Author’s response to reviews

Title: Trends and variation in the management of oesophagogastric cancer patients: A population-based survey.

Authors:

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Version: 4 Date: 18 November 2009

Author’s response to reviews: see over
How Reviewers’ and Editor’s comments were addressed

MS: 5151839230549681, ‘Recent population-based trends and variation in the management of oesophagogastric cancer patients’ by Georgios Lyratzopoulos, Josephine M Barbiere, Chetna Gajperia, Michael Rhodes, David Greenberg and Karen Wright.

Dear BMC HSR

We are grateful to the three Reviewers for a thorough and constructive review of our manuscript; and to the Editors for providing us with the opportunity to submit an improved version of our manuscript. We provide all the Reviewer comments verbatim below, along with our answers, annotated in blue fonts for legibility.

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REVIEWER 1

Reviewer’s report
Title: Recent population-based trends and variation in the management of oesophagogastric cancer patients
Version: 1 Date: 5 October 2009
Reviewer: Christopher B Forrest

Reviewer’s report:
This is a neatly constructed manuscript that was easy to read. It presented a pithy set of results lucidly and with generally adequate discussion.

Thank you.

I have just a few comments
1. The differences in rates of treatments between groups are terribly small, both in terms of historical trends that you reference in the background and your own data. You do not detect exposure-response effects. Lack of this coupled with a very week effect raises the concern for me that there may actually be no disparities, that your effects can all be explained by the limitations that you discuss. I think this point needs to be fleshed out more prominently in the discussion and your conclusions

Thank you for this comment. The effect size of deprivation differences is indeed limited for use of curative surgery (e.g. 25.9% vs 23.0% use, between least and most deprived patients). Confounding by stage or co-morbidity status could indeed be at least in part responsible. In contract, the effect size of deprivation differences for chemotherapy use is much more substantial, both in relative and absolute terms (e.g. 23.3% vs. 16.6% use, between least and most deprived patients). Therefore, the observed socioeconomic differences in chemotherapy use are much less likely to be the result of confounding by unadjusted for variables, for which no data was available. The Reviewer’s comment and the above observations have greatly helped us to improve the manuscript as following:

a) Both in the Abstract and the main text ‘Conclusions’, we particularly emphasise the finding relating to variation in chemotherapy use (as opposed to differential use of both chemotherapy and curative surgery).
b) In ‘Results’, 3rd para, 2nd sentence, we have drawn attention to the same issue by the insertion of a new phrase: ‘These differences were particularly prominent for chemotherapy use.’

c) In ‘Discussion’: i) we suitably modified the 1st paragraph in order to draw attention to the association of deprivation with chemotherapy use – in particular: ii) We have in addition included a new paragraph (2nd) with the following new material: (Please note that the sentence relating to the lack of apparent ‘linear’ effect of deprivation on curative surgery relates to related comments made by Reviewer 2).

‘Deprivation differences in use of curative surgery, although statistically significant, were relatively limited in both absolute and proportional terms (e.g. 26% compared with 23% use, in least and most deprived patients respectively). In contrast, socioeconomic treatment patterning was much stronger for chemotherapy use (e.g. 23% compared with 17% use, in least and most deprived patients respectively). Moreover, although the apparent effect of deprivation status on frequency of chemotherapy use was linear, no such consistent effect was observed for curative surgery use. These observations mean that data limitations (described below) could at least in theory be responsible for the observed socioeconomic difference in use of curative surgery. However, given the substantial effect size of deprivation status on use of chemotherapy, as well as its apparent linear effect, this is less likely to be the case for the observed socioeconomic variation in chemotherapy use, which is more likely to be genuine.’

2. Over the years, there has been tremendous attention given to improving cancer care in the UK. I think the manuscript could be strengthened by adding more of the policy context both in the background and your discussion.

Thank you, we have now referred to and suitably referenced the two key policy initiatives, the ‘NHS Cancer Plan, 2000’ and the ‘Cancer Reform Strategy, 2007’ (‘Background’ section, end of the penultimate paragraph).

3. And, a minor point, how much of the country did the registry cover? Please offer any further validation of the registry that may have been done in the past.

In the first paragraph of ‘Methods’, we now clarify that the Registry covers a population which is approximately 10% of the population of England. We also refer to the proportion of Death Certificate Only registration, which is a very good summary indicator of the quality of the registration process at the end of the same paragraph.

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REVIEWER 2

Reviewer's report
Title: Recent population-based trends and variation in the management of oesophagogastric cancer patients

This is an interesting article, which addresses an important question. The analyses are appropriate, and the manuscript is clearly written. The data sources is clearly described, and limitations of this are dealt with well.

Thank you.

I have only some minor comments which could be addressed prior to publication.

Discretionary Revisions
1. Page 3, 3rd last line: replace “may not explain” with “do not seem to fully explain”

   Thank you, addressed as advised.

Minor Essential Revisions
1. As a general rule, wherever an OR is quoted, it should be accompanied by a CI (e.g. in abstract).

   We have addressed as advised, with the inclusion of 95% CI in the Abstract, after OR values.

2. Analyses should be described as “multivariable” not “multivariate”.

   Changed as suggested throughout the document.

3. Table 1: I did not understand the definition of p* “adjusting for deprivation group only”, since deprivation group is the main explanatory variable? This P value should be the result of the chi-squared test surely? Also P** does not appear in the table (but does in the footnote) – perhaps the footnote of this table is incorrect?

   Thank you. On the first point, we used linear regression models entering deprivation group as a continuous variable, and we considered the obtained p value of the beta co-efficient of the deprivation group exposure variable as a test of significance for trend. (These models did not have any other exposure variables, other than deprivation group). This is an equivalent (but computationally easier) approach to other types of tests for trend, such as the chi-squared test for trend. This is now better annotated and explained at the footnote of Table 1.
   On the second point, this related to the fact that the complete model outputs for the multivariable regression models were presented in Additional File 2 – this is now properly annotated after the column heading ‘Multivariable Analysis’ at the top row of the Table.

4. Additional table 1: Why give P values from logistic regression for comparison of proportions?
In both Table 1 and Additional File 2-Table 1, we have now omitted the presentation of p values pertaining to categorical groups of continuous variables (i.e. for deprivation groups, age groups and diagnostic periods).

Major Compulsory Revisions
1. In describing the changes in treatment patterns over time, the authors do not consider the possibility that data quality may have changed.

Thank you. We acknowledge this as potential explanation of the observed findings, and discuss whether this is likely, in additional sentences added to the end of Paragraph 7 in 'Discussion'.

‘Similarly, it is possible that changes during the study period in data quality (including in the degree of treatment status ascertainment) may at least in part be responsible for some of the observed findings. However, there has been a high degree of consistency over time in cancer registration systems used in the UK, where cancer registration has been established over a number of decades. In addition, potential improvements in capturing treatment status could have perhaps explained the observed increase in chemotherapy use but are very unlikely to be responsible for the observed decrease in use of curative surgery. Furthermore, again, any changes over time in treatment status ascertainment would have been non-differential between patients of different gender and socioeconomic groups,[30] and cannot therefore be responsible for the observed gender and socioeconomic differences in use. For these three reasons, we believe that potential secular changes in data quality are unlikely to be responsible for the observed findings.’

2. Table 1: the patterns of inequalities in treatment appear to differ by outcome. For chemotherapy, there appears to be a linear decrease in likelihood of receiving this treatment across deprivation groups, whereas for curative surgery, the effect is driven by the most deprived (and possible the second most deprived) group. The authors appear to have used deprivation as a continuous variable without considering from the more detailed analysis whether this is appropriate. They also do not comment on this in the text. This however, is an important issue, with public health consequences.

Thank you for this useful comment that helped us to improve the manuscript as following:

1. In third paragraph of Results, 3rd sentence, we now draw attention to this observation as following:

‘For chemotherapy use there is an apparent linear decrease in frequency of use with increasing deprivation; however, for curative surgery use, there appears to be a (non-linear) ‘step’ effect, with socioeconomic variation mainly relating to the most (and perhaps the one but most) deprived group.’

2. In ‘Discussion’, 2nd (new) paragraph: We have included a new paragraph – in part it also addresses issues raised by Reviewer 1:
‘Deprivation differences in use of curative surgery, although statistically significant, were relatively limited in both absolute and proportional terms (e.g. 26% compared with 23% use, in least and most deprived patients respectively). In contrast, socioeconomic treatment patterning was much stronger for chemotherapy use (e.g. 23% compared with 17% use, in least and most deprived patients respectively). Moreover, although the apparent effect of deprivation status on frequency of chemotherapy use was linear, no such consistent effect was observed for curative surgery use. These observations mean that data limitations (described below) could at least in theory be responsible for the observed socioeconomic difference in use of curative surgery. However, given the substantial effect size of deprivation status on use of chemotherapy, as well as its apparent linear effect, this is less likely to be the case for the observed socioeconomic variation in chemotherapy use, which is more likely to be genuine.’

3. In general, in the ‘Conclusion’ section of both the abstract and the main text, we now draw attention to socioeconomic difference in use of chemotherapy (in particular) – as the strongest and more linear / more consistent association of treatment with deprivation (this also addresses observations made by Reviewer 1).

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REVIEWER 3

Reviewer's report
Title: Recent population-based trends and variation in the management of oesophagogastric cancer patients
Version: 1 Date: 26 October 2009
Reviewer: Elizabeth Davies
Reviewer's report:
Comments to editor
This seems a well-conducted study using cancer registration data to explore treatment trends and patterns for oesophagogastric cancer treatment for different social groups within one English region during 1995-2006. Cancer registry data has its limitations, which the authors recognise, but the analysis is well-conducted and its interpretation is strengthened by the clinical experience of co-authors. It provides a useful addition to the literature and makes some suggestions for future research. The study confirms earlier suggestions that curative surgery has increased and chemotherapy decreased and shows that these two treatments were used less often in deprived patients and surprisingly that chemotherapy less commonly in women. The main weakness of the study is no data on co-morbidity and low completeness for data on stage (44%). Surprisingly advanced stage disease was not associated with deprivation or sex, but this should be explored on more complete and larger datasets.

Thank you.

Minor essential revisions
The abstract needs to mention
1) kind of analysis performed i.e. logistic regression analysis
   Addressed as suggested, in 3\textsuperscript{rd} sentence of Abstract Results
2) subgroups considered and factors adjusted for
   Addressed as suggested, in 3\textsuperscript{rd} sentence of Abstract Results
3) low completeness for stage and no data on co-morbidity at least
   Addressed as suggested, in 2\textsuperscript{nd} sentence of Abstract Results.

It might exclude mention of “ordinal group” for deprivation or make this sentence a bit clearer.

   We now use ‘increasing’ (deprivation group), instead of ‘ordinal’.

Methods

A sentence on specific geographical areas included in Eastern Region to orientate international readers (and some UK ones) to exactly where these patients come from.

   Addressed as suggested.

A fuller explanation of the IMD. The current sentence is a little complex and may not be understandable to clinical or non-English audiences

   Thank you, we have re-written this paragraph, amplifying the methodological issues and in addition we now provide a new reference to the government office website responsible for production of Index of Multiple Deprivation statistics.

The paragraph on information available on surgical treatment needs some attention. One sentence appears to extend over six lines.

   We have addressed by constructing two sentences instead of one.

Minor discretionary revisions

Results

Add mean ages of men and women to first paragraph results

   Addressed as suggested, see 1\textsuperscript{st} paragraph of Results.

Reordering the keys in figures 1 and 2 to follow the order in the graph or the last point would make them slightly easier to read and interpret.

   Addressed as suggested by ‘opening up’ ‘treatment group’ to its component treatments.
Table 1 needs to include p** within it. Currently it is in the key only.

Thank you, Reviewer 2 also queried this. This related to the fact that the complete model outputs of multivariable regression were presented in Additional File 2 – this is now properly annotated after the column heading ‘Multivariable Analysis’ at the top row of the Table.

It might be useful to show unadjusted and adjusted odds ratios so that the two can be compared.

Addressed as suggested – see Table 1.

The columns in the additional files could be placed in the same order.

Addressed as suggested.

The first sentence of the conclusion could be stated more directly. This paragraph could ideally restate the time period, areas studied and the kind of data used.

Addressed as suggested.

Elizabeth Davies
Victoria Coupland

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EDITOR’S COMMENT

Please could you also clarify whether the registry data you used is publicly available, or whether you obtained permission to use it?

The data are not directly publicly available, but cancer registries in the UK have policies for release of anonymised (non-identifiable) data to researchers, with the aim of generating evidence that can be of use to improving patient care. The data used in this study was provided with the permission of the Registry. More information about the regulatory environment underpinning the function of UK Cancer Registries can be found at the UK Association of Cancer Registries website http://82.110.76.19/.

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In conclusion, we have been able to address all the constructive comments, and improve the manuscript. We are looking forward to hearing from you.

With best wishes

Georgios Lyratzopoulos, MD, FFPH, FRCP, MPH, DTM&H, Ptychio Iatrikes

(On behalf of all authors)