confounders which we simply wanted to adjust for if important.

All of these variables were investigated univariately for associations with the main and secondary outcomes. We then proceeded to build the multivariate models; only GP and practice characteristics remained significant. Therefore, Frequency of PSA testing and Inform patient prior to testing were not part of the multivariate models. Their associations with outcome were investigated and adjusted for significant GPs/practice characteristics. This is stated in the footnote of table 5.

Table 1 (which is now labelled Table 5) has been simplified.

11. In the Discussion,
   a. The first sentence should mention Ireland

   We have revised this as suggested.

   b. The paper must recognise that PSA testing is not the only cause of the rise in
detection rates of prostate cancer: aetiological factors, and biopsy practice, and pathological examination of prostate tissue whether from TURP or from biopsy must also be mentioned.

This has been acknowledged in the discussion section of the paper

c. The authors have a tendency to use their results to make statements about the causes of certain associations when in fact they can only make indirect assumptions eg ‘younger GPs, those involved in research…were more likely to be guided by the published evidence’ – the authors did not actually present any data on whether GPs were influenced by published evidence, and similarly ‘these beliefs were sincerely held’…….’ and ‘unlikely to be due to either patient demand…’.

We have tempered our conclusions.

d. ‘attendance at meetings on PSA’ – this is particularly interesting – who organised the meetings, which specialities were present, and what information and messages were given about PSA testing?

Unfortunately we did not collect information on who organized these meeting or the content of the meetings . Please also see our response to point 1 or reviewer 3.

e. A limitation is that fact that there were no data on the influences of urologists, pathologists and patients.

We accept that this is a limitation of the current paper and in retrospect we see that we might have asked GPs about the influence that urologists and pathologists had had on their PSA testing practice. However we did conduct a separate survey of urologists and radiologists in Ireland and a manuscript on this is currently in preparation.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests
Reviewer's report

Title: Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: A national survey of general practitioners

Version: 1 Date: 8 August 2008
Reviewer: Melina Gattellari

Reviewer's report:
Thank you for the opportunity to review this manuscript. This is a well written article reporting findings from a national survey of Irish GPs about PSA screening for prostate cancer. While a number of previous studies have addressed this issue, this submission extends existing work by considering a more varied set of predictors of GP self-reported behaviour, including GPs' own uptake of PSA screening and their knowledge about the issues relevant to PSA screening. I have recommended the following revisions:

Minor Essential Revisions:

1) Subjects and questionnaire administration: The authors state that they have described the creation of their GP data base elsewhere. While referring to previously published work is widely used by authors, I feel that it would be necessary to describe how the data base was created as this methodological detail would allow the reader to make a decision about the likely representativeness of the GPs targeted by the study.

We have included details on the establishment of the GP database in section ‘Subjects and questionnaire administration.

2) As a reader, I would have appreciated a table which outlines the characteristics of respondents, and more importantly, the n's and percentages associated with the questionnaire responses. Such a table would enable the researchers to present both the questions asked and the responses given to each of the questionnaire items. While I appreciate that not all questionnaire items need to be presented in this way, the n's and percentages of key variables should be displayed in a table.

A table describing the characteristics of the respondents has now been included (Table 1). A table has also be included detailing the n's and percentages of questionnaire responses to the questions on knowledge of prostate cancer risk factors (Table 2) and the positive predictive value of PSA (Table 3).

3) It is not usual scientific convention to start sentences with numbers (eg "29% of GPs frequently...." page 9.

We have changed all sentence beginning with numbers to text.

4) Much detail is presented in the tables of multivariate analyses. This level of detail may be distracting to the readers who may wish to refer to the tables to identify key and essential results. A few suggestions for simplifying these results:
a) only present the univariate and multivariate (adjusted) ORs and 95% CIs for those variables that are statistically significant in the multivariate analyses. b) Eliminate referent group OR as this is always 1 and instead indicate referent category using an asterisk; c) the column for "no" is redundant as row percentages for no and yes sum to 100% and the denominators are presented. d) Instead of a separate column for 95%CI, indicate the CIs within brackets that immediately follow the presentation of the OR. d) Do not report the univariate p-values and instead only report the multivariate p-values.

These tables have been simplified following the reviewers suggestions.

4) When presenting results in tables, I would report variables and response categories as these were presented in the questionnaire (for example, was OK a response category for GPs answers to questions assessing PPV?).

The "correct" response category was defined from the results of the metaanalysis of Mistry and Cable 2003. A Table showing the responses received has been included have been included in the manuscript (28).

5) I would recommend moving results of comparisons between responders and non-responders from the discussion to the end of the results section.

The comparison between responders and non-responders has been moved to the discussion to a final section in the results section titled ‘Non-response bias’.

6) I would recommend including in the methods details of how responses were combined and perhaps justify those combinations. For example, did GPs report their workload as less than or greater than or equal to 8 weeks? If not, the authors should justify their selected cut-off. Similarly, it seems that many variables in the analyses were reduced to dichotomous variables, whereas it is unclear that this is how the questions and response sets were presented to the GPs.

We have included in the methods section details of how variables were reduced to dichotomous variables.

Major Compulsory Revisions:
1) The multivariate statistical analysis presented in Table 1 may be affected by multicollinearity between the predictor variables (or unstable parameter estimates). The unadjusted OR for gender is 0.96 and the percentages are equal, yet the multivariate analysis shows a statistically significant effect of gender with an increased odds of testing amongst female GPs compared with male GPs. However, I wonder whether females are less likely to be full-time, principal members of practices and to work more than 8 sessions per week? The estimate of workload also appears problematic as the odds ratio in the univariate model changes indicates an increased odds of testing associated with practising
for at least 8 sessions per week, but the multivariate model indicates a reduced odds of testing for those GPs practising for at least 8 sessions per week. If these variables are highly correlated, then an independent assessment of these variables in a multivariate model may be compromised by collinearity and create statistical instability. A diagnostic of instability is when parameter estimates change signs (ie from negative to postive, as appears to have happened with the assessment of gender and number of sessions per week), and/or inflated standard errors (and corresponding wide confidence intervals). I am therefore concerned that the model is not valid as it is currently reported. My recommendation would be to remove variables from the model that create instability in the parameter estimates (ie probably remove gender first and then test the effect of the remaining variables). I would recommend the authors refer to Hosmer and Lemeshow’s text on logistic regression analysis for guidance on identifying and dealing with parameter instability.

The reviewer is correct in that female GPs were indeed less likely to be full-time and to work more than 8 sessions/week. On the basis of the comments from the reviewer, we tested for multicollinearity in the multivariate model and found no evidence for multicollinearity was found.

The effect of gender is diluted from the univariate to the multivariate analysis precisely because of confounding by full- time status. Being part-time was associated with a decreased likelihood of PSA testing, and women are likely to be part-time, however women were not less likely to test compared to male. We investigated whether there were any notable interactions between gender, no of session and full time status; no significant interaction were found.

Hosmer & Lemeshow’s test was not significant. Giving the sample size, it may be assumes that the model fit was ok. Therefore, we feel our model is valid.

Please also see our response to point 8 from reviewer 1, which describes how we approached the model fitting and dealt with closely related variables.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests
Reviewer's report
Title: Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: A national survey of general practitioners
Version: 1 Date: 5 August 2008
Reviewer: Anna Gavin
Reviewer's report:
The question posed by the authors is an important one and this work provides answers to these questions. The methods are appropriate and well defined and include consideration of non responders. The discussion and conclusions support the data. It is interesting to note the lack of differences observed between public and private patients.

Minor essential revisions
1. The authors should note in the discussion that while attendance at meetings re PSA had no influence on the testing practices that this depends on the content of the meetings ie whether they encourage or discourage PSA testing.

We have added as a limitation of the study the fact that we did not have any information on the meeting attended by the responding GPs.

2. There is no reference in the text to Table 2

There is reference to Table 2 in the text – which is now actually Table 5.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests
Reviewer's report
Title: Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: A national survey of general practitioners
Version: 1 Date: 14 August 2008
Reviewer: joan austoker

Reviewer's report:
This is an interesting paper on a topic of great interest to primary care. The paper is well written and the results, although not unexpected, do add to the body of knowledge on the topic.

Minor Essential Revisions

1. In the methods section it would be helpful to understanding and interpreting the results if the 37 closed questions are provided in a table. Also, more detail is required about the patient management scenarios.

*More detail on the questionnaire used has been included in the methods section. The questionnaire has been made available to the editor and to any interested parties upon request to the authors (see our response to question ** from reviewer 1)*

2. In the section on outcomes, it states that "GP and practice characteristics were considered as potential explanatory variables" - which characteristics are you referring to?

*GP and practice characteristics were factors such as the GP's age, whether they had trained/worked outside Ireland, whether they worked full or part-time, how many sessions a week they did, whether they were a solo practitioner, etc. We have included more details on this in the methods section.*

3. In the results under information needs it refers to at least one of the topics listed - which topics?

*A table on the topics had been included – Table 4*

4. In the discussion the word 'screen' is frequently used e.g., line 2 of the discussion. It would be better to insert 'testing'.

*We have replaced 'screening' with 'testing' in paragraph 1 of the discussion.*

5. The tables are far too detailed and as a result it is very difficult to ascertain what they are trying to put across. A greatly simplified version of both tables would improve the readability of the paper.

*We have simplified the tables.*

Level of interest: An article whose findings are important to those with closely
related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests
Reviewer's report
Title: Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: A national survey of general practitioners
Version: 1 Date: 28 July 2008
Reviewer: Suzanne Steginga

Reviewer's report:
This study address an important question: why do General Practitioners continue to increasingly screen for prostate cancer in the absence of evidence to support this practice?

Strengths of the study are that it includes a large sample, the response rate is quite acceptable for a study of this kind (unsolicited survey), and the survey tool was relatively broad in scope. It is also of great interest that it as undertaken in a country that until recently has had no national policy on screening. It was also good to see that the issue of at what age GPs would screen patients was included and that there was some attempt to look at non-responders.

I am not sure I would agree with the conclusion that GPs test because of a belief in the utility of testing. The GPs had poor knowledge about prostate cancer; they were more likely to test if they had had a personal experience with prostate cancer detection in their practice or themselves personally (salient experience rather than evidence based decision).

In making our argument we mean that the GPs themselves appear to genuinely believe that PSA testing is useful/valuable. We are not making any inference that this is an evidence-based thought process or evidence-based decision that they have reached. In fact we agree with what the reviewer appears to be suggesting that GPs views are not driven by the evidence, or having the correct "knowledge" about the performance characteristics of the test, or prostate cancer, but rather are being influenced by salient personal experience (as the reviewer calls it).

These findings would be better discussed with regard to the literature in non-systematic decision making and barriers to uptake of evidence based care. It is unfortunate that the authors didn’t test GP fear of medico-legal consequences as this may well be a strong predictor of behaviour. A comment that there was a high endorsement by GPs of the need for further education on this topic, this is worthy of note and discussion and recommendation by the authors.

Barriers to uptake of evidence based care - she is right that this is an issue.

We agree that the threat of medico-legal consequences might be a strong predictor of behaviour. In subsequent qualitative work among GPs, we have been able to explore in more depth the reasons why GPs do so many PSA tests and this has indeed come up as an important factor. GPs felt that it would be desirable to have national guidelines on the use of PSA testing and one of the major reasons for this is because it would afford them some "protection" against the possibility of medico-legal consequences. We are in the
process of analysing this data at the moment and intend to submit it for publication in coming months. We have referenced the work of Dunn and Sorum in the discussion.

We also agree with the reviewer that the fact that GPs themselves felt the need for further education on the topic is noteworthy, and have commented on this in the discussion.

Some possible references:


