

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Patient Reported Outcomes of Cancer Survivors in England 1 to 5 years after Diagnosis: a cross-sectional survey.
AUTHORS	Glaser, Adam; Fraser, Lorna; Corner, Jessica; Feltbower, Richard; Morris, Eva; Hartwell, Greg; Richards, Sir Mike; Wagland, Richard

VERSION 1 - REVIEW

REVIEWER	Simon N Rogers Professor, EPRC, Edge Hill University and Consultant Oral and Maxillofacial Surgeon, Aintree University Hospital, UK I have no competing interests.
REVIEW RETURNED	23-Dec-2012

GENERAL COMMENTS	<p>This is a very well undertaken and presented piece of clinical outcomes research. PROMS in cancer is very important. The study comprises of a very large cohort albeit restricted to breast, colorectal, prostate and non-hodgkins. It is not clear why these four were selected. Was it because they are common forms of cancer or was there an expected theoretical expected difference of outcome based on patient and clinical characteristics?</p> <p>Allowing comparison to Health Survey (2008) and General Practice Survey adds value to the study as does the other facets such as the relationship with the presence of one or more long-term condition. Cancer patients surviving into older age will have other comorbidities that impact on their Patient Report Outcome yet are not directly related to their cancer. It can be hard to tease this out and apportion weighting.</p> <p>There is an acceptable response rate for the cross-sectional survey (66%). Though two reminders were sent to non-responders. There is a cost associated with this. Also confirmation that the patient is alive as sending a questionnaire to a dead patient can cause considerable family distress.</p> <p>The PROMs used are appropriate. There are various measures such as EQ-5D, FACT (cancer specific), Social Difficulties Inventory (SDI), Experience of care etc. The data tends to focus on the EQ-5D.</p> <p>It is not clear which questionnaire was used to assess the fear of recurrence and dying. Also is this something that is expected to be common following cancer, however the severity of this concern might be low. Perhaps more mention around recurrence fears is appropriate given that 47% reported fear of recurrence. In many ways it is a natural and healthy reaction to having cancer. The fact that a quarter had fear of dying again might be reasonable and needs to be compared to normative data.</p> <p>Deprivation influenced response rate and outcome. This is a challenge when trying to assess PRO in the more vulnerable groups of society. What solutions are there to attempt to address this?</p> <p>Very good presentation of data – the detail in the tables is to be</p>
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	<p>commended.</p> <p>The study has two aims. Firstly to determine feasibility of PROM in assessing QOL. This is already well established and this study tests a limited aspect of 'feasibility'. Linking to this the authors' second aim is to inform the development of a national PROMS programme for cancer. It is unclear how this study does that.</p> <p>There are issues around the conclusion of this study. Questionnaires are already acknowledged as feasible and acceptable to most survivors. There are significant challenges to routinely collecting PROMS. Most HRQOL questionnaires have limited utility in the identification of specific needs as they are limited by the questionnaire items themselves, range, wording, scoring. Comparing HRQOL across service provides as an outcome is not without it problems based on patients priorities in cancer, response shift, adaptation, limitations inherent in HRQOL questionnaires, confounding variables.</p> <p>The key messages are weak – they are already well appreciated (first two appoints) or ill-advised (third point). HRQOL measures as used in this study are likely to fail to give clinically meaningful health economics comparison across provides and fail to really facilitate service provision across the diverse needs at cancer patients have.</p>
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REVIEWER	<p>A/Prof Michael Jefford Consultant Medical Oncologist Australian Cancer Survivorship Centre, A Richard Pratt Legacy Peter MacCallum Cancer Centre Melbourne, Victoria, Australia</p> <p>I recently authored a paper with Glaser, Richards I spent part of my sabbatical in 2011 working with Glaser, Richards and briefly Hartwell, Corner</p>
REVIEW RETURNED	08-Jan-2013

THE STUDY	research question, methods could be more clearly stated
RESULTS & CONCLUSIONS	results and discussion can be improved
GENERAL COMMENTS	<p>This is an important, interesting paper describing the largest population-based evaluation of European cancer survivors' PROs</p> <p>It confirms the feasibility of collecting data in this manner and provides useful baseline data</p> <p>One aspect that should be mentioned is that we don't know how many people are disease-free and how many are living with advanced cancer. It's worth stating this. Some studies have included 'survivors' who are cancer-free, making comparisons with this study somewhat problematic. The authors might consider describing QoL for people who are apparently disease-free and for those who report that they are living with cancer</p> <p>The paper is strong, but could be improved by considering aspects below</p> <p>Abstract</p> <ul style="list-style-type: none"> - Objectives do not really reflect the results. Surely the objectives include a desire to describe PROs, determine predictors of QoL, as well as look at feasibility, etc - Results – 'QoL scores were stable over time' – careful, as people

	<p>were not followed longitudinally</p> <p>Article summary</p> <ul style="list-style-type: none"> - Article focus - “to inform the development of a national PROMS programme for cancer” – this is not really discussed in the paper (but probably should be) - Strengths and limitations – 4th bullet (face and content validity) – questionnaires were not reviewed by consumers (patients, survivors) so I don’t know whether this is a strength or a weakness <p>Introduction</p> <ul style="list-style-type: none"> - final paragraph – ‘determine the feasibility of routinely collecting’ – consider adding the ‘how’ here – perhaps “by considering response rate, completion, participant complaints” - same paragraph – add extra goals – to report QoL and describe associations between QoL and other disease / patient factors <p>Methods, study design</p> <ul style="list-style-type: none"> - why 1, 2, 3, 5 years? Why not 1, 3, 5, 8 (as an example)? There seems a lot of sampling - add the ‘<5%’ line from the discussion in here in reference to private centres <p>Methods, cohort identification</p> <ul style="list-style-type: none"> - ‘covered 70 of 160 (43%) acute NHS Trusts’ – are these typical of all NHS Trusts? - Explain ‘Demographic Batch Service’ - ‘a dedicated freephone telephone helpline’ – add what the purpose of this was. Was it for assistance / to make a complaint? Were people adequately advised of the purpose of the service? <p>Methods, questionnaire design and content</p> <ul style="list-style-type: none"> - add more about development – the process of consultation with patient groups, etc - briefly describe the rationale for including each of the measures, eg why ask about exercise? (but not about smoking, drinking, etc) - comment on readability of the final questionnaires – the front page of the survey looks like it would frighten off people with health literacy difficulties - generic content – describe the validity of ‘self-reported response to treatment and disease status’ and also reporting of long-term conditions - describe the ‘experience of care’ survey - how was fear of recurrence and fear of death assessed (ie what tools) – this is important as there are many instruments available - have all the data from the measures been reported? If not, why not? - FACT measures are really intended for use around treatment. This needs to be acknowledged (i.e they’re not really ‘survivorship’ measures) - cognitive testing – was there pretesting to determine that people understood and answered correctly? - Why were the questions on feeling like a man (prostate ca) or a woman (breast ca) omitted? <p>Methods, data analysis</p> <ul style="list-style-type: none"> - is the categorization of QoL into high , medium, low a standard procedure? If so, reference it. If not, explain this <p>Results</p>
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	<ul style="list-style-type: none"> - response rates - no difference in RR by sex – this data is not shown - demographics of respondents – breast ca respondents similar age profile to incident cases – seems odd as you might expect that people would be 1, 2, 3, 5 years older than incident cases. Add whether other cancer types are reflective of the age expected in the population - missing data – ‘no evidence ... missing data was related to the order of the questions’ – was different order tried? Or do you mean that missing data was no more common at the end c/w earlier questions? - Generic PROMS – worth adding in the data for “percentage reporting anxiety or depression symptoms decreased significantly” as this is likely to be of interest. Adding comparisons to the general population (or mentioning in the discussion) would be interesting - Breast cancer (page 13, lines 28-30) “Increasing age ... better outcomes in EQ5D” – not really, as 85+ have an OR of 1.61 - Colorectal cancer (lines 54, 55) – regarding the comment ‘whilst undergoing treatment’ – people undergoing treatment are likely those with advanced or recurrent cancer. Has this been examined? Worth mentioning when describing the initial study sample - NHL, page 14, line 49 – “QoL seemed to improve with time from diagnosis” – qualify this to say that they are not the same patients who have been followed longitudinally - CRC and prostate ca (page 14, lines 15-21 and page 15, lines 19-28) – this seems like quite selective reporting from the disease-specific FACT measures. Consider how to present this data more completely (for all cancer types) - Fear of recurrence and dying – this data is important and worth describing in more detail (perhaps not in a supplementary table). Also, include whether these fears are related to psychological morbidity / inferior QoL. <p>Discussion</p> <ul style="list-style-type: none"> - This generally lacks oomph, and restates the results a little too much. I’m still left with a feeling of ‘so what?’ and ‘so what now?’ - There is a major focus on the EQ5D and associations with inferior QoL. Other factors that might impact QoL were not recorded, eg ongoing physical symptoms, depression – explain why all factors known to impact QoL were not included - It would be useful to include consideration of (i) other large studies of cancer survivors (e.g. compare to reference #2 – what does this data add?), (ii) consideration of possible mechanisms – why / how do the significant factors (eg age, deprivation, LTC, disease status) impact on QoL? (iii) potential interventions based on the data, (iv) future steps – will the survey be repeated? Why / when? - There should also be discussion of the possibility that treatments have changed over the 1-5 years and thus results might reflect treatment changes / change in practice - Comparison with the general population – odd to include a new table in the discussion – consider summarizing and moving to the results section. In this comparison, please justify the comparison – were the same QoL measures used? If not, how can data be compared? - Limitations – more needs to be said about the validity of self-report, use of measures that were not designed for a survivor population, effect of patient deaths, changes in treatments / treatment practices, missing data, etc - Where next for cancer PROMs in England? – NHS Outcomes Framework needs description – unlikely to be understood by non-UK
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	<p>readers (whereas the paper will be of broad international interest)</p> <ul style="list-style-type: none"> - Worth discussing how to get to elderly / low SES – probably some discussion of health literacy goes here - Page 17, lines 38-42 “the core components ... had been identified ... as being reliable and appropriate” – add more detail here. Is there really evidence that these measures work well for the elderly / low SES? - Page 20, lines 7/8 “...and are cost effective” – no data is shown to justify this - Page 20, lines 8-12 “...insights into where improvement efforts should be targeted to reduce the long-term burden of cancer and its treatments on the growing number of cancer survivors” – can you give some suggestions? - Final paragraph lacks impact <p>Table 1a</p> <ul style="list-style-type: none"> - suggest a solid vertical line to separate the 2 right columns as the %s work differently to the responders / non-responders columns (it’s a bit confusing) <p>Table 3a-c</p> <ul style="list-style-type: none"> - explain ‘physical activity’ as it’s not clear that this refers to increased activity <p>References</p> <ul style="list-style-type: none"> - several are incomplete, eg 16, 25
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VERSION 1 – AUTHOR RESPONSE

VERSION 2 – REVIEW

REVIEWER	<p>A/Prof Michael Jefford Consultant Medical Oncologist Australian Cancer Survivorship Centre, A Richard Pratt Legacy Peter MacCallum Cancer Centre Melbourne, Victoria, Australia</p> <p>I recently authored a paper with Glaser, Richards I spent part of my sabbatical in 2011 working with Glaser, Richards and briefly Hartwell, Corner</p>
REVIEW RETURNED	

GENERAL COMMENTS	<p>I feel that it is improved and requires little further amendment</p> <p>In the authors’ comments quite a bit is made about</p> <ol style="list-style-type: none"> 1. this data being a subset of the full dataset, which is available in a more detailed report, available online (referenced) 2. being cautious about over interpreting (subsets of) the data <p>It would be useful to include these two points within the introduction and/or results sections</p> <p>There is some inconsistency regarding point 2 as there is a lot of data analysis / interpretation and the authors report many significant associations.</p> <p>Some specific comments</p>
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	<p>Abstract, results section</p> <ul style="list-style-type: none"> - “there was an effect of deprivation on response rate” – state the direction of effect - “QoL scores were stable” – could the authors say “QoL scores were comparable’ (or ‘similar’) – it is less likely to imply longitudinal data (i.e. same patients being followed, with stable QoL scores) - include the year for the second general population report (for consistency) <p>Article summary</p> <ul style="list-style-type: none"> - Strengths and limitations – 4th bullet (face and content validity) – summarise the following, to indicate that consumers were involved (this is important) <p>THE QUESTIONNAIRES WERE REVIEWED BY CONSUMERS IN A PROCESS OF COGNITIVE TESTING AND THROUGH INVOLVEMENT OF ESTABLISHED NATIONAL ADVISORY GROUPS AND CONSULTATION WITH MAJOR CANCER CHARITIES. COGNITIVE TESTING DESCRIBED P9..</p> <p>Introduction</p> <ul style="list-style-type: none"> - final paragraph – ‘determine the feasibility of routinely collecting’ – re my previous comment about adding the ‘how’ – I meant how did you assess / judge feasibility – presumably by looking at response rate, completed PROs, lack of complaints, etc <p>Methods, study design</p> <ul style="list-style-type: none"> - previous comment ‘add the ‘<5%’ line from the discussion in here in reference to private centres’. Please add “(estimated to be less than 5% of cases)” so that it reads: “Patients attending private healthcare centres (estimated to be less than 5% of cases) were excluded as the aims of the study focused on the assessment of PROMS within the National Health Service (NHS) in England. - please add some text in response to previous comment, ‘covered 70 of 160 (43%) acute NHS Trusts’ – are these typical of all NHS Trusts? THERE IS NO WAY OF KNOWING THIS, BUT WE HAVE NO REASON TO SUSPECT THEY ARE NOT "TYPICAL". With any study of this kind, readers need to know whether participants are likely to be representative <p>Methods, questionnaire design and content</p> <ul style="list-style-type: none"> - (previous comment) comment on readability of the final questionnaires – the front page of the survey looks like it would frighten off people with health literacy difficulties - (previous comment) cognitive testing – was there pretesting to determine that people understood and answered correctly? - please add text in response to my previous comment, below. It is unusual to remove items that are part of well validated scales. Why were the questions on feeling like a man (prostate ca) or a woman (breast ca) omitted? ACTION TAKEN AS THESE QUESTIONS WERE FOUND TO BE CONFUSING AND UNACCEPTABLE TO THOSE PATIENTS/SURVIVORS PARTICIPATING IN THE COGNITIVE TESTING EXERCISE. <p>Methods, data analysis</p> <ul style="list-style-type: none"> - re my previous comment: is the categorization of QoL into high , medium, low a standard procedure? If so, reference it. If not, explain this A SECTION HAS BEEN ADDED TO THE "STUDY LIMITATIONS" IN THE DISCUSSION. <p>This should be stated within the methods section. I don't think the reader should have to get to the discussion to find out that this is not a standard approach</p> <p>Results</p> <ul style="list-style-type: none"> - response rates - no difference in RR by sex – this data is not shown THE FULL RESULTS ARE INT HE PREVIOUSLY MENTIONED AND REFERENCED DEPARTMENT OF HEALTH
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	<p>REPORT.</p> <p>Ok, could you please add 'see full report (ref#).' It might be worth doing this several times where data is not shown.</p> <p>- Generic PROMS – worth adding in the data for “percentage reporting anxiety or depression symptoms decreased significantly” as this is likely to be of interest. Adding comparisons to the general population (or mentioning in the discussion) would be interesting</p> <p>AGREE, BUT THIS IS IN THE FULL REFERENCED REPORT AND SPACE CONSTRAINTS PREVENTED INCLUSION.</p> <p>I would favour including this and removing a line or two of the restated results from the discussion</p> <p>Discussion</p> <p>- I still feel that the discussion restates the results too much and misses an opportunity to put the results in context. Would the authors consider adding (from previous comments): “consideration of (i) other large studies of cancer survivors (e.g. compare to reference #2 – what does this data add?), (ii) consideration of possible mechanisms – why / how do the significant factors (eg age, deprivation, LTC, disease status) impact on QoL? (iii) potential interventions based on the data”</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: Michael Jefford

Peter MacCallum Cancer Centre, Medical Oncology

Thank you for the opportunity to see the revised manuscript. I feel that it is improved and requires little further amendment

In the authors' comments quite a bit is made about

1.this data being a subset of the full dataset, which is available in a more detailed report, available online (referenced)

2.being cautious about over interpreting (subsets of) the data

It would be useful to include these two points within the introduction and/or results sections

There is some inconsistency regarding point 2 as there is a lot of data analysis / interpretation and the authors report many significant associations.

We have referenced the full report within the “Introduction” and added a further comment concerning the possibility of false positive results due to the number of statistical comparisons to the “limitations” section of the Discussion.

Some specific comments

Abstract, results section

- “there was an effect of deprivation on response rate” – state the direction of effect

This has been clarified.

- “QoL scores were stable” – could the authors say “QoL scores were comparable’ (or ‘similar’) – it is less likely to imply longitudinal data (i.e. same patients being followed, with stable QoL scores)

This has been amended as suggested.

- include the year for the second general population report (for consistency)

This has been added.

Article summary

-Strengths and limitations – 4th bullet (face and content validity) – summarise the following, to indicate that consumers were involved (this is important)

THE QUESTIONNAIRES WERE REVIEWED BY CONSUMERS IN A PROCESS OF COGNITIVE TESTING AND THROUGH INVOLVEMENT OF ESTABLISHED NATIONAL ADVISORY GROUPS AND CONSULTATION WITH MAJOR CANCER CHARITIES. COGNITIVE TESTING DESCRIBED P9..

This has been summarised and added to the “Article summary”.

Introduction

-final paragraph – ‘determine the feasibility of routinely collecting’ – re my previous comment about adding the ‘how’ – I meant how did you assess / judge feasibility – presumably by looking at response rate, completed PROs, lack of complaints, etc

This has been clarified within the final paragraph of the Introduction.

Methods, study design

-previous comment ‘add the ‘<5%’ line from the discussion in here in reference to private centres’. Please add “(estimated to be less than 5% of cases)” so that it reads: “Patients attending private healthcare centres (estimated to be less than 5% of cases) were excluded as the aims of the study focused on the assessment of PROMS within the National Health Service (NHS) in England. This has been added as suggested.

- please add some text in response to previous comment, ‘covered 70 of 160 (43%) acute NHS Trusts’ – are these typical of all NHS Trusts? THERE IS NO WAY OF KNOWING THIS, BUT WE HAVE NO REASON TO SUSPECT THEY ARE NOT “TYPICAL”. With any study of this kind, readers need to know whether participants are likely to be representative
We have acknowledged this limitation in the Methods.

Methods, questionnaire design and content

-(previous comment) comment on readability of the final questionnaires – the front page of the survey looks like it would frighten off people with health literacy difficulties
The questionnaires were cognitively tested as now described in the manuscript (see other comments). No objections were identified during this process.

-(previous comment) cognitive testing – was there pretesting to determine that people understood and answered correctly?

The questionnaires were cognitively tested as now described in the manuscript (see other comments). During this process no issues with comprehension were identified.

- please add text in response to my previous comment, below. It is unusual to remove items that are part of well validated scales.

Why were the questions on feeling like a man (prostate ca) or a woman (breast ca) omitted? The ACTION WAS TAKEN AS THESE QUESTIONS WERE FOUND TO BE CONFUSING AND UNACCEPTABLE TO THOSE PATIENTS/SURVIVORS PARTICIPATING IN THE COGNITIVE TESTING EXERCISE.

An explanation for this decision has been included in the text.

Methods, data analysis

-re my previous comment: is the categorization of QoL into high , medium, low a standard procedure?

If so, reference it. If not, explain this A SECTION HAS BEEN ADDED TO THE "STUDY LIMITATIONS" IN THE DISCUSSION.

This should be stated within the methods section. I don't think the reader should have to get to the discussion to find out that this is not a standard approach

This has been clarified in the Methods section.

Results

-response rates - no difference in RR by sex – this data is not shown THE FULL RESULTS ARE IN THE PREVIOUSLY MENTIONED AND REFERENCED DEPARTMENT OF HEALTH REPORT.

Ok, could you please add 'see full report (ref#).' It might be worth doing this several times where data is not shown.

This suggestion has been added to the Results.

-Generic PROMS – worth adding in the data for "percentage reporting anxiety or depression symptoms decreased significantly" as this is likely to be of interest. Adding comparisons to the general population (or mentioning in the discussion) would be interesting AGREE, BUT THIS IS IN THE FULL REFERENCED REPORT AND SPACE CONSTRAINTS PREVENTED INCLUSION.

I would favour including this and removing a line or two of the restated results from the discussion Further detail about these results has been added to the text.

Discussion

-I still feel that the discussion restates the results too much and misses an opportunity to put the results in context. Would the authors consider adding (from previous comments): "consideration of (i) other large studies of cancer survivors (e.g. compare to reference #2 – what does this data add?), (ii) consideration of possible mechanisms – why / how do the significant factors (eg age, deprivation, LTC, disease status) impact on QoL? (iii) potential interventions based on the data"

A direct comparison with other large studies, e.g. Reference 2 was not possible due to a different range of questions asked and a different cohort of cancer survivors (34% were breast survivors, 14% gynaecological, 13% prostate, 11% bowel, and results were not broken down according to cancer type). We felt that speculating about reasons for possible mechanisms and potential interventions was outside the scope of this pilot study.