

## 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

<b>TITLE (PROVISIONAL)</b>	Impact of route to diagnosis on treatment intent and 1-year survival in patients diagnosed with oesophago-gastric cancer in England
<b>AUTHORS</b>	Cromwell, David; Palser, Thomas; Hardwick, Richard; Riley, Stuart; Greenaway, Kimberley; van der Meulen, Jan

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Lucy Elliss-Brookes  Analytical Programme Manager National Cancer Intelligence Network, UK
<b>REVIEW RETURNED</b>	22-Oct-2012

<b>THE STUDY</b>	<p>Are the participants adequately described, their conditions defined, and the inclusion and exclusion criteria described?</p> <ul style="list-style-type: none"><li>• The definition of the routes to diagnosis need clarifying, particularly for GP referrals: GP referrals could fall into one of four categories: Routine, Urgent (non-Two Week Wait), Urgent (Two Week Wait) and Emergency. How do these equate to the two GP routes described?</li><li>• If urgent GP referral (suspected cancer) describes patients referred under the Two Week Wait referral system this should be stated. If this is the case it should then be noted that this does not cover all urgent GP referrals, and conversely that non-urgent referrals may include urgent non-Two Week Wait referrals. It should also be clarified how emergency GP referrals would be classified for this study.</li><li>• The authors suggest that emergency admission follows presentation at A&amp;E whereas this is not necessarily the case.</li><li>• 13% of patients were excluded because the route to diagnosis was entered for less than half of the patients within the trust (1,196 patients) or the route to diagnosis was missing (956). There is no explanation or justification given for excluding the former cohort of patients.</li><li>• There is geographical variation between Cancer Networks, it is possible that the excluded Trusts may have different routes to diagnosis to those included in the analysis, this could lead to a bias in this study towards non-emergency routes. These exclusions have not been sufficiently explored.</li></ul> <p>Are the patients representative of actual patients the evidence might affect?</p> <ul style="list-style-type: none"><li>• The authors state that the overall audit concluded 71% of all</li></ul>
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	<p>patients diagnosed in England during the audit period, and that exclusion of patients due to missing data meant the study had an estimated case ascertainment of 62%. The study does not explore this coverage or these exclusions in enough detail.</p> <ul style="list-style-type: none"> <li>• The case ascertainment of the audit is of relevance to this study but is not explored. 29% of diagnosed patients are not included but the authors have not considered why these patients might be missing from the audit or what impact this might have on the results, this is particularly relevant as results are expressed as a percentage of all patients.</li> <li>• Elliss-Brookes et al report similar one year survival rates for GP referral routes but lower one year survival for patients presenting via emergency routes. This would suggest an under-reporting of emergency presentation in this study and the potential omission of emergency presentations with poorer one year survival.</li> </ul> <p>Are the abstract/summary/key messages/limitations accurate?</p> <ul style="list-style-type: none"> <li>• The limitations stated are not accurate. 29% of newly diagnosed cases are missing before further exclusions whereas the authors state that the limitations stem from the exclusion of patients due to missing data on route to diagnosis and treatment intent.</li> </ul> <p>Are the references up to date and relevant? (If not, please provide details of significant omissions below.)</p> <ul style="list-style-type: none"> <li>• A significant paper has been published in the British Journal Of Cancer since this study was submitted, along with detailed results by tumour type (published by the National Cancer Intelligence Network), this work and these results should be referenced and compared throughout the study: Elliss-Brookes L et al. Routes to diagnosis for cancer – determining the patient journey using multiple routine data sets. Br J Cancer 2012; 107: 1220–1226</li> <li>• Two other papers/articles have been published which may be of interest to the authors: Bottle A et al. Association between patient and general practice characteristics and unplanned first-time admissions for cancer: observational study. Br J Cancer 2012; 107: 1213-1219; Hamilton W. Emergency admissions of cancer as a marker of diagnostic delay. Br J Cancer 2012; 107: 1205-1206</li> </ul>
<b>RESULTS &amp; CONCLUSIONS</b>	<p>Are they discussed in the light of previous evidence?</p> <ul style="list-style-type: none"> <li>• These results need to be discussed in light of detailed findings published by Elliss-Brookes et al.</li> </ul>
<b>GENERAL COMMENTS</b>	<ul style="list-style-type: none"> <li>• These results add insight to previously published routes to diagnosis results in particular with respect to treatment intent and information on comorbidity and performance status.</li> <li>• The large proportions of patients missing from the study (29% before exclusions, 38% after exclusions) are not discussed in sufficient detail.</li> <li>• The impact of the missing patients on the proportion of patients for each route to diagnosis is not explored.</li> </ul>
<b>REVIEWER</b>	<p>N Davies Consultant Surgeon</p>

	Royal Bournemouth and Christchurch Hospital Trust
	I contibuted data to the National Oesophago-gastric Cancer Audit
<b>REVIEW RETURNED</b>	23-Oct-2012

- The reviewer completed the checklist but made no further comments.

## VERSION 1 – AUTHOR RESPONSE

### Response to reviewer comments

#### Comment 1:

The definition of the routes to diagnosis need clarifying, particularly for GP referrals: GP referrals could fall into one of four categories: Routine, Urgent (non-Two Week Wait), Urgent (Two Week Wait) and Emergency. How do these equate to the two GP routes described?

If urgent GP referral (suspected cancer) describes patients referred under the Two Week Wait referral system this should be stated. If this is the case it should then be noted that this does not cover all urgent GP referrals, and conversely that non-urgent referrals may include urgent non-Two Week Wait referrals. It should also be clarified how emergency GP referrals would be classified for this study.

#### Comment 1 Response

We have clarified the routes to diagnosis definitions in the paper.

The study used definitions from the UK National Cancer Dataset that was current at the start of the study. The urgent GP referral (suspected cancer) corresponds to patients referred under the Two Week Wait category. The other GP category combines to the Routine and Urgent (non-Two Week Wait). Emergency GP referrals would be classified as an emergency admission in this study.

#### Comment 2

The authors suggest that emergency admission follows presentation at A&E whereas this is not necessarily the case.

#### Comment 2 Response

We have clarified the definition of emergency admission, with reference to the National Cancer Dataset.

#### Comment 3

13% of patients were excluded because the route to diagnosis was entered for less than half of the patients within the trust (1,196 patients) or the route to diagnosis was missing (956). There is no explanation or justification given for excluding the former cohort of patients.

#### Comment 3 Response

We reported the patient and hospital levels of the missing data to highlight the structure of the missing data. In particular, the risk of bias due to having an unrepresentative sample increases with lower case-ascertainment.

More information is given in the results on the 10 NHS trusts that were excluded because of poor case-ascertainment.

#### Comment 4

There is geographical variation between Cancer Networks, it is possible that the excluded Trusts may have different routes to diagnosis to those included in the analysis, this could lead to a bias in this study towards non-emergency routes. These exclusions have not been sufficiently explored.

#### Comment 4 Response

In the discussion, we have expanded on the limitations due to our incomplete sample. There was no relationship between the proportion of patients being diagnosed via the different routes within the networks, and (1) the proportion of expected cases submitted by NHS trusts and (2) the level of missing data. The networks with the higher and lowest values had good completeness of data. The excluded trusts are not uncharacteristic.

#### Comment 5

The authors state that the overall audit included 71% of all patients diagnosed in England during the audit period, and that exclusion of patients due to missing data meant the study had an estimated case ascertainment of 62%. The study does not explore this coverage or these exclusions in enough detail.

#### Comment 5 Response

This comment is addressed in comments 3, 4, and 6

#### Comment 6

The case ascertainment of the audit is of relevance to this study but is not explored. 29% of diagnosed patents are not included but the authors have not considered why these patients might be missing from the audit or what impact this might have on the results, this is particularly relevant as results are expressed as a percentage of all patients.

#### Comment 6 Response

Proportions derived from samples only differ in systematic ways from the population mean if the sample is unrepresentative. We provided information on the representativeness of the sample in the discussion, but have expanded the text and added figures to show how patient characteristics of the analysed data compare to the excluded cases and HES data used to estimate case-ascertainment.

#### Comment 7

Ellis-Brookes et al report similar one year survival rates for GP referral routes but lower one year survival for patients presenting via emergency routes. This would suggest an under-reporting of emergency presentation in this study and the potential omission of emergency presentations with poorer one year survival.

#### Comment 7 Response

We have made a note about the potential under reporting of emergency presentations in the study. We also note other reasons for the apparent difference. In particular, the category of "emergency admission" from the National Cancer dataset and the NCIN definition of emergency presentation may not be equivalent. It is possible that the more complex routes to diagnosis in the Ellis-Brookes et paper influenced their estimate.

#### Comment 8

The limitations stated are not accurate. 29% of newly diagnosed cases are missing before further

exclusions whereas the authors state that the limitations stem from the exclusion of patients due to missing data on route to diagnosis and treatment intent.

**Comment 8 Response**

The discussion about the case-ascertainment in the study has been clarified in answers to be points 3, 4 and 6.

**Comment 9**

A significant paper has been published in the British Journal of Cancer since this study was submitted, along with detailed results by tumour type (published by the National Cancer Intelligence Network), this work and these results should be referenced and compared throughout the study: Elliss-Brookes L et al. Routes to diagnosis for cancer – determining the patient journey using multiple routine data sets. Br J Cancer 2012; 107: 1220–1226

The results need to be discussed in light of detailed findings published by Elliss-Brookes et al.

**Comment 9 Response**

The paper has been updated to refer to this study.

**Comment 10**

Two other papers/articles have been published which may be of interest to the authors: Bottle A et al. Association between patient and general practice characteristics and unplanned first-time admissions for cancer: observational study. Br J Cancer 2012; 107: 1213-1219; Hamilton W. Emergency admissions of cancer as a marker of diagnostic delay. Br J Cancer 2012; 107: 1205-1206

**Comment 10 Response**

The paper has been updated to refer to these studies

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Lucy Elliss-Brookes Analytical Programme Manager National Cancer Intelligence Network (NCIN) United Kingdom
<b>REVIEW RETURNED</b>	09-Jan-2013

- The reviewer completed the checklist but made no further comments.